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To study the incidence of early onset sepsis among the late preterm and term neonates in a tertiary care Centre

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Introduction

Neonatal sepsis is a significant cause of morbidity and mortality among newborn infants. It is divided into neonatal early-onset sepsis (EOS) and neonatal late-onset sepsis [1]. Neonatal EOS is defined as the onset of symptoms before 7 days of age, although some experts limit the definition to infections occurring within the first 72 hours of life [2].

Approximately 400,000 newborns die every year globally due to neonatal sepsis [2]. In developing countries, due to a limited level of early diagnosis and treatment, the mortality rate by neonatal sepsis is about three times that of the developed countries [4]. The overall rate of neonatal EOS, defined as a positive blood or cerebrospinal fluid (CSF) bacterial culture at <72 hours of age, is 0.98 infections per 1000 live births, with rates inversely related to birth weight (BW) (0.57 per 1000 live births for > 2500 g BW) [5].

It is believed that EOS is mainly due to the maternal-fetal transmission of microorganisms during pregnancy or perinatally. Microorganism transmission to the blood circulation of neonates causes immune system reaction leading to systemic inflammatory response syndrome (SIRS), which may progress into sepsis, multiple organ failure, and death [6].

Early diagnosis and therapy may inhibit the progression of SIRS and prevent sepsis-related morbidity and mortality [7]. Determination of maternal risk factors and clinical and laboratory features are used for diagnosis of EOS. Important risk factors for EOS include the maternal medical history of urinary infection, vaginitis, early membrane rupture, and chorioamnionitis [8]. Clinical signs are nonspecific and subtle in neonatal EOS.

The unspecific clinical symptoms in neonates and the lack of sufficiently accurate biomarkers can lead to delay in diagnosis and initiation of the therapy, unnecessary

hospital admissions, and antibiotic resistance secondary to anti biotic misuse [9].

Blood culture is the gold standard laboratory test in the diagnosis of NS; however this method has significant limitations, which include false negativity secondary to maternal antibiotic use or low microorganism concentration, need 48 to 72 hours to get the results, false positivity secondary to contamination. Actually, the blood culture sensitivity in the diagnosis of sepsis is reported to be around 19% [10].

Many biomarkers have been tested for the accuracy in EOS diagnosis, including acute phase reactants, interleukins, and immuno globins [11-13]. C-reactive protein (CRP) is the most frequently studied inflammatory marker, which is also used in the follow-up of therapy. CRP is a sensitive but not a specific marker to diagnose sepsis, because of the increase in multiple non-infectious inflammatory events, other than sepsis, and the delay in the increase (10 to 12 hours) [14]. Another inflammatory marker, procalcitonin (PCT), increases in the first 3 to 4 hours from the beginning of symptoms and decreases to normal level in 24 hours [15]. Since peripheral blood smear test, another inflammatory marker, necessitates both appropriate laboratory conditions and personal experience, it's reliability in sepsis diagnosis in low [16]. All of these limitations regarding inflammatory markers cause the absence of a reliable biomarker that can be used in the early diagnosis of NS.

According to a growing number of studies, platelets are implicated in the pathophysiological pathways of sepsis and play a key role in organ dysfunction. Platelet activation is induced by inflammatory-coagulation reactions in sepsis and damaged endothelial cells, and these activated platelets can worsen coagulation disorders and systemic inflammatory reactions [17].

Low lymphocyte numbers may also be linked to a lower survival time in sepsis. Indeed, lymphopenia is a common hallmark of sepsis - induced immuno suppression, as it prevents microbial clearance and predisposes to serious infections, which are the leading cause of sepsis related death [18].

Aim of the study

To determine the incidence of early onset neonatal sepsis among late preterm and term neonates admitted in tertiary care Centre

Methodology

- Study design: Cross-sectional study
- Study duration: 19 months (January 2021 to July 2022)
- Study area: Rajarajeswari Medical College and Hospital, Bangalore.
- Study participants: Late preterm (more than or equal to 35weeks of gestation) and term (37-42 weeks of gestation) neonates admitted to RRMCH Bengaluru, with risk factors or clinical features suggestive of early onset neonatal sepsis.

Inclusion criteria

Inborn

Late preterm (more than or equal to 35 weeks of gestation) and Term neonates (37 weeks to 42 weeks of gestation) with suspicion of Early Onset Sepsis and are admitted to RRMCH

Outborn

Late preterm (more than or equal to 35weeks of gestation) and Term neonates (37weeks to 42weeks of gestation) with suspicion of Early Onset Sepsis and are admitted to RRMCH within 72 hrs. of life.

Exclusion criteria

1. < 35 weeks Period of gestation (preterm neonates)
2. Major congenital anomalies
3. Perinatal asphyxia
4. Preeclampsia
5. Neonates for whom parents decline consent

Method of collection of data

Late preterm (more than or equal to 35weeks of gestation) and term (37-42 weeks of gestation) neonates admitted to RRMCH Bengaluru, with risk factors or clinical features suggestive of early onset neonatal sepsis were included in the study. Clearance from the institutional ethical committee was taken before starting the study. Study participants were included in the study by Purposive Sampling technique.

Written informed parental consent was taken from the parents before collecting the data. A pre-tested, semi-structured questionnaire was used to collect information on socio-demographic variables and obstetric history by interview method. Presence of foul-smelling liquor alone or neonates with two of the risk factors mentioned in the operational definition were subjected to sepsis screen; and blood culture and sensitivity within 24hours of life. Neonates with clinical signs and symptoms suggestive of sepsis appearing within 72hours of life were also subjected to sepsis screen; and blood culture and sensitivity, soon after recognition of signs and symptoms. Clinical features of sepsis such as lethargy, poor sucking/feeding, temperature instability, hypoglycemia/hyperglycemia etc were documented. In order to do the sepsis screen, complete blood count (CBC) with peripheral smear and C-reactive Protein (CRP) was done. Components of sepsis screen included immature to total neutrophil (IT) ratio, CRP, WBC counts.

Statistical analysis

The data was collected and compiled in MS Excel. Descriptive statistics has been used to present the data. To analyse the data SPSS (Version 26.0) was used. Significance level was fixed as 5% ($\alpha = 0.05$. Qualitative variables are expressed as frequency and percentages. The chi-square test was used to compare proportions between groups, association of socio-demographic variables and adherence to treatment. When more than 20% of cells have expected frequencies < 5 Fischer's exact test of significance was used. A comparison of mean±SD of total leucocyte count, absolute neutrophil and lymphocyte counts, and CRP between the groups was done by an independent t-test. One way ANOVA was used to compare the means of blood parameters between 3 groups of sepsis. The diagnostic accuracy of NLR and CRP for neonatal sepsis was assessed by ROC curves and sensitivity, specificity was calculated. All the statistical analysis was carried out at 5% level of significance and a p-value of < 0.05 was considered as significant.

Operational definition

Risk factors or clinical features suggestive of early onset neonatal sepsis

The following neonates will be considered at risk for sepsis in this study:

1. Spontaneous prematurity
2. Foul smelling liquor
3. Rupture of membranes more than or equal to 18 hours
4. Prolonged labour (sum of 1st and 2nd stage of labour > 24 hrs.)
5. Single unclean or > 3 sterile vaginal examination(s) during labour

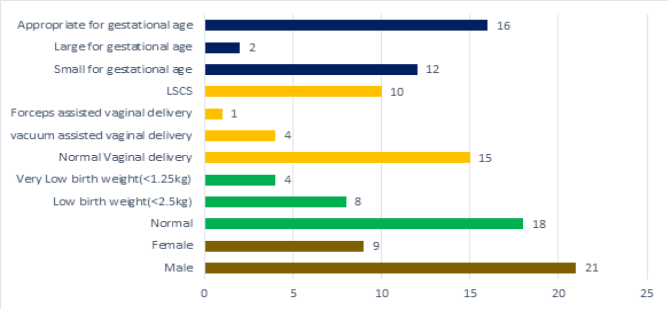
Presence of foul-smelling liquor alone or neonates with two of the above-mentioned risk factors were subjected to sepsis screen.

Results

Table 1: Demographic characteristics of study subjects

Variable	Frequency	Percentage
Gender		
Male	21	70
Female	9	30
Mean Gestational age	37.78±1.50	
Gestational age		
Late Preterm	7	23.3
Term	23	76.7
Mean Birth weight (in kgs)	2.71±0.68	
Birth weight		
Normal	18	60.0
Low birth weight(<2.5kg)	8	26.7
Very Low birth weight(<1.25kg)	4	13.3
Mean Birth weight (in kgs)	2.71±0.68	
Mode of Delivery		
Normal Vaginal delivery	15	50
vacuum assisted vaginal delivery	4	13.3
Forceps assisted vaginal delivery	1	3.3
LSCS	10	33.3
Size for gestational age		
Small for gestational age	12	40
Large for gestational age	2	6.7
Appropriate for gestational age	16	53.3

Figure 1: Demographic characteristics of study subjects

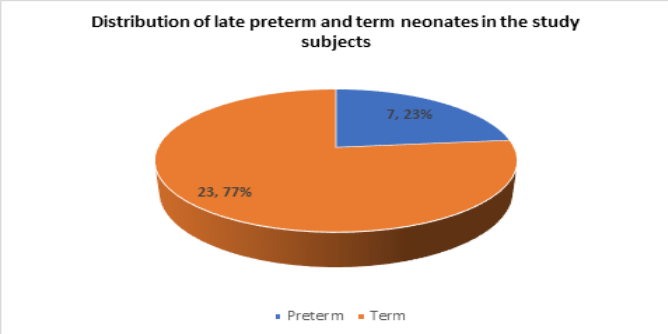


Among all the 30 inborn neonates 21 (70%) were males and 9 (30%) were females. The mean gestational age was 37.78±1.50 weeks. The mode of delivery for was normal vaginal for 15(50%) neonates and 10 (33.3%) neonates had LSCS. The mean birth weight of the neonates born were 2.71±0.68 kgs where 18(60%) were normal weight and 8 (26.7%) were low birth weight (<2.5kgs) and 4 (13.3%) were very low birth weight (<1.5kgs). Among the 3 neonates 16 (53.3%) had size appropriate to age and 12 (40%) neonates were small for the gestational age.

Table 2: Distribution of late preterm and term neonates in the study subjects

Variable	Frequency	Percentage
Preterm	7	23.3
Term	23	76.7
Total	30	100

Figure 2: Distribution of late preterm and term neonates in the study subjects

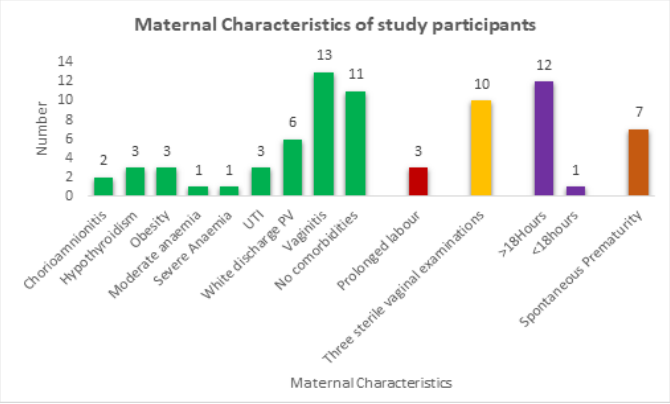


Twenty-three neonates were term gestation and 7 (23.3%) were late preterm.

Table 3: Maternal characteristics of study participants

Variable	Frequency	Percentage
Maternal illness		
Chorioamnionitis	2	6.7
Hypothyroidism	3	10.0
Obesity	3	10.0
Moderate anaemia	1	3.3
Severe Anaemia	1	3.3
UTI	3	10.0
White discharge PV	6	20.0
Vaginitis	13	43.3
No comorbidities	11	36.7
Prolonged labour		
Yes	3	10
No	27	90
Number of sterile vaginal examinations		
1	6	20
2	14	46
3	10	33.3
Prelabour Rupture of membranes		
>18Hours	12	92.30
<18hours	1	7.7
Spontaneous Prematurity		
Yes	7	23.3
No	23	76.7

Figure 3: Maternal characteristics of study participants



The maternal characteristics of study participants showed 11 (36.7%) had no maternal illness. Severe Anaemia was observed in 1 (3.3%) study participants. Hypothyroidism was reported in 3 (10%) of the participants. Three women had prolonged labour. Spontaneous pre maturity has been reported by 7 (23.3%). Prelab our rupture of membranes was reported in 13 mother and Duration after rupture of membranes was >18 hours for 12 (92.6%) and <18hrs for 1 (7.6%) of the mothers.

Table 4: Clinical manifestations among the neonates.

Clinical features	Frequency	Percentage
Poor sucking		
Yes	16	53.3
No	14	46.7
Lethargy		
Yes	10	33.3
No	20	66.7
Cold stress		
Yes	4	13.3
No	26	86.7
Fever		
Yes	4	13.3
No	26	86.7
Icterus		
Yes	4	13.3
No	26	86.7
Tachycardia		
Yes	3	10.0
No	27	90.0
Prolonged capillary refill time		
Yes	3	10
No	27	90
Hypoglycaemia		
Yes	3	10
No	27	90
Respiratory Distress		
Yes	10	33.3
No	20	66.7

Figure 4: Clinical manifestations among the neonates

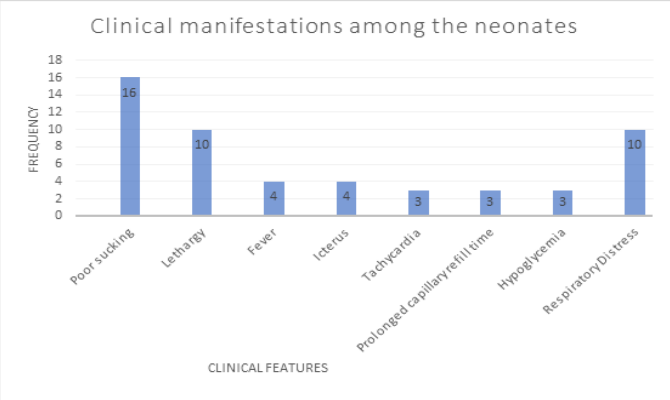


Table 4 and Figure 4 show the clinical manifestation observed in the neonates where majority i.e., 53.3% of them have poor sucking reflex. It has been observed that 10(33.3%) of them had respiratory distress and 3(10%) of the neonate had hypo glycaemia, and 3(10%) had prolonged capillary refill time. Cold stress, icterus and fever were the clinical manifestations observed in 4(13.3%) of the neonates. Lethargy was seen on 10(33.3%) of neonates and tachycardia in 3(10%) neonates.

Table 5: Systemic examination of neonates

Systemic examination	Frequency	Percentage
Respiratory System*		
Within normal limits	20	66.7
Tachypnoea	10	33.3
Retractions	3	10.0
SpO_2<95%	3	10.0
Grunt	4	13.3
Central Nervous system		
Within normal limits	19	63.3
Decreased activity	11	36.7
Per abdominal examination		
Within Normal limits	30	100
Cardio vascular system		
Within Normal limits	27	90.0
Tachycardia	3	10.0

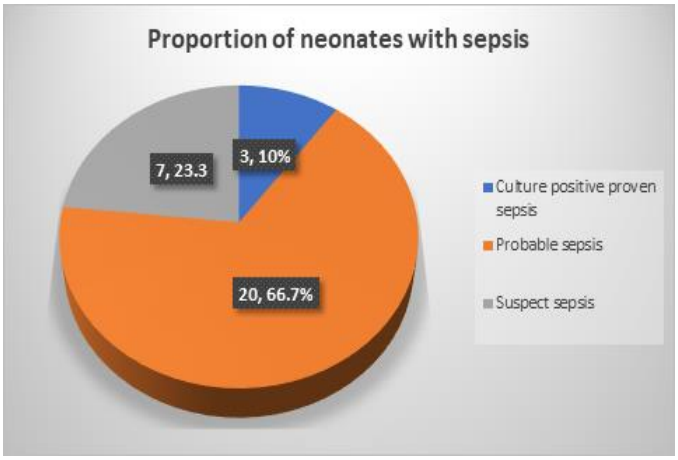
*Multiple responses

The systemic examination findings of the neonates shown in table. Per abdomen examination shows within normal limits for 100% neonates. In cardio vascular system examination tachycardia was reported in 3 neonates. Eleven (36.7%) of neonates showed decreased activity in central nervous system examination. Respiratory system examination showed within normal limits for 20 (66.2%) neonates and tachypnoea among 10 (33.3%).

Table 10: Proportion of neonates with sepsis in the sample

Variable	Frequency	Percentage
Culture positive proven sepsis	3	10.0
Probable sepsis	20	66.7
Suspect sepsis	7	23.3
Total	30	100.0

Figure 6: Proportion of neonates with sepsis



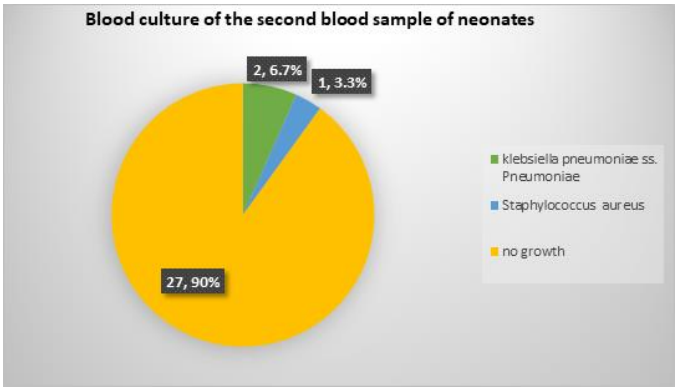
Among the neonates in the study 20(66.7%) were diagnosed as probable sepsis, 3(10%) as culture positive sepsis and 7(23.3%) with suspected sepsis.

Table 11: Organisms isolated in blood sample of neonates with proven sepsis

Variable	Frequency	Percentage
Klebsiella pneumoniae ss.	2	6.7
Staphylococcus aureus	1	3.3
No growth	27	90.0

Total	30	100.0

Figure 7: Organisms isolated in blood sample of neonates with proven sepsis



Out of 3 neonates with culture positive sepsis blood culture showed

klebsiella pneumoniae ss. Pneumoniae among 2(6.7%) and staphylococcus aureus among 1(3.3%).

Table 12: Demographic characteristics of groups

Variable	Culture positive proven sepsis (%)	Probable sepsis (%)	Suspect sepsis (%)	p-value
GENDER				
Male	3(100)	16(80.0)	2(28.6)	0.027
Female	0	4(20.0)	5(71.4)	
Gestational age				
Late Preterm	0	3(15.0)	4(57.1)	0.52
Term	3(100)	17(85.0)	3(42.9)	
Mean	39.16±0.15	38.0±1.37	36.57± 1.43	0.017
Birth weight				
Normal	3(100)	12(60.0)	3(42.9)	0.064
LBW (<2.5kg)	0	7(35.0)	1(14.3)	
Very LBW (<1.5kg s)	0	1(5.0)	3(42.9)	
Mode of Delivery				
NVD	3(100)	11(55.0)	1(14.3)	0.118
VAVD	0	3(15.0)	1(14.3)	
FAVD	0	1(5.0)	0	
LSCS	0	5(25.0)	5(71.4)	

***One-way anova**

Table 13 shows the demographic variables among the culture positive proven, Suspect and Proven sepsis groups. As per gender wise distribution, males are more in culture positive proven sepsis (100%) and Proven sepsis (80%). The association between gender and the sepsis group is found to be statistically significant.

As per gestational age wise distribution all babies in culture positive group were term gestation babies. In probable sepsis group majority (85%) i.e.,17 neonates were of term gestation and in suspect sepsis group 57% were late preterm.

All babies (100%) in culture positive proven sepsis group were delivered via normal vaginal delivery and 55% in probable sepsis group by normal vaginal delivery.

In the group of suspected sepsis 1(14.3%) neonates was of low birth weight and 3(42.9) neonates were very low birth weight.

Table 13: Association between maternal characteristics and neonatal sepsis

Variable	Culture positive proven sepsis (%)	Probable sepsis (%)	Suspect sepsis (%)	p-value
Maternal illness				
Present	3(15.8)	10(52.6)	6(31.6)	0.092
Absent	0	10(90.9)	1(9.1)	
Prolonged labour				
Yes	0	3(100)	0	0.435
No	3(11.1)	17(63.0)	7(25.9)	

Number of sterile vaginal examinations				
1	0	5(25.0)	1(14.3)	0.410
2	1(33.3)	8(40.0)	5(71.4)	
3	2(66.7)	7(35.0)	1(14.3)	
Rupture of membranes				
<18hours	0	1(10.0)	0	0.35
>18 hours	0	9(90.0)	3(100)	
Spontaneous Prematurity				
Yes	0	3(15.0)	4(57.1)	0.04
No	3(100)	17(85.0)	3(42.9)	

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