

# Risk factors of late-onset Neonatal Sepsis in Special Care Neonatal Unit of a Tertiary Care Hospital in Bangladesh

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## Abstract

**Introduction:** Late-onset neonatal sepsis is one of the most common causes of neonatal deaths in hospital as well as community in developing country like Bangladesh. It can present as meningitis, pneumonia, pyelonephritis, or gastroenteritis. Various risk factors play important role in its causation. In this study our main goal was to evaluate the risk factors of late onset neonatal sepsis in SCANU (Special Care Newborn Unit) of a tertiary care hospital.

**Methods:** This cross-sectional study was done in the SCANU of Dr. M.R. Khan Shishu Hospital and Institute of Child Health, Mirpur-2, Dhaka for 6 months. A total of 59 neonates with late onset sepsis in SCANU were included during the study period.

**Results:** The socio-demographic status of the neonates with late onset sepsis shows that, most of the neonates (44.1%) were between 24 to 28 days. Also, 54.24% patients were male

and 57.6% patients belong to middle economic status group. In the study, 79.7% had Cough with respiratory distress followed by 23.7% had cough only, 6.8% had fever, 52.5% had vomiting, abdominal distension, and 8.5% patients had Jaundice. Only 1.7% patients used bottles for feeding. Among neonates, the highest (49.15%) came with the risk factor of poor hygiene. The Majority (95%) of low-birth-weight neonates had patchy opacity resembling pneumonia in chest x-ray.

**Conclusion:** Poor hygiene is a high-risk factor for neonates with late onset sepsis. Bottle feeding had comparatively higher risk in developing late onset sepsis than formula feeding with spoon. Poor cord care is another risk factor.

**Keywords:** Late Onset Neonatal Sepsis (LOS), antibiotics, neonatal intensive care.

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## Introduction

Neonatal sepsis is a universal infection occurring in infants at  $\leq 28$  days of life and is an important cause of morbidity and mortality of newborns.<sup>1</sup> It is one of the major global public health challenges.<sup>2</sup> Neonatal sepsis is divided into early-onset sepsis (EOS) and late-onset

sepsis (LOS) as per the onset of age. Early-onset sepsis (EOS) occurs in the first 72 hours of life and late-onset sepsis (LOS) occurs beyond 72 hours.<sup>3</sup> EOS reflects transplacental or, more frequently, ascending infections from the maternal genital tract, whereas LOS is associated with the postnatal nosocomial or community environment, with the peak incidence reported to be between the 10th and 22nd day of life.<sup>4-7</sup> Since the early 1980s, epidemiological studies have observed a general reduction in EOS, probably due to advances in obstetric care and the use of prophylactic intra partum antibiotics to prevent infections caused by Group B Streptococcus.<sup>8,9</sup> Meanwhile, the incidence of LOS has increased in parallel with the improved survival of premature infants, especially in those with very low birth weight (VLBW).<sup>8-9</sup> Around 36.3% of neonates with gestational age (GA)  $< 28$  weeks had at least one episode of LOS, as compared with 29.6%, 17.5% and 16.5% of moderately preterm (GA of 29–32 weeks), late preterm (GA of 33–36 weeks) and term infants.<sup>6</sup>

Other well-recorded risk factors for LOS include the long-term use of invasive interventions, such as mechanical ventilation and intravascular catheterization, the failure of early enteral feeding with breast milk, a prolonged

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duration of parenteral nutrition, hospitalization, surgery and underlying respiratory and cardiovascular diseases.

Proper hand hygiene is the most important methods of preventing the spread of nosocomial infections. There are few studies showing that improving hand hygiene in NICU can reduce incidence of late onset sepsis. This is also true for community acquired infections.<sup>10</sup>

Inadequate cord care and poor maternal hygiene were also found to be important risk factors for late onset sepsis in many studies.<sup>11-12</sup> The probability for entering pathogenic micro-organisms through umbilical cord is high in low resource settings. This can also contribute to the prevailing sub-optimal hygienic conditions in baby's surrounding environment that can result in localized umbilical infection.<sup>12-13</sup>

It is already known to all that, breastmilk feeding within the first month of life has been shown to be protective against LOS development. Bottle feeding and feeding of artificial milk are other risk factors for sepsis as it bears risk of entrance of organism.<sup>14-15</sup>

Coagulase-negative staphylococci (CONS) have emerged as the predominant pathogens of LOS, accounting for 53.2%–77.9% of LOS in industrialized countries and 35.5%–47.4% in some developing regions.<sup>4-7, 9, 16-19</sup> Gram-negative bacilli responsible for neonatal LOS mainly include *Escherichia coli*, *Klebsiella*, *Enterobacter* and *Pseudomonas* species. The distribution pattern of causative pathogens varies across regions and may change over time within the same hospital due to demographic characteristics of patients, microflora colonization of the nosocomial environment and the policy of antibiotic use.<sup>9</sup>

In Bangladesh, very few studies have reported on the prevalence of neonatal sepsis condition in different areas of the country. Like other south Asian countries, the prevalence of sepsis among the neonates in Bangladesh is 69.35%.<sup>20</sup>

Neonatal sepsis contributes significantly to neonatal mortality. It was observed that sepsis contributed directly to 12% of neonatal mortality in a rural sub district of Bangladesh.<sup>21</sup> Ours, being an out born hospital, we deal mostly with cases of late onset neonatal sepsis. So, we conducted this study to evaluate the risk factors of late onset neonatal sepsis and to evaluate the clinical and laboratory features of those babies.

## Methods

A cross sectional study was conducted in the Special Care Newborn Unit (SCANU) of Dr. M. R. Khan Shishu

Hospital and Institute of Child Health, a tertiary care hospital of Dhaka city after approval by Research Ethics Committee over six months' period (from January 2020 to June 2020). This study was carried out after explaining the procedures in detail and a written informed consent was taken from parents and assurance about confidentiality was given. This study was performed among the neonates admitted with late onset sepsis (LONS). All cases with diagnosis of late onset neonatal sepsis were included in the study. Those neonates whose parents did not give consent were excluded from the study. The diagnosis was made by the consultants based on presence of any risk factors for late onset sepsis (e.g., formula feeding with spoon/ feeding of expressed milk or artificial milk with bottle/poor hygiene/ any hospital stays) and clinical features suggestive of sepsis or any investigations in favor of sepsis (raised C-reactive protein/ positive blood culture/ leucocytosis or leucopenia/ low platelet count). Poor hygiene was assessed by asking some questions to parents such as whether hand washing was done regularly during handling of baby such as diaper change and feeding, whether visitors wash hands before touching the baby and whether baby's clothes are washed daily. Poor cord care was defined as application of materials not recommended by the national guideline such as cow dung/ shurma/ applying heat/ chemicals etc. and not keeping the cord dry. Other than risk factors, clinical clues for diagnosing LONS were poor feeding or feeding difficulty, cough and cold, respiratory distress, persistent jaundice, convulsion, fever or hypothermia, abdominal distention, loose motion and umbilical sepsis. Besides clinical examination, blood sample was sent for complete blood count, CRP, electrolytes, random blood sugar, blood culture. Chest x-ray was done on admission and were repeated as required. Serum bilirubin and CSF study was done in relevant cases. C-Reactive Protein > 6 mg/L was considered as a positive screen result as per institutional protocol. Other relevant investigations were done depending on patient's condition. All the records of the study population were carefully reviewed and data including sociodemographic and clinical features consistent with sepsis, result of cultures, antibiotic sensitivity was entered into a data collection sheet. All data were analyzed using SPSS version 22. Descriptive statistics were calculated for all the variables, including frequencies and percentages. Paired sample t test was done to assess risk factors of Patchy opacity. P value of <0.05 was considered significant.

## Results

During the study period a total of 59 neonates were admitted with late onset neonatal sepsis. Table-1 shows

Socio-demographic status of the neonates where 44.1% belong to 24 to 28 days' age group. Also, 54.24% patients were male and 57.6% patients belong to middle economic status group.

**Table-I**

*Socio-demographic status of the neonates with late onset sepsis*

Socio-demographic status	N(59)	%
Mean age (days)	20.37±6.94	
Age:		
3 to 8 days	6	9.7
9 to 13 days	2	3.2
14 to 18 days	8	12.9
19 to 23 days	17	27.4
24 to 28 days	26	44.1
Gender:		
Male	32	54.24%
Female	27	45.76%
Parents Economic status:		
Middle	34	57.6%
Lower	25	42.4%

Table-II shows clinical profile of the neonates with late onset sepsis where 79.7% had cough with respiratory distress followed by, 52.5% had vomiting, 23.7% had cough only, 23.72% had less activity, 6.8% had fever.

**Table-II**

*Clinical Profile of the neonates with late onset sepsis*

Clinical Profile	N=59 Yes n (%)
Cough with respiratory distress	47(79.7)
Cough Only	14(23.7)
Less activity	14(23.72)
Fever	4(6.8)
Decreased urine output	4(6.78)
Convulsion	4(6.78)
Vomiting, abdominal distension and dehydrations	31(52.5)
Jaundice	5(8.47)
Skin rash/lesion	3(5.1)
Bleeding manifestation	0

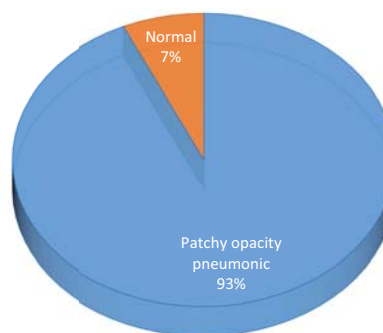
**Table-III**

*Distributions of the neonates with late onset sepsis according to lab investigations*

Description	N=59 (%)
Hb (g/dl):	
<12	33.90%
12-14	37.29%
>14	28.81%
PLC(μL)	
100000-300000	57.6%
>300000	42.4%
CRP(mg/L)	
<6	78%
6-10	18.6%
>10	3.4%
TC(μL)	
15000/mm <sup>3</sup> or more	2.9%
<15000/mm <sup>3</sup>	97.1%
Blood C/S:	
No growth	100%
Growth	0%

Table-III shows distributions of the patients according to lab investigations where 33.90% had Hb< 12 g/dl and 37.29% had Hb 12-14 g/dl. 57.6% had platelet count between 100000-300000 μL and there was no growth of Blood C/S.

In figure-1: chest X-ray status of the patients (n=59) showed majority of the patients (93.2%) had patchy opacity pneumonia.



**Fig-1:** Chest X-ray status of the neonates with patchy opacity pneumonia (n=59)

Table IV shows that poor hygiene was the highest (49.15%) among neonates who came with risk factors of late onset sepsis.

**Table-IV**

<i>Number of neonates who had risk factors for late onset sepsis</i>	
Risk Factor	Yes
Poor Hygiene	49.15%
Low birth weight (<2500gm)	33.90%
Low gestational age (<37 completed weeks)	30.51%
Previous antimicrobial exposure	27.11%
Bottle feeding (expressed milk & artificial milk)	25.64%
Poor Cord Care	18.64%
Formula feeding with spoon	18.64%

Table V shows that low birth weight neonates were mostly (95%) suffered by patchy opacity pneumonia. But in paired sample t test there was no significant difference among the different risk factors of patchy opacity pneumonia.

**Table V**

<i>Risk factors for patchy opacity pneumonia</i>		
Risk Factor	Frequency	Patchy opacity pneumonia
Poor hygiene	29	27 (93.10%)
Low birth weight (<2500gm)	20	19 (95%)
Lower gestational age (<37 completed weeks)	18	17 (94.44%)
Previous antimicrobial exposure	16	15 (93.75%)
Bottle feeding	15	14 (93.33%)
Poor Cord Care	11	10 (90.90%)
Formula feeding	11	10 (90.90%)

**Table VI**

<i>Paired sample t test for risk factors of Patchy opacity</i>									
Variables		Mean	Paired Differences				T	df	Sig. (2-tailed)
			Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
					Lower	Upper			
Pair 1	Risk factor - Poor hygiene	-.06897	.25788	.04789	-.16706	.02913	-1.440	28	.161
Pair 2	Risk factor - Low birth weight	-.05000	.22361	.05000	-.15465	.05465	-1.000	19	.330
Pair 3	Risk factor - Low gestational age (<37 completed weeks)	-.05556	.23570	.05556	-.17277	.06166	-1.000	17	.331
Pair 4	Risk factor - Previous antimicrobial exposure	-.06250	.25000	.06250	-.19572	.07072	-1.000	15	.333
Pair 5	Risk factor - Bottle feeding	-.06667	.25820	.06667	-.20965	.07632	-1.000	14	.334
Pair 6	Risk factor - Poor cord care	-.09091	.30151	.09091	-.29347	.11165	-1.000	10	.341
Pair 7	Risk factor - Formula feeding	-.09091	.30151	.09091	-.29347	.11165	-1.000	10	.341

**Table-VIII**

<i>Outcome of neonates with late onset sepsis</i>		
Variable	Number (n)	Frequency (%)
Duration of antibiotics		
7 days	34	58
3-5 days	25	42
Discharge status		
Discharged with advice	26	44
Discharged on request	29	49
Referred	04	7
Duration of hospital stay		
5 days	16	27.12
7 days	33	55.93
10 days	10	16.95

### Discussion

Late onset neonatal sepsis is commonly encountered in our NICU. They present with variety of features and many times causative risk factor is evident. In our study 44.1% patients belong to 24-28 days' age group which is slightly greater to one study where the median age at infection was 18 days (range 3-386 days).<sup>5</sup> As our hospital deals with outborn babies, so it may be the cause of getting older babies coming from community with preliminary diagnosis of late onset neonatal sepsis.

One study reported that, 57.8% were male and 42.2% were female also, 67.63% belong to middle economic status.<sup>12</sup> This was supported by our study where we found that, 54.24% patients were male and 57.6% patients belong to middle economic status group.

In one report, it is mentioned that, presence of infection at the umbilical cord, history of bottle feeding of the neonates and pre-existing maternal infection were significantly ( $p$ -value < 0.05) associated with neonatal sepsis.<sup>12</sup> Whereas in our study 1.7% patients used bottle for feeding and 98.3% didn't used bottle for feeding. Also, 35.6% maintained poor hygiene. These findings are consistent with other studies though frequency is variable due to variation in practice, education level of parents and community to community.<sup>12-14</sup>

In this study, we found that 27.11% neonates had previous anti-microbial exposure. Several clinical studies have also demonstrated that, early transient exposure to antibiotics increases the risk of late onset neonatal sepsis.<sup>22</sup>

One study reported that, fever is present in only 10 to 15% of neonates but, when sustained (e.g., > 1 hour), generally indicates infection. Other symptoms and signs include respiratory distress, neurologic findings (e.g., seizures, jitteriness), jaundice (especially occurring within the first 24 hours of life without Rh or ABO blood group incompatibility, vomiting, diarrhea, and abdominal distention).<sup>23</sup> We found similar results. In our study chest X-ray status of the patients showed where majority of the patients (93.2%) had patchy opacity pneumonia. In other study chest X-ray findings in neonatal pneumonia cases were (62%) which is lower than our study.<sup>24-25</sup>

Recent national surveillance data from UK reported that the vast majority of organisms isolated from LOS blood samples (95%-97%) were susceptible to gentamicin+flucloxacillin and gentamicin+amoxicillin/penicillin, suggesting that the current guideline for empirical therapy is adequate and most LOS cases can be appropriately treated by narrow-spectrum antibiotics.<sup>13</sup> However, in our study we used combined cefotaxime + Amikacin; Meroperum + vancomycin/colomycin antibiotic therapy and these types of antibiotics were found sensitive in another study conducted in Bangladesh.<sup>26</sup> Ninety eight percent patients need O2 followed by 58% stayed in hospital for 7 days and 42% need 3-5 days of antibiotic treatment. After treatment 44% patients got discharged with advice followed by 49% were discharged on request. Seven percent neonates were referred due to lack of NICU support.

### Conclusion

From our study we can say that, poor cord care and bottle feeding are important risk factors for late onset sepsis in neonates. Significant number of babies had previous antimicrobial exposure which is alarming.

### Limitation

The study findings reflect situation of a part of the city, not the whole capital. So large multi-centered study can be done for a better picture.



## Recommendation

Increasing awareness among parents regarding hand hygiene, umbilical cord care and reducing bottle feeding can be easy measures to decrease late onset neonatal sepsis.

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