



BACTERIAL RESISTANCE MARKERS IN SEPSIS OF NEWBORN IN ZLITEN MEDICAL CENTER

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Abstract

Background A lot of newborn patients with sepsis need antibiotic treatment, but some antibiotics are ineffective and cause bacteria to develop resistance markers (a gene that produces a protein that makes cells that express this protein resistant to antibiotics). Choosing antibiotics wisely can lower the mortality rate and promote the prudent use of antibiotics.

Aim We analyze the pattern of antibiotic use and the sensitivity patterns of antibiotics to support the rational use of antibiotics in neonate patients with sepsis.

Material and method Total sample of 211 blood sample were collected from neonate showing with clinical signs of sepsis at Zletin Medical Center during January-December 2022 year 2022 was *Staphylococcus epidermidis*, and the most antibiotic-resistant bacteria was *Acinetobacter*. The sample was then cultivated, and resistance markers assessed using Phoenix BD CPO.

Result The sample were divided into no bacterial growth and bacterial growth. we found that 165 sample (78.19%) have not bacterial growth and 44 samples (20.85%) have bacterial growth *Staphylococcus epidermidis* (20.45%), *Klebsiella pneumonia* (9.09%), *Staphylococcus hemolyticus* (11.36%), *Acinatobacter baumannii/calcoaceticus complex* (2.36%), *Pseudomonas putida* (2.72%), *Klebsilla oxytoca* (2.72%), *Echereshia coli* (2.72%), *Staphylococcus aureus* (2.72%).

Conclusion Based on the results of the trials, the most bacteria causing sepsis in the neonatal department at Zliten Medical Center during the year 2022 was *Staphylococcus epidermidis*, and the most antibiotic-resistant bacteria was *Acinetobacter*.

INTRODUCTION

Neonatal sepsis is blood infection that occurs in infants younger than 90 days old [1]. Early onset sepsis is seen in the first week of life. Late onset sepsis occur after 1 week through 3 months of age. It is the cause of substantial morbidity and mortality. Precise estimates of neonatal sepsis burden vary by setting. Early-onset sepsis remains a common and serious problem for neonates, especially preterm infants [2]. Group B *Streptococcus* (GBS) is the most common etiologic agent, while *Escherichia coli* is the most common cause of mortality [3]. Current efforts toward maternal intrapartum antimicrobial prophylaxis have significantly reduced the rates of GBS disease but have been associated with increased rates of Gram-negative infections, especially among very-low-birth-weight infants. Sepsis is one of the pathological conditions that, when it spreads more, can cause death [4]. These births were in polluted environments, which made it easier for children to develop sepsis, and sepsis can be treated. There are many types of bacteria that cause sepsis, the most important of which are family members [5]. Including *Staphylococcus aureus*, *Staphylococcus viridians*, and *Streptococcus*. To health workers, especially in hospitals and laboratories. It was found in a study in India she was outside the hospital, and these children were admitted to the hospital after they had blood poisoning because more *Pneumoniae*, in addition to *Pseudomonas aeruginosa* and Gram-positive bacteria, which includes *Staphylococcus*, and some fungi such as *Candida* [6]. Infants with neonatal sepsis may have the following symptoms [7]; Body temperature changes, breathing problems and meningitis, diarrhea or decreased bowel movements, low blood sugar, reduced movements, reduced sucking, seizures, slow or fast heart rate [7].

Sepsis disproportionately affects vulnerable groups, such as newborns, pregnant women and people living in low-resource setting [8]. According to the world Health Organization report, about 85% of sepsis cases and deaths related to this disease occur in these groups [9]. Approximately half of the 49 million cases of sepsis annually occur among children, and cause 2.9 million deaths, most of which can be prevented if the condition is diagnosed early and treated appropriately, and these deaths are often the result of diarrheal disease or lower respiratory infections [10]. Infection causes about 31% of these deaths [11].

Thirty-eight percent of all deaths under the age of five occur during the neonatal period, the first four weeks of an infant's life, killing nearly four million infants annually, three-quarters of which occur in the first week after birth [12]. Infection is the main cause of death in newborns after the first week. There is risk of death in infants with low birth weight. Those with low birth weight who have infections caused by *Candida* or bacteria are more likely to die. Those who recover from infection usually do not benefit from long-term problems. But those who are infected with the infection of the lungs, those who remain in prison, may have a delay in growth, or mental paralysis, or disorders, or a deficiency in hearing [12].

Complications of neonatal sepsis, one of the most serious complications of sepsis is inflammation of the membrane surrounding the brain (meningitis). Newborns with meningitis may be very slow (lethargy), coma, have seizures, or bulge a soft spot between the bones of the skull (fontanelle), and often die if not treated promptly.

Diagnosis of sepsis in the newborn, culture of blood, and sometimes urine. Spinal puncture with cerebrospinal fluid transplantation [13]. Doctors' diagnosis sepsis based on the newborn symptoms and test results. They do several tests, including blood tests, to try to identify the bacteria, virus, or fungus causing the infection. Blood culture, sometimes urine cultures, and spinal taps (lumbar puncture) are also done. For cultures, doctors take samples of blood, cerebrospinal fluid, and urine, and try to culture the bacteria in the samples in laboratory and identify them. respiratory to chest x-ray [14].

Treatment of sepsis in newborns is intravenous antibiotics, in addition to treatment with antibiotics, other treatments may be necessary, such as assisted breathing with a ventilator, intravenous infusion of fluids, blood, and plasma, and support of blood pressure and circulation with drugs. And treatment of neonate with sepsis by surgery, the doctor may resort to surgical intervention to remove the source of infection, such as opening an abscess or removing infected or dead tissue [15]. Treatment of sepsis in neonate by herbs is still a challenge even with the development of modern antibiotics and intensive

care technologies; Therefore, scientists continue to search for remedies that can stop infection, including herbal medicine [16]. Although many plants have proven their activity in the treatment of blood inflammation, there is need to conduct more clinical studies to confirm their effectiveness [17]. The aim of the study to know the bacterial resistance markers in sepsis of newborn.

MATERIAL AND METHODS

Research Design

The blood samples were examined from newborns with sepsis for signs of bacterial resistance of bacteria to antibiotics using device Phoenix BD CPO.

Population and Sample

This study included 211 samples obtained from newborns with sepsis at Zliten Medical Center. It was conducted during January-December 2022.

Location And Time

The research was conducted at the laboratory of Zliten Medical Center. It was from 1/1/2022 to 31/12/2022.

Phoenix BD CPO System

Provide accurate, rapid identification and susceptibility results for most clinically significant aerobic and facultative anaerobic Gram-negative and Gram-positive bacteria, as well as identification of yeast and yeast-like organisms. This device used In Zliten Medical Center library to know and identifying the appropriate antibiotics to treat infection from bacteria, so that it determines the extent of sensitivity and resistance of bacteria to antibiotics, The BD Phoenix™ system provides on-panel doubling dilutions of antimicrobials and built-in detection of resistance, including for example MRSA, ESBL, HLAR. Depending on BD Phoenix™ panel type and organism identification [23].

Data Analysis

Our data of results was analyses by SPSS program.

RESEARCH RESULT

The results by using Phoenix PD CPO showed that (21.32%) of blood sample had bacterial growth, and (78.67%) of blood sample have not bacterial growth of blood sample have not bacterial growth. (Figure 1) It was the highest percentage of bacterium types *Staphylococcus heamolitics* it was (5) sample at rate of (11.1%), after which came bacteria *klebseilla pneumonia* it was (4) sample at rate of (8.88%), where each represented one sample with a rate of (2.22%) for each of them. And it was (18) sample prepared manually, as the results showed (2) *Candida* samples, and (16) bacteria samples (Figure 2).

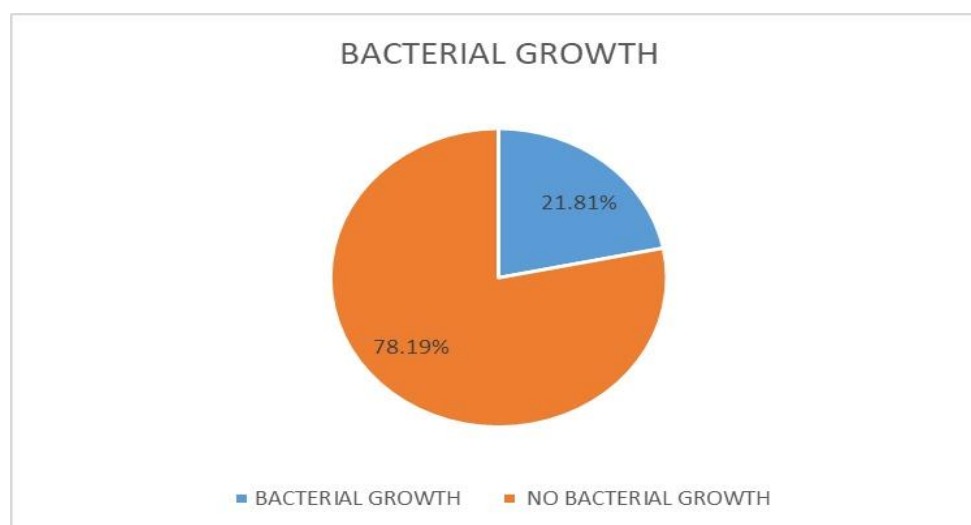


Figure 1: Percentage of growth bacteria and no growth bacteria causing sepsis in neonate at Zliten Medical Center.

As for sensitivity of the isolates to antibiotics, Gram- positive bacteria showed resistance Beta-lactam antibiotics (Figure 2). All of these gram-negative strains showed high sensitivity to the antibody it was high for beta- lactam antibiotics, which were included in the study mamely Ampicillin, Amoxicillin, Penicillin, Ceftazidime, Cefotaxime, in addition to their resistance Totrimethoprine, Tetracycline, Torflexin, Vancomycin, Profloxacin, Amikacin, gram-negative bacteria show d high resistance to most types of antibiotics used, especially Topromycin and Amikacin, and low resistance to Ciprofloxacin and Gentamycin (Figure 4).

Table (1) Types of antibiotics with percentage of bacterial resistance.

Antibiotic	Percentage of bacterial resistance
Amikacin	8.33%
Gentamicin	58.33%
Ertapenem	25%
Imipenem	50%
Meropenem	8.33%
Cephalothin	41.66%
Cefuroxime	50%
Cefoxitin	33.33%
Cefatazidim	16.66%
Ceftrixone	33.33%
Cefepime	33.33%
Aztreonam	33.33%
Ampicillin	25%
Amoxacillin-Clavulanate	83.33%
Piperacillin-Tazobactam	16.66%
Colistin	8.33%
Trimethoprim-Salfamethoxazole	41.66%
Nitrofurantoin	16.66%
Ciprofloxacin	50%
Gentamicin	8.33%
Ceforotaxim	33.33%
Ampicillin	100%
Penicillin G	41.66%
Oxacillin	33.33%
Linezolid	33.33%
Mupirocin high level	16.66%
Moxifloxacin	16.66%
Tetracyclin	33.33%
Rifampin	8.33%
Vancomicin	16.66%
Fucidic acid	8.33%
Cefotaxim	8.33%
Cefuroxime	16.66%
Teicoplanin	25%
Clindamycin	25%
Erythromicin	50%

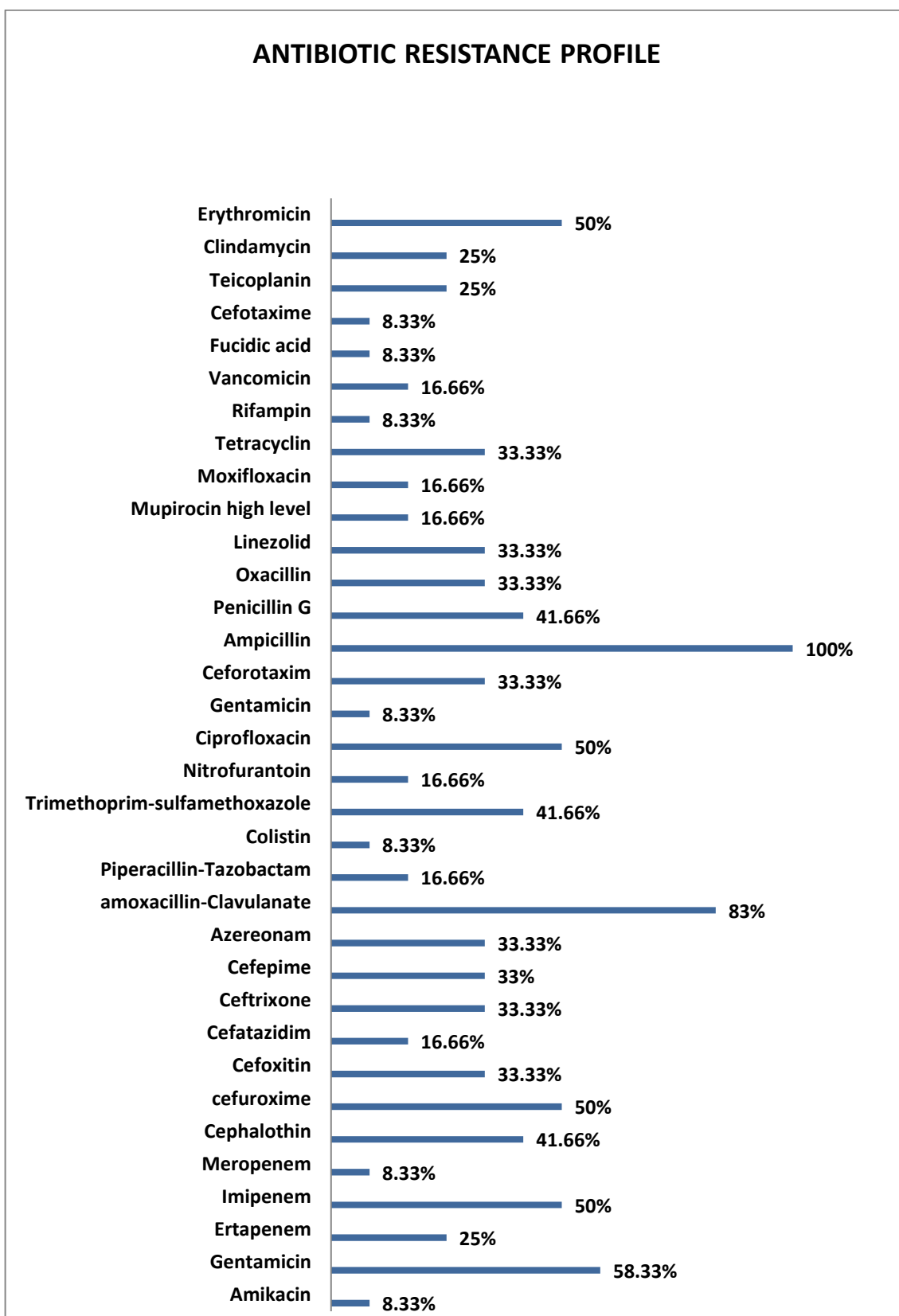


Figure (2): Percentage of resistance profile for a lot of antibiotics causing sepsis for neonate at Zliten Medical Center in 2022, The result shows Ampicillin (100%) most ineffective one and Amikacin, Meropenem, Colistin, Gentamicin, Rifampin, Fucidic acid and Cefotaxime as the most effective antibiotics.

Table (2) Represents the number of isolates with the percentage of isolates with the percentage of infection with sepsis of various types of bacteria.

Bacteria name	Sample number	Percentage%
S.epidermidis	9	20%
K.pneumonia	4	8.88%
Pseudomonas putida	1	2.22%
S.heamolytics	5	2.22%
K.oxytoca	1	2.22%
Enterococcus faccalis	1	2.22%
S.aureus	1	2.22%
k.ozaenea	1	2.22%
E.coli	1	2.22%
S.capitis	1	2.22%
Staphylococcus.spp	7	15.55 %
Streptococcus.spp	9	20%
Acinetobacter baumannii/calcoaceticus complex	1	2.22%
S.hominis	1	4.44%
Gram negative bacteria	1	2.22%

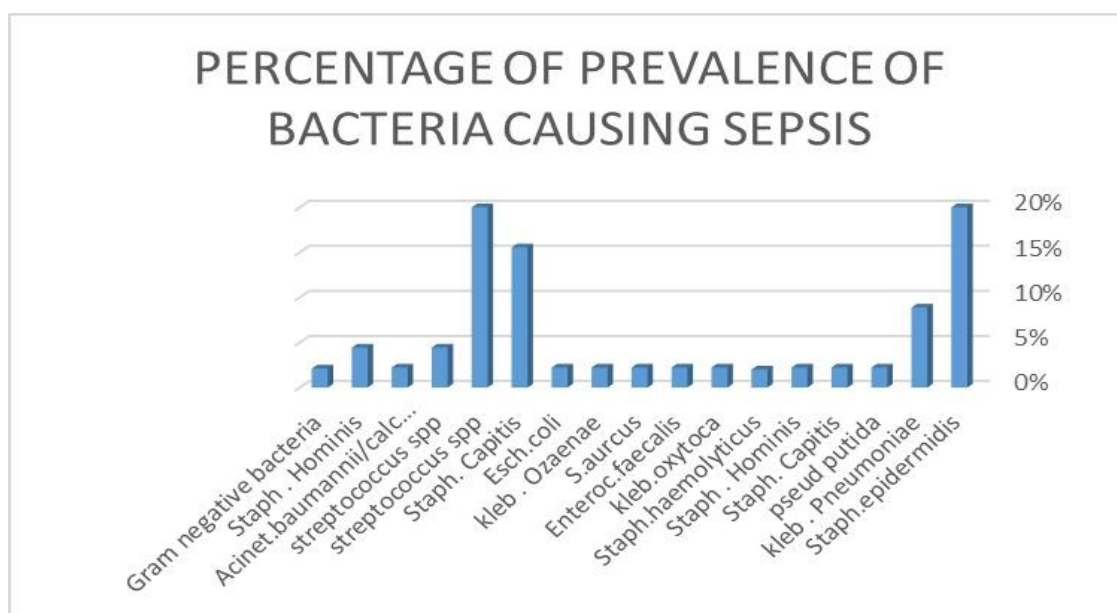


Figure 3: Percentage of bacteria causing sepsis for each type of bacteria in neonate at Zliten Medical center.

Table (3) Resistance marker for each bacterium.

Bacteria	MRSA	HLMR	BLPS	ESBL	SIMLsbP	ALERT	MDR
S. epidermidis	3	4	1	0	0	0	0
K. pneumonia	0	0	0	3	0	0	1
S. hemolyticus	3	1	0	0	1	0	0
P. putida	0	0	0	0	0	0	1
K. oxytoca	0	0	0	0	0	1	0
E. faecalis	0	0	0	0	0	0	1
S. capitis	1	0	0	0	0	0	0
K. ozaenae	0	0	0	1	0	0	0
E.coli	0	0	0	1	0	1	1
S. aureus	1	0	0	0	0	0	0
S.hominis	0	1	1	0	0	0	0
Acinetobacter baumannii/calcoaceticus complex	0	0	0	0	0	0	1

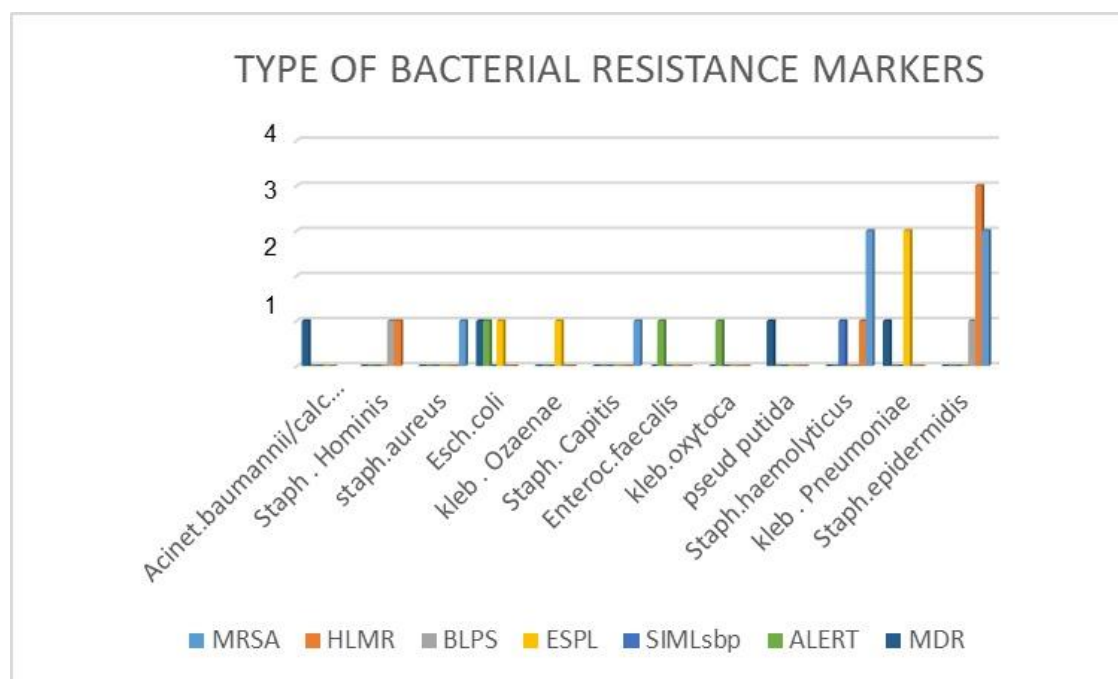


Figure 4: Resistance marker of bacteria causing sepsis in neonate at Zliten Medical Center, MRSA=Methacilline resistance S. aureus, HLMR=High level mupicocin resistance staphylococcus, BLPS=Beta lactamase producing staphylococcus, ESPL=Etended spectrum Beta lactamase, SIMLsb=Staphylococcus inducible MLsb, ALERT=Potential carbapenemase produce, MDR=Multipl drug resistance.

DISCUSSION

In our study, it turned out that the sample that have bacterial growth were (45) sample, and (26) samples were prepared by device Phoenix BD CPO, and (19) samples were prepared manually.

The lowest percentage of bacteria causing sepsis was *Acinetobacter baumannii/calcoaceticus complex*, *Pseudomonas putida*, *Klebsiella oxytoca*, *Enterococcus faecalis*, *Staphylococcus capitis*, *Klebsiella ozaenea*, *E. coli*, *Staphylococcus aureus* as percentage of each of which (2.2%), only this result came in agreement with (Mahapatra) [18] which found that the highest percentage of bacteria for sepsis was *Enterobacteria*. The results differenced with (Gales et al) [19], which showed that the most types causing sepsis are *E.coli* as for gram- positive bacteria, it did *Staphylococcus epidermidis* in the first place, it percentage was (20.45%) these results agree with (Sabiopaz et al) [20] followed by bacteria *Staphylococcus heamolytics* it percentage was (11.1%). Moreover, Gram-negative bacteria, it shows *Streptococcus spp* in first place the percentage was (20%), and observed in our study (2) sample was *Candida* it percentage was (4.4%).

We found four samples of *K.pneumoniae*, have multiple drug resistance [resistance marker] according to the Phoenix BD device, indicating that it is 100% resistance to all types of antibiotics.

In our study, four sample of *S.epidermidis* which have resistance markers was methicillin resistance staphylococcus, high level mupcocin resistant staphylococcus, beta lactamase produsing staphylococcus and staphylococcus inducible MLsb phenotype.

While *S.hominis* was two sample have B-lactamase producing staphylococcus and high level mupicocin resistance staphylococcus.

And five samples of *S.heamolyticus* have methicillin resistant staphylococcus, high level mupicocin resistant staphylococcus and staphylococcus inducible MLsb phenotype.

Acinetobacter baumannii/Calcoaceticus complex, *P.putida* and *Enterococcus faecalis* have multiple drug resistance so resistance to all antibiotics was one sample for each one. One sample of *K.oxytoca* and *E.coli* have potential carbapenemase produce, while *E.coli* have too extended spectrum beta-lactamase.

S.capitis and *S.aureus* have methicillin resistance staphylococcus, while *K.ozaeana* have extended spectrum beta-lactamase. In our study we noticed that the neonate which have sepsis by bacteria which have AIERT and MDR, they did not respond to treatment due to the bacteria is resistance to all antibiotics and mortality was among neonate infected by bacteria for example *K.pneomoniae*, *E.coli*, *Enterococcus faecalis*, *P.putida* and *acinetobacter baumannii/calcoaceticus complex*.

Neonatal sepsis is infection that specifically refers to the presence of bacterial infection in the bloodstream of newborn (such as meningitis, pneumonia, pyelonephritis, gastroenteritis) in the presence of fever [24].

Clinical criteria such as circulatory collapse or respiratory failure cannot be relied upon because these signs do not appear until very late in infants and when they do appear, death is imminent and difficult to prevent [25]. Infant sepsis can be divided into two major categories: Early sepsis refers to infection that begins within the first week of newborn is life (while some believe it only occurs within the first 725 hours of life) [26]. Infant sepsis is leading cause of neonatal death in developing countries, both in and out of hospital [27]. It is difficult to rule out sepsis in children less than 90 days of age who present with fever (defined as temperature greater than 38 celsius) by clinical detection except in cases of obvious bronchiolitis (a viral infection, not bacterial one) [28]. Currently, in the case of suspected infant sepsis, complete blood count, blood culture, and examination of the cerebrospinal fluid, including culture [29].

The child must also be immediately admitted to the hospital and treatment started as a case of confirmed infection, even before the results of the tests appear, for period of 48 hours, or until the results of the culture exclude the presence of bacteria [30].

In generally, Ampicillin with Gentamicin is first line of antibiotics to treatment of neonate with sepsis, but in our study, we noticed that all types of bacteria causing to sepsis of neonate at Zliten Medical Center in 2022 is resistant to ampicillin so can not to use to treatment.

Conclusion

Based on experiments, it can be some bacteria have resistance markers is MDR and ALERT which mean resistance to all antibiotics so not give effect to treat of sepsis in newborn, in general resistance of bacteria to antibiotic is moderate in newborn with sepsis at Zliten Medical Center.

Limitations:

The using (PCR) for identification of the gene causing resistance.

Strengths:

Phoenix BD new updated were used.

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