

Original Article

Determining the main risk factors associated with neonatal death from sepsis in Neonatal Intensive Care Unit (NICU) in Benghazi Medical Centre (BMC) during 2020

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Abstract:

Neonatal sepsis has known to be the third most common leading cause of death during the neonatal period worldwide. It accounts for nearly 26% of neonatal mortality in the developing countries. Hence, understanding the causes of death in NICU and highlighting the modifiable factors associated with death could possibly reduce infant mortality. Aim: this study was to assess the contributing factors of death from neonatal sepsis (early and late) among neonates died in NICU at Benghazi Medical Centre in 2020. methodology: This study was a descriptive, retrospective and cross-sectional design. Death certificates for neonates died from sepsis in NICU at BMC were collected from 1-3-2023 to 31-3-2023 march. The data was analyzed by using (SPSS version 28), Chi-square and *p. value of* < 0.05 was considered statistically significant for all statistical tests. Results: The neonates with BW < 2.5 Kg were more likely to die from neonatal sepsis 75% than with the neonates > 2.5 Kg that rate was less at 24.5%. Male neonates showed more predominance of death from sepsis than females at 64% and 35.8 % respectively. The majority of death occurs among preterm neonates (81%) in EOS 54.7%, whereas, LOS death was about 45.3%. Conclusion: The outcomes of the current study demonstrated that, being premature 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 in the current study. Ensuring the early detection of STI, UTI and trans placental infections among mothers, by routine antenatal screening to decrease its impact on the neonate.

Key words: Preterm, Early Onset Sepsis, late Onset Sepsis, risk factors, neonatal death.

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Introduction

fourth most frequent cause of death in neonatal period from 2014-2019 in NICU in Benghazi Medical Centre (8,9) . However, in 2020 a study conducted in Benghazi Pediatric Hospital demonstrated that most frequent causes of neonatal-related deaths were prematurity, then neonatal sepsis in the first week of life (10). Furthermore, there were similar findings reported from Al-Bayda Medical Centre in 2021, that highlighted that prematurity and its complications such as sepsis, then birth asphyxia were the most common causes of neonatal mortality. Hence, the rate of neonatal death in the hospital was about 7.6%(11).

Sepsis 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(12). The higher rates of EOS in the developing countries is reported to be high as a result of inadequate antenatal care, high rate of birth at home, unhygienic birth and umbilical cord care practices, and late recognition of conditions that pose a risk of infection in the mother or baby(13) . Late onset neonatal sepsis (LOS) occurs after 72 hours from the neonatal birth until 28 days of their life (3) .Invasive procedures, such as frequent blood sampling, intubation, mechanical ventilation, catheter or probe insertion, insufficient breastfeeding, long-term parenteral nutrition, low stomach acid and surgical interventions especially increase the risk of late-onset sepsis(13).

1.2 Risk Factors Associated with the Newborn:-

Globally, around 2.4 million neonatal death occur during the first month of their lives in 2019. Daily more than 6700 neonatal death occur, around one third of all neonatal mortality occur during the first day of life and by the end of the first week more than three quarters of death occur(1) . Nationally, according to a report from Tripoli medical center, 65.3% of the neonatal deaths occurred in the first week of neonatal life, while 21.5% died the late neonatal period. In mainly from prematurity and its complications such as sepsis(2) .The sepsis or as it known as blood stream infection could be bacterial, viral, or fungal(3). this infection clearly occur when these pathogenic microorganisms enter into the bloodstream in the first 28 days of neonatal life causing devastating systemic infection known as neonatal sepsis (NS)(3). Systemic signs of circulatory collapse characterize neonatal sepsis(4).Severe sepsis invasions leading to one, two, or more organ dysfunctions such as cardiovascular organ dysfunction or acute respiratory distress syndrome, which is without timely treatment, can rapidly lead to tissue damage, organ failure, and death(5). NS accounts for nearly 26% of neonatal mortality in developing countries(6) .According to WHO estimations around 400 000 to 700 000 of neonatal death from sepsis reported in 2018. Approximately 75% of these deaths happened in South-East Asia and Sub-Saharan Africa (7) .

Neonatal sepsis has also known to be the third most common leading cause of death during the neonatal period worldwide. (5) While in Benghazi, neonatal sepsis was reported to be the

of group B streptococcus and E. coli. Later, the few organisms in the vaginal vault are able to proliferate rapidly after PROM. Thus, organisms usually reach the bloodstream by fetal aspiration or swallowing of contaminated amniotic fluid, leading to bacteremia(16) .

- Intrapartum maternal fever (>38 °C),
- Delivery earlier than 37 weeks of gestation,
- Maternal group B streptococcal (GBS) colonization and having a history of GBS-infected baby in a previous pregnancy, detection of GBS positive bacteriuria during pregnancy, positive intrapartum nucleic acid amplification tests for GBS increases the risk of early neonatal sepsis (17) .
- Maternal history of urinary tract infections, and sexual transmitted infections during the index pregnancy (3) .
- Mode of delivery (caesarean section or vaginal delivery) (3) .

More importantly, understanding the causes of death in NICU and highlighting the modifiable factors associated with death could possibly reduce infant mortality (10) .As this emphasized by the WHO estimations that found that, the early detection and treatment of the cases can prevent about 84% of neonatal sepsis-related mortality (18) . Thus, The aim of this study was to assess the contributing factors of death from sepsis (early and late) among neonates died in NICU at Benghazi Medical Centre in 2020.

2. Methodology: This study was conducted in the neonatal intensive care

- Prematurity (< 37weeks): Premature babies with low birth weight, have a risk of developing sepsis three to ten times higher than full-term babies with normal birth weight develop. Moreover, low levels of transplacental maternal IgG levels in preterm babies are among the substantial risk factors for acquiring sepsis (14) .
- Low birth weight (less than 2500g)
- Fetal distress (14).
- Low APGAR score (Appearance, Pulse, Grimace, Activity, Respiration) (15) .
- Resuscitation of the baby (14).

1.3 Maternal risk factors:-

- Multiple pregnancies increase the risk of early-onset sepsis,
- Chorioamnionitis is estimated to be one of the most important risk factors in early-onset neonatal sepsis, Chorioamnionitis is defined as an acute inflammation of fetal membranes and amniotic fluid. It often develops due to the micro infusion of amniotic fluid because of prolonged rupture of membranes. Fever, leukocytosis, foul-smelling or intense discharge, abdominal tenderness in the mother and fetal tachycardia are among the clinical findings of chorioamnionitis. (14)
- Premature rupture of membranes (PROM)(> 18 hours):Many mothers with low-density colonization give birth to babies with high-density colonization that lead them to a major risk. Amniotic fluid contaminated with meconium or vernix caseosa promotes growth

number of neonates died from the sepsis during the year 2020 become 53 neonates. The data was analyzed by using the Statistical package for Social Sciences (SPSS version 28 software), Chi-square and *p. value of* < 0.05 was considered statistically significant for all statistical tests.

Results:

Table (1) Shows that most of the newborns are from the preterm neonates, where their percentage was 81.1% in this study, and the percentage for the post-term and term neonates each of them represents 9.4%.

units (NICU) at the department of neonates in Benghazi medical center, in Benghazi. Libya. This study used a descriptive, retrospective cross sectional design, this approach used all death certificates for neonates died from sepsis in NICU at the department of neonates at Benghazi Medical Centre, these certificates included the age of infants at death and sepsis related complications, birth weight and gender. The obtained death certificates recorded from 1-2-2020 to 31 -12- 2020

This study targeted the neonates died from sepsis in NICU in BMC. All the death certificates with missed information were excluded from the study. Thus, the total

Table (1) distribution of neonatal death according to the age groups

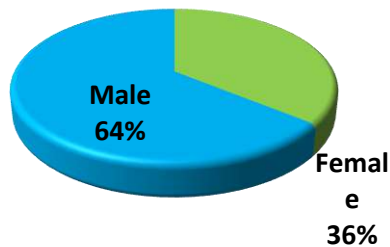


Figure No. (1) Shows that the variable is the type of newborn child, the majority of which are males, with a percentage of 64.2%, and in contrast, from females, where their percentage was 35.8%, in the study sample.

Age Groups	Frequency	%
post-term	5	9.4%
Preterm	43	81.1%
Term	5	9.4%
Total	53	100%

Figure (1) Distribution of neonatal death according to the gender

Figure (2) the mortality complications of sepsis

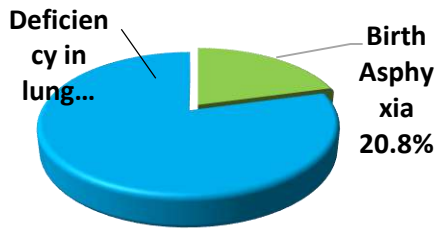


Figure No. (2) shows that the variable is the mortality complication of sepsis of newborn child, the majority of which are suffered with Deficiency in lung function, with a percentage of 79.2%, while Birth asphyxia percentage was 20.8%, in the study sample.

Table (2) the classification of neonatal death according to the time of sepsis onset.

Times of neonatal sepsis onset	Frequency	%
Early onset sepsis	29	54.7%
late onset sepsis	24	45.3%
Total	53	100%

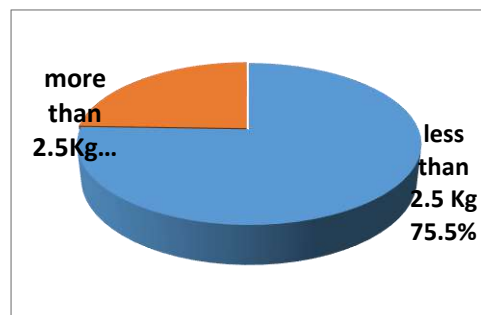


Table No. (2) Shows that the variable is the time of neonatal sepsis onset, the majority of death occurs in Early onset sepsis, with a percentage of 54.7%, whereas, Late onset sepsis death was about 45.3%, in the study sample.

Figure(3)distribution of neonatal death according to the birth weight

Figure No. (3) Shows that the variable is Birth weight of neonates, the vast majority of death occurs among the group less than 2.5 Kg, with a percentage of 75.5%, and nearly the quarter, for the category

more than 2.5 Kg, where their percentage in this study was 24.5%.

Table (3) the relationship between the neonatal death according to birth weights and time of sepsis onset

Classification of sepsis	Total	P_value
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birth-weight		Early onset sepsis	Late onset sepsis		Chi-Square	
less than 2.5 Kg	N	24	16	40	1.837	0.212
	%	45.3%	30.2%	75.5%		
greater than 2.5 Kg	N	5	8	13		
	%	9.4%	15.1%	24.5%		
Total	N	29	27	53		
	%	54.7%	45.3%	100%		

Table No. (3) Shows the relationship between the variables (Classification of sepsis EOS&LOS) and (birth-weight). The neonates with birth weight less than 2.5 Kg were more likely to die from neonatal sepsis 75% than with the neonates more than 2.5 Kg that rate was less at 24.5%. In addition, it can be noticed that newborns with birth weight less than 2.5 Kg were more likely to die in EOS at rate 45% than

in LOS, which represented 30%. On the other hand, the newborns weighed more than 2.5 kg Where less likely to die in EOS than LOS their ratios were 9.4%, 15% respectively. where the relationship is not statistically significant using chi-square (1.837) and the probability value (0.212), which is more than the level of statistical significance (0.05).

Table (4) the relationship between the neonatal death according to gender and time of sepsis onset

Gender	Classification of sepsis			Total	Chi-Square	P_value
		Early onset sepsis	late onset sepsis			
Female	N	8	11	19	1.901	0.138
	%	15.1%	20.8%	35.8%		
Male	N	21	13	34		
	%	39.6%	24.5%	64.2%		
Total	N	29	24	53		
	%	54.7%	45.3%	100%		

Table No. (4) describe the association between the variables (Classification of sepsis) and Gender. This study found that the highest incidence of neonatal death from sepsis has shown among males more than females at 64% and 35.8 % respectively. For the female infants 15.1% of them had died in early onset sepsis, and 20.8% of them had died in the late-onset

sepsis. On the other hands, the male newborns 39.6% of them had died in early onset sepsis and 24.5% had died in late-onset sepsis, where the relationship is not statistically significant using chi-square (1.901) and the probability value (0.138), which is more than the level of statistical significance (0.05).

Table (5) clarifies the relationship between the gestational age groups and the Classification of sepsis.

gestational age	Classification of sepsis		Total	Chi-Square	P_value
	Early onset sepsis	late onset sepsis			
Post-tem	N	1	4	3.443	0.179
	%	1.9%	7.5%		
Preterm	N	26	17		
	%	49.1%	21.1%		
Term	N	2	3		
	%	3.8%	5.7%		
Total	N	29	24		
	%	54.7%	45.3%		
			53	100.0%	

Table No. (5) explains the association between the variables classification of sepsis and the gestational age. It can be seen that the highest rates of death from neonatal sepsis were noticeable among preterm neonates at 81%. Of whom 49% of preterm died in EOS, and 21% of them died in the LOS. Regarding term and post term died neonates, the incidence of sepsis was similar for the both groups in

the rate 9.4%, but the difference observed among the time of sepsis onset between the two groups and for both LOS higher than EOS 7.5% for the post term and 5.7% for the term died neonates. Where the relationship is not statistically significant using chi-square (3.443) and the probability value (0.179), which is more than the level of statistical significance (0.05).

Table(6) the relationship between the mortality complications of sepsis and the Classification of sepsis.

mortality complications of sepsis		Classification of sepsis		Total	Chi-Square	P-value
		Early onset sepsis	late onset sepsis			
Birth asphyxia	N	4	7	11	1.887	0.194
	%	7.5%	13.2%	20.8%		
Deficiency in lung function	N	25	17	42		
	%	47.2%	32.1%	49.2%		
Total	N	29	24	53		
	%	45.7%	45.3%	100%		

Table No.(6) Shows the relationship between the variables Classification of sepsis and mortality complication of sepsis. it is important to highlight that, the rate of neonates who died in EOS with deficiency in lung function 47%, was higher than those neonates who died in EOS with a complication like birth asphyxia 7.5%. However, in the previous category death in LOS was higher than EOS 13%, 7.5% respectively. Where the relationship is not statistically significant using chi-square (1.887) and the probability value (0.194), which is more than the level of statistical significance (0.05).

Discussion:

The findings of this study demonstrated that, there was a predominance of death among preterm neonates 81% over the death among term and post-term neonates for both the rate was 9.4%. This consistence with a study by Birrie E, et al they highlighted that death among premature neonates is 4.4 times more likely as compared to post-term death (19). Additionally, Neonates born at term have a lower risk of neonatal sepsis

compared to premature <37 weeks of gestational age. Very low birth weight (VLBW, <1500g) or extremely low birth weight (ELBW) neonates(20) .This due to poor host defenses among preterm neonates, thus they are more sensitive to suffer from neonatal sepsis. In other words, postnatal infection does not usually occur in full term Babies. This is due to the transplacental passage of maternal IgG antibodies that acquired after 28 weeks of pregnancy and completes its maximal speed during the third trimester. Very preterm babies do not have this protection, and therefore are at risk to develop a severe infection like sepsis(5) .

Moreover, there were various studies in the literature in the line with the current study findings. A study conducted in NICU of Benghazi Pediatric Hospital in 2020 established that the most frequent cause of neonatal death were prematurity, then neonatal sepsis, and congenital heart disease(10) Furthermore, another study done by Aggarwal. A, et al in 2013 used World Health Organization (WHO) verbal autopsy tool in determining major causes

of neonatal deaths. Their findings explained the four most common causes of neonatal deaths were sepsis (29.1%), preterm birth (27.8%), birth asphyxia (27.2%), and congenital anomalies (11.5%) (21).

Much more study in Misurata, neonatal mortality rate was 1.2% and the death rate in the Special Care Baby Unit was 10.06% during the study period. The majority of deaths (88%) occurred during the early neonatal period. The causes of neonatal deaths were prematurity (37.5%), birth asphyxia (20%), neonatal sepsis (18%) congenital malformations (10%) and other different reasons (13.7%) (22).

The current study findings also explained that early onset sepsis was more prevalent at 54.7%, than late onset sepsis, which represented 45% of prevalence. These findings agreed with a previous study (4) which reported the EOS was much more common than LOS. Other studies showed higher prevalence of EOS in Indonesia 63% and Australia 32% than LOS (12, 23). Nonetheless, some studies showed contrast results like a study by Pillay D, and colleagues Late-onset sepsis (86.8%) predominated over early-onset sepsis (13.2%) (24). From the table (3) the findings emphasized that the neonates with birth weight less than 2.5 Kg were more likely to die from neonatal sepsis 75% than with the neonates more than 2.5 Kg their rate was less at 24.5%. In addition, it can be noticed that newborns with birth weight less than 2.5 Kg were more likely to die in EOS at rate 45% than in LOS, which represented 30%. The relationship is not statistically significant using chi-square (1.837) and the probability value (0.212), which is more than the level of statistical significance

(0.05). These findings disagreed with the previous study results that demonstrated VLBW neonates requiring prolonged hospitalization are more susceptible to LOS, due to limited infection control interventions resulting in hospital-acquired outbreaks, particularly in neonatal intensive care units (NICU) (25). In addition, a study in Saudi also disagreed with the current findings, they found that neonates with low birth weight (<1500g) had LOS 60.8% and 27.3% had EOS (26). More importantly, Approximately 50% of non-breast fed babies whose mother had positive vaginal CMV cultures during their birth can get the viable virus at 3-6 weeks of age developing LOS (27). An interesting study by proved that maternal and neonatal screening for CMV infection should be done for the babies delivered <34 weeks of gestation (28). Their study was supported by the American Academy of Pediatrics (AAP) that stated mothers who deliver infants at <32 weeks of pregnancy can be screened for CMV (28).

From table (4) it is clear that the highest incidence of neonatal death from sepsis has shown among males more than females at 64% and 35.8% respectively. Furthermore, the male neonates who had died in early onset sepsis 39.6% were more than neonates who had died in late-onset sepsis 24.5%, where the relationship is not statistically significant using chi-square (1.901) and the probability value (0.138), which is more than the level of statistical significance (0.05). Supportive studies in Egypt and Saudi, explained that the male neonates were more infected with sepsis in comparison with female neonates. This is related to the mechanisms of regulating the synthesis of gamma-globulin, that are possibly

situated on X chromosomes in the male newborns. The X chromosome is responsible for the dimorphic nature of the inflammatory response during endotoxemia by diversifying the leukocyte response. Therefore confers less immunological protection compared to female newborns (5,12,29). Furthermore, males neonates are more sensitive to adverse perinatal and postnatal environmental conditions, and are more likely to be born preterm and with a lower birth weight, both of which increase the risk of neonatal sepsis (30).

The current study explained the association between the Classification of sepsis and the gestational age. Neonatal sepsis death occurred mainly due to prematurity at 81%. Of whom 49% of EOS neonates were premature, while 21% of the neonates with LOS were premature. The relationship is not statistically significant using chi-square (3.443) and the probability value (0.179), which is more than the level of statistical significance (0.05). Basically, neonatal deaths in the first week of life are more likely associated with pregnancy issues and maternal health. Whereas, neonatal deaths after 7 -28 day of life are usually associated with the neonate surrounding environment (31).

As Maternal factors accounted for 45 (56%) of the neonatal deaths. These were rupture of the membrane (16, 20%) antepartum hemorrhage (10, 12.5%), infections (sepsis) (9, 11.2%), pre-eclampsia (3, 3.7%) and others (8.7%). (22)

Recommendations

From table (6) the rate of neonates who died in EOS with deficiency in lung function 47%, was higher than those neonates who died in EOS with a complication like birth asphyxia 7.5%. The relationship is not statistically significant using chi-square (1.887) and the probability value (0.194), which is more than the level of statistical significance (0.05). This finding agreed with a study(32) in Egypt by these results also agreed with other studies (33, 34) that were done by they found that respiratory distress was from the most prevalent complication of sepsis. Actually, neonatal resuscitation at birth was found to be a significant risk factor for neonatal sepsis. Since, newborns who had a history of resuscitation at birth were 2.3 times had higher rate of death from septicemia, as compared to newborns who had not been resuscitated. Resuscitation may be performed with contaminated equipment, introducing microorganisms into the lungs and because of prematurity and undeveloped immune system, leads the neonates to higher risk of complications that result in death in LOS. Whereas, death from EOS complication occurs more often from chorioamnionitis and aspiration of the neonates to infected amniotic fluid secretions in the birth canal, leading to pneumonia and sepsis manifested by neonatal asphyxia. (19) Hence, improving obstetric and neonatal care will at least reduce the death due to prematurity and infection like sepsis (22).

- Ensuring the early detection of STI, UTI and transplacental infections among mothers, by routine

antenatal screening to decrease its impact on the neonate.

- Improving the awareness of the staff working in NICU regarding; the importance of classification of sepsis in the medical records or death certificates, also maternal and neonatal risk factors, the predominant pathogens causing sepsis, this helps in designing better hospital-based management strategies.
- It is important to train health professionals to deal with pre-term labor, prematurity and their complications, with adherence to infection control practices to reduce the neonatal morbidity and mortality.
- The WHO verbal autopsy tools should be used in the neonatal department particularly in NICU, to control the causes leading to prematurity and sepsis. The WHO verbal autopsy tools can provide practically good evaluations of the

most common causes of neonatal mortality especially in countries where neonatal death is high.

- Moreover, efforts should also be made to raise awareness of the staff on using ICD- 10 codes to simply help the staff in better reporting for the causes of death to help them in understanding the main risk factors of neonatal death.

6. Conclusion: The outcomes of the current study demonstrated that, being premature 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 in the current study. The early detection and treatment of the cases can prevent the vast majority of neonatal sepsis-related mortality, that are usually implicated from inadequate maternal health during pregnancy, and inadequate care of newborns after delivery.

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