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Antibiotic Susceptibility Test of *Escherichia Coli* and *Staphylococcus Aureus*

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Abstract— *Escherichia coli* and *Staphylococcus aureus* the most frequently and common bacteria cause serious disease in human. Health facilities will be able to restrict the inappropriate use of antibiotics and take proactive measures to stop the spread of drug-resistant bacteria by identifying their antimicrobial patterns. In order to better understand the current state of antimicrobial resistance and to improve infection treatment by avoiding the use of unnecessary antibiotics that could accelerate the emergence of bacterial resistance, the aim of this research was to ascertain the antibiotic susceptibility of isolates of S. aureus and E. coli from a variety of clinical samples. A total of 100 (*S. aureus* and *E. coli*) isolates from different form samples were collected from Al-Hussain hospital, Al-Musayyib General Hospital, Al-Kafeel Hospital, Obstetrics Hospital, Alnaqaa laboratory, Aljawadin laboratory and Al-Rasul laboratory. The Kirby-Bauer disk diffusion method was used to test all isolates for antibiotic susceptibility and identify their profiles of antibiotic resistance. The results showed that Urine samples were the higher collected from females while nasal swabs were higher from males. Other important finding is presence of hetero-resistance phenomena in both bacteria. *E. coli* was highly resistant to Amoxicillin-Clavalanic acid (94%), Trimethoprim-Sulfamethoxazole (64%), Nalidixic acid (60%), Trimethoprim (58%), and moderate resistance to Ciprofloxacin (48). Whereas, the highest sensitivity rates were seen with Meropenem antibiotic (94%), Tobramycin (54%), Levofloxacin (52%). While S. aureus show highly resistant to Cefoxitin (94%), Erythromycin (72%), and moderate resistance to Sulfamethoxazole (36%) and show sensitivity to Rifampin (88%), Clindamycin (72%), Levofloxacin (66%), Trimethoprim (60%), and Gentamicin (64%). The current study represents that *E. coli* was highly resistant to Amoxicillin-Clavalanic acid while showed high sensitivity rates with Meropenem. On the other hand, *S. aureus* show highly resistant to Cefoxitin while showed high sensitivity rates with Rifampin and both bacteria showed hetero resistance phenomena.

***Index Terms*—Antibiotic resistant, *E. coli*, *S. aureus*, (HR) hetero-resistance, (MRSA) methicillin- resistant staphylococcus aureus.**

1. Introduction

Bacteria are the microorganisms (such as *E. coli* and *S. aureus*) that most frequently cause infectious diseases in human [1]. Sometimes bacteria develop very strong infections that the body's immune system cannot fight and resolve. For this reason, scientists develop the discovery of antibiotics (1928 penicillin, the first true antibiotic, was discovered by Alexander Fleming [2]) to enhance the immune system and kill the bacteria. In which antibiotic has a direct influence on slow or inhibits grow of microbes [3]. However, and as a result of bacteria's ability to fight and survive in an inappropriate condition, these bacteria become able to withstand when exposed to lethal concentrations of antibiotics and now many bacteria are resistant to multiple antimicrobial agents [1]. Bacteria can resist the effects of antibiotics in two primary ways: firstly, Modify or bypass the target that the antibiotic acts on. And, secondly Disrupt the antibiotic's specific target by releasing particular enzymes [4].

The point was initially made in 1944 on the fact that not all strains of *S. aureus* were killed when cultures were treated with high quantities of penicillin, and that some strains were able to survive [5]. After that in 1950, *E. coli* resistance it first discovered and it was against sulfonamides drug [6]. *E. coli* is a part of the normal flora, it is additionally one of the most significant pathogens that affect both humans and animals. It can cause intestinal and extra-intestinal conditions like urinary tract infections, gastroenteritis, meningitis, peritonitis, and septicemia. Because of this, its resistance to antibiotics makes it extremely dangerous [7]. Furthermore, β-lactamase-producing E. Coli strains have multiple resistance to β-lactam antibiotics, including penicillins, cephalosporins, cephamycins, and carbapenems (ertapenem) [8]. In 1960, MRSA was identified by British scientists, and the United States saw its first case of this "superbug" in 1968. Over time, MRSA strains evolved resistance to various penicillin-related drugs. *Methicillin-resistant Staphylococcus aureus* (MRSA) can cause very serious infection such as pneumonia, sepsis, urinary tract infection, and skin infection[5]. Additionally, this strain is very expanded and leads to increase in the mortality and morbidity rate [2]. By comparison, gram-positive (*S. aureus*) and gram-negative (*E. coli*) different in their susceptibility and resistance to antibiotics. These differences attributed to it is cell wall structure [42]. (See figure1)

Although sensitivity differences among negative bacteria and gram positive, it's generally use special mechanism includes; bacteria produce enzyme destroy the antimicrobial agent, impermeability of bacterial cell to antibiotic, mutations, bacterial efflux pump that expels antibiotic, alternation in special metabolic pathway [9]. Patients had fewer possibilities for treatment as well as higher rates of morbidity and death consequently with ongoing increases in antibiotic resistance.

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The expense of treating these illnesses has risen dramatically as a consequence [7]. According to the Centers for Disease Control (CDC), a realistic estimate is that more than 2 million Americans get ill with antibiotic-resistant infections every year, accounting for more than 23,000 fatalities [10]. A study was carried out to evaluate the sensitivity of E. coli and S. aureus that were isolated from various clinical samples. This was done in order to gain an accurate picture of the current state of antimicrobial resistance and to improve infection treatment by avoiding the use of unnecessary antibiotics that might accelerate the development of bacterial resistance.

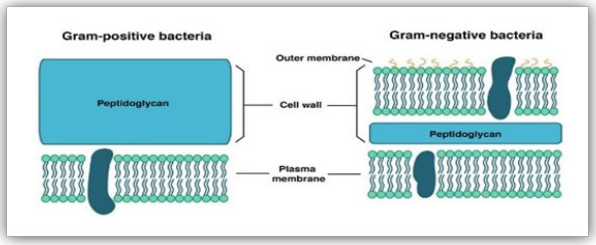


Fig. 1. Cell wall structure of gram positive and gram negative [gram negative: with outer phospholipids layer and thin peptidoglycan, gram positive: outer thick peptidoglycan]

2. Materials and Method

A. Sample Collection

During December 2020 to February 2021. A total of 100 isolates of *S. aureus* and *E. coli* (in which 50 for each bacteria) from different samples (urine, blood, pus, sputum and swab …etc.) were obtained randomly from Al-Hussain hospital, Al-Musayyib General Hospital, Al-Kafeel Hospital, Obstetrics Hospital, Alnaqaa laboratory, Aljawadin laboratory and Al-Rasul laboratory. After the bacteria were sent to the microbiology lab at the Public Health Center of the Karbala governorate and the Department of Clinical Laboratories, College of Applied Medical Sciences, Karbala University, the bacterial isolates were re-identified

B. Procedure Antibiotic Susceptibility Tests

Table 1
Antibiotic discs

	Antibiotic discs	Abbreviation	Concentration
1.	Nalidixic Acid	NA	30mg
2.	Levofloxacin	LEV	5*Mg*
3.	Meropenem	MRP	10*Mg*
4.	Amoxicillin Clavalanic Acid	AMC	20/10mcg
5.	Tobramycin	TOB	30*Mg*
6.	Ciprofloxacin	CIP	5*Mg*
7.	Trimethoprim	TMP	5mcg
8.	Trimethorpim Sulphamethxazal	SXT	23.75*Mg*
9.	Rifampin	RA	5mg
10.	Clindamycin	DA	10mcg
11.	Gentamicin	CN	10 mg
12.	Erythromycin	E	5 mg
13.	Cefoxitin	FOX	30 mcg

To evaluate the patterns of antibiotic resistance in each isolate, antibiotic susceptibility tests were conducted using the Kirby-Bauer disk diffusion method. Antibiotic sensitivity tests were performed using freshly produced overnight cultures. On Mueller Hinton Agar (Himedia, India), an aliquot (100µL) of each isolate suspension, equal to a 0.5% McFarland Standard, was spread plated. Different antibiotic discs used in the current study and their concentrations are shown in table 1. Measurements of inhibition zone diameters were made, and the results were interpreted using values from the National Committee on Clinical Laboratory Standards (2020). The normal microbiological methods were followed in order to identify the bacteria [12].

3. Results

A total of 100 bacterial clinical isolates, the percentage of female to male were 46%, 54% respectively. From the study, it showed that Urine samples were the higher collected 54 % (female 36% while male 18%), followed by nasal swab 14% (female 2% while male 12%) as shown in figure 2. In the present study, antibiotics susceptibility test for the clinical isolates was applied. The results show that 94% of *E. Coli* strains are exceedingly resistant to amoxicillin-clavulanic acid, Trimethoprim-Sulfamethoxazole (64%), Nalidixic acid (60%), Trimethoprim (58%), and moderate resistance to Ciprofloxacin (48%), Tobramycin (46%), Levofloxacin (30%). Whereas, the highest sensitivity rates were seen with Meropenem antibiotic (94%) as shown in table 2. On the other hand, *S. aureus* show highly resistant to Cefoxitin (94%), Erythromycin (72%) and moderate resistance to Trimethoprim (40%), Sulfamethoxazole (36%) and show sensitivity to Rifampin (88%), Clindamycin (72%), Levofloxacin (66%), Gentamicin (64%) as shown in table 3.

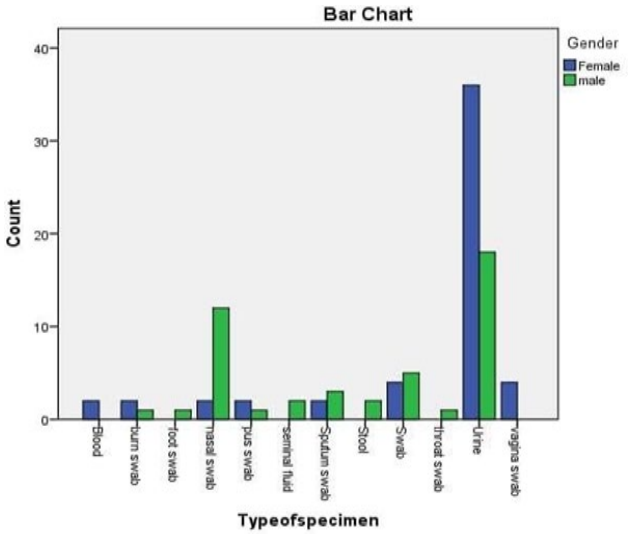


Fig. 2. Frequencies of type of specimens with gender

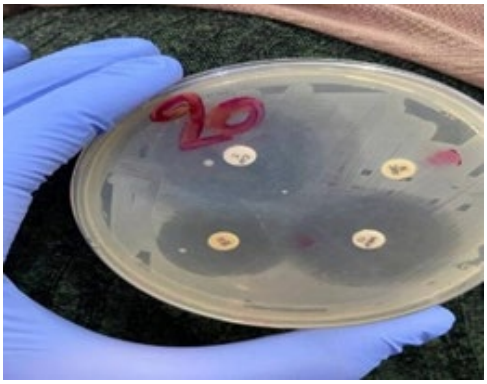
Additionally, six isolates from *E. coli* and seven from *S. aureus* showed the presence of a hetero-resistance phenomenon (Figure 3).

Table 2
Antibiotics susceptibility results for *E. coli*

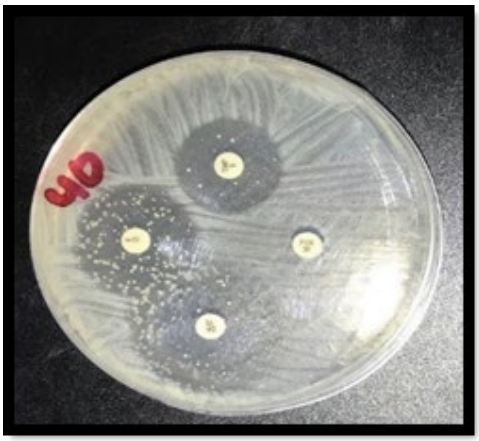
Antibiotics	Sensitive	Intermediate	Resistant	Total
Nalidixic Acid	17 (34.00%)	3 (5.60%)	30 (60.00%)	50 (100.00%)
Levofloxacin	26(52.00%)	9 (18.00)	15 (30.00%)	50(100.00%)
Meropenem	47(94.00%)	1 (2.00%)	2 (4.00%)	50 (100.00%)
Amoxicillin Clavalanic Acid	2 (4.00%)	1 (2.00%)	47 (94.00%)	50 (100.00%)
Tobramycin	27(54.00%)	(0.00%)	23 (46.00%)	50 (100.00%)
Ciprofloxacin	18 (36.00%)	8(16.00%)	24(48.00%)	50 (100.00%)
Trimethoprim	18 (36.00%)	3(6.00%)	29(58.00%)	50(100.00%)
Trimethorpim Sulphamethxazal	18(36.00%)	(0.00%)	32(64.00%)	50(100.00%)

Table 3
Antibiotics susceptibility results for *S. aureus*

Antibiotics	Sensitive	Intermediate	Resistant	Total
Trimethoprim	30 (60.00%)	(0.00%)	20 (40.00%)	50 (100.00%)
Levofloxacin	33 (66.00%)	8 (16.00%)	9 (18.00%)	50 (100.00%)
Clindamycin	36 (72.00%)	(0.00%)	14 (28.00%)	50 (100.00%)
Gentamicin	32 (64.00%)	7 (14.00%)	11 (22.00%)	50 (100.00%)
Erythromycin	9 (18.00%)	10 (10.00%)	36 (72.00%)	50 (100.00%)
Ciprofloxacin	29 (58.00%)	7 (14.00%)	14 (28.00%)	50 (100.00%)
Rifampin	44 (88%)	2 (4.00%)	4 (8.00%)	50 (100.00%)
Cefoxitin	3 (6.00%)	(0.00%)	47 (94.00%)	50 (100.00%)
Sulfamethoxazole	30 (60.00%)	2 (4.00%)	18 (36.00%)	50 (100.00%)



(a)



(b)

Fig. 3. a) Shows Hetero-resistance phenomenon of *E. coli* isolate for ciprofloxacin and Nalidixic acid, b) shows Hetero-resistance phenomenon of *S. aureus* isolate for Trimethoprim, Clindamycin and Erythromycin

4. Discussion

In this study, 100 isolates of *E. coli* and *S. aureus* examined for different types of antibiotics. Infections produced by antibiotic-resistant bacteria are regarded a hazard worldwide because of the difficulty in treating them and the increase in the expense thereof. [1]. This study showed that the active antibiotics against *S. aureus* was Rifampin followed by clindamycin and levofloxacin, this is agreed with Egypt-ion study [13] and in Kabul, Afghanistan [14]. Additionally, *S. aureus* was sensitive to Trimethoprim, Ciprofloxacin and Gentamicin [15]-[17]. *E. coli* was very sensitive to Meropenem [18], Levofloxacin [19] and Tobramycin this is agreed with Iraqi study (2018) [20]. Although that, over and improper use of antimicrobial drugs, these antibiotics can be bought without prescription, especially in developing countries [21] leads to demonstrate of bacterial resistance [9]. In this study, E. coli and *S. aureus* showed resistance against many antibiotics (Table 2, 3). *S. aureus* was very resistant against Cefoxitin and this act as a marker for presence of methicillin-resistant strain of *Staphylococcus aureus (MRSA)* [22]. (MRSA) is a significant human pathogen that causes infections in hospitals, animals, and communities that have a high death rate and increased or longer hospital stay [23]. Liang *et al*. reported that One of the main mechanisms of resistance to β-Lactam was the expression of β-Lactamase enzyme [24]; also, other Study showed 61% of *S. aureus* isolates was produce high level of enzyme [13]. Other mechanisms of *Staphylococcus* resistance were reported such as plasmid profile and efflux mechanism [13]. Recent study showed that, urinary tract infection was more common in female than male (Figure 2), and this result agreed with other study, that indicated to the reason of shortened urethra in women [18]. Our study also found that nasal infection was more in male sex than female. Male volunteers had higher nasal carriage of S. aureus than female volunteers, which may have been attributed in part to the female volunteers' greater propensity to regularly clean their nasal cavities, as shown by the results of the standardized questionnaire. As a result, it was crucial to regularly clean the nasal cavity in people who were exposed to increased rates of S. aureus carriage [25].

Moreover, the results demonstrated that six isolates of *E. coli* showed the presence of Herero- resistance phenomenon to Trimethoprim sulphamethxazal, Tobramycin, Levofloxacin, Ciprofloxacin, Nalidixic acid and seven isolates of *S. aureus*

showed the presence of same phenomenon to Erythromycin, Clindamycin, Trimethoprim, and Cefoxitin. This study concurred with the majority of publications that suggested bactericidal antibiotics, such as aminoglycosides, β-lactams, glycopeptides, antimicrobial peptides, fluoroquinolones, and the nitroimidazole antibiotic metronidazole, were responsible for the occurrences of heteroresistance [26]. Herero-resistance can be described as resistance to certain antibiotics expressed by a subgroup of a microbiological population that is normally thought to be sensitive to these antibiotics [21]. These resistant organisms are found in around one sub-clone out of every 105–106 colonies, which is equivalent to the typical rate of mutation [27]. First observed in 1947 with Haemophilus influenza, this phenomenon was later observed with gram-positive bacteria [28], *Staphylococcus aureus*, *coagulase-negative staphylococci* [29], *Enterococcus faecium* [33], *Streptococcus pneumonia* [32], *Mycobacterium tuberculosis* [31], *Acinetobacter baumannii* [30] and *Cryptococcus neoformans* [34]. Furthermore, *S. aureus* is the species for which the occurrence has been documented more frequently and thoroughly studied. Heteroresistance to Methicillinand Oxacillinis dependent on the mecA gene, which produce a penicillin-binding protein with reduced affinity, resulting in strain-specific variable resistance to beta-lactam antibiotics ranging from borderline to high [27]. It demonstrated that chromosomal alterations unrelated to mecA may also result in a tiny percentage of highly methicillin-resistant subclones in addition to this resistance [35]. Several investigations have found that the mechanisms of resistance in gram-negative subpopulations with sustained heteroresistance involve antibiotic efflux and/or influx [36]. However, heteroresistance could be a tool for natural evolution to drug resistance, because it allows bacteria to explore the possibility of growth in the presence of antibiotics [37]. In the absence of competition from the inhibited susceptible cells, the resistant subpopulations may multiply easily, creating a new resistant population [38]. However, because the formation of resistance can occasionally be accompanied by a loss of virulence, the establishment of resistant strains in vitro may not always have therapeutic ramifications [39]. Subsequently, Overuse of antibiotics may be the excessive use of antibiotics could be the reason for development of these isolates throughout the population, which causes the bacteria to become resistant to the antibiotic and potentially lead to treatment failure [40], [41].

5. Conclusion

The current study represents that *E. coli* was highly resistant to Amoxicillin-Clavalanic acid while showed high sensitivity rates with Meropenem. On the other hand, *S. aureus* show highly resistant to Cefoxitin while showed high sensitivity rates with Rifampin and both bacteria showed heteroresistance phenomena.

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