

## Risk Factors for Neonatal Sepsis in Sulaimania Pediatrics Teaching Hospital

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**Abstract:** A prospective case-control study was performed to determine the maternal and neonatal risk factors for Septicemia in neonates aged ( $\leq 28$ ) days admitted to the neonatal care unit in Sulaimania Pediatrics Teaching Hospital over a period of ten months from 1<sup>st</sup> of March 2021 to 31<sup>st</sup> of December 2022. One hundred ten cases with neonatal sepsis diagnosed by positive blood culture and 110 control culture-negative cases selected were studied; early onset neonatal sepsis (EONS) ( $\leq 7$  days age) forms 41.8%, while late-onset neonatal sepsis (LONS) (from 8-28days age) forms 58.2%. Our study shows there is an association between age at presentation, gender, weight, gestational age, maternal diseases, early rupture membrane (EROM), previous admission, and increased risk of development of neonatal sepsis. 62.7% percent of studies were male, 56.3% were premature, gram-positive bacteria were the predominant isolates both in early-onset neonatal sepsis and late-onset neonatal sepsis, *Staphylococcus aureus* was the commonest organisms detected; it forms (16.4%). Out of 110 cases, the mortality rate was 18.9% (55%) in late-onset neonatal sepsis and (45%) in early-onset neonatal sepsis. As conclusion, a gram-positive bacterium (specially *Staphylococcus aureus*) was the leading bacterial agent of neonatal sepsis in our environment, and the relative high frequency of nosocomial infection mandates the intensification of preventive control measures to limit the spread of infection.

**Keywords:** Neonatal sepsis; IgG; Low birth weight; and Febrile illness.

## INTRODUCTION

Neonatal sepsis is a clinical syndrome characterized by systemic signs of infection accompanied by bacteremia and occurring in the first month of life. The incidence of serious neonatal sepsis is variable [Seale, A.C. *et al.*, 2014-Simonsen, K.A. *et al.*, 2014]. Rates between 0.22 % and 11.2 % have been reported from the developed world, with mortality rates between 9-15%. From the developing world, rates of 10-30% are reported, with mortality between 30 - 45%. While other reports show that neonatal sepsis occurs in 1-21 infants per 1000 live births with a mortality rate as high as 30-69% of affected infants, developing countries have both the highest incidence and the highest mortality rates [Bizzarro, M.J. *et al.*, 2005-Weston, E.J. *et al.*, 2011]. A number of agents may infect newborns in the uterus, intrapartum, or postpartum. Intrauterine transplacental infections of significance to the fetus and/or newborn include rubella, cytomegalovirus (CMV), toxoplasmosis, parvovirus B19, and varicella. Although herpes simplex virus (HSV), human immunodeficiency virus (HIV), hepatitis B virus (HBV), hepatitis C virus (HCV), and tuberculosis (TB) can each result in transplacental infection, the most common mode of transmission for these agents is intrapartum during labor and delivery with passage through an infected birth canal (HIV, HSV, HBV) or Postnatal from contact with an infected mother or caretaker

(TB) [Stoll, B.J. *et al.*, 2011-Polin, R.A, 2012]. Any micro inhabiting the maternal genitourinary or lower gastrointestinal tract may cause intrapartum and postpartum infection. Neonatal sepsis may be categorized as early or late onset. 85% of newborns with early-onset infection present within 24 hours, 5% present at 24-48 hours, and a smaller percentage of patients present between 48 hours and six days of life. Onset is most rapid in premature neonates. Early-onset sepsis syndrome is associated with the acquisition of microorganisms from the mother.

Transplacental infection or an ascending infection from the cervix may be caused by organisms that colonize in the mother's genitourinary tract, with the acquisition of the microbe by passage through a colonized birth canal at delivery [Visser, V.E. *et al.*, 1979-Manroe, B.L. *et al.*, 1979]. The microorganisms most commonly associated with early-onset infection include group B streptococcus (GBS), *Escherichia coli*, *Haemophilus influenzae*, and *Listeria monocytogenes*. The fetal immune system develops in a sterile and protected environment and, therefore, lacks antigenic experience. It must also be modulated in order to co-exist with the mother's immune system. Soon after birth, the newborn is exposed to the "hostile world" of bacteria, viruses, fungi, and parasites and must

immediately defend itself. The immunologic competence of the neonate progresses rapidly in the first three months of life as the cells involved in acquired immunity mature and gain antigenic experience. During this period, the neonate also depends upon components of the innate or antigen-independent immune system, including phagocytes, natural killer cells, antigen-presenting cells, humoral mediators of inflammation, and complement [Lloyd, B.W. *et al.*, 1989-Gabay, C. *et al.*, 1999].

## PATIENTS AND METHODS

This is a prospective case/control study conducted on neonates (<28 days). One hundred ten blood culture-positive cases and 110 control cases who were healthy infants with no signs and symptoms of sepsis were studied.

The data was collected from the neonatal ward for ten month period from 1<sup>st</sup> of March 2021 to 31<sup>st</sup> of December 2022 in Sulaimania Pediatrics Teaching Hospital.

The relevant prenatal data adopted in this study were age at presentation, gender, weight, gestational age, mode of delivery, maternal fever, prolonged rupture membrane, meconium aspiration, and prior admission to the hospital.

Neonates were classified into two groups according to the age of onset of symptoms: the early onset (EONS), when the symptoms of sepsis started within the first seven days of life, which comprised (46) patients, and the late onset sepsis (LONS) when the symptom occurs after seven days of life till 28 days of life which comprised (64) patients.

The commonest causative microorganism was *Staphylococcus aureus*, as shown in Table (1). Statistical analysis was performed by SPSS 16.0. Odd ratio was used for the estimation of relative risk. P values <0.05 were regarded as significant.

## RESULTS

**Table 1:** Causative microorganisms for neonatal sepsis, according to positive blood culture

<b>Gram-positive</b>	<b>Frequency</b>	<b>Percent</b>
Staph. aureus	36	16.4
GBS	16	7.3
Srep. viridance	2	0.9
Strep. fecalis	2	0.9
Strep. pneumone	1	0.5
Strep. pyogenes	1	0.5
<b>Gram-negative</b>	<b>Frequency</b>	<b>Percent</b>
E. coli	20	8.6
E. aerogenes	15	7.3
S. typhi	7	3.2
Pseudomonus	5	4.1
Klebsiella	3	1.4
Proteus	2	0.9
<b>Total</b>	<b>110</b>	<b>100%</b>

**Table 2:** Characteristics of Cases and Controls

Variables	Case No. (%)	Control No (%)
<b>Age at presentation</b>		
Early ( $\leq 7$ days)	46 (41.8)	75 (68.2)
Late ( $> 7$ days)	64 (58.2)	35 (31.8)
<b>Gender</b>		
Male	69 (62.73)	47 (42.73)
Female	41 (37.27)	63 (57.27)
<b>Weight (Gm)</b>		
$> 2500$ gm	47 (42.73)	10 (9.1)
$\geq 2500$ gm	63 (57.27)	100 (90.9)
<b>Gestational age (Weeks)</b>		
Preterm ( $< 37$ wk.s)	62 (56.36)	16 (14.55)
Full-term ( $\geq 37$ wk.s)	48 (43.64)	94 (85.45)
<b>Mode of delivery</b>		
C/S	56 (50.9)	65 (59.1)
NVD	54 (49.1)	45 (40.9)
<b>Maternal fever (last week of pregnancy)</b>		
Positive	41 (37.27)	11 (10)
Negative	69 (62.73)	99 (90)
<b>prolonged rupture of membrane (<math>&gt; 24</math> hours)</b>		
Positive	28 (25.5)	10 (9.1)
Negative	82 (74.5)	100 (90.9)
<b>Prior admission to hospital</b>		
Positive	42 (38.2)	16 (14.5)
Negative	68 (61.8)	94 (85.5)
<b>Meconium aspiration</b>		
Positive	5 (4.5)	1 (0.9)
Negative	105 (95.5)	109 (99.1)

**Table 3:** Relative risk of neonatal sepsis with the gestational age

Association between variables and status (case and control)			Odds Ratio	95% Confidence Interval		P-value
	Case (N)	Control (N)		Lower	Upper	
Gestational age (Weeks)						
Preterm ( $< 37$ wk.s)	62	16	2.351	1.820	3.036	0.000
Full-term & post-term ( $\geq 37$ wk.s)	48	94	0.310	0.197	0.487	

Neonatal sepsis was significantly associated with prematurity (p value=0.000), odd ratio 2.35 (95%

C.I. 1.8 to 3.03). as shown in (Table-3).

**Table 4:** Relative risk of neonatal sepsis with weight

Association between variables and status (case and control)			Odds Ratio	95% Confidence Interval		P-value
Weight (Gm)	Case (N)	Control (N)		Lower	Upper	
$< 2500$ gm	47	10	2.13 .286	1.69 .161	2.67 .509	0.000
$\geq 2500$ gm	63	100				

The risk for neonatal sepsis who weighing  $< 2500$ gm was (OR 2.3, 95% CI 1.34 to 4.12) &

the P value (0.000) was highly significant, as shown in (Table-4)

**Table 5:** Relative risk of gender with neonatal sepsis

Association between variables and status (case and control)				Odds Ratio	95% Confidence Interval		P-value
					Lower	Upper	
<b>Gender</b>		<u>Case (N)</u>	<u>Control (N)</u>				
<b>male</b>		47	<b>69</b>	1.509	1.13	2.00	0.002
<b>Female</b>	41		63	.669	.511	.875	

Although gender was a minor risk factor, but it was highly significant with the male gender,

with a P-value (0.002), Odd ratio of 2.351, (95% C.I. 1.820 to 3.036), as shown in Table (5).

**Table 6:** Association between neonatal sepsis& age at diagnosis

Association between variables and status (case and control)				Odds Ratio	95% Confidence Interval		P-value
					Lower	Upper	
Age at presentation		<u>Case (N)</u>	<u>Control (N)</u>				
≤7days		46	75	.588	.449	.770	0.000
>7days		64	35	1.75	1.298	2.388	

Those with late presentation are at more risk (OR 1.75, 95% CI 1.298 to 2.388) for

developing neonatal sepsis& the P value (0.000) was highly significant, as shown in Table-6.

**Table 7:** Relative risk of early rupture membrane

Association between variables and status (case and control)				Odds Ratio	95% Confidence Interval		P-value
					Lower	Upper	
PROM (> 24 hours)	<u>case-control</u>	Positive	28				
negative	10	100		1.635	1.275	2.097	0.001
	82			.479	.277	.829	

Neonatal sepsis was significantly associated with early rupture of membrane (>24 hours), P-

value (0.001), Odd ratio 1.63, (95% C.I. 1.275 to 2.097). as shown in Table-7.

**Table 8:** Relative risk of previous admission& neonatal sepsis

Association between variables and status (case and control)				Odds Ratio	95% Confidence Interval		P-value
					Lower	Upper	
Prior admission to the hospital							
<u>Case (N) Control (N)</u>							
Positive	42	16		1.725	1.356	2.195	0.000
Negative	68	94		.475	.307	.736	

**Table 9:** Relative risk between maternal diseases& neonatal sepsis

Association between variables a status (case and control)		d	Odds Ratio	95% Confidence Interval		P-value
				Lower	Upper	
Maternal fever & UTI	<u>case</u>	<u>control</u>	.359	.209	.616	0.000
Negative	69	99				
positive	41	11				

**Table 10:** Association between neonatal sepsis& type of delivery

Association between variables and status (case and control)		Odds Ratio	95% Confidence Interval		P-value	
			Lower	Upper		
Type of delivery	C a s e (N)	Control (N)	1.182	.90	1.551	0.139
C/S	54	45				
NVD	56	65				

**Table 11:** Association between neonatal sepsis & meconium aspiration

Association between variables and status (case and control)			Odds Ratio	95% Confidence Interval		P-value
				Lower	Upper	
Meconium aspiration	<u>case</u>	<u>control</u>	1.698	1.158	2.491	0.106
Yes	5	1				
No	105	109				

**Table 12:** Case fatality rate in early and late neonatal sepsis among 110 cases

Cases	EONS N (%)	LONS N (%)	Total
Cases	46 (41.81%)	64 (58.19%)	110 (100%)
Death	9 (45%)	11 (55%)	20 (100%)

## DISCUSSION

Neonatal sepsis remains an important cause of mortality & morbidity in this age group despite the progress in hygiene, new effective antimicrobial agents & advances in early diagnosis and treatment. The study had showed that neonatal sepsis occurs more frequently among premature neonates. This result agrees with the studies of other workers, which suggest that prematurity is an important predisposing for factor sepsis. In the neonate, a possible explanation for this result is that premature infants lack well developed immune system or them prolong hospitalization, which increases the risk of nosocomial infection. LBW neonates were considered high risk for neonatal sepsis. This study is similar to the study of other workers [Cortese, F. *et al.*, 2016].

The present study indicates that males are more affected than female neonates; this result is compatible with the data reported by other workers. Such results suggest the possibility of sex-linked factors in host susceptibility. The study revealed that late presentation was a major risk

factor for neonatal sepsis; this is compatible with the study done in Kirkuk. This may be related to the character of our patients since most cases are either referred from the district hospital or presented after a period of hospitalization as a nosocomial infection, which is mostly manifested after (8th) day of life. [Sullins, A.K. *et al.*, 2013]

Maternal factors like premature rupture of the membrane significantly increase the risk of infection; this result is comparable to the study of other workers. By 24 hours of membrane rupture, the incidence of early-onset disease with group B streptococcus (GBS) increases significantly; longer than 18 hr is an appropriate cut-off for an increased risk of neonatal infection. Greater than 24 hours, microscopic evidence of inflammation of membranes is uniformly present. This study showed a strong relationship between the history of previous hospitalization and the development of neonatal sepsis as a result of nosocomial infection. The infant's skin, respiratory tract, conjunctivae, and gastrointestinal tract umbilicus may be colonized from the environment, leading to the

possibility of late-onset sepsis from an invasive microorganism.

This study showed a significant relation between maternal illness during the last weeks of the third trimester, such as maternal UTI and fever, and the development of neonatal sepsis. This study is in agreement with the studies done in Baghdad, Nepal, and Indonesia. Transplacental infection or an ascending infection from the cervix may be caused by organisms that colonize in the mother's genitourinary tract, with the acquisition of the microbe by passage through a colonized birth canal at delivery. Our study showed no significant relation between babies born by C/S and the development of neonatal sepsis. This result is incompatible with that done in Indonesia, which showed that Cesarean section (C/S) is a risk factor of developing neonatal sepsis. Meconium aspiration syndrome and development of neonatal sepsis, although the p-value was not significant, the odd ratio was (1.69), which it means there is some risk of developing sepsis among those infants with meconium aspiration syndrome; this result is in agreement with that done in Indonesia [Shane, A.L. et al., 2017]. Possible explanation for that is. However, meconium is sterile when aspirated into the lung; it may stimulate the release of cytokines and other vasoactive substances that lead to cardiovascular and inflammatory responses in the fetus and newborn. Meconium aspiration includes airway obstruction, chemical irritation, infection, and surfactant inactivation. However, it is likely that most cases of severe MAS are related in intrauterine pathologic processes, primarily asphyxia, and infection, rather than the aspiration of meconium by itself.

## CONCLUSION

Early rupture of membrane, maternal fever and UTI, Gender, LBW, late presentations, history of previous admission, and invasive procedure are significant risk factors for the development of neonatal sepsis.

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