



Determining the Main Causes of Neonatal Sepsis in the Neonatal Intensive Care Unit in Benghazi Medical Centre in 2022

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Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

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ABSTRACT

Background: Neonatal sepsis is considered the most common leading cause of morbidity and mortality among neonates mainly in developing countries. In the resource-poor settings, the most frequently reported cause of bacterial neonatal sepsis was from *Klebsiella pneumoniae*, *Acinetobacter baumannii*, and *Escherichia coli* in addition to *Staphylococcus aureus*. Whereas in the developed countries, *Streptococci agalactia* (Group-B *Streptococcus* (GBS) and *E. coli* are most prevalent.

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 was 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

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mothers with UTIs (52%), respectively. about 190 (52%) mothers whose neonates were infected with sepsis were suffering from urinary tract infections during pregnancy and delivery. As well as 125 (34%) mothers were suffering from leaking amniotic fluids for more than 18 hours before delivery. Finally, 50 (14%) neonates were infected with hospital-acquired pneumonia.

Conclusion: it is concluded that *Staphylococcus aureus* (39%) was the most common pathogen responsible for the mother's UTIs in this study. In addition, 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 maternal illnesses increase the risk of infection in 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; bloodstream infections.

1. INTRODUCTION

There is no doubt that the first critical hours until 28 days after neonatal birth are highly susceptible life periods, as neonates may be exposed to certain health problems that lead to their death [1]. Unfortunately, the vast majority of neonatal mortality (99%) occurs in developing nations [2]. Besides that, about 4 million cases of neonatal deaths that had occurred in developing countries were attributed to neonatal infections [3].

This infection could be bacterial, viral, or fungal; these pathogenic microorganisms when entering into the bloodstream in the first 28 days of neonatal life cause a devastating systemic infection known as Neonatal Sepsis (NS) [4]. Neonatal sepsis is considered the most common leading cause of morbidity and mortality among neonates mainly in developing countries [5].

The causative microorganisms of neonatal sepsis vary according to geographical differences and countries. Since etiology of the sepsis seen in the Low-income countries (LMICs) differs from those implicated in the High-income countries (HICs). In low-middle-income countries such as India or Jordan, the causative agents of EOS and LOS are similar. In resource-poor settings, the most frequently reported cause of bacterial neonatal sepsis was from *Klebsiella pneumoniae*, *Acinetobacter baumannii*, and *Escherichia coli* in addition to *Staphylococcus aureus*. Whereas in the developed countries, *Streptococci agalactia* (*Group-B Streptococcus* (GBS) and *E. coli* are the most prevalent [6].

Postnatal bloodstream infections and the pathogenic responsible organisms are widely categorized into two categories according to the time of the symptom's onset:

1.1 Early-Onset Neonatal Sepsis (EOS)

Occurs after 48 hours or less and up to 72 hours from the birth, which is more often associated with infections that are vertically transmitted from the mother to her fetus during the pregnancy or delivery [7]. (I.e. Maternal history of urinary tract infections, and sexually transmitted infections during the index gestation [4].

Most newborns have symptoms within 6 hours of birth, [8] and 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" [8].

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

"Klebsiella pneumoniae is a Gram-negative enteric bacillus, non-motile, and opportunistic pathogen. This organism is 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 is due to its multidrug resistance and hypervirulent-pathotype" [9].

"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". [10] "*Citrobacter* belongs to the family *Enterobacteriaceae* and some strains of this genus can cause serious opportunistic infections, particularly involving the urinary and respiratory tracts" [11].

1.2 Late-Onset Neonatal Sepsis (LOS)

Occurs after 72 hours from the neonatal births and up to 28 days of their life, which is usually acquired, from the surrounding environment and using invasive procedures [4]. "The *Staphylococci* are responsible for 30 to 60% of late-onset cases and are the most frequently due to using intravascular devices (mainly central venous catheters)" [8].

"Also, *Acinetobacter baumannii* is a Gram-negative bacillus, an opportunistic pathogen, that is aerobic, pleomorphic, and non-motile. An *A. baumannii* has a high incidence among immune-compromised individuals" [12]. "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)" [13].

"*Enterobacter* Gram-negative, non-spore-forming bacteria of the family *Enterobacteriaceae*. It is also part of the commensal micro flora of the human gut and are common pathogen of human infections, particularly hospital-acquired infections" [14]. "In addition, *E. coli* is recognized as a vital cause of late-onset sepsis, especially in extremely LBW newborns" [8].

"Contaminated respiratory equipment is usually suspected in outbreaks of hospital-acquired *Pseudomonas aeruginosa* pneumonia or sepsis" [8]. "*Candida* species are among the most predominant human fungal pathogens universally and are considered the fourth most common cause of hospital-acquired bloodstream infections in the USA" [15]. "People who received broad-spectrum antibiotics are more susceptible to invasive candidiasis, as well as premature newborns" [16]. "As *Candida* species occur in 12 to 18% of extremely LBW infants and are increasingly important causes of late-onset sepsis" [8].

1.3 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, and respiratory syncytial virus [8]. "Disseminated herpes simplex virus was 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" [17]

"Furthermore, certain viral maternal infections (rubella, cytomegalovirus) protozoal (*Toxoplasma gondii*), and treponemal (*Treponema pallidum*) pathogens can be transmitted to the fetus hematogenous or transplacentally, but most are acquired by the ascending route in utero or through passing the fetus from the colonized birth canal" [8].

Regarding Cytomegalovirus CMV, about 1% to 4% of women who have never been infected with CMV become infected during pregnancy [18]. There is evidence that during pregnancy and lactation, CMV is reactivated in 96% of the healthy immune-competent seropositive mother (i.e. Presence of CMV deoxyribonucleic acid (DNA) in breast milk), then transferring during lactation to the preterm neonate [19,20]. Moreover, between 20% and 58% of viral DNA detected in the colostrum within the first days of life, has proved to cause a severe disease like sepsis in preterm babies [21].

In the United States, cytomegalovirus CMV infection is considered 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 [22]. Additionally, the most common nonbacterial organisms associated with stillbirth and neonatal death cases were cytomegalovirus, parvovirus, syphilis, and herpes virus [23].

This study aims to address the most frequent causing organisms among neonates infected with sepsis in the NICU at Benghazi Medical Centre in 2022.

2. 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 2022, and the pathogens causing sepsis among neonates and mothers, maternal risk factors.

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

3. RESULTS

3.1 Rates of Neonatal Sepsis among Neonates Admitted to NICU in 2022

The total number of neonatal deliveries in Benghazi Medical Centre (BMC) during 2022 was 13445 infants, and the total number of neonatal admissions to NICU was 1350 infants. The total number of neonatal sepsis admissions was 365 cases. Fig. 1 explains the rate of admission to NICU from sepsis, which represented about 27 % of the total admission, while the rest 73% was for admission from other causes.

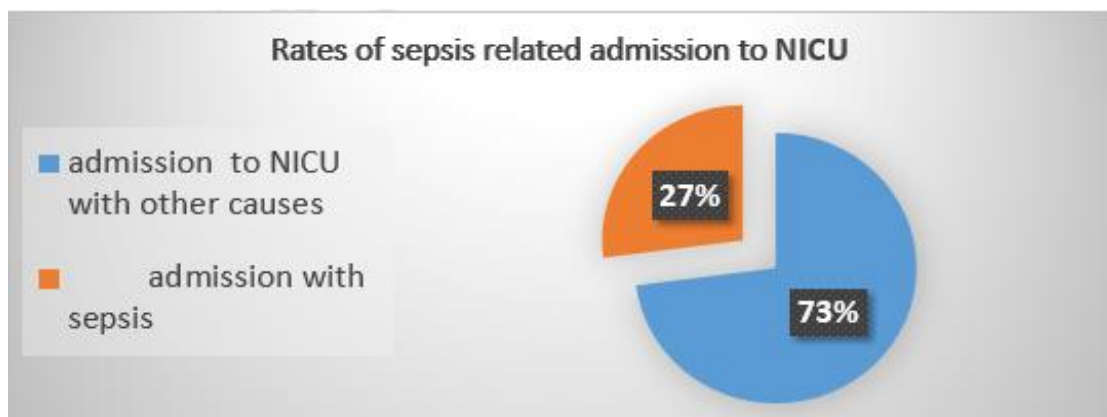


Fig. 1. Demonstrates the rates of sepsis among neonates admitted to NICU during 2022

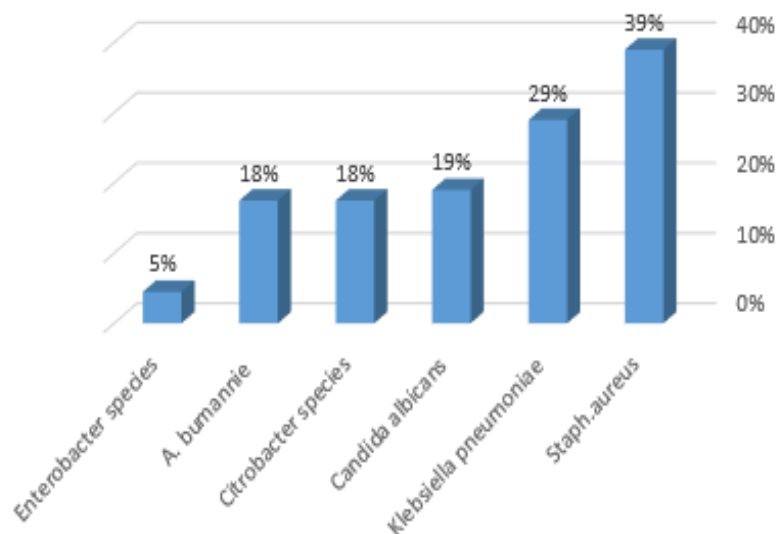


Fig. 2. Types of the bacteria isolated from the neonates infected with sepsis in NICU during 2022

3.2 Types of bacteria isolated from the neonates infected with sepsis in NICU during 2022

It can be noticed from Fig. 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 at *Acinetobacter baumannii* (19%), and finally *Enterobacter species* recorded the lowest rates (6%).

3.3 The Main Risk Factors Associated with the Neonatal Sepsis

Table 1 revealed that about 190 (52%) mothers whose neonates were infected with sepsis were suffering from urinary tract infections during pregnancy and delivery. As well as 125 (34%) mothers were suffering from leaking amniotic fluids for more than 18 hours before delivery. Finally, 50 (14%) neonates were infected with hospital-acquired pneumonia.

3.4 Types of the Bacteria Isolated from the Mothers Infected with UTIs

It is clear from Fig. 3. that *Staphylococcus aureus* (39%) was the most common pathogen

responsible for the mother's UTIs in this study, followed by *Klebsiella pneumoniae* 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%).

4. DISCUSSION

Regarding the Fig. 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 at *Acinetobacter baumannii* at (19%), and finally *Enterobacter species* recorded the lowest rates (6%).

From the literature, there were similar findings as [24] reported that *S. aureus* was the most frequent pathogen in East and West Africa. further work done by Pillay et al in 2021 reported that *K. pneumoniae* was classified as one of the three leading causes of EOS, with *coagulase-negative staphylococcus* (CoNS) and *A. baumannii* [25]. Additionally, in developing countries the most frequently reported cause of bacterial neonatal sepsis in one order or another is *Klebsiella pneumoniae*, *Acinetobacter baumannii*, and *Escherichia coli* in addition to *Staphylococcus aureus* [26].

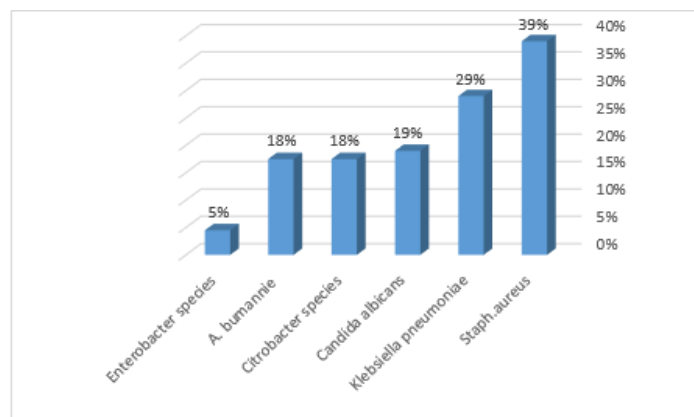


Fig. 3. Types of the bacteria isolated from the mothers infected with UTIs

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

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

It is important to highlight that *S. aureus* infections were reported to be more frequent, especially in patients with catheters. A study in the UK agreed 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 [27]. In addition, another study found nearly similar outcomes, since the isolated *S. aureus* was reported as the most common cause of late sepsis cases, followed by *K. pneumoniae* and *S. epidermidis* [28]. Moreover, Pillay D, and colleagues revealed the commonest pathogens that were isolated *coagulase-negative staphylococci* (53.5%), *Klebsiella pneumoniae* (11.6%), *enterococci* (9.3%), and *Acinetobacter baumannii* (7.7%) [25].

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 [29]. This can be emphasized by the fact that long-term hospitalization is recognized as one of the main factors associated with the increased risk of neonatal mortality from sepsis [7].

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 have existed since a study reported *Candida spp.* Is the third most frequent cause of late-onset neonatal sepsis particularly in premature babies with long-term hospitalization and babies weighing <1500 gr [30] In simple words, limited infection prevention control (IPC) and hygienic practices in LMICs, regardless of the time of its onset, it results in all infections being hospital-acquired [31].

It is clear from 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. Also 125(34%) of mothers were suffering 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 acquired the sepsis.

These results indicate that maternal UTIs as the most laboratory-proven leading cause of neonatal sepsis. More interestingly, a study by Rafi M A, et al, 2020, evidenced that mothers who faced UTIs during the gestational period, had their babies were five times more likely to

develop neonatal sepsis [32]. Furthermore, a study by Azami M et al emphasized these results, as they found that neonates born to mothers who got UTI during pregnancy had a 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 [33].

Furthermore, a 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 [34].

From Fig. 3 *Staphylococcus aureus* (39%) was the most common pathogen responsible for the mother's UTIs in this study, followed by *Klebsiella pneumonia* at about (29%), and then *Candida albicans* (19%), after *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 the membrane, that leads to the leaking of amniotic fluid then in turn causes the pathogenic organisms to transmit into the amniotic sac, after that the aspiration of the baby to the infected amniotic fluid may occur and causes birth asphyxia, that later leads to neonatal sepsis. These findings were also evident in different studies one 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 [35].

Another study also showed that neonatal resuscitation at birth was a substantial risk factor for neonatal bloodstream infections. As, newborns who had a history of resuscitation at birth were 2.3 times had higher rate of death from sepsis, in comparison with those who had not been resuscitated. Resuscitation may be performed with contaminated equipment, and because of prematurity and an undeveloped

immune system, that leads the neonates to a higher risk of complications such as death in LOS. Whereas, chorioamnionitis and aspiration of the neonates to infected amniotic fluid secretions in the birth canal, lead to pneumonia and sepsis manifested by neonatal asphyxia, which more often results in death from EOS complications [36].

A recent study also proved that prematurity with lower birth weight, being a male neonate, and having a history of resuscitation at birth all of these were identified as risk factors for neonatal sepsis [37].

Thus, 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 increases their possibility of admission to NICU after hours from birth.

5. CONCLUSION

This study revealed that *Staphylococcus aureus* and *Klebsiella pneumoniae* were the most predominant bacteria isolated from the maternal UTIs and their neonates who were infected with sepsis. In addition to 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.

CONSENT

It is not applicable.

ETHICAL APPROVAL

Ethical approval was obtained from the Ethics Committee of the Faculty of Public Health.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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