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Original Article

Risk Factors Associated with Early and Late-onset of Neonatal Sepsis in Duhok City

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ABSTRACT

Backgrounds and objectives: Neonatal sepsis refers to bacterial, fungal, protozoan infections or any viral agents or pathogens which inter to the newborns blood stream after the birth. Neonatal Sepsis is the main reason of deaths in non-developed countries. There is an overall prevalence of 54.67% in Iraq. The present study intends to explore the demographic and clinical affecting factors of early and late onset of neonatal sepsis of a sample population in Duhok city. The predictors of neonatal sepsis diagnosis were determined accordingly.
Methods: This cross-sectional study shows 110 neonates who were diagnosed with early or late onset of neonatal sepsis. A pediatrician diagnosed the patients through physical and clinical assessment.
Results: The prevalence of early and late onset of neonatal sepsis was 52.73% and 47.7%, respectively. The Apgar scores of less than seven and more than seven were risk factors for early and late-onset of neonatal sepsis, prolonged rupture of the membranes greater than18 hours and multiple gestations are common in patients with early onset of neonatal sepsis.
Conclusions: The study showed that the early onset of neonatal sepsis or late-onset of neonatal sepsis was associated with Apgar score and prolonged rupture of the membranes.
Keywords: Early Onset of Neonatal Sepsis; Late-Onset of Neonatal Sepsis; Risk Factors

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INTRODUCTION

Neonatal sepsis refers to bacterial, fungal, protozoan infections or any viral pathogen instantly after the delivery[1]. Neonatal inflammation indicates to the infections of newborns through the first-month of existence, surrounding infections in the eyes, mouth, skin, and the umbilicus.. The mostly ways of newborn infections are during the broken skin in the umbilical cord [1,2]. Early neonatal period refers to the first seven days of newborn's life, while the late neonatal period means the period from after seven days to 28 days of life. [2].
Maternal sepsis is the main factor leading to death of newborns with prevalence one from ten deaths. For more than 95% of maternal deaths are associated to maternal infections which happens in the societies where incomes are low. [3]. One million newborn deaths are related with

maternal infection every year [4].Reduction in the neonate and child mortality is a significant world goal to achieve health for all. During the last quarter of the century, the emphasis has paid to the reduction in under-five childhood mortality largely through vaccination, oral rehydration therapy (ORS), and control of respiratory tract infections. while, this changes did not have marked influence among neonates leading to converting of infant mortality at an any age [5].In developing countries newborn infection is considered a common reason of neonatal morbidity and mortality [6]. Insufficient care and inappropriate pregnancy treatment, including a lack of hygiene during the obstetric and delivery, contributes to the poor care of neonates.
[5-6].It's evaluated that three million newborns and 1.2 million children complain from sepsis globally. [7].

Neonatal sepsis in Kurdistan and Iraq

A study conducted in three hospitals in Baghdad to identify the leading microorganism of bacteria and viruses, as well the qualification factors studied 150 weakened and sensitive newborns, among sensitive newborns, the incidence of newborn infection it was 54.67% [8]. Immature newborn, weakness, inflammation of urinary and reproductive system of mothers, and cesarean section delivery, leads to predispose, newborns neonatal sepsis [8-9]. In early and late onset of neonatal sepsis, Staphylococci were the predominant pathogen in both EOS and LOS sepsis. While a large rate of this pathogen was coagulase-negative in LONS. Generally gram-positive bacteria have the most frequent level rather than positive bacteria, whereas Fungi and Toxoplasma showed no significant Effect or fewer roles in neonatal sepsis among newborns in Iraqi community.
To avoid increasing the percentage of deaths among neonates we should taking in account the early detection and diagnosis of the microbes as soon as possible. [9-11] A study conducted in Duhok reported that 25.39% of the neonates diagnosed with neonatal sepsis, including 61.9% in patients their age less than7 days [9].In another study conducted in Erbil city, 425 newborn patients were diagnosed with neonatal infections, including 53% in ages less than seven days and 47% in patients between seven and 28 days. [10]
The purpose of this study was to discover the demographic and clinical risk factors of early and late neonatal sepsis in a sample population in Duhok city. Also, the predictors of early and late-onset of neonatal sepsis diagnosis were considered in this study.

METHODS

This cross-sectional study targeted patients attending the out-patient clinic of a pediatric hospital were consecutively screened for diagnostic criteria of different types of neonatal sepsis. The patients who were recruited in a purposive way from the Neonatal Intensive Care Unit (NICU) of Heevi Pediatric Hospital in Duhok between 1st February 2018 and 27th December 2018.
The newborns who were involved in this study were the neonates diagnosed with clinical futures of newborn infections in early or late stage of neonatal infection in Duhok city. The investigators attempted to include all cases who attended the hospital between the mentioned time periods. The following patients were included in the study: Male or female, aged from birth to 28 days, diagnosed with early or late onset of neonatal sepsis, admitted to the hospital. The patients whose parents did not accepted to participation were excluded from the study. Also, the patients who had other medical conditions were not included in the study.

Baseline information was collected through self-reported by mothers and included information of newborn and parents such as age, gender, education, gestational age, and mode of delivery. The discovering of newborn infection or sepsis was established by the pediatrician, and according to the following clinical criteria, temperature instability; account of heart-bit (180 bit/minute, or 100 bit/minute; the rate of respiration more than 60 breaths/min, desaturations; lethargy/altered mental status; glucose intolerance (plasma glucose >10 mmol/liter); feed intolerance. [11].

Leukocytosis (WBC count >34000×109/l); leukopenia (WBC count <5000×109/l); immature neutrophils >10%; premature: the rate of total neutrophil >0.2; thrombocytopenia <100000× 109/l; CRP (C - reactive protein) >10 mg/l or 2 SD (Sta. Deviation) above normal value; procalcitonin >8.1 mg/dl or 2 SD above normal value; IL-6 or IL-8 >70 g/ml. [11,13] The Apgar score is a method of newborn health assessment against infant mortality. Which is calculated based on score of where 1 to 10 scores. Where high point indicate the baby's health status is good. Appearance (skin color); pulse (heart rate), Grimace response (reflexes), activity (muscle tone), respiration are included as indicators [12]. Preterm Premature Rupture of Membranes is defined as occurring prior to 37 week's gestation when the amniotic fluid is leaking prior to exit the baby out of the mother's vagina due to tearing of the membrane in more than 24 hours [13].

The difference between general and clinical characteristics of the patients diagnosed with early neonatal sepsis was examined through Chi-square and Fishers' exact test. Besides, the predictors of neonatal sepsis (early and late) were examined through Univariate analysis of variance. The null hypothesis was rejected in a P-value of equal or less than 0.05.

The program that which used to calculate our data were performed in SPSS (Statistical Package for Social Sciences) version 25.

The ethical approval of the present investigation was obtained from the Scientific Research Davison of Duhok General Directorate of Health on 20/06/2017. The verbal consent was taken from all mothers before data collection, and the guarantee was given for the confidentiality of their personal I information.

RESULTS

Of the total 110 patients diagnosed with neonatal sepsis and included in the study, the prevalence of EONS and LONS were 52.73% and 47.7%, respectively. The research did not discovered an important difference in gender distribution (P= 0.345), maternal age (38.5% between 31 and 40 years in EONS and 43.1% between 21 and 30 years in LONS; P=0.387), education level of mothers (P=0.407) between mother of neonates infected by ENOS and LNOS. Moreover, the study doesn't shows large differences in gestational age of the mother between two groups of the study (55.8% between 37 and 42 weeks in EONS and 53.4% in LONS; P=0.367), see Table 1.

The multiple gestations in EONS and LONS were 59.6% and 48.3%, respectively, with no significant difference (P=0.234). Also, the study did not report the considerable difference in the mode of delivery (44.2% by cesarean section in ENOS and 55.2% in LNOS; P=0.252) and twin gestation (P=0.938), see Table 1.

Table 1: General characteristics between patients in early and late onset of neonatal sepsis

General characteristics (n=110)	Early Onset (n=52, 47.27%)	Late Onset (n=58, 52.73%)	P-value (Two-sided)
Gender of infant			
Male	28 (53.8)	26 (44.8)	0.345*
Female	24 (46.2)	32 (55.2)	
Maternal age of mother			
< 20 year	13 (25)	9 (15.5)	0.387**
21-30 years old	18 (34.6)	25 (43.1)	
31-40 years old	20 (38.5)	24 (41.4)	
> 40 year	1 (1.9)	0 (0)	
Educational status of mother			
None	15 (28.8)	12 (20.7)	0.407*
Primary	14 (26.9)	13 (22.4)	
Secondary	12 (23.1)	22 (37.9)	
Tertiary	11 (21.2)	11 (19)	
Gestational age of mother			
<37 Weeks	21 (40.4)	27 (46.6)	0.367**
37-42 W	29 (55.8)	31 (53.4)	
>42 Weeks	2 (3.8)	0 (0)	
Multiple gestations			
Yes	31 (59.6)	28 (48.3)	0.234*
No	21 (40.4)	30 (51.7)	
Mode of Delivery			
Vaginal Delivery	29 (55.8)	26 (44.8)	0.252*
Cesarean Section	23 (44.2)	32 (55.2)	
Twin gestation			
Yes	14 (26.9)	16 (27.6)	0.938*
No	38 (73.1)	42 (72.4)	

*Chi-square and **Fishers' Exact tests were performed for statistical analyses. The numbers are in frequency (percentage).

Table 2 showed that there is no relationship between ENOS and LNOS study groups in maternal fever (P=0.763), maternal group B streptococcal colonization, UTI (P=0.792), prematurity rupture of membrane before the onset of labor (P=0.488), foul-smelling liquor (P=0.103), birth weight (P=0.170), resuscitation at birth (P=0.603), fetal tachycardia (P=0.365), fetal abnormalities (P=0.314), invasive procedures (P=0.899), hand washing (P=0.994) and PROM (P=0.047), see Table 2. Whereas the majority of the patients with EONS had Apgar score less than 7 (71.2%) compared to the majority with Apgar, score of more than 7 (63.8%) in LONS (P=<0.0001). Meconium-stained amniotic fluid was more prevalent in ENOS; 75.0% compared to 56.9%, respectively (P=0.046), see table 2.

Table 2: Comparison of clinical characteristics between patients with early and late-onset of neonatal sepsis

General characteristics	Early-Onset (n=52)	Late-Onset (n=58)	P-value (Two-sided)
Prolonged rupture of the membranes*	34(65.4)	27(46.6)	0.047
Maternal Fever	29(55.8)	34(58.6)	0.763
Maternal group B Streptococcal colonization, UTI**	31(59.6)	36(62.1)	0.792
Prematurity rupture of membrane before the onset of labor.	2(61.5)	32(55.2)	0.488
Foul Smelling Liquor	34(85.4)	29(50)	0.103
Apgar score (1min)			0.0001>
>than7	37(71.2)	21(36.2)	
<than 7	15(28.8)	37(63.8)	
Birth Weight			0.170
>than 2.5 Kg	37(71.2)	34(58.6)	
≤than 2.5 Kg	15(28.8)	24(41.4)	
Resuscitation at Birth	33(63.5)	34(58.6)	0.603
Meconium-stained amniotic fluid	39(75.0)	33(56.9)	0.046
Fetal tachycardia	26(50)	34(58.6)	0.365
Fetal abnormalities	12(23.1)	9(15.5)	0.314
Inadequate hand washing	35(67.3)	39(67.2)	0.994
Invasive procedures	47(90.4)	52(89.7)	0.899

Chi-square was performed for all statistical analyses. The numbers are in frequency (percentage).

*PROM: the prolonged rupture of the membranes > 18 hrs.
**UTI: Urinary tract infection

The predictors of ENOS and LNOS were examined in univariate analysis model in Table 3. The study showed that having multiple gestations is a predictor of ENOS (P=0.013). Also, the lower Apgar score predicts ENOS, and higher Apgar score predicts LNOS.

Table 3: Univariate analysis of variance of early and late neonatal sepsis

Dependent Variable: Early and Late Neonatal Onset				
Risk Factors	**Mean Square**	**F Score**	**P-Value**	**Effect Size**
Gender	0.173	0.790	0.377	0.009
Maternal Age	0.111	0.506	0.679	0.018
Mother Education	0.242	1.104	0.352	0.038
Gestational Age	0.204	0.931	0.398	0.022
prolonged rupture of the membranes	0.535	2.447	0.122	0.028
Maternal Fever	0.208	0.952	0.332	0.011
Urinary tract infections	0.052	0.236	0.628	0.003
Multiple Gestation	1.412	6.455	0.013	0.071
Premature rupture of membrane*	0.007	0.030	0.863	0.000
Mode of delivery	0.018	0.081	0.777	0.001
Foul Smelling Liquor	0.383	1.748	0.190	0.020
Inadequate hand Washing	0.004	0.020	0.887	0.000
Apgar Score	3.283	15.005	0.000	0.152
Birth weight	0.031	0.141	0.709	0.002
Resuscitation at Birth	0.041	0.188	0.666	0.002
Meconium-stained amniotic fluid	0.204	0.930	0.338	0.011
Twin Gestation	0.091	0.414	0.522	0.005
Fetal Tachycardia	0.064	0.291	0.591	0.003
Fetal Abnormalities	0.065	0.296	0.588	0.004
Invasive Procedures	0.169	0.772	0.382	0.009

*PRM: Prematurity rupture of membrane before the onset of labor.

DISCUSSION

In the present study the general and clinical risk factors of neonatal sepsis in a sample population of neonates were determined. In the study, gender of neonate was not determined to be a predictor of neonatal sepsis. There are contradictory reports about the dangerous of gender for neonatal sepsis [14]. Sexual dimorphism from the human immune response is quite clear; female babies produce the more active of cellular immune reaction so that they are more resistant to the infection. [15]. The differences with the present study could be due to the sample size or study design. Mother's maternal age and level of education was not significantly associated with neonatal sepsis [16, 17], possibly due to the lack of mother information and experience about newborn care. Prolong rapture of membrane (≥18 hours) was shown to not be associated with neonatal sepsis; Other researches in other communities shows the same results to the results of our study[18, 19]. One of the most common reason of upgrade of pathogens to rise from vagina and cervical canal in to the amniotic fluid and fetal sac are easy and late tearing of the membrane as asphyxia which leading to sepsis [19, 20]. In the present study, intrapartum fever was not shown a significant influence in the newborn infection and sepsis. The newborns were delivered from mothers with high body temperature during delivery have six times higher odds of developing sepsis compared to newborns that delivered from mothers their body temperature were normal during the labor. [19, 21]. Intra partum fever is an indicator of maternal infections that are frequently transmitted to the baby inside the uterus or through the delivery canal when the newborn pass through this canal, which always leading to early-onset sepsis [22, 19].

The study determined that those infants with Apgar score less than seven usually are affected by EONS and the infants with Apgar score greater than seven affect by LNOS ($P<0.0001$). The previous study have shown that Apgar score less than seven in the first minute have a risk of 14.05 times (95% CI 5.487-35.987) to the EONS occurrence. A study considered that the EONS happens in newborns with Apgar score less than seven in the early minutes rises 11.1 times with a significant ratio P-value 0.001 [14]. Also there were a same results and it was very closed to the previous study which shows a high significant rate in neonates with Apgar less than seven with p value 0.002 [23, 24]. Generally there were a relationship between the Apgar score in the moment of first life span of the newborn and the Hydrogen Potential (pH) cord blood and during delivery depression, but there was no relationship with the consequences, while the Apgar score refers to the changes which happen in the infant's health condition and the performance of resuscitation applied. [25]. Several factors can cause perinatal hypoxia-ischemia, while in the consistent consequences which performed from the previous study, explained that low Apgar score in the first minute may be due to the infants infection factors which happens from the perinatal period, usually a number of weeks, immediately before and after birth [24, 25].Birth weight, resuscitation at birth, meconium-stained amniotic fluid, twin gestation, fetal tachycardia, fetal abnormalities, poor feeding were not found to be predisposing factors of newborn infection or sepsis in this study in disagreement with some studies in the literature review [26]. This study shows that adequate hand washing before and after clinical procedures is not

a significant predictor of late onset of neonatal sepsis. More than quarter of neonatal mortality is related to sepsis or infections. Caregivers, mothers and nurses hygiene and hand washing with soap and detergents usually decrease neonatal sepsis and infections. A study examined the effect of plenty handwashing advancing the hand washing style and behavior of mothers. In Nepal there was a significant difference between mothers who wash their hands several times rather than mothers who did not wash their hands or has washing their hand few times, and the first group were at 44% lower risk of neonatal infection and death rather than the second group [27]. In a study conducted between two groups of mothers, which shows that good handwashing with detergents and antiseptic agents were significantly increased before and after breastfeeding, feces contact among case mothers than among controls. [28] therefore, the hygiene of mothers and hand washing with detergents before and after fecal attaches were less frequent rather than the spread of this style marked among mothers of small children in developing communities, which confirms the large barriers to hand washing progressed by mothers of newborns [28].Lastly, the study showed that invasive clonal procedure is not a predictor for neonatal sepsis types. In another study shows that the lumbar puncture (LP) meningitis can be the main indicator of neonatal sepsis in approximately 3% sample size; subsequently cerebrospinal fluid aspiration analysis ought to be considered in the majority of newborns with late-onset of neonatal sepsis prior using of antibiotics. [20]. When septicemia or blood infection, are shows in the positive blood culture and clinical picture, this refers to presence of EONS, LP, so LP should be delayed in that cases [29] There are several blood investigations other than culture used to detect sepsis. I: T ratio, micro ESR (Erythrocyte Sedimentation Rate) [30].

STRENGTH AND LIMITATION

The strong point of the present investigation must be searched in the study design as the mostly of the previous studies focused on cross-sectional design rather than a comparative design. The study was performed in one clinical setting, precluding us from generalizing the findings to other settings across the country.

CONCLUSION

There was evidence in the analyzing statistics which obvious that Apgar score is only a predictable factor of early and late onset of newborn sepsis. The majority of the subjects who were infected by ENOS had long term tearing down of the membranes longer than 18 hours, and their mothers had multiple gestations.

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CONFLICTS OF INTEREST

The authors announced that there were no conflicts of interest.

AUTHORSHIP

The corresponding author claims that all authors of the present study had sufficient contribution to study design, review, concept, assessment, diagnosis, and analysis.

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