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Antimicrobial Resistance Profile of Different Clinical Isolates against Augmentin, Imipenem and Ceftriaxone

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Background: Antibiotic resistance is a growing global public health concern because it jeopardizes the effective control and treatment of bacterial infections. The purpose of this study was to determine the bacterial profiles and susceptibility patterns to Imipenem, Augmentin, and Ceftriaxone in various clinical specimens from Al Saleem laboratory in Benghazi, Libya.
Methods: Two separate studies were carried out. Each experiment lasted three months. The patients' clinical samples included wound swabs, urine, sperm, blood, high vaginal swabs, and cerebrospinal fluid. Bacterial species were isolated and identified using standard microbiological

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methods in each study. Kirby-Bauer disc diffusion was used to conduct antimicrobial susceptibility tests from September 2020 to November 2020.
Results: There were 711 isolates obtained from 535 female and 503 male patients. The most common organisms isolated from specimens were *E. coli* spp, *Klebsiella* spp, and *Staph aureus*.
Conclusion: Bacterial resistance levels to various antibiotics varied greatly. We found that Augmentin has less activity against gram negative bacteria isolated from clinical specimens, whereas Imipenem has a much stronger effect on isolates than Augmentin. Appropriate monitoring of prevalent pathogenic organisms and their sensitivities will assist clinicians in making appropriate antibiotic treatment choices to avoid the spread of antimicrobial resistance.

Keywords: Augmentin; E. coli spp; imipenem; Klebseilla spp; wound swab; urine.

1. INTRODUCTION

Antimicrobial resistance is a growing issue in the twenty-first century and is regarded as the most serious threat to global public health [1]. Ceftriaxone sodium, an aminothiazol-cephalosporin, is a third-generation cephalosporin. Ceftriaxone (Rocephin) is the generic name for this medication. Ceftriaxone is used to treat many community-acquired infections and can be administered intravenously or intramuscularly; it has been widely used due to its improved stability against traditional -lactamases. Ceftriaxone is a bactericidal agent that works by inhibiting the synthesis of bacterial cell walls [2,3]. Ceftriaxone is active in the presence of certain beta-lactamases, penicillinases, and cephalosporinases from Gram-negative and Gram-positive bacteria [2]. Resistance to Ceftriaxone is primarily caused by beta-lactamase hydrolysis, changes in penicillin-binding proteins (PBPs), and decreased permeability [4]. Ceftriaxone has been shown to be active against Gram-negative bacteria and Gram-positive bacteria [5,6]. P-Lactam antibiotics are unable to destroy growing bacteria, with the exclusion of Imipenem, which is demanded to kill non-growing Gram-negative bacteria [7].

Imipenem remnants are the most effective active medication against 100% of bacteria strains [8]. Augmentin is a broad-spectrum antibacterial agent that has been available for clinical use in a variety of indications for over 20 years. It is still one of the most commonly used antibiotics in clinical practice, primarily for treating respiratory tract infections [9]. Amoxicillin/clavulanate was initially developed in response to a need for an oral broad-spectrum antibiotic that was effective against -lactamase-producing pathogens. Augmentin retained amoxicillin's good activity against -lactamase-negative strains, restored its activity against -lactamase-producing strains like *S. aureus, E. coli*, and *H. influenzae*, and broadened its activity against *Klebsiella pneumoniae* and anaerobic *Bacteroides fragilis* (most strains of the latter produce -lactamase) [10]. The β-lactamase-inhibiting properties of clavulanic acid [11] were combined with the good oral absorption and potent broad-spectrum antimicrobial activity of amoxicillin in tablets containing amoxicillin trihydrate and potassium clavulanate to rewrite text. Amoxicillin/clavulanate was first introduced as augmentin in the United Kingdom in 1981 [12], and later throughout the world. Augmentin has been shown to have increased activity against Enterobacteriaceae, staphylococci, and enterococci in *in vitro* studies in Europe and the United States [13]. The study aimed to identify the bacteria responsible for community-acquired infections and determine their susceptibility to the antibiotics Augumentin, Ceftriaxone, and Imipenem.

2. METHODS AND MATERIALS

Two separate studies were carried out, each lasting three months. Bacteria were isolated and identified in each study, and antibiotic sensitivity tests were performed. In terms of isolates and samples, a comparison was made between the two studies. The isolates and samples from which they were isolated, as well as their sensitivity patterns to the antibiotics tested on them, were compared in the two studies.

Bacterial Strain Collection: In this study, 711 pathogenic bacteria were isolated. Outpatients' urine cultures were 455 (75.3%), wound swabs 73 (12%), semen 48 (7.9%), high vaginal swab 16 (2.6%), blood culture 7 (1.2%), body fluids 4 (0.7%), and CSF 1 (0.2%). The investigation included all gram-negative and gram-positive bacteria isolated from clinical specimens by Al-saleem laboratory between August 2020 and November 2020. The bacteria were identified using standard procedures in the microbiology

department [14]. The study only considered samples that contained a significant number of recognized pathogens.

Testing for Susceptibility: The microbiology department conducted the following disk susceptibility testing. At 37Co, Augmentin, Imipenem, and Ceftriaxone were tested for gram-positive and gram-negative bacteria on Mueller-Hinton agar [15]. McFarland Standards is used in the antimicrobial susceptibility testing procedure to compare the bacterial suspension to Standard McFarland before swabbing on Muller Hinton agar. Checking and adjusting the densities of bacterial suspensions that can be used for identification and susceptibility tests is part of quality control. However, in the microbiological laboratory, the concentration used for antimicrobial susceptibility testing and culture media performance testing is 0.5 McFarland standards [16].

Identification of Bacteria: The clinical specimens were completely collected by standard microbiological technique for the identification and isolation of pathogenic bacteria. The samples were then cultured on Chocolate agar, MacConkey agar, Blood agar, Mannitol Salt Agar, and CLED agar, and incubated aerobically at 37 C for 24 hours, depending on the source of the specimens. The clinical isolates were identified using biochemical tests such as Triple sugar iron, urease test, motility test, Indole and Citrate utilization (MIS). Clinical strains of *Staphylococcus aureus*, *Escherichia coli* spp, *Klebsiella* spp, *Proteus* spp, *Citrobacter* spp, *Enterobacter* spp, and *Streptococcus* spp were thus isolated from clinical samples [15,17].

Methodology: The data was analyzed by SPSS programs version 20.

3. RESULTS

3.1 Gender Distribution among Patients in the First Study (n=604)

From 280 (46.3%) female and 324 (53.6%) male patients, 604 bacterial isolates were obtained (Table 1).

3.2 Gender Distribution among Patients in the Second Study (n=107)

107 bacterial isolates were obtained from 77 (71.9%) female patients and 30 (28%) (Table 2).

3.3 Clinical Specimen Distribution from Patients in the First Study (n=604)

Outpatient urine cultures (75.3%), superficial swabs (12%), semen (7.9%), high vaginal swab (2.6%), blood culture (1.2%), body fluids (0.7%), and CSF (0.2%) yielded 604 bacterial isolates (Table 3).

3.4 Clinical Specimen Distribution from Patients in the Second Study (n=107).

Based on age and gender, 439 specimens were accepted. Urine (83.1%), semen (6.5%), blood (1.8%), swabs (4.6%), high vaginal swabs (2.8%), and CSF (0.9%) were used to collect specimens (Table 4).

3.5 Isolate Distribution in Clinical Specimens Collected from Patients in the Initial Study (n=604)

The most common organisms isolated from the study subjects were *Escherichia coli* spp (39.7%) and *Klebseilla* spp (19.0%). *Staph aureus* (11.8%), *streptococcus pneumonia*e (11.6%), *Enterobacter* spp (7.0%), *pseudomonas* spp (6.5%), *streptococcus pyogen* (4.8%), *Proteus* spp (2.0%), *Citrobacter* spp (0.5%), and *Acinetobacter* spp and *Enterococcus faecalis* (0.2%) were also isolated (Table 5).

3.6 Isolate Distribution in Clinical Specimens Collected from Patients (n=107)

The most common pathogens were *Escherichia coli* 43 (40.1%) and *Staphylococcus aureus* 17 (15.8%) (Table 6).

Table 1. Shows the gender distribution of patients (n=604)

Gender	Number	Percentage
Female	280	46.3%
Male	324	53.6%
Total	604	99.9%

Table 2. Shows the gender distribution of patients (n=107)

Gender	Number	Percentage
Female	77	71.9%
Male	30	28 %
Total	107	100%

Table 3. Clinical specimen distribution from patients in the first study (n=604)

Sample	Frequency	Percentage
Urine	455	75.3
Wound swab	73	12
Semen	48	7.9
High Vaginal Swab	16	2.6
Blood	7	1.1
Body fluids	4	0.6
Cerebrospinal fluid	1	0.1
Total	604	100.0

Table 4. Clinical specimen distribution from patients in the second study (n=107)

Sample	Frequency	Percentage
Urine	89	83.1
Semen	7	6.5
Wound swab	5	4.6
High Vaginal Swab	3	2.8
Blood	2	1.8
Cerebrospinal fluid	1	0.9
Total	107	100.0

Table 5. Isolate distributions in clinical specimens collected from patients in the first study (n=604)

Bacteria	Frequency	Percentage
***E. coli* spp**	240	39.7
***Klebsiella* spp**	96	15.9
staph aureus	71	11.8
streptococus pneumoniae	70	11.6
***Enterobacter* spp**	42	7.0
***pseudomonas* spp**	39	6.5
streptococcus pyogen	29	4.8
***Proteus* spp**	12	0.2
Streptococcus agalactia	3	0.5
***Acinetobacter* spp**	1	0.2
Enterococcus faecalis	1	0.2
Total	604	100.0

3.7 Resistance Ratio against Ceftriaxone among Different Clinical Isolates (n=604)

Because they did not respond to standard therapy, organisms in the intermediate zones were not considered sensitive pathogens. Ceftriaxone was found to be highly effective against *E. coli* spp. but ineffective against *Streptococcus pneumonia*e and *Klebsiella* spp. Table 5 summarizes Ceftriaxone sensitivity patterns against various pathogens (Table 7).

3.8 Resistance and Sensitivity Rates of Imipenem Isolates (n=107)

Table 7 shows the results of susceptibility testing for the most common pathogens. Most *E. coli* 37

(34.6%) and *Staph aureus* 17 (15.9%) isolates were susceptible to Imipenem among culture-confirmed cases. The current study demonstrated that the antibiotic Imipenem has high activity against these bacteria (Table 8).

3.9 Resistance and Sensitivity Rates of Augmentin Isolates (n=107)

Augmentin was effective against 28.9% of the gram-positive bacteria (n=31). *Staph aureus*, the most common gram-positive bacteria isolate (17 (15.9%), has a susceptibility pattern to Augmentin of 13 (12.1%). 43 (40.2%) E. coli spp. were resistant to Augmentin, while 23 (21.5%) were sensitive. Augmentin showed a 33.6% resistance rate in gram negative bacterial isolates (n=67). Pseudomonas strains were resistant to Augmentin in 5 (4.7%) of the cases tested (Table 9).

Table 6. Isolate distribution in clinical specimens collected from patients (n=107)

Bacteria	Frequency	Percentage
***E. coli* spp**	43	40.1
Staph aureus	17	15.8
Streptococcus pneumoniae	14	3.2
***Klebseilla* spp**	12	11.2
***Enterobacter* spp**	6	5.6
Enterococcus faecalis	5	4.6
***Pseudomonas* spp**	5	4.6
Streptococcus pyogen	3	2.8
***Ctirobacter* spp**	1	0.9
Streptococcus agalactia	1	0.9
Total	107	100.0

Table 7. Resistance ratios to Ceftriaxone among different clinical isolates (n=604)

Bacteria	Ceftriaxone			Total
	I	R	S	
***Acinetobacter* spp**	0 0.0%	0 0.0%	1 .2%	1 .2%
***Citrobacter* spp**	0 0.0%	3 .5%	0 0.0%	3 .5%
Enterococcus faecalis	0 0.0%	1 .2%	0 0.0%	1 .2%
***E-coli* spp**	8 1.3%	112 18.5%	120 19.9%	240 39.7%
***Enterobacter* spp**	0 0.0%	18 3.0%	24 4.0%	42 7.0%
***Klebsiella* spp**	12 2.0%	38 6.3%	46 7.6%	96 15.9%
***Proteus* spp**	2 .3%	7 1.2%	3 .5%	12 2.0%
***pseudomonas* spp**	3 .5%	12 2.0%	24 4.0%	39 6.5%
Staph aureus	8 1.3%	52 8.6%	11 1.8%	71 11.8%
Streptococus pneumoniae	0 0.0%	39 6.5%	31 5.1%	70 11.6%
streptococcus pyogen	0 0.0%	13 2.2%	16 2.6%	29 4.8%
Total	33 5.5%	295 48.8%	276 45.7%	604 100.0%

Note: I-Intermediate; R-Resistance; S-Susceptibility

Table 8. Shows the resistance and sensitivity rates of Imipenem isolates (n=107)

Bacteria	Imipenem		Total
	R	S	
***Ctirobacter* spp**	0 0.0%	1 0.9%	1 0.9%
***E. coli* spp**	6 5.6%	37 34.6%	43 40.2%
***Enterobacter* spp**	2 1.9%	4 3.7%	6 5.6%
Enterococcus faecalis	2 1.9%	3 2.8%	5 4.7%
***Klebseilla* spp**	2 1.9%	10 9.3%	12 11.2%
***Pseudomonas* spp**	0 0.0%	5 4.7%	5 4.7%
Staph aureus	0 0.0%	17 15.9%	17 15.9%
Streptococcus pyogen	1 .9%	2 1.9%	3 2.8%
Streptococcus pneumoniae	2 1.9%	12 11.2%	14 13.1%
Streptococcus agalactia	0 0.0%	1 .9%	1 .9%
Total	15 14.0%	92 86.0%	107 100.0%

Table 9. Resistance and sensitivity rates of Augmentin isolates (n=107)

Bacteria	Augmentin			Total
	I	R	S	
***Ctirobacter* spp**	0 0.0%	0 0.0%	1 0.9%	1 0.9%
***E. coli* spp**	0 0.0%	23 21.5%	20 18.7%	43 40.2%
***Enterobacter* spp**	0 0.0%	1 0.9%	5 4.7%	6 5.6%
Enterococcus faecalis	0 0.0%	1 0.9%	4 3.7%	5 4.7%
***Klebseilla* spp**	1 0.9%	7 6.5%	4 3.7%	12 11.2%
***Pseudomonas* spp**	0 0.0%	5 4.7%	0 0.0%	5 4.7%
Staph aureus	0 0.0%	4 3.7%	13 12.1%	17 15.9%
Streptococcus pyogen	0 0.0%	0 0.0%	3 2.8%	3 2.8%
Streptococcus pneumoniae	0 0.0%	3 2.8%	11 10.3%	14 13.1%
Streptococcus agalactia	0 0.0%	1 0.9%	0 0.0%	1 .9%
Total	1 0.9%	45 42.1%	61 57.0%	107 100.0%

3.10 Ceftriaxone Resistance Profiles of Clinical Isolates (n=604)

All of the isolates were tested for resistance to third-generation cephalosporins (Ceftriaxone). 29 (8.48%) of 295 bacterial isolates were resistant to Ceftriaxone. However, 276 (45.7%) and 33 (5.5%), respectively, of the isolates remain susceptible and intermediate to Ceftriaxone (Table 10).

3.11 MICs of Imipenem for the Various Bacterial Isolates Tested (n=107)

The results of susceptibility testing against isolates are shown in Table 5. The 107 gram-positive and gram-negative bacteria tested 92 (86%) were susceptible to Augmentin, whereas only 15 (14%) were resistant to augmenting. On the other hand, very low resistance levels were observed against Imipenem (Table 11).

3.12 MICs of Augmentin for the Various Bacterial Isolates Tested (n=107)

The isolate of various bacteria was sensitive 232 (52.8%) to Augmentin and resistant 206 (46.9%) (Table 12).

4. DISCUSSION

Antibiotic resistance is a major public health concern that affects everyone. Several bacteria have developed resistance to a wide range of antibiotics in recent years as a result of antibiotic abuse and misuse. (WHO, 2000) In this study, we considered and measured the resistance of certain gram negative and gram positive bacteria to Augmentin, Imipenem, and Ceftriaxone in a region of our country. From September to November 2020, Al- Saleem laboratory examined 711 bacterial isolates from both studies, with 357 (50.2%) female patients and 354 (49.7%) male patients. Urine (n=544), sperm (n=55), blood (n=9), swab (n=78), HIV (n=19), and cerebrospinal fluid (n=2) were among the samples collected.

The CLSI, 2015 was taken into account when developing the standards for understanding the results. The "intermediate" category in this study is intended to connect antibiotics and bacterial samples. Blood and tissue response levels could be lower than in susceptible samples [3].

Gram-negative bacteria are the most common cause of bacterial infections, but gram-positive pathogens can also be present. Previous

Table 10. Ceftriaxone resistance profiles of clinical isolates (n=604)

Ceftriaxone		
Susceptibility patterns	**Frequency**	**Percent**
Intermediate	33	5.5
Resistance	295	48.8
Sensitive	276	45.7
Total	604	100.0

Table 11. MICs of Imipenem for the various bacterial isolates tested (n=107)

Imipenem		
Susceptibility patterns	**Frequency**	**Percent**
Resistance	15	14.0
Sensitive	92	86.0
Total	107	100.0

Table 12. MICs of Augmentin for the various bacterial isolates tested (n=107)

Augmentin		
Susceptibility patterns	**Frequency**	**Percent**
Intermediate	1	.9
Resistance	45	42.1
Sensitive	61	57.0
Total	107	100.0

research in Northern Ethiopia, India, and the United States discovered a disparity in gram-positive bacteria prevalence [18,19,20].

The prevalent use of brood spectrum antibiotics has led to the occurrence of antibiotic resistant strains of bacterial group; including *E. coli*. spp. [21]. High degrees of resistance have been mostly detected in bacteria that source common health problems. In the present study large numbers of the isolated bacteria strains were resistant to ceftriaxone drugs which are in agreement with WHO [1] reports.

Antibiotic-resistant strains of bacteria, including *E. coli*, have resulted from the widespread use of broad-spectrum antibiotics [21].

The majority of these isolates were *Escherichia coli* spp, a gram-negative bacterium, and the majority of them came from urine. This finding is consistent with other research findings that reported that *Escherichia coli* spp had the highest isolates from urine specimens [22,23].

50% of *E. coli* spp isolates were resistant to Ceftriaxone. This could be due to the high level of adaptive change. Resistant organisms pass on their resistant genes to their offspring through replication or conjugation, in which plasmids carrying the resistant gene are exchanged between adjacent organisms [1,24].

However, this study shows that Augmentin's effectiveness against Gram-positive bacteria is increasing. This dose matches the previous comparable study [18,25]. *Streptococcus pneumoniae, Enterobacter* spp., and *Enterococcus faecalis* were also isolated.

According to disk diffusion, 15.9% of *Staph aureus* were susceptible to imipenem. Resistance to imipenem was found in 1.9% of Streptococcus pneumonia cases. *Pseudomonas* spp and *Staph aureus* were both completely susceptible to imipenem. The susceptibility of Pseudomonas to imipenem was found to be higher in 91.7% to 86% of reports from other countries [26,27]

In 5 (4.7%) cases, all Pseudomonas strains were resistant to Augmentin. This finding is consistent with a previous study in Libya, which discovered Pseudomonas resistance to Augmentin via disk diffusion [28].

This uropathogen is the most prolific producer of extended spectrum beta-lactamase (ESBL), severely limiting therapeutic options for urinary tract infections Karlowsky et al., [29].

As a result, isolates of these strains have relatively high resistance development abilities. Wong et al., [30] Furthermore, the majority of *Escherichia coli* spp isolated from the entire specimen was resistant to the action of Ceftriaxone in the current study. One cause of resistance to beta-lactam antibiotics such as Ceftriaxone is the production of betalactamase enzymes by bacteria such as Gram negative bacteria *E. coli* spp, which produce the enzyme beta-lactamase AmpC. This enzyme can hydrolyze the ceftriaxone antibiotic's betalactam ring, rendering it ineffective [31].

Since 2004, the percentage of *E. coli* spp infections that are resistant to Ceftriaxone has increased significantly [32]. Other research findings revealed that the most resistant bacteria were *Escherichia coli* spp. [33,34]. Other studies found that *Klebseilla* spp had the highest resistance to Ceftriaxone [35].

In this study, the majority of *Streptococcus pneumoniae* were more resistant to Ceftriaxone. However, it is consistent with other studies conducted in various areas that reported the strains' resistance to Ceftriaxone. *Staphylococcus aureus* strains were more resistant to Ceftriaxone, which contradicts a previous study in which the majority of the strains were susceptible. Fantasy et al., 2018 similarly, an *in vitro* antimicrobial study conducted in Karachi, Pakistan, revealed that the majority of the isolated *Staph aureus* strains were resistant [36].

Ceftriaxone resistance was found in *Proteus* spp isolates tested. In Senegal, an *in vitro* antimicrobial study revealed that the majority of the isolated Enterobacteriaceae strains were resistant to Ceftriaxone Breurec et al., [37]. Infection from sterile body fluids is one of the most common diseases in developing countries [38,23].

The percentage of positive cultures in this study of (CSF, blood) samples received in the microbiology laboratory was 2.8%, which is lower than the 14.78% found in an Indian study [19]. Augmentin's inactivity against *Escherichia coli*, *Klebsiella* spp., and Pseudomonas spp. increased significantly. Previous research has shown that clavulanic acid does not inhibit the majority of *E. coli* [39]. Augmentin has been

shown *in vitro* to have increased activity against Enterobacteriaceae, staphylococci, and enterococci in the United States and Europe [13,40,41].

5. CONCLUSION

Antibiotic resistance levels in bacteria varied greatly. In this study, the activity of Augmentin against gram negative bacteria isolated from clinical specimens was found to be lower. Simultaneously, Imipenem is much more effective against isolates than Augmentin. Imipenem appears to be a more effective antibiotic in the treatment of these bacteria than Augmentin because they account for the vast majority of organisms implicated in clinical disease. Ceftriaxone is rapidly becoming a first-line antibiotic for both gram negative and gram positive bacteria. Appropriate monitoring of prevalent pathogenic organisms and their sensitivities will assist clinicians in making appropriate antibiotic therapy choices to prevent antimicrobial resistance from spreading.

6. RECOMMENDATION

According to the findings, Ceftriaxone is the best drug for treating patients. Antimicrobial stewardship programs are critical for screening and controlling antimicrobial intake, which could help to halt the antimicrobial resistance disaster.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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