Qurina Scientific Journal – QSJ ·

ISSN: 2959- 7463

Antibiogram susceptibility and multidrug Resistance of *Staphylococcus aureus* Isolated from Al-Jalaa Hospital for Surgery and Accidents - Benghazi - Libya

[1]Dareen El shareef Jadullah, [2]Wafa Mustafa F Bozarida
[1,2] Faculty of pharmacy, Qurina International University, Benghazi– Libya.

[1] Email: dareenelshareef@qiu.edu.ly.
[2] Email: wafabozarida@qiu.edu.ly.

Abstract

Background: *Staphylococcus aureus* is a major pathogen of increasing importance due to increasing in antibiotic resistance and a major cause of nosocomial infection. **Aim:** This study was aimed to identify the prevalence and antimicrobial susceptibility pattern of *Staphylococcus aureus* bacteria isolated from patients in AL-Jalaa hospital for accidents & surgery - Benghazi - Libya. **Methods:** A total of 108 samples were randomly selected from different wards and outpatient department. Samples collected was taken from both gender with different age. Specimen isolates was obtained from (urine, swap, tip, Endotracheal tube and blood). The bacterial identification and sensitivity was carried out using BD Phoenix system (BD Diagnostics, Sparks, MD, USA). The descriptive cross-sectional study was carried out in the Clinical Microbiology laboratory from January 2023 to April 2023. By inoculation in culture media and aerobic incubation at 37°C were done in accordance with the standard micro-biological procedure. Significant bacterial growth on culture of the specimens was processed for identification on the basis of colony morphology, Gram staining, catalase test and coagulase test. Antimicrobial susceptibility test (AST) was done by the Kirby-Bauer disk diffusion method. IBM SPSS software version 28 was used for data analysis. Chi square test used to determine the difference between each variable in the study $P < 0.05$ statistically significant. **Results:** our results shows that staph cocci was resistant to majority of antibiotics , as found resistant to in majority of patients penicillin (104), followed by Ciprofloxacin in (103), then Cefeimpe in (102), Nalidixic acid and Ceftriaxone in (101), Teicarcillin-Clavulanic acid in (100), Nitrofurantoin in (99) Imipenem and Cephalothin in (98), Piperacillin in (96), while a moderate resistance was found in amoxicillin in (56) against this on the other hand found only one antibiotic (Clindamycin) highly sensitive to staph cocci with lower resistance rate. **Conclusion:** Staphylococci found resistant to the majority of antibiotics used in anti-sensitivity test as it's a play a major role in infection in hospitals and consider a big health issue. Also the use of broad spectrum antibiotic irrationally increases without proper plan, lack of surveillance, suitable antibiotics detection through the period of management and infection control, lead to failure of management process. A further evaluation and study required to study the resistance of staphylococci toward antibiotics specially Methicillin Resistant *Staph aureus*.

Keywords- Antibiogram, *Staphylococcus aureus*, Hospitalized, patients.

I. INTRODUCTION

A. Staphylococci :

Staphylococci are typical Gram-positive bacteria forming irregular clusters of cocci. Staphylococci are widespread in nature, although they are mainly found on the skin, skin glands and mucous membranes of mammals and birds, but can cause infection under certain circumstances. *S. aureus* is more pathogenic than the other common members of the genus, *S. epidermidis* and *S. saprophyticus*. *S. epidermidis* has been known to cause various hospital-acquired infections (such as prosthetic or indwelling devices), whereas *S. saprophyticus* is mainly associated with urinary tract infections in young females who are sexually active. Disease processes with *S. aureus* are numerous.[1] The staphylococci are non-motile, non-spore forming facultative anaerobes that grow by aerobic respiration or by fermentation. Most species have a relative complex nutritional requirement, however, in general they require an organic source of nitrogen, supplied by 5 to 12 essential amino acids, e.g. arginine, valine, and B vitamins, including thiamine and nicotinamide. [2] [3] Members of this genus are catalase-positive and oxidase-negative, distinguishing them from the genus streptococci, which are catalase-negative, and have a different cell wall composition to staphylococci.[3] Staphylococci are tolerant to high concentrations of salt [3] and show resistance to heat [4].
Pathogenic staphylococci are commonly identified by their ability to produce coagulase, and thus clot blood.[5] This

ISSN: 2959- 7463

distinguishes the coagulase positive strains, *S. aureus* (a human pathogen), and *S. intermedius* and *S. hyicus* (two animal pathogens), from the other staphylococcal species such as *S. epidermidis*, that are coagulase-negative (CoNS).

B. Identification of Staphylococci in the Clinical laboratory:

Structure: Staphylococci are Gram-positive cocci about 0.5 – 1.0 µm in diameter. They grow in clusters, pairs and occasionally in short chains. The clusters arise because staphylococci divide in two planes. The configuration of the cocci helps to distinguish micrococci and staphylococci from streptococci, which usually grow in chains.

Catalase Test : The catalase test is important in distinguishing streptococci (catalase-negative) & staphylococci which are catalase positive. The test is performed by flooding an agar slant or broth culture with several drops of 3% hydrogen peroxide. Catalase-positive cultures bubble at once. The test should not be done on blood agar because blood itself will produce bubbles. [6]

Isolation and Identification: The organism is isolated by streaking material from the clinical specimen (or from a blood culture) onto solid media such as blood agar, tryptic soy agar or heart infusion agar. Specimens likely to be contaminated with other microorganisms can be plated on mannitol salt agar containing 7.5% sodium chloride, which allows the halo-tolerant staphylococci to grow. Ideally a Gram stain of the colony should be performed and tests made for catalase and coagulase production, allowing the coagulase-positive *S aureus* to be identified quickly. Another very useful test for *S aureus* is the production of thermostable deoxyribonuclease. *S aureus* can be confirmed by testing colonies for agglutination with latex particles coated with immunoglobulin G and fibrinogen which bind protein A and the clumping factor, respectively, on the bacterial cell surface. These are available from commercial suppliers (e.g., Staphaurex). The most recent latex test (Pastaurex) incorporates monoclonal antibodies to serotype 5 and 8 capsular polysaccharides in order to reduce the number of false negatives. (Some recent clinical isolates of *S aureus* lack production of coagulase and/or clumping factor, which can make identification difficult). [7]

B. *Staphylococcus aureus :*

Staphylococcus aureus is a major pathogen of increasing importance due to the rise in antibiotic resistance.[8] It is distinct from the CoNS (e.g. *S. epidermidis*), and more virulent despite their phylogenic similarities. [9][10] The species named aureus, refers to the fact that colonies (often) have a golden colour when grown on solid media, whilst CoNS form pale, translucent, white colonies. [11]

To date the *S. aureus* genome databases have been completed for 7 strains, 8325, COL, MRSA, MSSA, N315, Mu50, and MW2 (Web ref. 1-6). The average size of the S. aureus genome is 2.8Mb. [12]

Epidemiology of Staphylococcus aureus Infections:

Because *S aureus* is a major cause of nosocomial and community-acquired infections, the traditional method for typing *S aureus* is phage-typing. This method is based on a phenotypic marker with poor reproducibility. Also, it does not type many isolates (20% in a recent survey at the Center for Disease Control and Prevention), and it requires maintenance of a large number of phage stocks and propagating strains and consequently can be performed only by specialist reference laboratories. Many molecular typing methods have been applied to the epidemiological analysis of *S aureus*, in particular, of methicillin-resistant strains (MRSA). Plasmid analysis has been used extensively with success, but suffers the disadvantage that plasmids can easily be lost and acquired and are thus inherently unreliable. Methods designed to recognize restriction fragment length polymorphisms (RFLP) using a variety of gene probes, including rRNA genes (ribotyping), have had limited success in the epidemiology of MRSA. In this technique the choice of restriction enzyme used to cleave the genomic DNA, as well as the probes, is crucial. Random primer PCR offers potential for discriminating between strains but a suitable primer has yet to be identified for *S aureus*.

Clinical Manifestations of S aureus: *S aureus* is notorious for causing boils, furuncles, styes, impetigo and other superficial skin infections in humans. It may also cause more serious infections, particularly in persons debilitated by chronic illness, traumatic injury, burns or immunosuppression. These infections include pneumonia, deep abscesses, osteomyelitis, endocarditis, phlebitis, mastitis and meningitis, and are often associated with hospitalized patients rather than healthy individuals in the community. *S aureus* and *S epidermidis* are common causes of infections associated with indwelling devices such as joint prostheses, cardiovascular devices and artificial heart valves.

S. aureus associated infections: This bacterium is found naturally on the skin and in the nasopharynx of the human body. It can cause local infections of the skin, nose, urethra, vagina and gastrointestinal tract, most of which are minor and not life-threatening [13]. Over 4% of patients admitted into one of 96 hospitals in England between 1997 and 1999 for surgery acquired a nosocomial infection, which is defined as an infection where there was no evidence the infection was present or incubating prior to hospitalization (Central Public Health Laboratory, UK, 2000). The environment within a hospital also supports the acquisition of resistant *S. aureus*

strains. The same study found 81% of the infections were caused by *S. aureus*, and 61% of these were methicillin resistant. The skin and mucous membrane are excellent barriers against local tissue invasion by *S. aureus*. However, if either of these is breached due to trauma or surgery, *S. aureus* can enter the underlying tissue, creating its characteristic local abscess lesion [14] and if it reaches the lymphatic channels or blood can cause septicaemia.[15] The basic skin lesion caused by an *S. aureus* infection is a pyogenic abscess. However, *S. aureus* can also produce a range of extracellular toxins, such as enterotoxin A-E, toxic shock syndrome toxin- 1 (TSST-1) and exfoliative toxins A and B.[10] Ingestion of enterotoxin produced by *S. aureus* in contaminated food can cause food poisoning. [11] TSST-1 is the toxin responsible for toxic shock syndrome (TSS) and is only caused by strains carrying the TSST-1 gene.[9] TSS infections are commonly associated with menstruating women, particularly those using tampons. The exfoliative toxins are associated with staphylococcal scalded skin syndrome (SSSS). SSS consists of three entities, toxic epidermal necrolysis, scarlatiniform erythema, and bullous impetigo [14] all of which damage the epidermal layer of the skin & infection rates following orthopaedic surgery are 1-2% for total hip arthroplasty (Sanderson, 1991); 4% for total knee arthroplasty [15]; 2-25% 42 L.G. Harris *et al.; S. aureus* adhesions for open fractures [16] and ~1.5% for closed fractures [17] *S. aureus* has been found to be a common cause of metal-biomaterial, bone-joint and soft-tissue infections. [18][19]

Treatment of Staph aureus:

The excessive use of antibiotics has led to the emergence of multiple drug resistant *S. aureus* strains. Penicillin was introduced for treating *S. aureus* infections in the 1940s, and effectively decreased morbidity and mortality. However, by the late 1940s, resistance due to the presence of penicillinase emerged. The staphylococci are very capable of evolving resistance to the commonly used antimicrobial agents, such as, erythromycin ampicillin, and tetracycline. In most cases, resistance to antibiotics is coded for by genes carried on plasmids, accounting for the rapid spread of resistant bacteria (Soon after the introduction of methicillin, Jevons described the emergence of methicillin resistant *S. aureus* Methicillin resistance staph cocci aureus which have since spread worldwide as nosocomial pathogens. [20] Vancomycin, a glycopeptide has been the most reliable antibiotic against Methicillin resistance staph cocci infections; however, in 1996 the first Methicillin resistance staph cocci to acquire vancomycin intermediate resistance was isolated in Japan[21].

C. *Antibiotic resistance :*

Resistance to beta-lactams antibiotics:

Penicillin belongs to the beta-lactam group of antibiotics and has a beta-lactam ring in its structure, which binds to PBP on the cell wall of bacteria, inactivates it, and prevents bacterial cell wall synthesis. The resistance mechanism of *S. aureus* against beta-lactam agents occurs by two means: beta-lactam penicillinase and the mecA gene. The first mechanism requires the production of penicillinase enzyme [20],[21] or beta-lactamase enzymes. [22] which are located on plasmids and encoded by blaZ. This enzyme breaks down the beta-lactam ring in the beta-lactam antibiotic structure, thus inactivating the antibiotic. [23] The second defense mechanism requires the acquisition of the mecA gene, which encodes PBP2a protein, and assists in bacterial cell wall synthesis even in the presence of beta-lactam antibiotics [24] [21][25][22] MRSA carries the mecA gene, which confers resistance to most beta-lactam products.[26] The mecA gene is located on a mobile chromosomal DNA fragment, chromosomal cassette type SCCmecA, and is only present in MRSA strains.[24][20][21][27][28] Evolution of the second mechanism of MRSA resistance has two different theories. The single clone hypothesis suggests the vertical transfer of mecA gene elements into S. aureus on one occasion, followed by formation of the MRSA clone, and subsequent global distribution of the resistant genes. [28]

D. *Resistance to Glyco-peptides :*

Vancomycin, discovered by Edmund Kornfeld in 1953 [29] belongs to the glycopeptide antibiotic class and is considered the drug of choice to treat infections caused by MRSA. The first case of vancomycin resistance was documented in Japan in 1996. The strains were characterized by intermediate resistance to vancomycin; therefore, these strains were called vancomycin intermediate *S. aureus* (VISA).[29][21][30] Additional resistant strains were observed in many other countries. In 2002, the first case of vancomycin-resistant *S. aureus* (VRSA) was recorded in a clinical isolate in the USA. [31]

E. *Resistance to Tetracyclines :*

Tetracyclines are bacteriostatic [32] and broad-spectrum antibiotics. They inhibit protein synthesis by working precisely on 30s ribosomal subunits and blocking tRNA. Resistance to tetracycline is developed by two methods: protection of the ribosome, which is encoded by tetM and tetO genes, and the efflux pump system, which is encoded by tetK and tetL genes carried by plasmid. [33]

F. *Resistance to Fluoroquinolone :*

The fluoroquinolone antibiotic class inhibits DNA synthesis by attacking DNA gyrase enzymes, encoded by gyrA and gyrB genes, and topoisomerase IV, encoded by ParC and ParE genes. The mechanism of fluoroquinolone resistance arises

from mutations in the target gyrase or topoisomerase IV, or by changing antibiotic permeability into the bacterial cell. Additionally, resistance evolution to fluoroquinolone occurs due to the multidrug efflux pump system and is mediated by the norA gene. [32] [33]

G. *Resistance to Aminoglycosides :*

Aminoglycosides are used to treat different bacterial infections, including infections caused by *S. aureus*.[32][34] This antibiotic class interrupts protein synthesis and binds to 30S ribosomal subunits. [32][34] Resistance to aminoglycosides occurs via three pathways, including mutations in the ribosomal binding site to antibiotics, modifications to aminoglycoside-modifying enzymes (AMEs) that result in drug inactivation [32][34][35] and the efflux pump system .

H. *Resistance to ansamycins :*

The excessive use and misuse of antibiotics leads to resistance in *S. aureus* and the emergence of MRSA strains. As mentioned earlier, vancomycin is the target drug of choice to treat clinical conditions caused by MRSA, but incidences of VRSA have increased recently. Thus, rifampicin, a member of the ansamycin class of antibiotics, is used in combination with vancomycin to treat MRSA conditions. It is worth noting that rifampicin is the only working antibiotic in cases of multidrug-resistant tuberculosis. Thus, caution should be taken when using rifampicin for non-tuberculosis infections [36] [37] as a number of rifampicin resistant MRSA (RIF-R-MRSA) cases have been recorded. For example, a study conducted in China demonstrated that the incidence of RIF-R-MRSA was 15.5% in 2004, however, it reached 50.2% four years later. [37] Rifampicin interrupts protein synthesis by inhibiting transcription, which is achieved by blocking RNA polymerase. [32] [38] On the other hand, rifampicin resistance is mediated by a mutation in the rpoB gene, which encodes a beta distinct unit of RNA polymerase. [32]

I. *Resistance to clindamycin and fusidic acid :*

Clindamycin belongs to the lincosamide class of antibiotics. It disrupts protein synthesis in the bacterial cell by binding to the 50S ribosomal subunit. [38] Resistance to lincosamides occurs through methylation of its receptor binding site on the ribosome, consequently altering the target cell. Methylation is mediated by an enzyme called methylase and is encoded byerm genes. [32]

J. Aim of the study :

This study aimed was to identify the prevalence and antimicrobial susceptibility pattern of *Staphylococcus aureus* bacteria isolated from patients in AL-Jalaa hospital for accidents & surgery - Benghazi – Libya.

II. METHODS AND MATERIALS

A. *Ethical approval:*

This study was approved from Qurina International University – Faculty of pharmacy, and AL-jalaa hospital for accidents & surgery, consent was taken from patients before the study.

B. *Study design:*

This was experimental descriptive study was done in inpatients admitted to surgical wards and out patients of AL-jalaa hospital for accidents & surgery, from January 2023 to April 2023.

C. *Sample collections and isolation:*

1. A total of 108 samples were randomly selected from different departments (female surgical ward A, male surgical ward A, intensive care unit, burn shock room, and outpatient department at AL-jalaa hospital for accidents & surgery). Samples collected were taken from both genders (Male and Female) with different age. Specimen isolates was obtained from (urine, swap, tip of folly catheter, endotracheal tube and blood).

2. All the culture and sensitivity reports of Staph cocci from hospitalized patients and outpatient department were analyzed. The bacterial identification and sensitivity was carried out using BD Phoenix system (BD Diagnostics, Sparks, MD, USA) & the guidelines of Clinical and Laboratory Standard Institute were used in the lab.

3. By inoculation in culture media and aerobic incubation at 37°C were done in accordance with the standard microbiological procedure. Significant bacterial growth on culture of the specimens was processed for identification of Staph cocci on the basis of colony morphology, Gram staining, catalase test and coagulase test. Antimicrobial susceptibility test (AST) was done by the Kirby-Bauer disk diffusion method.

4.Antibiotics used for assess bacterial susceptibility included (Amoxicillin, Imipenem, Ticarcillin-Clavulanic Acid, Cefeimpe, Ertapenem, Cloroamphenicol, Ciprofloxacin, Tetracycline, Ceftriaxone, Nitrofuranntoin, Gentamicin, Vancomycin, Cephalothin, Nalidixic Acid, Penicillin,

ISSN: 2959- 7463

Cefoxitin, Clindamycin, Amoxicillin-Clavulanate, Piperacillin, Kanamycin).

D. Statistical analysis:

IBM SPSS software version 28 was used for data analysis. Data was comprised of gender, samples from patients, and wards of hospitals as frequencies and percentages. Chi square test was employed to determine the difference between each variable in the study.

III. RESULTS AND DISCUSSION

A total 108 isolated swabs were obtained from inpatients in surgical and out patients department in AL-Jalaa hospital for accidents & surgery, as found near half the samples obtained from outpatient department, while 23.1% from male surgical ward A, sharing the same percent 11.1 % intensive care unit and female surgical ward A, and last burn shocks room taking the less percent with 10.2%. As seen in table and figure (I).

Table (I): *The department frequency and percent* **:**

Department			
		Frequency	Percent
valid	Outpatient department (OPD)	48	44.4 %
	Burn shocks room (BSSR)	11	10.2 %
	Intensive care unit (ICU)	12	11.1 %
	Male surgical ward A (MSWA)	25	23.1 %
	Female surgical ward A (FSWA)	12	11.1 %
	Total	108	100 %

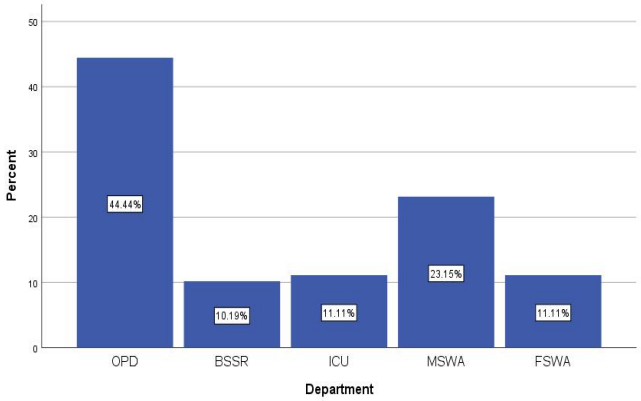

Figure (I): *The department percentage curve.*

As seen in table and figure (II), Which describe the gender of patients enrolled in the study as 53.7 % of them was male while female taking the rest percent with 46.3 %.

Table (II): *The sex frequency and percentage:*

Sex		Frequency	Percent
Valid	Male	58	53.7 %
	Female	50	46.3 %
	Total	108	100 %

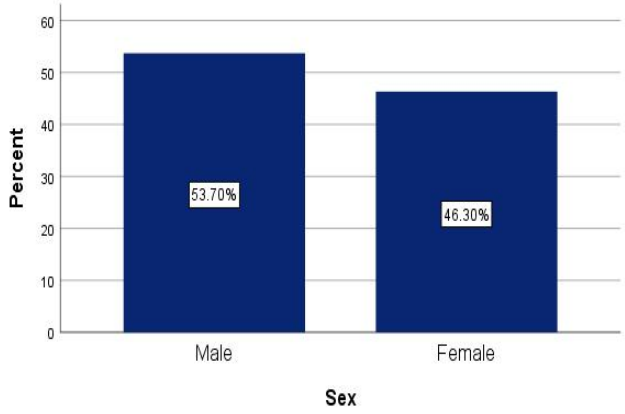

Figure (II): *The sex percentage curve .*

Table and figure (III) shows source of samples as most of the samples were swaps from site of the wound with 70.4%, second blood with 16.7%, third was urine with 10.2%, while Tip take only 1.9 %, and Endotracheal tube (CTT) is the less percent with 0.9%.

ISSN: 2959- 7463

Table (III): *The sample frequency and percentage:*

Sample			
		Frequency	Percent
Valid	Urine	11	10.2 %
	Swab	76	70.4 %
	Tip of folly catheter	2	1.9 %
	Endotracheal tube (CTT)	1	0.9 %
	Blood	18	16.7 %
	Total	108	100 %

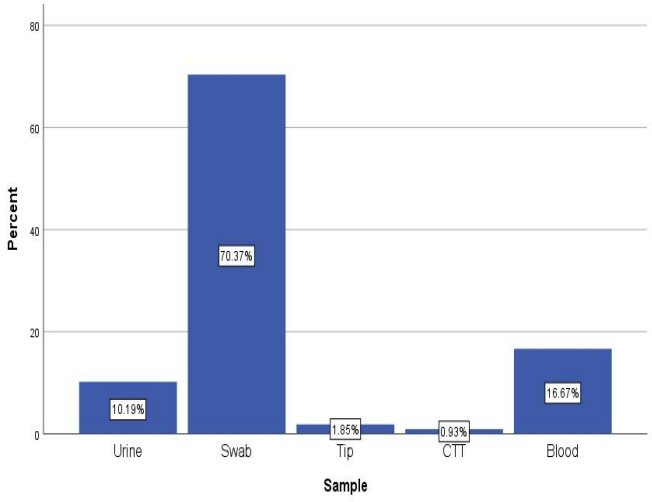

Figure (III): *The sample percentage curve.*

From the following table and figure (IV) we notice that staph cocci was resistant to majority of antibiotics, as found resistant to Penicillin (PA) in majority of patients (104), followed by Ciprofloxacin in (103), then Cefeimpe (FEP) in (102), Nalidixic acid (NA) and Ceftriaxone (CTX) in (101), Teicarcillin-Clavulanic acid (TGC) in (100), Nitrofurantoin (FA) in (99) Imipenem (IPM) and Cephalothin (CL) in (98), Piperacillin (PB) in (96), Chloramphenicol (C) in (93),Vancomycin (VA) in (88), Gentamicin (GN) in (86), Ertapenem (ETP) and Tetracycline (TE) in (79), Cefoxitin (CN) and Augmentin (AUG) in (78), Kanamycin (K) in (75) of them, while a moderate resistance was found in amoxicillin (AMC) in (56), on the other hand clindamycin was the only antibiotic found highly sensitive to staph cocci with lower resistance rate (80) patients.

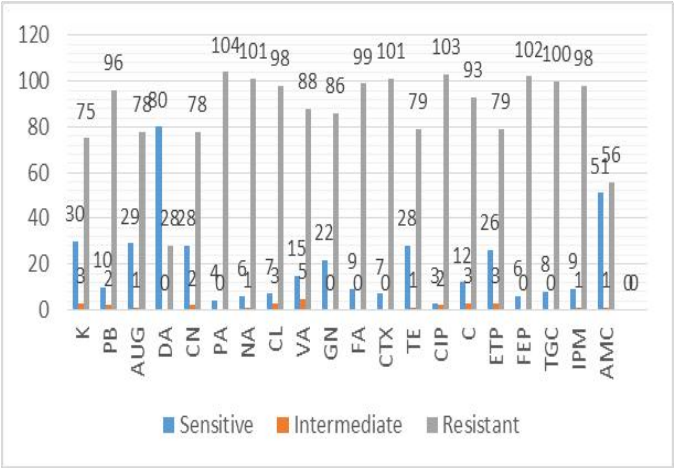

Figure (IV): Antimicrobial susceptibility pattern of *Staphylococcus aureus* to different antibiotics.

From the following tables and figures (V,VI), we notice that the probability value = 0.000, which is less than the probability value (α=0.05), which indicates the existence of a highly significant relationship between the two variables (department & sex).

Table (V): *The relation between department & sex:*

Cross tabulation of (Department & Sex)				
		sex		Total
		Male	Female	
Section	Outpatient department	22	26	48
	Burn shocks room	9	2	11
	Intensive care unit	6	6	12
	Male surgical wards A	21	4	25
	Female surgical ward A	0	12	12
Total		58	50	108

ISSN: 2959- 7463

Table (IV): *Antimicrobial susceptibility pattern of Staphylococcus aureus to different antibiotics:*

Antiprogram																			
	AMC	**IPM**	**TGC**	**FEP**	**ETP**	**C**	**CIP**	**TE**	**CTX**	**FA**	**GN**	**VA**	**CL**	**NA**	**PA**	**CN**	**DA**	**AUG**	**PB**	K
Sensitive	51	9	8	6	26	12	3	28	7	9	22	15	7	6	4	28	80	29	10	30
Intermediate	1	1	0	0	3	3	2	1	0	0	0	5	3	1	0	2	0	1	2	3
Resistant	56	98	100	102	79	93	103	79	101	99	86	88	98	101	104	78	28	78	96	75

Table (VI): *The relation between department & sex by Chi-Square Tests:*

Chi-Square Tests			
	Value	df	Asymptotic Significance (2-sided)
Pearson Chi-Square	27.908[a]	4	0
N of Valid Cases	108		

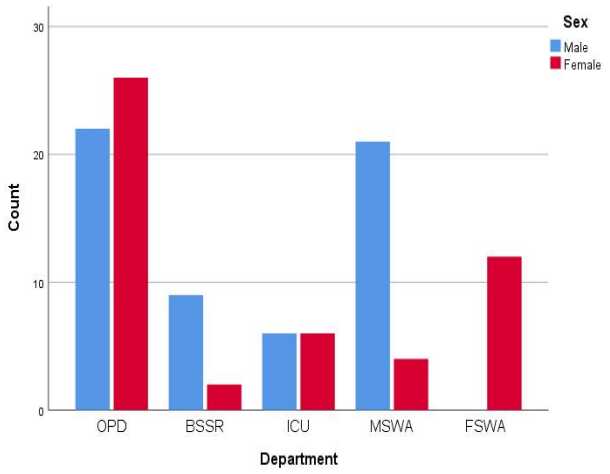

Figure (V): *The relation between department and sex curve .*

From the following tables (VII, VIII) and figure (V) we note that the probability value = 0.005, which is less than the probability value (α =0.05), which indicates the existence of a significant relationship between the two variables (department & sample).

Table (VII): *The relationship between section & sample:*

Cross tabulation of (Section & sample)							
		Sample					Total
		Urine	Swab	Tip	CTT	BLOOD	
Section	Outpatient department	9	35	0	0	4	48
	Burn shocks room	1	7	1	0	2	11
	Intensive care unit	0	6	1	1	4	12
	Male surgical wards A	1	16	0	0	8	25
	Female surgical wards A	0	12	0	0	0	12
Total		11	76	2	1	18	108

Table (VIII): *The relationship between section & sample by Chi-Square Tests:*

Chi-Square Tests			
	Value	df	Asymptotic Significance (2-sided)
Pearson Chi-Square	34.268[a]	16	0.005
N of Valid Cases	108		

ISSN: 2959- 7463

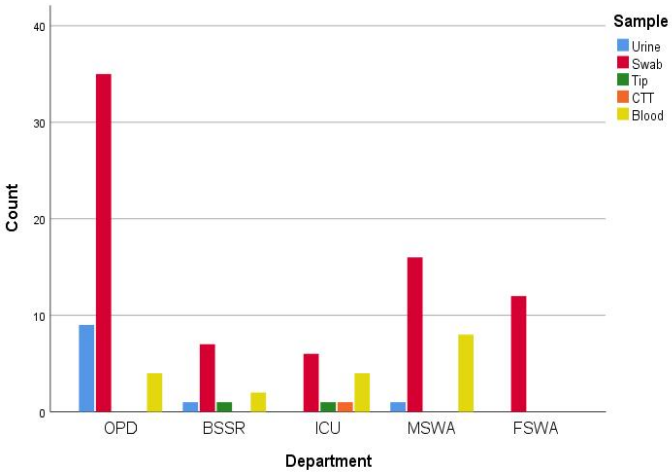

Figure (VI): *The relation between department & sample curve.*

In the figure (VII) shows the growth of *Staphylococcus aureus* gram positive bacteria is alpha hemolysis on Macconkey agar

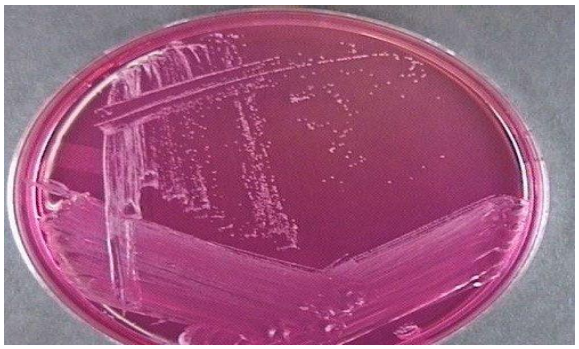

Figure (VII): *The growth of Staphylococcus aureus in MacConkey Agar.*

As show in the figure (VIII) these in gram stain from we shown that the *Staphylococcus aureus* is gram positive.

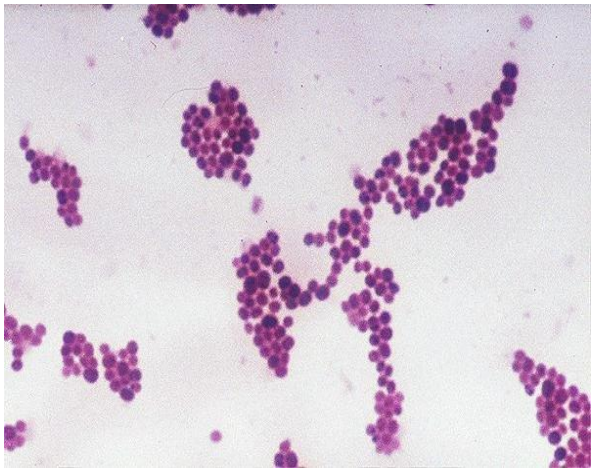

Figure (VIII): The gram stain of *Staphylococcus aureus.*

This study was based and examine the presence of *Staph aureus* using clinical samples from different wards and outpatient department in AL-Jalaa hospital, as *Staph aureus* found resistant to majority of antibiotics used in the study, according to the antibiogram results most of the resistant antibiotics consider broad spectrum ones reflect the un appropriate use of them in treatment of patients. Anti-sensitivity test *S. aureus* isolates against commonly used antibiotics showed that the overall resistance to antibiotics was alarmingly higher in Ciprofloxacin in as found resistant to (103) of patients from (108), followed by Cefeimpe in (102), Nalidixic acid and Ceftriaxone in(101), Teicarcillin-Clavulanic acid in (100), Nitrofurantoin in (99) Imipenem and Cephalothin in (98), PB in (96), Chloramphenicol in (93),Vancomycin in (88), Gentamicin in (86), as totally opposite to our result in degree of resistance a study by Abdullahi *et al*, observed resistance rates of 91.9%, 26.9%, 21.9% and 2.5% to Pencillin G, Cefoxitin, Augmentin and Imipenem respectively. [43] On the contrary, lower resistance was manifested by vancomycin (1.7%), Chloramphenicol (10.7%), Gentamicin (13.3%) and Cephalexin (20.3%) in study by Prashant Adhikari *et al.* [4] While regarding to regard to chloramphenicol, which appeared to have higher resistance rate in (93) of patients in comparing to a study by Prashant Adhikari *et al*, which has lower resistance rate (10.7%). This study shows only one antibiotic (Clindamycin) highly sensitive to *Staph aureus* with lower resistance rate, in contrary a study by Farooq Wani *et al.*, shows the lowest degree of resistance ranging from Levofloxacin, Moxifloxacin, Clarithromycin, Vancomycin and Teicoplanin.[44]

ISSN: 2959- 7463

IV. CONCLUSION

Our study shows that staphylococci found resistant to the majority of antibiotics used in anti-sensitivity test as it's a play a major role in infection in hospitals and consider a big health issue. Also the use of broad spectrum antibiotic irrationally increases without proper plan, lack of surveillance, suitable antibiotics detection through the period of management and infection control, lead to failure of management process. A further evaluation and study required to study the resistance of staphylococci toward antibiotics specially Methicillin Resistant *Staph aureus.*

REFERENCES

[1] Samuel Baron Medical Microbiology, 4th edition, University of Texas Medical Branch at Galveston, Galveston, Texas Galveston (TX): University of Texas Medical Branch at Galveston; 1996. ISBN-10: 0-9631172-1-1.

[2] Kloos WE, Schleifer KH (1986). Genus IV – Staphylococcus Rosenbach 1884. In: Sneath PHA, Mair NS, Sharpe ME, eds. Bergey's Manual of Systemic Bacteriology, Vol 2. Williams and Wilkins, Baltimore.

[3] Wilkinson BJ (1997) Biology. In: Crossley KB, Archer GL, eds. The Staphylococci in Human Diseases. Churchill Livingston, London. pp 1-38.

[4] Kloos WE, Lambe DW Jr (1991). Staphylococcus. In: Barlows A, Hausler WJ, Herrmann KL, Isenberg HD, Shadomy HJ, eds. Manual of Clinical Microbiology, 5th ed. ASM, Washington, D.C. pp 222-237.

[5] Kloos WE, Musselwhite MS (1975). Distribution and persistence of *Staphylococcus* and *micrococcus* species and other aerobic bacteria on human skin. *Appl Microbiol*; 30: 381-385.

[6] Bhakdi S, Tranum Jensen J. (1991). Alpha toxin of *Staphylococcus aureus. Microbiol Rev.* 55:733.

[7] Easmon CSF, Adlam C. (1983). Staphylococci and staphylococcal infections. Vols 1 and 2. Academic Press, London.

[8] Lowy FD (1998) Is *Staphylococcus aureus* an intracellular pathogen. Trends *Microbiol;* 8: 341-344.

[9] Waldvogel FA (1990). *Staphylococcus aureus* (including toxic shock syndrome), In: Mandell GL, Douglas RG, Bennett JE (eds.). Principles and Practice of Infectious Disease, 3rded. Churchill Livingston, London. pp 1489- 1510.

[10] Projan SJ, Novick RP (1997). The molecular basis of pathogenicity. In: Crossley KB, Archer GL, eds. The Staphylococci in Human Diseases. Churchill Livingston, London. pp 55-81.

[11] Howard BJ, Kloos WE (1987). Staphylococci. In: Howard BJ, Klass J II, Rubin SJ, Weissfeld AS, Tilton RC, eds. Clinical and Pathogenic Microbiology. Mosby, Washington D.C. pp 231-244.

[12] Kuroda M, Ohta T, Uchiyama I, Baba T, Yuzawa H, Kobayashi I, Cui L, Oguchi A, Aoki K, Nagai Y, Lian J, Ito T, Kanamori M, Matsumaru H, Maruyama A, Murakami H, Hosoyama A, Mizutani-Ui Y, Takahashi NK, Sawano T, Inoue R, Kaito C, Sekimizu K, Hirakawa H, Kuhara S, Goto S, Yabuzaki J, Kanehisa M, Yamashita A, Oshima K, Furuya K, Yoshino C, Shiba T, Hattori M, Ogasawara N, Hayashi H, Hiramatsu K (2001**). Whole genome sequencing of methicillin-resistant *Staphylococcus aureus.*** *Lancet*; **357**: 1225-1240.

[13] Shulman JA, Nahmias AJ (1972). Staphylococcal infections: clinical aspects. In: Cohen JO, ed. The Staphylococci. Wiley, New York pp 457-482.

[14] Elek S (1956). Experimental staphylococcal infections in the skin of man. *Ann NY Acad Sci*; 65: 85-90.

[15] Walenkamp GH (1990). Bacterial joint infections: a retrospective study for the source of infection. *Ned Tijdschr Geneeskd.*; 133: 2143-2144.

[16] Gustilo RB, Merkow RL, Templeman D (1990) The management of open fractures. *J Bone Joint Surg Am*; 72: 299-304.

[17] Boxma H (1995). Wound Infections in Fracture Surgery.The University of Amsterdam.

[18] PettyW, Spanier S, Shuster JJ, Silverthorne C (1985). The influence of skeletal implants on incidence of infection- Experiments in a canine model. *J Bone Joint Surg*; 67: 1236-1244.

[19] Barth E, Myrvik QM, Wagner W, Gristina AG (1989). *In vitro* and *in vivo* comparative colonization of *Staphylococcus aureus* and *Staphylococcus epidermidis* on orthopaedic implant materials. *Biomat*; 10: 325-328.

[20] Gnanamani A, Hariharan P, Paul-Satyaseela M. (2017). Staphylococcus aureus: Overview of Bacteriology, Clinical Diseases, Epidemiology, Antibiotic Resistance and Therapeutic Approach.

[21] Harris LG, Foster SJ, Richards RG.(2002). An introduction to Staphylococcus aureus, and techniques for identifying and quantifying *S. aureus* adhesins in relation to adhesion to biomaterials: review. *European cells & materials*;4:39-60.

[22] IWG-CSCC.(2009). Classification of staphylococcal cassette chromosome mec (SCCmec): guidelines for reporting novel SCCmec elements. Antimicrobial agents and chemotherapy;53(12):4961-7.

[23] Taylor TA, Unakal CG .(2020). *Staphylococcus aureus.* Stat Pearls. Treasure Island (FL): Stat Pearls Publishing LLC.

[24] Fuda C, Suvorov M, Vakulenko SB, Mobashery S. (2004). The basis for resistance to betalactam antibiotics by penicillin-binding protein 2a of methicillin-resistant *Staphylococcus aureus. The Journal of biological chemistry*; 279(39):40802-6.

[25] Liu J, Chen D, Peters BM, Li L, Li B, XuZ, *et al.*(2016). Staphylococcal chromosomalcassettes mec(SCCmec): A mobile genetic element in methicillin resistant *Staphylococcus aureus. Microb Pathog*; 101:56–67.

[26] Mehrotra M, Wang G, WM. J.(2000). Multiplex PCR for detection of genes for *Staphylococcus aureus* enterotoxins, exfoliative toxins, toxic shock syndrome toxin 1, and methicillin resistance. *J Clin Microbiol*;38:1032–5.

[27] Ito T, Hiramatsu K .(1998). Acquisition of methicillin resistance and progression of multiantibiotic resistance in methicillin-resistant *Staphylococcus aureus. Yonsei medical journal*;39(6):526-33.

[28] Hiramatsu K, Katayama Y, Matsuo M, Sasaki T, Morimoto Y, Sekiguchi A, *et al.* (2014). Multi-drug-resistant *Staphylococcus aureus* and future chemotherapy. *Journal of infection and chemotherapy : official journal of the Japan Society of Chemotherapy*; 20(10):593- 601.

[29] Khan MF.(2017). Brief History of *Staphylococcus aureus*: A Focus to Antibiotic Resistance. *EC Microbiology*; 5:36-9.

[30] Hiramatsu K, Hanaki H, Ino T, Yabuta K, Oguri T, Tenover F .(1997). Methicillin-resistant *Staphylococcus aureus* clinical strain with reduced vancomycin susceptibility. *The Journal of antimicrobial chemotherapy*; 40(1):135-6.

[31] Dm S, Boulton M, Stoltman G, D J, Stobierski MG, W B, *et al* .(2002). *Staphylococcus aureus* Resistant to Vancomycin—United States. *JAMA The Journal of the American Medical Association*; 288:824-5.

[32] Bitrus AA, Peter OM, Abbas MA, Goni MD .(2018). *Staphylococcus aureus*: A Review of Antimicrobial Resistance Mechanisms. Veterinary Sciences: Research and Reviews.;4(2).

[33] Emaneini M, Bigverdi R, Kalantar D, Soroush S, Jabalameli F, Khoshgnab BN, *et al.* (2013). Distribution of genes encoding tetracycline resistance and aminoglycoside modifying enzymes in *Staphylococcus aureus* strains isolated from a burn center. *Annals of burns and fire disasters;* 26(2):76.

[34] Foster TJ .(2017). Antibiotic resistance in *Staphylococcus aureus.* Current status and future prospects. *FEMS microbiology reviews*; 41(3):430-49.

ISSN: 2959- 7463

[35] Mahdiyoun SM, Kazemian H, Ahanjan M, Houri H, Goudarzi M .(2016). Frequency of Aminoglycoside-Resistance Genes in Methicillin-Resistant *Staphylococcus aureus* (MRSA) Isolates from Hospitalized Patients. *Jundishapur journal of microbiology*; 9(8):e35052.

[36] Rahimi F .(2016). Characterization of Resistance to Aminoglycosides in Methicillin-Resistant *Staphylococcus aureus* Strains Isolated From a Tertiary Care Hospital in Tehran, Iran. Jundishapur journal of microbiology; 9(1):e29237.

[37] Eng RH, Smith SM, Tillem M, Cherubin C. (1985). Rifampin resistance: development during the therapy of methicillin-resistant Staphylococcus aureus infection. *Archives of internal medicine*;145(1):146-8.

[38] Zhou W, Shan W, Ma X, Chang W, Zhou X, Lu H, *et al.*(2012). Molecular characterization of rifampicin-resistant Staphylococcus aureus isolates in a Chinese teaching hospital from Anhui, China. *BMC microbiology*; 12:240.

[39] Wilson D N .(2009). The A-Z of bacterial translation inhibitors. Critical reviews in biochemistry and molecular biology. 44(6):393-433.

[40] Alexander M Aiken, Irene M Mutuku *et al.*(2014). Carriage of *Staphylococcus aureus* in Thika Level 5 Hospital, Kenya: a cross-sectional study. Aiken *et al.* Antimicrobial Resistance and Infection Control; 3:22.

[41] Jyotshna Sapkota, Manisha Sharma, *et al* .(2019). Prevalence of Staphylococcus aureus Isolated from Clinical Samples in a Tertiary Care Hospital: A Descriptive Cross-sectional Study . *J Nepal Med Assoc*; 57(220):398-402.

[42] Prashant Adhikari, Deepak Basyal *et al.*(2023). Prevalence, antimicrobial susceptibility pattern and multidrug resistance of methicillin-resistant *Staphylococcus aureus* isolated from clinical samples at a tertiary care teaching hospital: an observational, cross-sectional study from the Himalayan country, Nepal. Adhikari P, *et al. BMJ Open*; 13:e067384. doi:10.1136/bmjopen-2022-067384.

[43] Farooq A Wani, Altaf Bandy, *et al.*(2020).Cross sectional study on methicillin resistant *Staphylococcus aureus* from the Aljouf region of Saudi Arabia. *Int J Clin Exp Med*;13(11):9172-9179.

[44] Abdullahi N and Iregbu KC.(2018). Methicillin-resistant *Staphylococcus aureus* in a central Nigeria tertiary hospital. *Annals of Tropical Pathology*; 9: 6.