

A descriptive case series of necrotising enterocolitis; occurrence at Aga Khan University Hospital

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Abstract

The objective of this study was to determine the frequency and outcome of preterm infants diagnosed with Necrotising Enterocolitis (NEC). In a case series, 320 preterm infants were enrolled during a period of 12 months at Aga Khan University Hospital, Karachi, a tertiary care hospital. Diagnosis and staging was done as per Bell's staging criteria. Possible confounders were filtered. Analysis was based on the form of treatment and symptom progression. During the study, NEC was observed in 29(9.06%) babies of which stages I, II and III were 69%, 24% and 7%, respectively. Outcome analysis showed that among the 29 neonates diagnosed with NEC, 23 were discharged and 6 expired. A 9% prevalence observed during the study suggests this to be a major challenge in neonatology. Mortality outcome of 21% diagnosed with NEC recommends an early diagnosis coupled with prompt and appropriate treatment and preventive measures to reduce the burden of NEC in future.

Keywords: Prematurity, Bell's Staging, Necrotising Enterocolitis.

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Introduction

In a national estimate, the rate of preterm birth ranged from 5% to 18%. As per Unicef, an estimated 8.6 lakh premature births are recorded annually in Pakistan of which 12% die due to prematurity related complications. Of the top 10 countries in the world accounting for two-thirds of the deaths due to preterm birth complications, Pakistan ranks second.¹

Before the advent of modern neonatal intensive care, NEC was not known to affect premature infants because of low rate of survival.² To depict the earliest presentation in infants, the terms "gangrenous enterocolitis" or "malignant enteritis" were used.³ Necrotising enterocolitis is defined as an acute inflammatory disease in the intestines, particularly of preterm new-borns, and is characterised by haemorrhagic necrosis of intestinal tissue which may lead

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to perforation and destruction of the gut.⁴ The occurrence of NEC varies, with studies reporting a variation of 1%-7% of neonatal intensive care admissions with equal prevalence among male and female infants.⁵ A study by Yee WH et al stated the occurrence of NEC to be 5.1% among pre-term infants with a gestational age of <33 weeks.⁶ A study conducted at AKUH more than two decades ago, reported the overall prevalence of NEC among new-borns to be 8.7% with an overall mortality of 44%.⁷ The mortality rate for NEC varied between 10-30% in developed countries but can be more than 50% in developing countries.⁶ With an increase in survival of preterm infants, an increase in the occurrence of NEC was noted.² Studies in Canada, Poland, the USA, and the UK report the prevalence to be 6.6%, 8.7%, 7.1%, and 14.4%, respectively in infants weighing less than 1,500 grams.⁸ A study done in Abbottabad reports an occurrence as high as 14.28%.⁹

To the best of our knowledge, only a few studies have been done in Pakistan that show the frequency of NEC in preterm neonates, so the aim of this study was to determine the occurrence of NEC in a developing country. The results of this study will provide data on the epidemiology of NEC and its outcome with information on the occurrence of the disease and a source to work on developing new practices for recognition and management so as to reduce morbidity and mortality.

Methods and Results

The study was conducted at the Aga Khan University Hospital (AKUH), Karachi, in the neonatal intensive care unit (NICU), step down unit, and well-baby nursery over a period of one year, after the approval of the synopsis. A non-probability (consecutive) sampling method was used. By taking the study design of a descriptive case series, a sample size was calculated by taking the prevalence of NEC among preterm infants as 5.1%.⁶ The study was conducted over a period of one year, and data for 320 preterm infants was collected. The terminology used in the study is described in the Supplementary Appendix.

After approval from the College of Physicians and Surgeons Pakistan and the Ethical Review Committee of AKUH, all subjects fulfilling the eligibility criteria were enrolled (Figure), and followed from birth till discharge from the

Supplementary Appendix: Operational Definitions.

S.N.	Terms	Operational Definitions
1.	Altered gastric aspirates	Aspirates containing altered feed, blood or bile
2.	Faecal occult blood	Blood detected on stool detailed report of neonates which is apparently not visible
3.	Temperature instability	An increase or decrease of rectal temperature of > 1.5oC within 3 hours regardless of whether or not upper (>38.5oC) and lower (<36oC) temperature was exceeded
4.	Bradycardia	A heart rate of less than 80 beats per minute
5.	Apnoea	A pause in breathing for more than 20 seconds
6.	Lethargy	Decreased activity in a neonate with or without poor neonatal reflexes
7.	Metabolic acidosis	An arterial pH <7.2 and base excess <-5
8.	Thrombocytopenia	A platelet count of less than 150 x 10 ⁹ /l
9.	Hypotension	Mean blood pressure less than 10th centile for birth weight and postnatal ag
10.	Intestinal dilatation	Radiological findings showing asymmetry or disorganized bowel pattern and paucity of gas in certain areas of intestine with dilatation in others
11.	Abdominal distension	Clinical assessment in respect to either bulging flanks, increased abdominal girth (more than 2 cm) or dilated bowel loops
12.	Abdominal tenderness	Clinical judgment of the neonatologist in terms of crying or grimacing of the neonate at the time of palpation of abdomen
13.	Pneumatosis intestinalis	Radiographic image showing gas within the wall of the bowel
14.	Generalized peritonitis	Inflammation of the bowel wall with perforation of bowel presenting with signs described above
15.	Pneumoperitoneum	Radiographic image showing air outside the bowel
16.	Outcome	Outcome will be determined among preterm neonates within one month after diagnosis of NEC on the basis of form of treatment required and symptom progression
17.	Non-surgical management	Neonates receiving conservative management either holding of feeds, antibiotic therapy or decompression of nasogastric bowel
18.	Surgical management	Neonates requiring intervention exploratory laparotomy, peritoneal drainage or intestinal resection with stoma formation
19.	Resolution of symptoms	Improvement of symptoms including feeding tolerance and progression of feed as per requirement
20.	Worsening of symptoms	Progression of symptoms from one stage to another (Modified Bell's criteria)
21.	Death	Death will be labelled on cessation of all vital functions including heart beat and breathing

hospital. Confidentiality was maintained for each patient's data.

Diagnosis of NEC was made by the neonatologist on the basis of Modified Bell's staging criteria.⁵ Data was collected on a pre-formed proforma and information was recorded. Staging and outcome in the form of survival, complications or mortality was recorded and analysed for patients fulfilling the diagnostic criteria of NEC.

Data was analysed using SPSS version 20.0. Descriptive statistics were done for demographics, gestational age, birth weight, gender, mode of delivery, Necrotising enterocolitis, staging, clinical features and outcome in terms of survival, complications, and mortality. Measures and outcome are defined in the supplementary appendix. Continuous variables like gestational age and weight at birth were presented as mean±standard deviation for quantitative variable. All possible confounders such as prior abdominal surgery or severe congenital abnormality were filtered at recruitment.

During the study period, a total of 320 preterm neonates were enrolled out of which 22 (7%) were born between 26-28 weeks, 131 (41%) between 28⁺¹-32 weeks, and 167 (52%) between 32⁺¹-34 week. None of the babies in the study were born at less than 26 weeks. Of the total, 178 (56%) were males and 142 (44%) females. Three hundred (94%) preterm neonates weighed more than or equal to one kilogram and 20 (6%) had a birth weight less than one kilogram. The mean gestational age was 31.88±1.83 weeks (range 26-34

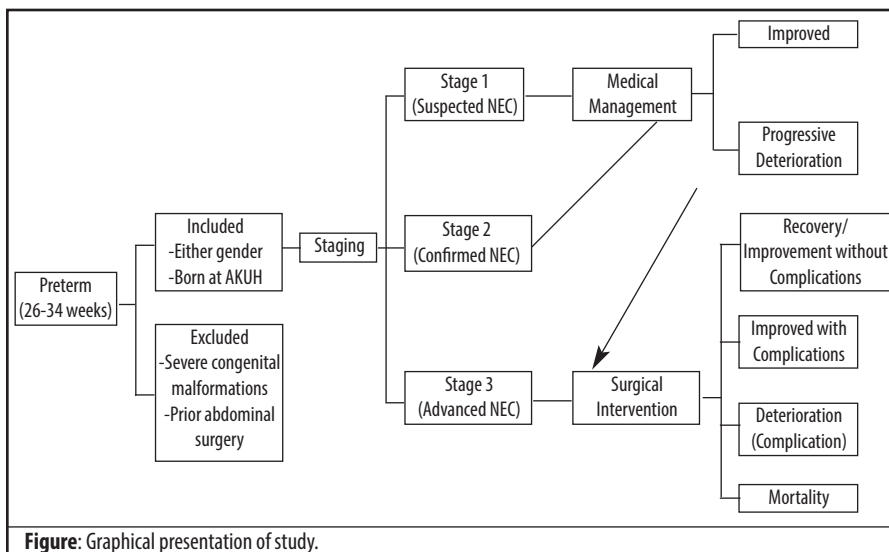


Figure: Graphical presentation of study.

Table-1: Clinical presentation in different Stages of NEC (n=29).

Clinical Presentation	Bell's Staging			Total Percentage	
	Stage I	Stage II	Stage III		
Gastrointestinal	Increasing gastric aspirate	19	5	1	86.2
	Mild abdominal distension	6	5	2	44.8
	Faecal occult blood	0	1	1	6.9
	Fresh blood per rectum	0	0	0	-
	Absent bowel sounds on auscultation	0	0	0	-
	Abdominal tenderness +/- abdominal mass	0	1	0	3.4
	Generalized peritonitis	0	0	0	-
Systemic	Temperature instability	1	0	0	3.4
	Apnoea	7	5	1	44.8
	Bradycardia	3	2	1	20.7
	Lethargy	6	5	0	37.9
	Hyponatraemia	2	1	1	13.8
	Mild metabolic acidosis	1	1	0	6.9
	Thrombocytopenia	4	3	2	31
	Hypotension	1	0	1	6.9
	Severe apnoea	0	1	0	3.4
	Radiological	Normal to mild ileus	20	1	0
Intestinal Dilatation		0	7	0	24
Pneumointestinalis		0	0	0	-
Portal vein gas		0	0	0	-
Ascites		0	0	0	-
Pneumoperitoneum		0	0	2	6.9

common radiological finding in both the cases of stage III NEC, whereas intestinal dilation was seen in stage II and normal to mild ileus in Stage I cases of NEC.

Risk estimation of demographics in neonates with NEC was also done with gender, weight at birth, and gestational age by using Chi square test (confidence interval 95%); it was noted that gestational age had a significant risk, estimate being 5.855 between 26-28 weeks, and low birth weight had a significant p-value of <0.05 (Table 2).

Two cases among 29 underwent surgical intervention. Of the 29 cases of necrotising enterocolitis, 23 (79.31%) improved without complications and 6 (20.69%) preterm neonates expired (1 due to surgical and 5 due to systemic complications).

Discussion

Necrotising enterocolitis continues to be the cause for considerable morbidity and mortality in preterm infants. The complex aetiology and multiple factors associated with the development of disease make its prevention a significant challenge. Bell et al classified NEC according to disease severity which was later modified.¹⁰ Another classification system published uses clinical and radiological findings to define NEC.¹¹ As compared to the previous study in this unit, the overall prevalence increased from 1.1 to 9.06%, probably due to increase in survival of infants of lower gestational age (26-34 weeks).⁷ In a study, the frequency in terms of staging of NEC according to Bell's criteria was noted to be 48 %, 39 % and 13 % for stage I, II, and III, respectively with stage III having a poor prognosis.¹² Similarly in our study, the occurrence of staging amongst infants diagnosed with NEC was noted to be 69%, 24%, 7% for stages I, II, and III respectively.

This study showed an inverse relationship between the occurrence of NEC with gestational age and birth weight, similarly observed in earlier studies. Severe NEC was described in infants at gestation of less than 30 weeks but not in all infants of birth weight less than one kilogram.⁵ It shows that lower birth weight babies had a higher percentage of NEC as compared to gestational age appropriate birth weight, i.e. 31% vs 8%.

Table-2: Comparison of demographics with NEC.

Variables	NEC present (n=29/%)			NEC absent (n=291/%)	p-value	Risk Estimate
	Stage I	Stage II	Stage III			
Gender	Male	10 (34.48)	4 (13.79)	1 (3.44)	0.698	1.189
	Female	10 (34.48)	3 (10.37)	1 (3.44)		
Weight	< 1 kg	1 (3.44)	3 (10.37)	1 (3.44)	0.001	0.194
	≥1 kg	19 (65.52)	2 (6.89)	1 (3.44)		
Gestational	26-28 weeks	4 (13.79)	2 (6.89)	1 (3.44)	0.002	5.855
Age	28 ⁺¹ -32 weeks	12 (41.42)	4 (13.79)	1 (3.44)	0.506	1.344
	32 ⁺¹ -34 weeks	4 (13.79)	1 (3.44)	0 (0)		
					0.011	0.352

NEC: Necrotising enterocolitis

weeks) and mean birth weight of the enrolled neonates was 1.700±0.480 kg (range from 0.46–3.40 kilograms). The duration of stay at the hospital was minimum five days and maximum 43 days with the age at diagnosis being minimum three and maximum 11 days. Three hundred and one (94%) had appropriate weight for gestational age and 19 (6%) had low birth weight.

The frequency of necrotising enterocolitis was 29 (9.06%) among preterm neonates, of which 20 (69%), 7 (24%), and 2 (7%) belonged to stage I, II, and III, respectively.

The frequency of the clinical features as per Bell's staging is described in Table 1. Gastrointestinal symptoms were the commonest observation, with increasing gastric aspirates most commonly noted in Stage 1 NEC and mild abdominal distension in stage II and III. Pneumoperitoneum was the

A stepwise approach in the management is reported depending on the disease severity, with medical management including discontinuation of oral feed, intravenous fluid therapy and decompression of the nasogastric bowel along with antibiotic therapy.⁸ An estimated 20-40% of infants diagnosed with NEC undergo surgical intervention with only 7% infants requiring intervention as observed in our study.¹³

As medical treatment improved over time, mortality in infants with NEC declined from 53.3% in a study done in 2011, to a mortality of 20.69% infants observed in the current study.¹⁴ The mortality in the present study was reported to be 6.79%, 10.38%, and 3.49% in stages 1, 2, and 3, respectively.

Conclusion

Necrotising enterocolitis continues to hold a substantial place in neonatal illnesses. Keeping in view the increasing survival of preterm babies, multi-centre studies involving larger sample size would direct towards better understanding the associations of this disease amongst neonates born in the same region.

Disclaimer: This is a Dissertation-based article.

Conflict of Interest: None.

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