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A Study on the Incidence and Risk Factors of Neonatal Sepsis in Regional Institute of Medical Sciences, Imphal

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Abstract:
Background: *Neonatal sepsis is a clinical syndrome of systemic illness accompanied by bacteraemia occurring in the first month of life. There is a paucity of studies on the incidence of neonatal sepsis and the risk factors associated with it in this part of the country and with above background, the study was conducted in a tertiary care centre.*
Aims and Objectives: *Study was conducted to determine the incidence and the risk factors of neonatal sepsis.*
Materials and Methods: *A hospital based prospective analytical study was conducted among 87 neonates with perinatal risk factors and clinical manifestation suggestive of neonatal sepsis admitted in the Paediatric ward, RIMS, Imphal from September 2018 to August 2020. Pre-designed pro-forma was used for complete clinical history, clinical examination and investigations. Blood was collected for sepsis screening and blood culture and sensitivity. Analysis was done using SPSS v21 for Windows.*
Results: *Perinatal risk factors was present in 87.4% (95% CI: 78.1%-93.2%) of the neonates admitted with suspicion of sepsis. The incidence of neonatal sepsis among the neonates with probable sepsis in our study was 13.8% (95% CI: 8.2%-23.3%). In-adequate antenatal visits, birth asphyxia and maternal UTI were the factors associated with neonatal sepsis.*
Conclusion: *In-adequate antenatal visits, birth asphyxia and maternal UTI were the factors associated with neonatal sepsis. There were no significant association for gender, low birth weight, prematurity, PROM, prolonged labor and maternal fever with the incidence of neonatal sepsis.*
Keywords: *Neonatal sepsis, Early onset sepsis (EOS), Late onset sepsis (LOS), sepsis screen*

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I. Introduction

Neonatal sepsis is a clinical syndrome of systemic illness accompanied by bacteremia occurring in the first month of life.[1] The term neonatal sepsis is used to designate a systemic condition of bacterial, viral origin that is associated with haemodynamic changes and other clinical manifestations and results in substantial morbidity and mortality. Despite years of clinical experience with the care of neonates with confirmed or suspected sepsis, challenges remain including the absence of a consensus definition of neonatal sepsis.[2]

According to World Health Organisation (WHO) estimates, there are about 5 million neonatal deaths each year, 98% of which occurring in developing countries. Neonatal sepsis is responsible for 30% to 50% of total neonatal deaths each year in developing countries.[3,4] Sepsis is the second major cause of mortality among neonates and it is estimated to cause 1.6 million deaths annually.[5] Sepsis and meningitis are the most commonly implicated factor.[6] Early onset neonatal sepsis (EOS) remains a major cause for neonatal mortality and morbidity. The case fatality in EOS ranges from 16.7% to 19.4%.[7,8]

The incidence of neonatal sepsis in India according to the data from National Neonatal Perinatal Database (NNPD) is 30 per 1000 live births. Among intramural births, *Klebsiella pneumoniae* was the most frequently isolated pathogen (32.5%), followed by *Staphylococcus aureus* (13.6%). Among extramural neonates, *Klebsiella pneumoniae* was again the commonest organism (27%), followed by *Staphylococcus aureus* (15%) and *Pseudomonas spp.* (13%).[9]

Globally, of the three million annual neonatal sepsis cases (2202/ 1,00,000 live births), India has the highest incidence of clinical sepsis (17,000/ 1,00,000 live births).[10] The case fatality rate of sepsis among neonates ranges between 25% to 65% in India.[11] Even these rates are believed to be underestimated by various literatures.[12-14]

Neonatal sepsis can be classified into two categories depending on the onset of symptoms[15]

Early onset sepsis (EOS): It presents within the first 72 hours of life. Infants with EOS usually presents with respiratory distress and pneumonia. The source of infection is generally the maternal genital tracts.[15,16]
The following risk factors seem to be associated with an increased risk of early onset sepsis[16]

1. Low birth weight (<2500gm) or prematurity
2. Febrile illness in the mother (>38^0C) with evidence of bacterial infection within 2 weeks prior to delivery
3. Foul smelling liquor
4. Rupture of membranes >24 hours
5. Single unclean or >3 sterile vaginal examinations during labor
6. Prolonged labor (sum of 1^{st} and 2^{nd} stage of labor ≥24 hours)
7. Perinatal asphyxia (Apgar score <4 at 1 minute).

Late onset sepsis (LOS): It usually presents after 72 hours of life. The infection in LOS is either hospital acquired (e.g. prolonged hospitalization, invasive procedure etc.) or community acquired (e.g. bottle feeding, poor hygiene, overcrowding, poor cord care etc.). Neonates usually present with septicemia, pneumonia or meningitis.[17,18]
Screening tests such as total and differential leukocyte count, band cells count, absolute neutrophil counts and C-reactive proteins (CRPs) assays may help in the diagnosis; however they lack the specificity to detect the pathogens and are not available in many centres in developing countries.[19] Hence blood culture still remains the gold standard test for confirmation.[20,21]
The varying microbiological pattern of septicemia in neonates and the impact of the risk factors in situations where intrapartum antibiotic prophylaxis administration is not well elucidated warrants the need for ongoing review of the incidence and risk factors so as to develop effective guidelines for management and prevention of neonatal sepsis. There is a paucity of studies on the incidence of neonatal sepsis and the risk factors associated with it in this part of the country and with above background, the study was conducted in a tertiary care centre to determine the incidence of neonatal sepsis and to determine the risk factors of neonatal sepsis among the neonates (0-28 days) with perinatal risk factors and clinical manifestation suggestive of neonatal sepsis admitted in the Paediatric ward and hence forth to reduce the neonatal morbidity and mortality.

II. Materials And Methods

This longitudinal study was carried out on patients of Department of Paediatrics at Regional Institute of Medical Sciences (RIMS), Imphal, Manipur from September 2018 to August 2020 to determine the incidence and the risk factors of neonatal sepsis among the neonates (0-28 days) with clinical manifestation suggestive of neonatal sepsis.
Study design: A hospital based longitudinal study
Study setting: Department of Paediatrics, RIMS, Imphal
Study duration: 2 years (Sept 2018-Aug 2020)
Study population: All neonates (0-28 days) with clinical manifestation suggestive of neonatal sepsis admitted in the Paediatric ward, RIMS during the study period
Inclusion criteria:

1. All neonates (0-28 days) with clinical manifestations suggestive of neonatal sepsis
2. Those who gave informed Consent/ Assent

Exclusion Criteria: Neonates with

1. Clinically suspected septicaemia and had received antibiotics prior admission
2. Birth weight <1000 gm.
3. Inborn errors of metabolism
4. Major congenital anomaly
5. Clinical symptoms of hypoglycaemia, hypocalcaemia or other metabolic causes
6. Birth from the mother with TORCH infections

Sample size: 87 by taking 6.03% as incidence rate (Bangi VA et al[22])
Sampling method: consecutive sampling

Procedure methodology:

Neonates with perinatal risk factors and clinical manifestations suggestive of neonatal sepsis admitted in Paediatric ward, RIMS according to the inclusion and exclusion criteria was enrolled in the study after informed consent and approval from the Research Ethics Board, RIMS, Imphal. A complete clinical history was taken using a pre-designed pro-forma following which clinical examination and investigations was done for the patients.

Blood routine examination and blood culture and sensitivity was done for all the patients and the values were recorded.

On the basis of the results of blood analysis and history of the patients, incidence and risk factors of neonatal sepsis was determined.

Study tools and instruments:

1. **Pre-designed proforma** for complete clinical history, clinical examination and investigations.
2. **Weighing machine:** Crown mechanical weight scale machine (digital weighing scale). Maximum capacity 20 kg (d=10gm), KONIG KN-BS10, Made in India.
3. **Stethoscope:** Littmann quality, K17H13477, Made in USA.
4. **Infantometer:** Indosurgical product. Product code 20014. Made in India.
5. **BactAlert PF plus,** manufactured by Biomerieux.

Sample collection:

Under aseptic and antiseptic precaution, blood sample was collected in sterile blood culture bottle, in sterile EDTA vial and sterile plain vial. It will be send immediately to Microbiology department for blood culture and sensitivity and CRP and Pathology department for sepsis screening.

Study variables:

Independent/ Predictor variables: Age, Gender, Socioeconomic status, Birth weight, Mode of delivery, Period of gestation, Place of delivery, Antenatal visits, Feeding history, APGAR score at 1 min, Risk factors, Sepsis screening report, Blood culture and sensitivity report

Dependent/ Outcome variables:

- Incidence of neonates with neonatal sepsis
- Risk factors associated with neonatal sepsis

Statistical analysis:

Data was entered and analysed using SPSS (IBM) Version 21.0 software for Windows (IBM Corp.in Armonk, NS, USA). Categorical variables like gender of the child, screening results are presented as frequency and percentages. Incidence of neonatal sepsis is presented as frequency and percentage with 95% confidence interval (95% CI). Association between categorical variables were performed using Chi-square test or Fisher's exact test. A p value of <0.05 was considered significant.

Ethical issues:

Commencement of the study was started after approval from the Research Ethics Board, RIMS, Imphal and informed consent was obtained from the parents for the study before recruitment. Confidentiality was maintained by limiting the identifying variables to the minimum.

(No. A/206/REB-Comm(SP)/RIMS/2015/438/56/2018)

III. Result

A longitudinal study was conducted in the Department of Paediatrics, RIMS, Imphal, from September 2018 to August 2020. A total of 87 neonates with a suspicion of neonatal sepsis admitted in the Paediatric ward were included in our study.

Table no 1 shows that 60.9% of the neonates were males with a M:F of 1.56:1.

Table no 1: Distribution of neonates by gender (N=87)

Gender of the neonate	Frequency	Percentage
Male	53	60.9
Female	34	39.1
Total	**87**	**100.0**

Table no 2 shows that 70.1% of the neonates were within three days of birth and the remaining 29.9% of the neonates were between 4-28 days of birth.

Table no 2: Distribution of neonates by days since birth (N=87)

Age category (days since birth)	Frequency	Percentage
1-3	61	70.1
4-28	26	29.9
Total	**87**	**100.0**

Table no 3 shows that majority (58.6%) of the neonates had normal birth weight in our study. Low birth weight was present in 41.4% of the neonates.

Table no 3: Distribution of neonates by birth weight (N=87)

Birth weight	Frequency	Percentage
Normal (≥2500 gram)	51	58.6
Low birth weight (<2500 gram)	36	41.4
Total	**87**	**100.0**

Table no 4 shows that 2/3rd of the neonates were form the middle socioeconomic class and 21.8% of the neonates were from the low socioeconomic class.

Table no 4: Distribution of neonates by socioeconomic status (N=87)

Socioeconomic status	Frequency	Percentage
Upper	10	11.5
Middle	58	66.7
Lower	19	21.8
Total	**87**	**100.0**

Table no 5 shows that majority of the neonates were term neonates (62.1%) and 11.5% of the neonates were born <34 weeks of gestation. Caesarean delivery was noted in 23.0% of the neonates. About 92.0% of the deliveries were institutional deliveries. However it is noteworthy to mention that 8.0% of the deliveries were home deliveries. Number of ANC visits was inadequate in more than 1/3rd (34.5%) of the neonates.

Table no 5: Distribution of neonates by antenatal and intra-natal characteristics (N=87)

Antenatal and intra-natal characteristics	Frequency	Percentage
Gestational age (weeks)		
≥37	54	62.1
34-37	23	26.4
<34	10	11.5
Mode of delivery		
Vaginal	67	77.0
Caesarean	20	23.0
Place of delivery		
Institutional	80	92
Home	7	8.0
ANC visits		
Adequate (≥4)	57	65.5
Inadequate (<4)	30	34.5

Table no 6 shows that perinatal risk factors was present in 87.4% (**95% CI:** 78.1%-93.2%) of the neonates admitted with suspicion of sepsis.

Table no 6: Prevalence of perinatal risk factors among the neonates suspected of sepsis (N=87)

Perinatal risk factors	Frequency	Percentage (95% CI)
Yes	76	87.4 (78.1-93.2)
No	11	12.6 (6.8-21.9)
Total	**87**	**100.0**

Table no 7 shows that PROM was the most common perinatal risk factor (48.3%) followed by prematurity (36.8%) and birth asphyxia (36.8%) among the neonates admitted with suspected sepsis. Prolonged labor was the least common risk factor and was observed in 9.2% of the neonates.

Table no 7: Distribution of neonates by perinatal risk factors (N=87)*

Perinatal Risk Factors	Frequency	Percentage
Premature rupture of membrane (PROM)	42	48.3
Prematurity	32	36.8
Birth asphyxia	30	34.5
Maternal urinary tract infection (UTI)	26	29.9
Maternal fever	16	18.4
Prolonged labor	8	9.2

***Multiple risk factors possible**

Table no 8 shows that the incidence of neonatal sepsis was 13.8% (**95% CI:** 8.2%-23.3%).

Table no 8: Incidence of neonatal sepsis among the neonates suspected of sepsis

Neonatal sepsis	Frequency	Percentage (95% CI)
Yes	12	13.8 (8.2-23.3)
No	75	86.2 (76.7-91.8)

Total	87	100.0

Table no 9 shows that home deliveries was more among those mothers with inadequate antenatal visits(23.3%) and it was found to be statistically significant (p<0.05).

Table no 9: Association of ANC visits and place of delivery

ANC visits	**Place of delivery**		**p value***
	Institutional (%)	Home (%)	
Adequate (≥4)	57 (100.0)	0	0.001
Inadequate (<4)	23 (76.7)	7 (23.3)	

***Fisher's exact test**

Table no 10 shows that there was significant association for socioeconomic status with the incidence of neonatal sepsis (p<0.05).

Table no 10: Association of socio-economic status with neonatal sepsis

Socio-economic status	**Neonatal Sepsis**		**P-value**
	Yes (%)	**No (%)**	
Upper	1 (10.0)	9 (90.0)	0.004
Middle	4 (06.9)	54 (93.1)	
Lower	7 (36.8)	12 (63.2)	

Table no 11 shows that there was significant association for place of delivery with the incidence of neonatal sepsis (p<0.05).

Table no 11: Association of place of delivery with neonatal sepsis

Place of delivery	**Neonatal Sepsis**		**P-value**
	Yes (%)	**No (%)**	
Institutional	8 (10.0)	72 (90.0)	0.006
Home	4 (57.1)	3 (42.9)	

***Fisher's exact test**

Table no 12 shows that maternal UTI was significantly associated with the incidence of neonatal sepsis (p<0.05).

Table no 12: Association of maternal UTI with neonatal sepsis

Maternal UTI	**Neonatal Sepsis**		**P-value**
	Yes (%)	**No (%)**	
Yes	5 (35.7)	9 (64.3)	0.021
No	7 (09.6)	66 (90.4)	

***Fisher's exact test**

IV. Discussion

Earlier diagnosis of sepsis would enable proper management and low probability of sepsis.[23] During the past two decades, health care delivery systems experienced many improvements, with rapid advancement of new technologies, advancement in the procedures, and an increase in provision of services such as neonatal intensive care. These improvements will prove to be helpful only when coupled with preventive measures, thus reducing the burden of neonatal mortality. Thus this study was conducted to decipher the incidence of neonatal sepsis in this part of the country where the resources are limited.

The incidence of neonatal sepsis among the neonates with probable sepsis in our study was 13.8% (95% CI: 8.2%-23.3%). The incidence in our study population was similar when compared to other studies conducted across the globe. The study by Medhat H et al[24] and Thapa S et al[25] had reported the incidence to be 8.6% and 10.8% respectively, which were low when compared to our study findings. A slightly higher incidence

than our study was reported by Pavan Kumar DV et al[26], Hayum M et al[27] and Jajoo M et al[28], who all reported the incidence to be 26.2%, 28.0% and 39.0% respectively.

The incidence of sepsis was found to be higher among the males but it was not statistically significant. A study by Chacko B et al[29] showed similar findings.

The incidence of sepsis was higher among those with low birth weight but it was not found to be statistically significant. A study by Mehdat H et al[24] and Palatnik A et al[30] also showed similar findings but was statistically significant. Bhat and Baby reported the low birth weight have a risk of EOS 10 times compared to the normal birth weight.[31] It is a well-known plausibility that the low birth weight babies usually are low in immunity and thus the higher chance of sepsis.

There was a significant association for maternal UTI with the incidence of neonatal sepsis. This finding may support for the reason that maternal UTI/STI is often associated with EOS, especially if untreated during the third trimester pregnancy or labor, and it may be associated with neonatal sepsis following the colonization of the birth canal by the infectious agent.

V. Conclusion

Earlier diagnosis of sepsis would enable proper management and low probability of sepsis. In-adequate antenatal visits, place of delivery, socio economic status and maternal UTI were the factors associated with neonatal sepsis. There were no significant association for gender, low birth weight, prematurity, PROM, prolonged labor and maternal fever with the incidence of neonatal sepsis.

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