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Prevalence of Antibiotics Resistance among Patients in Iraqi Hospitals

Wifaq M. Ali Alwatar[1*], Suha A. Al Fakhar[1], Saad Hasan Mohammed Ali[1], Khalil Ismail Abid Mohammed[1], Jenan M. Mousa[1]

[1]Clinical communicable Diseases Research Unit, College of Medicine, University of Baghdad, Baghdad, Iraq

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***Corresponding author:** Wifaq M. Ali Alwatar
Clinical communicable Diseases Research Unit, College of Medicine, University of Baghdad, Baghdad, Iraq

Abstract

Background: Antibiotics are medicines that fight bacterial infections. If they are used probably, they can save lives. Still there is a growing problem of antibiotic resistance. It happens when bacteria undergo some mutation and become able to resist the effect of an antibiotic. ***Objectives:*** This cross sectional study was to determine the prevalence of antibiotics resistance among group of patients and to know the causes that lead to antibiotic resistance crisis to compare the results with previous studies concerning this subject in order to identify the risks of antibiotic resistance to offer some solutions (if any) that can minimize this problem at Iraqi hospitals. ***Methodology:*** This cross sectional study was conducted from May to October 2019. The sample was 128 patients (their specimens were cultured and antibiotic sensitivity was tested) especially toward a group of antibiotic. ***Results:*** At the end of this study the result showed that a higher group of resistance especially to penicillin group and a lower rate to azithromycin, another finding was the bacteria which infect (admitted in patients) were resistant to multiple drugs than those which infect (out patients). ***Conclusion:*** A high resistance to penicillin group, Staphylococcus aureus was found to be the most resistant microorganism as culture results showed.

Keywords: Antibiotic resistance, culture, infection, antibiotics.

INTRODUCTION

Antibiotics are chemical materials of a natural origin mainly from fungi, if used properly it can save lives. Using antibiotics without caution can cause resistance [1]. Every time you take antibiotics, sensitive bacteria are killed. But resistant germs may be left to grow [2]. They can spread to other people and multiply causing infections that certain antibiotics cannot cure which makes it a challenge nowadays [3].

The rise of bacterial resistance to antibiotics in Middle Eastern countries which are devastated by wars, had made antibiotic resistance a slow-motion emergency facing many of these countries, for example, up to 60 percent of the infections we see in war-wounded patients from Iraq, Syria, and Yemen are antibiotic-resistant. The same holds true for the capacity for proper sterilization, hygiene, and care of patients with open fractures or other severe injuries that are highly susceptible to infection [4].

Increasingly, governments around the world are beginning to pay attention to this problem which is so serious that it threatens the achievements of modern medicine. Antimicrobial resistance (AMR) threatens the effective prevention and treatment of infections caused by bacteria, parasites, viruses and fungi [5].

The reasons for the widespread use of antibiotics in human medicine include increasing availability of antibiotics since the 1950, uncontrolled sale in many low or middle income countries, where they can be obtained over the counter without a prescription [6]. Releasing large quantities of antibiotics into the environment during pharmaceutical manufacturing without proper control increases the risk of those antibiotic-resistant strains [7, 8]. The development of new antibiotics by the pharmaceutical industry, a strategy that had been effective at combating resistant bacteria in the past are no longer effective due to emerging of new generations of resistant bacteria [9, 10].

There are many studies that discussed the mechanisms by which the resistance of bacteria developed, but the main one was to decrease drug uptake [11], the efflux pumps [12], enzymes that

inactivate a specific antimicrobial drug and the target alterations by mutation [13] as well as the nature of receptor [14].

The 1950s to 1970s represented the golden age of antibiotic discovery, where countless new classes of antibiotics were discovered to treat previously incurable diseases such as tuberculosis and syphilis [15]. However, since that time the discovery of new classes of antibiotics has been almost nonexistent, and represents a situation that is especially problematic considering the resiliency of bacteria shown over the time and the continued misuse and overuse of antibiotics in treatment [16]. The phenomenon of antimicrobial resistance caused by overuse of antibiotics was predicted by Alexander Fleming who said "The time may come when penicillin can be bought by anyone in the shops. Then there is the danger that the ignorant men may easily under-dose he and by exposing his microbes to nonlethal quantities of the drug make them resistant" [17, 18]. Without the creation of new and stronger antibiotics an era where common infections and minor injuries can kill, and where complex procedures such as surgery and chemotherapy become too risky, is a very real possibility [19]. Antimicrobial resistance threatens the world as we know it, and can lead to epidemics of enormous proportions of infection if preventive actions are not taken. In this day and age current antimicrobial resistance leads to longer hospital stays, higher medical costs, and increased mortality [20].

PATIENTS AND METHOD

Study population

Patients at local hospitals in Baghdad (Baghdad medical city) and Babil (Marjan teaching hospital) also (Ibn_Al Nafees) Hospital and private clinics and some private laboratories.

The patients who were expected of having bacterial resistance were sent to these hospitals for bacteriological culture and sensitivity testing.

The samples that were taken from these patients included (urine/blood/wound, throat and vaginal swab/sputum) were taken in this study.

Study Design

Descriptive cross sectional study was carried out on a sample of specimens from various sites (urine/blood/wound swab/sputum) during the period from June to October 2019 in bacteriology laboratories. Data collection was carried on June to September 2019 .

Study Sample

A total of 128 subjects (they were 49 male and 79 female) regarding the age range (22-89yrs).By using convenient sampling.

RESULTS

A hundred and twenty-eight individuals were included in the sample. 38.3% were males and 61.7% were females as shown in table (1).

Table 1: The percent of antibiotic resistance within males and females

	Frequency	Percent	Valid Percent
Males	**49**	**38.3**	**38.3**
Females	**79**	**61.7**	**61.7**
Total	**128**	**100.0**	**100.0**

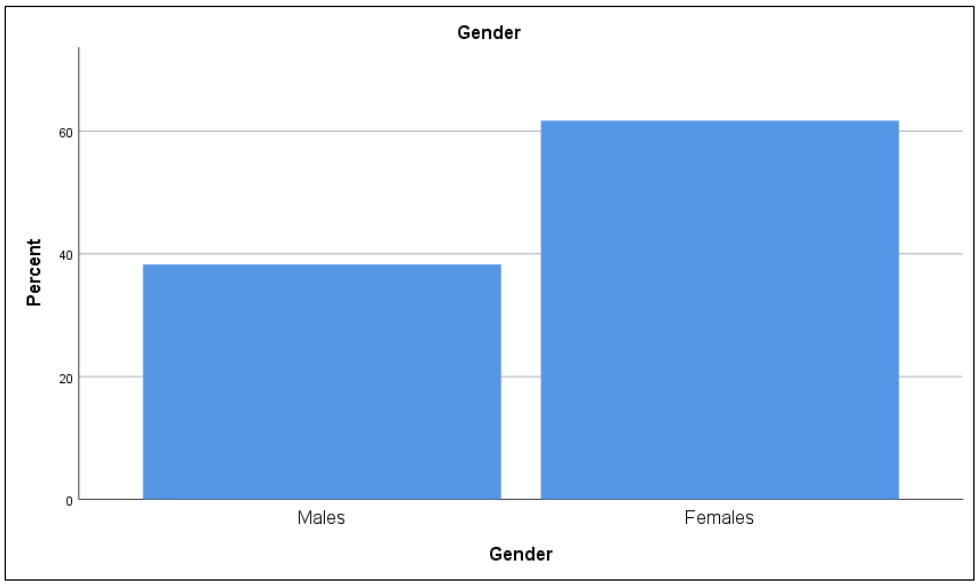

Figure 1: The percent of antibiotic resistance within males and females

The mean of their age is 40.66 years (SD = 13.89) and median is 40.00**.**

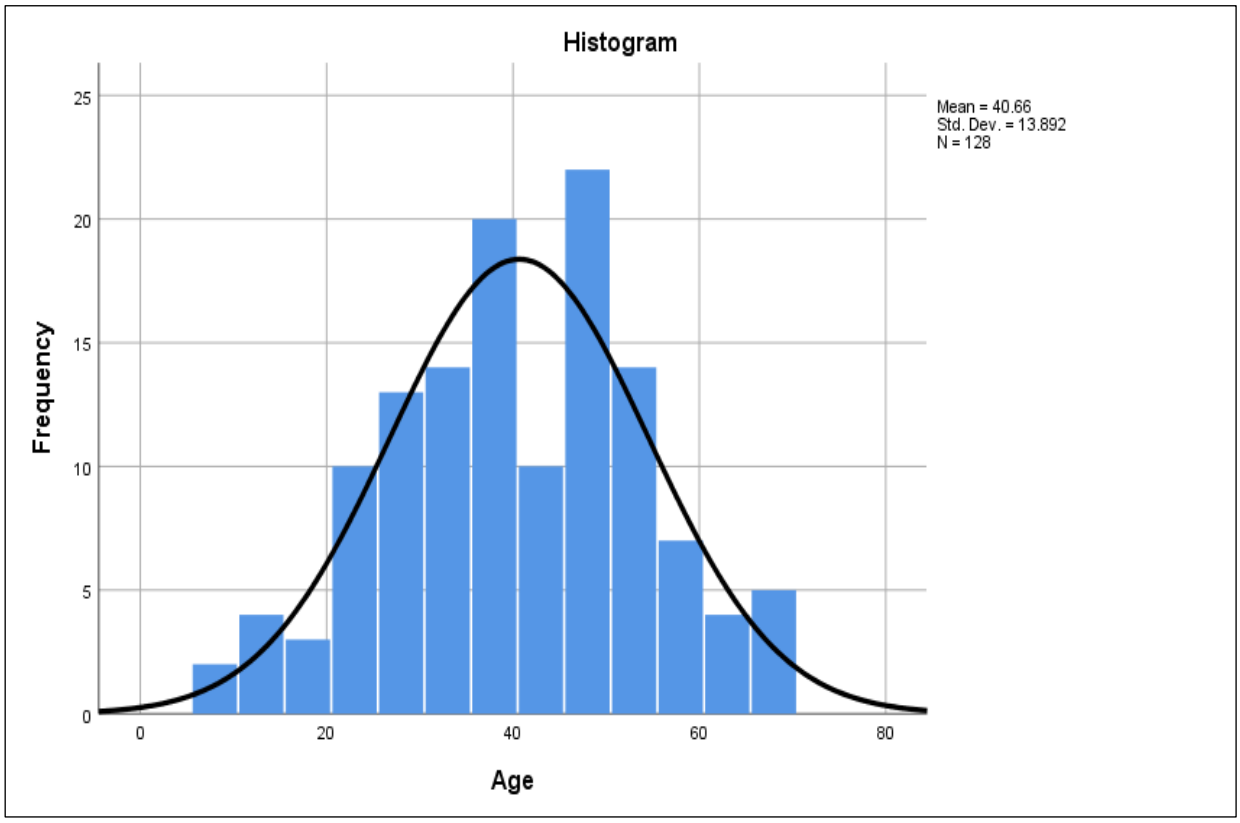

Figure 2: The age interval of the patient included in our study

Table 2: Distribution of cases

Diseases	*Frequency*	*Percent*	*Valid Percent*	*Cumulative Percent*
UTI	*17*	*13.3*	*20*	*20*
Chest infection	*4*	*3.1*	*4.7*	*24.7*
Endocarditis	*2*	*1.6*	*2.4*	*27.1*
Otitis media	*4*	*3.1*	*4.7*	*31.8*
Meningitis	*1*	*0.8*	*1.2*	*32.9*
Gastroenteritis	*4*	*3.1*	*4.7*	*37.6*
Bacteremia/Sepsis	*7*	*5.5*	*8.2*	*45.9*
Wound infection	*3*	*2.3*	*3.5*	*49.4*
Undiagnosed	*26*	*20.3*	*30.6*	*80*
Miscellaneous	*17*	*13.3*	*20*	*100*
Local infections	*85*	*66.4*	*100*	
Systemic infection (Multi-organ)	*43*	*33.6*		
Total	*128*	*100*		

More than half of individuals presented to the outpatient units (56.3%) while the remaining were in patients (43.8%).

Table 3: Admission statues of patients group

	Frequency	*Percent*	*Cumulative Percent*
Outpatient	*72*	*56.3*	*56.3*
Inpatient	*56*	*43.8*	*100*
Total	*128*	*100*	

The samples sent for culture varied but the majority, were urine samples (50.8%) followed by blood (18.8%) as shown in table (4).

Table 4: Types of study specimens collected in this study

Type of sample	*Frequency*	*Percent*	*Cumulative Percent*
Urine sample	*65*	*50.8*	*50.8*
Blood sample	*24*	*18.8*	*69.5*
Nasal swab	*7*	*5.5*	*75*
Ear swab	*4*	*3.1*	*78.1*
Sputum	*5*	*3.9*	*82*
Stool sample	*2*	*1.6*	*83.6*
Wound swab	*7*	*5.5*	*89.1*
High vaginal swab	*6*	*4.7*	*93.8*
Throat swab	*4*	*3.1*	*96.9*
Seminal fluid	*2*	*1.6*	*98.4*
Bone biopsy	*2*	*1.6*	*100*
Total	*128*	*100*	

Most of the urine samples showed growth of staphylococcus aureus, E.coli, and (klebsiella pneumonia, streptococcus viridians) showed less and almost equal percentage than the two organisms above. Blood samples showed growth of klebsiella pneumonia, staphylococcus auras, pseudomonas aureginosa at higher percentage than other organisms. Nasal swab almost showed no growth. High vaginal swab showed E.coli at highest percentage, followed by klebsiella pneumonia, then staphylococcus aureus. Ear swab showed staphylococcus aureus and streptococcus viridans. Throat swab showed main growth of staphylococcus aureus and enterococcus pyogen. Wound swab showed staphylococcus aureus and klebsiella pneumonia in almost equal percentage and less then pseudomonas aureginosa. Commonly isolated organisms were mostly Staphylococcus aureus (19.5%) followed by E. coli (11.7%). However, (35.2%) of the samples, showed no growth as shown in table (5).

Table 5: Types of bacteria isolated in culture growth results

Microorganism	*Frequency*	*Percent*	*Cumulative Percent*
Streptococcus Viridians	*4*	*3.1*	*3.1*
Staphylococcus aureus	*25*	*19.5*	*22.7*
E.coli	*15*	*11.7*	*34.4*
Enterococcus Pyogen	*6*	*4.7*	*39.1*
Pseudomonas aureginosa	*6*	*4.7*	*43.8*
Klebsiella pneumonia	*13*	*10.2*	*53.9*
Others	*14*	*10.9*	*64.8*
No growth	*45*	*35.2*	*100*
Total	*128*	*100*	

Resistance to antibiotics varied widely, Amoxicillin showed the most resistance (68.7%) while Cefotoxime and Azithromycin had the lowest (3.6%). Other antibiotics had a variable level of resistance as shown in table (6).

Among the patients in our study, 4 of them were having wound infection they were resistant to five types of antibiotic which are (amoxicillin, penicillin, erythromycin, vancomycin) and they were sensitive to only cefotoxime and ceftriaxone. Most of those patients were resistant to amoxicillin.

Table 5: Types of bacteria isolated in culture growth results

Antibiotic	*resistant frequency*	*resistance percent*
Amoxicillin	*57*	*68.70%*
Penicillin	*23*	*27.70%*
Gentamycin	*22*	*26.50%*
Ceftriaxone	*19*	*22.90%*
Nalidaxic acid	*17*	*20.4%*
Tetracycline	*14*	*16.90%*
Ciprofloxacin	*13*	*15.70%*
Erythromycin	*10*	*12%*
Nitrofurantoin	*10*	*12%*
Amikacin	*8*	*9.60%*
Imipenim	*8*	*9.60%*

Antibiotic	*resistant frequency*	*resistance percent*
Ceftazidime	*7*	*8.40%*
Vancomycin	*7*	*8.40%*
Ampicillin	*6*	*7.20%*
Chloramphenicol	*6*	*7.20%*
Piperacillin	*4*	*4.80%*
Azithromycin	*3*	*3.60%*
Cefotoxime	*3*	*3.60%*

Cross tabulation of age groups with culture results (organisms) showed no statistically significant results at (p ≤0 .223).

Pearson chi square (age)	***Value 33.579***	***Df 28***	***Significance 99% confidence interval 0.223***

The gender was not associated with cultures too at p value ≤0.961

Pearson chi square (gender with culture)	***Value 2.045***	***Df 7***	***Significance 99% confidence interval 0.961***

Cross tabulation of gender with the resistance to the total antibiotics showed no statistically significant results.

Pearson chi square gender with total resistance)	***Value 2.938***	***Df 7***	***Significance 99% confidence interval 0.913***

The diagnosis was not associated with the number of antibiotics the individual is resistant to at p value ≤0.131**.**

Pearson chi square (types of diagnosis)	***Value 67.847***	***Df 33***	***Significance 99% confidence interval 0.131***

There was no difference between outpatients and inpatients regarding the organisms isolated (p ≤0.809).

Pearson chi square (admission status)	***Value 3.888***	***Df 7***	***Significance 99% confidence interval 0.809***

However, there was a statistically significant association between the settings of which the patient presented (inpatient vs. outpatient) and the total number of antibiotics the patient is resistant to (p ≤0.010).

Pearson chi square (no. of AB and admission)	***Value 16.582***	***Df 7***	***Significance 99% confidence Interval 0.010***

With a trend of outpatients being resistant to antibiotics was ranging from 1 to 5 drugs while inpatients showed resistance for up to 8 antibiotics. Interestingly, age showed no significant correlation with total number of antibiotics the individual is resistant to (p ≤0.236, r = 0.097).

Table 7: Frequency of drug resistant among each diagnosis

Diagnosis	**Penicillin group**	**cephalosporins**	**Imipenim**	**Aminoglycosides**	**Erythromycin**	**Nalidaxic acid**
UTI	17	15	2	2	4	4
Chest infection	2	3	0	0	1	1
Endocarditis	2	2	2	1	0	2
Otitis media	3	2	0	1	3	2
Meningitis	1	1	0	1	4	2
Gastroenteritis	4	4	2	2	2	0
Bacteremia/Sepsis	7	5	1	3	0	3
Wound infection	3	2	0	1	1	0
Undiagnosed	26	22	0	18	1	3
Others	15	15	0	15	0	4

Others include cases with (stones, rheumatic fever, pharyngitis, vaginitis, neutropenia, Non Hodgkin lymphoma, fractures and leukemia).

Table 8: Correlations between age and number of drug resistance

Correlations between age and number of drug resistance		*Age*	*Total Resistance*
Age	*Correlation Coefficient*	*1.000*	*.097*
	Sig. (2-tailed)		*.236*
	N	*128*	*83*
Total Resistance	*Correlation Coefficient*	*.097*	*1.000*
	Sig. (2-tailed)	*.236*	
		83	*83*

DISCUSSION

Antibiotics are medications that destroy or slow down the growth of bacteria. They include a range of powerful drugs and are used to treat diseases caused by bacterial infections. Antibiotics cannot treat viral infections, such as common cold and flu.

Antibiotic resistance continues to be a global problem, affecting more than 500,000 people with possible bacterial infections across 22 reporting countries, according to who reports. In this cross sectional descriptive study, 128 cases studied the prevalence to antibiotic resistance. The mean of age of patients samples include were elderly but different age group from child to elderly showed no evidence association with number of antibiotic that the samples were resist to. Age showed no significant association with microorganisms résistance to antibiotic which can be explained that any microorganism can infect any age group with any microorganism were resistant to. Females were highly attendant to the laboratories to receive their culture results unlike males. Also gender showed no significance with number of drugs that the microorganisms resistance. Some samples showed no growth, because of other infections like fungal, viral infection or because of bad culture techniques [36].

Regarding the final diagnosis of patients, it was proved in (56) patients only and still not proven in (73) patient (referral from doctor because of certain signs and symptoms of infection .UTI was the most prevalent diagnosis within this study, and the least was meningitis. Otitis media, endocarditis, gastroenteritis, sepsis, wound infection were with similar proportions. While other infection were due to stones, rheumatic fever, pharyngitis, vaginitis, neutropenia, Non Hodgkin lymphoma and leukemia.

Staphylococcus aureus was the highest organism isolated from culture media followed by E.coli and klebsiella pneumonia then enterococcus pyogen, pseudomonas aureginosa, streptococcus viridans infection was the least and can be considered as normal flora and sometime can be the cause of infective endocarditis. Other organism showed lesser significant percentage like Neisseria meningitides, enterobacter cloacae, streptococcus pyogen, proteus mirabilis and streptococcus pneumonia.

Furthermore, one of the main goals of this study was to identify the antibiotics that had the highest and the lowest resistance rates among Iraqi patients and to relate that with the diagnosis of these patients. These groups in order are: the penicillin family carried the highest numbers of resistance in this study, showing that amoxicillin had the highest percentage and Piperacillin the lowest, which is related to B-lactamase producing organism mainly [37].

Ceftriaxone was the most used drug by the patients and surprisingly had the highest resistance, may be due to the over use in treatment of flu and common cold. That's why these patients were not showing any improvement in their symptoms, as result of cephalosporin B-lactamase type of resistance [38, 39].

Cefotoxime and ceftazidime had different percentages; perhaps it was contributed to the fact that they were less popular and less used [40]. For aminoglycosides family, gentamicin was the highest in its resistance and vancomycin the least, vancomycin remains the drug of choice for treatment of MRSA (methicillin-resistant staphylococcus aureus) infections which most of them occur in people who have been in hospitals or other health care settings, like nursing homes and dialysis centers, these infections typically are associated with invasive procedures or devices, such as surgeries, intravenous tubing or artificial joints. So using vancomycin to treat these infections can exhibit increased resistant to the drug mentioned above, known as vancomycin resistant staphylococcus aureus (VRSA) [41, 42].

VRSA are associated with persistent infections, vancomycin treatment failure, and poor clinical outcomes. Other antibiotics recorded different percentages of resistance depending on how much it was used, patient disease, age and other causes. Having a certain diagnosis was not associated with the numbers of antibiotics the individual is resistant to. However, if we excluded the undiagnosed cases, UTI patients carried the highest resistance to different types of antibiotics, for example 17cases were resistant to penicillin and 15 to cephalosporins, respectively. The higher rate of urinary tract infection in females was ought to the feature of female urogenetal tract (short female urethra) which makes it easy to be contaminated with fecal flora.

Aged males (particularly above 50 years old) tend to show an increased urinary tract infection (UTI), This was predisposed by the prostate infection and hypertrophy which leads to incomplete evacuation of urinary bladder due to urethral stenosis there leading to a residual volume of urine in the urinary bladder and this residual urine acts as good medium for bacterial growth in males .Comparing with previous study made in Al-Anbar in the west of Iraq UTI patients showed the higher resistance was amoxicillin and ampicillin [43]. In chest infection cases, cephalosporins were the highest, meningitis cases the patients carried resistant to erythromycin more than the other drugs. Sepsis patients showed more resistant to penicillin and cephalosporins, and wounded patients for penicillin. As we can see, the diagnosis of patients showed different percentages of resistance to different types of antibiotics [44].

Regarding patients setting, although the total resistance of outpatients were higher than inpatients, inpatients showed resistant to higher number of antibiotic compared to outpatients, due to the presence of much stronger strains of microorganisms inside hospitals wards, also the unnecessary overuse of broad spectrum antibiotics, since antibiotics are generally prescribed before the return of culture results to guide empirical antibiotic choice [45].

In compare with study in Iraq for antibiotic resistance pattern of bacteria isolated from urinary tract infection in 2013 the most common organism was E. coli which was isolated from patients. Followed by Proteus mirabilis, Pseudomonas aureginosa, Staphylococcus aureus, and Klebsiella pneumonia. Staphylococcus aureus isolates were highly resistant to ampicillin and amoxicillin. The overall assessment of the most antibiotics used for UTI treatment revealed that Amikacin [46]. While other study about Antibiotic resistance pattern of HA-MRSA strains isolated from leukemia patients in Baghdad, Iraq, among them, Staphylococcus aureus microorganisms accounted for the highest growth. Highest resistance for antibiotic was documented in MRSA, and then intermediate resistance was documented for VRSA [47].

International Society for Antimicrobial Chemotherapy in 2019, published an article was a cohort study of hospitalized patients receiving initial intravenous [I.V) antibiotic therapy followed by step-down oral therapy was conducted. The results were, treatment failure occurred in 15 patients (7.4%), there were bacterial resistance but there were no statistically significant differences between groups. Likewise, individual composite outcomes and secondary outcomes demonstrated no statistically significant differences [48].

Many studies demonstrated that increased environmental cleaning is associated with a reduction in Vancomycin-resistant enterococci (VRE)-positive environmental cultures. The emergence of drug-resistant bacteria is to some extent an inevitable consequence of the patterns of use of antibiotics in society today [49]. Given the time and cost required to bring new, more effective antimicrobial therapeutics to market, drug discovery may not be the most effective approach to limiting antimicrobial resistance. Rather, there is substantial evidence to support that more appropriate and careful use of antibiotics and even avoiding antibiotic treatment altogether in some cases, can significantly decrease or limit drug-resistant bacteria. In addition, relatively inexpensive and simple measures, such as microbial surveillance and prophylaxis, proper hygiene, the use of protective barriers, and environmental cleaning can translate into major savings in health care-related costs, and significant improvements in patient health and quality of care, the task is not insurmountable but will require a shift in behavior and attitudes among health care providers and patients [50-52].

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