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Isolation and Diagnosis of Bacteria in Bacteremia Patients and Study Their Resistance to Antibiotics in Kirkuk Hospitals

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Abstract

313 blood samples were collected from bacteremia patients, including 146 samples (30 from patients and 116 from outpatients) from Azadi teaching hospital, 36 samples from the dialysis unit at Kirkuk General Hospital, 126 samples (42 from inpatients and 84 from outpatients) from the Children's Hospital, and 5 samples from the Women's and Obstetrics Hospital in Kirkuk province, for the period from January 24, 2022, to September 10, 2022. The study, including the isolation and diagnosis of bacteria and the study of their resistance to antibiotics, The results show that 32 (17.87%) positive growth cultures were obtained from febrile patients, 3 (8.33%) from dialysis patients in the dialysis unit, and 15 (65.21%) from burn and wound patients. Fifty bacterial isolates were obtained, all of which were gram-positive.

Staphylococcus was the highest with 28 isolates, including [(11) *S.homoinis*, (4) *S.epidermidis* epidermidis, (2) isolates each of *S.haemolyticus* and *S. Wagner*, and (9) *Staphylococcus* spp.], while *Enterococcus faecalis* was one isolate. The gram-negative bacteria were [(11) *Pseudomonas aeruginosa*, (5) *Escherichia coli*, (2) isolates of *Enterobacter cloacae*, and followed by one isolate of *Raoultella terrigena*, *Acinetobacter* spp., and *Klebsiella* spp.). *Staphylococcus* spp. resistance to 20 antibiotics was studied, and the species *S.homoinis* showed 100% resistance to (Oxacillin, Benzylpenicillin, and Amoxicillin). Whereas *S.epidermidis* epidermidis was 100% antibiotic-resistant (Oxacillin, Benzylpenicillin, and Amoxicillin). *S. hemolyticus* was resistant to (erythromycin, benzylbeniclin, amosiclin, amikachin, gentamicin, torramichin, and tetracycline) by 100%. *S. warneri* was resistant to (oxacillin, benzylpenicillin, amoxicillin, and dusidic Acid) at a rate of one hundred percent.

Keywords: Bacteremia, Dialysis unit, Burns, Wounds, Infants.

1. Introduction

Blood in healthy people does not contain bacteria, so the presence of infection can affect the patient's life [1]. Bacterial infection is the most common cause of bacteremia, as the infection is limited to a specific place in the body and is helped by the movement of bacteria in the blood [1]. Bloodstream infection (BSI) is a growing public health concern worldwide and represents a serious infection with significant morbidity and mortality rates, especially in children and the elderly [2]. Bacteremia is one of the most common causes of death for patients in the hospital, and despite health progress, mortality rates remain unacceptably high. Some medical procedures can allow bacteria to pass into the blood of healthy patients from places that are usually colonized by bacteria, such as bladder urinary catheters or colonoscopies [1]. Septicemia due to bacterial infections is a leading cause of child mortality worldwide [3]. Severe septicemia can lead to severe organic weakness or septicasis, as well as irreversible low blood pressure by reviving fluids [4].

Bloodstream infections are associated with a high mortality rate [5], and [6] indicated that bacteremia may reach more than 200,000 patients per year, with the possibility of high prevalence and mortality, and that the method of blood culturing is the most sensitive way to detect bacteremia and is commonly obtained in patients with fever, chills, an increased number of white pellets, and peripheral infections. [1] indicated that the most frequent bacteremia causing infections are urinary tract (prostatitis or pyelonephritis), respiratory tract (pneumonia), blood vessels (infected catheters), digestive tract (cholecystitis or cholangitis), skin and soft tissues (cellulitis or myositis), or bones (osteoarthritis).

[7] noted that multiple factors make cirrhosis patients vulnerable to bacteremia or sepsis with a high mortality rate. According to [8], the respiratory system (18.0%), the digestive system (16.2%), and the urinary reproductive system (36.0%) were the three most common sources of bacteremia. Data obtained from 592 hospitals in Japan show positive blood culture samples in children, reaching 98,295 in 2010 and 109,611 samples in 2011, 115,172 samples in 2012 and 115,172 samples in 2013, 120,561 samples in 2014, 131,297 samples in 2015, and 138,452 in 2016 [9].

One of the genera causing bacteremia is Staphylococcus spp. bacteria, as the diagnosis of staphylococcii is largely based on the outward appearance of the colony as well as the production of various pigments varying from white to dark yellow [10].

Colonies on solid media are round, smooth, high, and radiant, but microscopic colonies are spherical cells with a diameter of about 1 micrometer arranged in irregular groups, appearing individually or appearing in pairs or quadrants and in chains in liquid culture media, and they are facultative anaerobic organisms [11]. Coagulase-negative staphylococci (CoNS) has received considerable attention in recent years as a pathogen, causing infection in both human and veterinary medicine, especially in weakened immunity, critical cases, long-term lying in the hospital, and in those cases containing medical devices in their bodies, such as catheters [12]. CoNS bacteria are able to cause clinically important bacteremia due to their natural environment on human skin and their ability to adhere to vital substances and form biofilm [13]. Others cause suppuration, abscesses, a variety of purulent infections, and even fatal septicemia [11]. Although staphylococcus bacteria are in many cases harmless, many of the ferocity factors they possess make them an opportunistic pathogen and one of the leading causes of hospital-acquired infections around the world [14].

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Staphylococcus hominis is a component of natural human bacteria and an opportunistic pathogen that can cause a variety of infections. S. hominis bacteria cause bacteremia, endocarditis, and endophthalmitis. However, abscesses rarely cause abscesses [15].

Staphylococcus epidermidis accounts for the majority of neonatal bacteremia cases. In addition, they have been shown to be associated with diseases of newborns such as bronchopulmonary dysplasia (BPD), white matter injury (WMI), necrotizing enterocolitis, and retinopathy of prematurity (ROP), which affect short- and long-term neonatal outcomes [16].

S.warneri has sometimes been isolated from bacteremia and endocarditis, which are commonly associated with prosthetic devices such as dialysis catheters [17].

While *S. haemolyticus* causes severe injuries such as meningitis, endocarditis, prosthetic joint infections, bacteremia, septicemia, peritonitis, and otitis, especially in patients with immunodeficiency [18].

2. Materials and Methods

2.1. Collecting samples

[7] noted that multiple factors make cirrhosis patients vulnerable to bacteremia or sepsis with a high mortality rate. According to [8], the respiratory system (18.0%), the digestive system (16.2%), and the urinary reproductive system (36.0%) were the three most common sources of bacteremia. Data obtained from 592 hospitals in Japan show positive blood culture samples in children, reaching 98,295 in 2010 and 109,611 samples in 2011, 115,172 samples in 2012 and 115,172 samples in 2013, 120,561 samples in 2014, 131,297 samples in 2015, and 138,452 in 2016 [9].

Three hundred and thirteen blood samples were collected, including: 146 samples (30 patient samples and 116 samples of outpatients) from Azadi Teaching Hospital; 36 samples from the dialysis unit at Kirkuk General Hospital; 126 samples (42 patient samples and 84 samples) from the Children's Hospital; and 5 samples from the Women's and Obstetrics Hospital in Kirkuk Province, for the period from January 2022 to September 2022.

2.2. Diagnosis of the sample

Blood samples from patients' were cultured in brain-heart infusion broth and incubated at 37°C for 24 hours. They were cultured on blood agar and MacConkey agar and incubated at 37 °C for 24 hours. All isolates were identified depending on their macroscopic size and diagnosed with the use of the API staph. Kit, the Compact System Vitek-2 for gram-positive bacteria, and the API 20E kit for gram-negative bacteria.

2.3. Resistance of Antibiotic

Bacteria sensitivity was tested using the Compact system Vitek –2 AST580.

3. Results and Discussion

3.1. Samples collection

[7] noted that multiple factors make cirrhosis patients vulnerable to bacteremia or sepsis with a high mortality rate. According to [8], the respiratory system (18.0%), the digestive system (16.2%), and the urinary reproductive system (36.0%) were the three most common sources of bacteremia. Data obtained from 592 hospitals in Japan show positive blood culture samples in children, reaching 98,295 in 2010 and 109,611 samples in 2011, 115,172 samples in 2012 and 115,172 samples in 2013, 120,561 samples in 2014, 131,297 samples in 2015, and 138,452 in 2016 [9].

Samples were collected from patients infected with or suspected of bacteremia and cultured in brain-heart infusion broth, and the results in **Figure 1** showed the percentage of positive and negative cultured growth. The percentage of positive growth culture was 15.97%, while the percentage of negative growth culture was 84.03%.

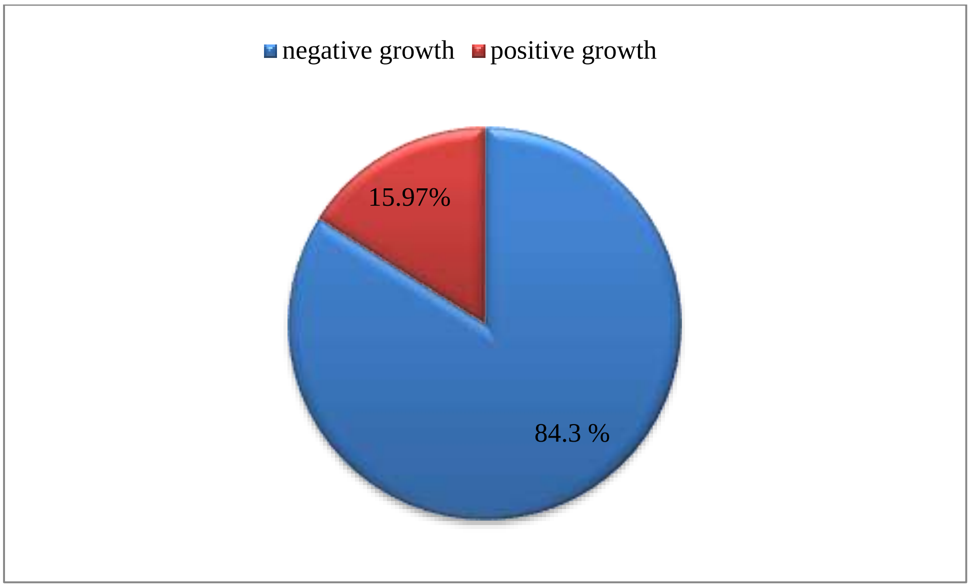

Figure1. The percentage of positive and negative growth culture.

[7] noted that multiple factors make cirrhosis patients vulnerable to bacteremia or sepsis with a high mortality rate. According to [8], the respiratory system (18.0%), the digestive system (16.2%), and the urinary reproductive system (36.0%) were the three most common sources of bacteremia. Data obtained from 592 hospitals in Japan show positive blood culture samples in children, reaching 98,295 in 2010 and 109,611 samples in 2011, 115,172 samples in 2012 and 115,172 samples in 2013, 120,561 samples in 2014, 131,297 samples in 2015, and 138,452 in 2016 [9].

This was noted by [19] in their study of 158 patients, including 107 cultured growth positives (80 bacterial, 27 fungal) and 51 cultured growth negatives.

[20] showed that 1,425 blood cultures were registered, with 179 (12.6%) positive cultures and 1.246 (87.4%) negative cultures. While [21] showed that 101 patients included 62 negative and 39

positive cultures in the bloodstream,

Table 1 shows the distribution of positive growth cultures according to the source of bacteremia, as the number of positive cultures was 32 (17.87%) from febrile patients, 3 (8.33%) from dialysis patients in the dialysis unit, and 15 (65.21%) from burn and wound patients.

Table 1. Distribution of positive growth culture according to the source of bacteremia .

Source of bacteremia	Total number of samples	Number of positive grown culture	Percentage %
Febrile	179	32	17.87
Dialysis patients (dialysis unit)	36	3	8.33
Burns and wounds	23	15	65.21

3.2. Diagnosis of positive-growth culture

Positive-growing cultures were cultured on blood agar and MacConkey agar, and all isolates were diagnosed macroscopically. Some of the isolates were shown in pink on MacConkey agar and the others were colorless depending on their fermentation and non-fermentation of lactose, while white and creamy isolates appeared on blood agar medium. Then the pure colonies were diagnosed with the use of a microscope; the gram-negative isolates were red, while the gram-positive isolates were seen in violation. **Table** 2 shows the number and proportions of positive and negative bacterial species of gram stain isolated from bacteremia patients, of which 29 (58%) were gram positive and 21 (42%) were gram negative bacteria.

Table 2. The number and percentage of gram positive and negative bacterial species isolated from bacteremia patients

Number of Total cultures Positive Isolates	Gram positive		Gram negative	
	Number	Percentage%	**Number**	**Percentage %**
50	29	58	21	42

As a result of an additional study done by [18], of 158 bacteremia patients, 45 (29%) were gram-positive bacteria, 35 (22%) were gram-negative bacteria, 27 (17%) were fungi, and 51 (32%) were negative growth. Al-rawazq et al. (2012) [22] indicated that 25% of blood culture samples from children with bacteremia were positive and 75% were negative. [23] Ibraheem (2005) noted that 15.5% of blood cultured samples from newborns showed positive growth.

While [21] indicated 101 patients had 39 blood cultures that were growth-positive, of which 16 (41%) were gram-negative, 18 (46.2%) were gram-positive bacteria, and 5 (12.8%) contained both positive and negative gram stains. [24] noted in his study that the most people with bacteremia among children were in the age group (1 day–1 year) at 64.89% percent.

3.3. Biochemical tests for isolates from bacteremia patients

The following biochemical tests were carried out for gram-positive cocci: cocci (Oxidase, Catalase, Hemolysin, Coagulase, Urease, and DNase (**Table** 3), and API E20 kit tests were conducted for negative gram stains [25].

Table 3. Biochemical tests for *Staphylococcus* spp. isolated from bacteremia patients.

Symbol isolates	Mannitol salt agar	DNase	urease	Coagulase		Hemolysis	oxidase	Catalase
				bound	free			
S6	+	+	+	-	-	-	-	+
S8	+	+	+	-	-	-	-	+
S9	+	+	-	-	-	-	-	+
S24	+	+	-	-	-	-	-	+
S25	+	+	+	-	-	-	-	+
S29	+	+	+	-	-	-	-	+
S30	+	+	+	-	-	-	-	+
31	\	-	-	\	\	+	\	-
S39	+	+	+	-	-	+	-	+
S41	+	+	+	-	-	+	-	+
S54	+	+	-	-	-	-	-	+
S73	+	+	-	-	-	+	-	+
S83	+	+	+	-	-	+	-	+
S86	+	+	+	-	-	+	-	+
S88	+	+	+	-	-	+	-	+
S90	+	+	+	-	-	-	-	+
S97	+	+	+	-	-	-	-	+
S 104	+	+	-	-	-	+	-	+
S106	+	+	+	-	-	+	-	+
S113	+	+	+	-	-	-	-	+

Table (3) shows that all isolates were positive for the DNase test except isolate (31), which was negative and catalase tested and all grew on mannitol salt agar. All isolates were negative for oxidase testing and free coagulase and bound coagulase tests. The isolates (S 31, S 39, S 41, S 73, S 83, S 86, S 88, S 104, and S 106) were positive for hemolysis, but isolates (S 6, S 8, S 9, S 24, S 25, S 29, S 30, S 54, S 90, S 97, and S 113) were negative, and the urease test was positive for all positive isolates except those (S 9, S 24, S 31, S 54, S 73, and S 104) that were negative.

Table 4. Number and percentage of isolated bacterial species of bacteremia patients.

Reaction with the gram stains	Genus	Species	Number	Percentage%
Gram positive bacteria	*Staphylococcus*	*Warneri(6,88)*	2	6.89
		Haemolyticus(73,104)	2	6.89
		Hominis(8,9,24,25,30,39,41,54,86,106,113),	11	37.93
		29,83,90,97 epidermidis	4	13.79
		Spp.	9	31.03
	Enterococcus	*Faecalis (31)*	1	3.44
Gram negative bacteria	*Raoultella*	*terrigena*	1	4.76
	Pseudomonas	*aeruginosa*	11	52.38
	Enterobacter	*cloacae*	2	9.52
	Escherichia	*coli*	5	14.28
	Klebsiella	*Spp.*	1	4.76
	Acinetobacter	*Spp.*	1	4.76

Table (4) shows the number and percentage of Staphylococcus spp. isolates from bacteremia patients that are negative for coagulase. The gram-positive bacteria were Staphylococcus hominis and S. epidermidis (37.33% and 13.79%), respectively; S. warneri and S. warneri and S. haemolyticus were 6.89%; and Enterococcus faecalis was 3.44%. While the gram-negative bacteria were presented by Pseudomonas 52.38% and Escherichia coli 14.28%, Enterobacter cloacae 9.52%, Raoultella terrigena, KlebsiellaSpp. and Acinetobacter Spp. were 4.76%.

[26], showed in their study that the main bacterial pathogens of gram positive bacteria in the bacteremia of newborns were *S. haemolyticus* (9.1%), *S. epidermidis* (7.1%) and *S. hominis* (5.1%), noted that the coagulase-negative Staphylococci (CONS) accounted for the majority of gram positive bacteria and showed *S. haemolyticus* of the most visible species.

[26] showed in their study that the main bacterial pathogens of gram positive bacteria in the bacteremia of newborns were S. haemolyticus (9.1%), S. epidermidis (7.1%), and S. hominis (5.1%). They noted that the coagulase-negative Staphylococci (CONS) accounted for the majority of gram-positive bacteria and showed S. haemolyticus as the most visible species.

[27] showed in their study that bacterial isolates from newborns were 21.23% of the gram-positive bacterium, followed by bacillia gram negative and yeasts, while [24] indicated that the percentage of S.epidermidis isolated from bacteremia patients was 54.78%.

3.4. Resistant *Staphylococcus* spp. isolated from bacteremia for antibiotics

Figure 2 shows the resistance of Staphylococcus hominis ssp. hominis, where all isolates were resistant to (Benzylpenicillin, Amoxicillin, and Oxacillin) by 100%, were resistant to (Fusidic Acid, Erythromycin, Tetracycline, Levofloxacin, Clindamycin) by (81.81, 63.63, 27.27, 54.54, and 18.18%), respectively, and resistant to (Amikacin, Gentamicin, Tobramycino Sulfamethoxazole/ Trimethoprim) by 36.36%, and resistant to (Moxifloxacin, Teicoplanin, Vancomycin, and Rifampicin) by 9.09%.

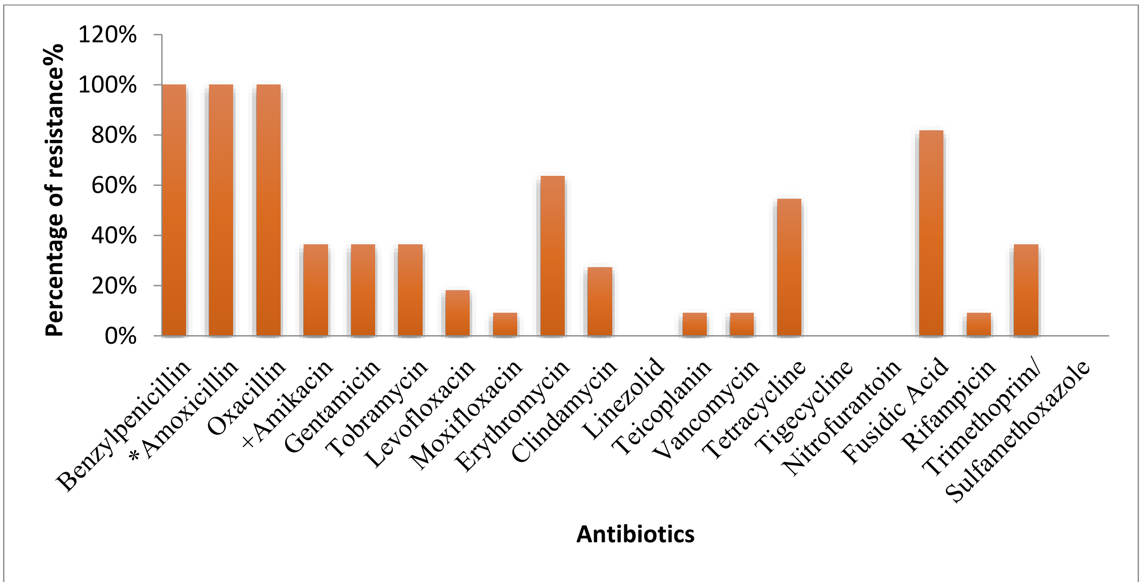

Figure 2. Resistance *Staphylococcus hominis* for antibiotics.

In *Staphylococcus epidermidis* isolates, all isolates were resistant to (Benzylpenicillin, Amoxicillin, Oxacillin) by 100%, (Amikacin, Tobramycin, Erythromycin, Tetracycline and Fusidic Acid) by 50%, and (Gentamicin, Levofloxacin, Moxifloxacin, Trimethoprim/ Sulfamethoxazole) by 25%, **(Table 3)**.

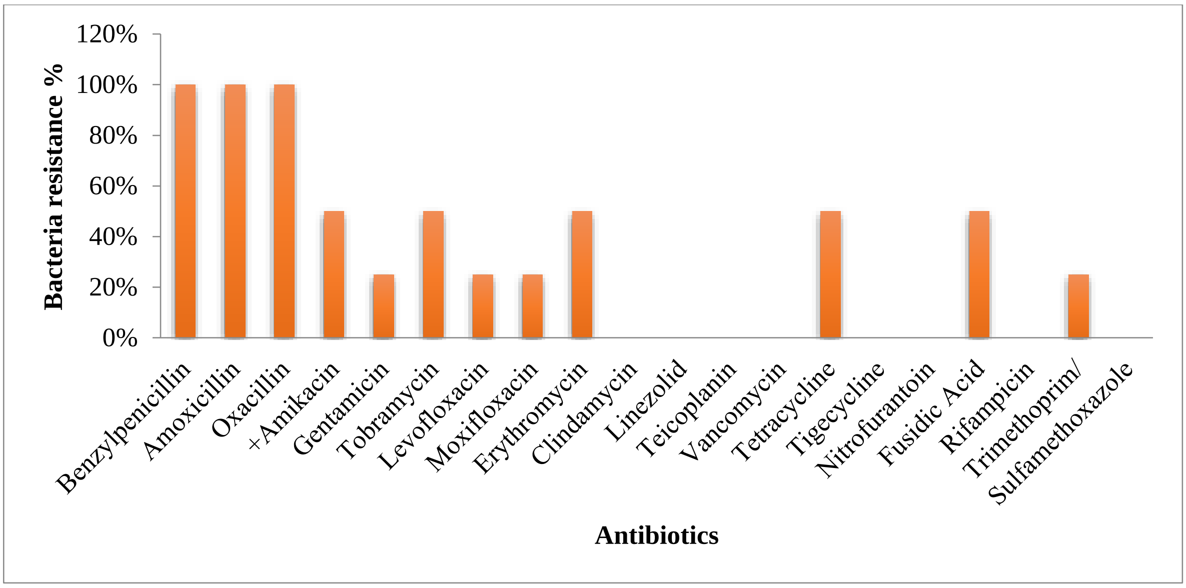

Figure 3. Resistance of *Staphylococcus haemolyticus* for antibiotics.

Figure 4 shows resistance of *Staphylococcus haemolyticus* to (Benzylpenicillin, Amoxicillin, Amikacin, Gentamicin, Tobramycin, Erythromycin, Tetracycline) 100%, and (Oxacillin, Levofloxacin, Moxifloxacin, Fusidic acid and Trimethoprim/Sulfamethoxazole) by 50%.

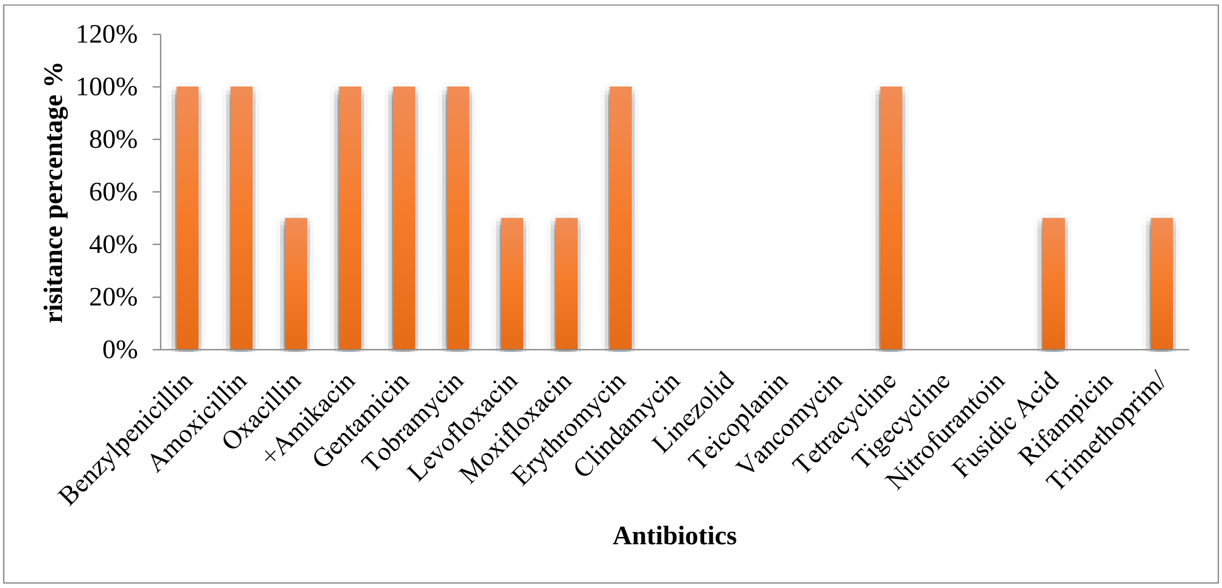

Figure 4. Resistance of *Staphylococcus warneri* for antibiotics.

Figure 5 shows the resistance of *Staphylococcus warneri* isolates to (Benzylpenicillin, Oxacillin, Amoxicillin and Fusidic acid) by 100% and antibiotics (Erythromycin and Clindamycin) by 50%

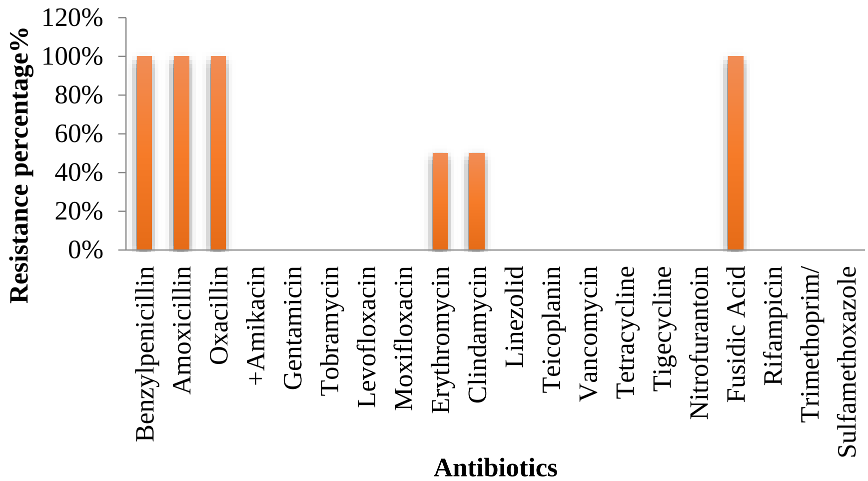

Figure 5. Resistance of *Staphylococcus warneri* for antibiotics.

[26] indicated that the S. hominis isolated from blood prematurely were resistant to antibiotics (Gentamicin, Ciprofoxacin, Levofoxacin, Moxifoxacin, Erythromycin, Clindamycin, Linezolid, Vancomycin, Tetracycline, Tigecycline, Nitrofurantoin, Rifampicin, Trimethoprim/ sulfamethoxazole by (37.5, 8, 25, 25, 0, 75, 50, 0, 25, 37.5, 0, 12.5,12.5, 25)%, respectively.

[28] showed that most clinical isolates in their study of S. haemolyticus and S. hominis were resistant to beta-lactams, lincosamides, macrolides, aminoglycosides as well as tetracycline, ciprofloxacin, trimethoprim/sulfamethoxazole, and also showed that most S.warneri isolates were resistant to macrolides and lincosamides and considered (cross-resistance) as well as tetracycline, and 36.8% were resistant to beta-lactams.

[26] indicated that *S. epidermidis* were resistant to (Gentamicin, Ciprofoxacin, Levofoxacin, Moxifoxacin, Erythromycin, Clindamicin, Linzolid, Vancomycin, Tetracycline, Tegisislin, Nitrofurantoin, Rifampicin, Trimthoprim/Sulfamthoxazole, and by (9, 9, 90 , 0 , 27.3, 36.3, 36.3, 9, 36.3, 45.4, 0, 0, 9, 54.5)) % respectively. *S. hemolytic* bacteria were resistant to (Gentamicin, Ciprofoxacin, Levofoxacin, Moxifoxacin, Erythromycin, Clindamicin, Linzolid, Vancomycin, Tetracycline, Tigecycline, Nitrofurantoin, Rifampicin, Trimthoprim/Sulfamthoxazole, and by (43, 10, 0, 0, 28.5,0, 28.5, 92.8, 50,90,90,85), respectively.

Staphylococcus spp. resistance to antibiotics is due to the presence of β-lactamase enzymes, targeting some bacterial ribosomes, leading to a reading pattern during the translation process, or because they have enzymes that are coded by genetic mobile elements, which may be involved in the genetic change of the topoisomerase enzyme as well as increased expression of the internal pump efflux [29- 33].

4. Conclusions

The results showed that most patients with clinical symptoms of bacteremia were febrile, while the highest positive culture was in wounds and burns patients, then febrile, followed by patients in the dialysis unit, and the negative coagulase staphylococcus was prevalent for all positive cultures.

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