RISK FACTORS ASSOCIATED WITH EARLY ONSET OF NEONATAL BACTERIAL SEPSIS IN BABIES BORN IN A RURAL TEACHING HOSPITAL- A PROSPECTIVE OBSERVATIONAL STUDY

Dr. NISHANTH. M[1],

Assistant Professor, Pediatrics, Dr.Pinnamaneni Siddhartha Institute of Medical Sciences, Gannavaram.

Dr.**SHAIK K JOHN MOHAMMAD ALISHA[2],**

Assistant professor, Pediatrics, Konaseema Institute of Medical Sciences, Amalapuram

Corresponding Author - Dr. MUJIBUR REHAMAN SHAIK,

Assistant Professor, Community Medicine, Siddhartha Medical College, Vijayawada.

Abstract:

Introduction: Early onset neonatal sepsis (EONS) remains a major cause for neonatal mortality and morbidity.To reduce neonatal mortality due to neonatal sepsis, preventive strategies are better than therapeutic measures.

AIM: To identify maternal and foetal risk factors associated with early onset neonatal bacterial sepsis (EONS), in babies born in a rural teaching hospital.

Methodology –During the study period, using simple random sampling method, total 204 neonates were selected. Of them, only 172 mothers of neonates (134 controls, 38 EONS cases) gave written informed consent.

Results- The birth weight was significantly low in babies who developed EONS (mean weight 2.39± 0.8) compared to that of the control group(mean weight 2.83±0.6).The Mean APGAR score at 5 minutes was significantly low in babies who developed EONS (7.15± 1.03) compared to that of the control group (9.3±0.9).Late preterm (GA 32 to 36 weeks) was a risk factor for EONS. Prematurity was significantly associated with EONS. Pregnancy domicile area of the mother was not associated with development of sepsis.

Conclusion-Ambuuse, Laryngoscope use, Oxygen use, ET intubation in the delivery room were not associated with EONS risk. Baby not undergoing or not needing gastric lavage in the delivery room was a protective factor against EONS.

Keywords: Neonatal sepsis, Low birth weight, preterm babies.

INTRODUCTION

Neonatal sepsis is the major cause of morbidity and mortality among neonates of developing countries.[1]Neonatal sepsis occurs in newborns of <28 days of life that can involve systemic infection, circulatory shock, and multisystem organ failure. Early-onset newborn sepsis (EONS) and late-onset neonatal sepsis (LONS) are the two kinds of neonatal sepsis (LONS). Infection and sepsis occurring within the first 24 hours to first week of birth are commonly termed as EONS.[2–4]After 24 hours or after the first week of life, LONS have been classified as lasting up to 28 days or one month.[5–7]According to various authors EONS is occurring within the first 72 hours of life and LONS as occurring after 72 hours of birth and lasting up to 28 days. [8–11]

Premature rupture of membranes, maternal fever within two weeks before delivery, and meconium stained liquor and foul-smelling liquor are some of the maternal causes of sepsis. Low birth weight and premature birth of the baby, low APGAR score at 1 minute and 5 minutes are the some foetal factors for sepsis.

EONS usually results from vertical transmission and, consequently, is associated with organisms that colonize the birth canal. Organisms can ascend to the amniotic fluid, colonizing the infant, or the infant may become colonized during passage through the birth canal. Invasive infection may occur if the skin barrier is breached.

Depending on the country, the organisms and infections mainly related with newborn sepsis varies. Pathogens include everything from gram-positive and gram-negative bacteria to viruses and fungi, with bacteria being the most common. Staphylococcus aureus, coagulase negative staphylococci (CONS), Streptococcus pneumoniae, Streptococcus pyogenes, Escherichia coli, Klebsiellapneumoniae, Pseudomonas aeruginosa, Salmonella typhi, and Group B streptococcus (GBS) are the most typically implicated bacteria.[12]The present study was conducted to identify the maternal and foetalrisk factors associated with early onset neonatal bacterial sepsis.

Aims and Objectives:
AIM:
To identify the maternal and foetalrisk factors associated with early onset neonatal bacterial sepsis (EONS) in babies born in a rural teaching hospital.
OBJECTIVES:
To identify the delivery room neonatal care factors (usage ofmucous sucker,laryngoscope,Ambu-bag, gastric lavage, Endotracheal intubation) and risk factors associated with EONS.

Methodology
This Observational study was conducted at Neonatal Intensive Care Unit (NICU), Department of Paediatrics, Pinnamaneni Siddhartha Institute Of Medical Sciences And Research Foundation, Gannavaram from December 2017 to June 2018. Live born neonates of 0-28 days with the features of sepsis who were admitted in NICU during the study period were considered as cases, and neonates admitted with features other than sepsis were taken as controls. **Ethics committee approval was obtained prior to the conduction of the study.During the study period, using simple random sampling method, total 204 neonates were selected. Of them, only 172 mothers of neonates (134 controls, 38 EONS cases) gave written informed consent.**
Mode of selection of subjects:
When any baby was suspected to be having Early Onset Neonatal Sepsis (EONS) according to the clinical context, two blood cultures were sent.
- In this study, EONS was defined as
➢ Bacterial sepsis within 1st seven days after birth.[13]
➢ When any 1 or 2 blood cultures sent in a culture media (on MacConkey (MC) agar, chocolate agar, and blood agar) within seven days after birth have grown pathogenic bacteria.
➢ When two blood cultures sent within seven days were not showing any bacterial growth, it was defined as No early onset of sepsis (**NOEOS).** It was taken as **control**.

➢ When clinically there was no need to send any blood culture in 1ˢᵗ seven days, it was taken as **control.**

➢ Due to logistics or difficulty in drawing blood samples in some babies 2ⁿᵈ blood culture could not be sent, the 1ˢᵗ blood culture sent did not show any pathogenic organism. Such babies were taken as **control.**

Variables measured:

1) Predictor variables:

• **Mother:** Meconium stained liquor, Premature rupture of membranes (PROM) duration in hours, domicile area (rural, urban) of a mother during pregnancy.

• **Baby:** Gender, baby birth weight [Low birth weight(LBW,2500gm),very low birth weight (VLBW, <1500 gm) and extremely low birth weight (ELBW, <1000 gm)], baby growth category [Large for gestational age(LGA)- >90ᵗʰ percentile, Average for gestational age(AGA)- 10ᵗʰ to 90ᵗʰ percentile, Small for gestational age (SGA)- <10ᵗʰ percentile], gestational age in weeks (Very preterm= 28-32 weeks, Late preterm= 32-36 weeks, Near Term= 36-37weeks, Term= 37-42 weeks).

• **Delivery room neonatal care factors:**usage ofmucous sucker,laryngoscope,Ambu-bag, endotracheal intubation, and gastric lavage done or not.

• **Others:** Meconium stained liquor, labour type (Spontaneous, Induced), Method of delivery (emergency or elective lower segment caesarean section, vaginal delivery), 1 minute APGAR score, 5 minutes APGAR score, 10 minutes SPO2 in the delivery room**,** hospital stay (in hours).

2) Outcome variable:

• EONS (blood culture positive in first seven days).

Statistical analysis:

Data was entered into a structured electronic data sheet (MS Excel 2007) and analyzed by Epi Info TM 7.1.5.2 of center for disease control, USA61 &Medcalc17.9.7, Belgium.[14] Mean and standard deviation of the quantitative variables of normal distribution were measured. Proportions were estimated for qualitative (categorical) variables. Significant group difference of continuous variables was found using T-test (parametric test) for normally distributed characteristics and Mann- Whitney test (Non parametric test) for non-normally distributed continuous variables. For categorical variables, significant group differences in the distribution of proportion were found using the chi-square test or Fisher's exact test. The risk factors for early neonatal bacterial sepsis were identified by multivariate logistic regression. P value less than 0.05 was taken as significant level.

Observation & Results

In this study, of the total 204 sample, 134 controls and 38 EONS cases were observed, and the following results were noted.

Table 1: Comparison between Controls and EONS

Parameter	Category	Controls (134)	EONS(38)	Statistical test used	P value
Domicile	Rural	114 (85.1%)	36(94.7%)	Chi-squared	0.115(Non

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	Urban	20 (14.9%)	2 (5.3%)	2.478; DF 1	Significant)
Gender of the baby	Female	77(57.5%)	22(57.9%)	Chi-squared 0.002; DF 1	0.96(Non Significant)
	Male	57(42.5%)	16(42.1%)		
Growth of the baby	AGA	104(77.6%)	31(81.6%)	Chi-squared: 0.716;DF 2	0.69(Non Significant)
	LGA	2(1.5%)	0(0%)		
	SGA	28(20.9%)	7(18.4%)		
Birth weight of the baby	Normal	112(83.6%)	20(52.6%)	Chi-squared: 30.802;DF 3	0.0001(Highly significant)
	LBW	22(16.4%)	11(28.9%)		
	VLBW	0(0%)	5(13.2%)		
	ELBW	0(0%)	2(5.3%)		
Gestational age	Late Preterm	2(1.5%)	8(21.1%)	Chi-squared 61.795;DF 3	0.0001(Highly Significant)
	Near Term	0(0%)	6(15.8%)		
	Term	132 (98.5%)	20(52.6%)		
	Very Preterm	0(0%)	4(10.5%)		
Meconium stained liquor	Present	4(3%)	10(26.3%)	Chi-squared 21.55;DF 1	0.0001(Highly Significant)
	Absent	130 (97%)	28(73.7%)		
Type of labour	Induced	74 (55.2%)	22(57.9%)	Chi-squared: 0.086;DF 1	0.770(Non Significant)
	Spontaneous	60 (44.8%)	16(42.1%)		
Method of Delivery	Elective LSCS	14(10.1%)	6(15.8%)	Chi-squared 0.986;DF 2	0.611(Non Significant)
	Emergency LSCS	44(31.9%)	12(31.6%)		
	Vaginal	80(58%)	20(52.6%)		

LSCS= lower segment caesarean section

Regarding comparison between Controls and EONS,except birth weight, gestational age, and meconium stained liquor,remaining all (domicile, gender, growth, birth weight, gestational age, type of labour, method of delivery) were statistically non significant (Table 1).

Table 2: Difference between neonates of EONS and Control in various parameters

Parameter	Controls (134) (Mean ± Standard deviation)	EONS(38) (Mean ± Standard deviation)	Statistics
Mean Premature rupture of membranes (PROM)	0.3 ± 1.8	1.8 ± 5.0	Mann-Whitney U 2170.5; P value 0.002(significant)
Mean APGAR score at 1 minute	7.0 ± 1.41	6.1 ± 1.42	Mann-Whitney U 1361.50; P value 0.0001(significant)
Mean APGAR score at 5 minutes	9.3 ± 0.9	7.15 ± 1.03	Mann-Whitney U728.00; P value 0.0001(significant)
Mean gestational age	38.6 ± 1.1	36.2 ± 2.7	Mann-Whitney U 1142.0; P value 0.001(significant)

Mean birth weight (in grams)	2836.0 ± 621.3	2390.5 ± 828.9	Independent T Test 5.010; P value 0.0001(significant)
Mean SPO2 at 10 minutes	95.9 ± 4.3	94.5 ± 3.9	Mann-Whitney U1838; P value 0.008 (significant)
Mean duration of hospital stay (in hours)	117.2 ± 56.1	474.6 ± 309.7	Mann-Whitney U303; P value 0.001 (significant)

As shown in table 2, PROM, mean APGAR score at 1 minute and 5 minutes, mean gestational age, mean birth weight, SPO2 at 10 minutes and duration of hospital stay (in hours) differed statistically at significant level between Controls and EONS.
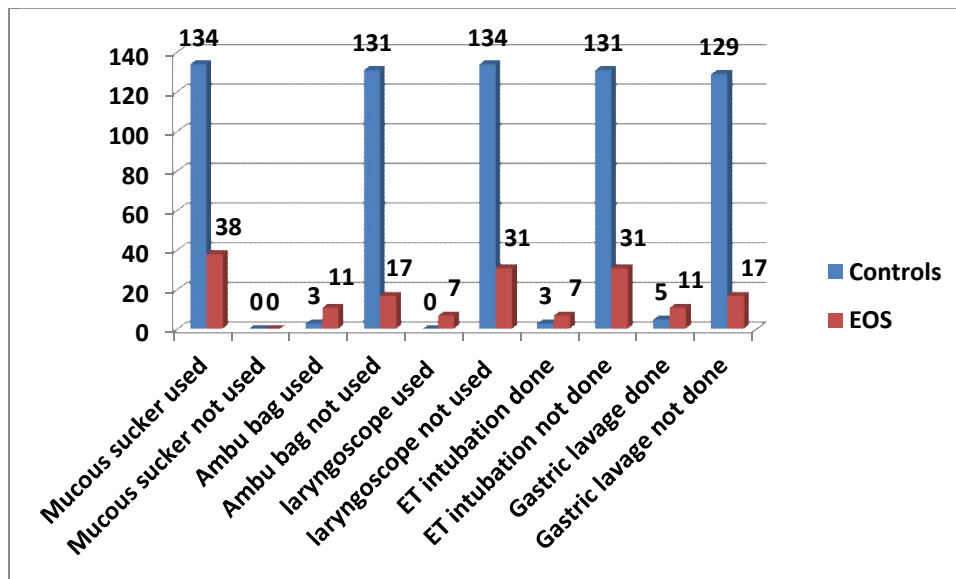
ET= Endotracheal

Figure 1: Characteristics of Neonatal Resuscitation

In this study, more number of EONS cases needed ambu bag usage and gastric lavage than the controls.Mucous sucker was used in all cases as well as in the controls Neonatal resuscitation measures were applied in majority of EONS cases than controls. (Figure 1).

Table 3: Distribution of organisms in EONS

EONS organisms	Frequency	Percent	95% C.I	
Acinetobacterbaumannii	2	5.26%	0.64%	17.75%
Burkholderia	1	2.63%	0.07%	13.81%
CONS	11	28.95%	15.42%	45.90%
Escherichia coli (E.coli)	3	7.89%	1.66%	21.38%

Enterococcus fecalis	1	2.63%	0.07%	13.81%
Klebsiella	9	23.68%	11.44%	40.24%
MRSA	5	13.16%	4.41%	28.09%
MSSA	2	5.26%	0.64%	17.75%
Pseudomonas aeruginosa	2	5.26%	0.64%	17.75%
Streptococcus species	2	5.26%	0.64%	17.75%
Total	38	100.00%		

CONS= Coagulase Negative Staphylococcus Aureus, MRSA= Methicillin Resistant Staphylococcus Aureus, MSSA= Methicillin Sensitive Staphylococcus Aureus

Distribution of organisms in EONS: As shown in table 3, regarding organisms found in culture, CONS was found in the majority of the EONS cases, followed by Klebsiella, MRSA, E.coli, and MSSA, AcinetobacterBaumannii, Pseudomonas Aeruginosa, Streptococcus species in equal number of cases.

Table 4: Multivariate logistic regression for risk factors of early-onset neonatal sepsis (EONS)

Parameter	Coefficient	Std. Error	Wald	P value	Odds ratio	95% C.I
Maternal PROM (in hours)	0.214	0.079	7.245	0.007	1.2387	1.05 to 1.44
Late preterm	2.222	0.971	5.230	0.022	9.2315	1.37 to 62.02
No need of Gastric lavage	-2.816	0.90441	9.6989	0.0017	0.0018	0.01 to 0.35
Higher APGAR score at 5minutes	-1.110	0.223	24.5795	<0.0001	0.3295	0.21 to 0.51
Constant	22.869	5.71577	16.0093	0.0001		

PROM - Premature rupture of membranes; C.I- Confidence Interval
*Only positive findings were displayed in table 4
Risk factors of early-onset neonatal sepsis (EONS): Regarding risk factors of early-onset neonatal sepsis (EONS) on multivariate logistic regression model, maternal PROM (in hours), late preterm were found as the risk factors for EONS, whereas no need of gastric lavage in the delivery room, and higher APGAR score at 5minutes were considered as protective factors against EONS (Table 4).

DISCUSSION

- In this study, the study design was a observational study, while it was a case-control study in the studies by Gebremedhin D et al.[15], Swankar K et al.[16], Shah GS et al.[17], Oddie S et al.[18], and Jajoo M et al.[19]
- In the present study, sample size of EONS was smaller which was similar to Gebremedhin D et al.[15], and Oddie S et al.[18] studies. The sample size of controls was of adequate size and cases, controls ratio was 1:3.5.
- Clinical setting of this study was similar to Swankar K et al.[16], Shah GS et al.[17], OddieS et al.[18], and Jajoo M et al.[19]
- Culture positivity of this study was 22.1%, which was similar to the study by Shah GS et al.[17], whereas higher (34%) incidence was reported by Sorsa A.[20]
- In this study CONS was found in the majority of the EOS cases which was similar to Sorsa A[20], Leal YA et al.[21], whereas NNPD report[22]showed that K.pneumoniae and S.aureus as predominant organisms. In the studies by Betty C et al.[23], and Tallur SS et al.[24], Pseudomonas and Klebsiella were the common organisms.

Multivariate logistic regression

- In the present study, on multivariate logistic regression, domicile and mode of delivery were not risk factors for sepsis, which was similar to Gebremedhin Det al.[15],while thesewere considered as risk factors for the studies by Siakwa M et al.[25], Woldu MA et al. [26], Chacko B and Sohi I[27], Hasan MS and Mahmood CB. [28]
- In this study, PROM was found to be a risk factor for EONS. A similar observation was found in the studies by Gebremedhin D et al.[15], Swankar K et al.[16], Shah GS et al.[17], Oddie S et al.[18], Sorsa A [20], Leal YA et el.[21], and Betty C et al.[23]
- In this study, Meconium stained amniotic fluid was not associated with EONS. Similar observation was reported by Oddie S et al.[18], and Betty C et al.[23]
- In this study, late preterm was risk factor for sepsis, while prematurity was the risk factor in the studies by Shah GS et al.[17], Sorsa A [20], Leal YA et el.[21],Siakwa M et al.[25], Chacko B and Sohi I[27], and Raghavan M et al.[29]
- In the present study low birth weight had an insignificant effect on the risk of neonatal sepsis, which was similar to the studies by Gebremedhin D et al.[15], Woldu MA et al.[26], and Hasan MS et al.[28]
- In this study higher APGAR at 5 minutes was a protective factor against EONS. Similar observation was found in the studies by GebremedhinDet al.[15]and Swankar Ket al.[16],Hasan MS et al.,[28] and Raghavan M et al.[29]
- Gastric lavage not done in the delivery room was a protective factor in this study. It was not observed in other studies.

CONCLUSION

In this study, PROM, late preterm increased the risk of EONS, while no need of Gastric lavage and high APGAR score at 5 minutes were protective factors against EONS. Thus both maternal and neonatal factors may lead to the development of EONS. Hence screening of early infections for proper diagnosisand adequate treatment of maternal infection will help in reducing the high-

risk pregnancy. In addition to this, adequate perinatal management of infections among neonates arerecommended to prevent neonatal morbidity and mortality due to sepsis.

CONFLICT OF INTEREST: There is no conflict of interest for the study

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