

# Outcome of Early Onset Sepsis and Clinical Profile of Very Low Birth Weight Neonates; A Cross Sectional Study.

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## ABSTRACT

**Background:** Septicaemia in neonates in the first month or before and after delivery is considered as major cause of mortality and morbidity in the developing countries despite the development of broad spectrum antimicrobial drugs. Early diagnosis of sepsis is necessary to increase the life expectation of neonates with sepsis. Moreover, sepsis induced mortality can be decreased via prevention of sepsis, timely diagnosis and intensive supportive care. **Methods:** The study involved 200 neonates weighing less than 1499 grams, delivered or admitted in extramural NICU with one clinical feature and one risk factor for sepsis as mentioned in the inclusion criteria were recruited for the study. Blood culture reports for promoting rational antibiotic use and clinical follow up of the child till completion of hospital stay was done to study outcome of neonatal septicemia and then treatment plan was modified accordingly. **Results:** 40% of bacteria culture cases were gram positive while 60% of bacteria culture cases were gram negative. Pulmonary hemorrhage (36%) followed by septic shock (30%) and hyaline membrane disease (27%) were the most common cause of death in the present study. 80% of gram negative and 20% of gram positive organisms were involved in all the deaths caused due to sepsis. The mortality rate was significantly higher for out born neonates (50%) as compared to inborn neonates (34%) out born neonates (50%) as compared to inborn neonates (34%). **Conclusion:** Present study confirmed the presence of major concern about the high rate of sepsis among very low birth weight infants. Antibiotic therapy should be considered in absence of clinical features if >2 risk factors of sepsis are present. Blood culture should be done in all suspected cases of neonatal septicemia, which provides early confirmation of sepsis. To keep the infection rates low, strict protocol for asepsis in neonatal units must be adhered to when handling these high-risk infants as prevention is better than cure.

**Keywords:** Neonates, sepsis, low birth weight, mortality.

## INTRODUCTION

Septicaemia in neonates in the first month or before and after delivery is considered as major cause of mortality and morbidity in the developing countries despite the development of broad spectrum antimicrobial drugs. Early sepsis is found to be the cause of 1-8 infants' mortality out of 1000 infants.<sup>[1]</sup>

Any systemic bacterial infection in a child less than one month of age confirmed by a positive blood culture is known as neonatal sepsis.<sup>[2]</sup> More than 50% of neonatal mortality accounts due to neonatal sepsis as its clinical features are non specific and symptomatology is mimicked by various other disorders affecting the newborn.<sup>[3]</sup>

The immature immune system contributes to the highly susceptibility of neonates to the wide range of organisms affecting this population. Mortality of lifelong consequences can be produced via early

sepsis even after prompt management and treatment. In India 28 causality is caused due to sepsis per 1000 births.<sup>[4,5]</sup> More than 20% of all very low birth weight infant deaths are caused by sepsis, and infants with sepsis are nearly three times as likely to die as those without sepsis, even after adjusting for gestational age, sex, and other co-morbidities.<sup>[4]</sup>

Continuous monitoring blood culture system as the diagnosis of bacteria is considered as the "gold standard" for the detection of sepsis. Early diagnosis of sepsis is necessary to increase the life expectation of neonates with sepsis. Moreover, sepsis induced mortality can be decreased via prevention of sepsis, timely diagnosis and intensive supportive care.

## MATERIALS AND METHODS

This was a prospective cross sectional study conducted at F. H Medical College from June 2017 to December 2017. A written informed consent was attained from the parents. The study involved 200 neonates weighing less than 1499 grams, delivered or admitted in extramural NICU with one clinical feature and one risk factor for sepsis as mentioned in the inclusion criteria were recruited for the study.

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Inclusion criteria for risk factors are Premature rupture of membranes, Chorioamnionitis, Maternal fever more than 100°F during or within 2 weeks of delivery, extent of labor exceeding twenty four hours, Foul smelling liquor more than three per vaginal examinations during labor, Urinary tract infection in mother, Active resuscitation required in labor room , Prolonged and difficult delivery with instrumentation, Birth asphyxia (APGAR <4 at 1 minute)

History of top feed, multiple pricks for blood sampling and clinical features are feed intolerance, Jaundice (predominantly direct hyperbilirubinemia), Abdominal distension Temperature instability-hypothermia /hyperthermia Apnoea, Respiratory distress, Convulsion, Shock Bleeding / petechiae / purpura Omphalitis. With proper consent of parents/guardians; a thorough antenatal, natal and postnatal history followed by general and systemic examination of neonates was done in every enrolled case. An area over the venipuncture site which is approximately of five cm was disinfected with seventy percent alcohol and allowed to dry, followed by application of povidone Iodine in concentric circles over the site and allowed to dry for at least one minute. Approximately 2 ml of blood was drained using a sterile syringe before administration of antibiotics and inoculated aseptically into a BACTEC PEDS PLUS/F Culture Vials. Blood culture reports for promoting rational antibiotic use and clinical follow up of the child till completion of hospital stay was done to study outcome of neonatal septicemia and then treatment plan was modified accordingly.

**Statistical analysis**

Chi-square test was used to obtained the Correlation of risk factors, clinical features with laboratory findings. p-value less than 0.05 was considered as significant.

**RESULTS**

Total 200 low birth weight neonates fulfilling the above inclusion criteria were included in the present study. Among 200 neonates 96 neonates were in born while 104 neonates were out born.

In the current study most of the neonates (60%) were from 31-34 week gestation age group range. Moreover, results revealed there was male predominance 1.4 : 1 in comparison of females. Birth weight distribution showed that the ratio of neonates with birth weight 1000-1499 grams 4.2:1 compare to birth weight less than 1000. Lower segment caesarean section (LSCS) was less commonly seen as compared to normal vaginal delivery. Furthermore, correlation of all the forsaid parameters with blood culture positivity has been shown in [Table 1].

**Table 1: Distribution and its correlation with culture positivity of neonates according to sex, gestational age, birth weight and mode of delivery.**

Variants		Total neonates (n=200)	Bacteria positive (n= 80)	Chi square	p value
Sex	Male	116	44 (38%)	0.235	>0.05
	Female	84	36 (42.8%)		
Gestational age (weeks)	≤ 30	60	22 (36.6%)	0.675	>0.05
	31-34	120	48 (40%)		
	35-37	20	10 (6%)		
Birth weight (grams)	<999	38	10 (6%)	0.542	>0.05
	1000-1499	162	70 (39%)		
Delivery mode	Vagina l	166	68	0.289	>0.05
	LSCS	34	12		

Table 2 shows that the prolonged rupture of membrane >24 hours (33%) was the most common risk factors in the current study whereas there were ≥3 per vaginal examination during labor (38%). Subjects with prolonged rupture of membranes (PROM) showed maximum number of culture positive (68%) followed by 60% urinary tract infection with mother. [Table 2]

**Table 2: Correlation of risk factors of sepsis with bactrias culture positivity.**

Variables	Bacteria positive	Percentage positivity	Isolates
Premature rupture of membranes > 24 hours (n=66)	44	68	Klebsiella, MRSA, Pseudomonas, S. aureus Acinetobacter, Enterobacter, Enterococcus
Urinary tract infection in mother (n=24)	14	60	Proteus, Citrobacter, Pseudomonas, Enterococcus, Acinetobacter, MRSA
>3 per vaginal examinations during labor (n=66)	28	43	Proteus, Citrobacter, Pseudomonas, Enterococcus, Acinetobacter, MRSA
Active resuscitation required in labor room (n=56)	22	38	Proteus, Citrobacter, Pseudomonas, Enterococcus, Acinetobacter, MRSA
Chorioamnionitis (n=6)	2	37	Klebsiella
Maternal fever >100° F during or within 2 weeks of delivery (n=26)	8	33	S. aureus, Enterococcus, MRSA, Klebsiella

Table 3 shows that more the number of risk factors present enhanced the probability of culture proven sepsis.

**Table 3: Bacteria blood culture positivity according to number of risk factors present.**

Number of risk factors present	Total neonates	Bacteria positive	Bacteria negative	Bacteria positive percentage
1	156	52	104	34
2	32	18	14	67
3	12	10	2	85
Total	200	80	120	

Table 4 shows the clinical features of sepsis and there correlation with bacteria positive neonates. Bleeding, temperature instability and respiratory distress were the most common clinical features present in the neonates suffering with sepsis.

**Table 4: Correlation between clinical features of sepsis with bacteria culture positivity.**

Presenting features	Frequency of occurrence	Bacteria positive	Bacteria positive percentage
Bleeding/ petechiae/ purpura	22	16	72
Temperature instability	40	20	52
Shock	26	12	47
Respiratory distress	172	64	38
Lethargy	22	8	37
Feed intolerance	6	2	35
Apnoea	38	10	28

**Table 5: Bacteriological profile of early onset sepsis.**

Organism	Frequency	Percentage
Gram positive bacteria		
Staphylococcus aureus	10	12.50
Enterococcus	6	7.5
MRSA	14	17.5
Gram negative bacteria		
Klebsiella	14	17.5
Pseudomonas	14	17.5
Acinetobacter	10	12.5
Proteus	2	2.5
Citrobacter	2	2.5
Enterobacter	8	10

40% of bacteria culture cases were gram positive while 60% of bacteria culture cases were gram negative. However, septecemia was more predominant in gram-negative septicemia (62.5%) compare to gram-positive septicaemia (37.5%). [Table 5]

Pulmonary hemorrhage (36%) followed by septic shock (30%) and hyaline membrane disease (27%) were the most common cause of death in the present study.80% of gram negative and 20% of gram positive organisms were involved in all the deaths caused due to sepsis. The mortality rate was significantly higher for out born neonates (50%) as compared to inborn neonates (34%) out born

neonates (50%) as compared to inborn neonates (34%). On the other hand, neonates having weight range 1000-1499 had mortality rate of 34.5%. Further results revealed that mortality was higher in early preterm belonging to  $\leq 30$  weeks and 31-34 weeks gestational age range which was 43% each as compared to late preterm neonates with gestational age range 35-37 weeks which was only 20%.

## DISCUSSION

In the present study early onset septicaemia is considered when sepsis occurred in neonates within 72 hours of life. Studies have shown that usually infection is acquired of birth canal or at the time reconstruction in labor room is found due to ascending infection which is followed by rupture of membranes or passage of the baby.<sup>[6,7]</sup>

Various causes of child mortality have been identified for neonatal deaths in India. Among these causes preterm birth complications and infections are the most important. Studies suggest that premature infants have two times more incidence of sepsis while it is more higher in very low birth weight neonates.<sup>[6,8]</sup>

Findings of the current study shows that there was no significant correlation between blood culture positivity and various variables like gender, birth weight, gestational age and mode of delivery. These findings are consistent with the findings of the earlier studies of Sarangi K et al, Maharaja P et al and Satyamurthi B et al as they recorded similar insignificant correlation between these variables and culture positivity in neonates.<sup>[9-11]</sup>

Results of the present study showed that 40% neonates were bacterial positive predominantly gram negative organism out of 200 neonates. Further, among bacterial positive organism gram negative bacteria's (62.5%) were abundantly found compare to gram positive bacteria (37.5). These findings are in full agreement with the previous studies of Hoque M et al and Sarangi K et al as they recorded bacterial positivity in 33% and 35.9% neonates respectively.<sup>[9,12]</sup> Similarly, Satyamurthi B et al,<sup>[11]</sup> Kalpana KL and Kayange N et al reported 34%,<sup>[13,14]</sup> 37% and 44% bacterial positivity in early sepsis of neonates with low birth weight. Further, in the current study most commonly involved bacteria were Pseudomonas, Klebsiella, MRSA. These results are very similar to the previous study of Hoque M et al,<sup>[12]</sup> as they recorded Acinetobacter (41.2%) was the most common isolated organism in early sepsis of neonates followed by Klebsiella pneumoniae (23.5%). Similarly, Lim WH et al<sup>[15]</sup> observed E. coli (40%) and Klebsiella (20%) were the most abundantly isolated bacteria in neonates with early onset septicaemia. Alike, Satyamurthi B et al,<sup>[11]</sup> reported that Klebsiella and S. aureus were most common cause for early onset of septicaemia in the neonates with low birth weight.

Various studies have reported that gram negative bacteria are among most common pathogen found involved in the genesis of sepsis. However, exact mechanism is still unclear.<sup>[10,16]</sup> Nonetheless, this can be explained by two different hypothesis for the mechanism of gram negative bacteria inducing harmful effects in neonates. One hypothesis suggest that invasion of bacterial organism to blood might be via injured or intact epithelium. This may in turn induce the systemic inflammatory responses which may result in failure of multiple organs. On the other hand another theory suggests that bacterial infections may persuade neuroendocrine dysregulation and mediators released in to systemic circulation.<sup>[17]</sup>

This high rate of culture positivity may be due to very low birth weight of neonates as decreased body weight neonates are more susceptible of infections via different causes like reduced level of immune cells which are transferred during the third trimester. In addition, the first line of defense against infection is compromised in very low birth weight neonates.<sup>[6,18-20]</sup>

Results of the current study revealed that prolonged rupture of membranes with a positivity rate of 67% followed by urinary tract in infection in mother with a positivity rate of 58% were most commonly associated with blood sepsis. These results are consistant with the previous studies of Maharaja P et al,<sup>[8]</sup> as they recorded that sepsis was positively correlated with prolonged rupture of membranes in low birth weight neonates. Similarly, Roy P et al,<sup>[21]</sup> observed that urinary tract in infection in mother and premature rupture of membranes are the most common risk factors which leads early sepsis in neonates.

Current study recorded that the number of risk factors and the risk of septicemia in the neonates simultaneously increased. These findings are very similar to the findings of Roy P et al,<sup>[21]</sup> as they observed increased incidence of sepsis in neonates along with increased number of risk factors.

Non-specificity of symptoms is the remarkable feature of the clinical manifestations of neonatal septicemia in different types bacterial sepsis. The earliest signs of sepsis are often subtle and nonspecific and need a high index of suspicion for early diagnosis.

Bleeding/purpura (72%) followed by temperature instability (50%) and shock (46%) were the most common clinical feature associated with the bacterial infection in the present study. These findings are in agreement with the earlier study of Maharaja P et al and Lim W H et al as they reported purpura and temperature instability among the most common clinical features of early sepsis in neonates.<sup>[10,15]</sup>

Mortality rate recorded in the current study was 41%. Multiple factors like inadequate early intervention from the place referral, a delay in referral and transport from peripheral health facilities to referral centres and improper transportation

without maintaining the warm chain are among the different causes lead to higher mortality rates as observed in out-born cases.

Pulmonary hemorrhage followed by the septic shock was the most common causes of neonate death in our study. Mortality in neonates in our study is mainly induced due to respiratory complications especially in preterm very low birth weight neonates. These findings are consistent with the previous study of Lim JW et al,<sup>[22]</sup> as they observed respiratory disorders were leading cause of neonatal casualty among neonates suffering with sepsis.

## CONCLUSION

Neonatal sepsis is a well-recognized cause of neonatal mortality and morbidity and more pronounced in VLBW infants. Present study confirmed the presence of major concern about the high rate of sepsis among VLBW infants. A detailed antenatal, natal and postnatal history should be taken to know the risk factors of septicemia. Clinical examination is of utmost importance for early suspicion of neonatal sepsis. Antibiotic therapy should be considered in absence of clinical features if >2 risk factors of sepsis are present. Blood culture should be done in all suspected cases of neonatal septicemia, preferably by BACTEC method which provides early confirmation of sepsis. Organisms causing neonatal sepsis and their antibiotic susceptibility vary from place to place. Antibiotics should be given according to culture and sensitivity rather than empirical treatment for better outcomes. To keep the infection rates low, strict protocol for asepsis in neonatal units must be adhered to when handling these high-risk infants as prevention is better than cure.

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