Usage Pattern of Drugs that are prescription in France and available OTC in Lebanon : Application on Antibiotics

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Doyen

THÈSE EN COTUTELLE PRÉSENTÉE

POUR OBTENIR LE GRADE DE

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ÉCOLE DOCTORALE de SOCIETES, POLITIQUE, SANTE PUBLIQUE (SP2)

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SPÉCIALITÉ Pharmacoloy (option Pharmacoepidemiology and Pharmacovigilance)

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Sous la direction de Nicholas MOORE
et de Pascale SALAMEH

Soutenue le 22/12/2017

Membre du Jury

M.Nicholas MOORE, Professeur, Université de Bordeaux	Directeur
Mme.Pascale SALAMEH, Professeur, Université Libanaise	Directeur
Mme.Maryse LAPEYER-MESTRE, Professeur, Université de Toulouse	Rapporteur
M.Hani DIMASSI, Professeur, Lebanese American University	Rapporteur
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M.Michel DUPON, Professeur, Université de Bordeaux	Examinateur
Mme. Aline HAJJ, Professeur, Université Saint-Joseph	Examinateur
M.Pierre-Marie PREUX, Professeur, Université de Limoges	Examinateur

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Résumé :

Contexte : les règlements distinguent habituellement les médicaments prescrits uniquement (prescription only medicines POM) et les médicaments en vente libre (over-the-counter OTC). Les premiers nécessitent une prescription médicale et les derniers sont disponibles pour l'automédication sans ordonnance. Au Liban comme dans les autres pays de l'Est de la Méditerranée, les médicaments théoriquement prescrits peuvent facilement être achetés sans ordonnance. Les antibiotiques sont parmi les classes de médicaments les plus fréquemment vendus sans ordonnance. L'utilisation inappropriée d'antibiotiques augmente le taux de résistance bactérienne et la fréquence de l'échec du traitement. Cette étude est menée pour déterminer le mode d'emploi des antibiotiques disponibles en tant qu'automédication au Liban, en comparaison avec leur utilisation comme médicaments uniquement prescrits en France.

Méthode : Tout d'abord, une revue approfondie de la littérature publiée (1990-2015) a été menée en utilisant les bases de données : Pubmed, Web of Science, Cochrane et Google Scholar, pour abus de médicaments disponibles sans ordonnance au Moyen-Orient ; les antibiotiques étaient parmi les médicaments les plus mal utilisés. Une étude prospective a ensuite été menée au Liban. Les données ont été collectées auprès de patients qui achetaient des antibiotiques avec ou sans ordonnance dans les officines sur une période d'un an (septembre 2015 à septembre 2016). En France, les données ont été extraites de la base de données Echantillon Généraliste de Bénéficiaires (EGB), contenant un échantillon représentatif permanent 1/97 du système d'assurance-maladie national français, qui contient toutes les prescriptions dispensées en France. Nous y avons mené des recherches pour identifier les modes d'utilisation des 5 antibiotiques les plus utilisés au Liban.

Résultats : La distribution moyenne de ces antibiotiques était plus élevée en France (18,6 DDD) qu'au Liban (10.6DDD). Cependant, le nombre moyen de dérogations au Liban était de 3,39 par an, plus élevé qu'en France (2 par an). Ce n'était pas différent entre les participants avec ou sans ordonnance. Le coamoxiclav a été largement consommé au Liban à la fois sous ordonnance et par automédication, alors que l'amoxicilline était le principal antibiotique consommé en France.62,4% des patients ont utilisé le bon antibiotique et 80,1% l'ont utilisé dans le dosage correct. Dans la suivi, la durée du traitement était inappropriée dans la majorité des cas (68,6%). Lorsque tous ces trois facteurs ont été additionnés, il s'avère que 83,6% des antibiotiques ont été utilisés de manière inappropriée. La pertinence de l'utilisation a été observée chez 27,6% et 16,4% des antibiotiques prescrits et non prescrits, respectivement.

Conclusion : Il est certain que l'automédication observée ou l'utilisation médicalement non surveillée d'antibiotiques est un risque majeur. Les premières mesures à prendre pour réduire celles-ci sont éducatives, pour les patients, les pharmaciens, les prescripteurs, l'industrie pharmaceutique et les autorités réglementaires.

Mots-clés : Antibiotique, automédication, OTC, Liban, France, mode d'utilisation, utilisation appropriée.

Titre : Modes d'utilisation des médicaments prescrits en France et disponibles sans ordonnance au Liban : Application sur les Antibiotiques

Abstract:

Background: Regulations usually distinguish between prescription-only (POM) and over-the-counter (OTC) medicines. The former requires medical prescription; the latter are available for self-medication (SM)without a prescription. In Lebanon as in other Eastern Mediterranean countries, theoretically prescription medicines can easily be purchased without a prescription. Antibiotics are among the most commonly sold drug classes without prescription. The inappropriate use of antibiotics increases the rate of bacterial resistance and the frequency of treatment failure. This study is conducted to determine the usage pattern of antibiotics available as self-medication in Lebanon, compared with their use as prescription only drugs in France.

Method: First, an extensive review of the published literature (1990–2015) was conducted using Pubmed, Web of Science, Cochrane and Google Scholar databases, for OTC medicine misuse and abuse in the Middle East. Antibiotics were among the most commonly misused medications. A prospective field study was then conducted in Lebanon. Data was collected from patients seeking antibiotics with or without prescription in community pharmacies over a 1-year period (September 2015 to September 2016). In France, data was extracted from the Echantillon Généraliste de Bénéficiaires (EGB) database,the permanent 1/97 representative sample from the French national healthcare insurance system which contains all dispensed prescriptions in France. It was searched in 2013 to identify usage patterns of antibiotics, of 5 antibiotics most commonly used in Lebanon.

Results: The average dispensing for these antibiotics was higher in France (18.6 DDD) than that in Lebanon (10.6DDD). However, the average number of dispensings in Lebanon was 3.39 per year, higher than that in France (2 per year). It was not different between participants with or without prescription. Coamoxiclav was widely consumed in Lebanon as both prescription and self-medication, whereas amoxicillin was the main antibiotic in France.62.4% of patients used the right antibiotic and 80.1% used it in correct dosage. The duration of treatment in the follow up was inappropriate in the majority of cases (68.6%). When all of these three factors were summed together, it turned out that 83.6% of antibiotics were utilized inappropriately. Appropriateness in use was seen in 27.6% and 16.4% of the prescribed and non-prescribed antibiotics respectively.

Conclusion: Misuse of antibiotics is an important issue for individuals and for public health. Obviously the observed self-medication or medically unsupervised utilization of antibiotics is a major risk. The first measures to take to reduce this are educational, for patients, pharmacists, prescribers, the pharmaceutical industry and the regulatory authorities.

Keywords: Antibiotic, Self-medication, OTC, Lebanon, France, Usage pattern, Appropriate use.

Title: Usage Pattern of Drugs that are prescription in France and available OTC in Lebanon: Application on Antibiotics

Aperçu:

Les règlements distinguent habituellement les médicaments sur ordonnance (prescription only medicines POM) et les médicaments en vente libre (over the counter OTC). Les premiers nécessitent une prescription médicale alors que ces derniers sont disponibles pour l'automédication (SM) sans ordonnance. Les médicaments OTC sont pris pour faciliter les services du système de soins de santé pour des usages préventifs et thérapeutiques basiques et simples. Les médicaments OTC sont des médicaments approuvés pour SM, car leur indication est facilement reconnue par les patients et généralement autolimitée, et le médicament est considéré comme sur et efficace (par exemple, les analgésiques de base tels que le paracétamol ou l'aspirine). Ainsi, les patients deviennent responsables de leur santé et commencent le traitement sans ordonnance, lorsqu'ils ont des symptômes.

Dans de nombreux pays en développement, y compris les pays du Moyen-Orient, l'automédication est très répandue, parce que les règlements ne sont souvent pas appliqués et certains médicaments sur ordonnance sont facilement disponibles en tant que SM. Les gens peuvent acheter des médicaments en vente libre qui ne devraient être vendus qu'avec une precription medicale. Le SM des médicaments sur ordonnance n'est en principe pas autorisé. Cependant, dans la pratique, dans de nombreux pays, la distribution des médicaments sur ordonnance (POM) par les pharmaciens sans prescription medicale n'est pas inhabituelle, en particulier pour le traitement à court terme des maladies courantes

Il en résulte une majorisation de l'utilisation irrationnelle des médicaments, y compris les medicaments POM, qui consitue un problème majeur dans le monde entier surtout où il existe une grande variété de produits qui peuvent être achetés même sans ordonnance, par contrast à d'autres pays où ils ne sont disponibles qu'avec une prescription valide, y compris la France. L'utilisation irrationnelle des médicaments, en particulier pour les médicaments POM obtenus sans ordonnance, peut entraîner une mauvaise utilisation et un risque évitable pour les patients et la communauté. Les antibiotiques sont considérés parmi les classes des médicaments les plus vendus dans les pays en développement sans ordonnance. L'utilisation inappropriée d'antibiotiques avec des doses incorrectes pour une période de temps inappropriée augmente le taux de résistance bactérienne et leur diffusion dans la population entraîne une fréquence plus élevée d'échec du traitement. Au Liban, comme dans la plupart des pays en développement, une prescription valide n'est pas généralement obligatoire pour obtenir des médicaments sur ordonnance (POM). À l'exception des narcotiques et des tranquillisants majeurs, les patients peuvent acheter un médicament POM sans ordonnance.

En France, les antibiotiques ne sont disponibles qu'aver une presciption medicale et, par conséquent, leur utilisation est captée dans des bases de données sur la population, y compris des registres de santé électroniques ou dans des bases de données sur les reclamations de remboursements. Alors qu'au Liban, comme la plupart des pays en développement, les antibiotiques peuvent être obtenus sans ordonnance. Les pharmacies sont la seule source de services de santé et de médicaments. Par conséquent, les patients qui cherchent des antibiotiques pourraient être capturés dans les pharmacies communautaires au Liban.

Objectif : Notre principale préoccupation est l'utilisation des antibiotiques en raison de son importance pour la santé publique et individuelle. Par conséquent, cette étude est menée pour étudier le mode d'utilisation des antibiotiques disponibles en tant qu'automédication au Liban alors qu'uniquement par prescription en France. Les autres objectifs étaient d'évaluer l'usage approprié des drogues et de souligner la nécessité pour les patients de recevoir des médicaments appropriés et en toute sécurité en fonction de leurs indications cliniques, à des doses qui correspondent à leurs conditions individuels, et pendant une période adéquate. Cette étude vise

également à évaluer la connaissance du public au Liban et sa sensibilisation au risque concernant l'automédication des antibiotiques. Il est également important de déterminer la sécurité et la conformité qui lui sont associées.

Méthode : Un examen approfondi de la littérature publiée (1990-2015) a été mené à l'aide des bases de données du pubmed, du web of science, du cochrane et du google scholar, pour sur la mauvaise utilisation de la médecine OTC (et) au Moyen-Orient. 72 documents ont été identifiés. Les antibiotiques étaient l'un des principaux médicaments mal utilisés au Moyen-Orient. Ils étaient les principaux médicaments évalués pour leur usage au liban et en france.

Au Liban, une étude prospective transversale a ensuite été réalisée dans le cadre de pharmacie communautaire. Les données ont été recueillies sur une période d'un an (septembre 2015 à septembre 2016) des 50 pharmacies communautaires (CP) réparties dans les six districts du Liban. Les participants éligibles ont été recrutés de façon aléatoire parmi des consommateurs présentant aux CP au Liban après avoir acheté des médicaments antibiotiques avec ou sans ordonnance. Les données ont été recueillies des participants deux fois, d'abord lors de l'achat, pour des informations a propos du médicament utilisé et de la condition pour laquelle il devrait être utilisé, puis en appelant le patient 30 jours après le début du médicament pour des données sur les habitudes d'utilisation et la sécurité et l'efficacité du médicament ainsi que sur l'adhésion au traitement et les causes de mauvaise utilisation. Le mode d'utilisation des antibiotiques a été décrit par le nombre de doses quotidiennes définies (Defined Daily Dose DDD) dispensées à chaque patient et utilisées pendant le suivi, ainsi que le nombre de demandes d'antibiotiques par an. La DDD a été obtenue du Centre collaborateur de l'OMS pour la méthodologie des statistiques des médicaments (http://www.whocc.no/atc_ddd_index/).

Puis une utilisation appropriée de l'antibiotique a été évaluée au Liban. cette utilisation a été décrite par le choix des antibiotiques dispensés, la durée de l'antibiotique utilisé et les doses journalières prescrites (Prescribed Daily Dose PDD) des antibiotiques consommés par chaque patient dans le suivi. La pertinence de l'antibiotique dispensé avec la plainte et la durée du client a été décidée en utilisant la ligne directrice de la Société des maladies infectieuses de l'Amérique (IDSA). Le PDD a été évalué par rapport à la dose quotidienne recommandée (Recommended Daily Dose RDD) du traitement sur la base du formulaire national de médicament (dictionnaire VIDAL®) (https://www.vidal.fr/). Un point a été attribué pour chaque utilisation correcte et 0 point pour une mauvaise utilisation, un mauvais choix de médicaments, une mauvaise durée (sous-utilisation ou utilisation excessive) ou un mauvais PDD. Plus tard, l'antibiotique distribué a été évalué en additionnant les scores donnés pour chaque élément. Un score total de 3, a été réfèré à un « traitement approprié » tandis que les scores inférieurs a 3 ont été définis comme « traitement inapproprié ».

La connaissance, l'attitude et le comportement des participants à l'étude ont également été évalués à l'aide d'une échelle de trois rapports (1 = accord, 2 = incertain, 3 = en désaccord) qui a été utilisé pour évaluer la réponse des participants. La cohérence interne des sections pour déterminer la connaissance et l'attitude à l'égard de l'utilisation des antibiotiques a été évaluée à l'aide du test α de Cronbach. L'alpha de Cronbach pour le score de connaissance et le score d'attitude étaient de 0,795 et 0,651 respectivement. Pour décrire les connaissances et les attitudes des participants, un score a été calculé en fonction du nombre de questions correctement répondues concernant l'utilisation d'antibiotiques. Le score de connaissance a été classé comme inadéquat ou adéquat. Le score d'attitude a été classé comme mauvais et ou bien. Chaque réponse correcte a été attribuée à 1 point alors que les réponses erronées ou incertaines ont été attribuées à 0 points. Ensuite, la somme des réponses pour chaque patient a été calculée. Le maximum score de connaissance et d'attitude était 13 points et 9 points respectivement. Ainsi, les scores de connaissances ont été catégorisés en inadéquats (0-6 / 13) ou adéquats (7-13/13) alors que le score d'attitude était divisé en mauvais (0-4 / 9) ou bien (5-9/9) comme variables dichotomiques. Les données ont été analysées à l'aide de statistiques descriptives et

du test du Chi-carré. Une régression logistique multi variée a été réalisée pour prédire les facteurs affectant la pertinence ou le score dichotomique de connaissance et d'attitude.

En France, les données ont été extraites de la base de données ‘echantillon généraliste de bénéficiaires’ (EGB), l'échantillon représentatif permanent 1/97 du système d'assurance français des soins de santé nationaux, qui contient toutes les prescriptions dispensées en France. Ces donnée ont été étudié en 2013 pour identifier les modes d'utilisation, les maladies chroniques concomitantes et les médicaments concomitants chez les utilisateurs d'antibiotiques. Les patients ont été suivis pendant 365 jours après la première distribution en 2013. Le mode d'utilisation de l'antibiotique a été décrit par le nom du médicament antibiotique dispensé, le nombre et la fréquence des doses par année, le nombre de doses quotidiennes définies (DDD) par épisode de distribution (défini comme la période de 30 jours suivant la distribution initiale) et le nombre total de DDD distribués par an. Les données ont été analysées à l'aide de SAS.

Enfin, nous comparons le mode d'utilisation des antibiotiques au Liban et en France. Le mode de distribution de 6 classes d'antibiotiques (coamoxiclav, amoxicilline, cefixime, cefuroxime, ciprofloxacine et clarithromycine) a été comparé entre le Liban et la France puisque ces antibiotiques étaient principalement dispensés au Liban (63%).

Résultats : une mauvaise utilisation des médicaments par l'automédication semble largement répandue au Moyen-Orient. Les caractéristiques du traitement individuel n'ont pas été clairement identifiées. Les pharmaciens, les amis ou les parents étaient les principales sources de SM. La connaissance et les attitudes des patients sont des facteurs importants contribuant à la mauvaise utilisation de ces médicaments. Les stratégies et les interventions visant à limiter l'utilisation abusive des médicaments étaient rarement identifiées dans la littérature. Les antibiotiques sont les principaux médicaments mal utilisés au Moyen-Orient.

Au Liban, 62,7% des 501 participants achètent des antibiotiques sans ordonnance. Les pharmaciens sont les principaux assistants (34,7%). L'amoxicilline / acide clavulanique était l'antibiotique le plus utilisé comme médicament (33,7%). La dispense moyenne globale était de 9,07 DDD pour une utilisation à court terme (<2 semaines). Dans le suivi, la DDD moyenne consommée par le patient était de 7,07 DDD et 62,5% des patients consommaient entre 1 et 7 DDD. La demande moyenne par année était de 3,35 ce qui était significativement plus élevé chez les patients sans ordonnance que ceux présentant avec une prescription ($p = 0,029$). Les hommes ont reçu plus de DDD que les femmes, mais le résultat n'était pas significatif. Les patients âgés de 25 à 50 ans avaient considérablement consommé plus que 1 DDD par jour (61,7%) par comparaison aux patients âgés de plus de 50 ans (41%, $p = 0,002$).

62,4% des patients ont utilisé le bon antibiotique et 80,1% l'ont utilisé dans le dosage correct. La durée du traitement était inappropriée dans la majorité des cas (68,6%). Lorsque tous ces trois facteurs ont été additionnés, il s'avère que 83,6% des antibiotiques ont été utilisés d’une manière inappropriée. La pertinence de l'utilisation a été de 27,6% et 16,4% des antibiotiques prescrits et non prescrits, respectivement.

L'échantillon de l'étude avait en général un faible score de connaissance (moyenne 6) et d’attitude (moyenne de 3,16). Une proportion élevée des participants libanais croyait que les antibiotiques sont utilisés pour traiter les symptômes du toux, du rhume, du maux de gorge (59%) ou les symptômes des infections virales (53%). 42% ont préféré prendre des antibiotiques de la pharmacie sans prescription médicale. Dans l'analyse de régression logistique multi variées, les femmes ont montré une meilleure connaissance de l'utilisation d'antibiotiques par rapport aux hommes (OR 1.59, IC 95% 1.01-2.53). Par comparaison aux participants âgés de plus de 50 ans, le niveau de connaissance adéquate des antibiotiques chez les personnes âgées de 25 à 50 ans était plus élevé (OR 3,66, IC 95% 1,79-7,49).

En France, 137 358 patients, représentant 25% de la population totale âgés de plus de 15 ans avaient au moins une dispensation d'antibiotique d'intérêt en 2013. L'amoxicilline était l'antibiotique le plus répandu (62,1%) suivi de l'amoxicilline et de l'acide clavulanique (39,0%) et la clarithromycine (11,3%). La distribution moyenne des doses quotidiennes définies (DDD) sur une année était plus élevée chez les hommes (35,5) que chez les femmes (34,6). L'utilisation moyenne des antibiotiques au cours d'une année montrait une augmentation avec l'âge de la moyenne de 28,4 DDD chez les patients âgés de 16 à 25 ans à 38,6 DDD chez les patients âgés de plus de 75 ans. L'amoxicilline et le coamoxiclav ont été les plus répandus dans tous les groupes d'âge.

Des différences ont été trouvées entre les modes d'utilisation des antibiotiques au Liban et en France. La moyenne de la distribution de ces antibiotiques était plus élevée en France (18,6 DDD) qu'au Liban (10,6 DDD). Cependant, la moyenne des distributions au Liban était de 3,39 par an plus élevée qu'en France (2 par an). Pas de différence trouvée entre les participants avec ou sans ordonnance. Le coamoxiclav est largement consommé au Liban à la fois comme antibiotique sur ordonnance et comme automédication alors que l'amoxicilline était le principal antibiotique consommé en France.

Conclusion : Cette étude confirme l'utilisation habituelle de l'automédication et la distribution de médicaments par les pharmaciens au Liban, par comparaison à la France, avec des distributions plus fréquentes de plus petites quantités de médicaments, ainsi avec une utilisation plus extensive d'un large spectre d'antibiotiques. Cela affecte tous les groupes d'âge, mais plus particulièrement les jeunes patients, et concerne de nombreuses maladies mineures potentiellement virales. Une utilisation abusive similaire d'antibiotiques et d'autres médicaments semble répandue au Moyen-Orient. La mauvaise utilisation des antibiotiques est un facteur majeur dans le développement de la résistance bactérienne aux antibiotiques, un problème majeur pour les individus et pour la santé publique. Évidemment, l'automédication observée ou l'utilisation médicale non surveillée d'antibiotiques est un risque majeur. La perception du patient et sa connaissance des antibiotiques est clairement erronée, avec peu de compréhension des raisons correcte de l'utilisation. La réputation générale de sécurité et d'efficacité des antibiotiques entraîne une automédication et une mauvaise utilisation. Il est nécessaire de s'opposer à l'automédication et à la mauvaise utilisation, ce qui devrait être abordé avec l'éducation et la formation avant de renforcer les réglementations. Cela réduit l'utilisation inappropriée d'antibiotiques. L'éducation concerne les patients, les pharmaciens, les prescripteurs, l'industrie pharmaceutique et les autorités réglementaires.

Au-delà des antibiotiques, susceptibles d'abus, d'autres médicaments pouvant être utilisé par automédication, sont également susceptibles d’abus. C'est le cas des opiacés, y compris les opiacés « faibles » tels que la codéine, ou d’autres médicaments psychotrope. Ces médicaments, pourraient être la cible de nouvelles enquêtes.

List of abbreviations:

8-MMMAS: The Morisky 8-Item Medication Adherence Scale

ANOVA: Analysis of Variance

ARMED: Data from Resistance Surveillance and Control in Mediterranean Region

ALD: Affections de Longue Durée

ATC: Anatomic Therapeutic Classification

β: Regression Coefficient

CDC: Center of Disease Control

CI: Confidence Interval

Cnam-TS: Caisse Nationale d'Assurance Maladie des Travailleurs Salarie´s

Coamoxiclav: Amoxicillin/clavulanic acid

CPs: community pharmacies

DDD: Defined daily dose

EGB: Echantillon Généraliste de Bénéficiaires

ENT: Ear Nose Throat

Erasme: The Extraction, Recherches, Analyses pour un Suivi Me´dico-Economique database

GTI : Gastrointestinal Tract Infection

IRB: Institutional Review Board

IDSA: Infectious Disease Society of America guideline

LL: Lebanese Pounds

Max: Maximum

Min: Minimum

MOH: Ministry of public health

MSA: Mutuelle Sociale Agricole

OTC: Over The Counter

ORa: adjusted odds ratio

P. correlation or r: Pearson Correlation

RDD: Recommended daily dose

RSI: Regime Social des Independants

SD: Standard Deviation

SE: Side Effects

SM: Self-medication

SPSS: The Statistical Package for the Social Sciences

SNIRAM: Système National d'Informations Inter-Régimes de l'Assurance Maladie database.

PDD: prescribed daily dose

POM: prescription only medicines

URTI: Upper Respiratory Tract Infection

UTI: Urinary Tract Infection

VIDAL: French national drug formulary

WHO: World Health Organization

Contents

Introduction:

Medicines play an important role in healthcare delivery, and when used properly, can help cure diseases, relieve symptoms, and alleviate patient suffering. Nonetheless, irrational use of medicines remains a major issue facing most health systems across the world. (World Health Organization, 2011b) This is more often the case in developing countries due to wide availability of prescription medicines for self-medication (SM) and of Over-The-Counter (OTC) medicines. WHO estimates that more than half of all medicines are prescribed, dispensed or sold inappropriately, and that half of all patients fail to take them correctly. (World halth Organization, 2004)

Appropriate use of drug is essential element in achieving quality of health and medical care for patients and the community. Rational use of drug requires that the patient receive the medication appropriate to their clinical needs, in doses that meet their own individual requirements for an adequate period of time and at lowest cost to them and their community. (World Health Organization, 1985)Examples of irrational use of medicines include: inappropriate self-medication, often of prescription-only medicines; inappropriate use of antimicrobials, often in inadequate dosage, for non-bacterial infections; non-adherence to dosing regimens; failure to prescribe in accordance with clinical guidelines. (World Halth Organization, 2012)

The World health organization (WHO) estimates around 50% of patients fail to take their medicines correctly. (World Health Organization, 2004) The problem of irrational medicine use is known to be worse in developing countries with weak health systems, where mechanisms for routine monitoring of medicine use are often not well developed or are at times non-existent. (Ofori-Asenso, Brhlikova, & Pollock, 2016)

Regulations usually distinguish between prescription only (POM) and over-the-counter (OTC) medicines. The former requires medical prescription whereas the latter are available for self-medication (SM) without a prescription. OTC medications are taken to facilitate Health Care System services for basic and simple preventive and therapeutic actions. OTC medicines are medicines that are approved for SM, because their indication is easily recognized by patients and usually self-limiting, and the medicine is thought to be safe and effective (e.g. basic analgesics such as paracetamol or aspirin). Thus patients become responsible for their health, and begin treatment without a prescription, when concerned by the symptoms. Globally, SM is on the rise due to the shift of many prescription medications to OTC. (A. Blenkinsopp & C. Bradley, 1996)

However, SM can also concern the use of prescription medicines, either as a reuse of medicines previously prescribed for another disease episode, or prescribed to others in order to treat self-diagnosed disorders or symptoms. SM may also concern prescription medicines if they are made irregularly available in pharmacies or elsewhere, even without the theoretically required prescription. Globally, self-medication has been reported as being on the rise. The World Health Organization has emphasized that self-medication must be correctly taught and controlled. (World Health Organization, 2011a)Self-medication has become quite common in developed (A. Blenkinsopp & C. Bradley, 1996) and more common in developing countries. (Kamat & Nichter, 1998)

In many developing countries including Middle East countries, self-medication is highly prevalent since regulations are often not enforced and some prescription drugs are easily available as SM. People can purchase drugs over-the-counter that legally should only be sold on prescription. SM with prescription medicines is in principle not authorized. However, in practice in many countries the dispensing of prescription medicines by pharmacists without a prescription is not unusual, especially for the short-term treatment of common diseases

Self-medication with prescription drugs is especially a problem in developing countries where pharmacies freely supply medicines over-the-counter, as do informal drug shops and small groceries. Doctors' consultations are expensive and repeated use of prescriptions is a way to economize. Sometimes people even self-medicate with prescription drugs on the advice of relatives or parents. The major factors that increase self-medication among population include: decrease in prescription coverage by the national health services, availability of over-the-counter products, and the effect of media in presentation of pharmaceutical products. (Figueiras, Caamano, & Gestal-Otero, 2000) In addition, cognitive related factors, such as knowledge of social norm and perceived severity of illness can predict self-medication behavior. (Figueiras et al., 2000)

Antibiotics are among the most commonly sold drug classes in the developing countries. (Buke, Ermertcan, Hosgor-Limoncu, Ciceklioglu, & Eren, 2003) In many Middle East countries including Lebanon antibiotics can be obtained as SM since having a valid prescription is not enforced. This results in the increased irrational use of medicines. Irrational use of prescription medications is a major problem worldwide especially in Lebanon where there is a wide variety of product which can be purchased even without a prescription, compared to other countries where they are available only with a valid prescription as prescription including France. The irrational use of medicines especially for prescription medicines obtained without prescription can result in potential misuse and unnecessary risk for patients and the community.

The incorrect use of antibiotics represents one of the main causes of antibiotic resistance. The bacteria if exposed to antibiotics develop some DNA mutations that make them resistant to the antimicrobial action. Moreover, the prolonged administration of these medicines leads to a natural selection process allowing the growth of resistant bacteria and the death of the sensitive ones. (Annual Report of the Chief Medical Officer, 2011) The indiscriminate consumption of antimicrobial drugs could be, in part, connected to the lack of knowledge about the correct antibiotic use by patients.

Several examples of resistant bacteria have been reported in literature including penicillin resistant Streptococcus pneumonia, vancomycin-resistant Enterococci, methicillin-resistant Staphylococcus aureus, multi-resistant Salmonellae, and multi-resistant Mycobacterium tuberculosis. (World Halth Organization, 2002) Several studies have discussed the correlation between antibiotic misuse, self-medication with antibiotic and antimicrobial resistance.

Data from Resistance Surveillance and Control in Mediterranean Region ARMED project showed increases of resistant rates in countries with high level of antibiotic consumption such as Eastern and Southern Mediterranean regions compared to low resistance rates in Northern countries. (Borg et al., 2006)This situation could be explained by the unregulated distribution of antibiotics, and their wide availability without prescription in developing countries which is not the case in most developed countries. (Sosa et al., 2010)

In France, antibiotics are obtained as prescription only medicines; their use is captured in French healthcare databases (SNIIRAM database). The French healthcare system is based on universal coverage by one of several healthcare insurance plans. The three reimbursement databases are the following: (1) The Extraction, Recherches, Analyses pour un Suivi Me´dico-Economique database (Erasme) (Fender & Weill, 2004)is the medical reimbursement database of the Caisse Nationale d'Assurance Maladie des Travailleurs Salarie´s (Cnam-TS) (http://www.ameli.fr)which covers all the medical reimbursement of all employees and their families. The computerized database includes almost 87% of the general population (i.e., 54.5 million individuals) and contains reimbursement data for the two years preceding the day it is interrogated.(2) The Regime Social des Independants (RSI) database is the medical reimbursement database of the system for the self-employed(http://www.le-rsi.fr)(approximately 3.3 million individuals) and contains reimbursement data for the three

years preceding the day it is interrogated.(3) The Mutuelle Sociale Agricole (MSA)(http://www.msa.fr) database is the medical reimbursement database of the system for all farmers and their employees, (approximately 3.6 million individuals) and contains reimbursement data for the 24–30 months preceding the day it is interrogated, according to the department concerned. (Martin-Latry & Begaud, 2010)

The SNIIRAM database merges anonymous information of reimbursed claims from all these plans, linked to the national hospital-discharge summaries database system (PMSI) and the national death registry. It now covers 98.8 % of the French population, over 66 million persons, from birth (or immigration) to death (or emigration), making it possibly the world's largest continuous homogeneous claims database. The power of the database is correlatively great, and its representativeness is near perfect, since it essentially includes the whole country's population. The main difficulty in using the database, beyond its sheer size and complexity, is the administrative process necessary to access it. (Bezin et al., 2017; Moulis et al., 2015; Tuppin, de Roquefeuil, Weill, Ricordeau, & Merliere, 2010) EGB (*Echantillon Généraliste de Bénéficiaires*) is the 1/97th random permanent representative sample of SNIIRAM, with planned 20-year longitudinal data (ten years at this time). Access to these databases has been recently clarified and improved. (Bezin et al., 2017)

In Lebanon, like most other developing countries, having a valid prescription is generally not enforced for receiving prescription-only drugs (POM). With the exception of narcotics and major tranquilizers, patients can buy any medication without a prescription. Community pharmacies are the only source of health services and medicines. Therefore, patients seeking antibiotics can be captured in community pharmacies. Many pharmacoepidemiological studies have been conducted in community pharmacies and described it as a feasible option. (Fendrick et al., 2004)

In Lebanon, the Lebanese Ministry of Public Health (MOH) laws regulate some prescription medications (psychiatric drugs, opioids derivatives), and the Pharmacy law prohibits dispensing prescription medications without a physician’s order. However, the governing rules and regulations are mostly not enforced. (Republic of Lebanon Ministry of Public Health. Laws and regulations)In addition, there is no clear and official list of OTC medications issued by the MOH which in practice leaves the door open for community pharmacies to sell a wide range of medications as OTC products. As a consequence, community pharmacists have increasing involvement in the self-management of minor and moderate illnesses as a result of the availability of this wider range of non-prescribed medicines and because they are faster and less expensive than public or private clinics. Such a situation encourages self-medication, including misuse of antibiotic. (M, Batiha, Tawalbeh, Tubaishat, & AlAzzam, 2015)

The use of antibiotics as SM is motivated by a complex set of factors including high cost of medical consultation, time constraints, accessibility, media campaigns and influence of friends and family, in addition to the misconceptions regarding the efficacy of antibiotics. (Afolabi, 2008; Belongia, Naimi, Gale, & Besser, 2002; Sosa et al., 2010) Doctors’ consultations are expensive and repeated reuse of prescriptions is a way to save money.

Our major concern is the antibiotic use due to its importance for both individual and public health concern. Studies in Lebanon about antibiotic usage are still scarce. Therefore, this study is conducted to compare the usage patterns of antibiotics as self-medication in Lebanon to that in a country which enforces prescription-only dispensing, such as France. A major objective is to see whether the drug status impacts on its usage. It is important also to assess whether an average person’s knowledge is sufficient enough to start a treatment without consulting with a doctor. Is the pattern of drug usage of antibiotic safe and effective? Is a pharmacist’s advice within so called pharmaceutical care, often marginally treated by pharmacist themselves, enough? What are the consequences and risks of being able to buy these drugs?

Objectives:

The main objectives of this study are:

- To determine the usage pattern of antibiotics available as self-medication in Lebanon and as prescription only in France.
- To assess the appropriate drug use, and emphasize the need that patients receive medications appropriately and safely according to their clinical needs, in doses that meet their own individual requirements, for an adequate period of time.
- To evaluate the knowledge and risk awareness regarding antibiotic self-medication among the general public in Lebanon.
- To determine the safety and compliance associated with self-medication of antibiotics.

Plan of the Thesis:

First, in chapter 1, we conduct a systematic review of self-medication misuse in the Middle East.

In chapter 2, we describe the self-medication use of antibiotics in Lebanon.

In chapter 3, we evaluate the appropriateness of self-medication use of antibiotics in Lebanon: was it the right choice of drug, in appropriate dose for the adequate duration.

In chapter 4, we assess the current knowledge, attitude and practice of Lebanese participants toward antibiotic.

In chapter 5, we describe the usage pattern of antibiotics (obtained on prescription only) in France.

In chapter 6 we discuss the findings in this study and compare the usage pattern of antibiotics between France and Lebanon.

Finally, chapter 7 is the overall conclusion of the Thesis.

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Chapter 1:

A Systematic review of self-medication misuse in the Middle East

In the Middle East, self-medication is highly prevalent since regulations are not enforced in many countries and some prescription drugs are easily available as SM. People are not only using non-prescription drugs but also prescription drugs, as self-medication products, without supervision.Few studies have described the act of self-medication misuse in the Middle East or Lebanon. However, before starting a field study of self-medication in Lebanon, we conducted a systematic review of published papers about self-medication misuse in the Middle East to identify different type of medicines involved. to verify its magnitude, and focus our field study on relevant targets.

We also aimed to describe current knowledge and understanding about the range of SM misuses and to identify the source for SM practice.

Khalifeh M, Moore N, Salameh P,Self-medication Misuse in the Middle East: a systematic literature review. Pharmacy Research and Perspective, 2017, 5 (4): 1-13.

Self-Medication Misuse in the Middle East: A Systematic Literature Review

Abstract:

Aims: Regulations usually distinguish between prescription-only (POM) and over-the-counter (OTC) medicines. The former requires medical prescription; the latter are available for SM of common minor or easily-treated ailments. However, in the Eastern Mediterranean countries, theoretically prescription medicines can easily be purchased without a prescription, as self-medication (SM) resulting in potential misuse and unnecessary risk for patients. The magnitude of this activity is uncertain. The aim of this paper, therefore, is to review the different types of medicines implicated in this misuse in the Middle East, and to describe current knowledge and understanding about POM misuse and the source of SM practice.

Methods: An extensive review of the published literature (1990–2015) was conducted using Pubmed, web of science, Cochrane and Google Scholar databases, for OTC medicine misuse and in the Middle East. 72 papers were identified. Medicines involved in misuse included: codeine containing products, topical anesthetics, topical corticosteroids, and antibiotics.

Results: Self-medication misuse of medicines seemed widespread. Individual treatment patterns were not clearly identified. Studies were not standardized, limiting the comparability between studies and the estimation of the scale of misuse. Pharmacists, friends or parents were found to be the main sources of SMs. Knowledge and attitudes are an important contributing factor in the misuse of these medications. Strategies and interventions to limit misuse were rarely identified in literature.

C**onclusion**: There is a massive problem involving a range of medicines. Standardization of studies is a prerequisite to the understanding and prevention of abusive self-medication.

Keywords: Self-medication, Prescription medicines, misuse, Middle East, Eastern Mediterranean countries.

Introduction:

Regulations usually distinguish between prescription-only (POM) and over-the-counter (OTC) medicines. The former requires medical prescription; the latter are available for SM of common minor or easily-treated ailments. Many patients may treat themselves and self-medicate, using either OTC medication or prescription medicines without prescription.

OTC medicines are medicines that are approved for self-medication (SM), because their indication is easily recognized by patients and usually self-limiting, and the medicine is thought to be safe and effective. Paracetamol and low-dose NSAIDs for pain relief are typical of these OTC medicines. However, SM is not limited to OTC medicines, and patients self-medicate with prescription medicines. These are medicines that may be have been prescribed and left over from a previous treatment episode, or bought directly from the community pharmacies without a prescription. The latter is in principle not authorized. However, in practice in many countries the dispensing of prescription medicines by pharmacists, without a prescription is not unusual, especially for the short-term treatment of common diseases.

SM has become quite common in developed (Blenkinsopp and Bradley 1996) and more common in developing countries(Kamat and Nichter 1998). In developing countries people are not only using OTC products as SM but also prescription medicines, as SM products, without supervision. SM has been studied in many different populations, showing that about 25-75% of the population consumes SM medicines(Wazaify, Shields et al. 2005). SM is highly prevalent in the community in Eastern Mediterranean countries. In Middle East, prescription medicines can easily be purchased without prescription, resulting in potential misuse and unnecessary risk. Patients may use medicines without a prescription from pharmacies, use old prescriptions, share medicines with friends/relatives, and use leftover medicines from previous prescription-based dispensing.

However, there is a relative lack of literature relating to SM misuse in the Middle East. There has been relatively little systematic research on this topic, partly due to the perception that SM misuse is not as problematic as other types of drug abuse. A single review article (Cooper 2013) has described the current knowledge of OTC medicine misuse and identifies the different types of OTC medicines implicated. A number of specific medicines have been implicated in literature including: opiate-based OTC analgesics, cough syrup containing dextromethorphan or pseudoephedrine, diphenhydramine and other antihistamines (Lessenger and Feinberg 2008). Moreover, since antibiotics are available without prescription in the middle East they were also included in the review.

Misuse has been defined as the incorrect use of an OTC product for a medical purpose, usually in terms of dosage or duration of use (Hughes, McElnay et al. 1999).

The aim of this article, therefore, is to undertake a comprehensive review to identify the different types of medicines that can easily be purchased as SM in Middle East and recognized as misused. Other objectives were to describe current knowledge and understanding about the range of SM misuses and to identify the source of SM practice.

Method:

Search Strategy:

Databases, namely Medline/Pubmed, Web of Science, Cochrane Library and other sources were used to identify peer reviewed papers dealing with the review theme in WHO Eastern Mediterranean countries. Search terms were identified through a pilot review of the literature and were used to identify articles through a systematic, standardized process.

The words/strings used for search and inclusion criteria were: using combinations of the following terms: "over the counter", "OTC", "non-prescription", "self-prescription medicines", "prescription medicines", "misuse", "abuse", "addiction", "dependency" and "nonmedical use", "irrational use", "inappropriate use", Arab and name of countries belonging to the WHO Eastern Mediterranean Region (EMRO). The search strategy is outlined in figure 1. The search was limited to publications between 1990 and July 2015. Reviews (Lessenger and Feinberg 2008, Al-Tawfiq, Stephens et al. 2010, Cooper 2013, Shehnaz, Agarwal et al. 2014) were used for reference mining but they were not included.

Article Selection:

For a paper to be included in the review, four criteria were jointly required: 1) SM or over the counter (OTC) or prescription medications since some are available without prescription in the community pharmacy in Middle East. 2) WHO Eastern Mediterranean country, 3) Publication from 1990 to July 2015, 4) Availability of abstract in English, French or Arabic.

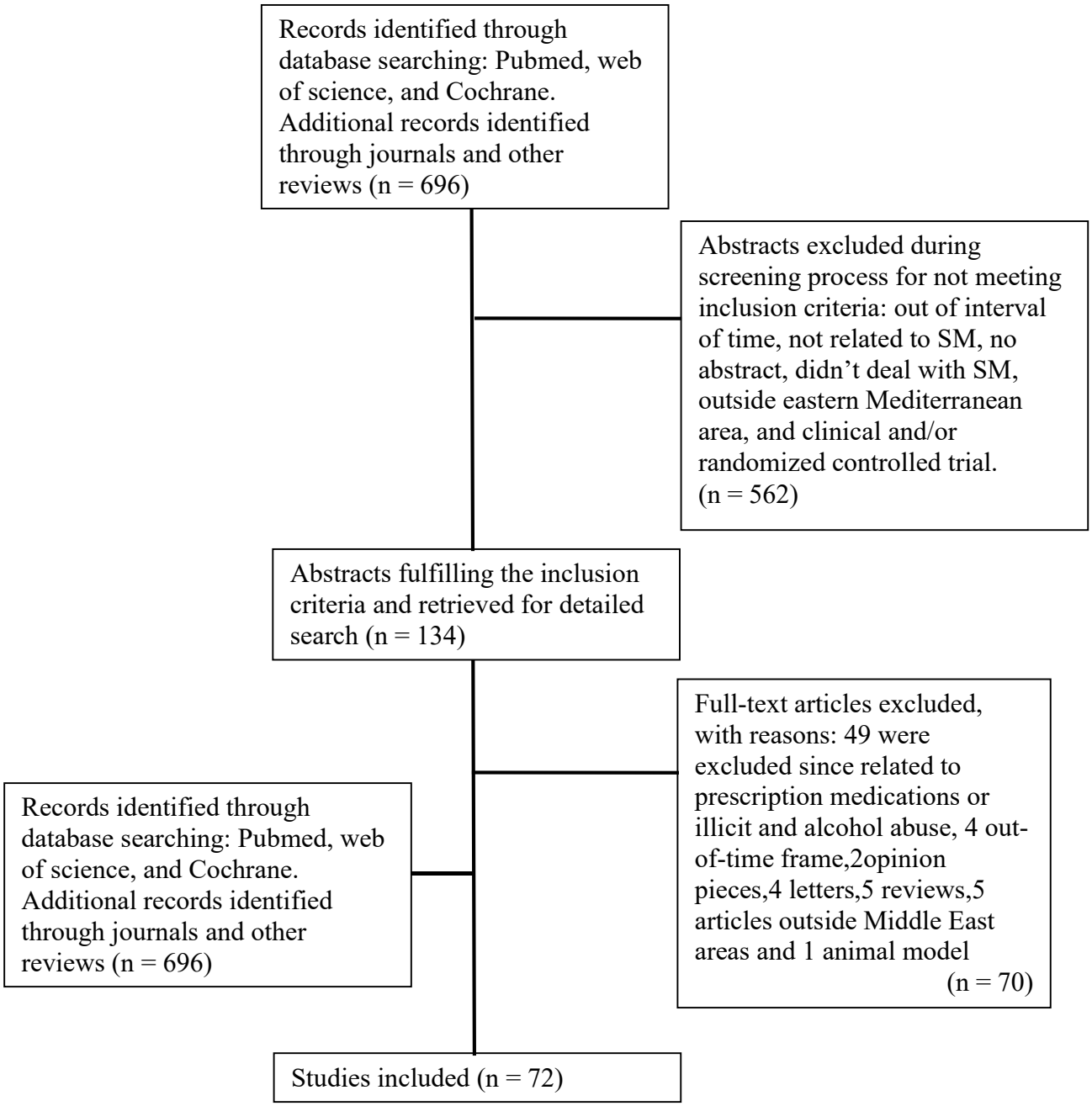
Exclusion criteria included non-English, French or Arabic language publications and reference exclusively to prescribed or illicitly obtained medicines. Articles related to alcohol or substance abuse were also excluded; although they represent an important category, they cover different objectives of the review theme related to SM misuse. Studies were also excluded via search limits if they were: review articles, on animal models; hospital-based studies; clinical and/or randomized controlled trials; editorials, letters, opinions or comment publication type.

Content reviews were performed to select articles that met these criteria. From the title review, articles were excluded if they were not relevant to the subject matter. Any articles with an ambiguous title or title suggestive of the topic were evaluated in the abstract review. Abstracts were reviewed for details that indicated the article may meet inclusion criteria. Finally, full text articles were reviewed and assessed to determine whether inclusion criteria were met. Full-text reviews were also conducted on review articles to identify additional articles from their bibliographies.

Data abstraction:

The following details were extracted from each study using an abstraction form: year of publication, country of origin, population sampled, recall period, and data pertaining to the study objectives.

Figure 1: Selection of articles



Results:

Literature search results

The database search yielded 696 publications for review. Fifty other records were added through other sources like health journals edited in Iran, Pakistan and Saudi Arabia and previous reviews for reference mining but they were not included. After excluding 562 articles for reasons of duplicated records, review articles, irrelevant topic, time of publication, availability of abstract, outside eastern Mediterranean area, and clinical and/or randomized controlled trial.

A secondary search was performed to elaborate the primary concept. 134 full-text articles were assessed of which 49 were excluded since they were related to prescription medications or illicit and alcohol abuse or medication storage and wastage, which did not meet our study objective. Another 21 articles (4 out-of-time- frame, 2 opinion pieces, 4 letters, 5 reviews, 5 articles outside Middle East area, and 1 animal model) were excluded. An additional 8 articles were added after reference screening. This resulted in 72 articles, which fulfilled the inclusion criteria. (**Figure 1**).

Study characteristics:

The studies in the 72 publications differed substantially in sample size, recall period, and location. These studies reviewing overall prevalence, frequencies and pattern of OTC misuse originated from different countries: Iran (n= 16), Pakistan (n= 12), Jordan (n= 11), Saudi Arabia (n=8), Lebanon (n=3), United Arab Emirates (n=4), Kuwait (n=2), Egypt (n=2), Syria (n=2), Yemen (n=2), Iraq (n=2), Palestine (n=2), Bahrain (n=2), Libya (n=1), Sudan (n=1), Oman (n=1). An additional paper included Lebanon, Egypt, Jordan, Tunisia and Libya (Scicluna, Borg et al. 2009). All the studies were cross-sectional in nature barring 1 case report (Risco and Millar 1992) and 1 prospective study (Nazarzadeh, Bidel et al. 2014). Most studies used self-administered questionnaires or face to face interviews for data collection. Mixed data collection techniques were also adopted.

Prevalence of SM:

SM was highly prevalent in the community in Eastern Mediterranean countries, ranging from 35.4% to 83% in Iran (Jafari, Khatony et al. 2015), 42.5% in Jordan (Yousef, Al-Bakri et al. 2008), 35.4% in Saudi Arabia (Alghanim 2011), and 68.1% in Pakistan (Syed, Mehreen et al. 2015). It is also well prevalent among adolescents in many Middle East countries including Jordan (87%) (M, Batiha et al. 2015), Palestine (98%) (Sawalha 2008), Kuwait (92%) (Abahussain, Matowe et al. 2005), Emirates (89.2%) (Shehnaz, Khan et al. 2013), Bahrain (44.8%) (James, Handu et al. 2006), and Pakistan (80.4%) (Mumtaz, Jahangeer et al. 2011).

Scale of SM misuse:

Methods used to describe the extent of OTC misuse varied. This variety is due to different methods and data sources, which make comparisons between countries difficult. Several studies relied on the perceptions or behavior of pharmacists (in Jordan, Palestine, Lebanon, Saudi Arabia, Egypt and Syria), whilst others relied on sampling the public, pharmacy customers or among university or school students.

Studies varied as to whether they focused on a particular product or on a range of products. Studies based on pharmacists' approaches appeared to generate more detailed and varied descriptions of medicines that may be misused. In Jordan, for example, antibiotics were commonly cited by pharmacists as being misused, as regulations restricting their supply were not always enforced (Albsoul-Younes, Wazaify et al. 2010). Similar studies were conducted in Palestine and Egypt by Sweileh et al (Sweileh, Arafat et al. 2004) and Elhoseeny (Elhoseeny,

Ibrahem et al. 2013), based on perception of community pharmacists. In Palestine, 66% of community pharmacists believe that there is an increase in misuse of OTC medicines (Sweileh, Arafat et al. 2004). Antitussives, analgesics, antihistamines, laxatives, decongestants and sedatives hypnotics and tranquilizers were also identified by pharmacists as misused OTC medicines (Sweileh, Arafat et al. 2004).

The use of nonprescription medicine among patients/consumers was reported by 66.9% of pharmacists to have increased in the past 4 years (Elhoseeny, Ibrahem et al. 2013). Iran Pharmacies sold 57% of prescription items without prescription (Zargarzadeh, Minaeiyan et al. 2008). Shehnaz study in the United Arab Emirates showed high prevalence of SM with antibiotics (53%) and sedative/hypnotics (27%) (Shehnaz, Khan et al. 2013).

Moreover, some studies showed that the practice of SM is influenced by pharmacists. In Syria, from 200 pharmacies visited, 87% agreed without insistence from the investigator to sell antibiotics without prescription. This figure increased to 97% when the investigators who were at first denied antibiotics insisted on having the antibiotics (Al-Faham, Habboub et al. 2011). In Saudi Arabia, only one attendant pharmacist refused to dispense medications without prescription. 17% dispensed urinary antiseptic only and 82% gave antibacterial agents (Al-Ghamdi 2001).

Medicines involved in SM misuse:

Medicines implicated in SM misuse belong to different pharmacologic groups: Codeine based products, tramadol, topical ocular anesthetic, topical corticosteroids. Antibiotics and antimalarial were also described as misused medicines in many articles as seen in table1.

Table1: Types of drugs misused in the retrieved publications:

Types of Drugs misused	***number of papers (n)***	***Countries***	***Prevalence of SM %***	***Study participants***	***Reference***
Analgesics (including codeine containing medicines)	4	Iran	28.7%	564 University students	(Sarahroodi, Maleki-Jamshid et al. 2012)
			60%	210 University and school students	(Sedighi, Ghaderi-Sohi et al. 2006)
		Saudi Arabia		504 University students	(Ibrahim, Alamoudi et al. 2015)
		Pakistan	55.4%	1380 Community participants	(Qazi, Bano et al. 2013)
		Jordan	32%	393 Pharmacists	(Albsoul-Younes, Wazaify et al. 2010)
Tramadol	2	Iran	56% 4.8%	162 Pharmacy customers 1894 School students	(Zabihi, Hoseinzaadeh et al. 2011)(Nazarzadeh, Bidel et al. 2014)
Antibiotics	38	Iran	35.8%	320 University staff	(Askarian and Maharlouie 2012)
			42.2%	195 University members	(Sarahroodi, Arzi et al. 2010)
			43%	272 Patients at clinics	(Jafari, Khatony et al. 2015)

Types of Drugs misused	*number of papers (n)*	*Countries*	*Prevalence of SM %*	*Study participants*	*Reference*
			53%	153 University females	(Sarahroodi and Arzi 2009)
			57.6%	572 Community participants	(Heidarifar, Koohbor et al. 2013)
		Jordan	40.7%	477 Patients at clinics	(Sawair, Baqain et al. 2009)
			46.3	480 pharmacy customers	(Al-Bakri, Bustanji et al. 2005)
			62%	37 Community participants	(Darwish, Abdelmalek et al. 2014)
			32%	174 Patients at clinics	(Scicluna, Borg et al. 2009)
			59.1%	1141 Community participants	(Shehadeh, Suaifan et al. 2012)
			N/A	1091 Pharmacy customers	(Alzoubi, Al-Azzam et al. 2013)
			68.8%	679 University students	(Suaifan, Shehadeh et al. 2012)
			N/A	393 Pharmacists	(Albsoul-Younes, Wazaify et al. 2010)
		Lebanon	32%	110 Pharmacists	(Farah, Lahoud et al. 2015)
			42%	340 Pharmacy customers	(Cheaito, Azizi et al. 2014)
			37%	119 Patients at clinics	(Scicluna, Borg et al. 2009)
		Pakistan	71.4%	780 University and school students	(Aslam, Mirza et al. 2013)
			N/A	1342 Households	(Sturm, van der Pol et al. 1997)
			30%Pharyngitis23%Gastroenteritis	851 Community participants	(Qazi, Bano et al. 2013)
			25% storage	158 Households	(Nasir, Hashmi et al. 2012)
			35.2%	572 University students	(Zafar, Syed et al. 2008)
			10.8% storage	158 Households	(Haider and Thaver 1995)
		Saudi Arabia	48%	353 School teachers	(Belkina, Al Warafi et al. 2014)
			11.6% for children	610 Community Parents	(Abobotain, Sheerah et al. 2013)

Types of Drugs misused	*number of papers (n)*	*Countries*	*Prevalence of SM %*	*Study participants*	*Reference*
			5%	1596 University and school students 88 Pharmacists	(Almalak, Albluwi et al. 2014) (Al-Ghamdi 2001)
		Syria	85%	365 Community participants	(Barah and Goncalves 2010)
			N/A	200 pharmacists	(Al-Faham, Habboub et al. 2011)
		UAE	40.2	300 University students	(Suleiman and Rubian 2013)
			46%	860 Community parents	(Abasaeed, Vlcek et al. 2009)
			11.4%	324 School students	(Shehnaz, Khan et al. 2013)
		Iraq	26%	300 Households	(Jassim 2010)
		Egypt	23.3%	884 Pharmacy customers	(Sabry, Farid et al. 2014)
			30%	300 Patients at clinics	(Scicluna, Borg et al. 2009)
		Kuwait	27.50%	680 Community participants	(Awad and Aboud 2015)
		Libya	43%	363 University students	(Ghaieth, Elhag et al. 2015)
			48%	286 Patients at clinics	(Scicluna, Borg et al. 2009)
		Oman	67%	718 Community participants	(Jose, Jimmy et al. 2013)
		Yemen	78.2%	367 School teachers	(Belkina, Al Warafi et al. 2014)
			60%	2000 Patients at clinics	(Mohanna 2010)
		Sudan	48.10%	1750 Households	(Awad, Eltayeb et al. 2005)
		Tunisia	20.00%	264 Patients at clinics	(Scicluna, Borg et al. 2009)
Antimalarial	2	Sudan	43.4%	1750 Households	(Awad, Eltayeb et al. 2005)
		Yemen			(Abdo-Rabbo 2003)
Topical Anesthetics	2	Iran	80.5%	390 Welders	(Sharifi, Sharifi et al. 2013)
		Saudi Arabia			(Risco and Millar 1992)
Topical Corticosteroids	1	Iraq	7.90%	1780 Patients at clinics	(Al-Dhalimi and Aljawahiry 2006)
Cough/cold products	3	Pakistan	N/A	864 University students	(Bano, Najam et al. 2012)

Types of Drugs misused	*number of papers (n)*	*Countries*	*Prevalence of SM %*	*Study participants*	*Reference*
		Jordan	N/A	393 Pharmacists	(Albsoul-Younes, Wazaify et al. 2010)
		Palestine	N/A	864 University students	(Sweileh, Arafat et al. 2004)
Decongestants	1	Jordan	N/A	393 Pharmacists	(Albsoul-Younes, Wazaify et al. 2010)
Laxatives	1	Palestine	N/A	97 Pharmacists	(Sweileh, Arafat et al. 2004)
Sedatives/Hypnotics and Benzodiazepines	3	Jordan	N/A	393 Pharmacists	(Albsoul-Younes, Wazaify et al. 2010)
		United Arab Emirates	N/A	324 School students	(Shehnaz, Khan et al. 2013)
		Jordan	N/A	393 Pharmacists	(Albsoul-Younes, Wazaify et al. 2010)

Analgesics:

Codeine is usually supplied and consumed as codeine-containing pain-killer tablets that mostly also contain acetaminophen. Both acetaminophen-codeine tablets and tramadol tablets are prescription medicines, but many pharmacies sell them without a prescription (Zabihi, Hoseinzaadeh et al. 2011). In Iran, Codeine-containing tablets, especially acetaminophen-codeine tablets are among the most requested medicines as OTC (Zargarzadeh, Minaeiyan et al. 2008). Headache was the most common problem (Sarahroodi, Maleki-Jamshid et al. 2012), and Sedighi showed that 91% of Iranian migraine sufferers used SM, mostly Acetaminophen and Codeine (Sedighi, Ghaderi-Sohi et al. 2006).

The prevalence of lifetime tramadol misuse among Iranian students was 4.7% (Nazarzadeh, Bidel et al. 2014). This is due to easy accessibility from pharmacies without prescription. For instance, 56% of patients requesting for tramadol did not have a prescription (Zabihi, Hoseinzaadeh et al. 2011).

Topical Anesthetics:

Topical ocular anesthetics are commonly misused among Iranian welders: 80.5% declared that they had used topical anesthetics at least once during their working lives (Sharifi, Sharifi et al. 2013). All were males. Mostly patients prefer self-treatment over seeking help from a physician, for cultural and financial reasons. The most commonly used topical anesthetic was tetracaine (Sharifi, Sharifi et al. 2013). Topical ocular anesthetic misuse is associated with many harmful adverse effects. A case report stated a 40-year-old patient in Saudi Arabia frequently self-administering topical oxybuprocaine drops had developed ocular ultrastructural alterations (Risco and Millar 1992).

Topical Corticosteroids:

Al-Dhalimi showed that topical corticosteroids were commonly misused by 7.9% of Iraqi patients presenting at the dermatological center for lightening the skin or mild acne. The most commonly used topical steroids were potent and highly potent corticosteroids including Clobetasole propionate and Betamethasone valerate. About half were aged 10–19 years. In

34.3% of cases, medical staff was responsible for recommending the medicines, including pharmacists (Al-Dhalimi and Aljawahiry 2006).

Cough/cold products and Laxatives:

Sweileh et al (Sweileh, Arafat et al. 2004) and Albasoul (Albsoul-Younes, Wazaify, Yousef, & Tahaineh, 2010) reported that antitussives, analgesics, antihistamines, decongestants and laxatives were identified by pharmacists as misused medicines (Sweileh W 2004). The antitussive products most misused were those containing the following combinations: (codeine phosphate/pseudoephedrine/triprolidine) (53.6%) or (ephedrine/ammonium chloride/ codeine phosphate/pheniramine maleate) (5.2%).

Antibiotics and Antimalarials:

Inappropriateness of antibiotic use is defined as suboptimal use of antibiotics to treat antibiotic responsive conditions, including use of overly broad agents, incorrect drug dosing or duration, and poor drug adherence (Sabry, Farid et al. 2014). Misuse of antibiotics is common in Eastern Mediterranean countries, with self-medication rates ranging from 32% to 42% as reported in Lebanon (Cheaito, Azizi et al. 2014), and from 32% to 62%% in Jordanian studies (Darwish, Abdelmalek et al. 2014)(Scicluna, Borg et al. 2009); rates as high as 57.6% were reported in Iran (Heidarifar, Koohbor et al. 2013), in Emirates (56%) (Abasaeed, Vlcek et al. 2009), Syria (85%) (Barah and Goncalves 2010), Tunisia (20%) (Scicluna, Borg et al. 2009) and Yemen (60%) (Mohanna 2010). 73.9% of Sudan population had used antibiotics or antimalarials without a prescription (Awad, Eltayeb et al. 2005).

Antibiotic SM was common among university and school students in Palestine (98%) (Sawalha 2008), Libya (46%) (Ghaieth, Elhag et al. 2015), United Arab Emirates (40%) (Sharifi, Sharifi et al. 2013), Saudi Arabia (48%) (Belkina, Al Warafi et al. 2014), Pakistan (from 71.4% to 80.4%) (Aslam, Mirza et al. 2013), and Iran (53%) (Sarahroodi and Arzi 2009). This practice was also observed among parents for their children. This practice was clear in Saudi Arabia (Darwish, Abdelmalek et al. 2014) and in the Scicluna study(Scicluna, Borg et al. 2009).

Respiratory tract symptoms were the main indication for which respondents indicated they would self-medicate. Antibiotics were mainly used for treatment of sore throat, cough, and flu. These results were found in Iran (Heidarifar, Koohbor et al. 2013), Iraq (Jassim 2010), Jordan (Sawair, Baqain et al. 2009)(Al-Bakri, Bustanji et al. 2005), Kuwait (Awad and Aboud 2015), Libya (Ghaieth, Elhag et al. 2015), Lebanon (Cheaito, Azizi et al. 2014), Pakistan (Qazi, Bano et al. 2013), Egypt (Sabry, Farid et al. 2014), Tunisia (Scicluna, Borg et al. 2009), and Saudi Arabia (Belkina, Al Warafi et al. 2014). Other reasons for self-medication were for urinary tract infections (Scicluna, Borg et al. 2009) or gastrointestinal symptoms (Mohanna 2010).

Poor compliance with antibiotic therapy has a great impact on antibiotic misuse. Most patients did not complete the full course of antibiotic and took them for less than 3 days. This was observed in many Middle East countries and ranged from 39% to 86% as seen in table 2. Reasons most frequently mentioned by patients for non-compliance were: rapid improvement of symptoms, forgetfulness and frequent dosing. (Al-Shammeri, Khoja et al. 1995) .

Table 2: Percentage of antibiotic compliance in the retrieved publications:

Countries	*% Antibiotic Compliance*	*Study Setting*	*Reference*
Jordan	39%	800 University students	(Suaifan, Shehadeh et al. 2012)
	40%	508 Community participants	(Darwish, Abdelmalek et al. 2014)
Kuwait	64%	680 Community participants	(Awad and Aboud 2015)
Iran	37.10%	542 Community participants	(Heidarifar, Koohbor et al. 2013)
	26.80%	564 University students	(Sarahroodi and Arzi 2009)
Libya	86%	363 University students	(Ghaieth, Elhag et al. 2015)
Oman	29%	718 Community participants	(Jose, Jimmy et al. 2013)
	56%	400 School teachers	(Belkina, Al Warafi et al. 2014)
Pakistan	42%	780 University and school students	(Aslam, Mirza et al. 2013)
Saudi Arabia	71.30%	300 Households	(Abobotain, Sheerah et al. 2013)
	61%	1200 School teachers	(Belkina, Al Warafi et al. 2014)
United Arab Emirates	75%	385 Women in clinics	(Suleiman and Rubian 2013)

The most common antibiotics used were amoxicillin or ampicillin among different Middle East countries including Libya, Tunisia, Egypt(Scicluna, Borg et al. 2009), United Arab Emirates (Abasaeed, Vlcek et al. 2009), Pakistan (Qazi, Bano et al. 2013), Iran (68.6%) (Heidarifar, Koohbor et al. 2013) and Jordan (Sawair, Baqain et al. 2009). In Saudi Arabia, fluoroquinolones were the most commonly dispensed antibiotic for urinary tract infections (82%) (Al-Ghamdi 2001). Amoxicillin-clavulanic acid was mostly used among Lebanese (48.9%)(Cheaito, Azizi et al. 2014)(Cheaito, Azizi et al. 2014), among university students in United Arab Emirates, (48.9%)(Suleiman and Rubian 2013) and in Pakistan (62.8%)(Aslam, Mirza et al. 2013). Metronidazole and TMP/ SMX were also commonly used in Pakistan (29.2%) (Qazi, Bano et al. 2013) and in Yemen (35%) (Mohanna 2010) respectively.

Sources and Reasons for Self-medication:

People tended to select medication based mainly on advice received from community pharmacist (see Table 3). Ease in access to antibiotics and availability of pharmacist consultation were the main factors resulting in an increase in the use of antibiotics. Cheaito et al reported that pharmacists were the main helpers for antibiotic self-medication (Cheaito, Azizi et al. 2014). Similar findings were in Sharif's study which showed that pharmacy was the main source of antibiotic self-medication (slightly more than 90%) (Sharifi, Sharifi et al. 2013) and among Libyan students (75%) (Ghaieth, Elhag et al. 2015).

Another study reported that the most common sources of information on medicines were parents or friends. In Jordan, 51.8% of adult patients use antibiotic based on a relative's advice (Shehadeh, Suaifan et al. 2012). Similar results were reported in many other Middle East countries. Prescription of antibiotics by physicians over phone is also an important contributing factor.

Use of leftover antibiotics is a major source for antibiotic use. Many patients tended also to keep antibiotics at home either for future use or for prophylaxis against infections(Ullah, Khan et al. 2013). In this case, antibiotics could be used without physician consultation. In Scicluna et al, (Scicluna, Borg et al. 2009)almost half of those interviewed admitted to having stored some type of antibiotic at home, which was not for current use.

The most common reasons for self-medication were prior experience of the disease or similar symptoms (Al-Azzam, Al-Husein et al. 2007, James, Handu et al. 2008, Yousef, Al-Bakri et al. 2008, Zafar, Syed et al. 2008, Scicluna, Borg et al. 2009, Mumtaz, Jahangeer et al. 2011, Jalilian, Hazavehei et al. 2013), certainty of its safety, (Jalilian, Hazavehei et al. 2013) prior consumption of the drug (Jalilian, Hazavehei et al. 2013), busy offices of physicians(Jalilian, Hazavehei et al. 2013, Shoaib, Rabia et al. 2013), and non-seriousness of the illness (James, Handu et al. 2008, Yousef, Al-Bakri et al. 2008, Mumtaz, Jahangeer et al. 2011, Jalilian, Hazavehei et al. 2013, Shoaib, Rabia et al. 2013) or low severity of disease (Ullah, Khan et al. 2013). Long waiting time to be seen by doctors (James, Handu et al. 2008, Yousef, Al-Bakri et al. 2008) and avoiding the cost of doctors' visits were also reported as common reasons for self-medication (Yousef, Al-Bakri et al. 2008)

Self-medication was significantly associated with age, male gender, education level and socioeconomic status. Young age, male, and having poor health status were more likely to practice self-medication (Alghanim 2011, Syed, Mehreen et al. 2015)(Yousef, Al-Bakri et al. 2008).

Table 3: Sources for Self-Medication:

Sources of SM	*Number of articles (n)*	*Country, %*	*references*
Pharmacists	23	Egypt, 13.1%, 30%	(Scicluna, Borg et al. 2009, Sabry, Farid et al. 2014)
		Iran 18.6%, 30%, 44.8%, 61.2%	(Sarahroodi and Arzi 2009, Heidarifar, Koohbor et al. 2013, Sharifi, Sharifi et al. 2013)(Askarian and Maharlouie 2012)
		Jordan 14.2%, 23.1%, 30%, 53.6%, 30%	(Al-Bakri, Bustanji et al. 2005, Yousef, Al-Bakri et al. 2008, Sawair, Baqain et al. 2009)(Scicluna, Borg et al. 2009)
		Lebanon 29.8%, 35%	(Cheaito, Azizi et al. 2014)(Scicluna, Borg et al. 2009)
		Libya 74%, 12%	(Scicluna, Borg et al. 2009)(Ghaieth, Elhag et al. 2015)
		Pakistan 33.49%	(Qazi, Bano et al. 2013)
		Yemen 55.1%	(Belkina, Al Warafi et al. 2014)
		Saudi Arabia 21.6%, 74%	(Alghanim 2011, Belkina, Al Warafi et al. 2014)
		Emirates 21.4%, 16.3%, 74%	(Shehnaz, Khan et al. 2013, Shehnaz, Khan et al. 2014)(Abasaeed, Vlcek et al. 2009, Mohanna 2010)
		Iraq 18.6%	(Al-Dhalimi and Aljawahiry 2006)
		Yemen N/A	(Abdo-Rabbo 2003)
		Tunisia 12%	(Scicluna, Borg et al. 2009)
Parents/Friends	19	Iran 0.6%, 6%, 54.7%, 40.1%	(Sharifirad, Pirzadeh et al. 2011)(Sarahroodi and Arzi 2009, Heidarifar, Koohbor et al. 2013, Sharifi, Sharifi et al. 2013)(Nazarzadeh, Bidel et al. 2014)
		Jordan 51.8%, 10.3%, 12%	(Sawair, Baqain et al. 2009, Scicluna, Borg et al. 2009, Shehadeh, Suaifan et al. 2012)
		Libya 26%, 11%	(Scicluna, Borg et al. 2009, Ghaieth, Elhag et al. 2015),
		Pakistan 20.09%	(Qazi, Bano et al. 2013)
		Yemen 7.3%	(Belkina, Al Warafi et al. 2014)
		Saudi Arabia 19.3%, 20.3%	(Belkina, Al Warafi et al. 2014)(Alghanim 2011)
		Emirates 20.2%	(Shehnaz, Khan et al. 2013, Suleiman and Rubian 2013)
		Iraq 20.7%	(Al-Dhalimi and Aljawahiry 2006)
		Yemen N/A	(Abdo-Rabbo 2003)
		Kuwait N/A	(Abahussain, Matowe et al. 2005)
		Egypt 11%	(Scicluna, Borg et al. 2009)

		Lebanon 10%	(Scicluna, Borg et al. 2009)
		Tunisia 13%	(Scicluna, Borg et al. 2009)
Physician advice or health professionals	5	Lebanon 50.8%	(Cheaito, Azizi et al. 2014)
		Emirates 25.8%	(Suleiman and Rubian 2013)
		Jordan 21.9%	(Yousef, Al-Bakri et al. 2008)
		Iran 27.2%	(Sharifi, Sharifi et al. 2013)
		Iraq 11.4%	(Al-Dhalimi and Aljawahiry 2006)
Dr. over phone	1	Jordan 37.5%	(Suaifan, Shehadeh et al. 2012)
Leftover	10	Iran 38.2%, 47.8%, 52%	(Sarahroodi and Arzi 2009, Askarian and Maharlouie 2012, Heidarifar, Koohbor et al. 2013)
		Iraq 45%	(Jassim 2010)
		Jordan 46%, 49%, 60%	(Shehadeh, Suaifan et al. 2012, Suaifan, Shehadeh et al. 2012, Darwish, Abdelmalek et al. 2014)
		Lebanon 19.4%	(Cheaito, Azizi et al. 2014)
		Emirates 1.1%, 28%	(Suleiman and Rubian 2013)(Abasaeed, Vlcek et al. 2009)
Stores at home for future use	2	Jordan 50%	(Scicluna, Borg et al. 2009)
		Tunisia 40%	(Scicluna, Borg et al. 2009)
		Libya 59%	(Scicluna, Borg et al. 2009)
		Lebanon 60%	(Scicluna, Borg et al. 2009)
		Egypt 40%	(Scicluna, Borg et al. 2009)
		Iraq 23%	(Jassim 2010)
		Emirates 27%	(Suleiman and Rubian 2013)
Self present based on: previous experience of symptoms or disease or knowledge	6	Iran 30.1% 48.5%, 75%	(Sarahroodi, Maleki-Jamshid et al. 2012)
		Jordan 27%, 53.1%	(Yousef, Al-Bakri et al. 2008, Sawair, Baqain et al. 2009)
		Yemen 17.1%	(Belkina, Al Warafi et al. 2014)
		Saudi Arabia 31.6%	(Belkina, Al Warafi et al. 2014)
previous treatment	3	Jordan 36.1%, 40%	(Scicluna, Borg et al. 2009)(Sawair, Baqain et al. 2009)
		Tunisia 45%	(Scicluna, Borg et al. 2009)
		Libya 48%	(Scicluna, Borg et al. 2009)
		Lebanon 88%	(Scicluna, Borg et al. 2009)
		Egypt 40%	(Scicluna, Borg et al. 2009)
		Iran N/A	(Jalilian, Hazavehei et al. 2013)
previous suggestion by physician or Dr. always prescribe the same antibiotic	2	Iran 32.6%	(Sarahroodi, Arzi et al. 2010)
		Lebanon 43%	(Scicluna, Borg et al. 2009)
		Egypt 11%	(Scicluna, Borg et al. 2009)
		Tunisia 21%	(Scicluna, Borg et al. 2009)
		Jordan 10%	(Scicluna, Borg et al. 2009)
		Libya 30%	(Scicluna, Borg et al. 2009)
old prescription	3	Yemen 20.6%	(Belkina, Al Warafi et al. 2014)
		Saudi Arabia 27.5%, 50.8%	(Alghanim 2011, Belkina, Al Warafi et al. 2014)
		Emirates 26%	(Mohanna 2010)

Doctor prescription to friend	1	Emirates 3.4%	(Suleiman and Rubian 2013)

Knowledge and Attitudes of self-medication:

Knowledge of self-medication is an important factor for drug misuse. In Egypt, 82.4% of the pharmacists considered the most common contributing factor for inappropriate self-medication use were lack of knowledge of patients/customers about the active ingredients in a branded product.(Elhoseeny, Ibrahem et al. 2013) Tawfiq's study showed that more than 60% of the respondents did not try to read the leaflets of their medications (Al-Tawfiq, Stephens et al. 2010).

The knowledge and attitude toward antibiotics are important contributing factors in the misuse of these medications. There is a limited understanding of which infections might require antibiotics and the safety and risks of such misusage. For instance, one Jordan study showed that 67.1% of the public believed that antibiotics treat common cold and cough. 28.1% misused antibiotics as analgesics (Shehadeh, Suaifan et al. 2012). Many patients thought they were used for viral infections (Alzoubi, Al-Azzam et al. 2013)(Darwish, Abdelmalek et al. 2014). Better knowledge was found to be a predictor for positive attitudes (Awad and Aboud 2015).

Discussion:

The current review summarizes a number of themes and data to inform understanding of self-medication misuse in Eastern Mediterranean area. In addition, it highlights the different medicines involved in self-medication misuse, their prevalence and their practice in different settings. Apparently, the uncontrolled consumption and monitoring of consumption of medicines in the Middle East is one reason for SM. This all is probably because of the easy availability of such medicines without prescription. So, people could misuse analgesics containing codeine, despite the availability of alternative active OTC medications such s paracetamol or NSAIDs. However, they are available as prescription medicines in some developed countries.

For example, in England (Paxton and Chapple 1996) and Scotland (Matheson, Bond et al. 2002) 69% and 68.5% of pharmacists considered there to be some form of OTC medicine misuse in their pharmacies. Consistently with this study findings different Eastern Mediterranean countries addressed in our review article.

This review showed that regardless of the type of studied samples (driven from general population or selected sub-groups of population) the reported prevalence of self- medication misuse in Eastern Mediterranean countries is very high. Therefore, high prevalence of misuse seems to be a health challenge in the Middle East. However, much still remains undone in this area in Eastern Mediterranean area. Many important researches remained unexplored in different countries of Middle East.

The inappropriate use of antibiotic is risky. This may include the use of antibiotics beyond the scope of their indications to treat ailments unrelated to bacterial infections or using antibiotic with incorrect dosages for inappropriate period of time. As a result, most antibiotics are used in unnecessary cases that would mostly recover without any antibiotic. For instance, people may self-medicate with antibiotic for treatment of mild ailments as throat or teeth symptoms, nasal congestion, cough, flu, and urinary discomfort. Although patients can use many alternative OTC medications as cough, decongestants, or antihistamine products for upper respiratory tract infections, many still prefer to use of antibiotics. Inappropriate use of antibiotics may eventually lead to antibiotic resistance.

The main sources for self-medication were previously prescribed pharmaceuticals stored in the household and those purchased in pharmacies. Prescribing of medicine based on Essential Medicine List formularies, information campaigns and regulatory reinforcement might control or reduce SM misuse. In Chile, the prohibition of OTC sales of antibiotic and a simultaneous public education campaign had an immediate and significant impact on the acquisition of antibiotic from pharmacies (Abasaeed, Vlcek et al. 2009). Similarly, sales of antibiotic without prescription in Zimbabwe decreased when the law against over-the-counter sales was strictly enforced (Avorn and Solomon 2000).

The use of leftover medications is a unique consequence of poor compliance with medications including antibiotics because it affords the patient opportunities to self-medicate with a partial supply of antibiotics. Over-prescription of antibiotics by physicians is also an important factor that increases patient self-medication. Awareness and educational programs for physicians and consumers appear promising to control the overuse of antibiotics, non-compliance and the use of leftovers.

Methodologically, studies are not standardized, which limits the quality of studies as well as comparability. Most of the studies were cross sectional descriptive studies often using self-administered questionnaires, face to face interviews, or pharmacists' perception. Many studies report data based on pharmacists’ perceptions of the problem of misuse and the profile of those

they considered to be affected, such as reported by Albsoul et al (Albsoul-Younes, Wazaify et al. 2010), Elhoseeny (Elhoseeny, Ibrahem et al. 2013), or Sweileh (Sweileh, Arafat et al. 2004). These study designs are similar to those conducted in Scotland (Matheson, Bond et al. 2002). Though these studies may have high response rate, they are still subjective.

Like all literature reviews, and despite our best effort to use standard methodology for such reviews, the possibility of a selection bias cannot be excluded, even though we did search for local language papers, that might have escaped other researchers. Lack of access to some of the databases in the field and to unpublished research reports were the main limitations in our attempt to shed light on OTC misuse behavior. Uninformative titles and abstracts are also a limitation. However, the main limitation in our analysis is the heterogeneous methodological nature and reporting of the studies. Even finding more studies hidden in obscure repositories would probably not have changed that conclusion. In addition, most studies were consistent and showed similar results on the widespread use of self-medication, so that again missing studies would not change these results.

Conclusion:

This review relating to self-medication misuse has found a massive problem involving a range of medicines. Considerable attention should be paid to the risks of future expansion of inappropriate self-medication. Better physician education of appropriate medication use is one approach that may encourage the prudent use of antimicrobial and other medicines. In addition, policy making should be implemented in Middle East area in order to restrict sales of prescription medications without prescription.

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Chapter 2:

Self-medication use of antibiotics in Lebanon

From the previous review of the medicines involved in SM misuse in the Middle East, we found that antibiotics were the main medicines identified as misuse in the Middle East. Antibiotics are important drugs. It would be difficult to overstate the benefit of antibiotics in treating bacterial infections, preventing spread of the disease and minimizing serious complications of the disease.

The increase in antibiotic resistant bacteria poses a threat to the continued use of antibiotics to treat bacterial infections. The overuse and misuse of antibiotics has been identified as a significant driver in the emergence of resistance. (Paterson, Hoyle, Ochoa, Baker-Austin, & Taylor, 2016) The World Health Organization states that resistance to antibiotics is one of the world's greatest public health problems: a major cause being the irrational use of medicines. (Goossens, Ferech, Vander Stichele, Elseviers, & Group, 2005; World Halth Organization, 2007)

The introduction of new antibiotics has generally outpaced the development of antibiotic resistance. However, drug resistance has contributed to an increasing number of health care problems. In the United States, according to a 2013 report by the Centers for Disease Control and Prevention, at least 2 million people annually "acquire serious infections with bacteria that are resistant to one or more of the antibiotics designed to treat those infections." And at least 23,000 people die annually from antibiotic-resistant infections. (Centers for Disease Control and Prevention, 2013)

The importance of these benefits, and the potential population and personal risks of misuse, especially concerning the selection of resistant bacteria, justify the careful use of antibiotics, and the need for prescription. Although antibiotics are indeed prescription medicines, they can be easily obtained as SM.

A report by the WHO noted high antibiotic resistance across the Eastern Mediterranean region, including Lebanon, with high levels of resistance of *Escherichia coli* to third-generation cephalosporins and fluoroquinolones, and of *Klebsiella pneumoniae* to third-generation cephalosporins.(World Health Organization, 2014)Particularly in Lebanon*, Escherichia coli* susceptibilityto fluoroquinolones has decreased during the past decade from 75% to 53%, and the prevalence of extended spectrum slactamase (ESsL) producing *Klebsiella pneumoniae* has increased from 12% to28%.(Araj et al., 2012; Baroud et al., 2013)Additionally, there is emergence of extensively drug resistant (XDR) *Acinetobacter, Pseudomonas,* and carbapenem-resistant *Enterobacteriaceae*.(Baroud et al., 2013; El-Herte, Kanj, Matar, & Araj, 2012)

Antibiotic-resistant infections can happen anywhere. Data show that most happen in the general community; however, most deaths related to antibiotic resistance happen in healthcare settings such as hospitals and nursing homes.(World Health Organization, 2004)

Antibiotics are now less effective in treating bacterial infections. The overuse and misuse of antibiotics are key factors contributing to antibiotic resistance. The general public, doctors and hospitals all play a role in ensuring proper use of the drugs and minimizing the development of antibiotic resistance.

Therefore, we conducted a prospective study to describe the community use of antibiotics and their usage pattern within Lebanese population as well as to explore patterns of age and gender specific use for patients obtaining antibiotics with or without prescription.

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Khalifeh M, Moore N, Salameh P,Community Usage Pattern of Antibiotics within Lebanese population, A prospective study. American journal of Pharmacological Sciences. 2017 5(2) 49-56

Community Usage Pattern of Antibiotics within Lebanese population: A Prospective Study

Abstract:

Introduction: Antibiotic misuse is a worldwide public health problem and a major cause of antibiotic resistance.

Objective: The aim of this study therefore was to describe the usage pattern of antibiotics in Lebanon.

Method: It is a prospective study in a community-based pharmacy setting in Lebanon. It uses a structured random interview to patients visiting community pharmacy seeking for antibiotics. Baseline characteristics and reason for self-medication were collected. Completing a self-administered questionnaire after 30 days provided information on safety, efficacy and usage pattern. Data were analyzed using descriptive statistics and Chi-square test.

Results: 62.7% of 501 participants bought antibiotic without prescription. Pharmacists were the main helpers (34.7%). Amoxicillin/clavulanic acid was the most used antibiotic as self-medication (33.7%). The overall average dispensation was 9.07 DDD for short term use (< 2 weeks). In the follow up, the average DDD consumed by patient was 7.07 DDD and 62.5% were dispensed between 1 to 7 DDD. The average request per year was 3.35 which was significantly higher in patients without prescription than with prescription (p= .029). Males were dispensed more DDDs than females but the result was not significant. Patients with ages from 25-50 years old had significantly consumed more than 1 DDD per day (61.7%) compared to patients with age above than 50 years old (41%, p=.002).

Conclusion: Antibiotic consumption in Lebanon is uncontrolled. Educational programs should be implemented for the public to reduce the usage of antibiotic.

Keywords: Self-medication, Antibiotic, Lebanon, Usage pattern, DDD.

Introduction:

Antibiotic misuse is a worldwide public health problem and a major cause of antibiotic resistance. (Ricciardi, Giubbini, & Laurenti, 2016) Antibiotic resistance is one of the most relevant problems in the healthcare: the growth of resistant microorganisms in healthcare settings is a worrisome threat, raising length to stay (LOS), morbidity and mortality in those patients. (Ricciardi et al., 2016)

The main reasons for the increase of antimicrobial resistance include unregulated drug availability and widespread attitude to antimicrobial misuse, including self-medication. (Okeke et al., 2005)

The use of antibiotics has therefore been frequently studied in different countries all over the world. Antibiotic use has been studied and compared in hospitals and in primary care. (Ferech et al., 2006; MacKenzie, Monnet, Gould, & Group, 2006; Molstad, Lundborg, Karlsson, & Cars, 2002; Ronning et al., 2003) However, the use of antibiotics at an individual level has until recently been studied in smaller groups of patients.

In Lebanon, like most other developing countries, having a valid prescription is not always enforced for receiving prescription-only medications (POM). Previous researches in Lebanon shows that the prevalence of self-medication of antibiotic is alarmingly high. (Cheaito, Azizi, Saleh, & Salameh, 2014)

However, no researches were done to study the usage pattern of antibiotics in Lebanon. The aim of this study therefore was to describe the usage pattern of antibiotic within Lebanese population living in Lebanon and to explore patterns of age and gender specific use.

Method:

Design and Study Population:

A prospective study was conducted in a community-based pharmacy setting in Lebanon. Data was collected over a 1-year period (September 2015 to September 2016) from 50 community pharmacies (CPs) distributed in the six districts in Lebanon: Beirut, South Lebanon, Nabatiyeh, Mount Lebanon, Bekaa, and North Lebanon.

Eligible participants were recruited randomly from consumers presenting at CPs in Lebanon after they had purchased antibiotic medication with or without prescription. The patients included were from both genders, aged 16 years and older, coming to purchase antibiotic. The patients were divided into two groups: those buying antibiotic with a prescription versus those buying them without prescription.

The Lebanese University, Faculty of Pharmacy Internal Review Board waived the need for written informed consent. The patients were informed about the objective of the study and were asked to give an oral consent. Only those who gave their voluntary informed oral consent were enrolled.

Sample size calculation

A sample size was calculated assuming a type I error of 5% and a study power of 80% and 95%CI. Based on a previous study, 40% of patients were exposed to non-prescribed antibiotics. (Cheaito et al., 2014) The minimal sample size necessary to show a twofold increase in the risk of exposure to non-prescribed antibiotics consists of 442 subjects: 186 patients for those buying antibiotic with prescription and 256 without prescription.

Procedure and Data Collection:

Data on antibiotic use was collected using a structured random interview conducted by pharmacists or interviewers who had been briefed about the study's aims and methods. Consecutive customers arriving at CPs seeking antibiotic were interviewed. Data was collected from the participants twice, first at purchase for data about drug used and the condition for which it was to be used, then by calling the patient 30 days after starting the medication, for usage patterns.

The questionnaire included many sections that were chosen following an extensive review of literature. The questionnaire was translated into Arabic and subjected to a process of forward and backward translation into English. It was pretested and validated first on 20 patients visiting 4 different pharmacies before starting the survey.

The questionnaire consisted of dichotomous and close-ended questions. It consisted of the following sections: socio-demographic data (age, sex, occupation, educational and marital status, monthly income, medical insurance, and the presence of a care provider at home), lifestyle data (smoking status, alcohol status, and involvement in sport activities), complaint for which the antibiotic is taken, the medication details (name, dose, duration and mode of administration as recommended to be taken), presence of comorbidities (defined as long-term diseases diagnosed by physicians) and background medications, as well as reasons and sources of self-medication.

Thirty days after starting the medication, patients were assessed about adherence and duration of antibiotic consumed, direction of use, and reasons for misuse.

Antibiotic use data:

This study included antibiotics used for systemic infections, excluded antivirals, antifungals, antiprotozoans and topical antimicrobial treatments. The trade names of the dispensed antibiotics were converted to their equivalent generic names using the Lebanese Medical Index. Antibiotics were classified according to the Anatomical Therapeutic Chemical class (ATC, http://www.whocc.no/ atc_ddd_index/).

Data analysis:

The usage pattern of antibiotics was described by the number of defined daily doses (DDD) dispensed to each patient and used during the follow up, as well as the number of request of antibiotic/year. Defined daily dose was defined as the average maintenance daily dose of a drug for its min indication in adults. The usage pattern was described using Anatomical Therapeutical Chemical Classification/Defined Daily Doses (ATC/DDD) system. (Table S1)

All data were entered and analyzed using SPSS version19 (the IBM Corporation, Armonk, NY). The explanatory variables were: socio-demographic, lifestyle, the condition for which antibiotic was used, source of antibiotic medication, reason for self-medication and frequency of antibiotic consumed per year. An appropriate bivariate analysis was done for every explanatory variable: Chi-2 for dichotomous variables to compare 2 percentages, T-test or ANOVA for nominal and ordinal variables to compare 2 means of 2 groups or more, and Pearson correlation for continuous variables. A p-value of 0.05 or less was considered to be statistically significant in all tests.

Results:

Baseline Characteristics:

Of a total of one thousand questionnaire distributed to CPs data from a total of 501 patients were recorded in the study (response rate = 50%). Among participants, 314 (62.7%) requested an antibiotic without prescription while 187 (37.3 %) had a medical prescription for their antibiotic. Both groups were homogenous regarding gender (p=0.154), age (p=0.532), education (p=0.285), Income (p=0.051), and presence of comorbidities (p=0.548) (Table 1).

Table 1: Characteristics of the study population

	Total participants N=501 (100%)	**Participants with medical prescription N= 187**	**Participants without medical prescription N= 314**	**p-value**
Gender				
Male	153 (30.5%)	50 (26.7%)	103 (32.8%)	0.154
Female	348 (69.5%)	137 (73.3%)	211 (67.2%)	
Age group				
16-25	244 (48.7%)	85 (45.5%)	159 (50.6%)	0.532
25-50	196 (39.1%)	78 (41.7%)	118 (37.6%)	
>50	61 (12.2%)	24 (12.8%)	37 (11.8%)	
Educational level				
Primary and less	153 (30.5%)	65 (34.8%)	88 (28%)	0.285
Secondary	69 (13.8%)	24 (12.8%)	45 (14.3%)	
University	279 (55.7%)	98 (52.4%)	181 (57.6%)	
Marital status				
Single	259 (51.7%)	90 (48.1%)	169 (53.8%)	0.217
Married	242 (48.3%)	97 (51.9%)	145 (46.2%)	
Currently working				
Yes	173(34.5%)	134 (71.7%)	194 (61.8%)	0.025
No	328 (65.5%)	53 (28.3%)	120 (38.2%)	
Family income (LL)				
<2000000	134 (74.4%)	38 (20.3%)	95 (30.3%)	.051
>2000000	46 (9.2%)	18 (9.6%)	27 (8.6%)	
Unemployment	323 (64.5%)	131 (70.1%)	192 (61.1%)	
Presence of comorbidities				
Yes	109 (21.8%)	38 (20.3%)	71 (22.6%)	0.548
No	392 (78.2%)	149 (79.7%)	243 (77.4%)	
Data presented as number (%) were performed using Chi2 respectively and a p-value < 0.05 is considered significant.				

A total of 392 patients (78.2%) had no associated medical conditions, while 109 (21.8%) suffered from chronic diseases, among which 21.8% had hypertension, 3.2% had asthma or COPD, 5.8% had dyslipidemia, 3.8% diabetes, 2.4% gastric diseases, and 3.6% osteoarthritis. 3 participants were pregnant and one had an allergy to penicillin.

Amoxicillin–clavulanic acid (coamoxiclav) combination was the most purchased antibiotic (33.7 %) followed by cephalosporins (21.2%). 33.9% of participants used antibiotics once per year. Coamoxiclav was the most frequently dispensed antibiotic without prescription (37.3%) followed by cephalosporins (21%), penicillins (17.2%), macrolides (6.1%) and fluoroquinolones (3.8%) respectively. The antibiotics dispensed with a prescription were, in the following descending order: coamoxiclav (27.8%), cephalosporins (21.4%), fluoroquinolones (17.6%), macrolides (14.4%) and penicillins (5.3%). (Table 2)

The most concern indications were for respiratory tract infections mainly tonsillitis (27.5%) and flu (17.6%), followed by oral and gastrointestinal tract infections (18.6%) and urinary tract infection (12.4%). Most patients bought antibiotic to treat respiratory tract infections: tonsillitis (30.3%), cold (22%) and cough (6.4%), oral and gastrointestinal tract infections: diarrhea (13.4%) and teeth infections (5.1%), skin and urinary tract infections (8.3%). Patients buying antibiotics for urinary tract infections had significantly more prescriptions ($p<0.05$). (Table 2)

Table 2: Self-medication practice among participants

	Total participants N=501 (100%)	Participants with medical prescription N= 187	Participants without medical prescription N= 314	p-value
Antibiotic Classes:				
Coamoxiclav	169(33.7%)	52 (27.8%)	117 (37.3%)	<.001
Amoxicillin or penicillins	64 (12.8%)	10 (5.3%)	54 (17.2%)	
Cephalosporins	106 (21.2%)	40 (21.4%)	66 (21.0%)	
Fluoroquinolones	45 (9%)	33 (17.6%)	12 (3.8%)	
Macrolides	46 (9.2%)	27 (14.4%)	19 (6.1%)	
Others	71 (14.2%)	25 (13.4%)	46 (14.6%)	
Antibiotic request/year				
1st time	186 (37.4%)	83 (44.3%)	103 (33.1%)	.032
More than 1 time	312(62.6%)	104 (55.6%)	208 (66.9%)	
Types of infection				
Respiratory tract infections:				
Tonsillitis	138 (27.5%)	43 (23%)	95 (30.3%)	.629
Cold	88 (17.6%)	19 (10.2%)	69 (22%)	.629
Sore throat	42 (8.4%)	6 (3.2%)	36 (11.5%)	.001
Cough	34 (6.8%)	14 (7.5%)	20 (6.4%)	.631
Otitis	32 (6.4%)	13 (7%)	19 (6.1%)	.320
Sinusitis	21 (4.2%)	10 (5.3%)	11 (3.5%)	.690
Chest tightness	14 (2.8%)	7 (3.7%)	7 (2.2%)	<.001
Runny nose or sneezing	10 (6.8%)	3 (1.6%)	7 (2.2%)	.079
Gastrointestinal infections:				
Diarrhea	60 (12%)	18 (9.6%)	42 (13.4%)	.394
Teeth infections	33 (6.6%)	17 (9.1%)	16 (5.1%)	.211
Urinary tract infections:	62 (12.4%)	36 (19.3%)	26 (8.3%)	.022
Skin infections:				
Skin infection	21 (4.2%)	12 (6.4%)	9 (2.9%)	.319
Acne	9 (1.8%)	6 (3.2%)	3 (1%)	.055
General:				
Fever	7 (1.4%)	3 (1.6%)	4 (1.3%)	.750
Pain	18 (3.6%)	5 (2.7%)	13 (4.1%)	.179
Others	35 (7%)	14 (7.4%)	17 (5.3%)	.750
Data presented as number (%) were performed using Chi2 respectively and a p-value < 0.05 is considered significant.				

Antibiotic utilization patterns:

The drugs were dispensed according to prescriptions from physician (37.3%), or through self-medication (62.7%). Self-medication practice was based mainly on pharmacist recommendation (34.7%). Of the self-medicated antibiotics, 25.2% were requested by the patients themselves based on previous experience with the same antibiotic. The remaining was based on advice from a friend and/or family member (18.5%) or physician on phone or previous prescription (21%). (Figure 1)

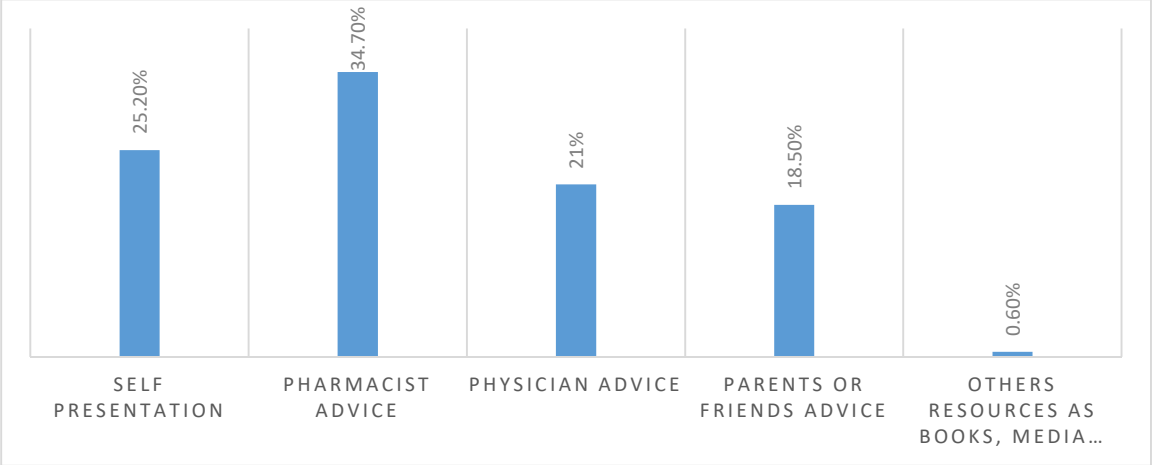

Figure 1: Sources of self-medication among participants requesting antibiotic without prescription

The main reason reported by patients for self-medication was previous successful use of antibiotic (40.4%), followed by saving time (25.2%), and ease access of medication from the community pharmacy (22.9%). The remaining reported reasons were fear of the disease to become worse (18.5%) or saving cost of physician prescription (18.5%). (Figure 2)

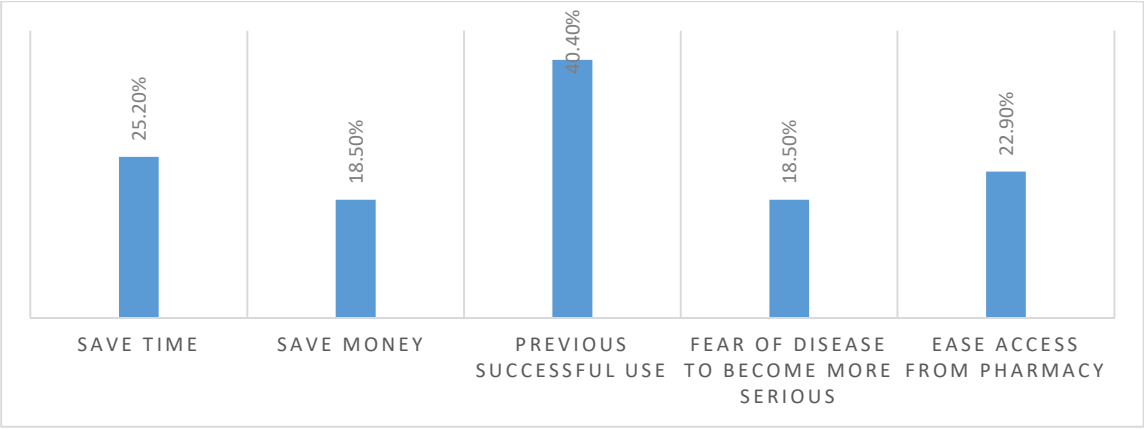

Figure 2: Reasons for self-medication among participants requesting antibiotic without prescription

Males bought significantly more coamoxiclav (43.8%, p=.003) followed by cephalosporins (16.3%), and fluoroquinolones (12.4%) while females bought more coamoxiclav (29.3%) and other penicillins (14.9%) followed by cephalosporins (23.3%) and macrolides (10.1%). Younger patients received more coamoxiclav (35.2%) while older patients more cephalosporins (29.5%) and fluoroquinolones (26.2%) and the result was statistically significant (p<.001). (Figure 3)

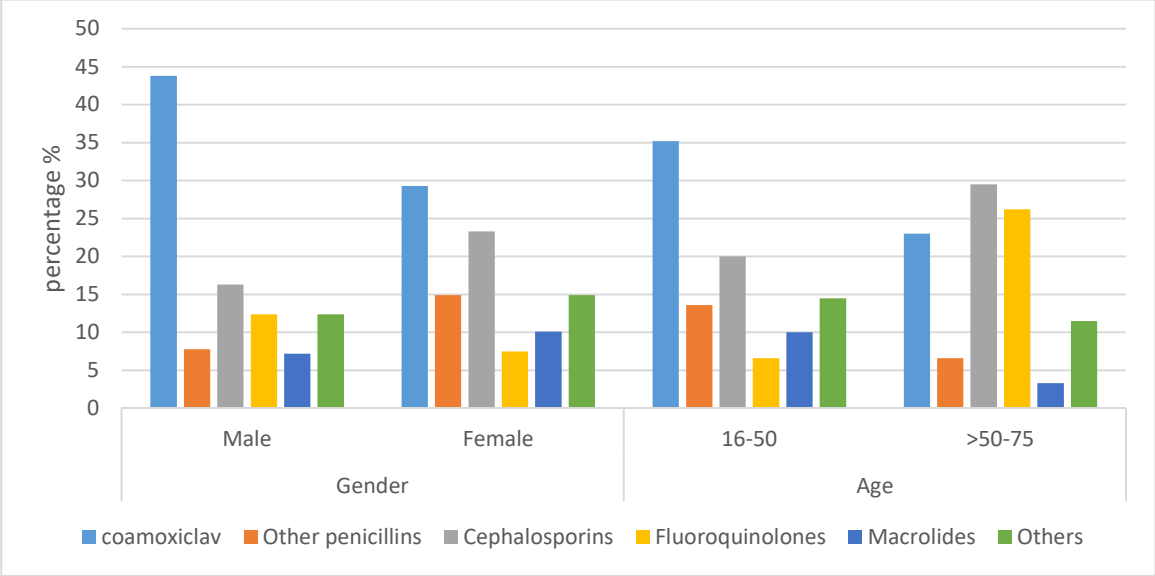

Figure 3 – Dispensing pattern of individual antibiotic:

At each dispensing patients received an average of 9.07 DDD. There was no significant difference in the number of DDDs dispensed between patients requesting antibiotic with or without prescription. 51.7% of females were dispensed between 1 to 7 DDD, while 58.2% of males were dispensed more than 8 DDD, however, the results were not statistically significant (p=.117). More patients above 50 years old were dispensed between 1 -7 DDD (55.7%) while only 47.7% of patients less than 50 years old were dispensed 1-7 DDD. (Table 3)

Table 3: Usage Pattern of antibiotics

	Total participants N=501 (100%)	**Participants with medical prescription N= 187**	**Participants without medical prescription N= 313**	**p-value**
Number of DDD/request				
Mean (SD)	9.07 +-5.06 (Min=1.5, Max=48)	9.23 (5.35)	8.97 (4.87)	.588 (95%CI= -.68-1.2)
1-7	244 (48.7%)	93 (49.7%)	151 (48.1%)	0.936
8-14	222 (44.3%)	81 (43.3%)	141 (44.9%)	
15-29	35 (7%)	13 (7%)	22 (7%)	
Number of DDD/follow-up				
Mean (SD)	7.07 +-4.93 (Min=0.2, Max=48)	7.93 (5.4)	6.54 (4.55)	.004 (95%CI= .45-2.33)
1-7	313 (62.5%)	107 (58.2%)	206 (68.4%)	.070
8-14	151 (30.1%)	67 (36.4%)	84 (27.9%)	
15-28	21 (4.2%)	10 (5.4%)	11 (3.7%)	
Number of DDD/day				
Mean (SD)	1.47+-.75 (Min=0.2, Max=4)	1.42 (.66)	1.49 (.79)	.29 (95%CI= -.19- .06)
<1	244 (48.7%)	95 (50.8%)	149 (47.5%)	.128
1.1-2	217 (43.3%)	83 (44.4%)	134 (42.7%)	
2-4	40 (8.0 %)	9 (4.8%)	31 (9.9%)	
Number of request/ year				
1	186 (37.1%)	83 (44.6%)	103 (33.2%)	.060
2-3	149 (28.7%)	51 (27.4%)	93 (30.0%)	
4-6	100 (21%)	31 (16.7%)	74 (23.9%)	
7-12	61 (12.2%)	21 (11.3%)	40 (12.9%)	
Data presented as number (%) were performed using Chi2 respectively and a p-value < 0.05 is considered significant.				

The average number of dispensings per year was 3.35. More than 50% requested antibiotics more than twice per year. Patients requesting antibiotic without prescription requested more antibiotic per year than patients with prescription. Only 33.2% of those requesting antibiotic without prescription were dispensed antibiotic once per year, compared to 44.6% for patients with prescription. (table 3)

Males were dispensed significantly more antibiotics over year than females (p=.003). More males were dispensed antibiotics between 2-3 times over a year (36.6%) while females were dispensed mainly once per year (42.9%). Younger patients received an average of 3.09 dispensings over year, less than older patients (average=5.18) (p<.001). (Table S1)

Follow-up usage pattern of antibiotic:

In the follow up, patients' consumption of DDD was an average of 7.07 DDD; 62.5% used between 1 to 7 DDD. The average number of DDD per day was 1.47 DDD. Patients with medical prescription used more DDDs (average=7.93) than patients without prescription (average=6.54) (p=.0.04). There was no significant difference in the number of DDDs used per day between patients requesting antibiotic with or without prescription. (Table 3)

In the follow up, the results show no statistical difference between the DDD consumed between gender groups. The percentages of patients consuming 1-7 DDD increased to 62.9% in younger patients, and to 77.2% in older patients (>50 years old) (p.009). Patients aged 25-50 years used significantly more often more than 1 DDD per day (61.7%) than patients above 50 (41%, p=.001). (table S2)

The average consumption per day of coamoxiclav, amoxicillin, or macrolides was 2.0, 1.4 and 1.41 DDD respectively. Amoxicillin, coamoxiclav, and clarithromycin had mean administered daily doses twice the number of DDD while the average number of DDD consumed per day of other antibiotics was 1.

Efficacy Follow up

Most patients (91.7%) had complete relief and only 1.2% didn't improve on antibiotic. In general, 86.4% have assessed the treatment with antibiotic as very good. 10.9% have described it as sufficient and 3.5% as bad. Most patients have experienced relief of symptoms after 1-4 days (70.7%). This might explain the under use of antibiotic treatment. 19.8% experienced relief of symptoms after 5-7 days and only 8.3% had experienced relief after 2 weeks. 17 (3.5%) participants switched to another antibiotic for reasons of not feeling better (n=16, 94.1%) or due to side effects (n=1, 0.2%). The major antibiotics switched to were ceftriaxone injection (n=3) or oral coamoxiclav (n=4).

Follow up on safety

Only 30 (6.6%) participants reported side effects. Gastrointestinal side effects were the main reported side effects (n=9), including diarrhea (n=5), abdominal pain (n=3), and vomiting (n=1). Skin allergic reactions and herpes were also reported in 13 cases. Other side effects reported were laziness (n=2), sedation (n=2), headache (n=2), and increasing appetite (n=1). One case of hospitalization was reported as due to exacerbation of the disease.

Discussion:

This study found a high rate of antibiotic self-medication (62.7%) originating from pharmacist advice or relatives' recommendations. The overall average dispensing of antibiotics was 9.07 DDD, indicating short term use (< 2 weeks). The usage pattern of antibiotics was not different between patients dispensed antibiotics with or without prescription; however, the number of request per year of antibiotic was significantly higher in patients practicing self-medication. Antibiotics were commonly dispensed in different infectious diseases and were commonly dispensed with cough or flu medicines, or analgesics (paracetamol, NSAIDs).

Easy availability of antibiotics without prescription from community pharmacies and the low price of some antibiotics explain the wide use of antimicrobial drugs whether needed or not. Moreover, the use of antibiotics is relatively safe and rarely associated with adverse effects. The prevalence of self-medication was relatively higher than that reported by Cheaito et al study (40%) which was restricted to Beirut and its suburbs. (Cheaito et al., 2014)

The average number of DDD per dispensing was not different between participants with or without prescriptions. Males had non-significantly higher average DDD consumption of antibiotics than females. In this study and in the study of Lombardy region, a greater prevalence was found in males than in females. (Bronzwaer et al., 2002; Majeed & Cook, 1996) This finding contrasts with another study done in the USA that showed that females were the main consumers of antibiotics in 2013. (Centers for Disease Control and Prevention, 2013) Females used more broad spectrum antibiotics, including cephalosporins and macrolides, concomitantly with more symptomatic infections of the genital and urinary tract system than males. (Blix, Engeland, Litleskare, & Ronning, 2007)

Higher use of antibiotics was observed in younger patients. Differences in patterns of use with regards to age could be explained by different types of infections. The shift from beta-lactams to more broad spectrum antibiotics such as cephalosporins and fluoroquinolones in the older age (>50 years), is not unexpected because the immune response lessens with age and the prevalence of UTIs increases with age. The use of more DDD in younger age should raise awareness regarding the increase risk of bacterial resistance over time.

The average number of requests per year was considered high i.e. 3.35 times. More than 50% requested antibiotics more than twice per year. This average rises significantly in patients requesting antibiotic without prescription. This could be attributed to therapeutic failure or to increase in bacterial resistance.Other problems with self-medication are self-diagnosis and buying of antibiotics in sub-therapeutic quantities tend to become cultural norms in countries with few regulations on the acquisition of non-prescribed antimicrobial drugs, (Drug Utilization Research Group, 1997), Moreover, antibiotic therapy was often used by patients without ruling out the possibility of viral infections which is more common in these cases of respiratory tract infections. This finding is consistent with results of other studies in Abu-Dhabi, (Abasaeed, Vlcek, Abuelkhair, & Kubena, 2009) Iran, (Heidarifar, Koohbor, Kazemian Mansourabad, Mikaili, & Sarahroodi, 2013) Jordan, (Sawair, Baqain, Abu Karaky, & Abu Eid, 2009) Lebanon (Cheaito et al., 2014) and Northern and Western Europe. (Grigoryan et al., 2008) This explains the rapid relief of signs and symptoms of many complaints. So, patients stop the antibiotic just when the symptoms of illness disappear.

Coamoxiclav was highly used among patients in this population. This result replicates findings reported in Lebanon (48.9%). (Cheaito et al., 2014) Similarly, in United Arab Emirates, it was the most commonly used (48.9%) (Sharif & Sharif, 2013) and in Pakistan. (62.8%)(Aslam & Mirza, 2013)[18] Although broad spectrum of antibiotics is effective against many bacterial infections and are relatively safe, this does not justify their uncontrolled use: prudent use of antibiotics promotes the use of narrow-spectrum targeted drugs when appropriate, to decrease

the chance of emergence of drug-resistant microbial strains. Incorrect use could cause the development of resistant bacteria and diminish the ability of the endogenous flora to resist colonization of harmful microorganisms, thereby leading to super infections by multi-resistant bacteria and yeasts. (Barbosa & Levy, 2000)

The average consumption per day of coamoxiclav, amoxicillin, or macrolides was 2.00, 1.4 and 1.41 DDD, respectively. Amoxicillin, coamoxiclav, and clarithromycin have mean daily doses twice the number of DDD. This study highlights the limits of DDD in estimating the daily doses consumed by patients per day. The effect, if any, of this increased dosage on bacterial resistance is unknown. Estimates of antibiotic use using DDD methods will remain open to criticism because the prescribed dosage, especially of antibiotics, often deviates from the “theoretical" daily dose, depending for instance on the location of the infection, pathogen susceptibility, or the excretory status of the patient. (Blix et al., 2007)

An important concern should be raised about residual antibiotics, i.e., antibiotics that were dispensed but not used. These may result in uncontrolled self-medication and inappropriate use. This could be quantified by comparing the overall DDD of antibiotic dispensed during episode to that actually used, during follow-up. The average DDD dispensed during the episode was 9.05, greater than that used during the follow-up. The average DDD used for each antibiotic class were around 2 DDDs less than what had been dispensed. Patients probably stopped the medication as soon as the symptoms disappear, either because of poor medical knowledge or use of the antibiotic for conditions for which the medication was not indicated. This results in using the antibiotic beyond the scope and increasing the daily dose of antibiotic and increasing the risk of antibiotic resistance.

This study is the first prospective study done in the Lebanese population of the usage pattern of antibiotic consumption. However, our study suffers from several limitations. To begin with, since not all pharmacists accepted to participate to the study, the sample may not be representative of Lebanese population. We might also expect a change in behaviour of the pharmacists in the presence of researchers, since the study addresses an illegal practice; Our results may be underestimating the reality of antibiotic self-medication. Second, there could also be a possibility of respondent and information bias, since the results of our study are based on a face-to-face questionnaire. Many persons did not agree to fill it out, which may also introduce a selection bias. Our study was limited to patients aged > 15 years old. Pediatric patients are also an important category group to measure extent of antibiotic use that could influence antibiotic resistance.

This study suffers from most consumer-based surveys issues, mostly the willingness or not of subjects coming to the pharmacy to spend tie filling a questionnaire or speaking to an interviewer. Patients may also be reluctant divulge information about disease of socioeconomic factors. As such our results represent only the part of the population that participated; mostly young, relatively healthy subjects who may have better educational level than older subjects. However, subjects in this study were recruited in various parts of the country. And difference in the spectrum of ages and professional status one might expect. The results are found were not unexpected and confirm to another studies done in the same area. (Cheaito et al., 2014; Sawair et al., 2009) The fact that we did find two third non-prescribed dispensing of antibiotics shows the respondents answer making information bias unlikely.

Conclusion:

This study reflects on the fact that antibiotic consumption in Lebanon is poorly controlled, with much misuse, often related to self-medication and non-prescribed use. To prevent this practice, health authorities have to implement educational programs for patients and pharmacists to emphasize the need for careful medical control of antibiotic prescriptions and regulations to reduce the usage of antibiotics.

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Table S1: Anatomically Therapeutic Classification system for systemic antibiotics

Antibiotic Class	ATC class
Penicillins :	J01C
Penicillins with extended spectrum	J01CA
Penicillin combination with B-lactamase inhibitors	J01CR
B-Lactamase-sensitive penicillins	J01CE
Cephalosporins:	J01D
First-generation cephalosporins	J01DAa
Second-generation cephalosporins	J01DAb
Third-generation cephalosporins	J01DAc
Fluoroquinolones	J01MA
Macrolides, lincosamides and streptogramins	J01F
Sulphonamides and trimethoprim	J01E
Aminoglycosides	J01G
Metronidazole	J01XD01
Tetracyclines	J01A

Table S2 – Dispensing pattern of antibiotic for gender and age groups:

	Gender					Age						
	Male		Female			16-25		25-50		>50-75		
Number of DDD/request	n	%	n	%	P-value	n	%	n	%	n	%	P-value
Mean (SD)	9.83 (5.77)		8.73 (4.67)		.025	8.68 (4.32)		9.86 (6.06)		8.07 (3.77)		.013
1-.7	64	41.8	180	51.7	.117	120	49.2	90	45.9	34	55.7	.097
7.5-14	76	49.7	146	42		112	45.9	85	43.4	25	41	
14.5-29	13	8.5	22	6.3		12	4.9	21	10.7	2	3.3	
Number of DDD/follow-up												
Mean (SD)	7.70 (5.76)		6.80 (4.51)		.095	6.50 (4.16)		8.11 (5.93)		6.05 (3.55)		.001
1-.7	89	61	224	66.1	.326	155	64.9	114	60.3	44	77.2	.009
7.5-14	48	32.9	103	30.4		79	33.1	60	31.7	12	21.1	
14.5-28	9	6.2	12	3.5		5	2.1	15	7.9	1	1.8	
Number of DDD/day												
Mean (SD)	1.56 (.8)		1.43 (.72)		.06	1.36 (.71)		1.63 (.76)		1.37 (.72)		<.001
<1	70	45.8	174	50	.112	135	55.3	75	38.3	34	55.7	.001
1.1-2	65	42.5	152	43.7		95	38.9	97	49..5	25	41.0	
2.-4	18	11.8	22	6.3		14	5.7	24	12.2	2	3.3	
Number of request/ year												
Mean (SD)	3.77 (3.64)		3.16 (3.41)		.073	2.99 (3.38)		3.22 (3.11)		5.18 (4.4)		<.001
1	39	25.5	147	42.9	.003	118	48.8	60	31.1	8	13.1	<.001
2-3	56	36.6	88	25.7		58	24	65	33.7	21	34.4	
4-6	36	23.5	69	20.1		40	16.5	50	25.9	15	24.6	
7-12	22	14.4	39	11.4		26	10.7	18	9.3	17	27.9	

Data presented as number (%) were performed using Chi2 respectively and a p-value < 0.05 is considered significant.

Chapter 3:

Appropriateness of self-medication use of antibiotics in Lebanon

After we identified the usage pattern of antibiotics in chapter 2, we aimed to evaluate the appropriateness of self-medication use of antibiotics within Lebanese population. The inappropriate use and overuse of antibiotics with incorrect dosages for inappropriate period of time increase the rate of bacterial resistance and their dissemination in the population leading to a higher frequency of treatment failures. (Grigoryan et al., 2006)

Antibiotics treat bacterial infections but not viral infections. Using antibiotic to treat viral infections can promote antibiotic-resistant properties in bacteria since it attacks the endogenous bacteria that are living in the body and not causing the disease. Antibiotics are important drugs, but they are over-prescribed and overused in self-medication for the treatment of minor disorders such as simple diarrhea, coughs and colds.

The overuse or misuse of antibiotics; especially taking antibiotics even when they are not the appropriate treatment, promotes antibiotic resistance. The appropriate use of antibiotics can help preserve the effectiveness of current antibiotics, extend their life span and protect the public from antibiotic-resistant infections. (World Health Organization, 2004)

Unfortunately, in Lebanon, very few studies have been conducted to target the emergence of resistant bacteria. One study, conducted at a tertiary healthcare center in Lebanon, showed an increased or fluctuating resistance to several bacteria, including *Acinetobacter* spp., *P. aeruginosa*, *E. coli*, *K. pneumonia*, *Enterococcus* spp., *Staphylococcus aureus*, *Streptococcus viridans* and *Streptococcus pneumonia.* (Araj et al., 2012) Furthermore, another healthcare center in Lebanon reported antibiotic susceptibility to several bacterial strains; by using a beta lactamase spectrum to define bacterial resistance, it was discovered that resistance was 31% for *E. coli* and 35% for *Klebsiella* in 2006. (Rafic Hariri Hospital Report, 2006) In 2010, the same hospital found that bacterial resistance increased to 43% for *E. coli* and48% for *Klebsiella.* (Rafic Hariri Hospital Report, 2010)

The suitability of effective antibiotic treatment regimens consists primarily of three variables: the choice of a drug appropriate for the indication, the dose and the duration of treatment. (Paterson, Hoyle, Ochoa, Baker-Austin, & Taylor, 2016) When antibiotics are used too often in sub-optimal dosages, bacteria become resistant to them.. People use sub-optimal dosages because they cannot afford the full course prescribed, or because they are not aware of the need to complete antibiotic courses. People may also tend to stop antibiotics as soon as they feel better. But the full treatment is necessary to kill the disease causing bacteria. Failure to do so can result in the need to resume treatment later and may promote the spread of antibiotic-resistant properties among harmful bacteria. (World Health Organization, 2004)

Although it is known that there is a problem of misuse in Lebanon, it has never been documented. Therefore, we aim in this chapter to evaluate the appropriateness of self-medication use of antibiotics in Lebanon. The appropriate use of antibiotic was described by the choice of antibiotics dispensed, duration of antibiotic used, and prescribed daily doses (PDD) of antibiotic consumed by each patient in the follow up. The suitability of the dispensed antibiotic for the customer's complaint and duration were decided using Infectious Diseas Scociety of America (IDSA) guidelines. Because of the absence of Lebanese guidelines, the IDSA guidelines are generally taught during medical education in Lebanon and are deemed to be the most important guidelines on an international level.

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Evaluation of Self-medication Use of Antibiotics within Lebanese population in Community Pharmacies: A Prospective Study

Abstract:

Introduction: Inappropriate self-medication by antibiotics could result in bacterial resistance. In Lebanon, like most other developing countries, having a valid prescription is not always enforced for receiving prescription-only drugs.

Objective: The aim of this study was to describe the community use of antibiotics within the Lebanese population. Moreover, it aims to assess follow up adherence and duration of antibiotics consumed.

Method: It is a prospective study in a community-based pharmacy setting in Lebanon. It uses a structured random interview to patients visiting a community pharmacy and seeking for antibiotics. Baseline characteristics and reason for self-medication were collected. Completing the questionnaire after 30 days provided information on adherence and usage pattern. Data were analyzed using descriptive statistics and Chi-square test. A multivariate logistic regression was performed to predict factors affecting appropriateness.

Results: 62.7% of 501 participants bought antibiotics without prescription. Amoxicillin/clavulanic acid was the most used antibiotic as self-medication (33.7%). 62.4% of patients used the right antibiotic and 80.1% used it in correct dosage. The duration of treatment was inappropriate in the majority of cases (68.6%). When all of these three factors were summed together, it turned out that 83.6% of antibiotics were utilized inappropriately. Appropriateness in use was seen in 27.6% and 16.4% of the prescribed and non-prescribed antibiotics respectively.

Conclusion: Our study shows great misuse of antibiotics and hence there is a need to increase awareness of the health risks related to inappropriate and uncontrolled use of antibiotics.

Keywords: Self-medication, Antibiotic, Lebanon, Misuse, Appropriate use.

Introduction:

Antibiotics are considered among the most commonly sold drug classes in the developing countries.(Buke et al., 2005) Irrational use of antibiotics is a global problem (Buke et al., 2005) and the rate of this problem and antibiotic resistance is increasing in Middle-East. (Al-Tawfiq, Stephens, & Memish, 2010) Resistance rates differ significantly between developing and developed countries. Indeed, data from the Resistance Surveillance and Control in the Mediterranean Region (ARMED) project showed an increase of antimicrobial resistance in countries with high levels of antibiotic consumption such as eastern and southern Mediterranean regions, compared to low resistance rates in northern countries. (Borg et al., 2006)

This situation could be explained by the unregulated distribution of antimicrobials, and their wide availability without prescription in developing countries which is not the case in most of the developed countries where antibiotics are not available without medical prescription. (Belongia, Naimi, Gale, & Besser, 2002; Byarugaba, 2004)Overuse and the inappropriate use of antibiotics with incorrect dosages for inappropriate period of time increase the rate of selecting resistant strains and their dissemination in the population leading to a higher frequency of treatment failure. (Grigoryan et al., 2006)

In Lebanon, like most other developing countries, having a valid prescription is not always enforced for receiving prescription-only medicines (POM). Previous researches in Lebanon showed that the prevalence of self-medication with antibiotics is alarmingly high (Cheaito, Azizi, Saleh, & Salameh, 2014) and revealed that the pattern of self-medication practice was inappropriate without further details.

The aim of this study therefore was to describe the community use of antibiotics within the Lebanese population living in Lebanon concerning appropriateness of use, dose and duration of antibiotic consumed and their conformity to IDSA guideline.

Method:

Design and Study Population:

A prospective study was conducted in a community-based pharmacy setting in Lebanon. Data was collected over a 1-year period (September 2015 to September 2016) from 50 community pharmacies (CPs) distributed in the six districts in Lebanon: Beirut, South Lebanon, Nabatiyeh, Mount Lebanon, Bekaa, and North Lebanon.

Eligible participants were recruited randomly from consumers presenting at CPs in Lebanon after they had purchased antibiotic medication with or without prescription. The patients included were from both genders, aged 16 years and older, coming to purchase antibiotic. The patients were divided into two groups: those buying antibiotic with a prescription versus those buying them without prescription.

The Lebanese University, Faculty of Pharmacy Internal Review Board waived the need for written informed consent. The patients were informed about the objective of the study and were asked to give an oral consent. Only those who gave their voluntary informed oral consent were enrolled.

Sample size calculation

A sample size was calculated assuming a type I error of 5% and a study power of 80% and 95%CI. Based on a previous study, 40% of patients exposed to non-prescribed antibiotics. (Cheaito et al., 2014) The minimal sample size necessary to show a twofold increase in the risk of exposure to non-prescribed antibiotics consists of 442 subjects: 186 patients for those buying antibiotic with prescription and 256 without prescription.

Procedure and Data Collection:

Data on antibiotic use was collected using a structured random interview conducted by pharmacists or interviewers who had been briefed about the study's aims and methods. Consecutive customers arriving at CPs seeking antibiotic were interviewed. Data was collected from the participants twice, first at purchase for data about drug used and the condition for which it was to be used, then by calling the patient 30 days after starting the medication, for usage patterns.

The questionnaire included many sections that were chosen following an extensive review of literature. The questionnaire was translated into Arabic and subjected to a process of forward and backward translation into English. It was pretested and validated first on 20 patients visiting 4 different pharmacies before starting the survey.

The questionnaire consisted of dichotomous and close-ended questions. It consisted of the following sections: socio-demographic data (age, sex, occupation, educational and marital status, monthly income, medical insurance, and the presence of a care provider at home), lifestyle data (smoking status, alcohol status, and involvement in sport activities), complaint for which the antibiotic is taken, the medication details (name, dose, duration and mode of administration as recommended to be taken), presence of comorbidities (defined as long-term diseases diagnosed by physicians) and background medications, as well as reasons and sources of self-medication.

Thirty days after starting the medication, patients were assessed about adherence and duration of antibiotic consumed, direction of use, and reasons for misuse.

Data analysis:

Appropriate antibiotic use was described by the choice of antibiotics dispensed, duration of antibiotic used, and prescribed daily doses (PDD) of antibiotic consumed by each patient in the follow up. The suitability of the dispensed antibiotic for the customer's complaint and duration were decided using IDSA guideline. Because of the absence of Lebanese guidelines, the IDSA guidelines are generally taught during medical education in Lebanon and are deemed to be the most important guidelines on an international level. The PDD was assessed in comparison to recommended daily dose (RDD) of treatment based on the manufacturer recommendation (French national drug formulary (***VIDAL***® dictionary) (https://www.vidal.fr/)).

One point was awarded for each correct use and 0 point will be awarded for misuse, wrong choice of medication, wrong duration (underuse or overuse), or wrong PDD. Later on, the dispensed antibiotic was assessed by summing up the scores given for each item. The total score obtained was 3, which refers to 'appropriate treatment' whereas the lower scores were defined as 'inappropriate treatment'.

Statistical analysis was performed using SPSS for Windows version 19. Frequencies and percentages of patient's characteristics, treated complaints, classes of antibacterial drugs dispensed and their appropriateness were calculated and presented. Chi-2 test was used to determine the associations between qualitative variables and other outcome measures. Stepwise multivariate logistic regression was then used to control for potential confounding variables and to calculate the odds ratios for potential independent variables for appropriateness. A p-value of 0.05 or less was considered to be statistically significant.

Results:

Baseline Characteristics:

Of a total of one thousand questionnaire distributed to CPs data from a total of 501 patients were recorded in the study (Response rate = 50%). Among participants, 314 (62.7%) have requested for antibiotic without prescription while 187 (37.3 %) had a medical prescription for their antibiotic. Both groups were homogenous regarding gender (p=0.154), age (p=0.532), education (p=0.285), income (p=0.051), and presence of comorbidities (p=0.548). The majority were females (69.5%) and between 16 and 50 years of age (87.8%). About half of the patients had a university degree (55.7%). (Table 1)

Table 1: Characteristics of the study population

	Total participants N=501 (100%)	**Participants with medical prescription N= 187**	**Participants without medical prescription N= 314**	**p-value**
Gender				
Male	153 (30.5%)	50 (26.7%)	103 (32.8%)	0.154
Female	348 (69.5%)	137 (73.3%)	211 (67.2%)	
Age group				
16-25	244 (48.7%)	85 (45.5%)	159 (50.6%)	0.532
25-50	196 (39.1%)	78 (41.7%)	118 (37.6%)	
>50	61 (12.2%)	24 (12.8%)	37 (11.8%)	
Educational level				
Primary and less	153 (30.5%)	65 (34.8%)	88 (28%)	0.285
Secondary	69 (13.8%)	24 (12.8%)	45 (14.3%)	
University	279 (55.7%)	98 (52.4%)	181 (57.6%)	
Marital status				
Single	259 (51.7%)	90 (48.1%)	169 (53.8%)	0.217
Married	242 (48.3%)	97 (51.9%)	145 (46.2%)	
Currently working				
Yes	173(34.5%)	134 (71.7%)	194 (61.8%)	0.025
No	328 (65.5%)	53 (28.3%)	120 (38.2%)	
Family income (LL)				
<2000000	134 (74.4%)	38 (20.3%)	95 (30.3%)	.051
>2000000	46 (9.2%)	18 (9.6%)	27 (8.6%)	
Unemployment	323 (64.5%)	131 (70.1%)	192 (61.1%)	
Presence of comorbidities				
Yes	109 (21.8%)	38 (20.3%)	71 (22.6%)	0.548
No	392 (78.2%)	149 (79.7%)	243 (77.4%)	

Data presented as number (%) were performed using Chi2 respectively and a p-value < 0.05 is considered significant.

A total of 392 patients (78.2%) had no associated medical conditions, while 109 (21.8%) suffered from chronic diseases, among which 21.8% had hypertension, 3.2% had asthma or COPD, 5.8% had dyslipidemia, and 3.8% for diabetes, 2.4% had gastric diseases, and 3.6% had osteoarthritis. 3 participants were pregnant and one had an allergy to penicillin.

Our results indicated that amoxicillin–clavulanic acid (coamoxiclav) combination was the most purchased antibiotic (33.7 %) followed by cephalosporins (21.2%). 33.9% of participants were using antibiotic once per year. Coamoxiclav was the most frequently dispensed antibiotic without prescription (37.3%) followed by cephalosporins (21%), penicillins (17.2%), macrolides (6.1%) and fluoroquinolones (3.8%) respectively. The antibiotics that were dispensed with a prescription, in the following descending order: coamoxiclav (27.8%), cephalosporins (21.4%), fluoroquinolones (17.6%), macrolides (14.4%) and penicillins (5.3%). (Table 2)
The most concern indications were for respiratory tract infections mainly tonsillitis (27.5%) and flu (17.6%), followed by oral and gastrointestinal tract infections (18.6%) and urinary tract infection (12.4%). Our study shows high percentage of non-prescribed acquisition of antibiotic to treat respiratory tract infections: tonsillitis (30.3%), cold (22%) and cough (6.4%), oral and gastrointestinal tract infections: diarrhea (13.4%) and teeth infections (5.1%), skin and urinary tract infections (8.3%). Patients buying antibiotics for urinary tract infections had significantly more prescriptions ($p<0.05$). (Table 2)

Table 2: Self-medication practice among participants

	Total participants N=501 (100%)	Participants with medical prescription N= 187	Participants without medical prescription N= 314	p-value
Antibiotic Classes:				
coamoxiclav	169(33.7%)	52 (27.8%)	117 (37.3%)	<.001
Amoxicillin or penicillins	64 (12.8%)	10 (5.3%)	54 (17.2%)	
Cephalosporins	106 (21.2%)	40 (21.4%)	66 (21.0%)	
Fluoroquinolones	45 (9%)	33 (17.6%)	12 (3.8%)	
Macrolides	46 (9.2%)	27 (14.4%)	19 (6.1%)	
Others	71 (14.2%)	25 (13.4%)	46 (14.6%)	
Antibiotic request/year				
1st time	186 (37.4%)	83 (44.3%)	103 (33.1%)	.032
More than 1 time	312(62.6%)	104 (55.6%)	208 (66.9%)	
Types of infection				
Respiratory tract infections:				
Tonsillitis	138 (27.5%)	43 (23%)	95 (30.3%)	.629
Cold	88 (17.6%)	19 (10.2%)	69 (22%)	.629
Sore throat	42 (8.4%)	6 (3.2%)	36 (11.5%)	.001
Cough	34 (6.8%)	14 (7.5%)	20 (6.4%)	.631
Otitis	32 (6.4%)	13 (7%)	19 (6.1%)	.320
Sinusitis	21 (4.2%)	10 (5.3%)	11 (3.5%)	.690
Chest tightness	14 (2.8%)	7 (3.7%)	7 (2.2%)	<.001
Runny nose or sneezing	10 (6.8%)	3 (1.6%)	7 (2.2%)	.079
Gastrointestinal infections:				
Diarrhea	60 (12%)	18 (9.6%)	42 (13.4%)	.394
Teeth infections	33 (6.6%)	17 (9.1%)	16 (5.1%)	.211
Urinary tract infections:	62 (12.4%)	36 (19.3%)	26 (8.3%)	.022
Skin infections:				
Skin infection	21 (4.2%)	12 (6.4%)	9 (2.9%)	.319
Acne	9 (1.8%)	6 (3.2%)	3 (1%)	.055
General:				
Fever	7 (1.4%)	3 (1.6%)	4 (1.3%)	.750
Pain	18 (3.6%)	5 (2.7%)	13 (4.1%)	.179
Others	35 (7%)	14 (7.4%)	17 (5.3%)	.750
Data presented as number (%) were performed using Chi2 respectively and a p-value < 0.05 is considered significant.				

Appropriateness of antibiotic:

There was statistical difference in the appropriateness between patients buying antibiotic with or without prescription regarding the drug choice (p=0.003), appropriate dose (p=0.036) and treatment duration (p=0.054). Moreover, the difference in global appropriateness was also statistically significant (p=0.003). (Figure 1)

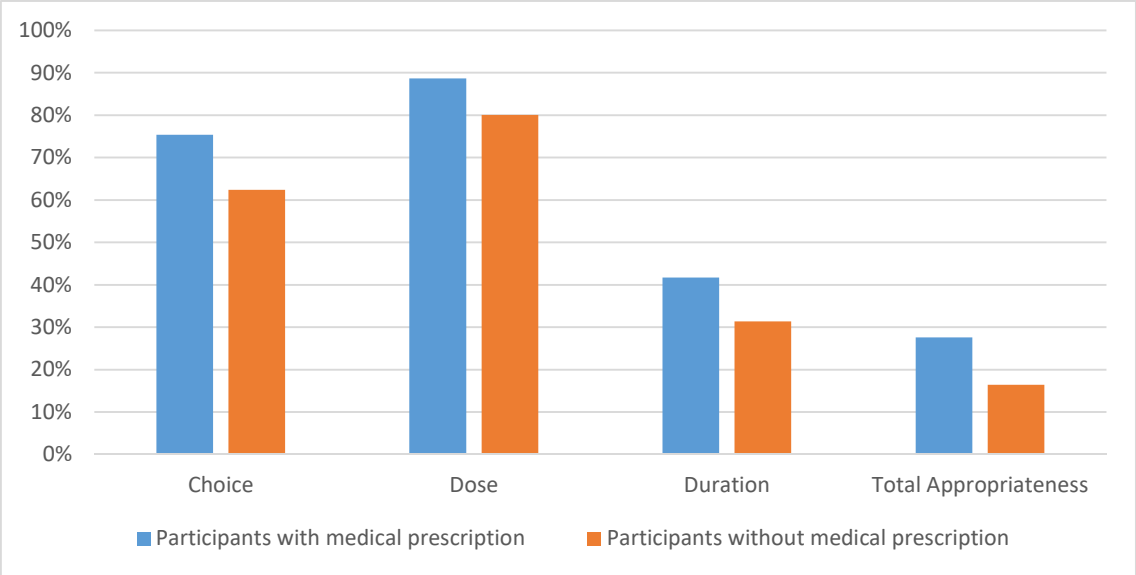

Figure 1: Percentages of appropriateness of choice, dose, duration and overall conformity between participants with prescription or self-medicated antibiotic

Our study has shown that 67.3% of patients have used the right antibiotic against 32.7% of patients have failed to do so. 47.1% used the first line treatment and 19.3% of patients have misused the antibiotic for conditions of sore throat, cough, flu, runny nose, chest tightness, pain and sneezing. 5.3% have used non-recommended drugs for their condition. In the majority of the cases, the dose used by patients was appropriate (88.7%). 9.5% have used low dosage and 5% have exceeded the right dose compared to VIDAL. However, the duration of treatment was inappropriate in majority of cases (58.3%), where the majority didn't complete the full course of antibiotic or used it for low duration (43.2%). When all of these three factors were summed together, it turned out that only 20.2% of antibiotic were used appropriately.

Appropriateness in use was seen in 27.6% and 16.4% of the prescribed and non-prescribed antibiotics, respectively. Among participants buying antibiotic without prescription, 62.4% were dispensed the right antibiotic for their complaint conditions. 32.2% misused the antibiotic and 5.4% used non-recommended drug for their condition. Most of the patients (80.1%) used the correct dose. The duration of treatment was inappropriate in majority of cases (68.6%). (Table 3)

Table 3: Percentages of appropriateness of choice, dose, duration and overall conformity between participants with prescription or self-medication antibiotic

	Total participants N=501 (100%)	Participants with medical prescription N= 187	Participants without medical prescription N= 314	p-value
Choice:				
Misuse	**137 (27.3%)**	**36 (19.3%)**	**101 (32.2%)**	**0.015**
1st line	**204 (40.7%)**	**88 (47.1%)**	**116 (36.9%)**	
2nd line	**133 (26.5%)**	**53 (28.3%)**	**80 (25.5%)**	
Not recommended	**27 (5.4%)**	**10 (5.3%)**	**17 (5.4%)**	
Dose:				
Low dose	**32 (9.5%)**	**9 (6.4%)**	**23 (11.7%)**	**.110**
Appropriate dose	**282 (83.7%)**	**125 (88.7%)**	**157 (80.1%)**	
Overdose	**23 (6.8%)**	**7 (5%)**	**16 (8.2%)**	
Duration:				
Short period	**171 (52.8%)**	**60 (43.2%)**	**111 (60.0%)**	**0.008**
Appropriate	**116 (35.8%)**	**58 (41.7%)**	**58 (31.4%)**	
Long period	**37 (11.4%)**	**21 (15.1%)**	**16 (8.6%)**	
Data presented as number (%) were performed using Chi2 respectively and a p-value < 0.05 is considered significant.				

Factors affecting antibiotic use appropriateness:

When studying the following factors affecting appropriateness: gender, age category, education levels, marital status, employment, family income, and presence of comorbidities, none of these studied factors have shown a significant difference with respect to choice and dose of antibiotic medication. While studying the duration conformity only presence of comorbidities showed a significant difference that was statically significant (p=.001), patients without comorbidities have shown greater appropriateness (70.7%). Only this factor has shown also a significant difference with respect to overall appropriateness (p=.032). (Table S1)

The appropriateness of choice of antibiotic was significantly different between the different conditions. Patients used the medication appropriately in cases of tonsillitis, diarrhea, teeth infection, urinary infection and skin infection. The dose of antibiotic was appropriate in case of tonsillitis, urinary infection. The treatment duration was appropriate in most cases of diarrhea, otitis, sinusitis. The overall appropriateness was significantly different between different conditions treated. The majority of patients were using antibiotic inappropriately in all indications except sinusitis (52% appropriate use, p<0.001). (Table S2)

Multivariate analysis:

We observed several factors affecting overall appropriateness (Table 4). Patients with sinusitis have better appropriateness compared to other complaints. Patients with tonsillitis and flu had less appropriateness. As the number of request per year increases, the overall appropriateness significantly decreases by 9%. Patients with dyslipidemia had also better appropriateness.

The following factors have shown a statistical difference of drug conformity. Pain, sore throat, cough, and flu were associated with significant less appropriateness. Diarrhea, teeth infections, and urinary tract infections were associated with better choice.

Self-medication negatively influenced the dosage appropriateness. Patients who used cephalosporins was associated with significant less appropriateness as well as fluoroquinolones.

Patients with increased antibiotic request per year have greater dose conformity. Patients with urinary infection have better dose adequacy. Consumption of other drugs at the time of dispensation has also positively influenced the dose conformity.

Many factors were found to be significantly associated with better duration conformity to IDSA guideline: sinusitis, and hypertension. Tonsillitis has negatively influenced the duration conformity. Presence of insurance has positively influenced the duration conformity.

Follow up on adherence

Current study shows that only 43.8% (n=213) completed the full course of antibiotic while 273 patients have admitted to underuse (94.9%) or overuse (5.12%). The most common reasons reported for under use were feeling better and symptoms were already resolved (86.8%), didn't feel better (5.12%), and feeling unwell (2.56%). The justifications for overuse were better control of disease and symptoms (2.56%), looking for faster healing (2.19%), and need more effect (0.36%). Moreover, 12 cases have increased the dose (4.8%).

Almost half of the sample patients reported stopping their medications when the disease is under control (51.2%) and only 12.9% reported forgetting to take their medications sometimes. 10.4% missed taking their medications for reasons other than forgetting. Moreover, only 3.3% of the patients reported cutting back their medications when they felt better or worse during the duration of treatment.

Table 4: Multivariate analysis among factors affecting appropriate choice, dose, duration, and overall appropriateness using Logistic regression

Multivariate Analysis	aOR	95% CI	p-value
overall appropriateness			
Predictors			
Presence of insurance	2.00	1.18-3.40	.01
Sinusitis	5.19	1.87-14.44	.002
Tonsillitis	.346	.19-.64	.001
Flu	.22	.087-..56	.002
Number of request per year	.904	.83-.98	.017
Dyslipidemia	4.27	1.65-11.08	.003
Appropriate Choice			
Pain	.212	.046-.98	.047
Flu	.222	.1-.51	<.001
Cough	.37	.13-1.07	.066
Tonsillitis	123.45	33.74-451.72	<.001
Sore throat	.12	.035-.422	.001
Diarrhea	27.44	8.04-93.61	<.001
Teeth infection	68.27	8.49-549.05	<.001
Urinary infection	11.07	4.53-27.05	<.001
Appropriate Dose			
OTC	.51	.24-1.06	.070
Antibiotic Classes:			.025
coamoxiclav	.61	.22-1.72	.353
Amoxicillin or penicillins	.42	.13-1.36	.148
Cephalosporins	.26	.09-.798	.018
Fluoroquinolones	.17	.03-.947	..043
Macrolides	4.52	.49-41.45	.182
Others	Reference		
Urinary tract infections	6.31	1.57-25.37	.009
Antibiotic request per year	1.99	1.04-3.84	.039
Water pipe	.45	.219-.904	.025
Taking other medications at the time of administering antibiotic	2.21	1.17-4.15	.014
Appropriate Duration			
Presence of Insurance	1.99	1.14-3.456	.014
Tonsillitis	.152	.083-.276	<.001
Sinusitis	4.32	1.26-14.76	.020
Hypertension	5.05	1.48-17.15	.009
aOR: adjusted odds ratio above 1 indicates increased n appropriateness and below 1 less appropriateness. CI: Confidence Interval Only factors significantly associated with better or worse appropriateness are shown.			

Discussion:

This study has revealed a high rate of antibiotic self-medication (62.7%). The easy availability of antibiotics without prescription from CPs and the low price for some antibiotics explains the wide use of antimicrobial drugs whether needed or not. The prevalence of self-medication was relatively higher than that reported by Cheaito et al study (40%) which was restricted to Beirut and its suburbs. (Cheaito et al., 2014)

In this pilot study, we found a high percentage of non-appropriateness of the used self-medicated antibiotics concerning treatment duration (64.2%) and overall appropriateness (77.6%). Antibiotic use was not conforming to the guidelines in the majority of cases. This could be explained by several factors including low adherence and rapid relief of symptoms. Poorer compliance with antibiotic therapy has been associated with the use of longer courses of therapy and regimens having more daily doses; (Kardas, Devine, Golembesky, & Roberts, 2005) patients also frequently report discontinuing antibiotic therapy when they begin to feel better or when adverse events occur. (Pechere, 2000)

The prescribed daily dose (PDD) of antibiotics consumed by each patient was highly appropriate (83.7%). This could be explained by several factors. First, a high percentage of self-medication antibiotics is based on pharmacists' advice (34.7%). We should not neglect the role of pharmacists in guidance of customers on the appropriate use of antibiotics. Secondly, 40.4% of self-medication antibiotics are based on previous experience or previous prescription for the same signs and symptoms; thus, physicians indirectly contributed to these self-medicated drugs. Moreover, many patients have requested antibiotic several times per year which explain the high percentage of conformity of dosage compared to VIDAL.

Furthermore, coamoxiclav was highly consumed which replicates findings to that reported in Lebanon (48.9%). (Cheaito et al., 2014) Similarly, in United Arab Emirates, it was the most commonly used (48.9%) (Sharif & Sharif, 2013) and in Pakistan (62.8%).(Aslam & Mirza, 2013) Although broad spectrum antibiotics are effective against many bacterial infections and are relatively safe, prudent use of antibiotics promotes the use of narrow-spectrum targeted drugs when appropriate in order to decrease the emergence of drug-resistant microbial strains. Incorrect use could cause the development of resistant bacteria and diminish the ability of the endogenous flora to resist colonization by harmful microorganism, thereby leading to super infections by multi-resistant bacteria and yeasts. (Barbosa & Levy, 2000)

The common use of antibiotic for minor illnesses is consistent with results of other studies in Abu Dabi, (Abasaeed, Vlcek, Abuelkhair, & Kubena, 2009) Iran, (Heidarifar, Koohbor, Kazemian Mansourabad, Mikaili, & Sarahroodi, 2013) Jordan, (Sawair, Baqain, Abu Karaky, & Abu Eid, 2009) Kuwait, (Awad & Aboud, 2015) Libya, (Ghaieth, Elhag, Hussien, & Konozy, 2015) Lebanon, (Cheaito et al., 2014) Egypt, (Sabry, Farid, & Dawoud, 2014) Saudi Arabia (Belkina et al., 2014) and Northern and Western Europe. (Grigoryan et al., 2008) The rapid relief of signs and symptoms of many complaints causes patients stopped treatment when the illness symptoms disappear and use it for several times over year. This usage pattern is one that typically results in the emergence of resistance.

Presence of comorbidities as dyslipidemia or hypertension have shown better overall appropriateness and better duration conformity. This could be explained by that patients with comorbidities are regular users of medical resources, see physicians and are used to take drugs as directed and have a high rate of POM.

Appropriateness of prescribing antibiotics was higher than that of self-medication although the overall appropriateness of prescribed antibiotics is still low (27.6%). This could be explained by several factors, such as the lack of simple and clear recommendations for treatment duration, the lack of clinical trials to assess the optimal treatment duration, variability in medical knowledge, and psychosocial factors involved in medical decision making. (Battikhi, 2002) Patients should be encouraged to the proper use of antibiotics using all appropriate public media. Physician's decision to prescribe an antibiotic may be influenced by pharmaceutical promotions and patient demand. As a result, interventions are required to improve the appropriate prescribing of antibiotics.

Our results show that patients with tonsillitis have less conformity to overall appropriateness and duration since based on the IDSA guideline the treatment should be completed for 10 days which is greater than the treatment duration of other complaints and the usual symptoms for tonsillitis resolve within a few days. Moreover, patients with fewer antibiotic request per year have better overall conformity. These are important findings, because inappropriate antibiotic use has contributed to the rising incidence of antimicrobial resistance. (McCaig, Besser, & Hughes, 2002)

Other problems with self-medication are self-diagnosis and buying of antimicrobial drugs in sub-therapeutic quantities, which tend to become cultural norms in countries with few regulations on the acquisition of non-prescribed antimicrobial drugs. (Drug Utilization Research Group, 1997) Patients with insurance have shown better duration conformity since they would buy the box of antibiotic and not in sub-therapeutic quantities.

This study is the first prospective study done in Lebanese population reflecting the appropriateness of antibiotic use and consumption. However, our study suffers from several limitations. To begin with, since not all pharmacists accepted to participate to the study, the sample may not be representative of Lebanese population. We might also expect a change in behavior of the pharmacists in the presence of researchers, since the study addresses an illegal practice; thus our results may be underestimating the reality of antibiotic self-medication practice. Second, there could also be a possibility of respondent and information bias, since the results of our study are based on a face to face questionnaire. Third, the sample was limited by its small size. Many people did not agree to participate, which may also introduce a selection bias. The small size of the sample affects also the power of tests to find significant differences. Additional large scale studies are recommended to take into account the cited limitations.

This study suffers from most consumer-based surveys issues, mostly the willingness or not of subjects coming to the pharmacy to spend tie filling a questionnaire or speaking to an interviewer. Patients may also be reluctant divulge information about disease of socioeconomic factors. As such our results represent only the part of the population that participated; mostly young, relatively healthy subjects who may have better educational level than older subjects. However, subjects in this study were recruited in various parts of the country. And difference in the spectrum of ages and professional status one might expect. The results are found were not unexpected and confirm to another studies done in the same area. (Cheaito et al., 2014; Sawair et al., 2009) The fact that we did find two third non-prescribed dispensing of antibiotics shows the respondents answer making information bias unlikely.

Conclusion:

This study reflects on the fact that antibiotic consumption in Lebanon is uncontrolled and that non-appropriateness to guidelines is common. In Lebanon, inadequate enforcement of drug regulations raised inappropriate antibiotics consumption. Patients should be educated about the proper use of drugs and the need for medical advices, especially for antibiotics considering the personal and populational risks of drug resistance. This should be accompanied by educational programs for pharmacists and physicians before reinforcing the regulatory aspects of drug prescription.

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Table S1: Sociodemographic factors affecting appropriate choice, dose, duration, and overall:

	non-appropriate Choice	Appropriate Choice	P-value	non-appropriate Dose	Appropriate Dose	P-value	Non-appropriate duration	Appropriate duration	p-value	Non Overall appropriate	Overall Appropriate	p-valu
Gender												
Male	49 (29.9%)	104 (30.9%)	0.823	18 (32.7%)	86 (30.5%)	0.743	59 (28.4%)	39 (33.6%)	0.323	114 (29.3%)	33 (32.7%)	0.51
Female	115 (70.1%)	233 (69.1%)		37 (67.3%)	196 (69.5%)		149 (71.6%)	77 (66.4%)		275 (70.7%)	68 (67.3%)	
Age group												
16-25	81 (49.4%)	163 (48.4%)	0.396	31 (56.4%)	132 (46.8%)	0.247	110 (52.9%)	49 (42.2%)	0.125	200 (51.4%)	41 (40.6%)	0.14
25-50	59 (36%)	137 (40.7%)		21 (38.2%)	116 (41.1%)		80 (38.5%)	51 (44%)		144 (37%)	47 (46.5%)	
>50	24 (14.6%)	37 (11%)		3 (5.5%)	34 (12.1%)		18 (8.7%)	16 (13.8%)		45 (11.6%)	13 (12.9%)	
Educational level												
primary and less	53 (32.3%)	100 (29.7%)	0.298	12 (21.8%)	88 (31.2%)	0.314	64 (30.8%)	31 (26.7%)	0.66	121 (31.1%)	28 (27.7%)	0.80
secondary	17 (10.4%)	52 (15.4%)		8 (14.5%)	44 (15.6%)		31 (14.9%)	16 (13.8%)		50 (12.9%)	14 (13.9%)	
university	94 (57.3%)	185 (54.9%)		35 (63.6%)	150 (53.2%)		113 (54.3%)	69 (59.5%)		218 (56%)	59 (58.4%)	
Marital status												
single	84 (51.2%)	175 (51.9%)	0.881	33 (60%)	142 (50.4%)	0.19	116 (55.8%)	53 (45.7%)	0.082	208 (53.5%)	46 (45.5%)	0.15
married	80 (48.8%)	162 (48.1%)		22 (40%)	140 (49.6%)		92 (44.2%)	63 (54.3%)		181 (46.5%)	55 (54.5%)	
Currently working												
yes	104 (63.4%)	224 (66.5%)	0.449	36(65.5%)	188 (66.7%)	0.862	147 (70.7%)	75 (64.7%)	0.264	262 (67.4%)	64 (63.4%)	0.47
no	60 (36.6%)	113 (33.5%)		19 (34.5%)	94 (33.3%)		61 (29.3%)	41 (35.3%)		127 (32.6%)	37 (36.6%)	
Family income (LL)												
<2000000	46 (28%)	87 (25.8%)	0.442	15 (27.3%)	72 (25.5%)	0.712	48 (23.1%)	28 (24.1%)	0.072	97 (24.9%)	27 (26.7%)	0.14
>2000000	11 (6.7%)	34 (10.1%)		7 (12.7%)	27 (9.6%)		16 (7.7%)	18 (15.5%)		31 (8.0%)	14 (13.9%)	
Unemployment	107 (65.2%)	216 (64.1%)		33 (60%)	183 (64.9%)		144 (69.2%)	70 (60.3%)		261 (67.1%)	60 (59.4%)	
Presence of comorbidities												

	non-appropriate Choice	Appropriate Choice	P-value	non-appropriate Dose	Appropriate Dose	P-value	Non-appropriate duration	Appropriate duration	p-value	Non Overall appropriate	Overall Appropriate	p-valu
No	121 (73.8%)	271 (80.4%)	0.091	48 (87.3%)	223 (79.1%)	0.161	179 (86.1%)	82 (70.7%)	0.001	312 (80.2%)	71 (70.3%)	0.03
Yes	43 (26.2%)	66 (19.6%)		7 (12.7%)	59 (20.9%)		29 (13.9%)	34 (29.3%)		77 (19.8%)	30 (29.7%)	
Daman												
No	54 (34%)	123 (69.5%)	0.52	145 (37.8%)	28 (28.3%)	0.079	24 (43.6%)	99 (35.6%)	0.26	86 (41.3%)	32 (28.1%)	0.01
Yes	105 (66%)	210 (66.7%)		239 (62.2%)	71 (71.7%)		31 (56.4%)	179 (64.4%)		122 (58.7%)	82 (71.9%)	
Antibiotic request												
1st time	56 (34.6%)	110 (32.7%)	0.68	24 (44.4%)	86 (30.5%)	0.045	68 (32.9%)	42 (36.2%)	0.54	131 (33.9%)	35 (34.7%)	0.89
More than once/ year	106 (65.4%)	226 (67.3%)		30 (55.6%)	196 (69.5%)		139 (65.3%)	74 (63.8%)		255 (66.1%)	66 (65.3%)	

Data presented as number (%) were performed using Chi2 respectively and a p-value < 0.05 is considered significant.

Table S2: Factors affecting appropriateness of choice, dose, duration and overall:

	Non-appropriate choice	Appropriate Choice	p-value	Non-appropriate Dose	Appropriate Dose	p-value	Non-appropriate duration	Appropriate duration	p-value	Non Overall Appropriate	Overall Appropriate	p-value
Antibiotic Classes:			0.314									0.024
coamoxiclav	57 (33.7%)	112 (66.3%)		17 (15.2%)	95 (84.8%)	0.026	71 (65.7%)	37 (34.3%)	0.061	134 (34.4%)	33 (19.8%)	
Amoxicillin or penicillins	25 (39.1%)	39 (60.9%)		10 (25.6%)	29 (74.4%)		32 (82.1%)	7 (17.9%)		58 (90.6%)	6 (9.4%)	
Cephalosporins	40 (37.7%)	66 (62.3%)		17 (25.8%)	49 (74.2%)		38 (59.4%)	26 (40.6%)		84 (21.6%)	20 (19.2%)	
Fluoroquinolones	11 (24.4%)	34 (75.6%)		4 (11.8%)	30 (88.2%)		20 (58.8%)	14 (41.2%)		34 (75.6%)	11 (24.4%)	
Macrolides	12 (26.1%)	34 (76.9%)		1 (2.9%)	33 (97.1%)		24 (70.6%)	10 (29.4%)		37 (80.4%)	9 (19.6%)	
Others	19 (26.8%)	52 (73.2%)		6 (11.5%)	46 (88.5%)		23 (51.1%)	22 (48.9%)		42 (65.6%)	22 (34.4%)	
Types of infection												
Respiratory tract infections:												
Tonsillitis	3 (1.8%)	135 (97.8%)	<.001	27 (20%%)	108 (80%)	0.135	114 (85.7%)	19 (14.3%)	<.001	121 (88.3%)	16 (11.7%)	0.002
Cold	60 (68.2%)	28 (31.8%)	<.001	4 (14.3%)	24 (85.7%)	0.761	20 (71.4%)	8 (28.6%)	0.404	82 (93.2%)	6 (6.8%)	<.001
Sore throat	36 (85.7%)	6 (14.3%)	<.001	1 (16.7%)	5 (83.3%)	0.982	4 (1.9%)	1 (20%)	0.458	41 (100%)	0	0.001
Cough	21 (61.8%)	13 (38.2%)	<.001	5 (38.5%)	8 (61.5%)	0.028	9 (69.2%)	4 (30.8%)	0.699	32 (94.1%)	2 (5.9%)	0.028
Otitis	13 (40.6%)	19 (59.4%)	0.335	3 (15.8%)	16 (84.2%)	0.949	8 (42.1%)	11 57.9%)	0.038	23 (71.9%)	9 (28.1%)	0.277
Sinusitis	5 (23.8%)	16 (76.2%)	0.373	2 (12.5%)	14 (87.5%)	0.672	4 (25%)	12 (75%)	0.001	10 (47.6%)	11 (52.4%)	<.001
Chest tightness	12 (85.7%)	2 (14.3%)	<.001	0	2	0.531	0	2	0.057	12 (85.7%)	2 (14.3%)	0.553
Runny nose or sneezing	5 (50%)	5 (50%)	0.24	2 (40%)	3 (60%)	0.149	1 (20%)	4 (80%)	0.038	8 (80%)	2 (20%)	0.961
Gastrointestinal infections:												
Diarrhea	4 (6.7%)	56 (93.3%)	<.001	10 (17.9%)	46 (82.1%)	0.733	19 (40.4%)	28 (59.6%)	<.001	27 (51.9%)	25 (48.1%)	<.001
Teeth infections	1 (3.1%)	31 (96.9%)	<.001	3 (9.7%)	28 (90.3%)	0.294	19 (63.3%)	11 (36.7%)	0.917	21 (67.7%)	10 (32.3%)	0.098
Urinary tract infections:	7 (11.3%)	55 (88.7%)	<.001	4 (7.3%)	51 (92.7%)	0.047	31 (57.4%)	23 (42.6%)	0.254	40 (65.6%)	21 (34.4%)	0.004
Skin infections:							4 (25%)	12 (75%)	0.001			
Skin infection	0	21 (100%)	0.001	6 (28.6%)	15 (71.4%)	0.117	13 (61.9%)	8 (38.1%)	0.821	15 (71.4%)	6 (28.6%)	0.357
Acne	7 (77.8%)	2 (22.2%)	0.004	0	2	0.531	1	1	0.674	8 (88.9%)	1 (11.1%)	0.477

General:												
Pain	16 (88.9%)	2 (11.1%)	>.001	1 (50%)	1 (50%)	0.196	0	2 (1.7%)	0.057	17 (94.4%)	1 (5.6%)	0.108
Data presented as number (%) were performed using Chi2 respectively and a p-value < 0.05 is considered significant.												

Chapter 4:

Knowledge, attitude and practice toward antibiotic

In previous chapters we assessed the usage pattern and appropriateness of antibiotic use in Lebanon. Several factors may enhance irrational antibiotics usage, which could be doctors' knowledge and experiences, (Cetinkaya, Karatas, Antmen, & Alhan, 2010) patients' expectations, lack of patient education, antibiotic selling without a prescription as well as economic reasons. (Oyetunde, Olugbake, & Famudehin, 2010) Patients' knowledge, attitude and behaviour play a significant role in using antibiotics.

There have been reports of a general lack of knowledge and public awareness ofthe basic principles of correct antibiotic use and indications. (Hawkings, Butler, & Wood, 2008) There are also common misconceptions regarding the use of antibiotics, especially for common indications like upper respiratory tract infections (URTIs), as it is believed that the use of antibiotics results in quick recovery and prevents more serious illness. (Richman, Garra, Eskin, Nashed, & Cody, 2001)

A review of antibiotic use in developing countries (Radyowijati & Haak, 2001) reported that people believed antibiotics as "an extraordinary medicine" or "a powerful medicine" or "a strong medicine" which are able to prevent and cure any diseases or symptoms.

The World Health Organization (WHO) identified three key issues for public involvement: improving access to medical facilities, decreasing unnecessary use of antimicrobials, taking a full course of treatment, and not giving out medication to other people or keeping left-overmedication for future needs. The WHO also urged member countries to initiate educational interventions for patients and the general population aimed at rationalizing the use of antibiotics to combat resistance. (World Health Organization, 2001)

Several countries have undertaken national campaigns to modify the public's misconceptions regarding the effectiveness of antibiotics, promote appropriate antibiotic use, and prevent the development of antibiotic resistance. (Mouhieddine et al., 2015) Population knowledge, attitudes and practices have been evaluated in many studies to identify a certain condition and a set of variables affecting that condition. The knowledge component assesses what people know, while the attitude component assesses what they feel and practice assesses their behaviour. There are no studies that target the Lebanese population to assess the knowledge and attitude concerning the usage of antibiotics.

In Lebanon, rare studies reported knowledge and attitude practice toward antibiotic among general public in Lebanon. Only two studies were done to explore knowledge and attitude in Beirut and its suburbs. Thus, our objective was to assess knowledge and attitude among general public in Lebanon and to identify the associated sociodemographic characteristics.

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Public Knowledge and Attitude towards Antibiotic Use in Lebanon

Abstract

Introduction: Antibiotic resistance is a major threat in global public health. This study aims to assess the public knowledge, attitude and practice towards antibiotic use among general public in Lebanon.

Method: It was a cross sectional study in a community-based pharmacy setting in Lebanon. It used a structured random interview to patients visiting community pharmacy seeking for antibiotics. Descriptive statistics were presented and multivariate logistic regressions were performed in data analysis.

Results: A total of 495 participated in the study. The study sample had in general low knowledge (average = 6) and attitude score (average=3.16). High proportion of Lebanese participants believed that antibiotics were used for treatment of common cough cold and sore throat symptoms (59%) or viral infections (53%). 42% preferred to take antibiotics from the pharmacy without physician prescription. In the multivariable logistic regression analysis, females showed better knowledge toward antibiotic use compared to males (ORa=1.59, 95%CI=1.01-2.53). Compared to participants aged >50 years old, the level of adequate knowledge was higher in those aged 25-50 years old (ORa=3.66, 95%CI=1.79-7.49).

Conclusion: This study identified important knowledge and attitude gaps among general public in Lebanon. Future antibiotic awareness campaigns and patient counselling should be implemented to reduce the risk of antibiotic resistance.

Keywords: antibiotic, knowledge, attitude, Lebanon

Introduction:

Antibiotic resistance is a major threat in global public health. The overuse and misuse of antibiotics may generate several problems, including the development of bacterial resistance, (Va¨a¨na¨nen, Pietila¨, & Airaksinen, 2006) adverse reactions, treatment failure and waste of resources. (Va¨a¨na¨nen et al., 2006)

The World Health Organization (WHO) identified three key issues for public involvement: improving access to medical facilities, decreasing unnecessary use of antimicrobials, taking a full course of treatment, and not giving out medication to other people or keeping left-over medication for future needs. The WHO also urged member countries to initiate educational interventions for patients and the general population aimed at rationalizing the use of antibiotics to combat resistance. (World Health Organization, 2001)

The lack of knowledge of medication such as antibiotics may greatly influence the probability of misuse or compliance. (Kandakai, Price, Telljohann, & Holiday-Goodman, 1996) Studies conducted elsewhere have demonstrated inappropriate practices such as sharing of antibiotics, (Kandakai et al., 1996) and the use of left over antibiotics. (Curry et al., 2006; Prakasam, Kumar, & Ramesh, 2011) There have been reports of a general lack of knowledge of correct antibiotic use and a lack of public awareness on the basic principles of antibiotic use, as well as indication for therapy. (Curry et al., 2006; Prakasam et al., 2011)

The World Health Organization (WHO) have also issued a Global Strategy for Containment of Antimicrobial Resistance in 2001 which urged member countries to initiate awareness and educational campaigns for patients and general community on appropriate use of antibiotics to combat antibiotic resistance. (World Health Organization, 2001) This was echoed by International Pharmaceutical Federation (FIP) in 2008 in its Statement of Policy on Control of Antimicrobial Drug Resistance (International Pharmaceutical Federation. FIP, 2008) and WHO Regional Office for South-East Asia (World Health Organization, 2010) in 2010.

In Lebanon, antibiotics are mostly accessed without prescription despite the presence of a law that bans such practices. Therefore, it is important to assess the public knowledge, attitude and practice of antibiotic use among Lebanese population. The findings from this study would provide useful data which could form the basis for educational campaigns on appropriate use of antibiotics, thus addressing any misconceptions among the public.

Method:

Design and study population

A cross sectional study was conducted in a community-based pharmacy setting in Lebanon. Data was collected over a 1-year period (September 2015 to September 2016) from 50 community pharmacies CPs distributed in six different districts in Lebanon: Beirut, South Lebanon, Nabatiyeh, Mount Lebanon, Bekaa, and North. Data on antibiotic use was collected using a structured random interview conducted by study researchers who had been briefed about the study's aims and methods. Consecutive customers aged 16 years and older arriving at community pharmacies seeking antibiotics for systemic infections were interviewed. The interview was based on a well-structured questionnaire, which had been pre-tested on a small pilot scale and subsequently modified to ensure that the data would provide reliable information.

The Lebanese University, Faculty of Pharmacy Internal Review Board waived the need for written informed consent. The patients were informed about the objective of the study and were asked to give an oral consent. Only those who were interested and who give their voluntary informed oral consent to participate in the study were enrolled.

Sample size calculation:

A sample size was calculated assuming a type I error of 5% and a study power of 80% and 95%CI. Based on a previous study, 40% of patients were expected to self-medicate with antibiotics. (Cheaito, Azizi, Saleh, & Salameh, 2014) The minimal sample size necessary to show a twofold increase in the risk of exposure to non-prescribed antibiotics consists of 442 subjects.

Data Collection

Data was acquired through a structured questionnaire filled by an interviewer. If a customer had more than one request, CPs filled out one documentation form per request. The questionnaire was obtained after wide review of literature. (Lim & Teh, 2012; Kim et al., 2011; Alzoubi et al., 2013; Awad & Aboud, 2015; Napolitano, Izzo, Di Giuseppe, & Angelillo, 2013) The questionnaire included many sections that were chosen following an extensive review of literature. The questionnaire was translated into Arabic and subjected to a process of forward and backward translation into English. It was pretested and validated first on 20 patients visiting 4 different pharmacies before starting the survey.

The questionnaire consisted of dichotomous, and close-ended questions. It consisted of 5 sections. The first section was related to sociodemographic characteristics including age, sex, occupation, educational and marital status, monthly income, medical insurance, and the presence of a care provider at home. Education was divided into five classes of illiterate, primary, complementary, secondary, and academic education levels. Work status was categorized into currently working, retired and never working, while marital status was categorized into married, single, and widow/divorced.

The second section consisted of 13 questions to evaluate respondent's knowledge bout antibiotics in four aspects: action and use (5 statements), side effects (4 sentences) and resistance (4 questions). A three-likert scale (1=agree, 2=uncertain, 3=disagree) was used to evaluate the participants' response. Nine attitude statements were included in section three, and

the participants were required to answer in three likert scale also. Finally, the fifth section included 6 statements to explore the patient and doctor relationship regarding prescribed antibiotic and the responses were measured using three-likert scale also.

Statistical analysis

Statistical analysis was done using SPSS version 19. Descriptive statistics of the respondents' knowledge and attitudes regarding antibiotic use and bacterial resistance were reported. After data cleaning, data was assessed. Percentages was used for multinomial variables, means and standard deviations for continuous variables. The internal consistency for the sections to determine knowledge of and attitude towards use of antibiotics was assessed using Cronbach's α test. The Cronbach's alpha for the knowledge score was 0.795 and 0.651 for the attitude score. To describe the knowledge and attitudes of the participants, a score was calculated according to the number of correctly answered questions targeting the knowledge and attitudes regarding antibiotic usage. The knowledge score was categorized as inadequate or adequate. The attitude score was categorized as poor and good. The knowledge and attitude scores were dichotomized based on median as a threshold. Each correct answer was assigned 1 point while wrong or uncertain responses were assigned 0 points. Then, the sum of the responses for each patient was calculated. The maximum knowledge score was 13 points and 9 points for the attitude score. Thus, the knowledge scores were categorized into inadequate (0-6/13) or adequate (7-13/13) while the attitude score was divided into poor (0-4/9) or good (5-9/9) as dichotomous variables. (Suaifan et al., 2012)(A. Awad, Eltayeb, Matowe, & Thalib, 2005)

Associations of demographic variables (gender, age, family income level, education level, employment and marital status) with knowledge and attitudes were first evaluated using a bivariate analysis by chi-squared test. The correlation test was used to examine the association between knowledge and attitude score. Multivariate analysis using Logistic regressions was used to assess the correlation between the Knowledge and attitude dichotomous score as dependent variables and sociodemographic characteristics as independent variables taking into account potential confounding variables that had a $p < 0.2$ in bivariate analysis. A p-value <0.05 was considered significant.

Results:

Baseline Characteristics

A total of 495 patients were recorded in the study. Table 1 shows the demographic characteristics of the participants. In this sample, females were more than males (69.9% vs 30.1%). The majority being between 16 and 50 years of age (88.3%), while 11.7% were >51 years of age. About half of patients had a university degree (56.2%), while 13.8% had secondary education, 30.3% had intermediate and elementary education. 34.3% were currently working. The monthly income with greatest prevalence among the respondents was 2000000 LL (62.2%). Almost 21.8% have concomitant comorbidities.

Table 1: Characteristics of the study population

	Total participants N=495 (100%)
Gender:	
Male	149 (30.1%)
Female	346 (69.9%)
Age group:	
16-25	244 (49.3%)
25-50	193 (39%)
>50	58 (11.7%)
Educational level:	
Primary and less	150 (30.3%)
Secondary	67 (13.5%)
University	278 (56..2%)
Marital status:	
Single	259 (52.3%)
Married	236 (47.7%)
Currently working:	
Employed	170 (34.3%)
Unemployed or retired	325 (65.7%)
Family income (LL):	
<2000000	131 (26.5%)
>2000000	44 (8.9%)
Unemployment	320 (64.6%)
Presence of comorbidities:	
Yes	109 (21.8%)
No	392 (78.2%)
Antibiotic request per year	
1st time	166 (33.5%)
More than once	326 (65.9%)
Presence of insurance on medication coverage	
Yes	313 (63.2%)
No	173 (34.9%)

Knowledge description

The study sample had in general low knowledge score (average = 6 points) (table 2).

Table 2: Knowledge and Attitude scores among participants

Level of Knowledge Mean (SD)	**Total Score 6.00 (2.73)**	**Number (%)**
Adequate	0-6	269 (54.3%)
Inadequate	7-13	226 (45.7%)
Attitude Mean (SD)	**Total Score 4.19 (1.96)**	**Number(%)**
Low	0-4	305 (61.7%)
Good	5-9	189 (38.3%)

Only 13.1% believed that antibiotics can kill bacteria. 54% and 59% responded that antibiotics can kill viruses and are effective against cough and cold. 54.3% of participants believed that antibiotics are effective in reducing fever and pain and can kill normal flora that live in the skin and gut. Almost 53% of participants realized that bacteria are becoming resistant to antibiotics and that the unnecessarily use of antibiotics has increased the risk of bacterial resistance. 25% believed that if antibiotics are taken for long period of time, the bacteria become more resistant to antibiotics and 36% believed that taken less doses did not decrease the bacterial resistance. Approximately, 45% of participants believed that antibiotics can cause side effects including hepatic and renal problems. Almost 65% stop taking antibiotic if they get side effects including skin allergic reaction. (Table 3)

Table 3: Knowledge Attitude and Patient Physician Relationship among participants

Knowledge for antibiotic:	**Correct Answer**	**Incorrect Answer**	**Uncertain**
Antibiotic Action			
Antibiotics work on most coughs and colds	110 (22.2%)	293 (59.2%)	92 (18.6%)
Antibiotics can kill bacteria	65 (13.1%)	351 (70.9%)	79 (16%)
Antibiotics can kill viruses	108 (21.8%)	267 (53.9%)	120 (24.2%)
Antibiotics are effective in reducing pain	269 (54.3%)	106 (21.4%)	120 (24.2%)
Antibiotics can kill the bacteria that normally live on the skin and in the gut	269 (54.3%)	75 (15.2%)	151 (30.5%)
Antibiotic Resistance:			
Bacteria are becoming resistant to antibiotics	264 (53.3%)	107 (21.6%)	124 (25.1%)
The unnecessarily use of antibiotics can increase the resistance of bacteria to them	269 (54.3%)	115 (23.2%)	111 (22.4%)
If antibiotics are taken less than the prescribed dose, bacteria become less resistant to antibiotics	178 (36%)	167 (33.7%)	150 (30.3%)
If antibiotics are taken for a long time, bacteria become more resistant to antibiotics	126 (25.5%)	211 (42.8%)	157 (31.7%)
Antibiotic Side effects:			
Antibiotic does not cause side effects	221 (44.6%)	159 (32.1%)	115 (23.2%)
Antibiotic may cause hepatic and renal problems.	234 (47.3%)	123 (24.8%)	138 (27.9%)
If you get side effects during a course of antibiotics treatment you should stop taking them as soon as possible	302 (61%)	92 (18.6%)	101 (20.4%)
If you get some kind of skin reaction when using an antibiotic, you should not use the same antibiotic again	344 (69.5%)	72 (14.5%)	79 (16%)
Patient Attitude	**Agree**	**Disagree**	**Uncertain**
Positive attitude			
I normally look at the expiry date of antibiotic before taking it	368 (73.5%)	83 (16.6%)	43 (8.6%)
Need for patient education.	370 (74.9%)	63 (12.8%)	61 (12.3%)
Negative Attitude			
I always complete the course of treatment with antibiotics even if I feel better.	240 (48.6%)	222 (44.9%)	32 (6.5%)
I stop taking the antibiotic if the symptoms do not improve after taking it.	240 (48.6%)	222 (44.9%)	32 (6.5%)
I prefer to be able to buy antibiotics from the pharmacy without a prescription.	208 (42.1%)	215 (43.5%)	71 (14.4%)

Patient Attitude	**Agree**	**Disagree**	**Uncertain**
I prefer to keep antibiotics at home in case there may be a need for them later	129 (26.1%)	301 (60.9%)	64 (13%)
I prefer to use an antibiotic if I have a cough for more than a week	166 (33.6%)	234 (47.4%)	94 (19%)
When I have a sore throat I prefer to use an antibiotic	151 (30.6%)	255 (51.6%)	88 (17.8%)
I share antibiotic with someone else in my family/friends with similar symptoms to mine	156 (31.6%)	263 (53.2%)	75 (15.2%)
Patient Physician Relationship	**Agree**	**Disagree**	**Uncertain**
Pharmacists often tell you how antibiotics should be used	376 (76.3%)	52 (10.5%)	65 (13.2%)
Doctors often take time to inform the patient during the consultation how antibiotics should be used	186 (37.7%)	222 (45%)	85 (17.2%)
Physicians routinely prescribed antibiotics to treat common cold symptoms	253 (51.3%)	150 (30.4%)	90 (18.3%)
I request antibiotic prescriptions from my physician	182 (36.9%)	248 (50.3%)	62 (12.8%)
I trust the doctor decision if she or he decides not to prescribe antibiotic	326 (66.1%)	101 (20.5%)	66 (13.4%)
I consult another physician to prescribe antibiotics if their physician disagreed to do so	168 (34.1%)	238 (48.3%)	87 (17.6%)

Five variables (age, education, employment and family income level and presence of insurance) showed a significant association (p-value<.005) with the respondents' knowledge regarding antibiotic use, according to the chi-squared test. Young age participants and those with higher educational level showed more adequate knowledge. Employed participants with higher income and with medical insurance showed better knowledge. Gender was not significantly associated with better knowledge of antibiotic use. (Table 4)

Table 4: Factors significantly associated with Public Knowledge toward antibiotic use:

	Level of Knowledge			Level of Attitude		
	Inadequate Knowledge	Adequate Knowledge	P-value	Poor Attitude	Good Attitude	p-value
Gender						
Male	88 (59.1%)	61 (40.9%)	.167	101 (68.2%)	47 (31.8%)	.052
Female	181 (52.3%)	165 (47.7%)		204 (59%)	142 (41%)	
Age group						
16-25	135 (55.3%)	109 (44.7%)	<.001	146 (59.8%)	98 (40.2%)	.559
25-50	90 (46.6%)	103 (53.4%)		120 (62.5%)	72 (37.5%)	
>50	44 (75.9%)	14 (24.1%)		39 (67.2%)	19 (32.8%)	
Educational level						
Primary and less	92 (61.3%)	58 (38.7%)	.004	102 (68.5%)	47 (31.5%)	.118
Secondary	44 (65.7%)	23 (34.3%)		41 (61.2%)	26 (38.8%)	
University	133 (47.8%)	145 (52.2%)		162 (58.3%)	116 (41.7%)	
Marital status						
Single	137 (52.9%)	122 (47.1%)	.498	161 (62.2%)	98 (37.8%)	.84
Married	132 (55.9%)	104 (44.1%)		144 (61.3%)	91 (38.7%)	
Currently working						
No	191 (58.8%)	134 (41.2%)	.006	191 (58.8%)	134 (41.2%)	.059
yes	78 (45.9%)	92 (54.1%)		114 (67.5%)	55 (32.5%)	
Family income (LL)						
<2000000	61 (46.6%)	70 (53.4%)	.004	97 (74.6%)	33 (25.4%)	.002
>2000000	17 (38.6%)	27 (61.4%)		27 (61.4%)	17 (38.6%)	
Unemployment	191 (59.7%)	129 (40.3%)		181 (56.6%)	139 (43.4%)	
Presence of comorbidities						
No	232 (59.6%)	157 (40.4%)	.064	232 (59.6%)	157 (40.4%)	.064
Yes	73 (69.5%)	32 (30.5%)		73 (69.5%)	32 (30.5%)	
Presence of Insurance or NSSF						
No	115 (66.5%)	58 (33.5%)	<001	114 (66.3%)	58 (33.7%)	.091
Yes	147 (47%)	166 (53%)		183 (58.5%)	130 (41.5%)	
Antibiotic request						
1st time	91 (54.8%)	75 (45.2%)	.912	109 (66.1%)	56 (33.9%)	.158
More than once/ year	177 (54.3%)	149 (45.7%)		194 (69.5%)	132 (40.5%)	

Data presented as number (%) were performed using Chi2 respectively and a p-value < 0.05 is considered significant.

Attitude and Patient Physician Relationship

The study sample had in general poor attitude score (mean= 4.19) (table 2). Almost 57.4% stopped taking the medication if the symptoms disappear. 42% preferred to take antibiotic from the pharmacy without physician prescription. About 33% preferred to take antibiotic in cases of cough, flu and sore throat. 26% preferred keeping antibiotic at home in case of emergency and 31% shared the antibiotics with someone else if he has similar signs and symptoms. Approximately 73% checked the expiry date of medication before taking it and that there was need for patient education about the appropriate use of antibiotics. (Table 3)

According to the chi-squared test, females showed better attitude compared to males toward the appropriate use of antibiotic (p=.052). Age and education were not significantly associated with better attitude of appropriate antibiotic use. (Table 4)

Approximately 76% of participants responded that pharmacists tell them how to administer antibiotic. 51% expected that physicians routinely prescribe antibiotics in case of cold symptoms and that 37% of physicians spent time to inform patient about the usage of antibiotics. 66% trusted physicians if they decided not to prescribe antibiotic and 34% consulted another physician if the first physician disagreed to prescribe antibiotic. (Table 3)

Practice

Almost half read the instructions on the label to see the correct usage and safe of medication. 26.4% told the pharmacist about the concurrent medication at the time of OTC. Greater than half of participants reported requesting antibiotic more than once per year. Almost 65% of participants reported returning to pharmacy if the symptoms do not improve and returning to physician.

Multivariable Analysis

In the multivariable logistic regression analysis (Table 5), females showed better knowledge score compared to males (ORa=1.59, 95%CI=1.01-2.53). Compared to participants aged >50 years old, the level of adequate knowledge of antibiotic was higher in those aged 25-50 years old (ORa=3.66, 95%CI=1.79-7.49). Compared to unemployed participants, those with higher income had better knowledge score (ORa=3.17, 95%CI=1.78-6.79). Participants with insurance on medication coverage had also better knowledge score (ORa=2.06, 95%CI=1.38-3.07).

Moreover, a step-wise multiple logistic regression was conducted on attitude of antibiotic usage (Table 5); three were shown to be significant predictors. Patients with comorbidities showed lower attitude score (ORa=.62, 95%CI= .38-1). Compared to unemployed participants with income <2000000 showed lower attitudes (ORa=.41, 95%CI=.26-.66) but those with income >2000000 didn't show significant difference in attitude toward appropriate antibiotic usage. Presence of medical insurance showed better attitude score (ORa=1.62, 95%CI=1.08-2.42).

Table 5: Multivariable logistic regression of Knowledge and Attitude score:

Multivariate Analysis	aOR	95% CI	p-value
Knowledge:			
Gender	1.59	1.01-2.53	.045
Age group			<.001
16-25	3.05	1.49-6.28	.002
25-50	3.66	1.79-7.49	.002
>50	1	Reference	
Income group			<.001
<2000000	1.73	1.07-2.77	.005
>2000000	3.17	1.78-6.79	.024
Unemployment	1	Reference	.003
Insurance of medication coverage	2.06	1.38-3.07	<.001
Attitude:			
Income group			.001
<2000000	.415	.26-.66	<.001
>2000000	.785	.41-1.51	.468
Unemployment	1	Reference	
Presence of comorbidities	.62	.38-1	.05
Insurance of medication coverage	1.62	1.08-2.42	.019

aOR: adjusted odds ratio above 1 indicates increased n appropriateness and below 1 less appropriateness. CI: Confidence Interval

Only factors significantly associated with better or worse appropriateness are shown.

Discussion:

The results of this study demonstrated the knowledge, attitudes and practice toward antibiotic use among general public in Lebanon. This will help in testing the adequacy of knowledge and provide further insight in designing future educational campaigns targeting general public to promote appropriate antibiotic use and help in reducing antibiotic resistance. The average knowledge and attitude score was low. This finding is similar to that of neighboring countries in Jordan. (Alzoubi et al., 2013) These results were supported by high proportion of Lebanese participants using antibiotic for common cough cold and sore throat symptoms. This means that that they are using antibiotic for diseases that do not require them. Other studies conducted in United Kingdom, (McNulty, Boyle, Nichols, Clappison, & Davey, 2007) Sweden, (Andre, Vernby, Berg, & Lundborg, 2010) Korea, (Kim, Moon, & Kim, 2011) Italy (Napolitano, Izzo, Di Giuseppe, & Angelillo, 2013) and United State (Filipetto, Modi, Weiss, & Ciervo, 2008) showed that many people thought that antibiotics are effective for common cold and cough symptoms and may be used for viral infections.

Participants were not well informed to the meaning of antibiotic resistance and were unaware of the spread of bacterial resistance. They didn't know that stopping the antibiotic early or as the symptoms disappear without completing the full course of antibiotic can increase the risk of antibiotic resistance. In our study, almost half of participants knew that antibiotics can kill normal flora that lives normally in the skin and gut which is similar percentage to that reported in Korea (57%) (Kim et al., 2011) but higher than that in UK (43%). (McNulty et al., 2007) Many participants were aware of antibiotic side effects where approximately 60% stopped taking antibiotic as soon as side effects occur and stopped taking it again later. But only 40% knew that antibiotic can cause hepatic or renal problems.

In term of attitudes our study showed that 42% preferred to take antibiotic from the pharmacy without physician prescription. Recent studies from Lebanon reported similar self-medication rate (40%). (Cheaito et al., 2014) It is similar to that reported in Mediterranean countries which ranged from 40.7% to 78% namely Jordan, (Shehadeh et al., 2012) United Arab Emirates, (Abasaeed, Vlcek, Abuelkhair, & Kubena, 2009) Iraq (Jassim, 2010) and Kuwait. (A. I. Awad & Aboud, 2015) In contrast it is higher than that reported in Hong Kong, Malaysia, UK and European countries which ranged between 4.8 to 9%. (European Commission, 2013; Lim & Teh, 2012; McNulty et al., 2007; Norris et al., 2010; You et al., 2008) This due to unregulated rules in Lebanon to restrict the self-medication use of prescribed antibiotic in community pharmacies. Hence, the current study highlights the need for further enforcement of regulations. Moreover, almost 48% stopped taking the medication if the symptoms disappear. This explains the rapid increase in bacterial resistance in Lebanon due to use of antibiotic beyond the scope.

About 33% preferred to take antibiotic in cases of cough, flu and sore throat. This explains the misconception present among the study participants regarding the role of antibiotic. A possible reason for inadequacy of knowledge in this area is the use of term "germ" rather than "bacteria" or "viruses" by the physicians during medical counseling. (Andre et al., 2010) Moreover, 26% preferred keeping antibiotic at home in case of emergency and 31% shared the antibiotics with someone else if he has similar signs and symptoms. This suggests that many Lebanese individuals share antibiotics with others and use them as necessary thus subjecting the Lebanese population to the problem of antibiotic misuse.

Approximately 76% of participants responded that pharmacists tell them how to administer antibiotic. This showed that many individuals obtained information about antibiotic use from pharmacists which highlight that pharmacists can have a vital role to play in public education

about the prudent use of antibiotics. Therefore, implementation of pharmaceutical care in community pharmacies can help to improve public knowledge and attitude towards antibiotics in Lebanon. Community pharmacists are the most accessible health care providers to the public, and can contribute to public knowledge about appropriate antibiotic use.

51% expected that physicians routinely prescribe antibiotics in case of cold symptoms It is well documented that overprescribing by physicians even in the absence of appropriate indications due to diagnostic doubt and patient demand are factors contributing to antibiotic resistance. (Franco, Altagracia Martinez, Sanchez Rodriguez, & Wertheimer, 2009; World Health Organization, 2001) Numerous reports have shown that patient's expectation is an important factor for antibiotic prescribing and that antibiotics are more likely to be prescribed under patient pressure. (Butler, Rollnick, Pill, Maggs-Rapport, & Stott, 1998; Kumar, Little, & Britten, 2003)

Our results identified demographic groups with poor knowledge toward antibiotic use, including persons with low educational status and those aged >50 years old. As we found, a higher educational level was associated with better knowledge and attitude(Van den Eng et al., 2003; You et al., 2008), and the elderly are less knowledgeable about antibiotics in general. (McNulty et al., 2007) Moreover, females and those with higher income or medical insurance show better knowledge and attitude score compared to males. Previous studies reported significant association between self-medication and age, male gender, education level and lower socioeconomic status. (Belkina et al., 2014; Jafari, Khatony, & Rahmani, 2015)

Participants' knowledge found to correlate positive attitude. Appropriate knowledge of antibiotics was identified to be a predictor for positive attitude towards antibiotic use. (Kim et al., 2011) These findings support the idea that the better knowledge on antibiotics usage and the potential for antibiotic resistance can change attitudes and behaviors regarding the appropriate use of antibiotic. An understanding of antibiotic use is important because personal decisions are based on these understandings. (Norris et al., 2010) They can impact physicians' prescription behavior, (Belongia, Naimi, Gale, & Besser, 2002) as well as lead to decreasing suboptimal use of antibiotics, such as using short courses and sub-therapeutic doses. (Norris et al., 2010)

This study has several limitations. While efforts were done to obtain representative samples, the over presentation of female gender and higher educational level indicate selection bias. This surveys were also filled using face to face questionnaire, therefore, there is a possibility of information and recall bias. Moreover, it is a cross sectional study, therefore, it does not allow causality to be attributed to the observed associations. Despite these limitations, this study provides important information for evaluating and improving knowledge, attitude and practice towards antibiotics use among general public in Lebanon.

Conclusion:

This study identified important knowledge and attitude gaps among general public in Lebanon. Future antibiotic awareness campaigns and patient counselling should be implemented to fill up the knowledge and attitude gaps as an effort against antibiotic resistance. This aim to reduce the risk of antibiotic resistance.

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Chapter 5:

Usage pattern of antibiotics in France

In the previous chapters we studied the usage pattern and appropriateness of antibiotic use in Lebanon.In contrast with Lebanon, in France, antibiotics are only obtained as prescription medicines. The community use of antibiotics can therefore be captured using the French Healthcare databases (EGB database).

EGB (*Echantillon Généraliste de Bénéficiaires*) is the 1/97th random permanent representative sample of SNIIRAM, with planned 20-year longitudinal data (ten years at this time). The database includes demographic data; healthcare encounters such as physician or paramedical visits, medicines, medical devices, lab tests (without results), chronic diseases (Affections de Longue Durée, ALDs), chronic medical conditions (ICD10 codes), hospitalisations with ICD10 codes for primary, linked and associated diagnoses, date and duration, procedures, diagnostic related groups and cost coding; date but currently not cause of death.(J. Bezin et al., 2017; Moulis et al., 2015; Tuppin, de Roquefeuil, Weill, Ricordeau, & Merliere, 2010)Each dispensing was described by the name of the antibiotic medication dispensed, number and frequency of dispensings per year, number of defined daily doses (DDD) per dispensing episode (defined as the 30-day period following the initial dispensing), and total number of DDD dispensed per year. The DDD was obtained from the WHO Collaborating Centre for drug statistics methodology (http://www.whocc.no/atc_ddd_index/). The recommended daily dose (RDD)was obtained from the 2012 French national drug formulary (VIDAL® dictionary, Paris).
The antibiotics we chose to describe in France are the 6 antibiotics most consumed in Lebanon. We also aim in this chapter to identify age and gender specific use of antibiotic as well as high antibiotic users who are considered an important category.

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Community Usage Patterns of antibiotics in France

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Abstract:

Objective: To describe the antibiotic usage pattern among outpatients in France and to explore patterns of age and gender specific use.

Methods: Data was extracted from the Echantillon Généraliste de Bénéficiaires (EGB) database, the permanent 1/97 representative sample from the French national healthcare insurance system which contains all dispensed prescriptions in France, was searched in 2013 to identify usage patterns, concomitant chronic diseases and concomitant medications in antibiotic users. Patients were followed for 365 days after first dispensing in 2013.

Results: A total of 137,358 patients, representing 25 % of the total population aged >15 years old had at least one dispensation of antibiotic of interest in 2013. Amoxicillin was the most commonly dispensed antibiotic (40.7%) followed by coamoxiclav (32.0%). The average dispensing of defined daily doses (DDD) over a year was higher in males (35.5) than in females (34.6). The average use of antibiotic over a year increased with age from average of 28.4 DDD in patients aged between 16 and 25 years old to 38.6 DDD in patients aged > 75 years old. Amoxicillin and coamoxiclav were the most commonly dispensed in all age groups.

Conclusion: Over 25% of the French population received antibiotic at least once per year, with differences related to gender and age. These should be considered when monitoring antimicrobial drug resistance and when planning educational interventions for health professionals, with the aim to improve the rational use of antibiotic drugs.

Keywords: antibiotic use, DDD, prescriptions, France population

Introduction:

Antibiotic resistance is a major health problem worldwide. The World Health Report 2007 highlighted the issue of antibiotic resistance as one of the major threats to public health security in the 21st century.(World Health Organization, 2007) Studies in Europe(Bronzwaer et al., 2002; Goossens, Ferech, Vander Stichele, Elseviers, & Group, 2005) indicate that resistance against antibiotics increases with higher consumption, which could be due to irrational use of antibiotics.(Franco, Altagracia Martinez, Sanchez Rodriguez, & Wertheimer, 2009) Furthermore, the decline in the development of novel antibiotics to combat the menace of antibiotic resistance has created a public health challenge to health policy makers, health-care workers, and the population around the world.(Wenzel, 2004)

Antibiotics are available only as prescription in France and therefore their use is captured in population databases, including electronic health records or claims reimbursement databases. The consumption of antibiotics is high among the French compared to other European countries with 30.1 defined daily doses (DDD)/1000 inhabitants/day in 2013 equivalent to 4.85 packages/1000inhabitants/day.(European Centre for Disease Prevention and Control, 2015) There is also a shift from the old narrow-spectrum antibiotics to new broad-spectrum antibiotics.(Goossens et al., 2005)

Penicillins were the most frequently used antibiotics in France, mostly broad spectrum penicillins alone or in combination with B-lactamase inhibitors. However, in Europe the use of cephalosporins has been rising for treatment of uncomplicated respiratory tract infection despite no recommendation for cephalosporin use in such circumstances.(Ho et al., 2001) This high cephalosporin use was due to the strikingly high use of oral third-generation cephalosporins i.e., cefixime. There is also an emergence of inappropriate use of macrolides (mainly with clarithromycin) or quinolones (mainly with ciprofloxacin).(Goossens et al., 2005) This inappropriate use will inevitably lead to the emergence of not only resistant pneumococci, but also of a host of resistant gram-negative organisms.(Guillemot et al., 1999)

In spite their widespread use, little is known of the usage patterns of antibiotics in France. Given that prescription antibiotics are recorded in the French claims databases, the aim of the present study therefore was to describe the usage pattern of these commonly used oral antibiotics in France and to explore patterns of age and gender specific use.

Method:

Data was extracted from the Echantillon Généraliste de Bénéficiaires (EGB) database, a permanent representative 1/97 sample of the nationwide Système National d'Informations Inter-Régimes de l'Assurance Maladie (SNIIRAM) database. (Julien Bezin et al.; Moulis et al., 2015; Tuppin et al., 2010) This database includes all reimbursed medical expenses, especially all dispensed drugs, as well as hospital discharge summaries and date but not cause of death. (J. Bezin et al., 2017; J. Bezin et al., 2014; Duong et al., 2016; Duong et al., 2014)

Study Population:

The study cohort included all patients in EGB aged >15 years with at least one dispensing of any antibiotic between 1 January and 31 December 2013. Patients in the study cohort were followed for 365 days after the first dispensing in 2013.

Demographic characteristics included age at the first antibiotic dispensing within the study period, gender and registration for chronic diseases (Affections de Longue Durée, ALDs). ALDs are diagnoses that result in full coverage of all medical expenses related to the disease. Prevalent ALDs were those that were present at the time of inclusion. Background medications and use of other drugs, including NSAIDs, paracetamol, aspirin, decongestants, antihistamines, cough products, aspirin, and anti-diarrheal drugs, anti-acidic drugs or antiasthmatics during follow-up were also identified by their anatomical, therapeutic and chemical (ATC) codes (http://www.whocc.no/atc_ddd_index/), which are included in the EGB database. Data abstracted included also data on hospital admissions, or deaths during the follow-up.

Exposure definition:

Each dispensing was described by the name of the antibiotic medication dispensed, number and frequency of dispensings per year, number of defined daily doses (DDD) per dispensing episode (defined as the 30-day period following the initial dispensing), and total number of DDD dispensed per year. The DDD was obtained from the WHO Collaborating Centre for drug statistics methodology (http://www.whocc.no/atc_ddd_index/). The recommended daily dose (RDD)was obtained from the 2012 French national drug formulary (VIDAL® dictionary, Paris).

In this study, we further looked of the antibiotic use of the patient group using many courses of antibiotics per year or for a longer period of time. After screening the database for high users, two cut-offs were tested, 60 and 90 DDDs/years, revealing groups of patients with less than 10% of users of antibiotic over a year. The cut-off of 90 DDDs was chosen and high users were defined as individuals using more than 90 DDDs over the period of a year. This is a rough estimate of use of antibiotics for 3 months.

Statistical analysis:

The statistical analyses were carried out using SAS® 9.2, and were limited to descriptive analyses. There was no prior hypothesis to test and no formal statistical comparisons were made. Considering the number of subjects in the samples, any descriptive difference greater than 0.1% could be considered statistically significant, and 95% confidence intervals (CIs) would be less than 1% of the point estimates.

Ethical approval:

The study was conducted using a fully anonymized database that, by decree, requires no specific ethical or data protection approval. It was registered with the French research institute INSERM overseeing body for the use of EGB data. Data used in the present study can be made available for any validation or verification, although, by law, the data cannot be forwarded or leave the country; all validations will need to be done on site.

Results:

In the EGB database, 137,358 patients aged >15 years old had at least one dispensation of antibiotic in 2013 (out of 609,205 individuals above the age of 15 in the database). Table 1 shows the demographic characteristics of antibiotic users. Females represented 56.3% of antibiotic users, yielding a crude prevalence for the use of antibiotics of 12.7% and 9.85% of the female and male French population, respectively. Their mean age was about 49 years old (± 19.2). 42.7% were between 26 and 50 years old, yielding a crude prevalence for antibiotic of 9.63% and 7.78% for those aged 50-75 years old and 50-75 years old respectively and about 2.5% for those aged 16-25 years old and >75 years old. Figure 1 shows the gender and age distribution for individuals dispensed at least one antibiotic in France in 2013.

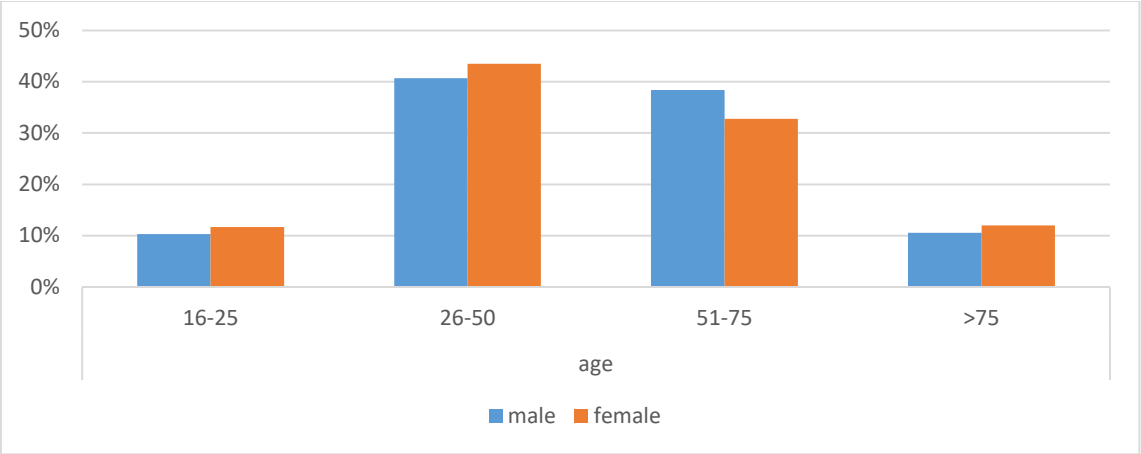

Figure 1: Gender and age specific 1-year prevalence for individuals dispensed at least one antibiotic prescription in France in 2013.

Table1: Demographic characteristics of antibiotic users

Characteristics	**Antibiotic (N= 137358)**
Age at first dispensation:	
Mean (SD)	49.2 (19.2)
SEM	0.05
Median (p25%-p75%)	48 (34, 6)
16-25	16116 (11.7%)
26-50	58681 (42.7%)
50-75	47385 (34.5%)
>75	15176 (11.1%)
Gender:	
Female	77351 (56.3%)
Male	60007 (43.6%)
% Substance users	
Amoxicillin	56959 (40.7%)
Coamoxiclav	44005 (32.0%)
Clarithromycin	15586 (11.4%)
Cefuroxime	8353 (6.08%)
Ciprofloxacin	8043 (5.86%)
Cefixime	5412 (3.94%)
Any prevalent ALD n(%):	
Presence of any ALD	47134 (34.3%)

ALD1: Cerebral vascular accident	1396 (1.02%)
ALD3: chronic arterial disease with ischemic events	2169 (1.58%)
ALD5: severe heart failure, severe valvular heart disease, serious arrhythmias, severe congenital heart disease.	4162 (3.03%)
ALD8: Type 1 diabetes and type 2 diabetes	8884 (6.47%)
ALD12: Severe arterial hypertension	3646 (2.65%)
ALD13: coronary infarction Coronary artery disease	4388 (3.19%)
ALD14: severe chronic respiratory insufficiency	2217 (1.61%)
ALD16: parkinson disease	399 (0.29%)
ALD22: severe active rheumatoid arthritis	839 (0.61%)
ALD24: ulcerative colitis and Crohn's disease scalable	556 (0.4%)
ALD30: Malignant tumor, malignant disease of lymphatic or hematopoietic tissue	8129 (5.92%)
ALD99: others	16969 (12.4%)
Dispensing of other medications in the follow-up:	
Other antibiotics	49266 (35.9%)
Paracetamol	102259 (74.4%)
Antihistamines	40261 (29.3%)
Codeine	26129 (19.1%)
Aspirin	4136 (3.01%)
NSAIDs	72030 (52.4%)
Antidiabetics	7720 (5.62%)
Antacid drugs	54710 (39.8%)
Antithrombotics	18835 (13.7%)
Antihypertensive drugs	1868 (1.36%)
Other cardiovascular drugs	34439 (25.1%)
Drugs for genitourinary system	32103 (23.4%)
Antiinfectous drugs	35434 (25.8%)
Antiasthmatics	87575 (63.8%)
Otological drugs	11278 (8.21%)
Antispasmodics	54710 (39.8%)
Antidiarrheals	38002 (27.7%)
Antiemetics	9715 (7.07%)
Topical antibiotics	17162 (12.5%)
Cough preparations	47840 (34.8%)
Nasal decongestants	51118 (37.2%)
Oral decongestants	362 (0.26%)

Amoxicillin was the most commonly dispensed antibiotic (40.7%) followed by amoxicillin/clavulanic acid (coamoxiclav) (32.0%) and clarithromycin (11.4%). 34.3% of patients had concomitant chronic diseases including diabetes, hypertension or other cardiovascular diseases.

At the time of antibiotic dispensing, patients also bought paracetamol (50.0%), followed by NSAIDs (21.8%), antihistamines (11.7%), nasal decongestants (19.1%), cough preparations (19.8%), anti-acid drugs (14.9%) or anti-asthmatics (11.9%).

During the 1-year follow-up, there was an average of 2 antibiotic dispensings (as shown in Table2). Over that year 55% had only one dispensing and 37.1% had 2 to 3 dispensings., Antibiotic users were dispensed an average of 35 DDD with a median of 24 DDD. 63.2% were dispensed ≤ 30 DDD (Table 2). The average per dispensing was 18.6 DDD. 41.1% were dispensed 8 to 14 DDD per dispensing.

Over this year, patients also bought paracetamol (74.5%), NSAIDs (50.7%), antihistamines (29.3%), anti-acid drugs (39.8%), antispasmodics (39.8%), cough preparations (34.8%)or decongestants (36.3%).

Table2: Dispensing Pattern of antibiotic users

	Antibiotic (N=232332)
Average DDD-dispensing	
Mean (SD)	18.6 (13.9)
SEM	0.028
Median (p25%-p75%)	16 (12, 24)
[1-7]	15392 (6.63%)
[8-14]	95513 (41.1%)
[15-21]	46077 (19.8%)
[22-29]	50523 (21.8%)
>29	24827 (10.7%)
Number of dispensings over a year	
Mean (SD)	1.78 (1.15)
SEM	0.002
Median (p25%-p75%)	1 (1, 2)
1	127784 (55%)
[2-3]	86090 (37.1%)
[4-6]	16854 (7.25%)
[7-12]	1594 (0.69%)
>12	10
Total number of DDD dispensed over a year	
Mean (SD)	35 (47.4)
SEM	0.098
Median (p25%-p75%)	24 (14, 42)
[1-7]	8610 (3.71%)
[8-14]	55636 (24.0%)
[15-30]	82620 (35.7%)
[31-60]	57334 (24.7%)
[61-90]	16508 (7.11%)
>90	11624 (5.00%)

The distribution of DDD at inclusion dispensing was slightly higher in males than in females but did not show a big difference between different age groups. Both were dispensed mainly 8-14 DDD per dispensation. The average consumption of DDD over a year was slightly higher in males (35.5) than in females (34.6) (Figure 2).

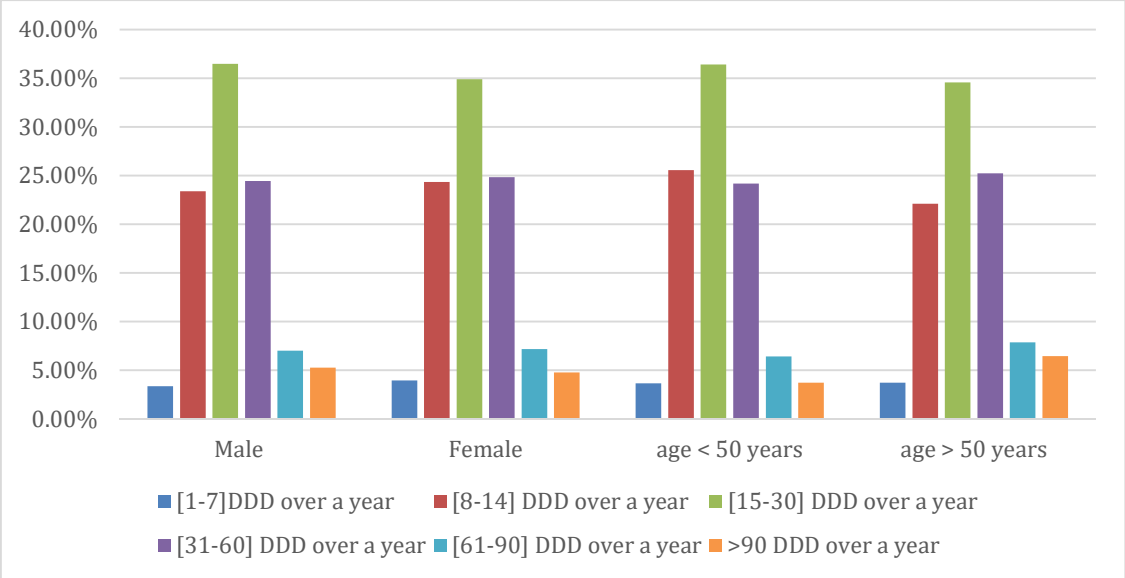

Figure 2: Average total Number of DDD dispensed per gender and age groups, over a year.

The average use of antibiotics over a year increased with age from an average of 28.4 DDD in patients aged between 16 to 25 years old to 38.6 DDD in patients aged > 75 years old (Figure 3).

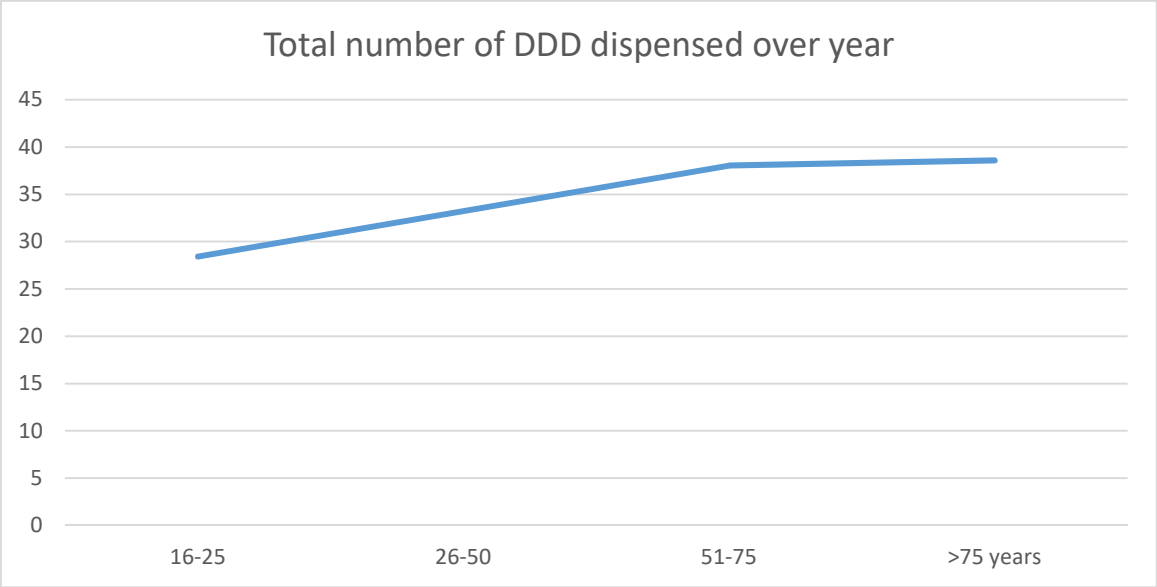

Figure 3: Average total number of DDD dispensed over year per age groups

Table 3 shows the different dispensing patterns for individual antibiotics. All were more commonly dispensed once per year except for cefixime, which was more often dispensed 2-3 times per year. They were dispensed with an average 8-14 DDD per dispensation except for

coamoxiclav, which was more dispensed as 22-29 DDD per dispensation and ciprofloxacin 1-7 DDD per dispensation. Over the course of one year, amoxicillin and coamoxiclav were more dispensed as 15-30 DDD over a year but the other antibiotics were dispensed as 1-14 DDD over a year.

Table3: Data and dispensing pattern for individual antibiotics

	Amoxicillin (N=115587)	**coamoxiclav (N=68526)**	**Cefixime (N=8618)**	**Cefuroxime (N=11037)**	**Ciprofloxacin (N=10467)**	**Clarithromycin (N=18097)**
Age at first dispensation: mean (SD)	48.2 (19.0)	50.4 (19.1)	54.9 (21.8)	48.6 (18.3)	57.1 (19.5)	49.5 (18.1)
SEM	0.056	0.073	0.23	0.17	0.19	0.13
Gender: Female	67697 (58.6%)	36630 (53.5%)	6578 (76.3%)	6613 (59.9%)	6242 (59.6%)	10711 (59.2%)
DDD (g)	1	1	0.4	0.5	1	0.5
RDD (g)	2	2	0.4	1	1	1
Number of DDD/box	3-14	3-12	4	2-8	3-6	5-30
Average DDD-dispensing						
Mean (SD)	18.47 (14.3)	23.92 (13.4)	9.53 (5.81)	9.67 (5.26)	11.6 (11.9)	13.5 (10.9)
SEM	0.04	0.05	0.06	0.05	0.12	0.08
Median (p25%-p75%)	14 (12, 24)	24 (16, 24)	8 (8, 8)	8 (8, 8)	12 (6, 12)	10 (10, 14)
[1-7]	4383 (3.79%)	55 (0.08%)	871 (10.1 %)	910 (8.24%)	4883 (46.7%)	4290 (23.7%)
[8-14]	56005 (48.5%)	11285 (16.5%)	6879 (79.8%)	8060 (73.0%)	3758 (35.9%)	9526 (52.6%)
[15-21]	24763 (21.4%)	15829 (23.1%)	583 (6.76%)	1829 (16.6%)	771 (1.67%)	2302 (12.7 %)
[22-29]	20723 (17.9%)	28354 (41.4%)	168 (1.95%)	151 (1.37%)	500 (4.78%)	627 (3.5%)
>29	9713 (8.40%)	13003 (19.0%)	117 (1.36%)	87 (0.79%)	555 (5.3%)	1352 (7.5%)
Number of dispensings over year						
Mean (SD)	1.69 (1.07)	1.82 (1.18)	2.18 (1.39)	1.74 (1.15)	2.07 (1.4)	1.84 (1.18)
SEM	0.003	0.004	0.015	0.01	0.014	0.009

Median (p25%-p75%)	1(1 ,2)	1 (1,2)	2 (1,3)	1 (1,2)	2 (1, 3)	1 (1, 2)
1	67564 (58.5%)	36562 (53.4%)	3401 (39.4%)	6287 (57.0%)	4683 (44.7 %)	9287 (51.3 %)
[2-3]	40504 (35.0%)	26025 (38.0%)	3961 (46.0%)	3933 (35.6%)	4427 (42.3%)	7240 (40.0 %)
[4-6]	6935 (6.00%)	5440 (7.94%)	1134 (13.2%)	728 (6.60%)	1193 (11.4%)	1424 (7.87%)
[7-12]	583 (0.50%)	495 (0.72%)	119 (1.38%)	89 (0.81%)	162 (1.55%)	146 (0.81%)
>12	1	4 (0.01%)	3 (0.03%)	0	2	0
Total number of DDD dispensed over a year						
Mean (SD)	33.0 (47.4)	42.3 (47.6)	30.8 (39.2)	23.1 (38.8)	35.46 (60.7)	29.4 (42.5)
SEM	0.14	0.18	0.42	0.37	0.59	0.32
Median (p25%-p75%)	24 (14, 37)	30 (24, 5)	20 (8, 38)	16 (8, 28)	18 (9, 41)	18 (10, 37)
[1-7]	2568 (2.22%)	33 (0.05%)	399 (4.63%)	528 (4.78%)	2496 (23.9%)	2586 (14.3%)
[8-14]	33524 (29.0%)	6308 (9.21%)	3046 (35.3%)	4985 (45.2%)	2058 (19.7%)	5715 (31.6%)
[15-30]	41987 (36.3%)	286324 (41.8%)	2197 (25.5%)	3098 (28.1%)	2415 (23.1%)	4289 (23.7%)
[31-60]	25956 (22.5%)	22031 (32.2%)	1991 (23.1%)	1728 (15.7%)	2017 (19.3%)	3611 (20.0%)
[61-90]	7074 (6.12%)	4895 (9.67%)	575 (6.67%)	413 (3.74%)	709 (6.77%)	1121 (6.14%)
>90	4478 (3.87%)	4895 (7.14%)	410 (4.76%)	284 (2.58%)	772 (7.38%)	784 (4.33%)

Individuals using > 90 DDD over a year represented 5.00% of the population using antibiotics. Those users were more commonly >50 years old (6.46%). However, gender difference was not pronounced (Figure 4). High users were most common with ciprofloxacin (7.38%) and coamoxiclav (7.14%) (Table 3).

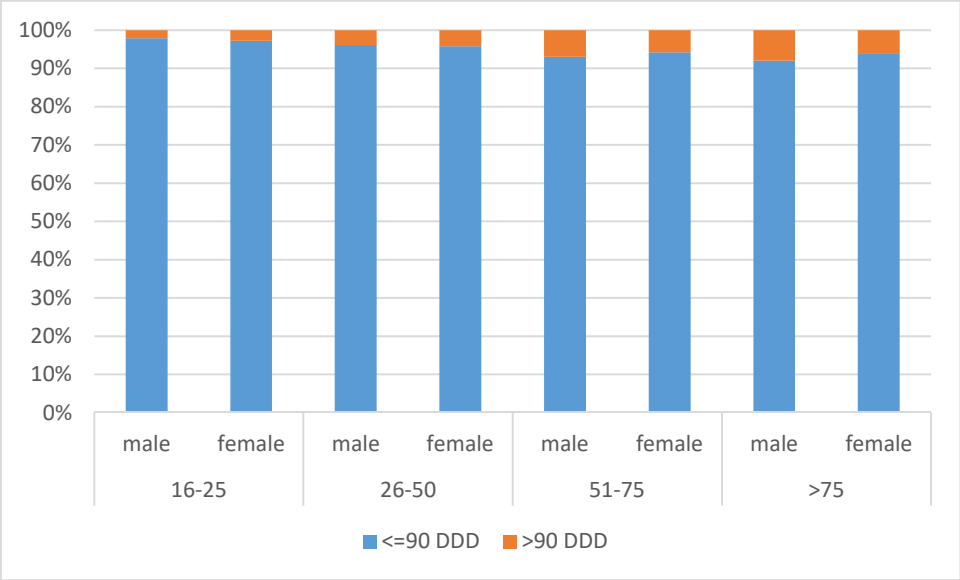

Figure 4: Age and gender distribution of patients dispensed antibiotic using under or above 90 defined daily doses (DDD) of antibiotic per year.

Amoxicillin and coamoxiclav were the most commonly dispensed in all age groups but as shown in figure 5 there was an increase in cefixime and ciprofloxacin dispensation in patients > 75 years old.

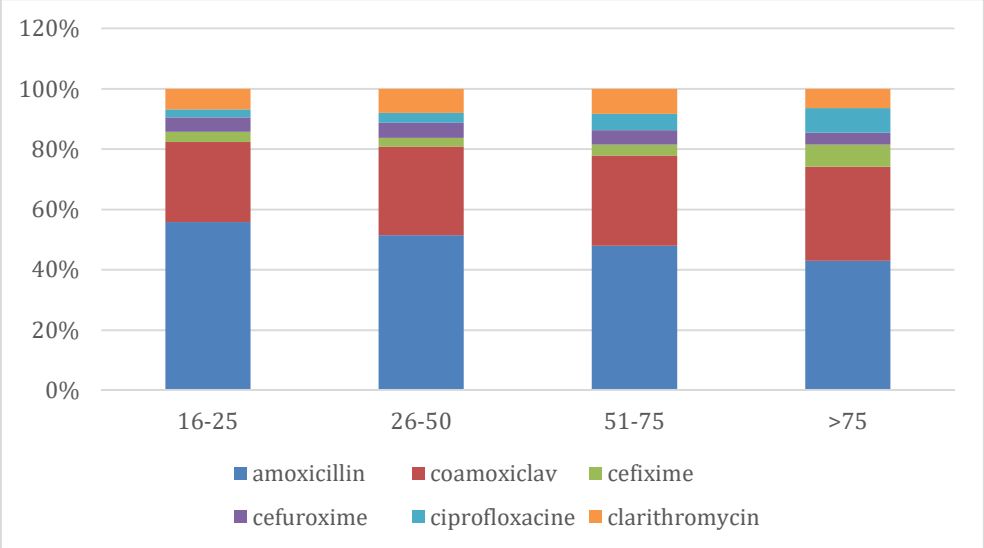

Figure 5: Type of antibiotic dispensed per age groups

Both males and females were commonly dispensed Amoxicillin and coamoxiclav; however, females were dispensed more cefixime, cefuroxime and ciprofloxacin as shown in figure 6.

Diseases of respiratory, circulatory and digestive system were the most common reasons for hospitalization among antibiotic users during antibiotic dispensing. Only 20 patients were hospitalized due to hepatic or renal drug induced disorders within a month of dispensing (0.02%). These patients had also been hospitalized for the same reasons before antibiotic dispensing.

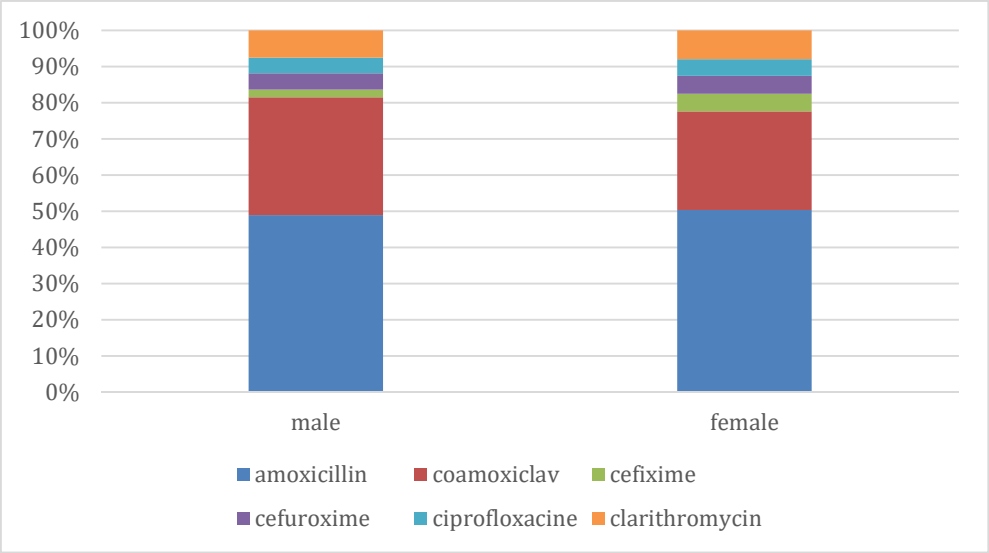

Figure 6: Type of antibiotic dispensed per gender

Discussion:

In this representative sample of the French population aged > 15years old, 22.5% of all patients were dispensed an antibiotic at least once in a year. The usage pattern of antibiotics suggested mainly upper respiratory or ENT infections since they were most commonly dispensed with cough, antihistamines, decongestants or analgesics (paracetamol, NSAIDs) and anti-acid drugs. Fifty per cent also bought paracetamol, which supports the use for acute infectious episodes – for example, ear, nose and throat infections.(Blin et al., 2010) The added risk of this combination on hepatotoxicity is unknown since very few patients were admitted for hepatotoxicity, which was also present before the antibiotic episode.

The average DDD dispensed was slightly higher in males than in females. In other countries the prevalence of antibiotic prescriptions remained higher in females than in males and also in the elderly, in this study and in the study of Lombardy region, a greater prevalence was found in males than in females.(Bronzwaer et al., 2002; Majeed & Cook, 1996) This finding is in contrast to another study done in the USA that shows that females were the main consumers of antibiotic in 2013.(Centers for Disease Control and Prevention, 2013)

Higher use of antibiotics was observed with increasing age. Differences in patterns of use with regards to age could be explained by different types of infections in different age groups. The high use of broad-spectrum antibacterials, including the shift from amoxicillin to more broad spectrum antibiotics such as coamoxiclav and cefixime in the elderly (75 years), is not unexpected because the immune response lessens with age and the prevalence of UTIs increases with age. This pattern might also be related to more bacterial resistance related to previous use of other antibiotics over time. In older patients who more frequently use other drugs than younger patients, additional attention should be focused to the increased risk of drug–drug interactions and antimicrobial resistance. This group of patients should therefore be of interest to specialists in microbiology, infectious diseases and pharmacology / pharmacotherapy.(Blix, Engeland, Litleskare, & Ronning, 2007)

Differences in the types of antibiotic used between gender groups may be explained by women having more symptomatic infections of the genital and urinary tract system then men.(Blix et al., 2007) This is shown in our data by the increased use of ciprofloxacin and cefixime by women.

It is also interesting to identify users of antibiotic > 90 DDDs over a year. This identifies patients with high antibiotics usage either for long period of time or due to repeated infections. A patient using 90 DDDs or more per year implies use in high doses or for > 3 months over the year. The high users create more problems with antibiotic resistance. High users were more common with ciprofloxacin and coamoxiclav. There is however a difference between coamoxiclav which has fewer but larger dispensings, and ciprofloxacin which has smaller dispensings. This may be explained by recurrence of urinary infections for ciprofloxacin and using coamoxiclav for longer lasting or resistant infections.

Gulliford et al.(Gulliford et al., 2009) observed that the prescription of antibiotics was higher in the treatment of respiratory tract infections (RTIs). Amoxicillin was the most frequently used antibiotic in all age groups, in males and in females. This is not surprising since amoxicillin is considered the first-choice antibiotic for most common respiratory infections. However, there was an increase in the average DDD per dispensing for coamoxiclav and cefixime with increasing age in comparison to other antibiotics. This may be related to high rate of antimicrobial resistance in France.(van de Sande-Bruinsma et al., 2008)

In 2013, the average amount dispensed per episode for cefixime, cefuroxime, ciprofloxacin and clarithromycin was 9.53, 9.67, 11.6, and 13.5 DDD respectively. This means that they are used for short term (< 2 weeks). This could contribute to the low number of post-dispensing hospital admissions for potential toxicity.

The average amount dispensed per episode for amoxicillin and coamoxiclav was high (18.5 and 23.9 respectively with medians of 14 and 24 respectively). The distribution of 70-80% of amoxicillin users was < 29 days and a few percent > 29 DDD per episode. This could be attributed to 2 or more short courses of antibiotics or to therapeutic failure.

It is important to link the distribution of the amount dispensed per episode with the recommended daily dose (RDD) and defined daily dose (DDD), and this study enabled us to determine the limits of DDD in estimating the daily doses consumed by patients per day. Amoxicillin and coamoxiclav have RDD twice number of DDD. This explains the high consumption of these antibiotics with distribution of 70-80% users were from 14 to 24 DDDs. This would represent an average of 9 RDD for amoxicillin, similar to that of the other antibiotics.

One concern of antibiotic usage is residual antibiotics, i.e., antibiotics that were dispensed but not used, leading to the constitution of stores of antibiotics that could lead to uncontrolled self-medication. In that respect, the existence of several box sizes could reduce this: for instance, most antibiotics exist in several box sizes, from 3 to 14 DDD for amoxicillin. In fact, since the RDD is double the DDD for instance for amoxicillin, that means the actual box size is 1.5 to 7 RDD, which allows for precise tailoring of the dispensing to the prescription. On the other hand, for instance cefixime exists only as 4 DDD preparations and the RDD is the same as DDD. For this drug dispensing is in multiples of 4 DDD, and any prescription that is not an exact multiple of 4 DDD will result in residual antibiotics or in wastage. However, without any information on the actual prescription and its duration, we cannot estimate the amount of residual antibiotics. However, it is likely that there is less residual antibiotics in patients with several smaller dispensings than in patients with single larger dispensings.

This study has some limits. In particular, the exposure to antibiotics could be underestimated, since self-medication from leftovers was not taken into consideration and could represent an important source of inappropriate antimicrobial use. Other limitations are common to most healthcare databases, i.e. the dearth of data concerning comorbidities, except long-term illnesses, the lack of information on drug indications and dose prescribed. This may be a major issue in countries where the amount (Blin et al., 2010; Wessling & Boethius, 1990) dispensed depends on prescription. In France, products are dispensed as boxes with a constant number of defined-strength tablets. The total quantity of drug dispensed is perfectly determined, and so the number of DDD dispensed, but this is not necessarily the exact amount actually prescribed.

Our study was limited to patients aged > 15 years old. However, pediatric patients are also an important category to measure extent of antibiotic use that could influence antibiotic resistance. In addition, the antibiotics in this study were limited to six substances and this could underestimate the extent of antibiotic usage although these antibiotics are considered the most frequent dispensed antibiotics in this area. They represent 59.4% of all antibiotics dispensed in France in 2013, based on Medicam.(Medic-am, 2013)

Conclusion:

Over 25% of the French population are dispensed antibiotics at least once per year. The increasing use of antibiotics with increasing age is not surprising, with a resulting risk of interactions. There is little doubt that antimicrobial drug consumption is important in antimicrobial drug resistance. However, additional factors such as age and gender should be taken into account when monitoring antimicrobial drug resistance and when planning educational interventions for health professionals, with the aim to improve the rational use of antibiotic drugs.

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Chapter 6:

Discussion;

Comparison of usage Pattern of antibiotic in France and Lebanon

Since their discovery in the 1920s, antibiotics have transformed our ability to treat infections. As antibiotic resistance increases, these lifesaving drugs do not work as well as they once did, and successfully treating common infections becomes more difficult. Antibiotic resistance is a growing problem across the world. The main driving factors behind antibiotic resistance are the overuse and misuse of antibiotics. Up to one-third to one-half of antibiotic use in humans is either unnecessary or inappropriate.(Centers for Disease Control and Prevention, 2013a)

Multi-resistant bacteria have become a major public health concern worldwide, and the discovery of new antibiotics is not helping much in fighting the newly emerging resistant bacteria. For example, southern and eastern Mediterranean regions have provided evidence of high rates of resistance, especially to penicillin, (Emslie & Bond, 2003) and unfortunately, the majority of the public remains ignorant of this distressing problem. (Spellberg et al., 2008)
Self-medication is a global problem especially in Middle East. Self-medication with antibiotic increases the risk for antibiotic misuse and therefore antibacterial resistance. Arguments against OTC use of antibiotic can also be persuasive. The real question, therefore, is where to draw the line. Today antibiotics are available as self-medication in Lebanon whereas in other countries such France they are available only on prescription

After we identified the usage pattern of antibiotics in France and Lebanon, we describe the usage pattern of antibiotic obtained by self-medication in Lebanon or obtained by prescription only in France,

The comparison of the usage pattern of antibiotics between a country with freely available antibiotics and one with restricted dispensing, can inform if drug status impacts on its use and whether prescription-only use could reduce misuse and the risk of antibacterial resistance.

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Discussion:

In Lebanon:

In Lebanon, self-medication of antibiotic is widely available (62.7%). This percentage is as high as that reported in neighboring countries in Jordan (59.1%) (Shehadeh et al., 2012) and in Syria (85%). (Barah & Goncalves, 2010) It is similar also to other countries in the Middle East such as Emirates (56%) (Abasaeed, Vlcek, Abuelkhair, & Kubena, 2009), Iran (57.6%) (Heidarifar, Koohbor, Kazemian, Mikaili, & Sarahroodi, 2013), or Yemen (60%) (Mohanna, 2010). However, it was relatively higher than that reported by Cheaito et al (40%) in a study that was restricted to Beirut and its suburbs. (Cheaito, Azizi, Saleh, & Salameh, 2014)

Antibiotic misuse is widely observed in Lebanon. Previous successful use of antibiotic and easy availability of antibiotic and availability of pharmacist consultation were the main factors resulting in an increase in the use of antibiotics. Similar results were reported in many other Middle East countries as in Emirate, pharmacies were the main source for antibiotics (74%) (Sharifi et al., 2013), in Jordan (53.6%) (Sawair, Baqain, Abu Karaky, & Abu Eid, 2009), in Libya (75%). (Ghaieth, Elhag, Hussien, & Konozy, 2015) and in Iran (61.2%). (Ghaieth et al., 2015) Parents or friends are an important source of self-medication. In Jordan, 51.8% of adult patients use antibiotics based on a relative's advice. (Shehadeh et al., 2012) Similarly in Iran (54.7%). (Heidarifar, Koohbor, Kazemian, et al., 2013) Prescription of antibiotics by physicians over phone was also an important contributing factor for misuse (Suaifan et al., 2012). Long waiting time to be seen by doctors (James, Handu, Khaja, & Sequeira, 2008; Yousef, Al-Bakri, Bustanji, & Wazaify, 2008) and avoiding the cost of doctors' visits were also reported as common reasons for self-medication. (Yousef et al., 2008) In addition, cognitive related factors, such as knowledge or social norm and perceived severity of illness can also predict self-medication behaviour. (Figueiras, Caamano, & Gestal-Otero, 2000)

Coamoxiclav was the most commonly used antibiotic among Lebanese participants, followed by cephalosporins. This result replicates findings reported in Lebanon (48.9%). (Cheaito et al., 2014), Libya, Tunisia, Egypt(Scicluna et al., 2009), United Arab Emirates (Abasaeed et al., 2009), Pakistan (Qazi, Bano, Zafar, Shoaib, & Yousuf, 2013), Iran (Heidarifar, Koohbor, Kazemian, et al., 2013) and Jordan (Sawair et al., 2009). Using broad spectrum antibiotics instead of narrow spectrum antibiotics even if they are safe and effective increases the chance of emergence of antibiotic resistance.

The overall appropriateness of antibiotics used without prescription is very low (16.4%). This is due to multiple factors including availability of antibiotics as self-medication, misconceptions of the correct indication and use of antibiotic, poor compliance to complete drug therapy, effect of influence of friends and family, and time constraints. (Afolabi, 2008; Belongia, Naimi, Gale, & Besser, 2002; Sosa et al., 2010)

The rapid relief of signs and symptoms related to the complaint disease causes patients to stop the antibiotic early: 31.4% of patients who self-medicate stop the antibiotic early when compared to the duration recommended in IDSA guideline. Poor compliance with antibiotic therapy has a great impact on antibiotic misuse. Most Lebanese participants did not complete the full course of antibiotic (72.4%). Low compliance was reported by many other countries including Jordan (40%) (Darwish, Abdelmalek, Abu Dayyih, & Hamadi, 2014), Kuwait (64%) (A. I. Awad & Aboud, 2015), United Arab Emirates (75%). (Suleiman & Rubian, 2013) Reasons most frequently mentioned by patients for non-compliance were: rapid improvement of symptoms, forgetfulness and frequent dosing. (Al-Shammeri, Khoja, & Al-Yamani, 1995) .

32.2% of patients who self-medicate misused antibiotics for symptoms related to viral infections or upper respiratory tract infections (URTIs). Our study identified the most common symptoms for which the participants would self-medicate themselves were mainly symptoms of cough and cold and other upper respiratory tract infections. This could be explained due to low participants' knowledge about the efficacy of antibiotics against bacteria, viruses, cough, cold and sore throat. This explains the misconception present among the study population regarding the role of antibiotic. The results of this study are similar to those reported in Middle East countries such as Jordan(Alzoubi et al., 2013; Shehadeh et al., 2012)or Kuwait, (A. Awad, Eltayeb, Matowe, & Thalib, 2005)or in European countries such as Greece, (Skliros et al., 2010) Britain, (McNulty, Boyle, Nichols, Clappison, & Davey, 2007) or Slovak Republic. (Tesaf, Foltan, Langsadl, & Binder, 2005) In Britain 38% of respondents did not know that antibiotics cannot resolve most cough and colds. (McNulty et al., 2007) In Slovak Republic patients thought that flu is a reason for antibiotic use. 67.1% of the public in Slovak Republic believed that antibiotics treat common cold and cough. (Tesaf et al., 2005) In Greece people tend to self-medicate for common cold and sore throat. (Skliros et al., 2010) Another study done in Europe showed that bronchitis and minor illnesses were the two main significant factors related to self-medication. (Grigoryan et al., 2008) In Jordan or Kuwait, many people thought that antibiotics were effective against cough, cold and many viral infections. (Alzoubi et al., 2013; A. Awad et al., 2005; Shehadeh et al., 2012)

The poor attitude and knowledge score in Lebanon was not surprising. This finding is similar to that of neighboring countries such as Jordan. (Alzoubi et al., 2013) These results were supported by the high proportion of Lebanese participants using antibiotic for common cough cold and sore throat symptoms.Our results identified demographic groups with poor knowledge and attitude toward antibiotic use. Young age, female, higher educational level and higher income with medical insurance show better knowledge and attitude score. Other studies in the Middle East reported significant association between self-medication and age, male gender, education level and lower socioeconomic status. (Belkina et al., 2014; Farah, Lahoud, Salameh, & Saleh, 2015; Jafari, Khatony, & Rahmani, 2015) Studies in Europe and Britain reported significant association between educational level (McNulty et al., 2007)and lower income (Grigoryan et al., 2008) with self-medication practices.

The incorrect use could cause the development of resistant bacteria and diminish the ability of the endogenous flora to resist colonization by harmful microorganisms, thereby leading to super infections by multi-resistant bacteria and yeasts. (Barbosa & Levy, 2000)There have been reports of a general lack of knowledge of correct antibiotic use and a lack of public awareness on the basic principles of antibiotic use, as well as indication for therapy. (Hawkings, Butler, & Wood, 2008) There are also common misconceptions regarding the use of antibiotics, especially for common indications like URTIs, as it is believed that the use of antibiotics results in quick recovery and prevents more serious illness.(Richman, Garra, Eskin, Nashed, & Cody, 2001)

The overall average dispensing of antibiotics was 9.07 DDD, indicating short term use (< 2 weeks). The average number of requests per year i.e., 3.35 times,was high. The usage pattern of antibiotics was not different between patients buying antibiotics with or without prescription; however, the number of yearly request of antibiotic was significantly higher in patients practicing self-medication. More than 50% requested antibiotics more than twice per year. This could be attributed to therapeutic failure, to increase in antibiotic resistance, or the treatment of viral affections.The average number of DDD per dispensing was not different between participants with or without prescriptions. Higher use of antibiotics was observed in younger patients. Differences in patterns of use with regards to age could be explained by different types of infections. The shift from beta-lactams to more broad spectrum antibiotics such as

cephalosporins and fluoroquinolones in the older age (>50 years), is not unexpected because the immune response lessens with age and the prevalence of UTIs increases with age. The use of more DDD in younger age should raise awareness regarding the increase risk of bacterial resistance over time.

The average DDD consumed by patient was 7.07 DDD and 62.5% were consumed between 1 to 7 DDD. This percentage is lower than that dispensed initially. This should raise concern for residual antibiotics i.e., antibiotics that were dispensed but not used. These may result in uncontrolled self-medication and inappropriate use. Patients probably stopped the medication as soon as the symptoms disappear, either because of poor compliance due to poor medical knowledge or use of the antibiotic for conditions for which the medication was not indicated. This results in using the antibiotic beyond the scope and increasing the daily dose of antibiotic and increasing the risk of antibiotic resistance.

The average consumption per day of coamoxiclav, amoxicillin, or macrolides was 2.00, 1.4 and 1.41 DDD, respectively. Amoxicillin, coamoxiclav, and clarithromycin have mean daily doses twice the number of DDD. This study highlights the limits of DDD in estimating the daily doses consumed by patients per day. The effect, if any, of this increased dosage on bacterial resistance is unknown. Estimates of antibiotic use using DDD methods will remain open to criticism because the prescribed dosage, especially of antibiotics, often deviates from the “theoretical" daily dose, depending for instance on the location of the infection, pathogen susceptibility, or the excretory status of the patient.(Polk, Fox, Mohaney, Letcavge, & MacDougall, 2007)

We compared the consumed prescribed daily dose (PDD) per day to the recommended daily dose in the French national drug formulary (VIDAL). The PDD of antibiotics consumed by each patient was highly appropriate (83.7%). This could be explained by the role of pharmacists in guidance of customers on the appropriate use of antibiotics. It is also due to previous experience or previous prescription of the same antibiotic; thus, physicians indirectly contributed to these self-medicated drugs. Moreover, many patients have requested antibiotic several times per year which explain the high percentage of conformity of dosage compared to VIDAL.

In France:

In France, 22.5% of all patients were dispensed an antibiotic at least once in a year. The average amount of DDD dispensed per episode was 18.6 DDD. This means that antibiotic was used for short term treatment, especially since DDD underestimate the actual PDD. If one considers that the actual dose used is twice the DDD, as in Lebanon, then the average duration of treatment will not be 18 days (from DDD) but more likely 9 days or less (from PDD). The indications of antibiotics appear to be mainly upper respiratory or ENT infections since they were most commonly dispensed with cough, antihistamines, decongestants or analgesics (paracetamol, NSAIDs) and anti-acid drugs. Fifty per cent also bought paracetamol, which supports the use for acute infectious episodes – for example, ear, nose and throat infections, or viral episodes.(Blin et al., 2010) Amoxicillin was the most frequently used antibiotic in all age groups, in males and in females. This is not surprising since amoxicillin is considered the first-choice antibiotic for most common respiratory infections.

The average DDD dispensed over a year was slightly higher in males than in females. Higher use of antibiotics was observed with increasing age. In this study and in the study of Lombardy region, a greater prevalence was found in males than in females and also in the elderly. (Blix, Engeland, Litleskare, & Ronning, 2007)This finding is in contrast to another study done in the USA that shows that females were the main consumers of antibiotics in 2013.(Centers for Disease Control and Prevention, 2013b)

Higher use of broad spectrum of antibiotics was observed with increasing age or in females including the shift from amoxicillin to more broad spectrum antibiotics such as coamoxiclav and cefixime in the elderly (75 years). This is not unexpected because the immune response lessens with age and the prevalence of UTIs increases with age. This pattern might also be related to more bacterial resistance related to previous use of other antibiotics over time. Women have more symptomatic infections of the genital and urinary tract system then men.(Blix et al., 2007)

In this study, we further looked at the antibiotic use of the patient group using many courses of antibiotics per year or for a longer period of time. After screening the database for high users, two cut-offs were tested, 60 and 90 DDDs/years, which represent fewer than 10% of users over a year. High users were defined as individuals using more than 90 DDDs over a year. This is a rough estimate of use of antibiotics for 3 months in a year. This helps us to identify patients using antibiotic for long period of time or repeated infections. High users were observed with increasing age and in males. This result is consistent with the study conducted in Norway. (Blix et al., 2007) High users were also observed with coamoxiclav and ciprofloxacin since ciprofloxacin is used for recurrent urinary tract infections and coamoxiclav for resistant infections. These users contribute more to antibacterial resistance.

The average amount dispensed for each antibiotic substance per episode was less than 14 DDD, which means that they are used for short term (<2 weeks). Comparing the RDD and DDD enable us to understand the limits of using DDD methods in estimating daily dose of antibiotic consumed by patient per day. This is identified for certain antibiotics especially for amoxicillin and coamoxiclav. Their RDD is 2 grams/day while their DDD is 1 gram/day. They have RDD double that of DDD. For example, amoxicillin and coamoxiclav have an average 18.5 DDD and 24 DDD respectively which is equivalent to 9 RDD and 12 RDD respectively. So, they can't be identified as high users within dispensation.

It is important also to link the amount of DDD dispensed to the information of the actual prescription. This enabled us to reduce the amount of residual antibiotics. In that respect, the existence of several box sizes could reduce this: for instance, most antibiotics exist in several box sizes, from 3 to 14 DDD for amoxicillin. In fact, since the RDD is double the DDD for instance for amoxicillin, that means the actual box size is 1.5 to 7 RDD, which allows for precise tailoring of the dispensing to the prescription. On the other hand, for instance cefixime exists only as 4 DDD preparations and the RDD is the same as DDD. For this drug dispensing is in multiples of 4 DDD, and any prescription that is not an exact multiple of 4 DDD will result in residual antibiotics or in wastage.

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Comparison of antibiotic Dispensing Patterns between France and Lebanon

Abstract:

Objective: Usage pattern of antibiotic is a major health concern for antibiotic resistance. To compare the usage pattern of antibiotics the usage pattern of antibiotics between a country with freely available antibiotics and one with restricted dispensing i.e. France.

Method: Data about antibiotic usage in France was extracted from healthcare database (EGB database) in 2013 to identify usage pattern of antibiotics. In Lebanon, data was obtained through a structured questionnaire filled in community pharmacy by patients requesting for antibiotic with or without prescription.

Result: The average of dispensing for these antibiotic was higher in France (18.6 DDD) than that in Lebanon (10.6DDD). However, the average of dispensings in Lebanon was 3.39 per year higher than that in France (2 per year). It was not different between participants with or without prescriptions. coamoxiclav is widely consumed in Lebanon as both prescription and as self-medication whereas amoxicillin was the main antibiotic consumed in France.

Conclusion: Antibiotics were more commonly dispensed in Lebanon when compared to France. Public awareness and educational programs should be implemented for patients and pharmacists to limit the self-medication use of antibiotics.

Keywords: France, Lebanon, Usage Pattern, Antibiotic, DDD.

Introduction:

The era of antibiotics transformed the treatment and outcome of infectious diseases. Antibiotics have marked a revolution in public health of human history by limiting the spread of infectious diseases and therefore saving millions of lives. However, irrational use of antibiotics is a global problem and the rate of this problem and antibiotics resistance is increasing in Middle-east. (Al-Tawfiq, Stephens, & Memish, 2010)Several reports from different countries (Al-Tawfiq et al., 2010)reveal high antibiotics self-medication world-wide. Antibiotic self-medication can produce harmful effects on both society and individuals such as antibiotics resistance.

Countries where over the counter antibiotic sales are strictly regulated have much lower prevalence rates of self-medication with antibiotics, ranging from 1 to 4 %. (Grigoryan et al., 2007) However, antibiotics are obtained without prescription in many developing countries. (Sosa et al., 2010)A review about antibiotic use in developing countries (Radyowijati & Haak, 2001) reported that people believed antibiotics as “an extraordinary medicine” or “a powerful medicine” or “a strong medicine” which are able to prevent and cure any diseases or symptoms. The knowledge and attitude toward antibiotics are important contributing factors in the misuse of these medications. There is a limited understanding of which infections might require antibiotics and the safety and risks of such misusage. (Khalifeh, Moore, & Salameh, 2017)

In France, antibiotics are available only as prescription and therefore their use is captured in population databases, including electronic health records or claims reimbursement databases. While in Lebanon like most other developing countries antibiotics can be obtained without prescription and can only be identified from field studies.(Fendrick et al., 2004) This study compares the usage pattern of antibiotics between France and Lebanon and explores patterns of age and gender specific use.

Method:

Data Source and Study population:

In France, data was extracted from the Echantillon Généraliste de Bénéficiaires (EGB) database, a permanent representative 1/97 sample of the nationwide Système National d'Informations Inter-Régimes de l'Assurance Maladie (SNIIRAM) database. (Bezin et al., 2017; Moulis et al., 2015; Tuppin, de Roquefeuil, Weill, Ricordeau, & Merliere, 2010)The study cohort included all patients in EGB aged >15 years with at least one dispensing of any antibiotic between 1 January and 31 December 2013. Patients in the study cohort were followed for 365 days after the first dispensing in 2013.

In Lebanon, a prospective study was conducted in a community-based pharmacy setting in Lebanon. Data was collected over a 1-year period (September 2015 to September 2016) from 50 community pharmacies (CPs) distributed in the six districts in Lebanon: Beirut, South Lebanon, Nabatiyeh, Mount Lebanon, Bekaa, and North Lebanon.

Eligible participants were recruited randomly from consumers presenting at CPs in Lebanon after they had purchased antibiotic medication with or without prescription. The patients included were from both genders, aged 16 years and older, coming to purchase antibiotic. Data on antibiotic use was collected using a structured random interview conducted by pharmacists or interviewers who had been briefed about the study's aims and methods. Data was collected from the participants twice, first at purchase for data about drug used and the condition for which it was to be used, then by calling the patient 30 days after starting the medication, for usage patterns.

Data Collection:

In France, demographic characteristics were included as age at the first antibiotic dispensing, gender and registration for chronic diseases (Affections de Longue Durée, ALDs), background medications and use of other drugs during antibiotic dispensing.

In Lebanon, the questionnaire of the following sections: socio-demographic data (age, sex, occupation, educational and marital status, monthly income, medical insurance, and the presence of a care provider at home), complaint for which the antibiotic is taken, the medication details (name, dose, duration and mode of administration as recommended to be taken), presence of comorbidities (defined as long-term diseases diagnosed by physicians) and background medications, as well as reasons and sources of self-medication.

Thirty days after starting the medication, patients were assessed about adherence and duration of antibiotic consumed, direction of use, and reasons for misuse.

Data Analysis:

Each dispensing was described by the name of the antibiotic medication dispensed, number and frequency of dispensings per year, number of defined daily doses (DDD) per dispensing episode (defined as the 30-day period following the initial dispensing). The DDD was obtained from the WHO Collaborating Centre for drug statistics methodology (http://www.whocc.no/atc_ddd_index/). The recommended daily dose (RDD)was obtained from the 2012 French national drug formulary (VIDAL® dictionary, Paris).

The dispensing pattern of 6 classes of antibiotics (coamoxiclav, amoxicillin, cefixime, cefuroxime, ciprofloxacin and clarithromycin) were compared between France and Lebanon since these antibiotics were the most commonly dispensed antibiotics in France (60%) based on Medicam.(Medic-am, 2013)

The comparison was limited to descriptive analysis and was carried out using SAS® 9.2 in France and SPSS version19 (the IBM Corporation, Armonk, NY) in Lebanon. Considering the number of subjects in the samples in France, any descriptive difference greater than 0.1% could be considered statistically significant. In Lebanon, an appropriate bivariate analysis was done using Chi-2 for dichotomous variables to compare 2 percentages and T-test or ANOVA for nominal and ordinal variables to compare 2 means of 2 groups or more. A p-value of 0.05 or less was considered to be statistically significant in all tests.

Ethical approval:

In France, the study was conducted using a fully anonymized database that, by decree, requires no specific ethical or data protection approval. It was registered with the French research institute INSERM overseeing body for the use of EGB data. In Lebanon, the Lebanese University, faculty of Pharmacy Internal Review Board waived the need for written informed consent. The patients were informed about the objective of the study and were asked to give an oral consent. Only those who gave their voluntary informed oral consent were enrolled.

Results:

In France, 137,358 patients aged >15 years old had at least one dispensing of an antibiotic in 2013. Females represented 56.3% of antibiotic users, 42.7% were between 26 and 50 years old. 34.3% of patients had concomitant chronic diseases including diabetes, hypertension or other cardiovascular diseases. At the time of antibiotic dispensing, patients also bought paracetamol (50.0%), followed by NSAIDs (21.8%), antihistamines (11.7%), nasal decongestants (19.1%), cough preparations (19.8%), anti-acid drugs (14.9%) or anti-asthmatics (11.9%). (Table 1)

In Lebanon, a total of 501 participants were recorded. Among participants, 314 (62.7%) requested an antibiotic without prescription while 187 (37.3 %) had a medical prescription for their antibiotic. Both groups were homogenous regarding gender (p=0.154), age (p=0.532). A total of 109 (21.8%) suffered from chronic diseases, among which hypertension, asthma or COPD, dyslipidemia, diabetes, gastric diseases, and osteoarthritis. At the time of antibiotic dispensing, patients also bought paracetamol (28.3%), followed by NSAIDs (20.9%), antihistamines (15.2%), cough preparations (6.52%), nasal decongestants (1.3%) or anti-acid drugs (1.74%). (Table 1)

In France, amoxicillin was the most commonly dispensed antibiotic (40.7%) followed by amoxicillin/clavulanic acid (coamoxiclav) (32.0%) and clarithromycin (11.4%). In Lebanon, coamoxiclav was the most purchased antibiotic (49.0 %) followed by cefuroxime (15.5%), amoxicillin (12.8%) and clarithromycin (11.7%). Coamoxiclav was the most frequently dispensed antibiotic without prescription (53%) followed by amoxicillin (16.9%), cefuroxime (15.1%), clarithromycin (8.2%) and cefixime (5.9%). The antibiotics dispensed with a prescription were, in the following descending order: coamoxiclav (41.9%), clarithromycin (17.7%), cefuroxime (16.1%), ciprofloxacin (10.5%), cefixime (8.1%) and amoxicillin (5.6%). (Table 1)
In Lebanon, 60.3% were dispensed 8-14 DDD per dispensing with an average 10.6 DDD. The average of dispensings was higher than that in France (3.39 per year). More than 50% of participants used antibiotics more than twice per year where 29.2% used antibiotics 2 to 3 times per year and 20.4% 4 to 6 dispensings per year. There was no significant difference between patients requesting antibiotic with or without prescription. Patients requesting antibiotic without prescription have requested mainly more 2-6 times per year (53.5%) while patients with prescription have requested mainly once per year (41.5%) but the result was not statistically significant. (Figure 1)

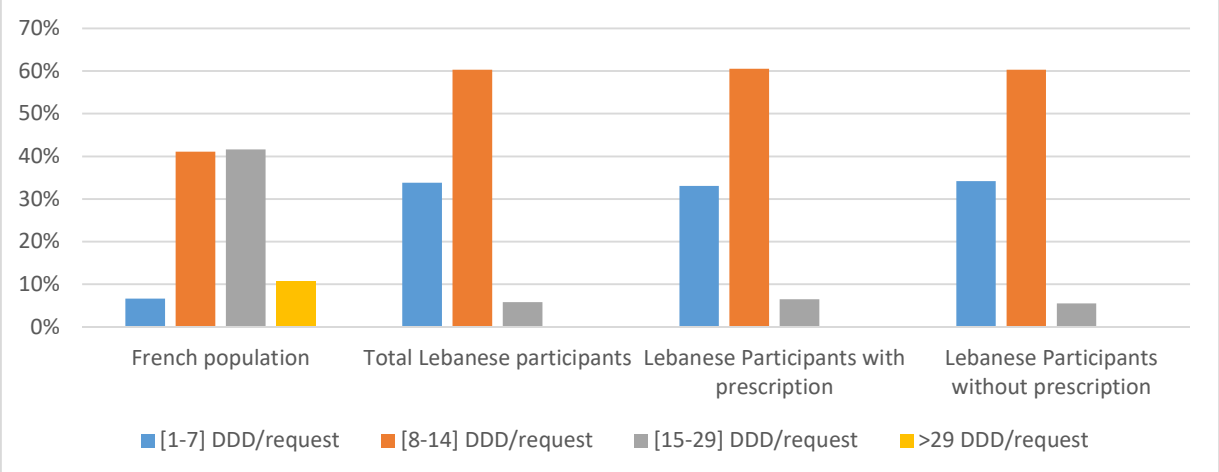

Figure 1: Distribution of DDD per dispensing for French and Lebanese participants

Table 1: Sociodemographic Characteristics of study participants:

	France	**Lebanon**			
Characteristics	Total participants (N=137358)	Total participants (N=343)	With prescription (N=124)	Without prescription (N=219)	p-value with vs. without prescription
Age at first dispensation					
16-25	16116 (11.73%)	155 (45.2%)	57 (46%)	115 (52.5%)	0.507
26-50	58681 (42.72%)	149 (43.4%)	54 (43.5%)	84 (38.4%)	
>50	62561 (45.7%)	39 (11.4%)	13 (10.5%)	20 (9.1%)	
Gender:					
Female	77351 (56.31%)	348 (70.3%)	91 (73.4%)	150 (68.5%)	
Male	60007 (43.69%)	102 (29.7%)	33 (26.6%)	69 (31.5%)	0.341
% Substance users					
Amoxicillin	56959 (40.7%)	44 (12.8%)	7 (5.6%)	37 (16.9%)	<.001
Amoxicillin/clavulanic	44005 (32.0%)	168 (49%)	52 (41.9%)	116 (53%)	
Cefixime	15586 (11.4%)	23 (6.7%)	10 (8.1%)	13 (5.9%)	
Cefuroxime	8353 (6.08%)	53 (15.5%)	20 (16.1%)	33 (15.1%)	
Ciprofloxacine	8043 (5.86%)	15 (4.4%)	13 (10.5%)	2 (13.3%)	
Clarithromycine	5412 (3.94%)	40 (11.7%)	22 (17.7%)	18 (8.2%)	
Presence of comorbidities	47134 (34.31%)	74 (21.6%)	25 (20.2%)	49 (22.4%)	0.632
Hypertension and other cardiovascular diseases	3646 (2.65%)	15 (4.4%)	5 (4%)	10 (4.6%)	
Osteoarthritis	839 (0.61%)	14 (4.1%)	6 (4.8%)	8 (3.7%)	
Diabetes	8884 (6.47%)	13 (3.8%)	14 (7.5%)	5 (1.6%)	
Chronic Respiratory insufficiency	2217 (1.61%)	11 (3.2%)	7 (5.6%)	4 (1.8%)	
Ulcerative colitis and chron's disease	556 (0.4%)	11 (3.2%)	6 (4.8%)	5 (2.3%)	
Dyslipidemia	4162 (3.03%)	15 (4.4%)	8 (6.5%)	7 (3.2%)	
Depression	943 (0.69%)	7 (2%)	3 (2.4%)	4 (1.8%)	
Cancer	8129 (5.92%)	1 (0.2%)	0	1 (0.3%)	

Data presented as number (%) were performed using Chi2 respectively and a p-value < 0.05 is considered significant.

In France, the average per dispensing was 18.6 DDD. 41.1% were dispensed 8 to 14 DDD per dispensing. The average of dispensings was 2 antibiotic dispensing per year. Over year 55% had only one dispensing and 37.1% had 2 to 3 dispensings. (Figure 2)

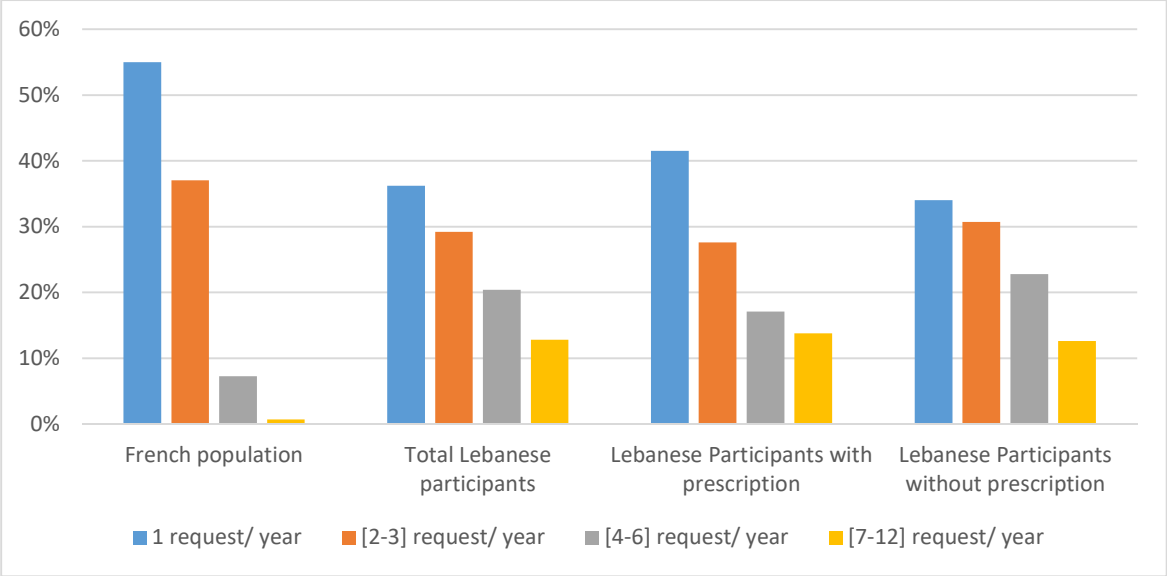

Figure 2: Distribution of the average request of antibiotic per year for French and Lebanese participants

In France, the distribution of DDD at inclusion dispensing was slightly higher in males than in females but did not show a big difference between different age groups. Both were dispensed mainly 8-14 DDD per dispensation. In Lebanon, the distribution of DDD didn't show a significant difference between age groups. Males were significantly dispensed more 8-14 DDD (74.5%) than female (54.4%, p<.001). (Figure 3)

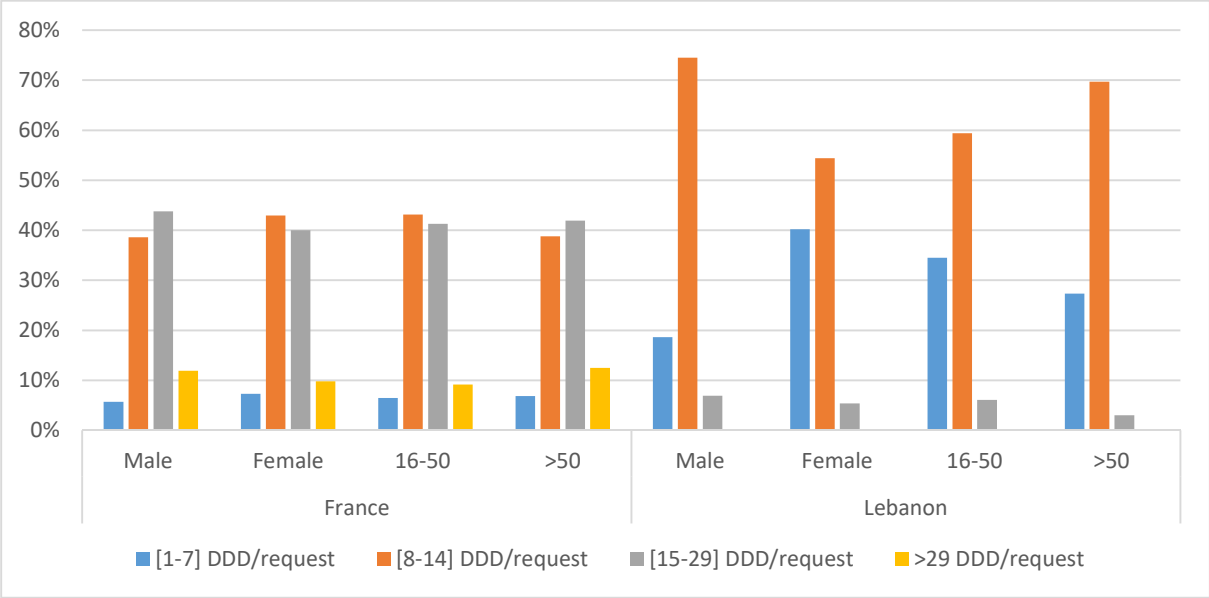

Figure 3: Distribution for DDD per dispensing for age and gender groups for French and Lebanese participants.

In France, number of dispensings per year didn't show a significant difference between gender and age groups. In Lebanon, Younger patients were dispensed mainly once per year (38.7%) while older patients have requested mainly 2-3 times per year (36.4%) (p=.013). In France, about half of the patients were dispensed mainly once per year. (Figure 4)

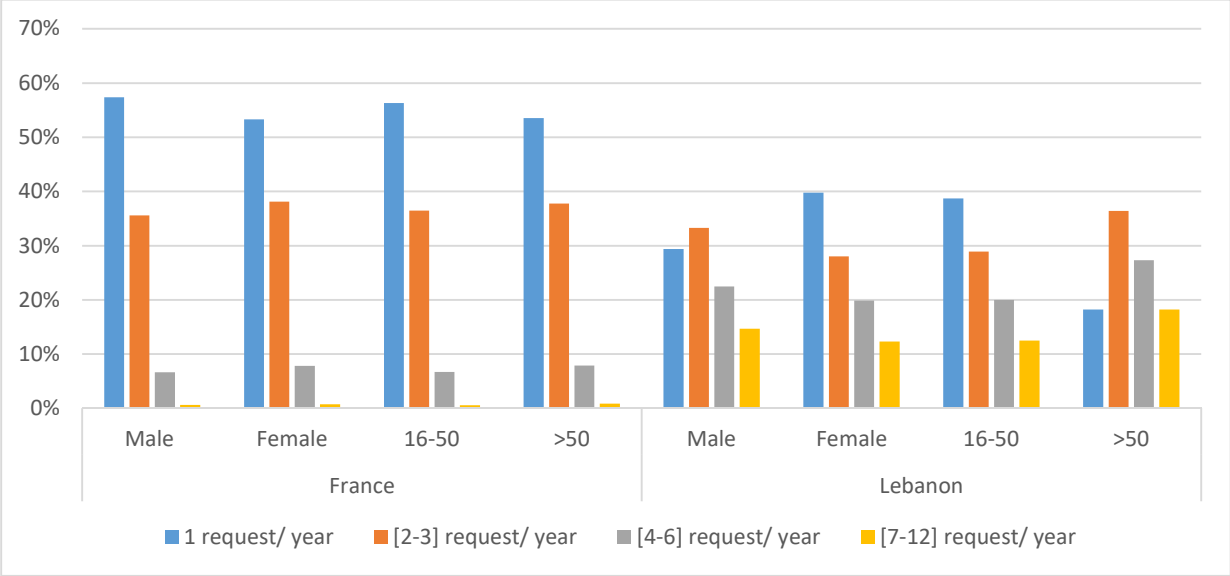

Figure 4: Distribution for the request per year of antibiotic for age and gender for French and Lebanese participants.

When comparing the dispensing pattern for antibiotic classes we found that in France all antibiotics were more dispensed with an average 8-14 DDD per dispensation except for coamoxiclav, which was more dispensed as 22-29 DDD per dispensation and ciprofloxacin 1-7 DDD per dispensation. They were more commonly dispensed once per year except for cefixime, which was more often dispensed 2-3 times per year. In Lebanon, all antibiotics were more commonly dispensed 1-7 DDD except for coamoxiclav and cefixime which were more dispensed as 8-14 DDD per dispensation. coamoxiclav and amoxicillin were more commonly dispensed 2-3 times per year while other antibiotics were more dispensed once per year. (Figure 5)

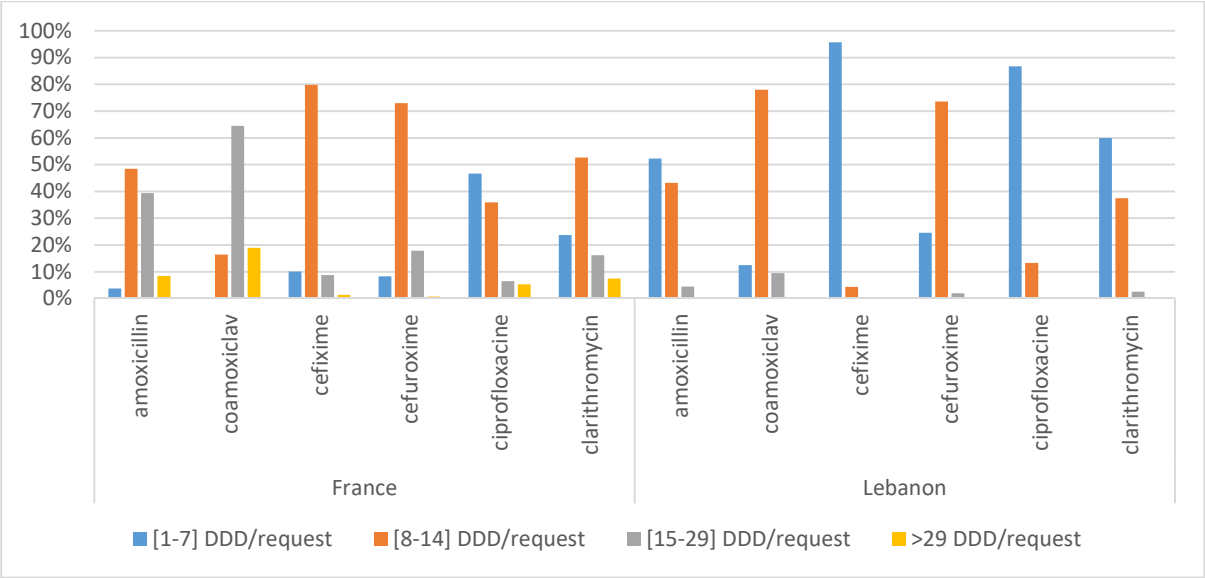

Figure 5: Distribution of the average of DDD per dispensing for the antibiotic substances for French and Lebanese participants.

In France, amoxicillin and coamoxiclav were the most commonly dispensed in all age groups but there was an increase in cefixime and ciprofloxacin dispensation in patients > 50 years old. Both males and females were commonly dispensed amoxicillin and coamoxiclav; however, females were dispensed more cefixime, cefuroxime and ciprofloxacin. In Lebanon, younger participants were dispensed more coamoxiclav (50%) followed by cefuroxime (13.9%),

amoxicillin (12.9%) and clarithromycin (12.9%) while older participants were dispensed more coamoxiclav and cefuroxime (30.3%) followed by amoxicillin and ciprofloxacin (12.1%). The result was statistically significant (p=.01). Males were mainly dispensed coamoxiclav (64.7%) followed by cefuroxime (13.7%) and clarithromycin (8.8%) while females dispense mainly coamoxiclav (42.3%), cefuroxime (16.2%), amoxicillin (15.4%), clarithromycin (12.9%) and cefixime (8.3%). The result was significant (p=.006). (Figure 6)

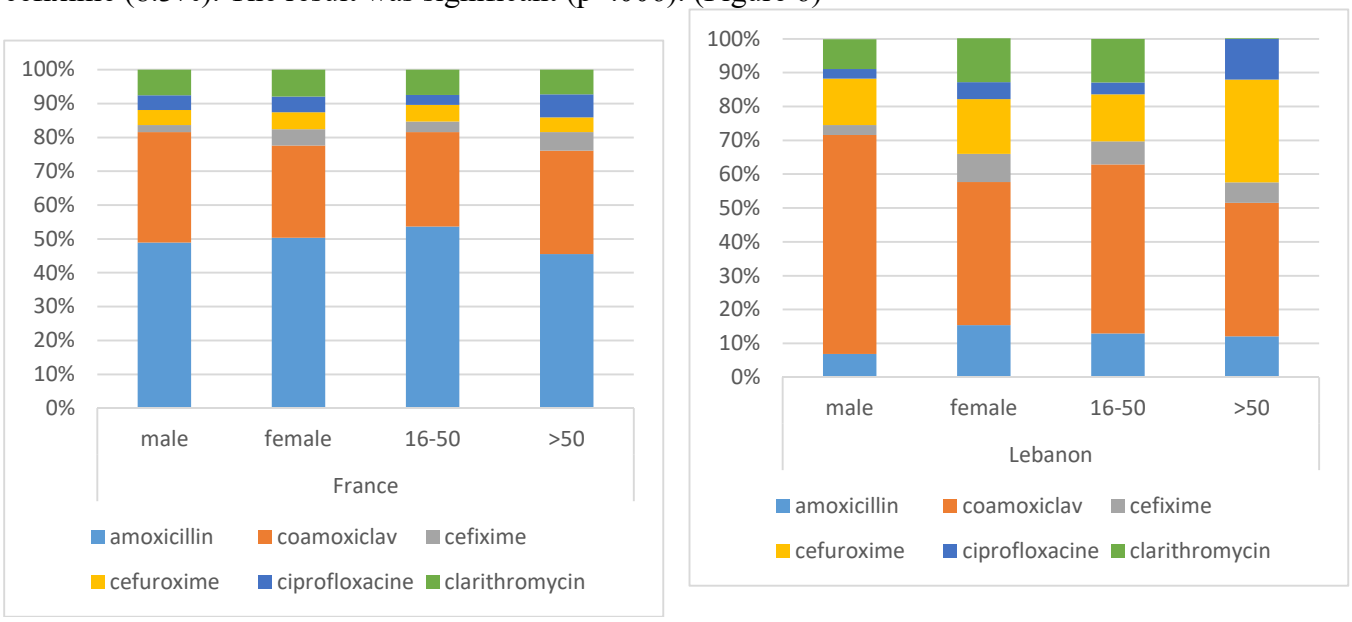

Figure 6: Distribution of antibiotic substance per gender and age groups for France and Lebanon

Discussion:

This study found clear differences between the usage patterns of antibiotics in Lebanon and in France. Coamoxiclav is widely consumed in Lebanon as both prescription and as self-medication whereas amoxicillin was the main antibiotic consumed in France. The average dispensing for these antibiotics was higher in France (18.6 DDD) than that in Lebanon (10.6DDD). However, the average number of dispensings in Lebanon was 3.39 per year, higher than in France (2 per year). It was not different between participants with or without prescriptions.

The usage pattern of antibiotic in both Lebanon and France suggested mainly upper respiratory tract infections (URTI). They were dispensed mainly with cough, antihistamines, decongestants and analgesics. In France, the indications for antibiotic use were not provided by French healthcare database due to lack of information on drug indication, though it can be presumed in most cases by the co-dispensed medications. In Lebanon, the most common indications for antibiotic use without prescription were URTI mainly tonsillitis and flu followed by gastrointestinal and urinary tract infections. Most patients reported the use of paracetamol, which supports the use of antibiotic for acute infectious episodes – for example, ear, nose and throat infections.(Blin et al., 2010)These findings are consistent with results of other studies in Abu-Dhabi, (Abasaeed et al., 2009) Iran, (Heidarifar, Koohbor, Kazemian Mansourabad, Mikaili, & Sarahroodi, 2013) Jordan, (Sawair et al., 2009) Lebanon (Cheaito et al., 2014) and Northern and Western Europe. (Grigoryan et al., 2008)

This explains the lower average of DDD per dispensing in Lebanon. This may be due to rapid relief of signs and symptoms of many complaints. Therapy was often used by patients without ruling out the possibility of viral infections which is more common in these cases of respiratory tract infections. So, patients stop the antibiotic just when the symptoms of illness disappear. Self-diagnosis and buying of antibiotics in sub-therapeutic quantities tend to become cultural norms in countries with few regulations on the acquisition of non-prescribed antimicrobial drugs. (Drug Utilization Research Group, 1997) This should raise awareness regarding the increase risk of bacterial resistance over time.

The average DDD dispensed for all antibiotic classes was lower in Lebanon when compared to France. The distribution of antibiotic users was mainly <14 days. This means that they are used for short term (<2 weeks), for acute infectious episodes. This difference in dispensation due to presence of different box sizes in the pharmacies. An important concern should be raised about residual antibiotics, i.e., antibiotics that were dispensed but not used. These may result in uncontrolled self-medication and inappropriate use. This could be quantified by comparing the overall DDD of antibiotic dispensed during episode to that actually used, during follow-up. Residual antibiotics could result in misuse of leftover of antibiotics for the treatment of minor infections.

It is an important concern also to link the difference DDD per dispensing with the number of DDD per formulation of antibiotic. The average number of DDD per box in France are 14, 12, 4, 8, 6, 5-30 for amoxicillin, coamoxiclav, cefixime, cefuroxime, ciprofloxacin, and clarithromycin. In Lebanon, the average number of DDD per box are 5-10, 14, 6, 10, 5 and 14 respectively. The number of DDD per box in Lebanon may explain the lower number of DDD per dispensing for these antibiotic classes when compared to France. Moreover, patients in Lebanon can buy antibiotic in sub therapeutic quantities (i.e. sachet) with lower number of DDD per dispensing and in lower therapeutic quantities. This explain the lower number of DDD per dispensing and may have an important impact on antibiotic resistance.

Another contributor to the differences between Lebanon and France may be the health insurance coverage: antibiotics are covered by the national healthcare insurance in France, so that they

are essentially free for the patient. The pharmacists will then dispense the whole amount that has been prescribed, even if it is not all used by the patient. In Lebanon, patients will pay for the drugs (and may be reimbursed later, eventually). There is a strong incentive to buy only the amount they think necessary. The difference in amount dispensed may result in differences in patient usage if patients in France and Lebanon use the whole amount dispensed, or not if in France as in Lebanon patients stop the drug when the symptoms resolve, and maybe reuse what is left at a later date.

No significant difference was found between different age groups in both Lebanon and in France. Males had significantly higher average DDD consumption of antibiotics than females. In these studies, and in the study of Lombardy region, a greater prevalence was found in males than in females. (Bronzwaer et al., 2002; Majeed & Cook, 1996). This finding is in contrast to another study done in the USA that shows that females were the main consumers of antibiotics in 2013.(Centers for Disease Control and Prevention, 2013b)Females used more broad spectrum antibiotics, including cefuroxime, cefixime and clarithromycin. This may be because females have more symptomatic infections of the genital and urinary tract system than males. (Blix et al., 2007)

In Lebanon, the average number of requests per year was considered high (3.39 times). More than 50% requested antibiotics more than twice per year while in France more than half were dispensed once per year. This could be attributed to therapeutic failure or to increase in bacterial resistance, or to unmeasured re-use in France of residual product from a previous dispensing.

Coamoxiclav was highly used among Lebanese patients (49%) followed by cefuroxime (15.5%). This result replicates findings reported in Lebanon (48.9%). (Cheaito et al., 2014) Similarly, in United Arab Emirates, it was the most commonly used (48.9%) (Sharif & Sharif, 2013) and in Pakistan (62.8%). (Aslam & Mirza, 2013) Coamoxiclav and cefuroxime were also dispensed mainly without prescription (53% and 15.9% respectively). In contrast, In France, amoxicillin was the main antibiotic dispensed (40.7%) followed by coamoxiclav (37.1%). This shows a big shift to broad spectrum antibiotic in Lebanon, maybe related to uncontrolled use of antibiotics, which could cause the development of more resistant bacteria and diminish the ability of the endogenous flora to resist colonization of harmful microorganisms, thereby leading to super infections by multi-resistant bacteria and yeasts. (Barbosa & Levy, 2000)

Higher use of broad spectrum of antibiotics was observed with increasing age in both Lebanon and France. Differences in patterns of use with regards to age could be explained by different types of infections in different age groups. The high use of broad-spectrum antibacterials, including the shift from amoxicillin to more broad spectrum antibiotics such as coamoxiclav, cefixime and cefuroxime is not unexpected because the immune response lessens with age and the prevalence of UTIs increases with age. This pattern might also be related to more bacterial resistance related to previous use of other antibiotics over time. In older patients who more frequently use other drugs than younger patients, additional attention should be focused to the increased risk of antimicrobial resistance.

Strength and Limitations of the study:

The comparison of the usage pattern of antibiotics between a country with freely available antibiotics and one with restricted dispensing, can inform if drug status impacts on its use and whether prescription-only use could reduce misuse and the risk of antibacterial resistance.

This study is the first to compare the usage pattern of antibiotics between a country with freely available antibiotics i.e. Lebanon and one with restricted dispensing i.e. France. It is the first study done in the Lebanese population of the usage pattern of antibiotic consumption.

However, this study has many limitations. The comparison suffers from an important limitation due to limited sample size in Lebanon when compared to France and different data sources where the data in Lebanon was obtained based on a prospective study while in France based on a database.

Our study was limited to patients aged > 15 years old. Pediatric patients are also an important category group to measure extent of antibiotic use that could influence antibiotic resistance.

In addition, the antibiotics in this study were limited to six substances and this could underestimate the extent of antibiotic usage although these antibiotics are considered the most frequent dispensed antibiotics in this area. They represent 59.4% of all antibiotics dispensed in France in 2013, based on Medicam.(Medic-am, 2013) and 68.5% in Lebanon. (Malak et al, 2017)

In Lebanon, since not all pharmacists accepted to participate to the study, the sample may not be representative of Lebanese population. We might also expect a change in behavior of the pharmacists in the presence of researchers, since the study addresses an illegal practice; Our results underestimate the reality of antibiotic self-medication. Second, there could also be a possibility of respondent and information bias, since the results of our study are based on a face-to-face questionnaire. Many persons did not agree to fill it out, which may also introduce a selection bias.

In Lebanon the study suffers from most consumer-based surveys issues, mostly the willingness or not of subjects coming to the pharmacy to spend time filling a questionnaire or speaking to an interviewer. Patients may also be reluctant divulge information about disease of socioeconomic factors. As such our results represent only the part of the population that participated; mostly young, relatively healthy subjects who may have better educational level than older subjects. However, subjects in this study were recruited in various parts of the country. And difference in the spectrum of ages and professional status one might expect. The results are found were not unexpected and confirm to another studies done in the same area. (Cheaito et al., 2014; Sawair et al., 2009) The fact that we did find two third non-prescribed dispensing of antibiotics shows the respondents answer making information bias unlikely.

In addition, the differences between the demographic characteristics of French and Lebanese users could indicate the selection bias of the Lebanese sample, or more likely differences in the age and gender structure of the Lebanese population, which is younger and more female than France.

In France, though the sample is exhaustive and unbiased, there are limitations: the indication for the use of the drug is not known even if it can sometimes be presumes from comedication; The exact quantity dispensed is known, but not the actual usage of the drug by the patient, whereas in Lebanon this information was obtained from the patient.

In both instances the exposure to antibiotics could be underestimated, since self-medication from leftovers was not taken into consideration and could represent an important source of inappropriate antibiotic use. Especially, the larger quantity dispensed in France and the smaller number of dispensing could also indicate that not all antibiotics were used in the initial dispensing, and the leftover could be used later, obviating the need for redispensing, and resulting in an apparently lower rate of dispensing.

Conclusion:

Lebanon show a greater number of dispensings per year compared to France and a wider use of broad spectrum of antibiotics. This difference is considered an important health concern in antimicrobial resistance. Existing regulations should be enforced to reduce the misuse of antibiotics among Lebanese population. Public awareness and educational programs should be implemented for patients and pharmacists to limit the self-medication use of antibiotics.

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Chapter 7:

Conclusion

This work confirms the habitual use of self-medication and pharmacist dispensing of antibiotics in Lebanon, compared to France with more frequent dispensings of smaller amounts of drugs with wider use of broad spectrum of antibiotics. This affects all age groups, but more specially the young patients, and concerns many minor, potentially viral diseases.

Similar misuse of antibiotics and other drugs seem prevalent over the Middle East. Misuse of antibiotics is a major driver in the development of antibiotic resistance, an issue for individuals and for public health. Obviously the observed self-medication or medically unsupervised utilization of antibiotics is a major risk.

Patient perception and knowledge of antibiotics is obviously flawed, with little understanding of the reasons for proper use. The general reputation of safety and efficacy of the antibiotics drives self-medication and misuse. There is a need to oppose self-medication and misuse, which should be approached with education and training before reinforcing regulations. This reduces the inappropriate use of antibiotics.

Education concerns patients, pharmacists, prescribers, the pharmaceutical industry and the regulatory authorities.

Patients should be taught through public awareness campaigns that antibiotics are not cure-alls, and that they should be used parsimoniously. Raising awareness of antimicrobial resistance and promoting behavioral change through public communication programs that target different audiences, especially the younger and if possible starting at school age. Including the indication of use of antibiotics and resistance in school curricula will also promote a better understanding and awareness from an early age. Patients should know that antibiotics are used for bacterial infections only and not for viral infections or for minor illnesses including: cough, cold and sore throat. It is important to educate patients about the importance of completing the full course of antibiotic to reduce antibiotic resistance. Patients should know that antibiotics are not “an extraordinary medicine” or “a powerful medicine” or “a strong medicine” which are able to prevent and cure any diseases or symptoms. It is also important to adopt consensual public relations policies to control antibiotic promotion to prescribers and in pharmacies. Patients should know that “Antibiotics are not automatic”, a successful campaign in France a few years ago that reduced both prescribing and use of antibiotics.

Pharmacists should be further trained in the proper use of antibiotics. Ideally they should only dispense antibiotics when the patient has a prescription. This may be difficult to implement in a country with a long-standing tradition of self-medication and pharmacist "prescription" of drugs that are thought to be innocuous and effective. At the least the pharmacists should be trained to limit dispensing of non-prescribed antibiotics, referring the patient to a physician in the case of an overt bacterial infection and dispensing analgesics and fever reducers or other comfort medication in the case of probable viral infections, explaining to the patient to come back or see the doctor if the symptoms persist more than a few days. And convincing them that "with antibiotics you'll get better within a week, it'll take 7 days without the antibiotics".

Prescribers should reinforce these messages, even though they are almost by definition not involved in these self-medication practices. They can especially warn against the reuse of prescriptions.

Drug companies and regulators should make available different pack sizes so that each dispensing is appropriate to the quantity needed. Alternatively, the dispensing could be adapted to the prescription, dispensing only the exact number of tablets required, as in the US for instance.

Regulatory authorities should accompany these actions with communication and training programs before changing laws or regulations that exist but are not applied.Reducing antibiotic misuse to prevent emergent resistance is a multipronged endeavor, that is the responsibility of all.Future studies should investigate a number of situations and patient categories who are important potential providers and victims of antibiotic resistance: Children; long-term users; and in-hospital use, where resistance most often emerge and can have dire consequences in fragile patients. We can also compare the antibiotic resistance between Lebanon and France in future studies.

Beyond antibiotics, which are prone to misuse, other drugs can be self-medicated, with a potential for abuse in addition to misuse. This is the case for opiates including "weak" opiates such are codeine (Khalifeh, Moore, & Salameh, 2016). Other drugs with a high potential for misuse and abuse such as some psychotropic drugs might also be the target of further investigations.

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Annexes

Publications and Conference presentations during PhD study:

Publications:

- Khalifeh M, Moore N, Salameh P, Self-medication Misuse in the Middle East: a systematic literature review. Pharmacy Research and Perspective, 2017, 5 (4): 1-13.
- Khalifeh M, Moore N, Salameh P, Evaluation of self-medication use of antibiotic in Lebanon, A prospective study. American journal of Pharmacological Sciences. 2017 5 (2), 31-39.
- Khalifeh M, Moore N, Salameh P, Knowledge and attitude of Lebanese Population toward antibiotic use. American Journal of Epidemiology and Infectious Disease. 2017, 5 (2), 35-41
- Khalifeh M, Moore N, Salameh P, Community Usage Pattern of Antibiotics within Lebanese population, A prospective study. American journal of Pharmacological Sciences. 2017 5(2) 49-56

Other Publications Outside the theses:

- Khalifeh M, Moore N, Salameh P, Self-medications with potential abuse in the Middle East: a systematic literature review. Int J Basic Clin Pharmacol. 2016 Dec;5(6):2298-2307
- Khalifeh M, Salameh P, AlHajje A, Awada S, Rachidi S, Bawab W, Hypertension in the Lebanese adults: Impact on health related quality of life. Journal of Epidemiology and Global Health. Volume 5, Issue 4, December 2015, Pages 327–336

Other Submitted Papers:

- Khalifeh M, Moore N, Lassalle R, Pichard S, Abouelfath A, Duong M, Salameh P, Community Usage Pattern of Antibiotics in France
- Khalifeh M, Moore N, Lassalle R, Pichard S, Abouelfath A, Duong M, Salameh P, Comparison of Usage Pattern of antibiotics between Lebanon and France.

Conference Participation:

- Oral presentation in 22nd Scientific International in The Social Avenues of the Research on April 14 and 15, 2016 at the Holy Spirit University of Kaslik.
- Oral and Poster conference presentation in the 23rd Scientific International conference LAAS in Lebanese University-Fanar
- Poster Presentation in the “Troisieme Journees Franco-Libanaise-JFL3 La Recherche au Service da la Communaute” in 29 et 30 October in Lebanese University Campus Hadath in 2015.
- Oral and Poster presentation "Ma These en 180sec" in Journal of Doctoral School JED in Bordeaux University in 2016 and 2017.
- Poster presentation in the “Forum de l’ecole doctoralle” in Lebanese university Campus Hadath in 27 September 2017.

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REVIEW

Self-medication misuse in the Middle East: a systematic literature review

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Keywords
Eastern Mediterranean countries, Middle East, misuse, over-the-counter, Prescription medicines, Self-medication

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Abstract

Regulations usually distinguish between prescription-only (POM) and over-the-counter (OTC) medicines. The former requires medical prescription; the latter are available for SM of common minor or easily treated ailments. However, in the Eastern Mediterranean countries, theoretical prescription medicines can easily be purchased without a prescription, as self-medication (SM) resulting in potential misuse and unnecessary risk for patients. The magnitude of this activity is uncertain. The aim of this article, therefore, is to undertake a comprehensive review to identify the different types of medicines that can easily be purchased as SM in Middle East and recognized as misused. An extensive review of the published literature (1990–2015) was conducted using Pubmed, web of science, Cochrane, and Google Scholar databases, for OTC medicine misuse in the Middle East. A total of 72 papers were identified. Medicines involved in misuse included: codeine containing products, topical anesthetics, topical corticosteroids, antimalarial, and antibiotics. Self-medication misuse of medicines seemed widespread. Individual treatment patterns were not clearly identified. Studies were not standardized, limiting the comparability between studies and the estimation of the scale of misuse. Pharmacists, friends, or parents were found to be the main sources of SMs. Knowledge and attitudes are an important contributing factor in the misuse of these medications. Strategies and interventions to limit misuse were rarely identified in literature. In conclusion, a massive problem involving a range of medicines was found in Middle East. Standardization of studies is a prerequisite to the understanding and prevention of misuse of self-medication.

Abbreviations

EMRO, Eastern Mediterranean Region; OTC, over-the-counter; POM, prescription-only; SM, self-medication.

Introduction

Regulations usually distinguish between prescription-only (POM) and over-the-counter (OTC) medicines. The former requires medical prescription; the latter are available for SM of common minor or easily treated ailments. Many patients may treat themselves and self-medicate, using either OTC medication or prescription medicines without prescription.

OTC medicines are medicines that are approved for self-medication (SM) because their indication is easily recognized by patients and usually self-limiting, and the medicine is thought to be safe and effective. Paracetamol and low-dose NSAIDs for pain relief are typical of these OTC medicines. However, SM is not limited to OTC medicines, and patients self-medicate with prescription medicines. These are medicines that may have been prescribed and left over from a previous treatment episode, or bought directly from the community pharmacies without a prescription. The latter is in principle not authorized. However, in practice in many countries the

dispensing of prescription medicines by pharmacists, without a prescription is not unusual, especially for the short-term treatment of common diseases.

SM has become quite common in developed (Blenkinsopp and Bradley 1996) and more common in developing countries (Kamat and Nichter 1998). In developing countries people are not only using OTC products as SM but also prescription medicines, as SM products, without supervision. SM has been studied in many different populations, showing that about 25–75% of the population consumes SM medicines (Wazaify et al. 2005). SM is highly prevalent in the community in Eastern Mediterranean countries. In Middle East, prescription medicines can easily be purchased without prescription, resulting in potential misuse and unnecessary risk. Patients may use medicines without a prescription from pharmacies, use old prescriptions, share medicines with friends/relatives, and use leftover medicines from previous prescription-based dispensing.

However, there is a relative lack of literature relating to SM misuse in the Middle East. There has been relatively little systematic research on this topic, partly due to the perception that SM misuse is not as problematic as other types of drug abuse. A single review article (Cooper 2013) has described the current knowledge of OTC medicine misuse and identifies the different types of OTC medicines implicated. A number of specific medicines have been implicated in literature including: opiate-based OTC analgesics, cough syrup containing dextromethorphan or pseudoephedrine, diphenhydramine, and other antihistamines (Lessenger and Feinberg 2008). Moreover, as antibiotics are available without prescription in the Middle East they were also included in the review.

Misuse has been defined as the incorrect use of an OTC product for a medical purpose, usually in terms of dosage or duration of use (Hughes et al. 1999).

The aim of this article, therefore, is to undertake a comprehensive review to identify the different types of medicines that can easily be purchased as SM in Middle East and recognized as misused. Other objectives were to describe current knowledge and understanding about the range of SM misuses and to identify the source of SM practice.

Materials and Methods

Search strategy

Databases, namely, Medline/Pubmed, Web of Science, Cochrane Library, and other sources, were used to identify peer-reviewed papers dealing with the review theme in WHO Eastern Mediterranean countries. Search terms were identified through a pilot review of the literature and were used to identify articles through a systematic, standardized process.

The words/strings used for search and inclusion criteria were as follows: using combinations of the following terms: "over the counter", "OTC", "non-prescription", "self prescription medicines", "prescription medicines", "misuse", "abuse", "addiction", "dependency," and "non-medical use", "irrational use", "inappropriate use", Arab and name of countries belonging to the WHO Eastern Mediterranean Region (EMRO). The search strategy is outlined in figure 1. The search was limited to publications between 1990 and July 2015. Reviews (Lessenger and Feinberg 2008; Al-Tawfiq et al. 2010; Cooper 2013; Shehnaz et al. 2014a,b) were used for reference mining but they were not included.

Article selection

For a paper to be included in the review, four criteria were jointly required: (1) SM or over-the-counter (OTC) or prescription medications as some are available without prescription in the community pharmacy in Middle East, (2) WHO Eastern Mediterranean country, (3) Publication from 1990 to July 2015, and (4) Availability of abstract in English, French or Arabic.

Exclusion criteria included non-English, French, or Arabic language publications and reference exclusively to prescribed or illicitly obtained medicines. Articles related to alcohol or substance abuse were also excluded; although they represent an important category, they cover different objectives of the review theme related to SM misuse. Studies were also excluded via search limits if they were as follows: review articles, on animal models; hospital-based studies; clinical and/or randomized controlled trials; editorials, letters, opinions, or comment publication type.

Content reviews were performed to select articles that met these criteria. From the title review, articles were excluded if they were not relevant to the subject matter. Any articles with an ambiguous title or title suggestive of the topic were evaluated in the abstract review. Abstracts were reviewed for details that indicated the article may meet inclusion criteria. Finally, full-text articles were reviewed and assessed to determine whether inclusion criteria were met. Full-text reviews were also conducted on review articles to identify additional articles from their bibliographies.

Data abstraction

The following details were extracted from each study using an abstraction form: year of publication, country of origin, population sampled, recall period, and data pertaining to the study objectives.

Results

Literature search results

The database search yielded 696 publications for review. Fifty other records were added through other sources like health journals edited in Iran, Pakistan, and Saudi Arabia and previous reviews for reference mining but they were not included. 562 articles were excluded for reasons of duplicated records, review articles, irrelevant topic, time of publication, availability of abstract, outside eastern Mediterranean area, and clinical and/or randomized controlled trial.

A secondary search was performed to elaborate the primary concept. A total of 134 full-text articles were assessed of which 49 were excluded as they were related to prescription medications or illicit and alcohol abuse or medication storage and wastage, which did not meet our study objective. Another 21 articles (four out of time frame, two opinion pieces, four letters, five reviews, five articles outside Middle East area, and one animal model) were excluded. An additional eight articles were added after reference screening. This resulted in 72 articles, which fulfilled the inclusion criteria. (Fig. 1).

Study characteristics

The studies in the 72 publications differed substantially in sample size, recall period, and location. These studies reviewing overall prevalence, frequencies, and pattern of OTC misuse originated from different countries: Iran ($n = 16$), Pakistan ($n = 12$), Jordan ($n = 11$), Saudi Arabia ($n = 8$), Lebanon ($n = 3$), United Arab Emirates ($n = 4$), Kuwait ($n = 2$), Egypt ($n = 2$), Syria ($n = 2$), Yemen ($n = 2$), Iraq ($n = 2$), Palestine ($n = 2$), Bahrain ($n = 2$), Libya ($n = 1$), Sudan ($n = 1$), and Oman ($n = 1$). An additional paper included Lebanon, Egypt, Jordan, Tunisia, and Libya (Scicluna et al. 2009). All the studies were cross sectional in nature barring 1 case report (Risco and Millar 1992) and 1 prospective study (Nazarzadeh et al. 2014). Most studies used self-administered questionnaires or face-to-face interviews for data collection. Mixed data collection techniques were also adopted.

Prevalence of SM

SM was highly prevalent in the community in Eastern Mediterranean countries, ranging from 35.4% to 83% in Iran (Jalilian et al. 2013; Jafari et al. 2015), 42.5% in Jordan (Yousef et al. 2008), 35.4% in Saudi Arabia (Alghanim 2011), and 68.1% in Pakistan (Syed et al. 2015). It is also well prevalent among adolescents in many Middle East countries including Jordan (87%) (ALBashtawy et al. 2015), Palestine (98%) (Sawalha 2008), Kuwait (92%) (Abahussain et al. 2005), Emirates (89.2%) (Shehnaz et al. 2013), Bahrain (44.8%) (James et al. 2006), and Pakistan (80.4%) (Mumtaz et al. 2011).

SM was also common for children and among pregnant women. Medication without prescription was given to 51.3% children in Pakistan (Haider and Thaver 1995), mostly consisting of unidentified medicines or analgesics/antipyretics. Good past experience (61.3%) with the medicine was the main reason for SM (Haider and Thaver 1995). In addition, more than 35% of the women self-medicated during pregnancy (Baghianimoghadam et al. 2013).

Scale of SM misuse

Methods used to describe the extent of OTC misuse varied. This variety is due to different methods and data sources, which make comparisons between countries difficult. Several studies relied on the perceptions or behavior of pharmacists (in Jordan, Palestine, Lebanon, Saudi Arabia, Egypt, and Syria), whereas others relied on sampling the public, pharmacy customers, or among university or school students.

Studies varied as to whether they focused on a particular product or on a range of products. Studies based on pharmacists' approaches appeared to generate more detailed and varied descriptions of medicines that may be misused. In Jordan, for example, antibiotics were commonly cited by pharmacists as being misused, as regulations restricting their supply were not always enforced (Albsoul-Younes et al. 2010). Similar studies were conducted in Palestine and Egypt by Sweileh et al. (2004) and Elhoseeny et al. (2013) based on perception of community pharmacists. In Palestine, 66% of community pharmacists believe that there is an increase in misuse of OTC medicines (Sweileh et al. 2004). Antitussives, analgesics, antihistamines, laxatives, decongestants, and sedatives hypnotics and tranquilizers were also identified by pharmacists as misused OTC medicines (Sweileh et al. 2004).

The use of nonprescription medicine among patients/consumers was reported by 66.9% of pharmacists to have increased in the past 4 years (Elhoseeny et al. 2013). Iran pharmacies sold 57% of prescription items without prescription (Zargarzadeh et al. 2008). Shehnaz study in the United Arab Emirates showed high prevalence of SM with antibiotics (53%) and sedative/hypnotics (27%) (Shehnaz et al. 2013).

Moreover, some studies showed that the practice of SM is influenced by pharmacists. In Syria, from 200 pharmacies visited, 87% agreed without insistence from the

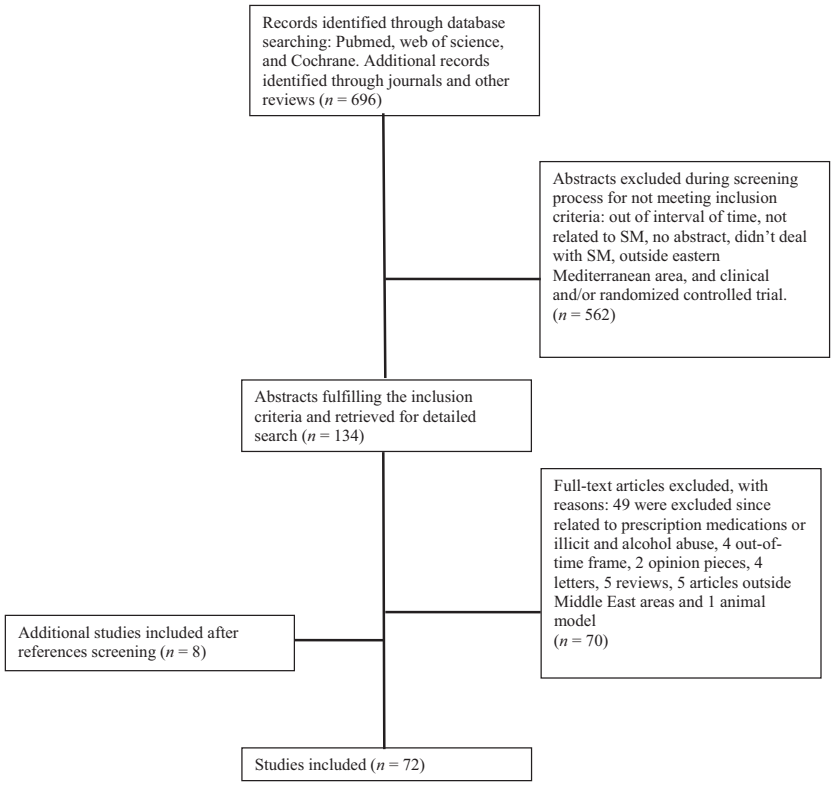

Figure 1. Selection of articles.

investigator to sell antibiotics without prescription. This figure increased to 97% when the investigators who were at first denied antibiotics insisted on having the antibiotics (Al-Faham et al. 2011). In Saudi Arabia, only one attendant pharmacist refused to dispense medications without prescription. Seventeen percent dispensed urinary antiseptic only and 82% gave antibacterial agents (Al-Ghamdi 2001).

Medicines involved in SM misuse

Medicines implicated in SM misuse belong to different pharmacologic groups: Codeine-based products, tramadol, topical ocular anesthetic, topical corticosteroids. antibiotics, and antimalarials were also described as misused medicines in many articles as seen in Table 1.

Analgesics

Codeine is usually supplied and consumed as codeine-containing pain-killer tablets that mostly also contain acetaminophen. Both acetaminophen–codeine tablets and tramadol tablets are prescription medicines, but many pharmacies sell them without a prescription (Zabihi et al. 2011). In Iran, Codeine-containing tablets, especially acetaminophen–codeine tablets are among the most requested medicines as OTC (Zargarzadeh et al. 2008). Headache was the most common problem (Sarahroodi et al. 2012), and Sedighi showed that 91% of Iranian migraine sufferers used SM, mostly Acetaminophen and Codeine (Sedighi et al. 2006).

The prevalence of lifetime tramadol misuse among Iranian students was 4.7% (Nazarzadeh et al. 2014). This is due to easy accessibility from pharmacies without prescription. For instance, 56% of patients requesting for tramadol did not have a prescription (Zabihi et al. 2011).

Topical Anesthetics

Topical ocular anesthetics are commonly misused among Iranian welders: 80.5% declared that they had used topical anesthetics at least once during their working lives (Sharifi et al. 2013). All were Men. Mostly patients prefer self-treatment over seeking help from a physician, for cultural and financial reasons. The most commonly used topical anesthetic was tetracaine (Sharifi et al. 2013). Topical ocular anesthetic misuse is associated with many harmful adverse effects. A case report stated a 40-year-old patient in Saudi Arabia frequently self-administering

Table 1. Types of drugs misused in the retrieved publications.

Types of Drugs misused	Number of papers (n)	Countries	Prevalence of SM %	Study participants	Reference
Analgesics (including codeine-containing medicines)	4	Iran	28.7%	564 University students	Sarahroodi et al. (2012)
			60%	210 University and school students	Sedighi et al. (2006)
		Saudi Arabia		504 University students	Ibrahim et al. (2015)
		Pakistan	55.4%	1380 Community participants	Qazi et al. (2013)
		Jordan	32%	393 Pharmacists	Albsoul-Younes et al. (2010)
Tramadol	2	Iran	56%	162 Pharmacy customers	Zabihi et al. (2011), Nazarzadeh et al. (2014)
			4.8%	1894 School students	
Antibiotics	38	Iran	35.8%	320 University staff	Askarian and Maharlouie (2012)
			42.2%	195 University members	Sarahroodi et al. (2010)
			43%	272 Patients at clinics	Jafari et al. (2015)
			53%	153 University females	Sarahroodi and Arzi (2009)
			57.6%	572 Community participants	Heidarifar et al. (2013)
		Jordan	40.7%	477 Patients at clinics	Sawair et al. (2009)
			46.3	480 pharmacy customers	Al-Bakri et al. (2005)
			62%	37 Community participants	Darwish et al. (2014)
			32%	174 Patients at clinics	Scicluna et al. (2009)
			59.1%	1141 Community participants	Shehadeh et al. (2012)
			N/A	1091 Pharmacy customers	Alzoubi et al. (2013)
			68.8%	679 University students	Suaifan et al. (2012)
			N/A	393 Pharmacists	Albsoul-Younes et al. (2010)
		Lebanon	32%	110 Pharmacists	Farah et al. (2015)
			42%	340 Pharmacy customers	Cheaito et al. (2014)
			37%	119 Patients at clinics	Scicluna et al. (2009)
		Pakistan	71.4%	780 University and school students	Aslam et al. (2013)
			N/A	1342 Households	Sturm et al. (1997)
			30% Pharyngitis 23% Gastroenteritis	851 Community participants	Qazi et al. (2013)
			25% storage	158 Households	Nasir et al. (2012)
			35.2%	572 University students	Zafar et al. (2008)
			10.8% storage	158 Households	Haider and Thaver (1995)
		Saudi Arabia	48%	353 School teachers	Belkina et al. (2014)
			11.6% for children	610 Community Parents	Abobotain et al. (2013)
			5%	1596 University and school students 88 Pharmacists	Almalak et al. (2014), Al-Ghamdi (2001)
		Syria	85%	365 Community participants	Barah and Goncalves (2010)
			N/A	200 pharmacists	Al-Faham et al. (2011)
		UAE	40.2	300 University students	Suleiman and Rubian (2013)
			46%	860 Community parents	Abasaeed et al. (2009)
			11.4%	324 School students	Shehnaz et al. (2013)
		Iraq	26%	300 Households	Jassim (2010)
		Egypt	23.3%	884 Pharmacy customers	Sabry et al. (2014)
			30%	300 Patients at clinics	Scicluna et al. (2009)
		Kuwait	27.50%	680 Community participants	Awad and Aboud (2015)
		Libya	43%	363 University students	Ghaieth et al. (2015)
			48%	286 Patients at clinics	Scicluna et al. (2009)
		Oman	67%	718 Community participants	Jose et al. (2013)
		Yemen	78.2%	367 School teachers	Belkina et al. (2014)
			60%	2000 Patients at clinics	Mohanna (2010)
		Sudan	48.10%	1750 Households	Awad et al. (2005)
		Tunisia	20.00%	264 Patients at clinics	Scicluna et al. (2009)
Antimalarial	2	Sudan	43.4%	1750 Households	Awad et al. (2005)
		Yemen			Abdo-Rabbo (2003)

(*Continued*)

Table 1. Continued.

Types of Drugs misused	Number of papers (n)	Countries	Prevalence of SM %	Study participants	Reference
Topical Anesthetics	2	Iran	80.5%	390 Welders	Sharifi et al. (2013)
		Saudi Arabia			Risco and Millar (1992)
Topical Corticosteroids	1	Iraq	7.90%	1780 Patients at clinics	Al-Dhalimi and Aljawahiry (2006)
Cough/cold products	3	Pakistan	N/A	864 University students	Bano et al. (2012)
		Jordan	N/A	393 Pharmacists	Albsoul-Younes et al. (2010)
		Palestine	N/A	864 University students	Sweileh et al. (2004)
Decongestants	1	Jordan	N/A	393 Pharmacists	Albsoul-Younes et al. (2010)
Laxatives	1	Palestine	N/A	97 Pharmacists	Sweileh et al. (2004)
Sedatives/Hypnotics and Benzodiazepines	3	Jordan	N/A	393 Pharmacists	Albsoul-Younes et al. (2010)
		United Arab Emirates	N/A	324 School students	Shehnaz et al. (2013)
		Jordan	N/A	393 Pharmacists	Albsoul-Younes et al. (2010)

topical oxybuprocaine drops had developed ocular ultrastructural alterations (Risco and Millar 1992).

Topical corticosteroids

Al-Dhalimi showed that topical corticosteroids were commonly misused by 7.9% of Iraqi patients presenting at the dermatological center for lightening the skin or mild acne. The most commonly used topical steroids were potent and highly potent corticosteroids, including Clobetasole propionate and Betamethasone valerate. About half were aged 10–19 years. In 34.3% of cases, medical staff was responsible for recommending the medicines, including pharmacists (Al-Dhalimi and Aljawahiry 2006).

Cough/cold products and laxatives

Sweileh et al. (2004) and Albsoul-Younes et al. (2010) reported that antitussives, analgesics, antihistamines, decongestants, and laxatives were identified by pharmacists as misused medicines (Sweileh 2004). The antitussive products most misused were those containing the following combinations: (codeine phosphate/pseudoephedrine/triprolidine) (53.6%) or (ephedrine/ammonium chloride/codeine phosphate/pheniramine maleate) (5.2%).

Antibiotics and antimalarials

Inappropriateness of antibiotic use is defined as suboptimal use of antibiotics to treat antibiotic-responsive conditions, including use of overly broad agents, incorrect drug dosing or duration, and poor drug adherence (Sabry et al. 2014). Misuse of antibiotics is common in Eastern Mediterranean countries, with self-medication rates ranging from 32% to 42% as reported in Lebanon (Cheaito et al. 2014) (Farah et al. 2015), and from 32% to 62%% in Jordanian studies (Darwish et al. 2014) (Scicluna et al. 2009); rates as high as 57.6% were reported in Iran (Heidarifar et al. 2013), in Emirates (56%) (Abasaeed et al. 2009), Syria (85%) (Barah and Goncalves 2010), Tunisia (20%) (Scicluna et al. 2009), and Yemen (60%) (Mohanna 2010). A percentage of 73.9 of Sudan population had used antibiotics or antimalarials without a prescription (Awad et al. 2005).

Antibiotic SM was common among university and school students in Palestine (98%) (Sawalha 2008), Libya (46%) (Ghaieth et al. 2015), United Arab Emirates (40%) (Sharifi et al. 2013), Saudi Arabia (48%) (Belkina et al. 2014), Pakistan (from 71.4% to 80.4%) (Aslam et al. 2013), and Iran (53%) (Sarahroodi and Arzi 2009). This practice was also observed among parents for their children. This practice was clear in Saudi Arabia (Darwish et al. 2014) and in the Scicluna study (Scicluna et al. 2009).

Respiratory tract symptoms were the main indication for which respondents indicated they would self-medicate. Antibiotics were mainly used for treatment of sore throat, cough, and flu. These results were found in Iran (Heidarifar et al. 2013), Iraq (Jassim 2010), Jordan (Sawair et al. 2009), Kuwait (Awad and Aboud 2015), Libya (Ghaieth et al. 2015), Lebanon (Cheaito et al. 2014), Pakistan (Qazi et al. 2013), Egypt (Sabry et al. 2014), Tunisia (Scicluna et al. 2009), and Saudi Arabia (Belkina et al. 2014). Other reasons for self-medication were for urinary tract infections (Scicluna et al. 2009) or gastrointestinal symptoms (Mohanna 2010).

Poor compliance with antibiotic therapy has a great impact on antibiotic misuse. Most patients did not complete the full course of antibiotic and took them for less than 3 days. This was observed in many Middle East countries and ranged from 39% to 86% as seen in Table 2. Reasons most frequently mentioned by patients

Table 2. Percentage of antibiotic compliance in the retrieved publications.

Countries	% Antibiotic Compliance	Study Setting	Reference
Jordan	39%	800 University students	Suaifan et al. (2012)
	40%	508 Community participants	Darwish et al. (2014)
Kuwait	64%	680 Community participants	Awad and Aboud (2015)
Iran	37.10%	542 Community participants	Heidarifar et al. (2013)
	26.80%	564 University students	Sarahroodi and Arzi (2009)
Libya	86%	363 University students	Ghaieth et al. (2015)
Oman	29%	718 Community participants	Jose et al. (2013)
	56%	400 School teachers	Belkina et al. (2014)
Pakistan	42%	780 University and school students	Aslam et al. (2013)
Saudi Arabia	71.30%	300 Households	Abobotain et al. (2013)
	61%	1200 School teachers	Belkina et al. (2014)
United Arab Emirates	75%	385 Women in clinics	Suleiman and Rubian (2013)

for noncompliance were as follows: rapid improvement of symptoms, forgetfulness, and frequent dosing (Al-Shammeri et al. 1995) .

The most common antibiotics used were amoxicillin or ampicillin among different Middle East countries including Libya, Tunisia, Egypt (Scicluna et al. 2009), United Arab Emirates (Abasaeed et al. 2009), Pakistan (Qazi et al. 2013), Iran (68.6%) (Heidarifar et al. 2013), and Jordan (Sawair et al. 2009). In Saudi Arabia, fluoroquinolones were the most commonly dispensed antibiotic for urinary tract infections (82%) (Al-Ghamdi 2001). Amoxicillin–clavulanic acid was mostly used among Lebanese (48.9%) (Cheaito et al. 2014), among university students in United Arab Emirates, (48.9%) (Suleiman and Rubian 2013), and in Pakistan (62.8%) (Aslam et al. 2013). Metronidazole and TMP/SMX were also commonly used in Pakistan (29.2%) (Qazi et al. 2013) and in Yemen (35%) (Mohanna 2010) respectively.

Sources and reasons for self-medication

People tended to select medication based mainly on advice received from community pharmacist (see Table 3). Ease in access to antibiotics and availability of pharmacist consultation were the main factors resulting in an increase in the use of antibiotics. Cheaito et al. (2014) reported that pharmacists were the main helpers for antibiotic self-medication. Similar findings were in Sharif's study which showed that pharmacy was the main source of antibiotic self-medication (slightly more than 90%) (Sharifi et al. 2013) and among Libyan students (75%) (Ghaieth et al. 2015).

Another study reported that the most common sources of information on medicines were parents or friends. In Jordan, 51.8% of adult patients use antibiotic based on a relative's advice (Shehadeh et al. 2012). Similar results were reported in many other Middle East countries. Prescription of antibiotics by physicians over phone is also an important contributing factor.

Use of leftover antibiotics is a major source for antibiotic use. Many patients tended also to keep antibiotics at home either for future use or for prophylaxis against infections (Ullah et al. 2013). In this case, antibiotics could be used without physician consultation. In Scicluna et al. (2009) almost half of those interviewed admitted to having stored some type of antibiotic at home, which was not for current use.

The most common reasons for self-medication were prior experience of the disease or similar symptoms (Al-Azzam et al. 2007; James et al. 2008; Yousef et al. 2008; Zafar et al. 2008; Scicluna et al. 2009; Mumtaz et al. 2011; Jalilian et al. 2013), certainty of its safety, (Jalilian et al. 2013), prior consumption of the drug (Jalilian et al. 2013), busy offices of physicians (Jalilian et al. 2013; Shoaib et al. 2013), and nonseriousness of the illness (James et al. 2008; Yousef et al. 2008; Mumtaz et al. 2011; Jalilian et al. 2013; Shoaib et al. 2013) or low severity of disease (Ullah et al. 2013). Long waiting time to be seen by doctors (James et al. 2008; Yousef et al. 2008) and avoiding the cost of doctors' visits were also reported as common reasons for self-medication (Yousef et al. 2008).

Self-medication was significantly associated with age, male gender, education level, and socioeconomic status. Young age, male, and having poor health status were more likely to practice self-medication (Alghanim 2011; Syed et al. 2015).

Knowledge and attitudes of self-medication

Knowledge of self-medication is an important factor for drug misuse. In Egypt, 82.4% of the pharmacists

Table 3. Sources for Self-Medication.

Sources of SM	Number of articles (n)	Country, %	References
Pharmacists	23	Egypt, 13.1%, 30%	Scicluna et al. (2009); Sabry et al. (2014)
		Iran 18.6%, 30%, 44.8%, 61.2%	Sarahroodi and Arzi (2009), Heidarifar et al. (2013), Sharifi et al. (2013), Askarian and Maharlouie (2012)
		Jordan 14.2%, 23.1%, 30%, 53.6%, 30%	Al-Bakri et al. (2005), Yousef et al. (2008), Sawair et al. (2009)), Scicluna et al. (2009)
		Lebanon 29.8%, 35%	Cheaito et al. (2014), Scicluna et al. (2009)
		Libya 74%, 12%	Scicluna et al. (2009), Ghaieth et al. (2015)
		Pakistan 33.49%	Qazi et al. (2013)
		Yemen 55.1%	Belkina et al. (2014)
		Saudi Arabia 21.6%, 74%	Alghanim (2011), Belkina et al. (2014)
		Emirates 21.4%, 16.3%, 74%	Shehnaz et al. (2013, 2014a,b), Abasaeed et al. (2009), Mohanna (2010)
		Iraq 18.6%	Al-Dhalimi and Aljawahiry (2006)
		Yemen N/A	Abdo-Rabbo (2003)
		Tunisia 12%	Scicluna et al. (2009)
Parents/Friends	19	Iran 0.6%, 6%, 54.7%, 40.1%	Sharifirad et al. (2011), Sarahroodi and Arzi (2009), Heidarifar et al. (2013), Sharifi et al. (2013), Nazarzadeh et al. (2014)
		Jordan 51.8%, 10.3%, 12%	Sawair et al. (2009), Scicluna et al. (2009), Shehadeh et al. (2012)
		Libya 26%, 11%	Scicluna et al. (2009), Ghaieth et al. (2015)
		Pakistan 20.09%	Qazi et al. (2013)
		Yemen 7.3%	Belkina et al. (2014)
		Saudi Arabia 19.3%, 20.3%	Belkina et al. (2014), Alghanim (2011)
		Emirates 20.2%	Shehnaz et al. (2013), Suleiman and Rubian (2013)
		Iraq 20.7%	Al-Dhalimi and Aljawahiry (2006)
		Yemen N/A	Abdo-Rabbo (2003)
		Kuwait N/A	Abahussain et al. (2005)
		Egypt 11%	Scicluna et al. (2009)
		Lebanon 10%	Scicluna et al. (2009)
		Tunisia 13%	Scicluna et al. (2009)
Physician advice or health professionals	5	Lebanon 50.8%	Cheaito et al. (2014)
		Emirates 25.8%	Suleiman and Rubian (2013)
		Jordan 21.9%	Yousef et al. (2008))
		Iran 27.2%	Sharifi et al. (2013)
		Iraq 11.4%	Al-Dhalimi and Aljawahiry (2006)
Dr. over phone	1	Jordan 37.5%	Suaifan et al. (2012)
Leftover	10	Iran 38.2%, 47.8%, 52%	Sarahroodi and Arzi (2009), Askarian and Maharlouie (2012), Heidarifar et al. (2013)
		Iraq 45%	Jassim (2010)
		Jordan 46%, 49%, 60%	Shehadeh et al. (2012), Suaifan et al. (2012), Darwish et al. (2014)
		Lebanon 19.4%	Cheaito et al. (2014)
		Emirates 1.1%, 28%	Suleiman and Rubian (2013), Abasaeed et al. (2009)
Stores at home for future use	2	Jordan 50%	Scicluna et al. (2009)
		Tunisia 40%	Scicluna et al. (2009)
		Libya 59%	Scicluna et al. (2009)
		Lebanon 60%	Scicluna et al. (2009)
		Egypt 40% Iraq 23%	Scicluna et al. (2009), Jassim (2010)
Self present based on: previous experience of symptoms or disease or knowledge	6	Emirates 27%	Suleiman and Rubian (2013)
		Iran 30.1% 48.5%, 75%	Sarahroodi et al. (2012)
		Jordan 27%, 53.1%	Yousef et al. (2008), Sawair et al. (2009)
		Yemen 17.1%	(Belkina et al. 2014)
		Saudi Arabia 31.6%	Belkina et al. (2014)

(*Continued*)

Table 3. Continued.

Sources of SM	Number of articles (n)	Country, %	References
Previous treatment	3	Jordan 36.1%, 40%	Scicluna et al. (2009), Sawair et al. (2009)
		Tunisia 45%	Scicluna et al. (2009)
		Libya 48%	Scicluna et al. (2009)
		Lebanon 88%	Scicluna et al. (2009)
		Egypt 40%	Scicluna et al. (2009)
		Iran N/A	Jalilian et al. (2013)
Previous suggestion by physician or Dr. always prescribe the same antibiotic	2	Iran 32.6%	Sarahroodi et al. (2010)
		Lebanon 43%	Scicluna et al. (2009)
		Egypt 11%	Scicluna et al. (2009)
		Tunisia 21%	Scicluna et al. (2009)
		Jordan 10%	Scicluna et al. (2009)
		Libya 30%	Scicluna et al. (2009)
Old prescription	3	Yemen 20.6%	Belkina et al. (2014)
		Saudi Arabia 27.5%, 50.8%	Alghanim (2011), Belkina et al. (2014)
		Emirates 26%	Mohanna (2010)
Doctor prescription to friend	1	Emirates 3.4%	Suleiman and Rubian (2013)

considered the most common contributing factor for inappropriate self- medication use was lack of knowledge of patients/customers about the active ingredients in a branded product Elhoseeny et al. (2013). Tawfiq's study showed that more than 60% of the respondents did not try to read the leaflets of their medications (Al-Tawfiq et al. 2010).

The knowledge and attitude toward antibiotics are important contributing factors in the misuse of these medications. There is a limited understanding of which infections might require antibiotics and the safety and risks of such misusage. For instance, one Jordan study showed that 67.1% of the public believed that antibiotics treat common cold and cough. A percentage of 28.1 misused antibiotics as analgesics (Shehadeh et al. 2012). Many patients thought they were used for viral infections (Alzoubi et al. 2013; Darwish et al. 2014). Better knowledge was found to be a predictor for positive attitudes (Awad and Aboud 2015).

Discussion

The current review summarizes a number of themes and data to inform understanding of self-medication misuse in Eastern Mediterranean area. In addition, it highlights the different medicines involved in self-medication misuse, their prevalence, and their practice in different settings. Apparently, the uncontrolled consumption and monitoring of consumption of medicines in the Middle East is one reason for SM. This all is probably because of the easy availability of such medicines without prescription. So, people could misuse analgesics containing codeine, despite the availability of alternative active OTC medications such s paracetamol or NSAIDs. However, they are available as prescription medicines in some developed countries. Similar findings are observed to that reported in many developed countries. For example, in England (Paxton and Chapple 1996) and Scotland (Matheson et al. 2002) 69% and 68.5% of pharmacists considered there to be some form of OTC medicine misuse in their pharmacies.

This review showed that regardless of the type of studied samples (driven from general population or selected subgroups of population) the reported prevalence of self-medication misuse in Eastern Mediterranean countries is very high. Therefore, high prevalence of misuse seems to be a health challenge in the Middle East. However, much still remains undone in this area in Eastern Mediterranean area. Many important researches remained unexplored in different countries of Middle East.

The inappropriate use of antibiotic is risky. This may include the use of antibiotics beyond the scope of their indications to treat ailments unrelated to bacterial infections or using antibiotic with incorrect dosages for inappropriate period of time. As a result, most antibiotics are used in unnecessary cases that would mostly recover without any antibiotic. For instance, people may self-medicate with antibiotic for treatment of mild ailments as throat or teeth symptoms, nasal congestion, cough, flu, and urinary discomfort. Although patients can use many alternative OTC medications as cough, decongestants, or antihistamine products for upper respiratory tract infections, many still prefer to use of antibiotics.

Inappropriate use of antibiotics may eventually lead to antibiotic resistance.

The main sources for self-medication were previously prescribed pharmaceuticals stored in the household and those purchased in pharmacies (Al-Bakri et al. 2005). Prescribing of medicine based on Essential Medicine List formularies, information campaigns, and regulatory reinforcement might control or reduce SM misuse. In Chile, the prohibition of OTC sales of antibiotic and a simultaneous public education campaign had an immediate and significant impact on the acquisition of antibiotic from pharmacies (Abasaeed et al. 2009). Similarly, sales of antibiotic without prescription in Zimbabwe decreased when the law against over-the-counter sales was strictly enforced (Avorn and Solomon 2000).

The use of leftover medications is a unique consequence of poor compliance with medications including antibiotics because it affords the patient opportunities to self- medicate with a partial supply of antibiotics. Overprescription of antibiotics by physicians is also an important factor that increases patient self-medication. Awareness and educational programs for physicians and consumers appear promising to control the overuse of antibiotics, noncompliance, and the use of leftovers.

Methodologically, studies are not standardized, which limits the quality of studies as well as comparability. Most of the studies were cross-sectional descriptive studies often using self-administered questionnaires, face-to-face interviews, or pharmacists' perception. Many studies report data based on pharmacists' perceptions of the problem of misuse and the profile of those they considered to be affected, such as reported by Albsoul-Younes et al. (2010), Elhoseeny et al. (2013), or Sweileh et al. (2004). These study designs are similar to those conducted in Scotland (Paxton and Chapple 1996; Matheson et al. 2002). Although these studies may have high response rate, they are still subjective.

Like all literature reviews, and despite our best effort to use standard methodology for such reviews, the possibility of a selection bias cannot be excluded, even though we did search for local language papers that might have escaped other researchers. Lack of access to some of the databases in the field and to unpublished research reports was the main limitations in our attempt to shed light on OTC misuse behavior. Uninformative titles and abstracts are also a limitation. However, the main limitation in our analysis is the heterogeneous methodological nature and reporting of the studies. Even finding more studies hidden in obscure repositories would probably not have changed that conclusion. In addition, most studies were consistent and showed similar results on the widespread use of self-medication, so that again missing studies would not change these results.

Conclusion

This review relating to self-medication misuse has found a massive problem involving a range of medicines. Considerable attention should be paid to the risks of future expansion of inappropriate self-medication. Better physician education of appropriate medication use is one approach that may encourage the prudent use of antimicrobial and other medicines. In addition, policy making should be implemented in Middle East area in order to restrict sales of prescription medications without prescription.

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Authors Contribution

Malak Khalifeh had the original idea, did the literature search, and wrote the original manuscript. Nicholas Moore had the original idea, and edited/amended the manuscript. Pascale Salameh had the original idea, and edited/amended the manuscript. All authors read and approved the final manuscript as submitted.

Disclosures

The authors declare no conflicts of interest.

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Community Usage Pattern of Antibiotics within Lebanese Population: A Prospective Study

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Abstract **Introduction:** Antibiotic misuse is a worldwide public health problem and a major cause of antibiotic resistance. **Objective:** The aim of this study therefore was to describe the usage pattern of antibiotics in Lebanon. **Method:** It is a prospective study in a community-based pharmacy setting in Lebanon. It uses a structured random interview to patients visiting community pharmacy seeking for antibiotics. Baseline characteristics and reason for self-medication were collected. Completing a self-administered questionnaire after 30 days provided information on safety, efficacy and usage pattern. Data were analyzed using descriptive statistics and Chi-square test. **Results:** 62.7% of 501 participants bought antibiotic without prescription. Pharmacists were the main helpers (34.7%). Amoxicillin/clavulanic acid was the most used antibiotic as self-medication (33.7%). The overall average dispensation was 9.07 DDD for short term use (< 2 weeks). In the follow up, the average DDD consumed by patient was7.07 DDD and 62.5% were consumed between 1 to 7 DDD. The average request per year was 3.35 which was significantly higher in patients without prescription than with prescription (p= .029).Males were dispensed more DDDs than females but the result was not significant. Patients with ages from 25-50 years old had significantly consumed more than 1 DDD per day (61.7%) compared to patients with age above than 50 years old (41%, p=.002). **Conclusion:** Antibiotic consumption in Lebanon is uncontrolled. Educational programs should be implemented for the public to reduce the usage of antibiotic.

Keywords: *self-medication, antibiotic, Lebanon, usage pattern, DDD*

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1. Introduction

Antibiotic misuse is a worldwide public health problem and a major cause of antibiotic resistance [1]. Antibiotic resistance is one of the most relevant problems in the healthcare: the growth of resistant microorganisms in healthcare settings is a worrisome threat, raising length to stay (LOS), morbidity and mortality in those patients [1].

The main reasons for the increase of antimicrobial resistance include unregulated drug availability and widespread attitude to antimicrobial misuse, including self-medication [2].

The use of antibiotics has therefore been frequently studied in different countries all over the world. Antibiotic use has been studied and compared in hospitals and in primary care [3,4,5,6]. However, the use of antibiotics at an individual level has until recently been studied in smaller groups of patients.

In Lebanon, like most other developing countries, having a valid prescription is not always enforced for receiving prescription-only medications (POM). Previous researches in Lebanon shows that the prevalence of self-medication of antibiotic is alarmingly high [7].

However, no researches were done to study the usage pattern of antibiotics in Lebanon. The aim of this study therefore was to describe the usage pattern of antibiotic within Lebanese population living in Lebanon and to explore patterns of age and gender specific use.

2. Method

2.1. Design and Study Population

A cross sectional prospective study was conducted in a community-based pharmacy setting in Lebanon. Data was collected over a 1-year period (September 2015 to September 2016) from 50 community pharmacies (CPs) distributed in the six districts in Lebanon: Beirut, South Lebanon, Nabatiyeh, Mount Lebanon, Bekaa, and North Lebanon.

Eligible participants were recruited randomly from consumers presenting at CPs in Lebanon after they had purchased antibiotic medication with or without prescription. The patients included were from both genders, aged 16 years and older, coming to purchase antibiotic. The patients were divided into two groups:

those buying antibiotic with a prescription versus those buying them without prescription.

The Lebanese University, Faculty of Pharmacy Internal Review Board waived the need for written informed consent. The patients were informed about the objective of the study and were asked to give an oral consent. Only those who gave their voluntary informed oral consent were enrolled.

2.2. Sample Size Calculation

A sample size was calculated assuming a type I error of 5% and a study power of 80% and 95%CI. Based on a previous study, 40% of patients were expected to self-medicate with antibiotics. [7] The minimal sample size necessary to show a twofold increase in the risk of exposure to non-prescribed antibiotics consists of 442 subjects: 186 patients for those buying antibiotic with prescription and 256 without prescription.

2.3. Procedure and Data Collection

Data on antibiotic use was collected using a structured random interview conducted by pharmacists or interviewers who had been briefed about the study's aims and methods. Consecutive customers arriving at CPs seeking antibiotic were interviewed. Data was collected from the participants twice, first at purchase for data about drug used and the condition for which it was to be used, then by calling the patient 30 days after starting the medication, for usage patterns.

The questionnaire included many sections that were chosen following an extensive review of literature. The questionnaire was translated into Arabic and subjected to a process of forward and backward translation into English. It was pretested and validated first on 20 patients visiting 4 different pharmacies before starting the survey.

The questionnaire consisted of dichotomous and close-ended questions. It consisted of the following sections: socio-demographic data (age, sex, occupation, educational and marital status, monthly income, medical insurance, and the presence of a care provider at home), lifestyle data (smoking status, alcohol status, and involvement in sport activities), complaint for which the antibiotic is taken, the medication details (name, dose, duration and mode of administration as recommended to be taken), presence of comorbidities (defined as long-term diseases diagnosed by physicians) and background medications, as well as reasons and sources of self-medication.

Thirty days after starting the medication, patients were assessed about adherence and duration of antibiotic consumed, direction of use, and reasons for misuse.

2.4. Antibiotic Use Data

This study included antibiotics used for systemic infections, excluded antivirals, antifungals, antiprotozoans and topical antimicrobial treatments. The trade names of the dispensed antibiotics were converted to their equivalent generic names using the Lebanese Medical Index. Antibiotics were classified according to the Anatomical Therapeutic Chemical class (ATC, http://www.whocc.no/ atc_ddd_index/).

2.5. Data Analysis

The usage pattern of antibiotics was described by the number of defined daily doses (DDD) dispensed to each patient and used during the follow up, as well as the number of request of antibiotic/year.The usage pattern was described using Anatomical Therapeutical Chemical Classification/Defined Daily Doses (ATC/DDD) system. (Table S1).

All data were entered and analyzed using SPSS version19 (the IBM Corporation, Armonk, NY). The explanatory variables were: socio-demographic, lifestyle, the condition for which antibiotic was used, source of antibiotic medication, reason for self-medication and frequency of antibiotic consumed per year. An appropriate bivariate analysis was done for every explanatory variable: Chi-2 for dichotomous variables to compare 2 percentages, T-test or ANOVA for nominal and ordinal variables to compare 2 means of 2 groups or more, and Pearson correlation for continuous variables. A p-value of 0.05 or less was considered to be statistically significant in all tests.

3. Results

3.1. Baseline Characteristics

Of a total of one thousand questionnaire distributed to CPs data from a total of 501 patients were recorded in the study. Among participants, 314 (62.7%) requested an antibiotic without prescription while 187 (37.3 %) had a medical prescription for their antibiotic. Both groups were homogenous regarding gender (p=0.154), age (p=0.532), education (p=0.285), Income (p=0.051), and presence of comorbidities (p=0.548) (Table 1).

A total of 392 patients (78.2%) had no associated medical conditions, while 109 (21.8%) suffered from chronic diseases, among which 21.8% had hypertension, 3.2% had asthma or COPD, 5.8% had dyslipidemia, 3.8% diabetes, 2.4% gastric diseases, and 3.6% osteoarthritis. 3 participants were pregnant and one had an allergy to penicillin.

Amoxicillin–clavulanic acid (coamoxiclav) combination was the most purchased antibiotic (33.7 %) followed by cephalosporins (21.2%). 33.9% of participants used antibiotics once per year. Coamoxiclav was the most frequently dispensed antibiotic without prescription (37.3%) followed by cephalosporins (21%), penicillins (17.2%), macrolides (6.1%) and fluoroquinolones (3.8%) respectively. The antibiotics dispensed with a prescription were, in the following descending order: coamoxiclav (27.8%), cephalosporins (21.4%), fluoroquinolones (17.6%), macrolides (14.4%) and penicillins (5.3%). (Table 2)

The most concern indications were for respiratory tract infections mainly tonsillitis (27.5%) and flu (17.6%), followed by oral and gastrointestinal tract infections (18.6%) and urinary tract infection (12.4%). Most patients bought antibiotic to treat respiratory tract infections: tonsillitis (30.3%), cold (22%) and cough (6.4%), oral and gastrointestinal tract infections: diarrhea (13.4%) and teeth infections (5.1%), skin and urinary tract infections (8.3%). Patients buying antibiotics for urinary tract infections had significantly more prescriptions (p<0.05) (Table 2)

Table 1. Characteristics of the study population

	Total participants N=501	Participants with medical prescription N= 187	Participants without medical prescription N= 314	p-value
Gender				
Male	153 (30.5%)	50 (26.7%)	103 (32.8%)	0.154
Female	348 (69.5%)	137 (73.3%)	211 (67.2%)	
Age group				
16-25	244 (48.7%)	85 (45.5%)	159 (50.6%)	0.532
25-50	196 (39.1%)	78 (41.7%)	118 (37.6%)	
>50	61 (12.2%)	24 (12.8%)	37 (11.8%)	
Educational level				
Primary and less	153 (30.5%)	65 (34.8%)	88 (28%)	0.285
Secondary	69 (13.8%)	24 (12.8%)	45 (14.3%)	
University	279 (55.7%)	98 (52.4%)	181 (57.6%)	
Marital status				
Single	259 (51.7%)	90 (48.1%)	169 (53.8%)	0.217
Married	242 (48.3%)	97 (51.9%)	145 (46.2%)	
Currently working				
Yes	173(34.5%)	134 (71.7%)	194 (61.8%)	0.025
No	328 (65.5%)	53 (28.3%)	120 (38.2%)	
Family income (LL)				
<2000000	134 (74.4%)	38 (20.3%)	95 (30.3%)	.051
>2000000	46 (9.2%)	18 (9.6%)	27 (8.6%)	
No answer	323 (64.5%)	131 (70.1%)	192 (61.1%)	
Presence of comorbidities				
Yes	109 (21.8%)	38 (20.3%)	71 (22.6%)	0.548
No	392 (78.2%)	149 (79.7%)	243 (77.4%)	
Data presented as number (%) were performed using Chi2 respectively and a p-value < 0.05 is considered significant.				

Table 2. Self-medication practice among participants

	Total participants N=501	Participants with medical prescription N= 187	Participants without medical prescription N= 314	p-value
Antibiotic Classes:				
coamoxiclav	169(33.7%)	52 (27.8%)	117 (37.3%)	<.001
Amoxicillin or penicillins	64 (12.8%)	10 (5.3%)	54 (17.2%)	
Cephalosporins	106 (21.2%)	40 (21.4%)	66 (21.0%)	
Fluoroquinolones	45 (9%)	33 (17.6%)	12 (3.8%)	
Macrolides	46 (9.2%)	27 (14.4%)	19 (6.1%)	
Others	71 (14.2%)	25 (13.4%)	46 (14.6%)	
Ab request/year				
1st time	170 (33.9%)	70 (37.4%)	100 (32.2%)	.132
More than 1 time	328 (65.5%)	117 (62.6%)	211 (67.8%)	
Types of infection				
Respiratory tract infections:				
Tonsillitis	138 (27.5%)	43 (23%)	95 (30.3%)	.629
Cold	88 (17.6%)	19 (10.2%)	69 (22%)	.629
Sore throat	42 (8.4%)	6 (3.2%)	36 (11.5%)	.001
Cough	34 (6.8%)	14 (7.5%)	20 (6.4%)	.631
Otitis	32 (6.4%)	13 (7%)	19 (6.1%)	.320
Sinusitis	21 (4.2%)	10 (5.3%)	11 (3.5%)	.690
Chest tightness	14 (2.8%)	7 (3.7%)	7 (2.2%)	<.001
Runny nose or sneezing	10 (6.8%)	3 (1.6%)	7 (2.2%)	.079
Gastrointestinal infections:				
Diarrhea	60 (12%)	18 (9.6%)	42 (13.4%)	.394
Teeth infections	33 (6.6%)	17 (9.1%)	16 (5.1%)	.211
Urinary tract infections:	62 (12.4%)	36 (19.3%)	26 (8.3%)	.022
Skin infections:				
Skin infection	21 (4.2%)	12 (6.4%)	9 (2.9%)	.319
Acne	9 (1.8%)	6 (3.2%)	3 (1%)	.055
General:				
Fever	7 (1.4%)	3 (1.6%)	4 (1.3%)	.750
Pain	18 (3.6%)	5 (2.7%)	13 (4.1%)	.179
Others	35 (7%)	14 (7.4%)	17 (5.3%)	.750
Data presented as number (%) were performed using Chi2 respectively and a p-value < 0.05 is considered significant.				

3.2. Antibiotic Utilization Patterns

The drugs were dispensed according to prescriptions from physician (37.3%), or through self-medication (62.7%). Self-medication practice was based mainly on pharmacist recommendation (34.7%). Of the self-medicated antibiotics, 25.2% were requested by the patients themselves based on previous experience with the same antibiotic. The remaining was based on advice from a friend and/or family member (18.5%) or physician on phone (21%). (Figure 1)

The main reason reported by patients for self-medication was previous successful use of antibiotic (40.4%), followed by saving time (25.2%), and ease access of medication from the community pharmacy (22.9%). The remaining reported reasons were fear of the disease to become worse (18.5%) or saving cost of physician prescription (18.5%). (Figure 2)

Males bought significantly more coamoxiclav (43.8%, p=.003) followed by cephalosporins (16.3%), and fluoroquinolones (12.4%) while females bought more coamoxiclav (29.3%) and other penicillins (14.9%) followed by cephalosporins (23.3%) and macrolides (10.1%). Younger patients received more coamoxiclav (35.2%) while older patients more cephalosporins (29.5%) and fluoroquinolones (26.2%) and the result was statistically significant (p<.001). (Figure 3)

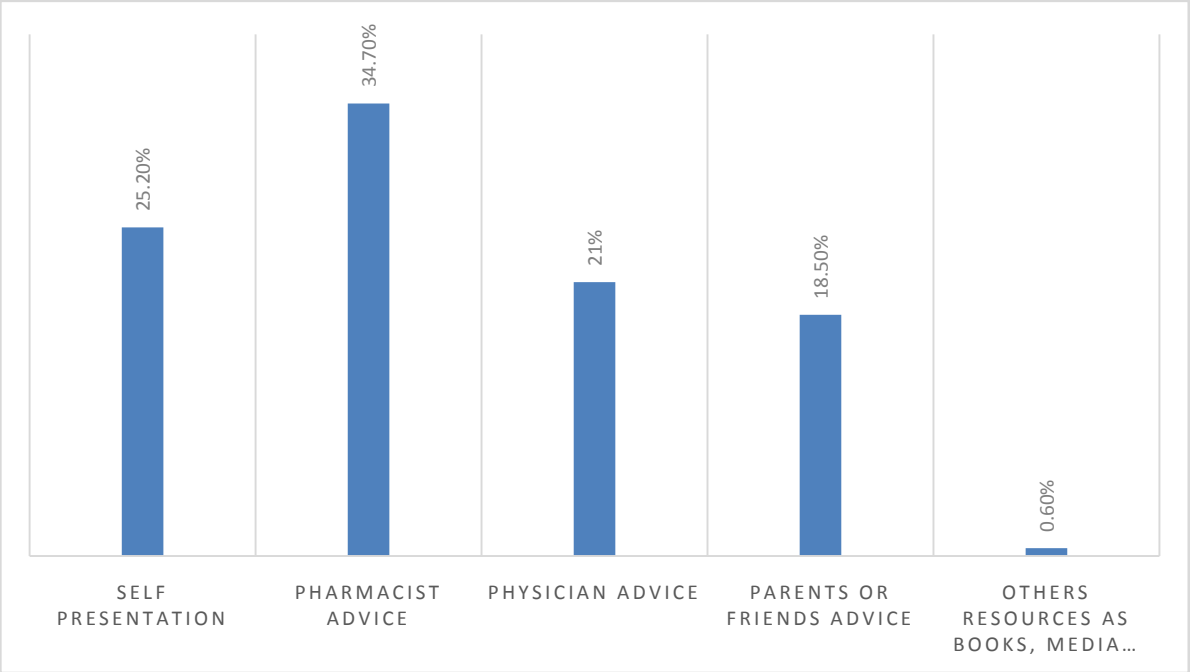

Figure 1. Sources of self-medication among participants requesting antibiotic without prescription

Figure 2. Reasons for self-medication among participants requesting antibiotic without prescription

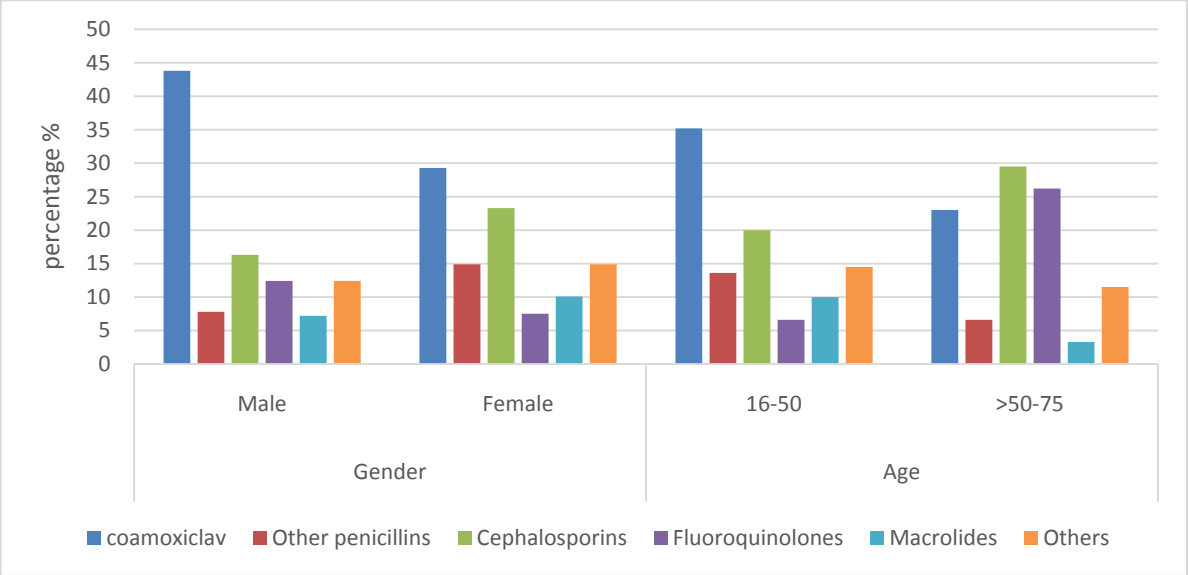

Figure 3. Dispensing pattern of individual antibiotic

Table 3. Usage Pattern of antibiotics

	Total participants N=357 (100%)	Participants with medical prescription N= 99 (30%)	Participants without medical prescription N= 258 (70%)	p-value
Number of DDD/request				
Mean	9.07 +-5.06 (Min=1.5, Max=48)	9.23 (5.35)	8.97 (4.87)	.588 (95%CI=-.68-1.2)
1-7	244 (48.7%)	93 (49.7%)	151 (48.1%)	0.936
8-14	222 (44.3%)	81 (43.3%)	141 (44.9%)	
15-29	35 (7%)	13 (7%)	22 (7%)	
Number of DDD/follow-up				
Mean	7.07 +-4.93 (Min=0.2, Max=48)	7.93 (5.4)	6.54 (4.55)	.004 (95%CI=.45-2.33)
1-7	313 (62.5%)	107 (58.2%)	206 (68.4%)	.070
8-14	151 (30.1%)	67 (36.4%)	84 (27.9%)	
15-28	21 (4.2%)	10 (5.4%)	11 (3.7%)	
Number of DDD/day				
Mean	1.47+-.75 (Min=0.2, Max=4)	1.42 (.66)	1.49 (.79)	.29 (95%CI=-.19- .06)
<1	244 (48.7%)	95 (50.8%)	149 (47.5%)	.128
1.1-2	217 (43.3%)	83 (44.4%)	134 (42.7%)	
2-4	40 (8.0 %)	9 (4.8%)	31 (9.9%)	
Number of request/ year				
Average:	**3.35 +-3.48(min=1, max 12)**	**3.08 (3.4**	**3.51 (3.52)**	**.182 95%CI (-1.1-.166)**
1	186 (37.1%)	83 (44.6%)	103 (33.2%)	.060
2-3	149 (28.7%)	51 (27.4%)	93 (30.0%)	
4-6	100 (21%)	31 (16.7%)	74 (23.9%)	
7-12	61 (12.2%)	21 (11.3%)	40 (12.9%)	

At each dispensing patients received an average of 9.07 DDD. There was no significant difference in the number of DDDs dispensed between patients requesting antibiotic with or without prescription. 51.7% of females were dispensed between 1 to 7 DDD, while 58.2% of males were dispensed more than 8 DDD, however, the results were not statistically significant (p=.117). More patients above 50 years old were dispensed between 1 -7 DDD (55.7%) while only 47.7% of patients less than 50 years old were dispensed 1-7 DDD. (Table 3)

The average number of dispensings per year was 3.35. More than 50% requested antibiotics more than twice per year. Patients requesting antibiotic without prescription requested more antibiotic per year than patients with prescription. Only 33.2%of those requesting antibiotic without prescription were dispensed antibiotic once per year, compared to 44.6% for patients with prescription. (Table 3)

Males were dispensed significantly more antibiotics over year than females (p=.003). More males were dispensed antibiotics between 2-3 times over a year (36.6%) while females were dispensed mainly once per year (42.9%).Younger patients received an average of 3.09 dispensings over year, less than older patients (average=5.18) (p<.001). (Table S2)

3.3. Follow-up usage pattern of antibiotic

In the follow up, patients' consumption of DDD decreased to an average of 7.07 DDD; 62.5% used between 1 to 7

DDD. The average number of DDD per day was 1.47 DDD. Patients with medical prescription used more DDDs (average=7.93) than patients without prescription (average=6.54) (p=.0.04). There was no significant difference in the number of DDDs used per day between patients requesting antibiotic with or without prescription. (Table 3)

In the follow up, the results show no statistical difference between the DDD consumed between gender groups. The percentages of patients consuming 1-7 DDD increased to 62.9% in younger patients, and to 77.2% in older patients (>50 years old)(p.009). Patients aged25-50 years used significantly more often more than 1 DDD per day (61.7%) than patients above 50 (41%, p=.001). (Table S2)

The average consumption per day of coamoxiclav, amoxicillin, or macrolides was 2.0, 1.4 and 1.41 DDD respectively. Amoxicillin, coamoxiclav, and clarithromycin had mean administered daily doses twice the number of DDD while the average number of DDD consumed per day of other antibiotics was 1.

3.4. Efficacy Follow up

Most patients (91.7%) had complete relief and only 1.2% didn't improve on antibiotic. In general, 86.4% have assessed the treatment with antibiotic as very good. 10.9% have described it as sufficient and 3.5% as bad. Most patients have experienced relief of symptoms after 1-4 days (70.7%). This might explain the under use of antibiotic treatment. 19.8% experienced relief of symptoms after 5-7 days and only 8.3% had experienced relief after 2 weeks. 17 (3.5%) participants switched to another antibiotic for reasons of not feeling better (n=16, 94.1%) or due to side effects (n=1, 0.2%). The major antibiotics switched to were ceftriaxone injection (n=3) or oral coamoxiclav (n=4).

3.5. Follow up on Safety

Only 30 (6.6%) participants reported side effects. Gastrointestinal side effects were the main reported side effects (n=9), including diarrhea (n=5), abdominal pain (n=3), and vomiting (n=1). Skin allergic reactions and herpes were also reported in 13 cases. Other side effects reported were laziness (n=2), sedation (n=2), headache (n=2), and increasing appetite (n=1).One case of hospitalization was reported as due to exacerbation of the disease.

4. Discussion

This study found a high rate of antibiotic self-medication (62.7%) originating from pharmacist advice or relatives' recommendations. The overall average dispensing of antibiotics was 9.07DDD, indicating short term use (<2 weeks). The usage pattern of antibiotics was not different between patients buying antibiotics with or without prescription; however, the number of request per year of antibiotic was significantly higher in patients practicing self-medication. Antibiotics were commonly dispensed in different infectious diseases and were commonly dispensed with cough or flu medicines, or analgesics (paracetamol, NSAIDs).

Easy availability of antibiotics without prescription from community pharmacies and the low price of some antibiotics explain the wide use of antimicrobial drugs whether needed or not. Moreover, the use of antibiotics is relatively safe and rarely associated with adverse effects. The prevalence of self-medication was relatively higher than that reported by Cheaito et al study (40%) which was restricted to Beirut and its suburbs [7].

The average number of DDD per dispensing was not different between participants with or without prescriptions. Males had non-significantly higher average DDD consumption of antibiotics than females. In this study and in the study of Lombardy region, a greater prevalence was found in males than in females [8,9] This finding contrasts with another study done in the USA that showed that females were the main consumers of antibiotics in 2013. [10] Females used more broad spectrum antibiotics, including cephalosporins and macrolides, concomitantly with more symptomatic infections of the genital and urinary tract system than males [11].

Higher use of antibiotics was observed in younger patients. Differences in patterns of use with regards to age could be explained by different types of infections. The shift from beta-lactams to more broad spectrum antibiotics such as cephalosporins and fluoroquinolones in the older age (>50 years), is not unexpected because the immune response lessens with age and the prevalence of UTIs increases with age. The use of more DDD in younger age should raise awareness regarding the increase risk of bacterial resistance over time.

The average number of requests per year was considered high i.e. 3.35 times. More than 50% requested antibiotics more than twice per year. This average rises significantly in patients requesting antibiotic without prescription. This could be attributed to therapeutic failure or to increase in bacterial resistance. Other problems with self-medication are self-diagnosis and buying of antibiotics in sub-therapeutic quantities tend to become cultural norms in countries with few regulations on the acquisition of non-prescribed antimicrobial drugs [12]. Moreover, antibiotic therapy was often used by patients without ruling out the possibility of viral infections which is more common in these cases of respiratory tract infections. This finding is consistent with results of other studies in Abu-Dhabi, [13] Iran, [14] Jordan, [15] Lebanon [7] and Northern and Western Europe [16]. This explains the rapid relief of signs and symptoms of many complaints. So, patients stop the antibiotic just when the symptoms of illness disappear.

Coamoxiclav was highly used among patients in this population. This result replicates findings reported in Lebanon (48.9%) [7]. Similarly, in United Arab Emirates, it was the most commonly used (48.9%) [17] and in Pakistan. (62.8%) [18]. Although broad spectrum of antibiotics is effective against many bacterial infections and are relatively safe, this does not justify their uncontrolled use: prudent use of antibiotics promotes the use of narrow-spectrum targeted drugs when appropriate, to decrease the chance of emergence of drug-resistant microbial strains. Incorrect use could cause the development of resistant bacteria and diminish the ability of the

endogenous flora to resist colonization of harmful microorganisms, thereby leading to super infections by multi-resistant bacteria and yeasts [19].

The average consumption per day of coamoxiclav, amoxicillin, or macrolides was 2.00, 1.4 and 1.41DDD, respectively. Amoxicillin, coamoxiclav, and clarithromycin have mean daily doses twice the number of DDD. This study highlights the limits of DDD in estimating the daily doses consumed by patients per day. The effect, if any, of this increased dosage on bacterial resistance is unknown. Estimates of antibiotic use using DDD methods will remain open to criticism because the prescribed dosage, especially of antibiotics, often deviates from the "theoretical" daily dose, depending for instance on the location of the infection, pathogen susceptibility, or the excretory status of the patient [20].

An important concern should be raised about residual antibiotics, i.e., antibiotics that were dispensed but not used. These may result in uncontrolled self-medication and inappropriate use. This could be quantified by comparing the overall DDD of antibiotic dispensed during episode to that actually used, during follow-up. The average DDD dispensed during the episode was 9.05, greater than that used during the follow-up. The average DDD used for each antibiotic class was less than what had been dispensed. Patients probably stopped the medication as soon as the symptoms disappear, either because of poor medical knowledge or use of the antibiotic for conditions for which the medication was not indicated. This results in using the antibiotic beyond the scope and increasing the daily dose of antibiotic and increasing the risk of antibiotic resistance.

This study is the first prospective study done in the Lebanese population of the usage pattern of antibiotic consumption. However, our study suffers from several limitations. To begin with, since not all pharmacists accepted to participate to the study, the sample may not be representative of Lebanese population. We might also expect a change in behavior of the pharmacists in the presence of researchers, since the study addresses an illegal practice; Our results may be under estimating the reality of antibiotic self-medication. Second, there could also be a possibility of respondent and information bias, since the results of our study are based on a face-to-face questionnaire. Many persons did not agree to fill it out, which may also introduce a selection bias. Our study was limited to patients aged > 15 years old. Pediatric patients are also an important category group to measure extent of antibiotic use that could influence antibiotic resistance.

This study suffers from most consumer-based surveys issues, mostly the willingness or not of subjects coming to the pharmacy to spend tie filling a questionnaire or speaking to an interviewer. Patients may also be reluctant divulge information about disease of socioeconomic factors. As such our results represent only the part of the population that participated; mostly young, relatively healthy subjects who may have better educational level than older subjects. However, subjects in this study were recruited in various parts of the country. And difference in the spectrum of ages and professional status one might expect. The results are found were not unexpected and confirm to another studies done in the same area [7,15]. The fact that we did find two third non-prescribed dispensing of antibiotics shows the respondents answer making information bias unlikely.

5. Conclusion

This study reflects on the fact that antibiotic consumption in Lebanon is poorly controlled, with much misuse, often related to self-medication and non-prescribed use. To prevent this practice, health authorities have to implement educational programs for patients and pharmacists to emphasize the need for careful medical control of antibiotic prescriptions and regulations to reduce the usage of antibiotics.

Conflicts of Interest

The authors declare no conflicts of interest.

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Table S1. Anatomically Therapeutic Classification system for systemic antibiotics

Antibiotic Class	ATC class
Penicillins :	J01C
Penicillins with extended spectrum	J01CA
Penicillin combination with B-lactamase inhibitors	J01CR
B-Lactamase-sensitive penicillins	J01CE
Cephalosporins:	J01D
First-generation cephalosporins	J01DAa
Second-generation cephalosporins	J01DAb
Third-generation cephalosporins	J01DAc
Fluoroquinolones	J01MA
Macrolides, lincosamides and streptogramins	J01F
Sulphonamides and trimethoprim	J01E
Aminoglycosides	J01G
Metronidazole	J01XD01
Tetracyclines	J01A

Table S2. Dispensing pattern of antibiotic for gender and age groups:

	Gender					Age						
	Male		Female			16-25		25-50		>50-75		
Number of DDD/request	n	%	n	%	P-value	n	%	n	%	n	%	P-value
Mean (SD)	9.83 (5.77)		8.73 (4.67)		.025	8.68 (4.32)		9.86 (6.06)		8.07 (3.77)		.013
1-.7	64	41.8	180	51.7	.117	120	49.2	90	45.9	34	55.7	.097
7.5-14	76	49.7	146	42		112	45.9	85	43.4	25	41	
14.5-29	13	8.5	22	6.3		12	4.9	21	10.7	2	3.3	
Number of DDD/follow-up												
Mean (SD)	7.70 (5.76)		6.80 (4.51)		.095	6.50 (4.16)		8.11 (5.93)		6.05 (3.55)		.001
1-.7	89	61	224	66.1	.326	155	64.9	114	60.3	44	77.2	.009
7.5-14	48	32.9	103	30.4		79	33.1	60	31.7	12	21.1	
14.5-28	9	6.2	12	3.5		5	2.1	15	7.9	1	1.8	
Number of DDD/day												
Mean (SD)	1.56 (.8)		1.43 (.72)		.06	1.36 (.71)		1.63 (.76)		1.37 (.72)		<.001
<1	70	45.8	174	50	.112	135	55.3	75	38.3	34	55.7	.001
1.1-2	65	42.5	152	43.7		95	38.9	97	49..5	25	41.0	
2.-4	18	11.8	22	6.3		14	5.7	24	12.2	2	3.3	
Number of request/ year												
Mean (SD)	3.77 (3.64)		3.16 (3.41)		.073	2.99 (3.38)		3.22 (3.11)		5.18 (4.4)		<.001
1	39	25.5	147	42.9	.003	118	48.8	60	31.1	8	13.1	<.001
2-3	56	36.6	88	25.7		58	24	65	33.7	21	34.4	
4-6	36	23.5	69	20.1		40	16.5	50	25.9	15	24.6	
7-12	22	14.4	39	11.4		26	10.7	18	9.3	17	27.9	

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Evaluation of Self-medication Use of Antibiotics within Lebanese Population: A Prospective Pilot Study

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Abstract **Objective:** The aim of this study was to assess the appropriateness of antibiotic used in community based pharmacy setting. **Method:** It is a cross sectional prospective study in a community-based pharmacy setting in Lebanon. It uses a structured random interview to patients visiting a community pharmacy and seeking for antibiotics. Baseline characteristics and reason for self-medication were collected. Completing the questionnaire after 30 days provided information on adherence and usage pattern. Data were analyzed using descriptive statistics and Chi-square test. A multivariate logistic regression was performed to predict factors affecting appropriateness. **Results:** 62.7% of 501 participants bought antibiotics without prescription. Amoxicillin/clavulanic acid was the most used antibiotic as self-medication (33.7%). 62.4% of patients used the right antibiotic and 80.1% used it in correct dosage. The duration of treatment was inappropriate in the majority of cases (68.6%). When all of these three factors were summed together, it turned out that 83.6% of antibiotics were utilized inappropriately. Appropriateness in use was seen in 27.6% and 16.4% of the prescribed and non-prescribed antibiotics respectively. **Conclusion:** Our study shows great misuse of antibiotics and hence there is a need to increase awareness of the health risks related to inappropriate and uncontrolled use of antibiotics.

Keywords: *self-medication, antibiotic, Lebanon, misuse, appropriate use*

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1. Introduction

Antibiotics are considered among the most commonly sold drug classes in the developing countries.[1] Irrational use of antibiotics is a global problem [1] and the rate of this problem and antibiotic resistance is increasing in Middle-East. [2] Resistance rates differ significantly between developing and developed countries. Indeed, data from the Resistance Surveillance and Control in the Mediterranean Region (ARMED) project showed an increase of antimicrobial resistance in countries with high levels of antibiotic consumption such as eastern and southern Mediterranean regions, compared to low resistance rates in northern countries. [3]

This situation could be explained by the unregulated distribution of antimicrobials, and their wide availability without prescription in developing countries which is not the case in most of the developed countries where antibiotics are not available without medical prescription. [4,5] Overuse and the inappropriate use of antibiotics with incorrect dosages for inappropriate period of time increase the rate of selecting resistant strains and their dissemination in the population leading to a higher frequency of treatment failure. [6]

In Lebanon, like most other developing countries, having a valid prescription is not always enforced for receiving prescription-only medicines (POM). Previous researches in Lebanon showed that the prevalence of self-medication with antibiotics is alarmingly high [7] and revealed that the pattern of self-medication practice was inappropriate without further details.

The aim of this study therefore was to describe the community use of antibiotics within the Lebanese population living in Lebanon concerning appropriateness of use, dose and duration of antibiotic consumed and their conformity to IDSA guideline.

2. Method

2.1. Design and Study Population

A cross sectional prospective study was conducted in a community-based pharmacy setting in Lebanon. Data was collected over a 1-year period (September 2015 to September 2016) from 50 community pharmacies (CPs) distributed in the six districts in Lebanon: Beirut, South Lebanon, Nabatiyeh, Mount Lebanon, Bekaa, and North Lebanon.

Eligible participants were recruited randomly from consumers presenting at CPs in Lebanon after they had

purchased antibiotic medication with or without prescription. The patients included were from both genders, aged 16 years and older, coming to purchase antibiotic. The patients were divided into two groups: those buying antibiotic with a prescription versus those buying them without prescription.

The Lebanese University, Faculty of Pharmacy Internal Review Board waived the need for written informed consent. The patients were informed about the objective of the study and were asked to give an oral consent. Only those who gave their voluntary informed oral consent were enrolled.

2.2. Sample Size Calculation

A sample size was calculated assuming a type I error of 5% and a study power of 80% and 95%CI. Based on a previous study, 40% of patients were expected to self-medicate with antibiotics. [7] The minimal sample size necessary to show a twofold increase in the risk of exposure to non-prescribed antibiotics consists of 442 subjects: 186 patients for those buying antibiotic with prescription and 256 without prescription.

2.3. Procedure and Data Collection

Data on antibiotic use was collected using a structured random interview conducted by pharmacists or interviewers who had been briefed about the study's aims and methods. Consecutive customers arriving at CPs seeking antibiotic were interviewed. Data was collected from the participants twice, first at purchase for data about drug used and the condition for which it was to be used, then by calling the patient 30 days after starting the medication, for usage patterns.

The questionnaire included many sections that were chosen following an extensive review of literature. The questionnaire was translated into Arabic and subjected to a process of forward and backward translation into English. It was pretested and validated first on 20 patients visiting 4 different pharmacies before starting the survey.

The questionnaire consisted of dichotomous and close-ended questions. It consisted of the following sections: socio-demographic data (age, sex, occupation, educational and marital status, monthly income, medical insurance, and the presence of a care provider at home), lifestyle data (smoking status, alcohol status, and involvement in sport activities), complaint for which the antibiotic is taken, the medication details (name, dose, duration and mode of administration as recommended to be taken), presence of comorbidities (defined as long-term diseases diagnosed by physicians) and background medications, as well as reasons and sources of self-medication.

Thirty days after starting the medication, patients were assessed about adherence and duration of antibiotic consumed, direction of use, and reasons for misuse.

2.4. Data Analysis

Appropriate antibiotic use was described by the choice of antibiotics dispensed, duration of antibiotic used, and prescribed daily doses (PDD) of antibiotic consumed by each patient in the follow up. The suitability of the dispensed antibiotic for the customer's complaint and duration were decided using IDSA guideline. Because of the absence of Lebanese guidelines, the IDSA guidelines are generally taught during medical education in Lebanon and are deemed to be the most important guidelines on an international level. The PDD was assessed in comparison to recommended daily dose (RDD) of treatment based on the French national drug formulary (VIDAL® dictionary) (https://www.vidal.fr/).

One point was awarded for each correct use and 0 point will be awarded for misuse, wrong choice of medication, wrong duration (underuse or overuse), or wrong PDD. Later on, the dispensed antibiotic was assessed by summing up the scores given for each item. The total score obtained was 3, which refers to 'appropriate treatment' whereas the lower scores were defined as 'inappropriate treatment'.

Statistical analysis was performed using SPSS for Windows version 19. Frequencies and percentages of patient's characteristics, treated complaints, classes of antibacterial drugs dispensed and their appropriateness were calculated and presented. Chi-2 test was used to determine the associations between qualitative variables and other outcome measures. Stepwise multivariate logistic regression was then used to control for potential confounding variables and to calculate the odds ratios for potential independent variables for appropriateness. A p-value of 0.05 or less was considered to be statistically significant.

3. Results

3.1. Baseline Characteristics

Of a total of one thousand questionnaire distributed to CPs data from a total of 501 patients were recorded in the study. Among participants, 314 (62.7%) have requested for antibiotic without prescription while 187 (37.3 %) had a medical prescription for their antibiotic. Both groups were homogenous regarding gender (p=0.154), age (p=0.532), education (p=0.285), income (p=0.051), and presence of comorbidities (p=0.548). The majority were females (69.5%) and between 16 and 50 years of age (87.8%). About half of the patients had a university degree (55.7%) (Table 1).

A total of 392 patients (78.2%) had no associated medical conditions, while 109 (21.8%) suffered from chronic diseases, among which 21.8% had hypertension, 3.2% had asthma or COPD, 5.8% had dyslipidemia, and 3.8% for diabetes, 2.4% had gastric diseases, and 3.6% had osteoarthritis. 3 participants were pregnant and one had an allergy to penicillin.

Our results indicated that amoxicillin–clavulanic acid (coamoxiclav) combination was the most purchased antibiotic (33.7 %) followed by cephalosporins (21.2%). 33.9% of participants were using antibiotic once per year. Coamoxiclav was the most frequently dispensed antibiotic without prescription (37.3%) followed by cephalosporins (21%), penicillins (17.2%), macrolides (6.1%) and fluoroquinolones (3.8%) respectively. The antibiotics that were dispensed with a prescription, in the following descending order: coamoxiclav (27.8%), cephalosporins (21.4%), fluoroquinolones (17.6%), macrolides (14.4%) and penicillins (5.3%). (Table 2).

Table 1. Characteristics of the study population

	Total participants N=501	Participants with medical prescription N= 187	Participants without medical prescription N= 314	p-value
Gender				
Male	153 (30.5%)	50 (26.7%)	103 (32.8%)	0.154
Female	348 (69.5%)	137 (73.3%)	211 (67.2%)	
Age group				
16-25	244 (48.7%)	85 (45.5%)	159 (50.6%)	0.532
25-50	196 (39.1%)	78 (41.7%)	118 (37.6%)	
>50	61 (12.2%)	24 (12.8%)	37 (11.8%)	
Educational level				
Primary and less	153 (30.5%)	65 (34.8%)	88 (28%)	0.285
Secondary	69 (13.8%)	24 (12.8%)	45 (14.3%)	
University	279 (55.7%)	98 (52.4%)	181 (57.6%)	
Marital status				
Single	259 (51.7%)	90 (48.1%)	169 (53.8%)	0.217
Married	242 (48.3%)	97 (51.9%)	145 (46.2%)	
Currently working				
Yes	173(34.5%)	134 (71.7%)	194 (61.8%)	0.025
No	328 (65.5%)	53 (28.3%)	120 (38.2%)	
Family income (LL)				
<2000000	134 (74.4%)	38 (20.3%)	95 (30.3%)	.051
>2000000	46 (9.2%)	18 (9.6%)	27 (8.6%)	
No answer	323 (64.5%)	131 (70.1%)	192 (61.1%)	
Presence of comorbidities				
Yes	109 (21.8%)	38 (20.3%)	71 (22.6%)	0.548
No	392 (78.2%)	149 (79.7%)	243 (77.4%)	
Data presented as number (%) were performed using Chi2 respectively and a p-value < 0.05 is considered significant.				

Table 2. Self-medication practice among participants

	Total participants N=501	Participants with medical prescription N= 187	Participants without medical prescription N= 314	p-value
Antibiotic Classes:				
coamoxiclav	169(33.7%)	52 (27.8%)	117 (37.3%)	<.001
Amoxicillin or penicillins	64 (12.8%)	10 (5.3%)	54 (17.2%)	
Cephalosporins	106 (21.2%)	40 (21.4%)	66 (21.0%)	
Fluoroquinolones	45 (9%)	33 (17.6%)	12 (3.8%)	
Macrolides	46 (9.2%)	27 (14.4%)	19 (6.1%)	
Others	71 (14.2%)	25 (13.4%)	46 (14.6%)	
Ab request/year				
1st time	170 (33.9%)	70 (37.4%)	100 (32.2%)	.132
More than 1 time	328 (65.5%)	117 (62.6%)	211 (67.8%)	
Types of infection				
Respiratory tract infections:				
Tonsillitis	138 (27.5%)	43 (23%)	95 (30.3%)	.629
Cold	88 (17.6%)	19 (10.2%)	69 (22%)	.629
Sore throat	42 (8.4%)	6 (3.2%)	36 (11.5%)	.001
Cough	34 (6.8%)	14 (7.5%)	20 (6.4%)	.631
Otitis	32 (6.4%)	13 (7%)	19 (6.1%)	.320
Sinusitis	21 (4.2%)	10 (5.3%)	11 (3.5%)	.690
Chest tightness	14 (2.8%)	7 (3.7%)	7 (2.2%)	<.001
Runny nose or sneezing	10 (6.8%)	3 (1.6%)	7 (2.2%)	.079
Gastrointestinal infections:				
Diarrhea	60 (12%)	18 (9.6%)	42 (13.4%)	.394
Teeth infections	33 (6.6%)	17 (9.1%)	16 (5.1%)	.211
Urinary tract infections:	62 (12.4%)	36 (19.3%)	26 (8.3%)	.022
Skin infections:				
Skin infection	21 (4.2%)	12 (6.4%)	9 (2.9%)	.319
Acne	9 (1.8%)	6 (3.2%)	3 (1%)	.055
General:				
Fever	7 (1.4%)	3 (1.6%)	4 (1.3%)	.750
Pain	18 (3.6%)	5 (2.7%)	13 (4.1%)	.179
Others	35 (7%)	14 (7.4%)	17 (5.3%)	.750
Data presented as number (%) were performed using Chi2 respectively and a p-value < 0.05 is considered significant.				

The most concern indications were for respiratory tract infections mainly tonsillitis (27.5%) and flu (17.6%), followed by oral and gastrointestinal tract infections (18.6%) and urinary tract infection (12.4%). Our study shows high percentage of non-prescribed acquisition of antibiotic to treat respiratory tract infections: tonsillitis (30.3%), cold (22%) and cough (6.4%), oral and gastrointestinal tract infections: diarrhea (13.4%) and teeth infections (5.1%), skin and urinary tract infections (8.3%). Patients buying antibiotics for urinary tract infections had significantly more prescriptions ($p<0.05$). (Table 2)

3.2. Appropriateness of Antibiotic

There was statistical difference in the appropriateness between patients buying antibiotic with or without prescription regarding the drug choice ($p=0.003$), appropriate dose ($p=0.036$) and treatment duration ($p=0.054$). Moreover, the difference in global appropriateness was also statistically significant ($p=0.003$). (Figure 1).

Our study has shown that 67.3% of patients have used the right antibiotic against 32.7% of patients have failed to do so. 47.1% used the first line treatment and 19.3% of patients have misused the antibiotic for conditions of sore throat, cough, flu, runny nose, chest tightness, pain and sneezing. 5.3% have used non-recommended drugs for their condition. In the majority of the cases, the dose used by patients was appropriate (88.7%). 9.5% have used low dosage and 5% have exceeded the right dose compared to VIDAL. However, the duration of treatment was inappropriate in majority of cases (58.3%), where the majority didn't complete the full course of antibiotic or used it for low duration (43.2%). When all of these three factors were summed together, it turned out that only 20.2% of antibiotic were used appropriately.

Appropriateness in use was seen in 27.6% and 16.4% of the prescribed and non-prescribed antibiotics, respectively. Among participants buying antibiotic without prescription, 62.4% were dispensed the right antibiotic for their complaint conditions. 32.2% misused the antibiotic and 5.4% used non-recommended drug for their condition. Most of the patients (80.1%) used the correct dose. The duration of treatment was inappropriate in majority of cases (68.6%). (Table 3)

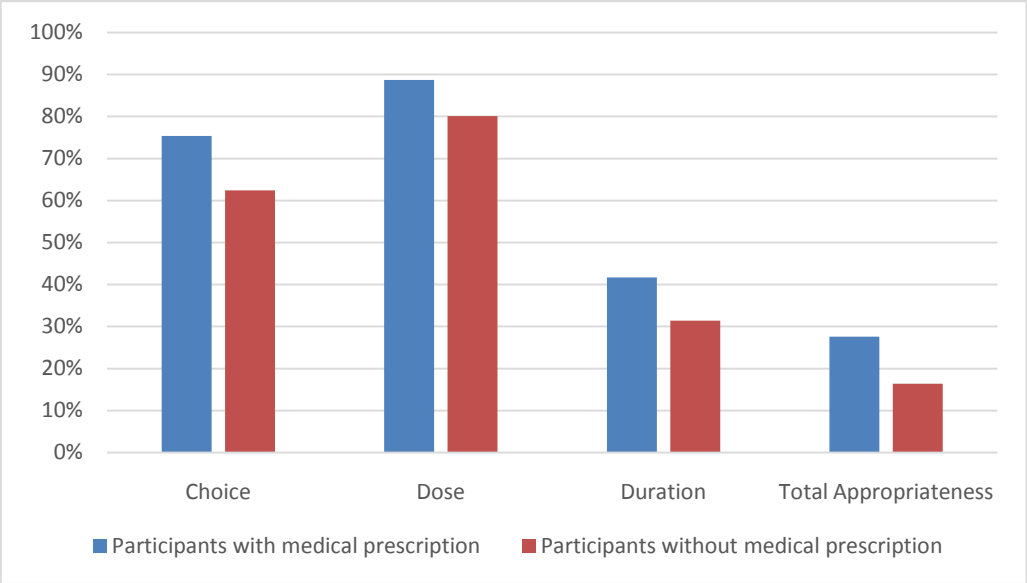

Figure 1. Percentages of appropriateness of choice, dose, duration and overall conformity between participants with prescription or self-medicated antibiotic

Table 3. Percentages of appropriateness of choice, dose, duration and overall conformity between participants with prescription or self-medication antibiotic

	Total participants N=501	Participants with medical prescription N= 187	Participants without medical prescription N= 314	p-value
Choice				
Misuse	137 (27.3%)	36 (19.3%)	101 (32.2%)	0.015
1st line	204 (40.7%)	88 (47.1%)	116 (36.9%)	
2nd line	133 (26.5%)	53 (28.3%)	80 (25.5%)	
Not recommended	27 (5.4%)	10 (5.3%)	17 (5.4%)	
Dose				
Low dose	32 (9.5%)	9 (6.4%)	23 (11.7%)	.110
Appropriate dose	282 (83.7%)	125 (88.7%)	157 (80.1%)	
Overdose	23 (6.8%)	7 (5%)	16 (8.2%)	
Duration				
Short period	171 (52.8%)	60 (43.2%)	111 (60.0%)	0.008
Appropriate	116 (35.8%)	58 (41.7%)	58 (31.4%)	
Long period	37 (11.4%)	21 (15.1%)	16 (8.6%)	

Data presented as number (%) were performed using Chi2 respectively and a p-value < 0.05 is considered significant.

3.3. Factors Affecting Antibiotic Use Appropriateness

When studying the following factors affecting appropriateness: gender, age category, education levels, marital status, employment, family income, and presence of comorbidities, none of these studied factors have shown a significant difference with respect to choice and dose of antibiotic medication. While studying the duration conformity only presence of comorbidities showed a significant difference that was statically significant (p=.001), patients without comorbidities have shown greater appropriateness (70.7%). Only this factor has shown also a significant difference with respect to overall appropriateness (p=.032). (Table S1)

The appropriateness of choice of antibiotic was significantly different between the different conditions. Patients used the medication appropriately in cases of tonsillitis, diarrhea, teeth infection, urinary infection and skin infection. The dose of antibiotic was appropriate in case of tonsillitis, urinary infection. The treatment duration was appropriate in most cases of diarrhea, otitis, sinusitis. The overall appropriateness was significantly different between different conditions treated. The majority of patients were using antibiotic inappropriately in all indications except sinusitis (52% appropriate use, p<0.001). (Table S2)

3.4. Multivariate Analysis

We observed several factors affecting overall appropriateness (Table 4). Patients with sinusitis have better appropriateness compared to other complaints. Patients with tonsillitis and flu had less appropriateness. As the number of request per year increases, the overall appropriateness significantly decreases by 9%. Patients with dyslipidemia had also better appropriateness.

Table 4. Multivariate analysis among factors affecting appropriate choice, dose, duration, and overall appropriateness

Multivariate Analysis	aOR	95% CI	p-value
overall appropriateness			
Predictors			
Presence of insurance	2.00	1.18-3.40	.01
Sinusitis	5.19	1.87-14.44	.002
Tonsillitis	.346	.19-.64	.001
Flu	.22	.087-..56	.002
Number of request per year	.904	.83-.98	.017
Dyslipidemia	4.27	1.65-11.08	.003
Appropriate Choice			
Pain	.212	.046-.98	.047
Flu	.222	.1-.51	<.001
Cough	.37	.13-1.07	.066
Tonsillitis	123.45	33.74-451.72	<.001
Sore throat	.12	.035-.422	.001
Diarrhea	27.44	8.04-93.61	<.001
Teeth infection	68.27	8.49-549.05	<.001
Urinary infection	11.07	4.53-27.05	<.001
Appropriate Dose			
OTC	.51	.24-1.06	.070
Antibiotic Classes:			.025
coamoxiclav	.61	.22-1.72	.353
Amoxicillin or penicillins	.42	.13-1.36	.148
Cephalosporins	.26	.09-.798	.018
Fluoroquinolones	.17	.03-.947	..043
Macrolides	4.52	.49-41.45	.182
Others	Reference		
Urinary tract infections	6.31	1.57-25.37	.009
Antibiotic request per year	1.99	1.04-3.84	.039
Water pipe	.45	.219-.904	.025
Taking other medications at the time of administering antibiotic	2.21	1.17-4.15	.014
Appropriate Duration			
Presence of Insurance	1.99	1.14-3.456	.014
Tonsillitis	.152	.083-.276	<.001
Sinusitis	4.32	1.26-14.76	.020
Hypertension	5.05	1.48-17.15	.009

aOR: adjusted odds ratio above 1 indicates increased n appropriateness and below 1 less appropriateness. CI: Confidence Interval
Only factors significantly associated with better or worse appropriateness are shown.

The following factors have shown a statistical difference of drug conformity. Pain, sore throat, cough, and flu were associated with significant less appropriateness. Diarrhea, teeth infections, and urinary tract infections were associated with better choice.

Self-medication negatively influenced the dosage appropriateness. Patients who used cephalosporins was associated with significant less appropriateness as well as fluoroquinolones. Patients with increased antibiotic request per year have greater dose conformity. Patients with urinary infection have better dose adequacy. Consumption of other drugs at the time of dispensation has also positively influenced the dose conformity.

Many factors were found to be significantly associated with better duration conformity to IDSA guideline: sinusitis, and hypertension. Tonsillitis has negatively influenced the duration conformity. Presence of insurance has positively influenced the duration conformity.

3.5. Follow up on Adherence

Current study shows that only 43.8% (n=213) completed the full course of antibiotic while 273 patients have admitted to underuse (94.9%) or overuse (5.12%). The most common reasons reported for under use were feeling better and symptoms were already resolved (86.8%), didn't feel better (5.12%), and feeling unwell (2.56%). The justifications for overuse were better control of disease and symptoms (2.56%), looking for faster healing (2.19%), and need more effect (0.36%). Moreover, 12 cases have increased the dose (4.8%).

Almost half of the sample patients reported stopping their medications when the disease is under control (51.2%) and only 12.9% reported forgetting to take their medications sometimes. 10.4% missed taking their medications for reasons other than forgetting. Moreover, only 3.3% of the patients reported cutting back their medications when they felt better or worse during the duration of treatment.

4. Discussion

This study has revealed a high rate of antibiotic self-medication (62.7%). The easy availability of antibiotics without prescription from CPs and the low price for some antibiotics explains the wide use of antimicrobial drugs whether needed or not. The prevalence of self-medication was relatively higher than that reported by Cheaito et al study (40%) which was restricted to Beirut and its suburbs. [7]

In this pilot study, we found a high percentage of non-appropriateness of the used self-medicated antibiotics concerning treatment duration (64.2%) and overall appropriateness (77.6%). Antibiotic use was not conforming to the guidelines in the majority of cases. This could be explained by several factors including low adherence and rapid relief of symptoms. Poorer compliance with antibiotic therapy has been associated with the use of longer courses of therapy and regimens having more daily doses; [8] patients also frequently report discontinuing antibiotic therapy when they begin to feel better or when adverse events occur. [9]

The prescribed daily dose (PDD) of antibiotics consumed by each patient was highly appropriate (83.7%). This could be explained by several factors. First, a high percentage of self-medication antibiotics is based on pharmacists' advice (34.7%). We should not neglect the role of pharmacists in guidance of customers on the appropriate use of antibiotics. Secondly, 40.4% of self-medication antibiotics are based on previous experience or previous prescription for the same signs and symptoms; thus, physicians indirectly contributed to these self-medicated drugs. Moreover, many patients have requested antibiotic several times per year which explain the high percentage of conformity of dosage compared to VIDAL.

Furthermore, coamoxiclav was highly consumed which replicates findings to that reported in Lebanon (48.9%). [7] Similarly, in United Arab Emirates, it was the most commonly used (48.9%) [10] and in Pakistan (62.8%). [11] Although broad spectrum antibiotics are effective against many bacterial infections and are relatively safe, prudent use of antibiotics promotes the use of narrow-spectrum targeted drugs when appropriate in order to decrease the emergence of drug-resistant microbial strains. Incorrect use could cause the development of resistant bacteria and diminish the ability of the endogenous flora to resist colonization by harmful microorganism, thereby leading to super infections by multi-resistant bacteria and yeasts. [12]

The common use of antibiotic for minor illnesses is consistent with results of other studies in Abu Dabi, [13] Iran, [14] Jordan, [15] Kuwait, [16] Libya, [17] Lebanon, [7] Egypt, [18] Saudi Arabia [19] and Northern and Western Europe. [20] The rapid relief of signs and symptoms of many complaints causes patients stopped treatment when the illness symptoms disappear and use it for several times over year. This usage pattern is one that typically results in the emergence of resistance.

Presence of comorbidities as dyslipidemia or hypertension have shown better overall appropriateness and better duration conformity. This could be explained by that patients with comorbidities are regular users of medical resources, see physicians and are used to take drugs as directed and have a high rate of POM.

Appropriateness of prescribing antibiotics was higher than that of self-medication although the overall appropriateness of prescribed antibiotics is still low (27.6%). This could be explained by several factors, such as the lack of simple and clear recommendations for treatment duration, the lack of clinical trials to assess the optimal treatment duration, variability in medical knowledge, and psychosocial factors involved in medical decision making. [21] Patients should be encouraged to the proper use of antibiotics using all appropriate public media. Physician's decision to prescribe an antibiotic may be influenced by pharmaceutical promotions and patient demand. As a result, interventions are required to improve the appropriate prescribing of antibiotics.

Our results show that patients with tonsillitis have less conformity to overall appropriateness and duration since based on the IDSA guideline the treatment should be completed for 10 days which is greater than the treatment duration of other complaints and the usual symptoms for tonsillitis resolve within a few days. Moreover, patients

with fewer antibiotic request per year have better overall conformity. These are important findings, because inappropriate antibiotic use has contributed to the rising incidence of antimicrobial resistance. [22]

Other problems with self-medication are self-diagnosis and buying of antimicrobial drugs in sub-therapeutic quantities, which tend to become cultural norms in countries with few regulations on the acquisition of non-prescribed antimicrobial drugs. [23] Patients with insurance have shown better duration conformity since they would buy the box of antibiotic and not in sub-therapeutic quantities.

This study is the first prospective study done in Lebanese population reflecting the appropriateness of antibiotic use and consumption. However, our study suffers from several limitations. To begin with, since not all pharmacists accepted to participate to the study, the sample may not be representative of Lebanese population. We might also expect a change in behavior of the pharmacists in the presence of researchers, since the study addresses an illegal practice; thus our results may be underestimating the reality of antibiotic self-medication practice. Second, there could also be a possibility of respondent and information bias, since the results of our study are based on a face to face questionnaire. Third, the sample was limited by its small size. Many people did not agree to participate, which may also introduce a selection bias. The small size of the sample affects also the power of tests to find significant differences. Additional large scale studies are recommended to take into account the cited limitations.

This study suffers from most consumer-based surveys issues, mostly the willingness or not of subjects coming to the pharmacy to spend tie filling a questionnaire or speaking to an interviewer. Patients may also be reluctant divulge information about disease of socioeconomic factors. As such our results represent only the part of the population that participated; mostly young, relatively healthy subjects who may have better educational level than older subjects. However, subjects in this study were recruited in various parts of the country. And difference in the spectrum of ages and professional status one might expect. The results are found were not unexpected and confirm to another studies done in the same area. [7,15] The fact that we did find two third non-prescribed dispensing of antibiotics shows the respondents answer making information bias unlikely.

5. Conclusion

This study reflects on the fact that antibiotic consumption in Lebanon is uncontrolled and that non-appropriateness to guidelines is common. In Lebanon, inadequate enforcement of drug regulations raised inappropriate antibiotics consumption. Patients should be educated about the proper use of drugs and the need for medical advices, especially for antibiotics considering the personal and populational risks of drug resistance. This should be accompanied by educational programs for pharmacists and physicians before reinforcing the regulatory aspects of drug prescription and dispensing.

Conflicts of Interest

The authors declare no conflicts of interest.

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Table S1. Sociodemoraphic factors affecting appropriate choice, dose, duration, and overall:

	non-appropriate Choice	Appropriate Choice	P-value	non-appropriate Dose	Appropriate Dose	P-value
Gender						
Male	49 (29.9%)	104 (30.9%)	0.823	18 (32.7%)	86 (30.5%)	0.743
Female	115 (70.1%)	233 (69.1%)		37 (67.3%)	196 (69.5%)	
Age group						
16-25	81 (49.4%)	163 (48.4%)	0.396	31 (56.4%)	132 (46.8%)	0.247
25-50	59 (36%)	137 (40.7%)		21 (38.2%)	116 (41.1%)	
>50	24 (14.6%)	37 (11%)		3 (5.5%)	34 (12.1%)	
Educational level						
primary and less	53 (32.3%)	100 (29.7%)	0.298	12 (21.8%)	88 (31.2%)	0.314
secondary	17 (10.4%)	52 (15.4%)		8 (14.5%)	44 (15.6%)	
university	94 (57.3%)	185 (54.9%)		35 (63.6%)	150 (53.2%)	
Marital status						
single	84 (51.2%)	175 (51.9%)	0.881	33 (60%)	142 (50.4%)	0.19
married	80 (48.8%)	162 (48.1%)		22 (40%)	140 (49.6%)	
Currently working						
yes	104 (63.4%)	224 (66.5%)	0.449	36(65.5%)	188 (66.7%)	0.862
no	60 (36.6%)	113 (33.5%)		19 (34.5%)	94 (33.3%)	
Family income (LL)						
<2000000	46 (28%)	87 (25.8%)	0.442	15 (27.3%)	72 (25.5%)	0.712
>2000000	11 (6.7%)	34 (10.1%)		7 (12.7%)	27 (9.6%)	
unemployed	107 (65.2%)	216 (64.1%)		33 (60%)	183 (64.9%)	
Presence of comorbidities						
No	121 (73.8%)	271 (80.4%)	0.091	48 (87.3%)	223 (79.1%)	0.161
Yes	43 (26.2%)	66 (19.6%)		7 (12.7%)	59 (20.9%)	
Daman						
No	54 (34%)	123 (69.5%)	0.52	145 (37.8%)	28 (28.3%)	0.079
Yes	105 (66%)	210 (66.7%)		239 (62.2%)	71 (71.7%)	
Ab request						
1st time	56 (34.6%)	110 (32.7%)	0.68	24 (44.4%)	86 (30.5%)	0.045
More than once/ year	106 (65.4%)	226 (67.3%)		30 (55.6%)	196 (69.5%)	
	Non-appropriate duration	**Appropriate duration**	**p-value**	**Non Overall appropriate**	**Overall Appropriate**	**p-value**
Gender						
Male	59 (28.4%)	39 (33.6%)	0.323	114 (29.3%)	33 (32.7%)	0.511
Female	149 (71.6%)	77 (66.4%)		275 (70.7%)	68 (67.3%)	
Age group						
16-25	110 (52.9%)	49 (42.2%)	0.125	200 (51.4%)	41 (40.6%)	0.143
25-50	80 (38.5%)	51 (44%)		144 (37%)	47 (46.5%)	
>50	18 (8.7%)	16 (13.8%)		45 (11.6%)	13 (12.9%)	
Educational level						
primary and less	64 (30.8%)	31 (26.7%)	0.66	121 (31.1%)	28 (27.7%)	0.801
secondary	31 (14.9%)	16 (13.8%)		50 (12.9%)	14 (13.9%)	
university	113 (54.3%)	69 (59.5%)		218 (56%)	59 (58.4%)	
Marital status						
single	116 (55.8%)	53 (45.7%)	0.082	208 (53.5%)	46 (45.5%)	0.155
married	92 (44.2%)	63 (54.3%)		181 (46.5%)	55 (54.5%)	
Currently working						
yes	147 (70.7%)	75 (64.7%)	0.264	262 (67.4%)	64 (63.4%)	0.478
no	61 (29.3%)	41 (35.3%)		127 (32.6%)	37 (36.6%)	
Family income (LL)						
<2000000	48 (23.1%)	28 (24.1%)	0.072	97 (24.9%)	27 (26.7%)	0.145
>2000000	16 (7.7%)	18 (15.5%)		31 (8.0%)	14 (13.9%)	
unemployed	144 (69.2%)	70 (60.3%)		261 (67.1%)	60 (59.4%)	
Presence of comorbidities						
No	179 (86.1%)	82 (70.7%)	0.001	312 (80.2%)	71 (70.3%)	0.032
Yes	29 (13.9%)	34 (29.3%)		77 (19.8%)	30 (29.7%)	
Daman						
No	24 (43.6%)	99 (35.6%)	0.26	86 (41.3%)	32 (28.1%)	0.018
Yes	31 (56.4%)	179 (64.4%)		122 (58.7%)	82 (71.9%)	
Ab request						
1st time	68 (32.9%)	42 (36.2%)	0.54	131 (33.9%)	35 (34.7%)	0.89
More than once/ year	139 (65.3%)	74 (63.8%)		255 (66.1%)	66 (65.3%)	

Table S2. Factors affecting appropriateness of choice, dose, duration and overall:

	Non-appropriate choice	Appropriate Choice	p-value	Non-appropriate Dose	Appropriate Dose	p-value
Antibiotic Classes:			0.314			
coamoxiclav	57 (33.7%)	112 (66.3%)		17 (15.2%)	95 (84.8%)	0.026
Amoxicillin or penicillins	25 (39.1%)	39 (60.9%)		10 (25.6%)	29 (74.4%)	
Cephalosporins	40 (37.7%)	66 (62.3%)		17 (25.8%)	49 (74.2%)	
Fluoroquinolones	11 (24.4%)	34 (75.6%)		4 (11.8%)	30 (88.2%)	
Macrolides	12 (26.1%)	34 (76.9%)		1 (2.9%)	33 (97.1%)	
Others	19 (26.8%)	52 (73.2%)		6 (11.5%)	46 (88.5%)	
Types of infection						
Respiratory tract infections:						
Tonsillitis	3 (1.8%)	135 (97.8%)	<.001	27 (20%%)	108 (80%)	0.135
Cold	60 (68.2%)	28 (31.8%)	<.001	4 (14.3%)	24 (85.7%)	0.761
Sore throat	36 (85.7%)	6 (14.3%)	<.001	1 (16.7%)	5 (83.3%)	0.982
Cough	21 (61.8%)	13 (38.2%)	<.001	5 (38.5%)	8 (61.5%)	0.028
Otitis	13 (40.6%)	19 (59.4%)	0.335	3 (15.8%)	16 (84.2%)	0.949
Sinusitis	5 (23.8%)	16 (76.2%)	0.373	2 (12.5%)	14 (87.5%)	0.672
Chest tightness	12 (85.7%)	2 (14.3%)	<.001	0	2	0.531
Runny nose or sneezing	5 (50%)	5 (50%)	0.24	2 (40%)	3 (60%)	0.149
Gastrointestinal infections:						
Diarrhea	4 (6.7%)	56 (93.3%)	<.001	10 (17.9%)	46 (82.1%)	0.733
Teeth infections	1 (3.1%)	31 (96.9%)	<.001	3 (9.7%)	28 (90.3%)	0.294
Urinary tract infections:	7 (11.3%)	55 (88.7%)	<.001	4 (7.3%)	51 (92.7%)	0.047
Skin infections:						
Skin infection	0	21 (100%)	0.001	6 (28.6%)	15 (71.4%)	0.117
Acne	7 (77.8%)	2 (22.2%)	0.004	0	2	0.531
General:						
Pain	16 (88.9%)	2 (11.1%)	>.001	1 (50%)	1 (50%)	0.196
	Non-appropriate duration	**Appropriate duration**	**p-value**	**Non Overall Appropriate**	**Overall Appropriate**	**p-value**
Antibiotic Classes:						0.024
coamoxiclav	71 (65.7%)	37 (34.3%)	0.061	134 (34.4%)	33 (19.8%)	
Amoxicillin or penicillins	32 (82.1%)	7 (17.9%)		58 (90.6%)	6 (9.4%)	
Cephalosporins	38 (59.4%)	26 (40.6%)		84 (21.6%)	20 (19.2%)	
Fluoroquinolones	20 (58.8%)	14 (41.2%)		34 (75.6%)	11 (24.4%)	
Macrolides	24 (70.6%)	10 (29.4%)		37 (80.4%)	9 (19.6%)	
Others	23 (51.1%)	22 (48.9%)		42 (65.6%)	22 (34.4%)	
Types of infection						
Respiratory tract infections:						
Tonsillitis	114 (85.7%)	19 (14.3%)	<.001	121 (88.3%)	16 (11.7%)	0.002
Cold	20 (71.4%)	8 (28.6%)	0.404	82 (93.2%)	6 (6.8%)	<.001
Sore throat	4 (1.9%)	1 (20%)	0.458	41 (100%)	0	0.001
Cough	9 (69.2%)	4 (30.8%)	0.699	32 (94.1%)	2 (5.9%)	0.028
Otitis	8 (42.1%)	11 57.9%)	0.038	23 (71.9%)	9 (28.1%)	0.277
Sinusitis	4 (25%)	12 (75%)	0.001	10 (47.6%)	11 (52.4%)	<.001
Chest tightness	0	2	0.057	12 (85.7%)	2 (14.3%)	0.553
Runny nose or sneezing	1 (20%)	4 (80%)	0.038	8 (80%)	2 (20%)	0.961
Gastrointestinal infections:						
Diarrhea	19 (40.4%)	28 (59.6%)	<.001	27 (51.9%)	25 (48.1%)	<.001
Teeth infections	19 (63.3%)	11 (36.7%)	0.917	21 (67.7%)	10 (32.3%)	0.098
Urinary tract infections:	31 (57.4%)	23 (42.6%)	0.254	40 (65.6%)	21 (34.4%)	0.004
Skin infections:	4 (25%)	12 (75%)	0.001			
Skin infection	13 (61.9%)	8 (38.1%)	0.821	15 (71.4%)	6 (28.6%)	0.357
Acne	1	1	0.674	8 (88.9%)	1 (11.1%)	0.477
General:						
Pain	0	2 (1.7%)	0.057	17 (94.4%)	1 (5.6%)	0.108

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Public Knowledge and Attitude towards Antibiotic Use in Lebanon

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Abstract **Introduction:** Antibiotic resistance is a major threat in global public health. This study aims to assess the public knowledge, attitude and practice towards antibiotic use among general public in Lebanon. **Method:** It was a cross sectional study in a community-based pharmacy setting in Lebanon. It used a structured random interview to patients visiting community pharmacy seeking for antibiotics. Descriptive statistics were presented and multivariate logistic regressions were performed in data analysis. **Results:** A total of 495 participated in the study. The study sample had in general low knowledge (average = 6) and attitude score (average=3.16). High proportion of Lebanese participants believed that antibiotics were used for treatment of common cough cold and sore throat symptoms (59%) or viral infections (53%). 42% preferred to take antibiotics from the pharmacy without physician prescription. In the multivariable logistic regression analysis, females showed better knowledge toward antibiotic use compared to males (ORa=1.59, 95%CI=1.01-2.53). Compared to participants aged >50 years old, the level of adequate knowledge was higher in those aged 25-50 years old (ORa=3.66, 95%CI=1.79-7.49). **Conclusion:** This study identified important knowledge and attitude gaps among general public in Lebanon. Future antibiotic awareness campaigns and patient counselling should be implemented to reduce the risk of antibiotic resistance.

Keywords: *antibiotic, knowledge, attitude, Lebanon*

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1. Introduction

Antibiotic resistance is a major threat in global public health. The overuse and misuse of antibiotics may generate several problems, including the development of bacterial resistance, [1] adverse reactions, treatment failure and waste of resources. [1]

The World Health Organization (WHO) identified three key issues for public involvement: improving access to medical facilities, decreasing unnecessary use of antimicrobials, taking a full course of treatment, and not giving out medication to other people or keeping left-over medication for future needs. The WHO also urged member countries to initiate educational interventions for patients and the general population aimed at rationalizing the use of antibiotics to combat resistance. [2]

The lack of knowledge of medication such as antibiotics may greatly influence the probability of misuse or compliance. [3] Studies conducted elsewhere have demonstrated inappropriate practices such as sharing of antibiotics, [3] and the use of left over antibiotics. [4,5] There have been reports of a general lack of knowledge of correct antibiotic use and a lack of public awareness on the basic principles of antibiotic use, as well as indication for therapy. [4,5]

The World Health Organization (WHO) have also issued a Global Strategy for Containment of Antimicrobial Resistance in 2001 which urged member countries to initiate awareness and educational campaigns for patients and general community on appropriate use of antibiotics to combat antibiotic resistance. [2] This was echoed by International Pharmaceutical Federation (FIP) in 2008 in its Statement of Policy on Control of Antimicrobial Drug Resistance [6] and WHO Regional Office for South-East Asia [7] in 2010.

In Lebanon, antibiotics are mostly accessed without prescription despite the presence of a law that bans such practices. Therefore, it is important to assess the public knowledge, attitude and practice of antibiotic use among Lebanese population. The findings from this study would provide useful data which could form the basis for educational campaigns on appropriate use of antibiotics, thus addressing any misconceptions among the public.

2. Method

2.1. Design and Study Population

A cross sectional prospective study was conducted in a community-based pharmacy setting in Lebanon. Data was collected over a 1-year period (September 2015 to

September 2016) from 50 community pharmacies CPs distributed in six different districts in Lebanon: Beirut, South Lebanon, Nabatiyeh, Mount Lebanon, Bekaa, and North. Data on antibiotic use was collected using a structured random interview conducted by study researchers who had been briefed about the study's aims and methods. Consecutive customers aged 16 years and older arriving at community pharmacies seeking antibiotics were interviewed. The interview was based on a well-structured questionnaire, which had been pre-tested on a small pilot scale and subsequently modified to ensure that the data would provide reliable information.

The Lebanese University, Faculty of Pharmacy Internal Review Board waived the need for written informed consent. The patients were informed about the objective of the study and were asked to give an oral consent. Only those who were interested and who give their voluntary informed oral consent to participate in the study were enrolled.

2.2. Sample Size Calculation

A sample size was calculated assuming a type I error of 5% and a study power of 80% and 95%CI. Based on a previous study, 40% of patients were expected to self-medicate with antibiotics. [8] The minimal sample size necessary to show a twofold increase in the risk of exposure to non-prescribed antibiotics consists of 442 subjects.

2.3. Data Collection

Data was acquired through a structured questionnaire filled by an interviewer. If a customer had more than one request, CPs filled out one documentation form per request. The questionnaire was obtained after wide review of literature. (Lim & Teh, 2012; Kim et al., 2011; Alzoubi et al., 2013; Awad & Aboud, 2015; Napolitano, Izzo, Di Giuseppe, & Angelillo, 2013) The questionnaire included many sections that were chosen following an extensive review of literature. The questionnaire was translated into Arabic and subjected to a process of forward and backward translation into English. It was pretested and validated first on 20 patients visiting 4 different pharmacies before starting the survey.

The questionnaire consisted of dichotomous, and close-ended questions. It consisted of 5 sections. The first section was related to sociodemographic characteristics including age, sex, occupation, educational and marital status, monthly income, medical insurance, and the presence of a care provider at home. Education was divided into five classes of illiterate, primary, complementary, secondary, and academic education levels. Work status was categorized into currently working, retired and never working, while marital status was categorized into married, single, and widow/divorced.

The second section consisted of 13 questions to evaluate respondent's knowledge bout antibiotics in four aspects: action and use (5 statements), side effects (4 sentences) and resistance (4 questions). A three-likert scale (1=agree, 2=uncertain, 3=disagree) was used to evaluate the participants' response. Nine attitude statements were included in section three, and the participants were required to answer in three likert scale also. Finally, the fifth section included 6 statements to explore the patient and doctor relationship regarding prescribed antibiotic and the responses were measured using three-likert scale also.

2.4. Statistical Analysis

Statistical analysis was done using SPSS version 19. Descriptive statistics of the respondents' knowledge and attitudes regarding antibiotic use and bacterial resistance were reported. After data cleaning, data was assessed. Percentages was used for multinomial variables, means and standard deviations for continuous variables. The internal consistency for the sections to determine knowledge of and attitude towards use of antibiotics was assessed using Cronbach's α test. The Cronbach's alpha for the knowledge score was 0.795 and 0.651 for the attitude score. To describe the knowledge and attitudes of the participants, a score was calculated according to the number of correctly answered questions targeting the knowledge and attitudes regarding antibiotic usage. The knowledge score was categorized as inadequate or adequate. The attitude score was categorized as poor and good. Each correct answer was assigned 1 point while wrong or uncertain responses were assigned 0 points. Then, the sum of the responses for each patient was calculated. The maximum knowledge score was 13 points and 9 points for the attitude score. Thus, the knowledge scores were categorized into inadequate (0-6/13) or adequate (7-13/13) while the attitude score was divided into poor (0-4/9) or good (5-9/9) as dichotomous variables. [9,10]

Associations of demographic variables (gender, age, family income level, education level, employment and marital status) with knowledge and attitudes were first evaluated using a bivariate analysis by chi-squared test. The correlation test was used to examine the association between knowledge and attitude score. Multivariate analysis using Logistic regressions was used to assess the correlation between the Knowledge and attitude dichotomous score as dependent variables and sociodemographic characteristics as independent variables taking into account potential confounding variables that had a $p < 0.2$ in bivariate analysis. A p-value <0.05 was considered significant.

3. Results

3.1. Baseline Characteristics

A total of 495 patients were recorded in the study. Table 1 shows the demographic characteristics of the participants. In this sample, females were more than males (69.9% vs 30.1%). The majority being between 16 and 50 years of age (88.3%), while 11.7% were >51 years of age. About half of patients had a university degree (56.2%), while 13.8% had secondary education, 30.3% had intermediate and elementary education. 34.3% were currently working. The monthly income with greatest prevalence among the respondents was 2000000 LL (62.2%). Almost 21.8% had concomitant comorbidities.

Table 1. Characteristics of the study population

	Total participants N=495 (100%)
Gender:	
Male	149 (30.1%)
Female	346 (69.9%)
Age group:	
16-25	244 (49.3%)
25-50	193 (39%)
>50	58 (11.7%)
Educational level:	
Primary and less	150 (30.3%)
Secondary	67 (13.5%)
University	278 (56..2%)
Marital status:	
Single	259 (52.3%)
Married	236 (47.7%)
Currently working:	
Employed	170 (34.3%)
Unemployed or retired	325 (65.7%)
Family income (LL):	
<2000000	131 (26.5%)
>2000000	44 (8.9%)
No answer	320 (64.6%)
Presence of comorbidities:	
Yes	109 (21.8%)
No	392 (78.2%)
Antibiotic request per year	
1st time	166 (33.5%)
More than once	326 (65.9%)
Presence f insurance on medication coverage	
Yes	313 (63.2%)
No	173 (34.9%)

3.2. Knowledge Description

The study sample had in general low knowledge score (average = 6 points). Only 13.1% believed that antibiotics can kill bacteria. 54% and 59% responded that antibiotics can kill viruses and are effective against cough and cold. 54.3% of participants believed that antibiotics are effective in reducing fever and pain and can kill normal flora that live in the skin and gut. Almost 53% of participants realized that bacteria are becoming resistant to antibiotics and that the unnecessarily use of antibiotics has increased the risk of bacterial resistance. 25% believed that if antibiotics are taken for long period of time, the bacteria become more resistant to antibiotics and 36% believed that taken less doses do not decrease the bacterial resistance. Approximately, 45% of participants believed that antibiotics can cause side effects including hepatic and renal problems. Almost 65% stopped taking antibiotic if they get side effects including skin allergic reaction. (Table 2)

Five variables (age, education, employment and family income level and presence of insurance) showed a significant association (p-value<.005) with the respondents' knowledge regarding antibiotic use, according to the chi-squared test. Young age participants and those with higher educational level showed more adequate knowledge. Employed participants with higher income and with medical insurance showed better knowledge. Gender was not significantly associated with better knowledge of antibiotic use. (Table 3).

Table 2. Knowledge Attitude and Patient Physician Relationship among participants

Knowledge for antibiotic:	**Correct Answer**	**Incorrect Answer**	**Uncertain**
Antibiotic Action			
Antibiotics work on most coughs and colds	110 (22.2%)	293 (59.2%)	92 (18.6%)
Antibiotics can kill bacteria	65 (13.1%)	351 (70.9%)	79 (16%)
Antibiotics can kill viruses	108 (21.8%)	267 (53.9%)	120 (24.2%)
Antibiotics are effective in reducing pain	269 (54.3%)	106 (21.4%)	120 (24.2%)
Antibiotics can kill the bacteria that normally live on the skin and in the gut	269 (54.3%)	75 (15.2%)	151 (30.5%)
Antibiotic Resistance:			
Bacteria are becoming resistant to antibiotics	264 (53.3%)	107 (21.6%)	124 (25.1%)
The unnecessarily use of antibiotics can increase the resistance of bacteria to them	269 (54.3%)	115 (23.2%)	111 (22.4%)
If antibiotics are taken less than the prescribed dose, bacteria become less resistant to antibiotics	178 (36%)	167 (33.7%)	150 (30.3%)
If antibiotics are taken for a long time, bacteria become more resistant to antibiotics	126 (25.5%)	211 (42.8%)	157 (31.7%)
Antibiotic Side effects:			
Antibiotic does not cause side effects	221 (44.6%)	159 (32.1%)	115 (23.2%)
Antibiotic may cause hepatic and renal problems.	234 (47.3%)	123 (24.8%)	138 (27.9%)
If you get side effects during a course of antibiotics treatment you should stop taking them as soon as possible	302 (61%)	92 (18.6%)	101 (20.4%)
If you get some kind of skin reaction when using an antibiotic, you should not use the same antibiotic again	344 (69.5%)	72 (14.5%)	79 (16%)
Patient Attitude	**Agree**	**Disagree**	**Uncertain**
Positive attitude			
I normally look at the expiry date of antibiotic before taking it	368 (73.5%)	83 (16.6%)	43 (8.6%)
Need for patient education.	370 (74.9%)	63 (12.8%)	61 (12.3%)
Negative Attitude			
I stop taking the antibiotic if the symptoms do not improve after taking it.	240 (48.6%)	222 (44.9%)	32 (6.5%)
I stop taking the antibiotic if the symptoms do not improve after taking it.	240 (48.6%)	222 (44.9%)	32 (6.5%)
I prefer to be able to buy antibiotics from the pharmacy without a prescription.	208 (42.1%)	215 (43.5%)	71 (14.4%)
I prefer to keep antibiotics at home in case there may be a need for them later	129 (26.1%)	301 (60.9%)	64 (13%)
I prefer to use an antibiotic if I have a cough for more than a week	166 (33.6%)	234 (47.4%)	94 (19%)
When I have a sore throat I prefer to use an antibiotic	151 (30.6%)	255 (51.6%)	88 (17.8%)
I share antibiotic with someone else in my family/friends with similar symptoms to mine	156 (31.6%)	263 (53.2%)	75 (15.2%)
Patient Physician Relationship	**Agree**	**Disagree**	**Uncertain**
Pharmacists often tell you how antibiotics should be used	376 (76.3%)	52 (10.5%)	65 (13.2%)
Doctors often take time to inform the patient during the consultation how antibiotics should be used	186 (37.7%)	222 (45%)	85 (17.2%)
Physicians routinely prescribed antibiotics to treat common cold symptoms	253 (51.3%)	150 (30.4%)	90 (18.3%)
I request antibiotic prescriptions from my physician	182 (36.9%)	248 (50.3%)	62 (12.8%)
I trust the doctor decision if she or he decides not to prescribe antibiotic	326 (66.1%)	101 (20.5%)	66 (13.4%)
I consult another physician to prescribe antibiotics if their physician disagreed to do so	168 (34.1%)	238 (48.3%)	87 (17.6%)

Table 3. Factors significantly associated with Public Knowledge toward antibiotic use:

	Level of Knowledge			Level of Attitude		
	Inadequate Knowledge	**Adequate Knowledge**	**P-value**	**Poor Attitude**	**Good Attitude**	**p-value**
Gender						
Male	88 (59.1%)	61 (40.9%)	.167	101 (68.2%)	47 (31.8%)	.052
Female	181 (52.3%)	165 (47.7%)		204 (59%)	142 (41%)	
Age group						
16-25	135 (55.3%)	109 (44.7%)	<.001	146 (59.8%)	98 (40.2%)	.559
25-50	90 (46.6%)	103 (53.4%)		120 (62.5%)	72 (37.5%)	
>50	44 (75.9%)	14 (24.1%)		39 (67.2%)	19 (32.8%)	
Educational level						
Primary and less	92 (61.3%)	58 (38.7%)	.004	102 (68.5%)	47 (31.5%)	.118
Secondary	44 (65.7%)	23 (34.3%)		41 (61.2%)	26 (38.8%)	
University	133 (47.8%)	145 (52.2%)		162 (58.3%)	116 (41.7%)	
Marital status						
Single	137 (52.9%)	122 (47.1%)	.498	161 (62.2%)	98 (37.8%)	.84
Married	132 (55.9%)	104 (44.1%)		144 (61.3%)	91 (38.7%)	
Currently working						
No	191 (58.8%)	134 (41.2%)	.006	191 (58.8%)	134 (41.2%)	.059
yes	78 (45.9%)	92 (54.1%)		114 (67.5%)	55 (32.5%)	
Family income (LL)						
<2000000	61 (46.6%)	70 (53.4%)	.004	97 (74.6%)	33 (25.4%)	.002
>2000000	17 (38.6%)	27 (61.4%)		27 (61.4%)	17 (38.6%)	
No answer	191 (59.7%)	129 (40.3%)		181 (56.6%)	139 (43.4%)	
Presence of comorbidities						
No	232 (59.6%)	157 (40.4%)	.064	232 (59.6%)	157 (40.4%)	.064
Yes	73 (69.5%)	32 (30.5%)		73 (69.5%)	32 (30.5%)	
Daman						
No	115 (66.5%)	58 (33.5%)	<001	114 (66.3%)	58 (33.7%)	.091
Yes	147 (47%)	166 (53%)		183 (58.5%)	130 (41.5%)	
Ab request						
1st time	91 (54.8%)	75 (45.2%)	.912	109 (66.1%)	56 (33.9%)	.158
More than once/ year	177 (54.3%)	149 (45.7%)		194 (69.5%)	132 (40.5%)	

Data presented as number (%) were performed using Chi2 respectively and a p-value < 0.05 is considered significant.

3.3. Attitude and Patient Physician Relationship

The study sample had in general poor attitude score (mean= 4.19). Almost 57.4% stopped taking the medication if the symptoms disappear. 42% preferred to take antibiotic from the pharmacy without physician prescription. About 33% preferred to take antibiotic in cases of cough, flu and sore throat. 26% preferred keeping antibiotic at home in case of emergency and 31% shared the antibiotics with someone else if he had similar signs and symptoms. Approximately 73% checked the expiry date of medication before taking it and that there was need for patient education about the appropriate use of antibiotics. (Table 2)

According to the chi-squared test, females showed better attitude compared to males toward the appropriate use of antibiotic (p=.052). Age and education were not significantly associated with better attitude of appropriate antibiotic use. (Table 3)

Approximately 76% of participants responded that pharmacists tell them how to administer antibiotic. 51% expected that physicians routinely prescribe antibiotics in case of cold symptoms and that 37% of physicians spent time to inform patient about the usage of antibiotics. 66% trusted physicians if they decided not to prescribe antibiotic and 34% consulted another physician if the first physician disagreed to prescribe antibiotic. (Table 2)

3.4. Practice

Almost half read the instructions on the label to see the correct usage and safe of medication. 26.4% told the pharmacist about the concurrent medication at the time of OTC. Greater than half of participants reported requesting antibiotic more than once per year. Almost 65% of participants reported returning to pharmacy if the symptoms do not improve and returning to physician.

3.5. Multivariable Analysis

In the multivariable logistic regression analysis (Table 4), females showed better knowledge score compared to males (ORa=1.59, 95%CI=1.01-2.53). Compared to participants aged >50 years old, the level of adequate knowledge of antibiotic was higher in those aged 25-50 years old (ORa=3.66, 95%CI=1.79-7.49). Compared to unemployed participants, those with higher income had better knowledge score (ORa=3.17, 95%CI=1.78-6.79). Participants with insurance on medication coverage had also better knowledge score (ORa=2.06, 95%CI = 1.38-3.07).

Table 4. Multivariable logistic regression of Knowledge and Attitude score:

Multivariate Analysis	aOR	95% CI	p-value
Knowledge			
Gender	1.59	1.01-2.53	.045
Age group			<.001
16-25	3.05	1.49-6.28	.002
25-50	3.66	1.79-7.49	.002
>50	1	Reference	
Income group (LL)			<.001
<2000000	1.73	1.07-2.77	.005
>2000000	3.17	1.78-6.79	.024
No answer	1	Reference	.003
Insurance of medication coverage	2.06	1.38-3.07	<.001
Attitude			
Income group (LL)			.001
<2000000	.415	.26-.66	<.001
>2000000	.785	.41-1.51	.468
No answer	1	Reference	
Presence of comorbidities	.62	.38-1	.05
Insurance of medication coverage	1.62	1.08-2.42	.019

aOR: adjusted odds ratio above 1 indicates increased n appropriateness and below 1 less appropriateness. CI: Confidence Interval
Only factors significantly associated with better or worse appropriateness are shown.

Moreover, a step-wise multiple logistic regression was conducted on attitude of antibiotic usage (Table 4); three were shown to be significant predictors. Patients with comorbidities showed lower attitude score (ORa=.62, 95%CI= .38-1). Compared to unemployed participants with income <2000000 showed lower attitudes (ORa=.41, 95%CI=.26-.66) but those with income >2000000 didn't show significant difference in attitude toward appropriate antibiotic usage. Presence of medical insurance showed better attitude score (ORa=1.62, 95%CI=1.08-2.42).

4. Discussion

The results of this study demonstrated the knowledge, attitudes and practice toward antibiotic use among general public in Lebanon. This will help in testing the adequacy of knowledge and provide further insight in designing future educational campaigns targeting general public to promote appropriate antibiotic use and help in reducing antibiotic resistance. The average knowledge and attitude score was low. This finding is similar to that of neighboring countries in Jordan. [11] These results were supported by high proportion of Lebanese participants using antibiotic for common cough cold and sore throat symptoms. This means that that they are using antibiotic for diseases that do not require them. Other studies conducted in United Kingdom, [12] Sweden, [13] Korea, [14] Italy [15] and United State [16] showed that many people thought that antibiotics are effective for common cold and cough symptoms and may be used for viral infections.

Participants were not well informed to the meaning of antibiotic resistance and were unaware of the spread of bacterial resistance. They didn't know that stopping the antibiotic early or as the symptoms disappear without completing the full course of antibiotic can increase the risk of antibiotic resistance. In our study, almost half of participants knew that antibiotics can kill normal flora that lives normally in the skin and gut which is similar percentage to that reported in Korea (57%) [14] but higher than that in UK (43%). [12] Many participants were aware of antibiotic side effects where approximately 60% stopped taking antibiotic as soon as side effects occur and stopped taking it again later. But only 40% knew that antibiotic can cause hepatic or renal problems.

In term of attitudes our study showed that 42% preferred to take antibiotic from the pharmacy without physician prescription. Recent studies from Lebanon reported similar self-medication rate (40%). [8] It is similar to that reported in Mediterranean countries which ranged from 40.7% to 78% namely Jordan, [17] United Arab Emirates, [18] Iraq [19] and Kuwait. [20] In contrast it is higher than that reported in Hong Kong, Malaysia, UK and European countries which ranged between 4.8 to 9%. [12,21,22,23,24] This is due to unregulated rules in Lebanon to restrict the self-medication use of prescribed antibiotic in community pharmacies. Hence, the current study highlights the need for further enforcement of regulations. Moreover, almost 48% stopped taking the medication if the symptoms disappear. This explains the rapid increase in bacterial resistance in Lebanon due to use of antibiotic beyond the scope.

About 33% preferred to take antibiotic in cases of cough, flu and sore throat. This explains the misconception present among the study participants regarding the role of antibiotic. A possible reason for inadequacy of knowledge in this area is the use of term "germ" rather than "bacteria" or "viruses" by the physicians during medical counseling. [13] Moreover, 26% preferred keeping antibiotic at home in case of emergency and 31% shared the antibiotics with someone else if he has similar signs and symptoms. This suggests that many Lebanese individuals share antibiotics with others and use them as necessary thus subjecting the Lebanese population to the problem of antibiotic misuse.

Approximately 76% of participants responded that pharmacists tell them how to administer antibiotic. This showed that many individuals obtained information about antibiotic use from pharmacists which highlight that pharmacists can have a vital role to play in public education about the prudent use of antibiotics. Therefore, implementation of pharmaceutical care in community pharmacies can help to improve public knowledge and attitude towards antibiotics in Lebanon. Community pharmacists are the most accessible health care providers to the public, and can contribute to public knowledge about appropriate antibiotic use.

51% expected that physicians routinely prescribe antibiotics in case of cold symptoms It is well documented that overprescribing by physicians even in the absence of appropriate indications due to diagnostic doubt and patient demand are factors contributing to antibiotic resistance. [2,25] Numerous reports show that patient's expectation is an important factor for antibiotic prescribing and that antibiotics are more likely to be prescribed under patient pressure. [26,27]

Our results identified demographic groups with poor knowledge toward antibiotic use, including persons with low educational status and those aged >50 years old. As we found, a higher educational level was associated with better knowledge and attitude [23,28], and the elderly are

less knowledgeable about antibiotics in general. [12] Moreover, females and those with higher income or medical insurance show better knowledge and attitude score compared to males. Previous studies reported significant association between self-medication and age, male gender, education level and lower socioeconomic status. [29,30]

Participants' knowledge found to correlate positive attitude. Appropriate knowledge of antibiotics was identified to be a predictor for positive attitude towards antibiotic use. [14] These findings support the idea that the better knowledge on antibiotics usage and the potential for antibiotic resistance can change attitudes and behaviors regarding the appropriate use of antibiotic. An understanding of antibiotic use is important because personal decisions are based on these understandings. [22] They can impact physicians' prescription behavior, [31] as well as lead to decreasing suboptimal use of antibiotics, such as using short courses and sub-therapeutic doses. [22]

This study has several limitations. While efforts were done to obtain representative samples, the over presentation of female gender and higher educational level indicate selection bias. This surveys were also filled using face to face questionnaire, therefore, there is a possibility of information and recall bias. Moreover, it is a cross sectional study, therefore, it does not allow causality to be attributed to the observed associations. Despite these limitations, this study provides important information for evaluating and improving knowledge, attitude and practice towards antibiotics use among general public in Lebanon.

5. Conclusion

This study identified important knowledge and attitude gaps among general public in Lebanon. Future antibiotic awareness campaigns and patient counselling should be implemented to fill up the knowledge and attitude gaps as an effort against antibiotic resistance. This aim to reduce the risk of antibiotic resistance.

Conflicts of Interest

The authors declare no conflicts of interest.

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Contribution of Authors

Malak Khalifeh shared the original idea, did the study, and wrote the original manuscript.

Nicholas Moore shared the original idea, and edited/amended the manuscript.

Pascale Salameh shared the original idea, and edited/amended the manuscript.

All authors read and approved the final manuscript as submitted.

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