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Research Article

Relationship between gestational age and mode of delivery with neonatal septicemia

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ABSTRACT

Background: Newborn infants are at much higher risk for developing sepsis than children and adults because of their immature immune system especially premature infants. In spite of the efforts of Government and non-government sectors, neonatal sepsis constitutes a major cause of morbidity and mortality in neonates of this region. Our aim of study was to find out the relationship between gestational age and mode of delivery with neonatal septicaemia.
Methods: A hospital based study was done between 1st June 2014 to 31st May 2015 at NICU of tertiary care center, Indore. Both qualitative and quantitative data was collected from bed side. Chi square test and Binary logistic regression were used for the analysis. We calculated odds ratios (OR) and their 95% confidence intervals (95% CI) P-value <0.05 was considered to be statistically significant.
Results: Among the 399 NICU patients studied, our study showed male(62.4%) preponderance as compared to female(37.6%) in neonatal infection, out of which 35.3% cases were reported to be neonatal septicaemia making male(37.8%)more prevalent than female(31.3%). Preterm were having 1.49 [CI (0.95, 2.35)] times risk of developing septicaemia as compared to term neonates ($p<0.05$). Patients under study showed 83.5% were born with normal vaginal delivery (NVD) and 16.5% via caesarean section, among this neonates born via NVD is 2.29[CI=(1.22,4.3)] times more risk of developing NNS as compared to caesarean section($p<0.05$).
Conclusions: The analysis shows that neonatal infection is having more preponderance with preterm male neonates, born with normal vaginal delivery. Keeping in view these facts, a comprehensive but achievable and sustainable program should be implemented to reduce neonatal septicaemia.

Keywords: Neonatal septicaemia, NICU, Paediatrics

INTRODUCTION

Of the total 130 million infants born each year worldwide, 4 million die in the first 28 days of life.[1] Three-quarters of neonatal mortality occur in the first week, and more than one-quarter occur in the first 24 hours.[1,2] 40% of deaths under the age of 5 years worldwide accounts for Neonatal deaths. Hence, the UN Millennium Development Goal 4 is aimed at reducing childhood mortality by two-thirds by 2015 and reducing neonatal deaths in high-mortality countries. The direct cause accounting for as much as 24% of neonatal deaths according to the World Health Organization (WHO) and the most significant problem in current obstetric practice is preterm birth.[3] Rates of preterm birth range between 7-16% and are similar worldwide.[3] The WHO estimates that 1 million deaths per year (10%) of all deaths in under five years old) are due to neonatal sepsis and that 42% of these deaths occur in the first week of life. Globally, the main direct causes of neonatal mortality are thought to be preterm birth (28%), severe infections (26%), and asphyxia (23%).[2]

Symptoms of infection along with systemic signs in the first 4 weeks of life due to bacteraemia represent the clinical syndrome defined as neonatal sepsis. The pathogenic bacteria after gaining access into the bloodstream cause an exaggerated infection without much localization (septicaemia) or may predominantly localise to the lung (pneumonia) or the meninges (meningitis). It can be classified as before 72 hours of life (early-onset neonatal sepsis-EONS) or late (late-onset neonatal sepsis-LONS).

The objective of the study was to find out the neonatal outcome in relation to gestational age, mode of delivery and various diagnostic markers in neonatal septicaemia (early and late).

METHODS

It was a hospital based retrospective observational study conducted in the Department of Paediatrics, Sri Aurobindo Institute of Medical Sciences, Indore, MP.

This study was carried out from 1st June 2014 to 31st May, 2015.The study population included patients admitted in paediatrics NICU from different parts of Central India. Data was collected from the medical record department of the patient from NICU. The variable collected were age, sex, weight, mode of delivery, gestational age, and diagnostic markers. Total of 399 cases were included in the study having both early and late onset septicaemia, along with other neonatal diseases. Estimation of complete blood count was done by Coulter Counter for which minimum of 2ml blood is collected and results of total count and differential count are obtained. Results of differential were reconfirmed by microscopically (manually). The CRP-latex is a slide agglutination test for the qualitative and semi quantitative detection of C - reactive protein (CRP) in human serum (serum 1 ml). Latex particles coated with goat IgG anti-human CRP are agglutinated when mixed with samples containing CRP.

Inclusion criteria

Preterm births <37 weeks was include and term between >37 weeks and <42 weeks. Neonates (<28 days) were included as a study group, 0-7 days age were assigned as early onset neonatal septicaemia, and>7 but < 28 days were late onset neonatal septicaemia. Normal vaginal delivery and caesarean section was included in the study.

Outcome variables

The levels of total leukocyte count, C - reactive protein (CRP), lymphocytes, neutrophils and mode of delivery, gestational age and sex were assessed in relation to neonatal septicaemia.

Explanatory variables

Factor at individual level were Age, Sex, Gestational age, Mode of delivery, Early and late onset neonatal septicemia.

Data management and statistical analysis

Analysis was done using descriptive statistics and testing of hypothesis. The data was analysed using MedCalc software (trial Version). A p-value of <0.05 (two-tailed) was used to establish statistical significance**.**

RESULTS

Out of 399 cases, male (62.4%) showed preponderance as compared to female (37.6%) in neonatal infection, out of which 35.3% cases were reported to be neonatal septicaemia making male (37.8%) more prevalent than female (31.3%).

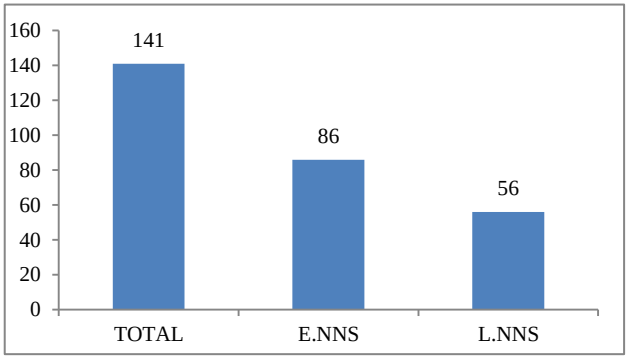

Figure 1: Predicting total number of neonatal sepsis cases (early and late).

Table 1: Comparison of diagnostic markers in early onset neonatal septicaemia.

		Mean± SD Confidence interval	p-value
WBC	Early (86)	13981.73±7108.4 CI(11277.83,16685.62)	0.792[x]
	Late (56)	13440.70±.7479.9 CI(10206.13,16675.26)	
CRP	Early (86)	34.76±31.19 CI(22.89, 46.62)	0.677[x]
	Late (56)	31.17±30.17 CI(18.13,44.22)	
Neutrophil	Early (86)	57.86±22.81 CI(49.19,66.54)	0.972[x]
	Late (56)	57.61 ±27.382 CI(45.77,69.45)	
Lymphocyte	Early (86)	34.31±18.90 CI(27.12,41.5)	0.248[x]
	Late (56)	28.13±18.90 CI(19.95,36.31)	

[x] statistically not significant (p>0.05).

Figure 1 depicts that 141 (35.3%) cases were diagnosed to be neonatal septicaemia [86 (33.3%) were early onset

neonatal sepsis and 56 (39.0%) were late onset neonatal sepsis.

Table 2: Cross tabulation between Socio demographic factors and neonatal sepsis.

Variables		Neonatal sepsis			p-value	Odds ratio
		Yes	No	Total		
Age	Early(<24hours)	86(33.33%)	172(66.67%)	258	0.257 *	1
	Late(>24hours)	55(39.0%)	86(60.99%)	141		1.279[CI(0.835,1.958)]
Sex	Male	94(37.8%)	155(62.20%)	249	0.194 *	1.329[CI(0.865,2.043)]
	Female	47(31.3%)	103(68.7%)	150		1
Gestational age	1(<37weeks)	102(38.6%)	162(61.4%)	264	0.084 *	1.491[CI(0.948,2.346)]
	2(37-42 weeks)	38(29.7%)	90(70.3%)	128		1
	3(>42 weeks)	1(14.3%)	6(85.7%)	7	0.397*	0.395[CI(0.046,3.391)]
Mode of delivery	Normal vaginal delivery	127(38.1%)	206(61.9%)	333	0.009#	2.290[CI(1.219,4.300)]
	Caesarean section	14(21.2%)	52(78.8%)	66		1

* statistically not significant (p>0.05); # statistically significant (p<0.05).

Table 1 shows that levels of WBC [13981.73 (CI: 11277.83, 16685.62)], CRP [34.76 (CI: 22.89, 46.62)] and lymphocytes [34.31 (CI: 27.12,41.5)] were markedly raised in Early onset Neonatal sepsis as compared to Late onset Neonatal sepsis WBC [13440.70 (CI: 10206.13, 16675.26)], CRP [31.17 (CI: 22.89, 46.62)], lymphocytes [28.13 (CI: 19.95,36.31)] (p>0.05).According to the study it is obvious to make out that among the selected markers: CRP,WBC, lymphocytes, neutrophils first three markers were more significant in establishing the early onset neonatal septicaemia as compared to late onset neonatal septicaemia. Neutrophil in our perspective didn't show much significance.

Table 2 preterm were having 1.49 [CI (0.95, 2.35)] times risk of developing septicaemia as compared to term neonates (p<0.05). Amongst them 83.5% were born with normal vaginal delivery (NVD) and 16.5% via caesarean section, out of which neonates born via NVD is 2.29 [CI (1.22,4.3)]times more risk of developing neonatal septicaemia as compared to caesarean section(p<0.05). Thus it is easy to conclude that among the various age groups, preterm neonates are more vulnerable in developing the fatal condition neonatal septicaemia, normal vaginal delivery is also markedly associated with more chance of having sepsis making the chance of early mortality and morbidity among neonates.

DISCUSSION

Infants are generally more prone to develop infections than adults. Poor hygienic conditions pose an increased risk of sepsis in a new-born due to an inadequately developed immune system. Neonatal sepsis still continues to account for the majority of neonatal morbidity and mortality inspite of marked improvements in its diagnosis and management especially in developing countries.Sepsis is the commonest cause of neonatal morbidity and mortality. It is responsible for about 30-50% of total neonatal deaths.[4,5] Sepsis related morbidity and mortality is largely either preventable or treatable with rational antimicrobial and supportive therapy. LBW is a strong risk factor for neonatal sepsis due to multiple reasons. Unsafe delivery or unclean delivery at inappropriate place is another important predisposing factor for sepsis. The WHO estimated the burden of mortality for neonatal sepsis in 2004 ('Global Burden of Disease') based partly on work by Lawn et al.[2] Neonatal infections (mainly sepsis and pneumonia and excluding diarrhoeal diseases) accounted for 26% of all neonatal deaths in 2004 (1 million deaths in total, based on 2000 mortality data). The absolute number of deaths from infections was highest in Southeast Asia, while the mortality rate in neonates from infections was highest in Sub-Saharan Africa. Alternatively, UNICEF (State of the World's Children 2009) suggests that neonatal sepsis could account for up to 50% of all neonatal deaths.[6] Bacterial sepsis is considered as one of the important cause for neonatal mortality (deaths in the first 28 days of life).[7-11]

Neonatal septicaemia with gestational age

In contrast to our study, Caughey et al found that the rates of immediate neonatal morbidity increased with increasing gestational age.[12] Accurate determination of these rates was important in the determination of gestational age at which the risk of continuing the pregnancy outweighed the risk of induction of labour. Another study by Alexander et al compared labour characteristics and neonatal outcomes of pregnancies at 40, 41 and 42 weeks' gestation.[13] Neonatal outcomes were similar in the three groups. In our study Preterm were having 1.49 [CI (0.95, 2.35)] times risk of developing septicaemia as compared to term neonates (p<0.05) making preterm preponderance.

Neonatal septicaemia with mode of delivery

Otoide et al evaluated whether routine induction of labour at 41-42 weeks of gestation has an increased risk for

operative delivery, maternal or foetal complication compared with spontaneously initiated labour of similar gestation.[14] There was no significant difference in caesarean section rates in the induction group, compared with spontaneously initiated labour. Foetal complications were similar. Patients under study showed 83.5% were born with normal vaginal delivery (NVD) and 16.5% via caesarean section, among this neonates born via NVD is 2.29 [CI=(1.22,4.3)]times more risk of developing NNS as compared to caesarean section ($p<0.05$).

Neonatal sepsis and CRP

CRP is an acute phase protein synthesised in the liver in response to inflammatory cytokines. At the time of an acute phase response the levels of CRP may rise up a thousand fold and these tend to fall rapidly due to its short half-life (19hours) as soon as the source of infection (often microbial) has been eliminated.[15] In our study the mean CRP level for early onset neonatal sepsis was [mean 34.76 (CI: 22.89, 46.62)] which was little higher than late onset neonatal septicemia [mean 31.17 (CI: 18.13, 44.22)].This showed that early neonates are more prone for having higher level of CRP.

Neonatal sepsis and total leukocyte count

Total leukocyte counts are of limited value in the diagnosis of septicaemia in new-borns.[16] Total leukocyte counts are particularly unreliable indicators of infection during the first several hours of early-onset (within 48 hours of birth) sepsis because they are normal at the time of initial evaluation in more than one third of infants with proven bacteraemia.[17-29] Conversely, among neonates evaluated for suspected sepsis, far less than half of neonates with reduced (<5000 cells/mm^3) or elevated (>20,000 cells/mm^3) cell counts are ultimately identified to be infected.[17,19,21,28]

The current study signifies that in early onset sepsis, total count are showing more significant increase in early neonatal sepsis as compared to late onset sepsis. The mean value of WBC [mean 13981.73 (CI: 11277.83, 16685.62)] in early onset is higher as compared to late onset [mean 13440.70 (CI: 10206.13, 16675.26)].

Neonatal sepsis and lymphocytes

Lymphocyte counts can rise or fall on the basis of changes in (1) input of lymphocytes into the circulation, (2) margination (including sequestration in the spleen or lymph nodes), and (3) regress from or destruction within the circulation. Although perinatal changes in corticosteroid concentrations may be involved in regulating fetal and neonatal lymphocyte concentrations, other humoral factors such as catecholamine's, cytokines, and growth factors might also contribute.[29,30] Our study emphasised that early onset neonatal septicaemia [mean-34.31 (CI: 27.12, 41.50)]

Neonatal sepsis and neutrophil

Absolute neutrophil count < 2.0×10^9/L in a neonate is defined as neonatal neutropenia and reportedly it is present in approximately 8% of all patients admitted into NICU.[31,32] In the United States, this translates to 32,000 NICU admissions with neutropenia per year.[32,33] In our hospital based study neutrophil did not proven to be significant for neonatal sepsis. Early onset neonatal septicaemia [Mean-57.86 (CI: 49.19, 66.54)], late onset neonatal septicaemia [Mean-57.61 (CI: 45.77, 69.45)].

CONCLUSION

From this study it can be reassured that neonatal infection is having more preponderance with preterm male neonates, born with normal vaginal delivery and predictive markers are useful in identifying/predicting sepsis. Out of various hematological and biochemical parameters CRP, WBC, and lymphocyte count were found to be elevated in early onset sepsis. Serial measurement of infection markers will certainly improve the diagnostic sensitivity of these tests, because in most circumstances it is not certain at which stage of the infection the specimen should be taken for analysis. In addition, the use of multiple markers, in particular, combining an early sensitive marker with a late specific test will further enhance the diagnostic accuracy of these mediators in identifying infected cases. These tests are simple and cost effective.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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