Original Research Article

Risk factors for necrotizing enterocolitis in neonates: a prospective study

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ABSTRACT

Background: Necrotizing enterocolitis (NEC) is mostly limited to preterm babies due to immaturity of gut. NEC is one of important cause of neonatal mortality and morbidity in the neonatal intensive care units all over the world. Aim of study is to find the antenatal and post-natal risk factors associated with necrotizing enterocolitis in neonates admitted to NICU.

Methods: A prospective study was conducted on 45 neonates with necrotizing enterocolitis fulfilling the predetermined inclusion criteria. A detailed antenatal history including all maternal risk factors, birth history including the need for resuscitation and type of resuscitation was recorded. The gestational assessment was done by the New Ballard Score.

Results: Pregnancy induced hypertension accounts as a risk factor to most of the cases of NEC 18 (40%), followed by setting for sepsis 12 (26.6%), least being gestational diabetes mellitus 1 (2.2%).

Conclusions: Prematurity is found to be the most common risk factor followed by patent ductus arteriosus and sepsis. Most common antenatal risk factor was PIH (Pregnancy induced hypertension).

Keywords: Gestational diabetes mellitus, Necrotising enterocolitis, New Ballard score, Pregnancy induced hypertension, Prematurity

INTRODUCTION

Necrotising enterocolitis is one of the common problems of preterm babies. Its incidence is variable among different centres and even in a given centre depending on the bacterial ecology of neonatal intensive care unit feeding practices, obstetric resuscitation procedures and other variable.

There are less studies in India and authors should have their own data regarding incidence and risk factor associations with NEC. So, authors conducted this study to know what could be associated factors for NEC in their unit in South India.

It is one of the important cause of mortality and morbidity in preterm babies.¹ NEC predominantly affects the premature neonates in the neonatal intensive care units with an average weight less than 1500 grams.²

The disease rarely occurs in normal full term neonates.³ The risk is inversely proportional to gestational age and weight at birth. IUGR may be additional specific risk factors.

The aim of the study was to find the antenatal and post-natal risk factors associated with Necrotizing Enterocolitis in neonates admitted to NICU.

METHODS

The present study was a prospective study of 45 neonates with necrotizing enterocolitis fulfilling the predetermined inclusion criteria. The study was conducted over a period of 24 months (September 2015 to August 2017) in the Department of Pediatrics, Alluri Sitarama Raju Academy of Medical Sciences, Eluru, Andhra Pradesh, India.

Inclusion Criteria

Preterm, term and post term neonates admitted to NICU who showed clinical sign and symptoms suggestive of NEC (abdominal distention, aspirate more than 25%, altered aspirate in a sick looking neonate, gastrointestinal bleeding, pneumatosis intestinalis on abdominal radiograph as per modified bell's staging criteria for NEC).⁴

Both inborn and out born babies were included. Babies who died within 24hrs and those born with congenital gastrointestinal anomalies were excluded.

Caregivers of infants who satisfy the the inclusion criteria were approached for participation in this study in NICU of ASRAM medical college, Eluru, Andhra Pradesh, India. An information sheet providing the details of the study was provided and the nature of the study was verbally explained in a clearly understandable language. Written consent was obtained from caregivers. Enrollment of the infant and recording of the baseline information was done.

All the babies with clinical picture suggestive of NEC were included into the study. A detailed antenatal history including all maternal risk factors, birth history including the need for resuscitation and type of resuscitation was recorded. The gestational assessment was done by the New Ballard Score.⁵

Routine clinical examination including cardiovascular, respiratory, abdominal and neurological assessment was done on admission and everyday thereafter, vital parameters like temperature, blood pressure, and oxygen saturation are recorded for all babies. Necessary hematological, biochemical, microbiological and radiological investigations were done as and when required.

Statistical analysis

In this study population was 45. Data were analysed using SPSS version 20. In the entire tests p value <0.005 was taken as significant.

RESULTS

A total of 679 neonates were admitted in NICU during the study period, out of which 45 neonates suffered with NEC. The incidence of NEC in our unit was 6.62%.

In the present study, of the 45 cases admitted with NEC 43 were pre terms and only 2 were term babies., which was statistically significant with p value <0.00001.

Females (25) were predominantly affected compared to males (20) with M: F ratio of 1:1.13.

In the present study, Pregnancy induced hypertension accounts as a risk factor to most of the cases of NEC 18 (40%), followed by Setting for sepsis 12 (26.6%), least being gestational diabetes mellitus 1 (2.2%) Table 1.

Table 1: Distribution of antenatal risk factors.

Antenatal risk factors	Number of cases	%
PIH	18	40%
Oligohydramnios	9	20%
Polyhydramnios	5	11.1%
GDM	1	2.2%
Setting for sepsis	12	26.6%
Antenatal steroids	17	37.7%

In the present study, prematurity was the major risk factor associated with cases of NEC accounting for 43 (95.5%). Hyperbilirubinemia, sepsis, blood product transfusion is observed in 88.88%.

Intraventricular hemorrhage, pulmonary arterial hypertension was observed in 15.5% and 8.8% of cases respectively.

Table 2: Post-natal risk factors for NEC.

Risk factors	Cases	%
Prematurity	43	95.5%
Early enteral feeds	31 FF	68.8%
	4 EBM	
Shock	33	73.3%
Sepsis	40	88.88%
Perinatal Asphyxia	20	44.44%
RDS	24	53.33%
Polycythemia	13	28.88%
Intraventricular hemorrhage	7	15.5%
Pulmonary arterial hypertension	4	8.8%
Patent ductus arteriosus	22	48.8%
Mechanical ventilation/CPAP	29	64.4%
Blood product transfusion	40	88.8%

FF=Formula feeding, EBM=Expressed breast milk.

Early enteral feeds were given to 31 (68.8%) babies, out of which 27 are given expressed breast milk and 4 were given formula feeds. All the 4 breast milk fed babies suffered with stage 1 NEC and recovered while formula fed babies progressed to stage 2 and 3 NEC, required

more aggressive management and prolonged stay. Hyperbilirubinemia/neonatal jaundice was the most common associated comorbidity in cases of NEC accounting for 41 (91.1%) of cases. The bilirubin cut off values is taken according to the AAP hyperbilirubinemia charts.

Majority of the cases received blood product (Packed RBC/FFP/Platelet concentrates) transfusion 40 (88.8%) Table 2.

DISCUSSION

Necrotising enterocolitis, one of the gut related disorder which mainly affects premature babies and ELBW. In term babies it seldom occurs when there are associated conditions like sepsis, or hypotension.⁶ Further, survivors of NEC are likely to suffer poor growth, and gastrointestinal, and neurodevelopment sequelae because of the complications related to NEC.^{6,7} To improve the outcome of this condition, prevention, early diagnosis and timely intervention are the corner stone.

In the present study, 45 neonates were included, who satisfied the inclusion criteria and were diagnosed as necrotizing enterocolitis by the clinical presentation at admission or during hospital stay. During the study period, about 679 neonates are admitted to our NICU, out of which 45 neonates who had signs and symptoms suggestive of NEC were selected for the study. The overall incidence varies from 2-5% of all NICU admissions.⁸⁻¹¹ But, in the present study it is 6.62% of all NICU admissions and, 0.7% of live births in the study unit. In a study the incidence of NEC was 6.2% which is close to the incidence in the present study.¹² However, the possible reasons for slightly higher incidence in the present study is, more number of preterms admitting to our hospital as it was the only tertiary care referral center in the vicinity and increased survival of the preterm due to early interventions and shift in the preterm

management to a more organized and protocol based care. This slight variation may also be due to the differences in patient populations in the studies, different management policies, and the inclusion of varying numbers of out born babies in some series.

The study included 43 premature and 2 mature babies (95.55% and 4.44% respectively) thus the difference is statistically significant ($P < 0.00001$) and prematurity account for the most important risk factor for development of NEC. Eighty one percent were less than 2000gms and 76% less than 36 weeks of gestation.¹³

Antenatal risk factors for NEC

Maternal characteristics such as pregnancy-induced hypertension, gestational diabetes mellitus, setting for sepsis, polyhydramnios, oligohydramnios and antenatal steroids were included as maternal risk factors in the present study. Pregnancy induced hypertension is the most common associated variable with 18 (40%) cases. In a study by Beeby PJ, PIH was seen in 38% of cases which is comparable with the present study.¹⁴

In the present study, antenatal steroids were given in only 17 (37.7%) cases which is significantly low compared to the other studies by Boo N, 76% and Beeby PJ, 72% and Qian T, 58.8%.^{12,14,15} The reason could be late recognition of danger signs by quacks and delayed referral to the qualified gynecologist in rural India, where the present study is conducted.

In the present study, setting for sepsis was seen in 12 (26.6%) of cases of NEC which is comparable to the study done by, Qian T et al, 28.2%.¹⁵ In a study by Boo N, it was slightly higher 39%.¹²

Gestational diabetes mellitus is associated with only 1 (2.2%) case and the other studies by Qian T (4.5%) and Boo N (3.3%) also showed the similar results.

Table 3: Comparison of various antenatal risk factors between present study and other studies.

Antenatal risk factors	Present study n (%)	Qian T et al (%) ¹⁵	Boo N et al (%) ¹²	Beeby PJ et al (%) ¹⁴
PIH	18 (40%)	14.5%	-	38%
Gestational diabetes mellitus	1 (2.2%)	4.55%	3.3%	
Oligohydramnios	9 (20%)	-	-	-
Polyhydramnios	5 (11.1%)	-	-	-
Antenatal steroids	17 (37.7%)	58.8%	76%	72%
Setting for sepsis	12 (26.6%)	28.2%	39%	39%

Postnatal risk factors of NEC

Out of 45 neonates, 43 are preterm and remaining 2 babies were term babies. Prematurity was the major risk factor being responsible for majority of cases (95.5%).

Infection (sepsis) was the second most common risk factor in the present study (88.8%) in contrast to other studies. Infection (sepsis) was noticed in 88.8% of cases in the present studying in contrast to other studies by Narang A (28.5%) and Boo N (49.3%).^{16,12}

The reason for this could be that the present study is done in a tertiary care hospital where most of the babies are referred after early neonatal period for further management. Shock was associated risk factor in 33 cases (73.3%). Moderate to severe birth asphyxia is seen in 20 cases (44.4%) and Hyaline membrane disease in 24 cases (53.3%). Starting of enteral feeds was the next most important risk factor associated with necrotizing enterocolitis (68.8%). Most of the neonates were preterm thus initiated on nasogastric tube feeds with expressed breast milk, due to inability to suck and swallow. These newborns have more than one risk factor for NEC.

A meta-analysis of nine trials (n=754) did not detect a significant effect of early trophic feeding versus enteral fasting on incidence of NEC: typical relative risk 1.07 (95% CI 0.67, 1.70); typical risk difference 0.01 (95% CI -0.04, 0.05).¹⁷

In the present study, hyaline membrane disease is associated with 53.3% cases which is comparable to the study done by Beeby PJ, where it was 52.4%.¹⁴ But in another study done by Boo N, 2.4% of cases with NEC are having hyaline membrane disease which was higher compared to the present study.¹² The difference could be due to various antenatal factors like antenatal steroids and variation in other management protocols. In another study done by Narang A.¹⁶ RDS is a risk factor in 35.1% of babies. The higher incidence in present study is due to relatively more number of preterm babies and increased survival of preterm due to advances in management.

Infection (sepsis) is noticed in 88.8% of cases in the present study in contrast to other studies by Narang A, (28.5%) and Boo N, (49.3%).^{16,12} The reason for this could be that the present study is done in a tertiary care hospital where most of the babies were referred after early neonatal period for further management. So, most of the babies are presenting with clinical sepsis.

Asphyxia is one of the risk factors for NEC in term as well as preterm babies. In present study it is noted in 44.44% which is comparable to the study done by Narang A, which showed 45.5%. This gross deviation may be due to conducting most of the preterm deliveries in poorly equipped centers without qualified personnel in Neonatal resuscitation in most of the places of India.

Polycythemia as a risk factor is seen in 26.66% of cases which is comparable to the results in Narang A et al, where it was seen in 27% of cases.¹⁶ Hyper viscosity associated with polycythemia resulting in ischemia of gut and the partial exchange transfusion through the umbilical vessels for its treatment collectively may predispose these newborns to necrotizing enterocolitis.

In the present study, Mechanical ventilation/CPAP required in 29 (64.4%) cases whereas in a study by Thomas c, Krishnan L 49.4% cases are treated with CPAP/mechanical ventilation.¹⁸ But in a study by

Guthrie, 73% of the babies required either CPAP/mechanical ventilation.⁷

Patent ductus arteriosus is associated in 22 (48.8%) cases in the present study and similar results were seen in studies done by Boo NY (48.6%), Beeby PJ, (41.9%). But in an Indian study by Narang A, PDA was seen in 18.7% of cases only. Possible reason being, the study was done year 1993 and lack of appropriate diagnostic facilities could have contributed to the lower incidences.^{12,14,16}

Neonatal jaundice/hyperbilirubinemia is seen in 41(91.1%) cases in the present study and in a study by Thomas c, Krishnan L, it is 67.6%.¹⁸

Intra ventricular hemorrhage is noticed in 15.5% of the cases in the present study and it is comparable to the study done by Qian T where it was 15.8%.¹⁵ But in a study by Boo N, IVH was seen in 41.9% of cases of NEC.¹²

In the present study, 40 cases are transfused with blood products (packed RBC/FFP/platelet concentrates) and pulmonary arterial hypertension was diagnosed in 4 (8.8%) cases. No of cases were less which was the limitation of present study

CONCLUSION

Authors found that PIH is associated with an increased risk for NEC independent of birth weight. Among various postnatal risk factors, prematurity is found to be the most common risk factor. Sepsis and PDA found to be strongly associated with the incidence of NEC. All the breast milk fed babies came under stage 1 NEC while formula fed babies progressed to stage 2 and 3 NEC. Authors findings also support the view that breast milk is associated with a reduced risk for NEC.

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