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THE COST-EFFECTIVENESS ANALYSIS AND DRUG USE TREND OF THE MOST COMMONLY USED ANTIBIOTICS IN SAUDI ARABIA

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Abstract:

Aim: *Antibiotic drug resistance can result from the inappropriate use of antibiotics, which is a global concern. The purpose of this study was to evaluate the cost-effectiveness and pattern of drug use. To encourage their sensible use, studies are carried out to examine the pattern of antibiotic prescriptions, their adherence to accepted practices, and the financial impact on the patients.*

Method: *The study was intended to be a cross-sectional, single-center retrospective pharmacy database investigation of cost-utility relationships for the five most widely prescribed antibiotics in Saudi Arabia. The study included data spanning from January 1, 2019, to December 31, 2019. Frequencies and percentages of the demographic traits were displayed, together with the Wilson 95% confidence intervals for the proportions. The adherence of Saudi Arabia's antibiotic prescription practices to the National Antimicrobial Guidelines was compared using the chi-square test (for P-value computation).*

Results*: The highest percentage of patients (35.97%) came from the 18–35 age group, and the lowest percentage (1.82%) was from the 72–88 age group. The greatest number of units administered was 22487 for amoxicillin and clavulanic acid, which was given to 42.93% of patients; the lowest number was 8.04% for ciprofloxacin (4215). Cefdenir had the longest therapeutic duration (7.23 days), while azithromycin had the shortest length (3.58 days). Cefdenir 38.66SR (10.31 USD) had the highest cost, while Cefuroxime 12.43SR (3.31 USD) had the lowest estimated cost.*

Conclusion: *Because of their broad spectrum of activity against a variety of microorganisms, our study found that amoxicillin and clavulanic acid were the most commonly utilized first-line medicines in the treatment of bacterial infections. Before prescribing, laboratory testing to determine the type of bacterium could stop the emergence of medication resistance and preserve the antibiotic for later use. For any indication that might encourage the prudent use of antibiotics, cost-benefit analyses of the medications must be carried out.*

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INTRODUCTION:

Due in large part to the development of antibiotics during this time, infectious diseases became less common in 1900 and drastically decreased in 2000.Antimicrobials are the substances that combat harmful microorganisms. Among the antimicrobials that are most frequently employed are antibiotics.[2]The increasing use of antibiotics poses the risk of antibiotic resistance, which could be the cause of the rise in world mortality rates.[3] The World Health Organization (WHO) advises against using antibiotics excessively because of their alarmingly high rate of side effects.[4] Between 1930 and 1962, about 20 new types of antibiotics were developed worldwide.[5] Depending on their chemical or molecular structures, several common types of antibiotics include tetracycline, beta-lactams, macrolides, quinolones, aminoglycosides, sulphonamides, glycopeptides, and oxazolidinones.[6]

The beta-lactam medication class is well recognized for its antibiotics, monobactams, carbapenems, and cephalosporins. Combining amoxicillin with clavulanic acid, a substance that inhibits the bacterial penicillinase enzyme, augments the antibacterial activity of amoxicillin. This is known as augmentin.[7] Cephalosporins are the most commonly recommended antibiotics by UK doctors, perhaps due to their structural and mechanism of action similarities with penicillin.[8] There are five generations of these cephalosporins, with the later generations being more potent in treating infections brought on by Gram-negative bacteria.[9] The macrolide group of antibiotics, which includes clarithromycin, erythromycin, and azithromycin, works by preventing the synthesis of proteins in bacteria.[10] Tetracyclines work by attacking ribosomes and preventing bacteria from synthesizing proteins. They are divided into generations according to how they are synthesized. This class of antibiotics includes oxytetracycline, doxycycline, chlortetracycline, and so on.[6] Quinolones are strong, all-purpose antibiotics that work by preventing the synthesis of bacterial DNA. Despite having a number of gastrointestinal and central nervous system side effects, they are one of the most often given drugs for different infections in both hospital and outpatient settings.[11] Strong, all-purpose antibiotics known as aminoglycosides work via inhibition of synthesis of protein . Among the medications in this class are tobramycin, gentamycin, kanamycin, and neomycin. They were first used as first-line chemotherapeutic medicines, but in the 1980s, cephalosporin, fluoroquinolone, and carbapenams—which were discovered to be less toxic and to have a wider spectrum of action—replaced them. Their limited oral bioavailability necessitates parenteral administration.[12] Synthetic antibiotics known as sulphonamides prevent bacterial growth by blocking the conversion of p-amino benzoic acid to dihydropteroate, which is a mediator of bacterial DNA synthesis. For oral administration, they are offered as individual medications or combinations. Sulphonamides are available in ocular dose forms, suppositories, and lotions.

There are sulfonamides for topical and oral use. Inflammatory bowel disease, burns, UTIs, vaginitis, and other conditions are treated with them.[13] Although parenteral administration is sometimes used for severe systemic infections, oral administration of antibiotics is the most usual method. For the treatment of certain skin illnesses, such as cellulitis and acne, topical methods are preferred.[14] Antibiotic abuse and misuse, for example, in hospitals and the community, is a global concern since it can result in antibiotic resistance, unfavorable side effects, hospitalization, and financial hardship for the patient due to the high cost of care. Therefore, research on medication consumption and cost-effectiveness are carried out to examine the pattern of drug prescriptions made by doctors and their financial impact to promote their rational use. The purpose of this study is to analyze the cost-effectiveness of the five antibiotics that are most frequently used in hospital settings, as well as their drug usage patterns.

METHOD:

The study's design called for a cost-utility analysis of the five most often prescribed antibiotics in Saudi Arabia as well as a single-centered, cross-sectional retrospective pharmacy database assessment of prescribing trends. Information for the time frame of January 1, 2019, to December 31, 2019, was taken from Al-Mana General Hospital in Khobar, Saudi Arabia's electronic pharmacy records. Electronic drug dispensing records from the inpatient and outpatient pharmacy departments were obtained together. Microsoft Excel 2013 was used to archive all of the recovered data. All of the patient data that was retrieved about those receiving antibiotic therapy was sorted into groups based on how frequently the top five different antibiotics were prescribed, and those groups were then labeled with five different categories.

The five most often used antibiotics in the hospital under study were cefuroxime, azithromycin,

ciprofloxacin, amoxicillin and clavulanic acid, and cefdenir. The study included patients of all genders, ages, and nationalities who were taking any combination or single of the five medicines listed above. The study excluded patients who did not receive a prescription or medication from any of the five antibiotics listed above. The WHO defined daily dose and the National Antimicrobial Guidelines, which were established as a standard measure of drug consumption and offer a rough estimate of the prescribing pattern of various antibiotics taken for the management of various infectious diseases, were used to calculate the daily price of each drug.

The average cost of each unit dose of each prescription was used to determine the cost analysis of every medication under study.The National Antimicrobial Guidelines are the protocols and guidelines that the study center (hospital) uses to address various infectious infections, and these are the last criteria that were used to analyze the prescribing patterns. The WHO anatomical therapeutic chemical classification code, or ATC, was used to code all five of the aforementioned antibiotics based on their availability in dose form and mode of administration. These include cefdenir (ATC code: J01DD15), cefuroxime (ATC code: J01DC02), azithromycin (J01FA10, S01AA26), amoxicillin and clavulanic acid (ATC code: J01CR02), and ciprofloxacin (ATC code: J01MA02, S01AE03, S02AA15).

Data analysis:

Frequencies and percentages of demographic traits were displayed, together with Wilson 95% confidence ranges for proportions. The adherence of Saudi Arabia's antibiotic prescription practices to the National Antimicrobial Guidelines was compared using the chi-square test (for P-value computation). Microsoft Excel 2013 and SPSS version 26 (SPSS Institute Inc., Cary, NC, USA) were used for all statistical analyses. A P-value of less than 0.05 was deemed statistically significant.

RESULTS:

According to baseline demographic data (Table 1), of the 52 372 patients who were studied and administered antibiotics, 51.64% (CI: 51.21–52.07; n = 27 046) of the patients were males, and 48.36% (CI: 47.93–48.79; n = 25 326) of the patients were females. The age group of 18–35 years had the highest percentage of patients documented at 35.97% (CI: 35.57–36.39; n = 18 842). This was followed by 0–17 years (29.51%; CI: 29.13–29.91; n = 15 459), 36–53 years (21.93%; CI: 21.59–22.3; n = 11 489), and 54–71 years 10.73% (CI: 10.48–11.01; n = 5624). For the age range of 72–88 years, the percentage was notably low at 1.82% (CI: 1.72–1.95; n = 958). Saudis made up a larger percentage, 58.21% (CI: 57.8–58.64; n = 30 490), than non-Saudis, 41.78% (CI: 41.36–42.2; n = 21 882).

Table 1 Baseline demographic characteristics of the studied patients

Characteristics	Total 52 372, % (95% CI) (*n*)
Gender	
Male	51.64 (51.21–52.07) (27 046)
Female	48.36 (47.93–48.79) (25 326)
Age (years)	
0–17	29.51 (29.13–29.91) (15 459)
18–35	35.97 (35.57–36.39) (18 842)
36–53	21.93 (21.59–22.3) (11 489)
54–71	10.73 (10.48–11.01) (5624)
72–88	1.82 (1.72–1.95) (958)
Nationality	
Saudi	58.21 (57.8–58.64) (30 490)
Non-Saudi	41.78 (41.36–42.2) (21 882)

As can be seen in Figure 1, among the five most popular antibiotics, amoxicillin had the highest number of units prescribed (22 487), while ciprofloxacin had the lowest number (4215).The remaining antibiotics were prescribed as cefuroxime (12 737), azithromycin (8349), and cefdenir (4546), in decreasing sequence of dosage.

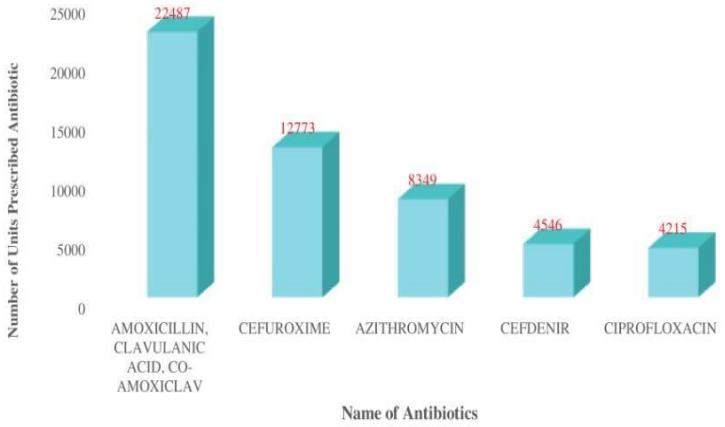

Figure 1 Five different most common prescribed antibiotics in studied hospital.

The majority of patients (42.93%; CI: 42.52–43.36; n = 22 487) received the medication amoxicillin, clavulanic acid (ATC code: J01CR02), which is available in oral solid and liquid parenteral dosage form with a standard dose of 6.67–20 mg/ kg, 1.67–5 mg/ kg. The distribution of patients among the different age groups is as follows: Among those with significant P values <0.05 were those aged 0–17 years (17.89%; CI: 17.56–18.22; n = 9371), 18–35 years (12.89%; CI: 12.62–13.19; n = 6754), 36–53 years 8.05% (CI: 7.83–8.30; n = 4219), 54–71 years 3.57% (CI: 3.42–3.74; n = 1873), and 72–88 years 0.51% (CI: 0.46–0.59; n = 270).

The parenteral dosage form of azithromycin (ATC Code: J01FA10, S01AA26) comes in oral solid and liquid, eye and ear drop, and typical adult dose of 500 mg OD or 10 mg/kg OD, one drop of 1% solution. BD was administered to 15.94% (CI: 15.64–16.27; n = 8351) of the patients, distributed as follows across the age groups:
With a significant P value <0.05, the following age groups had significant differences: 0–17 years 5.41 (CI: 5.23–5.62; n = 2838), 18–35 years 5.51% (CI: 5.22–5.71; n = 2888), 36–53 years 3.04% (CI: 2.91–3.20; n = 1597), 54–71 years 1.57% (CI: 1.48–1.69; n = 827) and 72–88 years 0.38% (CI: 0.33–0.44; n = 201).

Cefdenir (ATC Code: J01DD15) is available in oral solid and liquid dosage forms. Its standard dose is 300–600 mg OD or 14 mg/kg. This medication was administered to 8.68% (CI: 8.44–8.93; n = 4546) of the patients, who were distributed among the following age groups: 0–17 years 4.53% (CI: 4.36–4.71; n = 2375), 18–35 years 1.91% (CI: 1.81–2.04; n = 1003), 36–53 years 1.31% (CI: 1.22–1.41; n = 688), 54–71 years 0.81% (CI: 0.74–0.89; n = 425), and 72–88 years 0.10% (CI: 0.09–0.14; n = 55) with a significant P value <0.05.

8.04% (CI: 7.82–8.29; n = 4215) of the patients received the antibiotic ciprofloxacin (ATC Code: J01MA02, S01AE03, S02AA15) in oral solid and liquid, eye and ear drop, parenteral dosage form with a standard dose of 14–40 mg/kg, two drops hourly in the affected eye. The patients were distributed among the following age groups: Among the age groups with significant P values <0.05 were 0–17 years (0.26%; CI: 0.23–0.32; n = 140), 18–35 years (2.82%; CI: 2.69–2.98; n = 1481), 36–53 years (2.63%; CI: 2.50–2.77; n = 1380), 54–71 years (1.94%; CI: 1.84–2.07; n = 1020), and 72–88 years (0.37%; CI: 0.32–0.43; n = 194).

Table 2 displays the average therapy length for the major antibiotics under study. Cefdenir had the greatest duration (7.23 days), followed by ciprofloxacin (7.09 days), amoxicillin, clavulanic acid (6.44 days), cefuroxime (3.88 days), and azithromycin (3.58 days). Cefdenir 38.66SR (10.31 USD) had the greatest cost, according to the cost-utility study. Azithromycin 22.26SR (5.94 USD), amoxicillin, clavulanic acid 17.75SR (4.73 USD), and ciprofloxacin 15.15SR (4.04 USD) were the next most expensive. Cefuroxime was expected to cost the least, at 12.43SR (3.31 USD).

Drug (ATC code)	Average therapy of duration in days	Average cost in unit dose, prescription wise in SR (USD)
Amoxicillin, clavulanic acid (J01CR02)	6.44	17.75 (4.73)
Azithromycin (J01FA10, S01AA26)	3.58	22.26 (5.94)
Cefdenir (J01DD15)	7.23	38.66 (10.31)
Cefuroxime (J01DC02)	3.88	12.43 (3.31)
Ciprofloxacin (J01MA02, S01AE03, S02AA15)	7.09	15.15 (4.04)

DISCUSSION:

Our research showed that, with the exception of elderly patients over the age of 72–88, there was little variation in the proportion of adults, children, and men who received antibiotic prescriptions. Similar information is included in a WHO report that claims antibiotic resistance poses a major threat to everyone, anywhere in the world, and that it can impact people of all ages and nationalities.[15] Amoxicillin and clavulanic acid were prescribed the most units out of the five most widely used antibiotics; this is consistent with previous research.[16] This may be because, as previous research has shown, it is the safest and most effective first-line recommended antibacterial treatment for treating ear infections, dental infections, and mild to severe upper respiratory tract infections.

This may be because, as demonstrated by a previous study that also demonstrated adherence to the National Antimicrobial Guidelines, MOH, Saudi Arabia, it is the safest and most effective first-line preferred antimicrobial agent for treating dental infections, ear infections, and mild to major upper respiratory tract infections.[17, 18] Our study's second option, cefuroxime, is comparable to previous findings and may be used as an empirical treatment for a variety of community-acquired illnesses.[19] In terms of pragmatic pneumonia management in the community, azithromycin treatment was found to be just as effective as cefuroxime, and it is equally well-tolerated.[20]

Clinical data suggests that Cefdenir is a useful medication that is generally well tolerated for treating minor to severe skin or respiratory tract toxicities in children, adults, and young people, especially when treating common community-acquired infections.[21]

An FDA-approved antibiotic drug in the fluoroquinolone class, ciprofloxacin is a suitable therapy choice for individuals with mixed infections or those who have variables that make them more susceptible to Gram-negative infections. It treats bacterial infections, including pneumonia and urinary tract infections. However, unless there are no other options, antibiotics shouldn't be used to treat infections due to their serious adverse effects.

According to the cost-utility analysis, the cost of cefdenir, which had the longest therapy duration, was highest, while the cost of amoxicillin and clavulanic acid, which had moderate therapy durations, was moderate. This is consistent with the previous comparative analysis, which demonstrated that the choice of antibiotic(s) utilized had an impact on treatment costs but that age or gender had no effect on the cost of antibiotic medication therapy.

CONCLUSIONS:

Because of their broad spectrum of activity against a variety of microorganisms, beta-lactam and beta-lactamase inhibitor combinations (such as amoxicillin plus clavulanic acid) were most frequently employed as first-line treatments for bacterial infections. In cases of hepatic and renal impairment, the dosage of the combination of amoxicillin and clavulanic acid should be closely watched. The least desired option was ciprofloxacin, a fluoroquinolone, because of its toxicity and risk of bacterial resistance. It is not advised to use them as children's first-line antibiotic treatment agents.

Drug prescriptions that are appropriate and their dosages should be checked to make sure they follow national recommendations. Antibiotic prescriptions that are inappropriate or unnecessary can lead to the emergence of drug resistance and unfavorable side

effects, which can eventually lengthen hospital stays for patients and increase financial burden.

Before writing a prescription, laboratory testing to determine the type of bacterium could stop the emergence of medication resistance and preserve the antibiotic for later use. Cost-benefit analyses of antibiotics must be carried out for each indication that may support their appropriate use, as concerns regarding drug resistance and less funding for the research of novel antibiotics are becoming more pressing.

Study place:

A study utilizing retrospective observation was conducted at the Al-Mana Group of Hospitals (AGH) located in Saudi Arabia. AGH Al-Khobar is a 250-bed private teaching hospital that offers 74 outpatient clinics to serve the Saudi Arabian population's healthcare needs.

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