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Antibiotics in Lebanese Surface Waters: Estimation of Population Exposure and Identification of High-Risk Drugs

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Abstract

The evaluation of the environmental risk of antibiotics and their byproducts is an important topic around the world viewing the increase of use of antibiotics and the absence of conventional water treatment plants. The objective of the study is to determine the consumption of antibiotics and evaluate their potential health hazard as contaminants of the Lebanese surface waters. Data of 704 antibiotics consumed in 2019 were provided by the Ministry of Public Health (MOPH). Following the analysis of the data multiple parameters were calculated including: yearly consumption of single active ingredients, yearly consumption of therapeutically equivalent drug, and Predicted Environmental Concentrations. Compounds were classified into categories based on the Predicted Environmental Concentrations (PECs). The top 7 most consumed antibiotics are: amoxicillin, ciprofloxacin, levofloxacin, clarithromycin, cefuroxime, cefexime, and metronidazole. Using the PEC value of the single active ingredients and their therapeutically equivalent compounds, the mentioned seven compounds were identified as high risk. This study sheds the light on the need of additional analysis of antibiotics while focusing on high risk compounds. Proper regulations must be implemented to secure safe and proper management of waste water.

Keywords: Antibiotics; Environmental Risk; Water Treatment Plants; Predicted Environmental Concentrations; Lebanon

Introduction

Infectious diseases kill over 17 million people a year according to the WHO. Nearly 50,000 men, women and children are dying every day from infectious diseases [1]. At least 30 new diseases have emerged in the last 20 years and now together threaten the health of hundreds of millions of people. For many of these diseases, there is no treatment, cure or vaccine [2].

Infectious diseases remain among the leading causes of morbidity and mortality in the Middle East, with diseases such as pneumonia, gastroenteritis, malaria, and tuberculosis presenting a major burden in our region.

Infectious diseases are caused by pathogenic microorganisms, such as bacteria, viruses, parasites or fungi; the diseases can be spread, directly or indirectly, from one person to another.

Lebanon carries a double burden of disease: health problems related to infectious diseases, such as acute respiratory infections and measles, persist while chronic degenerative diseases, such as diabetes, hypertension, high blood pressure and cancer, have considerably augmented [2].

Antibiotics are used to treat or prevent some types of bacterial infection. They work by killing bacteria or preventing them from spreading.

There are hundreds of different types of antibiotics, that can be identified into different groups including but not limited to Penicillins (such as penicillin and amoxicillin) – widely used to treat a variety of infections, including skin infections, chest infections and urinary tract infections. Cephalosporins (such as cephalexin) – used to treat a wide range of infections, but some are also effective for treating more serious infections, such as septicemia and meningitis. Aminoglycosides (such as gentamicin and tobramycin) – tend to only be used in hospital to treat very serious illnesses such as septicemia, as they can cause serious side effects, including hearing loss and kidney damage; they're usually given by injection, but may be given as drops for some ear or eye infections. Tetracyclines (such as tetracycline and doxycycline) – can be used to treat a wide range of infections but are commonly used to treat acne and a skin condition called rosacea. Macrolides (such as erythromycin and clarithromycin) – can be particularly useful for

treating lung and chest infections, or as an alternative for people with a penicillin allergy, or to treat penicillin-resistant strains of bacteria. Fluoroquinolones (such as ciprofloxacin and levofloxacin) – are broad-spectrum antibiotics that were once used to treat a wide range of infections, especially respiratory and urinary tract infections. These antibiotics are no longer routinely used because of the risk of serious side effects [3].

As a new pollutant in the environment, antibiotics are one of the most important pollutants in sewage treatment plants. Continuous entering of the antibiotics to the environment has led them to be considered as the metastable pollutants. Some antibiotics are metabolized in the human body, whereas 10–90% of them remain unchanged and are excreted in the urine and feces. These molecules enter the sewage in the form of connected, metabolite or parent compounds. Therefore, the municipal wastewater system is one of the major antibiotic carriers to the environment. Hospitals are considered as the main sources of antibiotic distribution in the municipal wastewater treatment plants.

The potential ecological hazards of the antibiotics drove much attention in the recent years. The emergence of resistant strains is probably due to the continuous exposures to low concentrations of the antibiotics which is viewed as one of the three big dangers by the WHO. Non-target organisms can also be affected by the antibiotics. The chronic toxicity of antibiotics for aquatic species has been documented. This includes a decrease in the population of phytoplankton and zooplankton, negative effects on the reproductive system such as species infertility and reduction of the eggs fertility, and disrupting the gender balance of the aquatic species such as fishes [4].

In Lebanon, the case is not less dangerous. Environmental risk assessment of antibiotics and their transformation products is a major concern worldwide; studies have been conducted to analyze antibiotics consumption trends, availability in surface water and population exposure [5]. Ecotoxicological studies are not available in Lebanon so far. This work is the first of its kind to shed the light on the consumption trends in Lebanon, to predict the presence of associated contaminants in surface waters, and to assess the correlated risks.

The aim of the study is to investigate the consumption of antibiotics and asses their potential health hazard toxic effects as contaminants in the environment.

Materials and Methods

Five steps approach:

1- Study the consumption of antibiotics drugs in Lebanon during 2019
2- Compute the concentration of antibiotics in surface water
3- Investigate the exposure of the Lebanese population to antibiotics
4- Assess the long term-risk associated with the exposure and the potential effect on countries on the Mediterranean Sea

Antibiotics consumption

The antibiotics drug data were collected as per the ministry of public health (MOPH) antibiotic therapeutic class classification. The consumption data over the year 2019 was as well delivered by. All dosage forms available on the Lebanese market were covered including tablets, capsules, suspension, and injectables.

Data collection and concentration in surface water

Records for the consumption of 704 antibiotics were provided for the year of 2019 (Table 1). The total amount of active ingredients consumed over the year was calculated based on the following:

- For every brand drug, Consumption per year (in mg) was calculated using the following formula: number of boxes consumed x the number of units in each box x the amount of active ingredients in each unit (in mg).
- Drugs with the same active ingredient were grouped together and their consumption accumulated.
- Different active ingredients belonging to the same pharmacologic or chemical class were grouped together.
- Cumulative concentration was calculated by summing the total consumption per year.

Drug Class	Active Ingredients Included	Conversion Factor Used*
Penicillin Derivatives	benzylpenicillin, phenoxymethylpenicillin, amoxicillin, ampicillin, cloxacillin, fluoxacillin, piperacillin,	1500mg amoxicillin = 1000 mg ampicillin = 2000mg cloxacillin = 1000mg fluoxacillin
Cephalosporins	cefixime, ceftriaxone, cefdinir, cefpodoxime, cefuroxime, cefadroxil, cefepime, cephalexin, cefditoren, cefaclor, ceftazidime, cefradine, ceftibuten, cefotaxime, ceftaroline, cefazolin, cefprozil, ceftolozane,	400mg cefixime= 600mg cefdinir = 400mg cefpodoxime = 500mg cefuroxime = 1000mg cefadroxil = 1000mg cephalexin = 400mg cefditoren = 1500mg cefaclor= 1000mg cefradine = 400mg ceftibuten = 1000mg cefprozil
Carbapenems	ertapenem, imipenem/cilastatin, meropenem	1000mg ertapenem=2000mg imipenem = 3000mg meropenem
Monobactams	aztreonam	
Beta lactamase inhibitor	tazaobactam, avibactam, clavulanic acid	

Drug Class	Active Ingredients Included	Conversion Factor Used*
Glycopeptides	vancomycin, teicoplanin	2000mg vancomycin =800mg teicoplanin
Aminoglycosides	amikacin, gentamicin, tobramycin	15mg/kg amikacin = 15mg/kg gentamicin = 15mg/kg tobramycin
Tetracyclines	doxycycline, tetracycline	200mg doxycycline=1000mg tetracycline
Glycylcycline	tigecycline	
Macrolides	azithromycin, clarithromycin, spiramycin	500mg azithromycin =500mg clarithromycin
Lincomycin	clindamycin	
Polymixins	colomycin, colistimethate Sodium	
Sulfonamides	sulfamethoxazole/ trimethoprim	
Oxazolidiones	linezolid	
Nitroimidazole	metronidazole	
Fluoroquinolones	ciprofloxacin, gemifloxacin, levofloxacin, moxifloxacin, norfloxacin, ofloxacin, prulifloxacin	1500mg ciprofloxacin= 1500mg levofloxacin = 320mg Gemifloxacin = 400mg moxifloxacin = 400mg norfloxacin = 400mg ofloxacin
Ansamycin	rifampicin	

*The conversion factor used is based on the therapeutically equivalent antibiotics. Therapeutically equivalent antibiotics were grouped into one class [6]
Table 1: Table presenting the active ingredients in each class of antibiotics and the factors that were used in the conversion

Exposure based classification

The human and aquatic life are at a greater danger from the highly used compounds that reach the aquatic environment in larger quantities. Thus, the risk classification is based on the quantity consumed. The classification of compounds based on exposure is done using Predicted Environmental Concentrations (PECs), according to Figure 1 (Table 2).

Thresholds for risk classification adopted in the analysis are 100 ng.L^{-1} (guidance by the FDA) and 10 ng.L^{-1} (guidance by EMEA) [7].

Two PEC values were determined:

- PEC_a assumes no metabolism of the active ingredient happens in the body, 100% of the active ingredient is excreted unchanged.

$$PEC_a = \frac{Consumption}{WWinhab \times inhab \times DF}$$

Where Consumption is the amount of active ingredient consumed per year (ng.$year^{-1}$) WWinhab is the water consumption per person per year, Inhab is the number of inhabitants of Lebanon and DF is the dilution factor from waste water treatment plants effluents to surface water.

- PEC_b is calculated when metabolism data is available for the drug. The fraction of active ingredient excreted unchanged (F_{exc}) is added to the equation.

$$PEC_b = \frac{Consumption}{WWinhab \times inhab \times DF} \times Fe \times c$$

- PEC_c is the Predicted environmental concentration in surface water that remains after treatment. Therefore, PEC_c is obtained by taking into consideration the fraction of pharmaceuticals removed by waste water treatment plants (F_{WWTP}). However, due to the absence of efficient treatment plants or the absence of data, the F_{WWTP} was assumed to be equal to zero. PEC_c and PEC_b values are therefore equal [5].

$$PEC_c = \frac{Consumption}{WWinhab \times inhab \times DF} \times Fe \times c \times (1 - F_{WWTP})$$

The following assumptions were made when using the formula:

- According to the EMEA guidelines, the amount of wastewater per inhabitant per day to be equal to 200 L. The yearly consumption (WWinhab) would therefore be equal to 7300 L.$inhab^{-1}$. $year^{-1}$
- The number of inhabitants in Lebanon was assumed to be equal to 6,000,000.
- The Dilution Factor was assumed to be equal to 10 as per the EMEA guidelines.
- The fraction of active ingredient excreted unchanged was assumed to be equal to 0.5 when data was not available.

Class	Risk*
Class IA	High risk compounds
Class IB	Potentially hazardous compounds but limited data
Class IIA	Potentially hazardous compounds
Class IIB	Unclassified risk
Class III	Very low risk
Class IV	Very low risk

*Depending on PEC_a and PEC_b values obtained for each drug, a different class was assigned to each drug. Drugs were categorized into 6 classes from the highest to the lowest risk

Table 2: Classification of compounds based on potential exposure (PEC_a and PEC_b values): risk categories

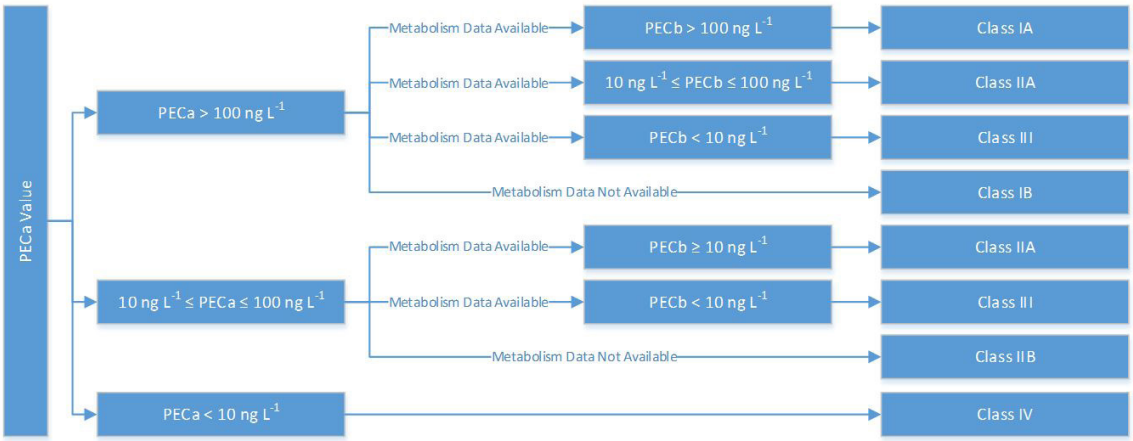

Figure 1: Classification of compounds based on potential PEC_a and PEC_b values

Risk quotients

The RQ Is calculated from an estimated exposure (PEC), divided by an estimated effect (PNEC: predicted no effect concentrations). PNEC values are estimated from short-term toxicological data (EC50 or LC50) using a security factor of 1000 to ensure that compounds with the potential to cause adverse effects is identified in the effect's assessment.

If a value less than 1, then there is an acceptable risk. In contrast, if the RQ greater than 1, there is an unacceptable level of risk and measures to reduce exposure should be taken.

RQ can be calculated using the formula below:

$$RQ = \frac{PECc}{PNEC}$$

Results

Antibiotics consumption in Lebanon

The antibiotics with the highest consumption in Lebanon during the year 2019 were the following (decreasing order): amoxicillin, ciprofloxacin, clarithromycin, levofloxacin, metronidazole, cefuroxime, and cefixime (Figure 2).

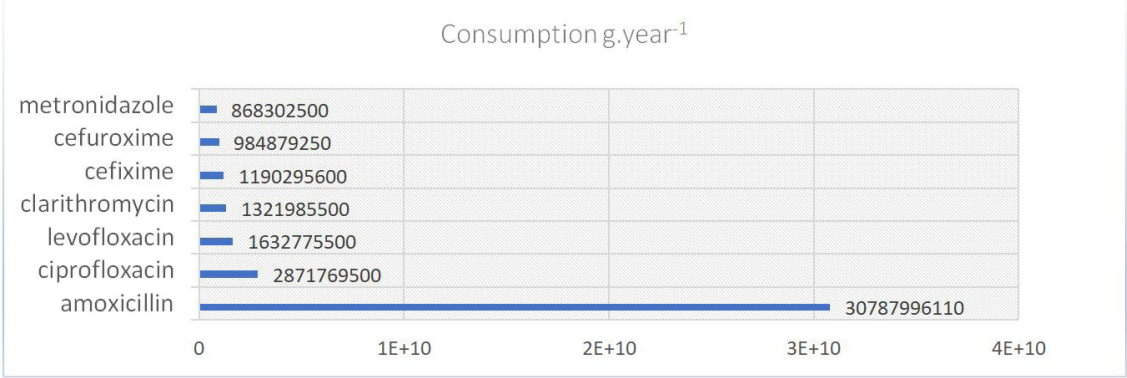

Figure 2: Top 7 most consumed antibiotics in Lebanon in 2019

The most consumed antibiotic during 2019 was amoxicillin, belonging to the class of penicillin derivatives. It works by inhibiting the bacterial cell wall synthesis by binding to one or more of the penicillin-binding proteins (PBPs) which in turn inhibit the final transpeptidation step of peptidoglycan synthesis in bacterial cell walls, thus inhibiting cell wall biosynthesis. Accordingly, consumption data of the penicillin derivative drugs were grouped together based on the conversion factors in Table 1. The consumption of the antibiotics (ampicillin, cloxacillin, and fluoxacillin) and their equivalent to amoxicillin is presented in Figure 3.

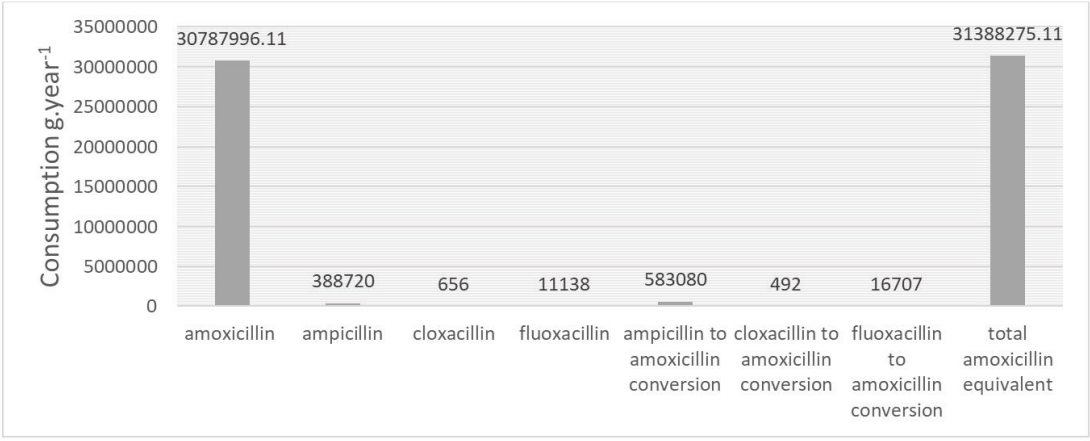

Figure 3: Consumption of amoxicillin, ampicillin, cloxacillin, fluoxacillin, and their equivalent (2019)

The second and third mostly consumed antibiotic in 2019 are ciprofloxacin and levofloxacin, respectively belonging to the class of fluoroquinolones. They work by inhibiting DNA-gyrase in susceptible organisms; inhibiting relaxation of supercoiled DNA and promotes breakage of double-stranded DNA [8].

The consumption data of the fluoroquinolone's derivatives were grouped together based on the conversion factors in Table 1. The consumption of the antibiotics (ciprofloxacin, levofloxacin, Gemifloxacin, moxifloxacin, norfloxacin, and ofloxacin) and their equivalent to ciprofloxacin is presented in Figure 4.

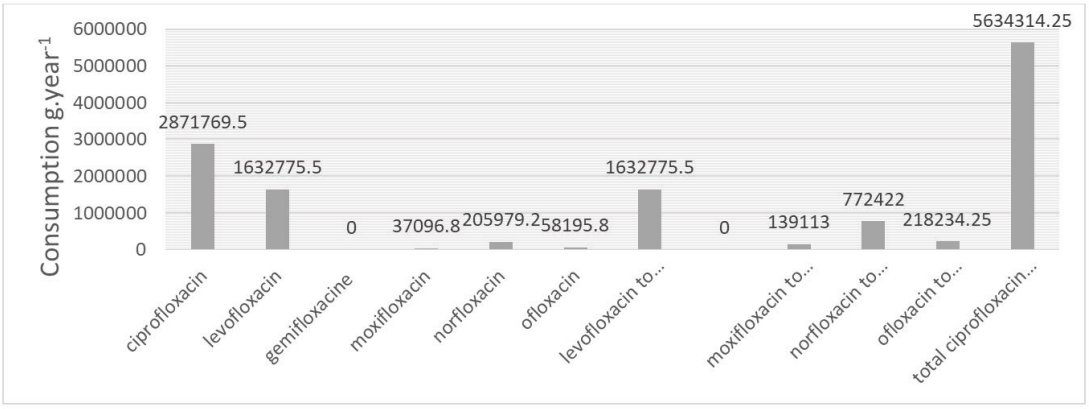

Figure 4: Consumption of ciprofloxacin, levofloxacin, gemifloxacin, moxifloxacin, norfloxacin, ofloxacin and their equivalent (2019)

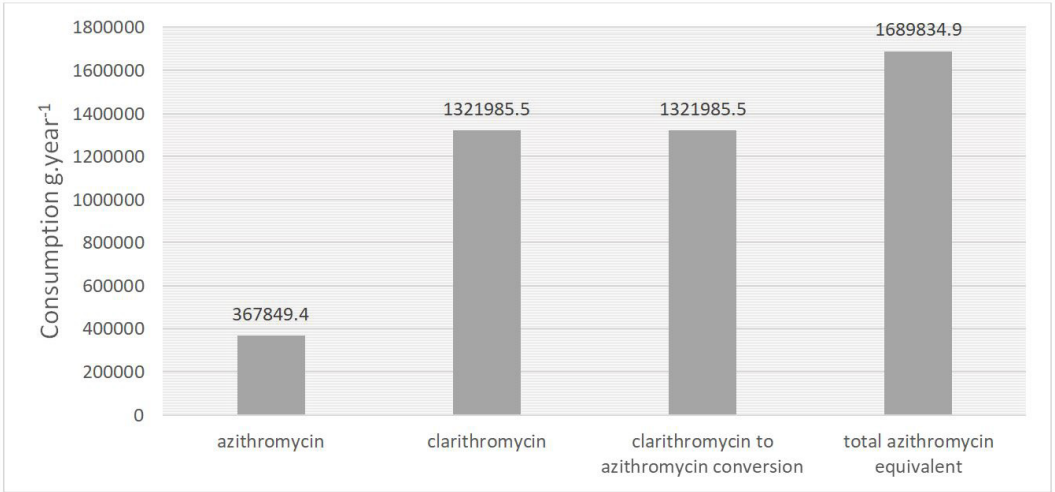

Figure 5: Consumption of azithromycin, clarithromycin, and their equivalent (2019)

The fourth mostly consumed antibiotic in 2019 is clarithromycin, belonging to the class of macrolides. They exert their antibacterial action by binding to 50S ribosomal subunit resulting in inhibition of protein synthesis. The 14-OH metabolite of clarithromycin is twice as active as the parent compound against certain organisms [9].

The consumption data of the macrolide's derivatives were grouped together based on the conversion factors in Table 1. The consumption of the antibiotics (azithromycin and clarithromycin) and their equivalent to azithromycin is presented in Figure 5.

The fifth and sixth drugs are cefixime and cefuroxime, respectively. They belong to the cephalosporins class. They inhibit bacterial cell wall synthesis by binding to one or more of the penicillin-binding proteins (PBPs) which in turn inhibits the final transpeptidation step of peptidoglycan synthesis in bacterial cell walls, thus inhibiting cell wall biosynthesis [10,11]. The consumption data of the cephalosporins were grouped together based on the conversion in Table 1. The consumption of the antibiotics (cefixime, cefdinir, cefpodoxime, cefuroxime, cefadroxil, cephalexin, cefditoren, cefaclor, cefradine, ceftibuten, and cefprozil) and their equivalent to cefixime is presented in Figure 6.

The seventh most commonly consumed antibiotic in 2019 is metronidazole, belonging to the nitroimidazole class. After diffusing into the organism, metronidazole interacts with DNA to cause a loss of helical DNA structure and strand breakage resulting in inhibition of protein synthesis and cell death in susceptible organisms [12].

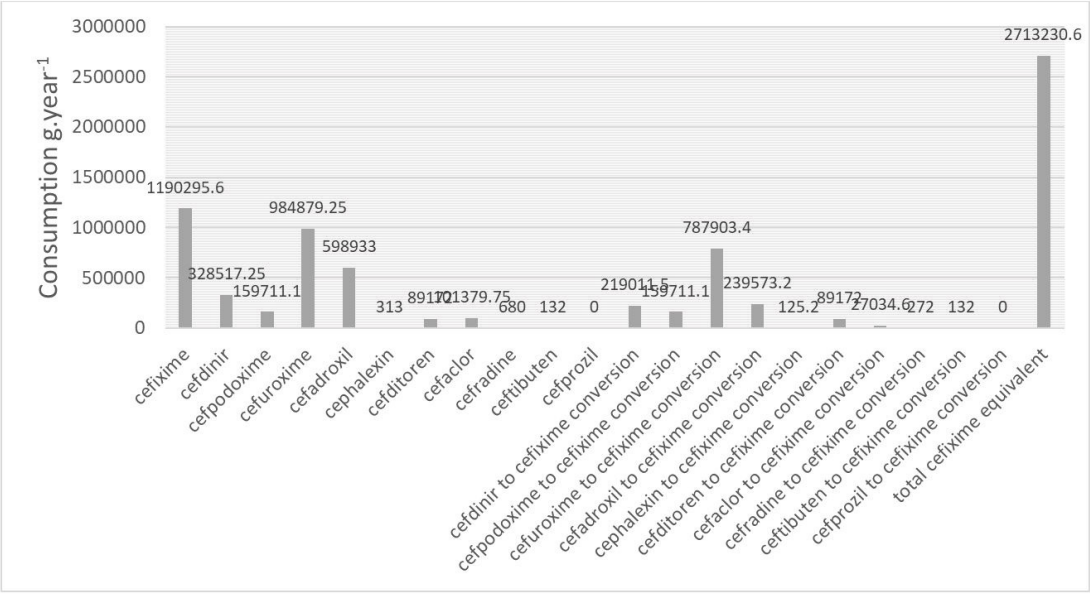

Figure 6: Consumption of cefixime, cefdinir, cefpodoxime, cefuroxime, cefadroxil, cephalexin, cefditoren, cefaclor, cefradine, ceftibuten, and cefprozil, and their equivalent (2019)

Exposure based classification

In order to understand better the exposure to the antibiotics multiple factors will be taken into consideration such as the excretion and waste water treatment plants removal rates. As a first step the PEC_a value was obtained, which is the concentration of each antibiotic in surface waters without transformation in the body and removal at WTTPs. The second step was to obtain the PEC_b value, which is the concentration of the antibiotics taking into consideration the drugs's metabolism in the body. The third step was ideally to calculate the PEC_c value, which the fraction of the drug removed by the WWTP. Due to the absence of competent WWTPs in Lebanon, the PEC_c value would be equal to PEC_b.

Tables 3 and 4 shows that nine of the antibiotics belong to class I high risk compounds, indicating a very high risk of environmental toxicity. In addition, multiple cephalosporins belong to the potentially hazardous class IIA. (Figure 7).

As a consequence, from the 704 antibiotics present on the Lebanese market and studied in this article, the six previously mentioned compounds should be further assessed.

Class IA	amoxicillin	**Class IV**	amikacin
	cefixime		avibactam
	cefuroxime		aztreonam
	ciprofloxacin		benzylpenicillin
	clarithromycin		cefazolin
	clavulanic Acid		cefotaxime
	levofloxacin		cefprozil
	metronidazole		cefradine
	piperacillin		ceftaroline
Class IIA	ampicillin		ceftazidime
	azithromycin		ceftibuten
	cefaclor		ceftolozane
	cefadroxil		cephalexin
	cefalexin		cilastatin
	cefdinir		cloxacillin
	cefditoren		colistimethate sodium
	cefpodoxime		colomycin
	ceftriaxone		fluoxacillin
	clindamycin		gemifloxacine
	doxycyline		imipenem
	gentamicin		linezolid
	lymecyclin		moxifloxacin
	norfloxacin		Phenoxymethyl-penicillin
	sulfamethoxazole		prulifloxacin
	tazobactam		rifampicin
	tetracyclin		spiramycin
	tetracycline		teicoplanin
	Trimethoprim		tigecycline
Class III	cefepime		tobramycin
	cefepime		
	ertapenem		
	meropenem		
	ofloxacin		
	vancomycin		

Table 3: Risk categorization of antibiotics based on environmental exposure data between the years 2019

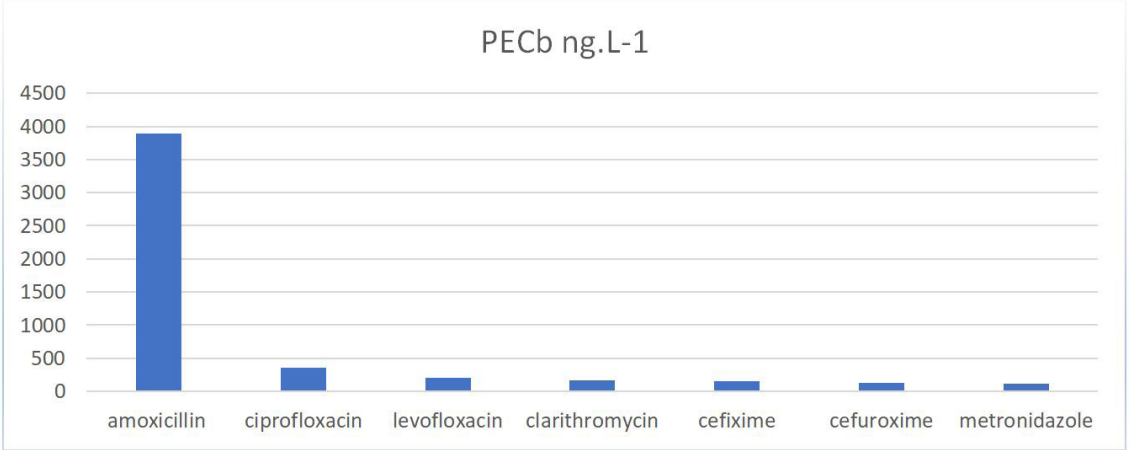

Figure 7: PEC_b value of the 7 priority antibiotics drugs in Lebanon

Active Ingredient	PEC_a	Class
amoxicillin	7775.21165	Class IA
amoxicillin equivalents	7926.806326	Class IA
ciprofloxacin	725.2377061	Class IA
ciprofloxacin equivalents	1422.891754	Class IA
levofloxacin	412.3417141	Class IA
clarithromycin	333.8546953	Class IA
azithromycin equivalents	426.7515156	Class IA
cefixime	300.5976805	Class IA
cefixime equivalents	685.200235	Class IA
cefuroxime	248.7217613	Class IA
metronidazole	219.2814268	Class IA

Table 4: PEC_a and risk categorization of the priority antibiotics between the years 2019

Discussion

Analysis of the results

Amoxicillin is the most commonly consumed antibiotic. The reason behind the increased consumption of amoxicillin and the penicillin derivatives (amoxicillin equivalents) is the relatively broad microorganisms' coverage they offer, the relative safety profile they offer, and the relatively low cost. The analysis of amoxicillin toxicity and the penicillin derivatives toxicity separately led to an underestimation of the risks.

Benzylpenicillin, phenoxymethylpenicillin, ampicillin, cloxacillin, fluoxacillin, and piperacillin are penicillin derivatives therefore the consumption of these antibiotics was grouped using conversion equivalence factors based on the potency of each antibiotic and the equivalent dose needed for a specific infection (Table 1). The PEC values obtained for the amoxicillin equivalent helped into risk categorization of the amoxicillin equivalent into class IA, designating that amoxicillin is a high-risk compound. Likewise, when amoxicillin was analyzed as a separate entity of the penicillin derivatives, it was also classified in IA. In Lebanon the consumption of amoxicillin/equivalents was equal to 1.78 mg. $Inhabitant^{-1}$ .Day^{-1}.

The second and third most commonly consumed antibiotic are ciprofloxacin and levofloxacin, respectively. The increased consumption of the antibiotics is due to their cheap price and prescription for most of the gram negative and respiratory infections. They belong to class IA, as high risk compounds. Gemifloxacine, moxifloxacin, norfloxacin, and ofloxacin are fluoroquinolones therefore the consumption of these antibiotics was grouped using conversion equivalence factors based on the potency of each antibiotic and the equivalent dose needed for a specific infection (Table 1). The PEC values obtained for ciprofloxacin equivalent helped into risk categorization of the ciprofloxacin equivalent into class IIA. The consumption of ciprofloxacin in Lebanon was 1422.89 mg. $Inhabitant^{-1}$. Day^{-1}.

The fourth most commonly consumed antibiotic is clarithromycin belonging to the class of macrolides. It is widely used due to its coverage of atypical infections. Clarithromycin is also classified in class IA, high-risk compound. Azithromycin is an antibiotic belonging to the macrolide's family as well. As a consequence, the consumption of clarithromycin was grouped with azithromycin using conversion equivalence factors based on the potency of each antibiotic and the equivalent dose needed for a specific infection (Table 1). The PEC value obtained for azithromycin equivalent led to its classification in class to IA. The separate PEC value of clarithromycin lead as well to its classification in class IA. The consumption of clarithromycin equivalents in Lebanon was 426.75 mg. $Inhabitant^{-1}$. Day^{-1}.

The fifth and sixth drugs are cefixime and cefuroxime, respectively. They belong to the cephalosporins class. They are widely prescribed in Lebanon due to their relatively broad coverage and their relatively safe profile. According to the PEC value both drugs also belong to class IA, high risk of toxicity. Cefixime, cefdinir, cefpodoxime, cefuroxime, cefadroxil, cephalexin, cefditoren, cefaclor, cefradine, ceftibuten, and cefprozil are cephalosporins derivatives therefore the consumption of these antibiotics was grouped using conversion equivalence factors based on the potency of each antibiotic and the equivalent dose needed for a specific infection (Table 1). The PEC value obtained for cefixime equivalent lead to its classification in class IA. The consumption of cefixime equivalents Lebanon are respectively 685.20 mg per $Inhabitant^{-1}$. Day^{-1}.

The seventh most commonly consumed antibiotic is metronidazole. It is mostly prescribed in Lebanon for the anaerobic infections. It belongs to class IA, another high-risk compound. The consumption of metronidazole in Lebanon was 219.28 mg $Inhabitant^{-1}$. Day^{-1}.

Actual risk

This article studied the risk inflicted by antibiotics as micro-pollutants based on their yearly consumption. Nevertheless, some antibiotics accumulate in the environment over the years suggesting a higher ecotoxicological risk. Among the top five most consumed antibiotics, amoxicillin may bioaccumulate in fish muscle tissues. As a consequence, this drug may occur in food leading to passive consumption of the antibiotic. The result would be undesirable effects on the consumer's health such as immunoallergic responses [13].

The presence and accumulation of fluoroquinolone antibacterial agents in aquatic environments have been widely reported; for example 249-405 ng L^{-1} of ciprofloxacin and 45-120 ng L^{-1} of norfloxacin were detected in domestic sewage in Switzerland. Higher concentrations of some fluoroquinolones (0.6-2 μg L^{-1}) were also detected in wastewaters in the United States. Median concentrations of 0.02 μg L^{-1} and 0.12 μg L^{-1} were reported for ciprofloxacin and norfloxacin, respectively, for samples from 139 surface streams across the United States. Additionally, ciprofloxacin in the range 0.7-124.5 μg L^{-1} was found in wastewater of a Swiss hospital [14].

The residues of pharmaceuticals are another factor to pay attention to it. The residues can be in the environment in the form of complex mixtures leading to a more alarming ecotoxicological association.

Impact on animals and humans

Investigations and researches regarding the toxicity of antibiotics in fish mostly from the aquatic environment are relatively rare. According to the ecological structure-activity relationship (EOCSAR) scan analysis, it is estimated that almost one third of antibiotics are very toxic to fish. The toxicity may range from morphologic to genetic changes. Changes in physiological and biochemical indicators typically come along with genotoxicity. The inhibition of the transcriptional of genes involved in inflammation, energy metabolism, and anti-oxidant responses is also considered as an example of genotoxicity found in liver and muscle tissues of fish [3].

Importance of waste water treatment plants

The chronic indirect exposure to antibiotics endangers both humans and other species in the environment. Chronic exposure to antibiotics would lead to higher resistance in the exposed organisms. The increase in infections rates in Lebanon and maluses of antibiotics without prescriptions and for a wrong diagnosis led to an upsurge in antibiotics consumption and consequently a higher amount if drug disposal in the environment. Thus, the presence of effective waste water treatment is essential and needed to take care of the released compounds in the environment [4].

Waste management challenge in Lebanon

This article projected the risks from a major source of antibiotics in surface waters, the drugs were consumed by patients either in a hospital setting or at home. Nevertheless, in Lebanon another source of micropollutants exist which is the expired/unused drugs in the importers' warehouses. The lack of a safe disposal of these drugs would put the environment in danger.

Need for regulation

Laws and regulations are needed to plan a safe disposal of antibiotics. This study was designed in order to emphasize on the need waste water treatment plants due to the presence of the risk imposed by antibiotics.

Future studies needed

This study handled a brand-new research topic in Lebanon and the Middle East as well. In this article the environmental concentrations in surface waters were estimated using predicted environmental concentrations based on consumption data provided by the Ministry of Public Health. Reports on the occurrence of antibacterials in surface water, ground water or drinking water by measurement of actual of the drug concentrations are absent, unfortunately.

Conclusion

In this article, it was projected for the first time a deep analysis of the consumption rate of 704 antibiotics on the Lebanese market between 2019. In the world today, the eyes are more on the fate of pharmaceuticals in the environment and their potential toxicity to living organisms. Antibiotics are a great advance in medicine but the misuse and overuse of them would lead to the development of antibiotic resistance, meaning that the bacteria will be unresponsive to antibiotics that used to work in the past.

The study showed that the most commonly prescribed antibiotics are: amoxicillin, ciprofloxacin, levofloxacin, clarithromycin, cefuroxime, cefixime, and metronidazole. The analysis of the toxicity based on the assessment of exposure allowed the identification of seven high-risk compound belonging to class IA. Ampicillin, several cephalosporins, in addition to monobactams and others were classified as potentially hazardous compounds. In this study, antibiotics belonging to the same class were combined together according to their potency and therapeutic equivalence towards a certain infection. This study showed that is essential to implement efficacious waste water treatment plants and impose laws and regulations to control the environmental pollution.

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Availability of data and materials

All data generated or analyzed during this study are included within the article except for the raw data provided that can be provided upon request.

Authors' contributions

Y. Saab was responsible for the conceptualization and design of the study, acquisition of the data analysis, interpretation, and critical revision of the manuscript. Z. Nakad developed the software needed for the calculations, processed the data, and developed all required graphs and tables. R. Zgheib worked on the computation and interpretation of data and drafted the article. All authors read and approved the final manuscript.

Competing interests

The authors declare they have no competing interests.

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Author's Information

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