

Management of necrotizing enterocolitis: experience at a tertiary care hospital in Oman

Kirtikumar J. Rathod^a, Asfaq A. Khan^b, Mathew Kripail^b, Muhammad Fazallulah^b, Zainab Al Balushi^a and Mohamed Abdellatif^b

Introduction Necrotizing enterocolitis (NEC) is the most common surgical emergency in the neonatal intensive care unit. The aim of this study was to determine the incidence of NEC and identify the factors predicting the surgical management and also to determine the mortality due to NEC at our tertiary care neonatal unit in Oman.

Materials and methods The parameters studied included sex-based differences, 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, presence of any antecedent associations, clinical features, radiological features, blood investigations, requirement of surgery, surgical findings, and outcome.

Results The study included 14 male and 12 female neonates. The mean gestational age at birth was 29.8 ± 3.7 weeks (range: 25–38 weeks). The mean birth weight was 1348.4 ± 774.1 g (range: 610–3900 g). The total incidence of NEC was 2.28%, whereas its incidence in neonates with birth weight less than 2500g was 4.47%. Surgical management was carried out for 11 (42.3%) patients. The mean platelet count in patients managed surgically was significantly lower compared with those managed

conservatively (106.5 vs. 218.1 cells/ μ l of blood, $P < 0.05$). Similarly, the mean C-reactive protein level was also higher in patients managed surgically compared with those managed conservatively (104 vs. 54 mg%, respectively, $P < 0.05$). Five of 26 (19.2%) patients died during the course of treatment.

Conclusion The incidence and mortality rate of NEC in Oman is similar to that in other countries. Low platelet counts and high C-reactive protein levels are the factors that can predict the need for surgical management. *Ann Pediatr Surg* 9:65–68 © 2013 Annals of Pediatric Surgery.

Annals of Pediatric Surgery 2013, 9:65–68

Keywords: C-reactive protein, necrotizing enterocolitis, thrombocytopenia

^aPediatric Surgery Unit, Department of Surgery and ^bNeonatology Unit, Department of Child Health, Sultan Qaboos University Hospital, Muscat, Oman

Correspondence to Kirtikumar J. Rathod, MBBS, MS, MCh, Pediatric Surgery Unit, Department of Surgery, PO Box 38, Postal Code 123, Al Khoudh, Sultan Qaboos University Hospital, Muscat, Oman
E-mail: drkirtirathod@gmail.com

Received 20 September 2012 accepted 3 January 2013

Introduction

Necrotizing enterocolitis (NEC) is one of the most common reasons for a neonatal surgical emergency. The increased survival rate of premature babies due to advances made in neonatal intensive care has led to an increase in the incidence of NEC [1]. However, despite the advancement in neonatal care, mortality due to NEC remains high [1,2]. The following study describes our two and half years of experience in managing NEC at a tertiary care hospital in Oman. The aim of the study was to determine the incidence and mortality rate due to NEC at our centre and also to compare various parameters between medically and surgically managed patients.

Patients and methods

Between January 2010 and May 2012, 1139 neonates were admitted at our neonatal intensive care unit (NICU), out of whom 26 were diagnosed with NEC. The data of all these children were collected from the hospital information system and analysed. Parameters studied included sex difference, gestational age at birth, birth weight, maternal risk factors, patient risk factors, day of life when feeding was started, type of feed, day of life when signs of NEC appeared, any antecedent associations, clinical features, radiological features, blood investigations, requirement of surgery, surgical findings and outcome. A comparison of all these parameters between the patients

managed nonsurgically and those managed surgically was also made. Statistical analysis was performed using statistical software SPSS V17 (IBM, Chicago, Illinois, USA). The study was approved by the hospital ethics committee.

Results

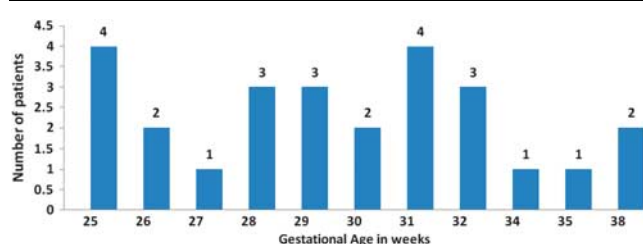
A total of 1139 patients were admitted to the NICU during the study period, out of whom 514 (45.1%) weighed less than 2500 g at birth and 49 (4.3%) died during this study period. Twenty-six patients with NEC, including 14 male and 12 female neonates, were studied. Incidence of NEC during the study period was 2.28% of total admissions. Mean gestational age at birth was 29.8 ± 3.7 weeks (range: 25–38 weeks). The mean birth weight was 1348.4 ± 774.1 g (range: 610–3900 g). The distribution of NEC patients as per gestational age and birth weight is shown in Figs 1 and 2, respectively. The incidence of NEC in patients with birth weight less than 2500 g was 4.47%.

Maternal risk factors included pre-eclampsia in four mothers, threatened abortion in three, absent end diastolic blood flow on Doppler ultrasonography in three and premature rupture of membranes in one mother. Twenty (76.9%) neonates had respiratory distress syndrome because of prematurity; 19 (73.1%) were mechanically ventilated; a central venous catheter was inserted in

19 (73.1%) patients; 14 (53.8%) patients required inotropic support; there was documented evidence of infection in 12 (46.1%) patients; 18 (69.2%) received blood transfusion (exchange transfusion in two); and 11 (42.3%) patients had patent ductus arteriosus as evident on echocardiography.

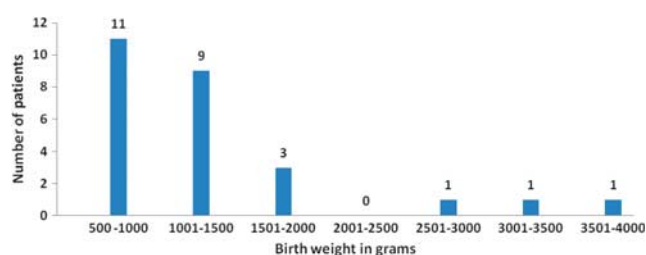
Enteral feeds were started from day 1 and continued up to day 7 of life. In 15 out of 26 (57.7%) patients, feeds were started on the second day of life. Seven (26.9%) babies were started on formula feed as breastmilk was not available for them. The average number of days of start of symptoms after admission was 17.5 days (range: 3–50 days). Feeds were changed in six babies, seven babies had features of sepsis and 10 received blood transfusion as preceding events before development of NEC.

Fig. 1



Distribution of necrotizing enterocolitis patients according to gestational age.

Fig. 2



Distribution of necrotizing enterocolitis patients as per birth weight.

Clinical features included abdominal distension, increased nasogastric tube aspirates, visible bowel loops and blood in stools. Abdominal radiographs showed distended small bowel loops in 10 patients, fixed loop on serial radiographs in four patients, pneumatosis intestinalis in six patients, pneumoperitoneum in five patients and ascitis in one patient.

The blood culture of two patients revealed the presence of coagulase-negative staphylococci (CONS); in two patients it showed *Pseudomonas aeruginosa* (with CONS in one), in one patient *Escherichia coli* and CONS and in another patient it showed *Klebsiella pneumoniae*; it was sterile in the rest of the patients. Occult blood in stools was positive for nine patients.

The mean duration for which patients were kept nil per oral was 9.5 days (range: 3–24 days). Antibiotics were given to all the patients for a mean duration of 11.2 days (range: 3–21 days). Total parental nutrition was given to 25 (96.1%) patients.

Laparotomy was performed in 11 (42.3%) patients. Five patients had pneumoperitoneum. Surgical findings and outcomes are shown in Table 1. The comparison of various study parameters in patients managed conservatively and by laparotomy is shown in Table 2. It can be seen that, except for raised C-reactive protein (CRP) and thrombocytopenia, all other parameters were similar in both the groups. The mean platelet count in patients managed surgically was significantly lower than that in patients managed medically (106.5 vs. 218.1 cells/ μ l of blood; $P = 0.0204$). Similarly the mean CRP level was also higher in patients managed surgically than in those managed medically (104 vs. 54 mg%; $P = 0.0414$).

Five (19.2%) patients died during the course of their treatment and 10.2% of the total deaths in the NICU during the study period were due to NEC.

Discussion

The reported incidence of NEC in premature and preterm neonates is 3–7% [3,4]. Mortality rates from NEC are high, ranging from 15 to 30% [3–5]. Cases of NEC are usually sporadic, although there have been reports of outbreaks. These outbreaks occur more

Table 1 Data of the patients managed by surgery

Patient	Indication of surgery	Surgical findings	Outcome
1	Fixed loops on radiograph	Caecum, ascending colon, transverse colon and splenic flexure necrotic	Alive
2	Severe pneumatosis intestinalis	Total gangrene gut	Died
3	Pneumoperitoneum	Terminal ileum to one-third of transverse colon resected for multiple perforation	Alive doing well
4	Fixed loops plus pneumatosis intestinalis	Descending colon and sigmoid colon gangrene	Alive
5	Pneumoperitoneum	Ileal perforation	Alive doing well
6	Pneumoperitoneum	Jejunal perforation with NEC of whole small and large bowel	Died
7	Fixed loop on radiograph	110 cm bowel 42 cm distal to duodenal jejuna flexure gangrenous	Died
8	Pneumatosis intestinalis and multiple air fluid levels on radiograph	Gangrene of terminal ileum, caecum and part of sigmoid colon	Alive
9	Pneumoperitoneum	Caecal perforation and total colonic gangrene sparing the rectum	Alive
10	Pneumoperitoneum	Gangrene of terminal ileum with perforations	Alive doing well
11	Air fluid levels on abdominal radiograph	Stricture of terminal ileum	Alive doing well

NEC, necrotizing enterocolitis.

Table 2 Comparison between the patients managed medically and those managed surgically

Sr. no.	Parameters	Medical management (n=15)	Surgical management (n=11)	P value ^b
1	Male : female ratio	9 : 6	5 : 6	0.6922
2	Mean \pm SD gestational age (weeks)	29.5 \pm 2.9	30.3 \pm 4.7	0.5923
3	Mean \pm SD birth weight (g)	1207.3 \pm 491.8	1540.9 \pm 1043.5	0.7596
4	Sepsis (n)	7	5	1.000
5	Central venous cannulation (n)	12	7	0.4065
6	Mechanical ventilation (n)	11	8	1.000
7	Blood transfusion (n)	9	9	0.3945
8	Respiratory distress syndrome (n)	11	9	1.000
9	Inotropic support (n)	7	7	0.4527
10	Positive radiology ^a (n)	9	10	0.1783
11	WBC count (cells/mm ³ of blood)	12 360 \pm 8951	8718.2 \pm 5773	0.2874
12	Absolute neutrophil count (cells/mm ³ of blood)	4586.7 \pm 5290	3390.9 \pm 3241	0.5506
13	Platelet count (cells/ μ l of blood)	218.1 \pm 143.2	106.5 \pm 109.1	0.0204
14	C-reactive protein (mg%)	55.1 \pm 64.2	104.7 \pm 66.2	0.0414
15	Positive blood culture (n)	3	3	1.000
16	Mortality (n)	2	3	0.6196

WBC, white blood cell.

^aPresence of either of pneumoperitoneum, pneumatosis intestinalis, portal venous gas or persistent fixed bowel loops on serial abdominal radiographs.

^bt-test and the Mann-Whitney test.

commonly in crowded nurseries. The incidence and mortality rates (2.28 and 10.2%, respectively) of NECs at our centre are consistent with those reported worldwide.

Prematurity and low birth weight are the two most consistent features associated with the development of NEC [6]. Twenty-four patients (92.3%) in the present study were premature, and 23 (88.5%) weighed less than 2500 g at birth. Another important association with NEC is the starting of enteral feeds [7]. Increased incidence of NEC in the babies given formula feeds has also been well documented in the literature [8]. In the present study 26.9% of babies received formula feeds before the onset of signs of NEC.

Many cases of NEC are managed medically, but roughly 20–40% of patients require surgical intervention [9]. Some of these cases are due to progression of disease during medical treatment, but many infants present acutely with severe disease requiring immediate operation.

A previous study from Oman performed by Samuel and Sajwany [10] reported 31 children aged between 48 days and 24 months who were initially treated for gastroenteritis, which later developed complications of NEC. The main initial complaints in these patients were diarrhoea and vomiting. Almost 88% of their patients had severe sepsis complicated by hypovolaemic shock and hypotension. All of their patients had bleeding in their rectum, abdominal distension and pneumatosis intestinalis [10]. Twelve patients (38.7%) in their study were managed surgically. Only two of their surgically managed patients survived, whereas only seven survived in the medically managed group. Thus, the total mortality in their series was 70.9%, which is very high compared with the 19.2% described in the present study.

Nair *et al.* [11] reported four neonates (birth weight: 810–1030 g) who developed NEC following an eye examination after topical instillation of mydriatics. However, they could not establish any casual relationship between the use of eye drops and the development of NEC. They suggested toxic effects of the eye drops

either by atropine-like activity of cyclopentolate on the gut or by the sympathomimetic action of phenylephrine causing splanchnic vasoconstriction. In the present study, 22 (84.6%) patients underwent an eye examination to rule out retinopathy of prematurity.

In our study thrombocytopenia and high CRP (at the time of appearance of the first clinical sign) were found to be the two factors positively associated in patients who required surgical management. There was no significant difference between gestational age, birth weight, presence of sepsis, presence of a central venous line, respiratory distress syndrome, need for mechanical ventilation, blood transfusion, inotropic support, leucocyte count and positive blood culture in patients managed conservatively and surgically. A low platelet count was a positive finding in patients who required surgical management ($P < 0.05$). Kenton *et al.* [12] had reported that a low platelet count is an important marker for gangrene of the bowel and it can be used as a direct indicator of the requirement for surgical intervention. Although our study showed the same, we were not able to ascertain the cutoff value of platelets indicating the need for surgery because of the small sample size.

Elevated CRP level was another important marker predicting the need for surgical management in the present study. Pourcyrous *et al.* [13] suggested that elevated CRP level can be used to differentiate paralytic ileus from NEC. Although CRP is a nonspecific marker of acute inflammatory states its elevated value can be used to identify patients with NEC who may require surgery.

The important limitation of our study is the small sample size, as the study was conducted in a recently established neonatal surgical centre in Oman.

We finally conclude that the incidence and mortality rates of NEC in Oman are similar to those reported in the literature. A low platelet count and high CRP levels at the time of onset of clinical features are the two important factors that can be used to predict the need for urgent surgical management in otherwise conservatively managed patients.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

References

- 1 Luig M, Lui K. Epidemiology of necrotizing enterocolitis – part II: risks and susceptibility of premature infants during the surfactant era: a regional study. *J Paediatr Child Health* 2005; **41**:174–179.
- 2 Kafetzis DA, Skevaki C, Costalos C. Neonatal necrotizing enterocolitis: an overview. *Curr Opin Infect Dis* 2003; **16**:349–355.
- 3 Lin PW, Stoll BJ. Necrotizing enterocolitis. *Lancet* 2006; **368**:1271–1283.
- 4 Llanos AR, Moss ME, Pinzón MC, Dye T, Sinkin RA, Kendig JW. Epidemiology of neonatal necrotizing enterocolitis: a population-based study. *Paediatr Perinat Epidemiol* 2002; **16**:342–349.
- 5 Sankaran K, Puckett B, Lee DS, Seshia M, Boulton J, Qiu Z, Lee SK. Variations in incidence of necrotizing enterocolitis in Canadian neonatal intensive care units. *J Pediatr Gastroenterol Nutr* 2004; **39**:366–372.
- 6 Henry MCW, Moss RL. Neonatal necrotizing enterocolitis. *Semin Pediatr Surg* 2008; **17**:98–109.
- 7 Kim SS, Albanese CT. Necrotizing enterocolitis. In: Grosfeld JL, O'neill JA, Coran AG, Fonlalsrud EW, editors. *Pediatric surgery*. 6th ed. Philadelphia: Mosby Elsevier; 2006. pp. 1427–1452.
- 8 Book LS, Herbst JJ, Atherton SO, Jung AL. Necrotizing enterocolitis in low birth weight infants fed an elemental formula. *J Pediatr* 1975; **87**:602–605.
- 9 Henry MCW, Moss RL. Surgical therapy for necrotizing enterocolitis: bringing evidence to the bedside. *Semin Pediatr Surg* 2005; **14**: 181–190.
- 10 Samuel M, Sajwany MJ. Necrotizing enterocolitis in children between the ages of 48 days and 24 months. *Pediatr Surg Int* 1994; **9**: 564–566.
- 11 Nair AK, Pai MG, Da Costa DE, Al Khusaiby SM. Necrotizing enterocolitis following ophthalmological examination in preterm neonates. *Indian Pediatr* 2000; **37**:417–421.
- 12 Kenton AB, O'Donovan D, Cass DL, Helmrath MA, Smith EO'B, Fernandes CJ, et al. Severe thrombocytopenia predicts outcome in neonates with necrotizing enterocolitis. *J Perinatol* 2005; **25**:14–20.
- 13 Pourcyrous M, Korones SB, Yang W, Boulden TF, Bada HS. C-reactive protein in the diagnosis, management, and prognosis of neonatal necrotizing enterocolitis. *Pediatrics* 2005; **116**:1064–1069.