Original Research Article

Determining the main causes of neonatal sepsis in Neonatal Intensive Care Unit in Benghazi Medical Centre in 2022

Abstract

Background: Infections are considered the primary indicator that reflects maternal illness, placental issues, or direct fetal infection, particularly in developing or low- middle-income countries. This infection could be bacterial, viral, or fungal; these pathogenic microorganisms enter the bloodstream in the first 28 days of neonatal life causing a devastating systemic infection known as **neonatal sepsis.**

Aim: This study aimed to determine the leading causes of neonatal sepsis in the Neonatal Intensive Care Unit (NICU) at Benghazi Medical Centre (BMC) in 2022.

Research methodology: a descriptive, retrospective cross-sectional study design. Data was collected from medical records of the NICU from the infection control office for a year [from January to December 2022]. The total number of neonatal sepsis admissions were 365 cases.

Results: *Staphylococcus aureus* (40%) and (39%) and *Klebsiella pneumoniae* (31%) and (29%) were the most common bacteria that isolated from the neonates infected with sepsis and their mothers with UTIs (52%), respectively.

Conclusion: it is concluded that, the history of maternal UTI, and leaking due to PROM, were identified as risk factors for neonatal sepsis in the current study. Lack of Antenatal care and failure to deal with the maternal illnesses increase the risk of infection to the baby. Thus, it is essential to identify and address the associated factors to reduce neonatal morbidity and mortality.

Keywords: *neonatal sepsis, causative organisms, neonatal death.*

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Introduction:

There is no doubt that the first critical hours until 28 days after neonatal birth are highly susceptible life periods, as the neonates may expose to certain health problems that lead to their death. [(1)] Globally, nearly 7.6 million children die yearly from preventable causes, and about 40% of them die in their neonatal period. [(2)] In fact, it is believed that the most common cause of stillbirths or neonatal deaths worldwide is the infections, which are considered as the main indicator that reflect the maternal illness, placental issues, or direct fetal infection particularly in the developing or low- middle income countries . Since yearly, the neonatal infections are accounted for about 4 million deaths of neonates in the developing countries [(3)] In addition, it is estimated that in low-income countries the most common cause of stillbirths was the infection (15.8%).[(4)]

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This infection could be bacterial, viral, or fungal; these pathogenic microorganisms when enter into the bloodstream in the first 28 days of neonatal life causing devastating

systemic infection known as neonatal sepsis.[5] Systemic signs of circulatory collapse characterize neonatal sepsis [6] ;hence, it has known to be the most common leading cause of morbidity and mortality among neonates mainly in the developing countries. [7]

Postnatal blood stream infections is widely categorized into two categories according to the time of the symptoms onset.

Early onset neonatal sepsis (EOS) occurs after 48 hours or less until 72 hours from the birth, which mainly due to infections that are vertically transmitted from mother to her fetus during the pregnancy or delivery. [8]

Late onset neonatal sepsis (LOS) occurs after 72 hours from the neonatal birth until 28 days of their life, which usually acquired from the neonates surrounding environment and using invasive procedures.[5]

The causative microorganisms of neonatal sepsis vary according to geographical differences and countries. Since etiology of the sepsis that seen in the LMICs differ from those implicated in the HICs. In low-middle income countries such as India or Jordan, the causative agents of EOS and LOS are similar. In the resource-poor settings, the most frequently reported cause of bacterial neonatal sepsis *Klebsiella pneumoniae, Acinetobacter baumannii* and *Escherichia coli* in addition to *Staphylococcus aureus*. whereas in the developed countries, *Streptococci agalactiae* (*Group-B Streptococcus* (GBS)) and *E. coli* are most prevalent.[9]

Unfortunately, the vast majority of neonatal mortality (99%) occur in the developing nations. [10] Depending on geographical area, hospital-acquired infections account for an estimated 4% to 56% of all deaths in the neonatal period. [11] It is reported that neonatal mortality from all different causes in the low-middle income countries represent around 34 per 1000 live birth during the first week of life, while in high income countries the rate is only 5 per 1000 live births. [7]

The pathogenic organisms have classified as well according to the most frequent time to onset:

1-Early-Onset neonatal Sepsis

EOS sepsis usually results from acquiring organisms during intrapartum period. Most newborns have symptoms within 6 hours of birth.[12] Most cases are caused by *Group B streptococcus* (GBS) and gram-negative enteric organisms (predominantly *Escherichia coli*). Vaginal or rectal cultures of women at term may show GBS colonization rates of up to 35%. At least 35% of their infants also become colonized. The density of infant colonization determines the risk of early-onset invasive disease, which is 40 times higher with heavy colonization. Although only 1/100 of infants colonized develop invasive disease due to GBS, > 50% of those present within the first 6 hours of life. [12]

In addition to other more causative organisms, that may causes **EOS:**

Klebsiella pneumoniae is a Gram-negative enteric bacilli, non-motile, and opportunistic pathogen. This organism found in the soil, water, plants, and sewage. *K. pneumoniae* is one of the most frequent pathogens isolated from the intensive care units (ICUs), and the predominant leading cause of neonatal sepsis. This due to its multidrug-resistance and hypervirulent-pathotype. [13]

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Citrobacter. spp. Gram-negative, facultatively anaerobic, motile, rod-shaped bacteria, they are often found in human feces, and may be isolated from a variety of clinical specimens, which have been associated with diarrhea and secondary infections in weakened persons, occasionally causing primary septicemia [14] *Citrobacter* belongs to the family *Enterobacteriaceae* and some strains of this genus can cause serious opportunistic infections particularly involving the urinary and respiratory tracts. [15]

2-Late-Onset neonatal Sepsis

LOS sepsis usually acquired from the surrounding environment**:**

The *Staphylococci* are responsible for 30 to 60% of late-onset cases and are most frequently due to using intravascular devices (mainly central venous catheters).

Also, *Acinetobacter baumannii* is a *Gram-negative bacillus*, and opportunistic pathogen, that is aerobic, pleomorphic and non-motile. An *A. baumannii* has a high incidence among immune-compromised individuals. [16]

ventilator-associated pneumonia and bloodstream infections are the most common leading cause of death from *A. baumannii* healthcare-associated infections, this can range from 5% in general hospital wards to 54% in the intensive care unit (ICU) [17]

Enterobacter Gram-negative, non-spore-forming bacteria of the family *Enterobacteriaceae* .It is also part of the commensal microflora of the human gut are common pathogens of human infections, particularly hospital-acquired infections [18]

In addition, *E. coli* is recognized as a vital cause of late-onset sepsis, especially in extremely LBW newborns.

Contaminated respiratory equipment usually suspected in outbreaks of hospital-acquired *Pseudomonas aeruginosa* pneumonia or sepsis.

Candida species are among the most predominant human fungal pathogens universally, and consider the fourth most common cause of hospital-acquired bloodstream infections in the USA.[19] people who received broad-spectrum antibiotics are more susceptible to invasive candidiasis, as well as premature newborns. [20] As Candida species occurring in 12 to 18% of extremely LBW infants and are increasingly important causes of late-onset sepsis. [12]

3-Early- and late-onset neonatal sepsis

Certain viral infections may manifest as early-onset or late-onset sepsis for example; disseminated herpes simplex, enterovirus, adenovirus, respiratory syncytial virus.[12] Disseminated herpes simplex virus found to cause late-onset neonatal sepsis. It has been reported that 85% of babies diagnosed with disseminated HSV infection and 50% of those with central nervous system involvement died before one year of age. Another viral factor in late-onset neonatal sepsis is enteroviruses. Enterovirus infections can present with nonspecific lethargy, poor nutrition, fever, restlessness, hypoperfusion, jaundice, meningoencephalitis, myocarditis, and hepatitis [21]

Furthermore, certain viral maternal infections (rubella , cytomegalovirus) protozoal(Toxoplasma gondii), and treponemal (treponema pallidum) pathogens can be transmitted to the fetus hematogenously or transplacentaly, but most are acquired by the ascending route in utero or through passing the fetus from the colonized birth canal.[12)]

Regarding Cytomegalovirus CMV, it is not surprising to say that about 1% to 4% of women who have never been infected with CMV become infected during pregnancy. [(22)] There is an evidence that during pregnancy and lactation CMV is reactivated in 96% of healthy immune-competent seropositive mother (i.e. Presence of CMV deoxyribonucleic acid (DNA) in breast milk), then transferring during lactation to the preterm neonate. [(23)(24)] Moreover, it is estimated that between 20% and 58% of viral DNA who has detected in the colostrum within the first days of life, it has proved to cause a severe disease like sepsis in the preterm babies. [(25)]

It is important to take in your account that in the United States, cytomegalovirus CMV infection is considered as the most well-known leading viral intrauterine infection. In addition, approximately half of all women in the USA are infected with CMV before their first pregnancy. [(26)] Moreover, it is estimated that the most common nonbacterial organisms associated with stillbirth and neonatal death cases were cytomegalovirus, and parvovirus, syphilis, and herpes virus. [(4)]

The aim of this study is addressing the most frequent causing organisms among neonates infected with sepsis in NICU at Benghazi Medical Centre in 2022

Materials and Methods

A descriptive, retrospective cross sectional study design was conducted in the neonatal intensive care units (NICU) at the department of neonates in Benghazi Medical Center (BMC), in Benghazi, Libya.

Data collection was using medical records from the infection control office in the neonatal intensive care unit. The medical records included the rate of sepsis in NICU from January to December during 2022, and the pathogens causing sepsis among neonates and mothers, maternal risk factors.

The total number of neonatal admission to NICU in 2022 was 1350 infants. The total number of neonatal sepsis admission was 365 cases.

Results:

1.Rates of neonatal sepsis among neonates admitted to NICU in 2022:

The total number of neonatal delivery in BMC during 2022 was 13445 infants, and the total number of neonatal admission to NICU was 1350 infants. The total number of neonatal sepsis admission was 365 cases. The figure (1) explained the rate of admission to NICU from the sepsis, which represented about 27 % of the total admission, while the rest 73% was for the admission from the other causes.

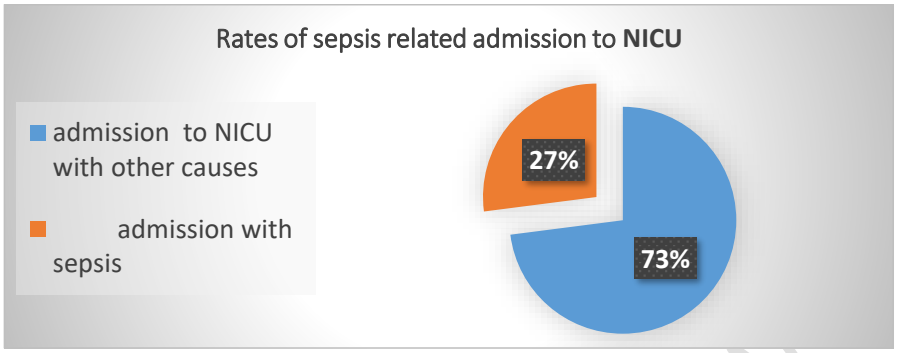

Figure (1) demonstrates the rates of sepsis among neonates admitted to NICU during 2022

2. Types of bacteria isolated from the neonates infected with sepsis in NICU during 2022:

It can be noticed from the figure (2) that, *Staphylococcus aureus* (40%) was the most common isolated bacteria from the neonates infected with sepsis. Followed by *Klebsiella pneumoniae* (31%), then *Candida albicans and Citrobacter species* (20%), and nearly the same rate *Acinetobacter baumannii* at (19%), finally *Enterobacter species* recorded the lowest rates (6%).

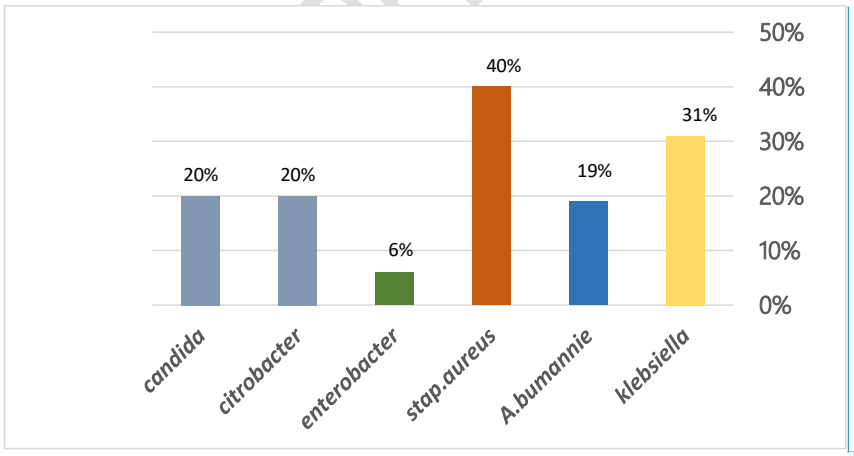

Figure (2) Types of isolated bacteria from the neonates infected with sepsis in NICU during 2022.

3.The main risk factors associated with the neonatal sepsis:

The table (1) revealed that the total number of sepsis among neonates admitted to NICU during 2022 was 365 cases. More importantly, 190 (52%) mothers whose neonates were

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nding order

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the risk factors of neonatal sepsis

infected with sepsis were suffering from urinary tract infections during pregnancy and delivery. As well as, 125 (34%) mothers were suffering from leaking of amniotic fluids for more than 18 hours before delivery. Finally, 50 (14%) neonates were infected with hospital-acquired pneumonia before they later acquire the sepsis.

How were you able to prove that they had hospital acquired pneumonia before sepsis? Remember this is a retr ospective study. You have to clearly define your defination of hospit al acquired pneumonia and sepsis **:Commented [m10]**

Table (1) The main risk factors of sepsis among the infected neonates.

Risk factors for neonatal sepsis	No. of cases	Total number of the infected cases
Mothers with Leaking	125	365
Mothers with UTIs	190	
Neonates with Hospital Acquired Pneumonia	50	

4. The most common causative organisms isolated from the mothers infected with UTIs.

It is clear from the table (2) that *Staphylococcus aureus* (39%) was the most common pathogen responsible for the mothers UTIs in this study, followed by *Klebsiella pneumonia* at about (29%), and then *Candida albicans* (19%), after that *Acinetobacter baumannii* and *Citrobacter species* found in (17.5%) cases, and the least common organism was *Enterobacter species* (4.5%).

Table (2) The most common isolated bacteria from the mothers infected with UTIs.

candida albicans	*citrobacter species*	*enterobacter species*	*Staphylococcus aureus*	*A.bumannie*	*klebsiella*
19%	17.5%	4.5%	39%	17.5%	29%

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Discussion:

It is noticed from the figure (1) that the rate of admission to NICU from the sepsis was about 27 %, while the rest 73% was for the admission from the other causes. Actually, these findings were different from the others that reported in literature, as they found that the most frequent cause of admission to NICU for both term and preterm is neonatal sepsis. [27]

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In addition to another findings that were reported by [28] about the main cause of neonatal admission to the special care baby unit at Misurata Central Hospital, which were low birth weight (26.4%), infection (sepsis) (23.8%), asphyxia (9.9%). [28] More interestingly, in Tripoli the main documented reasons for admission to the special care baby unit of the neonates who died were prematurity (43.9%), birth asphyxia (16.7%), and congenital malformations (15.9%), neonatal infections (sepsis) (14.6%). [29]

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In fact, it is important to take into your account that, the newborn outcome is a significant indicator of obstetrics and health care. Lack of pregnancy supervision and failure to prevent, detect, and deal with maternal illnesses increase the risk to the baby, which in turn increase their possibility of admission to NICU after hours from birth.

Regarding the figure (2), *Staphylococcus aureus* (40%) was the most common bacteria that isolated from the neonates infected with sepsis. Followed by *Klebsiella pneumoniae* (31%), then *Candida albicans* and *Citrobacter species* (20%), and nearly the same rate *Acinetobacter baumannii* at (19%), finally *Enterobacter species* recorded the lowest rates (6%).

From the literature there was similar findings as [30] reported that *S. aureus* was the most frequent pathogen for East and West Africa. In addition to another work has done by Pillay et al in 2021 reported that, *K. pneumoniae* classified as one of the three leading causes of EOS, with *coagulase-negative staphylococcus (CoNS)* and *A. baumannii*. [31] Really, these findings come in line with the other study that was stated, in the developing countries the most frequently reported cause of bacterial neonatal sepsis in one order or another *Klebsiella pneumoniae, Acinetobacter baumannii* and *Escherichia coli* in addition to *Staphylococcus aureus*.[32]

Actually, it is important to highlight that *S. aureus* infections were reported to be more frequent, especially in patients with catheters. As a study in the UK was in line with these findings, since, they found that from 117 sepsis episodes, *S. aureus* growth was determined in 50% of the cases that using the central catheters.[33]

Furthermore, in one order or another, the results agreed with a study by Özdemir et al, since the isolated *S. aureus* was reported as the most common cause of late sepsis cases, followed by *K. pneumoniae* and *S. epidermidis.*[34] Furthermore, Pillay D, and colleagues did supportive study, which demonstrated the common pathogens that were included *coagulase-negative staphylococci* (53.5%), *Klebsiella pneumoniae* (11.6%), *enterococci* (9.3%), and *Acinetobacter baumannii* (7.7%).[31]

In reality, a study by Shaw et al. revealed that the existence of *Enterobacteriaceae and staphylococci* was associated with LOS, which may associated with long hospitalization in NICUs.[35] This can be emphasized by the fact that says long-term hospitalization is recognized as one of the main factors associated with the increased risk of neonatal mortality from sepsis. [8]

Moreover, the current study findings listed *Candida albicans* and *Citrobacter species* (20%), as the third pathogens responsible for neonatal sepsis among the admitted cases. similar findings were existed, since a study reported *Candida spp*. As the third most frequent cause of late-onset neonatal sepsis particularly in premature babies with long-term hospitalization and babies weighing <1500 gr.[36] In simple words, limited infection prevention control (IPC) and hygienic practices in LMICs, regardless of the time of onset, result in all infections being hospital acquired. [37]

It is clear from the table (1) that among 365 cases of neonatal sepsis, about 190 (52%) of mothers whose neonates were infected with sepsis were suffering from urinary tract infections during pregnancy and delivery. As well as, 125(34%) of mothers were suffering

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from leaking of amniotic fluids for more than 18 hours before delivery. Finally, 50(14%) of neonates were infected with hospital-acquired pneumonia before they later acquire the sepsis.

In fact, these results indicates to the maternal UTIs as the most laboratory proved leading cause to neonatal sepsis. More interestingly, a study by Rafi M A,.et al, 2020, evidenced that mothers who faced UTIs during the gestational period, their babies were five times more likely to develop neonatal sepsis.[38] Furthermore, another study by Azami M et al emphasized these results, as they found the neonates born to mothers who got UTI during pregnancy had higher likelihood of developing sepsis than those born to mothers without prenatal UTI. This could be demonstrated by, the mothers who suffer from untreated UTIs even asymptomatic bacteriuria during pregnancy are more likely to have early rupture of membrane leading to pre-term delivery, chorioamnionitis and anemia. [39]

Furthermore, supportive study by Woldu, M A. et al revealed that, maternal urinary tract infections and sexually transmitted infections are often associated with early onset neonatal sepsis, particularly if untreated during the third trimester of gestation, and it may be associated with neonatal sepsis following the colonization of the birth canal by the infectious agent. [40]

From the table (2) *Staphylococcus aureus* (39%) was the most common pathogen responsible for the mothers UTIs in this study, followed by *Klebsiella pneumonia* at about (29%), and then *Candida albicans* (19%), after that *Acinetobacter baumannii* and *Citrobacter species* found in (17.5%) cases, and the least common organism was *Enterobacter species* (4.5%).

It is necessary to mention that, the pathogens that were isolated from maternal UTIs were similar to those organisms isolated from their infected neonates. in reality the current findings showed the association between UTI, and Premature rupture of membrane that leads to leaking of amniotic fluid then in turn causes the pathogenic organisms transmit into amniotic sac, after that the aspiration of baby to the infected amniotic fluid may occur and causes birth asphyxia, that later leads to neonatal sepsis. These findings were also evident by a study by Hasan and others in 2011, since they claimed that premature rupture of membrane and prolonged labor increases the chance of ascending microorganisms from the birth canal into the amniotic sac then birth asphyxia occurs which frequently leads to sepsis.[41]

Conclusion:

This study found different maternal and neonatal determinants of neonatal sepsis. A history of maternal UTI, and leaking due to PROM, were identified as the main associated factors for neonatal sepsis in the current study. As a result, it is critical to identify and address the associated factors to reduce neonatal morbidity and mortality. *Staphylococcus aureus* and *Klebsiella pneumoniae* were the most predominant bacteria that isolated from the maternal UTIs and their neonates whose infected with sepsis. s

ETHICAL APPROVAL:

Ethical approval was obtained from the Ethics Committee of faculty of public health.

References:

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