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EVALUATION RISK FACTORS OF NECROTIZING ENTEROCOLITIS;

CHILDREN HOSPITAL AND THE INSTITUTE OF CHILD HEALTH MULTAN.

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ABSTRACT… Introduction: Necrotizing enterocolitis (NEC) is a condition where the intestines become infected and can begin to die. Necrotizing enterocolitis is a serious condition that may require surgery, and has a high morbidity and mortality rate**. Objectives:** To evaluate the risk factors of necrotizing enterocolitis among neonates at children hospital Multan. **Study Design:** Descriptive Cross-sectional study. **Setting:** Neonatal Unit of Children Hospital and Institute of Child Health Multan. **Period:** October 2015 to September 2016. **Material and Methods:** A total of 79 neonates presented with necrotizing enterocolitis were enrolled for the possible causes. The parameters studied included gestational age at birth, birth weight, maternal risk factors, patient risk factors, age when feeding was started, type of feed, age when signs of NEC appeared, per feed increment, presence of any antecedent associations, clinical features, radiological features, blood investigations (complete blood counts, blood glucose, serum sodium, serum potassium, serum creatinine, liver function tests), ABGs, stool for occult blood and culture, septic screening and blood culture, management(medical or surgical) and outcome. The data was analyzed using SPSS-20. **Results:** Out of a total of 79 neonates, 48 (60.8%) were male and 31(39.2%) female. There were 71% infants who were younger than 32 gestational weeks and 67.7% under 1500 grams. The majority of neonates 62 (78.5%) commenced enteral feeds within the first 24 hours. First feeding was started at a mean 5.6 ± 3.85 (2-17) days. Prematurity was the commonest factor and present in 63 (79.9%) neonates. Abdominal distention was the commonest symptoms 55% followed by bilious vomiting in 15%. Blood culture was positive in 22 (27.8%) with predominance of gram negative microorganisms. According to Bell's staging, 54 (68.35%) neonates had stage I, 17 (21.5%) stage II, and 8 (10.1%) neonates were in stage III. **Conclusion: I**n most of the cases, the causes of necrotizing enterocolitis were present and prematurity was the main etiological factor. Cautiously introducing enteral feeds using expressed maternal breast milk and increasing feed volumes slowly is important in reducing the incidence amongst high risk individuals.

Key words: Neonates, Necrotizing Enterocolitis, Risk Factors.

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INTRODUCTION

Despite advances in the diagnosis and management of many neonatal diseases, NEC remains a serious disease for preterm and low birth babies.[1,2] It is very difficult to eliminate and has become an important research issue.[3] It is described as dysfunction of the intestine causing perforation, shock and may lead to death is serious cases.[4]

Population-based estimates of NEC range from 0.72 to 2.4 cases per 1,000 live births whereas the prevalence of NEC is around 7% around the world in the newborns having weight 500-1500 grams at birth.[5-8] The calculated mortality in NEC is 20-30%.[9] A systematic description of NEC is described in terms of staging system explained by Bell and colleagues.[10,11] The extreme inflammatory reaction started in the immuno reactive gut in NEC may cause systemic effects on organs like brain causing neuro developmental dysfunction in future life.[12,13]

The exact cause and Pathophysiology of NEC

is unknown.[14,15] In the long-term, severe NEC is associated with higher risk of nosocomial infection, malnutrition, growth failure, bronchopulmonary dysplasia, and neuro developmental delay.[14,16] Clinical features of NEC ranges from distension of abdomen, increased gastric residuals, vomiting, bloody stool, tenderness and abdominal discoloration.[17] Nonspecific clinical features include variability in temperature, lethargy, apneic spells and hypotension.[17]

Low birth weight and prematurity are the most important risk factor.[18] The Pathophysiology of NEC is poorly understood, but is likely multifactorial.[15]

Immaturity of the intestinal tract which predisposes damage to the gut and abnormal immune response to this injury. Abnormal bacterial colonization and genetic predisposition are important risk factors.[15] In a cohort study of 4039 ELBW infants, longer durations of initial empirical antibiotic (> 5 days) were associated with NEC or death.[19] The role of specific feeding strategies on NEC risk is also unclear.[20] It has been found that certain pharmacological agents (e.g., supplemental Vitamin E)[21], antenatal indomethacin[22] and histamine-2 receptor (H2) blocker therapy[23] may contribute to NEC risk in VLBW infants.

The current study was planned to search various risk factors causing NEC in neonates in our setup so that an effective strategy for their prevention and management can be carried out.

Material and Methods

It was a prospective descriptive study. The study was conducted at the neonatology unit of children hospital in the institute of child health Multan from October 2015 to September 2016.

Seventy nine newborns admitting in the neonatology unit through children OPD / emergency room and diagnosed as NEC were included. An informed written consent were taken from parents / guardians. The study was approved by the local ethical committee.

Differential diagnosis of NEC included sepsis, gastrointestinal obstruction, volvulus, isolated perforation, meconium ileus and hirschsprung disease, differentiated from NEC on the basis of clinically, complete blood count, C - reactive protein, blood culture, radiological findings (done by consultant radiologist) and expertise from paediatrics surgery department. Spontaneous gut perforation commonly occurs in the first few days of life and has not relation with feeding. It is characterized by minimal gut changes as shown by low serum levels of inflammatory cytokines. The use of indomethacin and glucocorticoid are the risk factors.

A detail history of the newborn including post gestational age, maternal diabetes, maternal hypertension and antenatal steroids was taken. Delivery details were also taken including the site of delivery (hospital, private clinic, home), root of delivery, duration of labour, resuscitation details and APGAR score of less than 3 at 1 and 5 minutes of age, polycythemia and exchange of transfusions. Feeding history was documented especially when feeding was initiated, nature of the feed, age of onset of NEC, per feed increment and dilution of milk. Increased gastric residuals, vomiting or bilious aspiration from the enteral tubes and bloody stools are associated with NEC in very low birth weight (VLBW) newborns.

Examination including vital signs, anthropometric measurements, gestation age by Ballard's score, apneic spells, temperature instability, poor perfusion or lethargy, hypotension, abdominal distention, measurement of abdominal girth, gastric residue or vomiting, ascites, tenderness and discoloration of abdomen, hepato-spleenomegaly, cardiovascular system(hypotension, capillary refill time and character of pulse) , respiratory system and necessary central nervous system was carried out.

Investigations were done including blood glucose, serum sodium, serum potassium, complete blood count, c-reactive protein for evidence of infection, Serum urea / creatinine, liver function tests (LFT's),), ABG,s, blood culture, guaiac positive stools and stool culture. Radiological findings

including gaseous distention, gasless abdomen, pneumatosis intestinalis and presence of free air under diaphragm (intestinal perforation) were noted. Ultrasound abdomen for ascites, intestinal obstruction, intestinal perforation and portal vein gas was done. Measurement of 'pulsatile index' with Doppler of superior mesenteric artery is also diagnostic. All these babies were finally grouped into three stages as per the modified Bell's classification.[10,11]

Stage 1 (Suspected NEC)

Signs and symptoms akin to sepsis, feeding intolerance, metabolic acidosis, Bloody stools plus minus. Distended and fixed loops with mucosal thickening on plain abdominal radiographs.

Stage 2 (Definite NEC)

All of above (stage 1) plus intestinal pneumatosis with or without gas in the biliary tree on abdominal x-ray.

Stage 3 (Complicated NEC)

All of the above (stage 2) with evidence of intestinal perforation plus minus ascites.

No laboratory examination is diagnostic of NEC but severe or persistent thrombocytopenia, neutropenia, high CRP, coagulopathy or acidosis indicates severe disease. Babies were kept nil by mouth (NPO) for a variable period of time depending on the severity of disease and stages of disease (3- days for stage-I, 7-10 days for stage II and 14 days or prolong for stage III) and parenteral antibiotics with metronidazole given. Total parenteral nutrition including aminovel on daily basis, intravenous lipid on every 3rd day to prevent the deficiency of essential fatty acids, 10% dextrose water (1/v), trace elements and multivitamins were started. Monitoring of patients done by daily measurements of abdominal girth, vital signs, erythema of abdominal wall, daily platelets count, hematocrit, ABG, S serum electrolyte, PT and APTT and cross table X-ray abdomen. Consultation with a pediatric surgeon was essential once the diagnosis of NEC confirmed. Indications of surgery are pneumoperitoneum, no response to medical treatment, fixed bowel loop, abdominal wall erythema and cellulitis. The surgery may include inserting drainage tube in peritonic cavity, resection of the disease part of the gut and enterostomy with creation of a stoma depending on the severity of disease. Trophic was started depending upon the condition of patients. The trophic feeding is defined as the use of minimal enteral feeds as less than 1 mL per hour with parenteral nutrition. Its benefits include less chances of feeding intolerance and is associated with decreased chances of NEC. The trophic feeding prevents the mucosal atrophy. Trophic feeding was given for prolong period. After tolerance of trophic feeding (no prefeeding residual and abdominal distension), proper feeding (human breast milk) started depending on the weight of patient and per day feed increased according to weight. After establishment of feed, patients were discharged and advised for regular follow up at outpatient department.

RESULTS

Out of a total of 79 neonates, 48 (60.8%) were male and 31 (39.2%) female. Mean gestational age was 30.3 ± 3.1 (range 25-36 weeks), mean birth weight was 1326 ± 380 (range 730-2150 grams) while 71% newborns were having gestational age < 32 weeks and 67.7% were under 1500 grams. Onset of NEC was at 11.2 ±8 (range 2-31 days). The majority of neonates, 62 (78.5%) started enteral feeds in the first 24 hours. First feeding was started at a mean 5.6 ± 3.85 (2-17) days while mean postnatal days of onset of NEC was 8.7 ± 7. (2-28).

Prematurity was the commonest finding and present in 63 (79.9%) neonates, followed by ventilator therapy in 50 (63.3%) and intraventricular hemorrhage 42 (53.2%). Mean APGAR score at 1 and 5 minutes was 5.2 ± 2.1 (1-9) and 7.2 ± 1.8 (3-10) respectively. Abdominal distention was the commonest symptoms 55% followed by bilious vomiting in 15%. Blood culture was positive in 22 (27.8%) with predominance of gram negative microorganisms in 17 infants. According to Bell's staging, 54 (68.35%) neonates had stage I, 17 (21.5%) stage II, and 8 (10.1%) neonates were in stage III. History of antenatal steroids was present in 63.4% of the cases.

Sign and Symptom	No. of Infants (%)
Abdominal distention	55%
Bilious vomiting	15%
Apnea	12%
Non-bilious vomiting	6%

Signs and symptoms at the time of admission

Risk Factors	No. of Patients (%)
Prematurity	63 (79.9%)
Asphyxia	5 (6.3%)
Prolonged membrane rupture	23 (29.1%)
Early membrane rupture	28 (35.4%)
Hypothermia	24 (30.3%)
Hypoxia	32 (40.5%)
Respiratory distress syndrome	34 (43.0)%
Hypotension	5 (6.3%)
Surfactant therapy	12 (15.1%)
Ventilator therapy	50 (63.3%)
Indomethacine treated-	11 (13.9%)
Anemia	31 (39.2%)
Polycythemia	8 (10.1%)
Thrombocytopenia	38 (48.1%)
Leucopenia	30 (37.9%)
Intraventricular hemorrhage	42 (53.2%)
Umbilical catheterization	33 (41.7%)
Feeding breast milk	8 (10.1%)

Risk Factors

DISCUSSION

Inspite advancement in the intensive care of newborns, the incidence of NEC has increased to 7% VLBW neonates.[5,14] There are more chances of hospital acquired infections, under nutrition, growth failure, retinopathy of prematurity, chronic lung diseases and even longer stay in the hospital for newborns with NEC. Mortality rate is 25-30%, morbidity is about 50-60% and 1/3rd of the patient required surgical intervention.[14,24]

NEC is inversely related to gestational age as 80% of the newborns are preterm.[25-27] In this study, the mean gestational age was 30.3 ± 3.1 weeks and birth weight 1326 ± 380 grams.

Hypoxia and RDS have been shown to be significantly associated in the development of NEC,[28] our study showed that 40.5% infants were having hypoxia and 43.0% RDS. So, gut hopoxia was a risk factor of NEC in newborns. In the term infant with NEC, risk factors for gut hypoxia are invariably present.[28]

This study showed that small amount of milk feeding was associated with less chances of NEC as compared to large amount of milk and increase in the amount of enteral feeds.

The study conducted by Dunn and colleagues showed that the early usage of hypocaloric milk formula in small amount is harmless.[29] Our study's results were consistent with those of Dunn and Colleagues and it proved again that small amounts of milk result in fewer complications as compared to large amount of milk. Increase in volume of enteral feeds at slow as compared to fast rates brings about several days delay in salvaging birth weight and establishing full enteral feeds but the long term clinical importance was unclear. Further randomized controlled trials are necessary to find out how the rate of daily addition in enteral feed volumes influence clinical outcomes in VLBW infants.[25] As we saw in the current study that longer period of low milk resulted in increase in enteral feeding time, and it was further found that complications like NEC an feeding intolerance were shrinked, so we can advocate this to enhance infant feeding management. Whereas, Rayyis and Colleagues stated that the NEC occurrence was uniform in different ways of increase in the volume of milk.[30] Breast milk protects against NEC. Breast milk has been found superior as far as general health of the infant is considered. Benefits like infant host defence, gastrointestinal function improvement, sensory neural development and some improvement in nutritional status can be obtained in premature infants who are fed with their mother's milk. In last 30 years, newborn morbidity related to infections has been reported as an important part of research and literature, NEC occurs more regularly in newborns given formula than those given breast milk.[28,31]

Umbilical artery catheterization may result in intestinal ischemia in premature infants with clot formation.[32,33] We found that umbilical catheterization was seen in 41.7 infants. Specific bacterial species are linked with NEC, and commonly occurring species are endemic to

nıcus and form the gastrointestinal colonization species of most premature neoborns.[34,35]

Some studies propose that coagulase negative staphylococci are most commonly responsible in NEC and related with elevated rates of mortality and morbidity.[36,37] We found that mostly gram negative microorganisms were isolated in blood cultures in our study.

The clinical consequences are more or less the same in different patient populations, either they are infants of VLBW or extreme maturity.[38] Early symptoms of NEC are very similar to sepsis neonatorum. There are variety of signs and symptoms, ranging from feeding intolerance to evidence of a fulminate intraabdominal catastrophe. Most commonly, the newborns are presented with abdominal distention, vomiting, increased gastric residual, lethargy, apneic spells, bradycardia or guaiac positive stool.[39] We found that abdominal distention (55.1%) was the most commonly occurring symptom in NEC.

Several approaches like withholding enteral feedings, using enteral antibiotics, feeding the infant with the mother's breast milk, giving probiotics and administering various growth factors have been found beneficial in preventing NEC. Stoppage of feedings may prove dangerous as it may lead to the prolonged use of parenteral nutrition, as well as to intestinal atrophy, increased permeability and inflammation, that might further result in late-onset sepsis. Delay in feeding actually enhance the severity of NEC if it occurs. An alternative for the prevention of NEC is to provide enteral feedings of small amounts of the mother's expressed breast milk.

CONCLUSION

In majority of the cases, the causes of NEC were present and Prematurity was the main etiological factor. Carefully initiating enteral feeds using expressed maternal breast milk and increasing feed volumes slowly is important in minimizing the incidence amongst high risk newborns. Evading of premature birth, use of antenatal steroids, frequent breast feeding seem to be a good strategy to cut down the incidence of NEC.

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PREVIOUS RELATED STUDY

Rehan-E-Kibria, Saif ud din Awan. NECROTIZING ENTEROCOLITIS IN PREMATURE BABIES; LAPAROTOMY VERSUS PERITIONEAL DRAINAGE (Original) Prof Med Jour 15(3) 350-353Jul, Aug, Sep, 2008.

Those who never change their mind never change anything.

– Unknown –

AUTHORSHIP AND CONTRIBUTION DECLARATION

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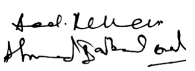
1	Abdur Rehman Malik	Introduction, Statistics, Discussion.	
2	Ahmed Iqbal Quddusi	Discussion.	
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4	Mukhtar Hussain Bhatti	Discussion.	