Exploratory laparotomy in the management of confirmed necrotizing enterocolitis

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Introduction **Necrotizing enterocolitis (NEC) is a serious gastrointestinal emergency in newborn infants. Surgical management includes primary peritoneal drainage and/or exploratory laparotomy with bowel resection. This study describes obstetric complications, postnatal comorbidities, surgical care and intermediate postoperative outcomes in all infants with surgically and/or histologically proven NEC, who underwent exploratory laparotomy at our tertiary referral centre.**

Materials and methods **We conducted a retrospective review between January 2005 and December 2010. Results are reported as median (range). Fisher's exact test (two tailed) was used for statistical analysis. A *P*-value of 0.05 or less was considered statistically significant.**

Results **A total of 71 infants had suspected (Bell's stage ≥ 1) NEC. Of them, 32 infants underwent laparotomy for stage 2–3 NEC. We excluded 11 infants with surgically and/or histologically proven spontaneous intestinal perforation. In the remaining 21 infants with confirmed NEC, median gestational age was 27 weeks (23–39 weeks) and median birth weight was 720 g (440–3510 g). NEC was suspected after a median 14 days of life (1–49 days of life). Fifteen patients (71%) were initially managed medically for a median total of 8 days (1–25 days). Laparotomy was performed after a median of 7 days (<1–35 days) from the suspicion of NEC. Eleven infants (52%) underwent bowel resection and enterostomy, four infants (19%) underwent bowel resection with primary anastomosis and one infant (5%) underwent proximal diverting jejunostomy. Bowel perforation was seen in seven patients (33%). Necrosis totalis was evident in five patients (24%). There were 12 postoperative deaths (57% mortality), and seven deaths (58%) occurred during the first 30 days. Infants who died were more likely to have had absent/reversed end-diastolic flow (*n*=5, *P*=0.64), intrauterine growth retardation (*n*=5, *P*=0.18) or a gestational birth weight between 501 and 750 g (*n*=9, *P*=0.08). In the surviving children (*n*=9), the median length of hospital stay was 134 days (87–190 days) and postoperative sequelae were frequently seen.**

Conclusion **The morbidity and mortality for infants with confirmed NEC who undergo laparotomy remain high in infants despite optimal medical and surgical care. *Ann Pediatr Surg* 11:123–126 © 2015 Annals of Pediatric Surgery.**

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Introduction

Necrotizing enterocolitis (NEC) is a serious gastrointestinal emergency in neonates, associated with significant morbidity and mortality [1]. It primarily affects preterm infants and those with very low birth weight (VLBW – i.e., birth weight < 1500 g) [2,3]. Bell's staging criteria is used to define the severity of NEC based on clinical, laboratory and radiographic signs. Patients can be classified with stage 1 (suspected), stage 2 (confirmed) or stage 3 (advanced) disease [4]. Surgery is considered in children with Bell's stage 2–3 NEC and includes primary peritoneal drainage (PPD) and/or exploratory laparotomy with bowel resection [5], although no consensus exists about the optimal intervention [6–8]. At our institution, PPD is used to stabilize a patient before laparotomy, but not as a definitive treatment. The aims of exploratory laparotomy are to control intra-abdominal sepsis, remove necrotic bowel and preserve as much bowel length as possible [5]. Resection of bowel necrosis is followed by either primary anastomosis or enterostomy.

This retrospective review outlines the obstetric complications, postnatal comorbidities, surgical care and postoperative outcomes in infants with surgically and/or histologically proven NEC at our tertiary referral centre between January 2005 and December 2010.

Materials and methods

The institutional review board of the John Radcliffe Hospital, Oxford, approved this study. All neonates with clinical, laboratory and radiographic signs of Bell's stage 2–3 NEC who underwent exploratory laparotomy at our institution between January 2005 and December 2010 were identified using the hospital database.

Patient demographics, obstetric complications, postnatal comorbidities, clinical, laboratory and radiographic signs of NEC, operative procedures, surgical findings and intermediate postoperative outcomes were reviewed using inpatient and outpatient records. The standardized electronic neonatal database was used to retrieve missing antenatal data. All infants with a surgically or histologically proven spontaneous intestinal perforation (SIP) were excluded from the study.

The following definitions are used throughout this study: for extreme prematurity, a gestation of less than 28

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weeks; for intrauterine growth retardation (IUGR), an estimated foetal weight less than 10th centile for gestational age; for neonatal hypoglycaemia, a serum glucose of less than 2.5 mmol/l during the first 24 h of life; for severe thrombocytopenia, a platelet count less than 50×10^9/l; and for VLBW, a birth weight less than 1500 g. Grades 3 and 4 intraventricular haemorrhage (IVH) was diagnosed on the basis of cranial ultrasonography (US), with grade 3 IVH diagnosed if the ventricles were enlarged by the blood, and grade 4 if there was bleeding into the brain tissues around the ventricles [9]. Results are reported as median (range). Statistical analysis involved the two-tailed Fisher's exact test, with a *P*-value of 0.05 or less considered to indicate statistical significance.

Results

A total of 71 infants had suspected (Bell's stage ≥ 1) NEC at our institution between January 2005 and December 2010. Of them, 32 underwent exploratory laparotomy. We excluded 11 patients who had surgically or histologically proven SIP, leaving 21 infants (30% of original cohort) with confirmed surgical NEC.

In the cohort of infants with surgical NEC, there were 12 boys (57%). The median gestational age was 27 weeks (23–39 weeks) and median birth weight was 720 g (440–3510 g). Sixteen neonates (76%) were classified as extremely premature and 19 (90%) infants had VLBW. There were six twin pregnancies, with only one set of twins in whom both infants were diagnosed with NEC stage 1 or higher. Fourteen patients (67%) were born through Caesarean section; of which, eight were emergency procedures. All obstetric complications are outlined in Table 1. The most common obstetric complications were absent or reversed end-diastolic flow [$n = 7$ (33%)], pre-eclamptic toxaemia [$n = 7$ (33%)] and IUGR [$n = 6$ (29%)].

Perinatal comorbidities

Median Apgar scores at 1 and 5 min were 6 (1–10) and 9 (3–10), respectively. Twenty infants (95%) had respiratory distress syndrome requiring mechanical ventilation on the first day of life. Neonatal hypoglycaemia was diagnosed in five babies (24%). Cranial US revealed grades 3 or 4 IVH in three infants (14%). Fourteen patients (67%) were diagnosed with patent ductus arteriosus, and four (19%) received indomethacin therapy. Severe thrombocytopenia was noted in six cases (29%) and disseminated intravascular coagulopathy occurred in two patients (10%). Sepsis was suspected initially in all cases. Eleven patients (52%) had positive blood cultures, including coagulase-negative *Staphylococcus* ($n = 9$), *Enterobacter cloacae* ($n = 2$) and *Candida* spp. ($n = 1$). One infant had two or more microorganisms.

Table 1 **Obstetric complications**

Conditions	Patients [*n* (%)]
Absent or reversed end-diastolic flow	7 (33)
Pre-eclamptic toxaemia	7 (33)
Intrauterine growth retardation	6 (29)
Antepartum haemorrhage	3 (14)
Premature rupture of the membranes	3 (14)
Oligohydramnios	2 (10)
Group B streptococcus infection	2 (10)
Chorioamnionitis	1 (5)
Thrombosis in pregnancy	1 (5)
Maternal HIV	1 (5)
Twin-to-twin transfusion syndrome	1 (5)

Enteral feeding

Eighteen (86%) infants were started on enteral feeds before NEC was suspected. Enteral feeds were started after a median of 3 days of life (1–17 days of life) and consisted of breast milk ($n = 13$) or formula milk ($n = 5$).

Necrotizing enterocolitis

NEC was suspected after a median of 14 days of life (1–49 days of life), with 81% of infants suspected to have NEC within 30 days of birth. A total of 21 patients (95%) presented with abdominal distension and six (29%) had rectal bleeding. Fifteen patients (71%) were treated conservatively with bowel rest, bowel decompression and broad-spectrum antibiotics. The medical treatment given to these patients lasted a median of 8 days (1–25 days). Seven patients (33%) received total parental nutrition preoperatively.

Indications for laparotomy included pneumoperitoneum, portal venous gas and/or pneumatosis intestinalis [$n = 15$ (71%)], failed medical treatment [$n = 4$ (19%)] or severe peritonitis [$n = 2$ (10%)]. Failed medical treatment was defined as failure to demonstrate a clinical improvement despite resuscitation, gut rest and treatment with intravenous antibiotics. Four infants (19%) had PPD before exploratory laparotomy, and all these infants had VLBW. Exploratory laparotomy was performed after a median of 21 days of life (1–52 days of life) and 7 days ($<$ 1–35 days) after NEC was suspected. The surgical findings and operative procedures are outlined in Table 2. Eleven patients (52%) underwent bowel resection and enterostomy and four patients (19%) underwent a resection and primary anastomosis. One patient underwent a proximally diverting jejunostomy. Bowel perforation was found in seven patients (33%): four (19%) with a single perforation and three (14%) with multiple perforations. Necrosis totalis was evident in five neonates (24%) in whom care was subsequently withdrawn.

Postoperative morbidity and mortality

Postoperative morbidities are outlined in Table 3. Two infants (10%) required planned relook laparotomy: both within 5 days of their initial laparotomy. In the first patient, more necrotic bowel (3 cm in the jejunum) was resected and additional enterostomies were formed. In the second patient, necrosis totalis was seen and care was withdrawn. Postoperative sepsis was confirmed in 11 patients (52%), and blood cultures were positive for coagulase-negative Staphylococcus ($n = 6$), *Klebsiella* spp. ($n = 3$), *E. cloacae* ($n = 2$), *Enterococcus faecalis* ($n = 1$) and *Serratia marcescens* ($n = 1$). Three patients had two or more bacteria.

There were 12 postoperative deaths (57% mortality). Seven deaths occurred during the first 30 days postoperatively. Factors that correlated with higher mortality included absent or reversed end-diastolic flow ($n = 5$),

Table 2 Surgical findings and management

Sex	Gestation (weeks)	Birth weight (g)	NEC suspected (day of life)	Laparotomy (day of life)	Findings	Procedure
Male	26 + 1	440	9	36	10 cm of necrotic ileum containing single perforation and inflammatory mass	Bowel resection and primary anastomosis
Female	29 + 0	520	14	14	5 cm of necrotic ileum with proximal perforation resected	Bowel resected, proximal ileostomy and mucous fistula. Relook laparotomy showed necrosis totalis
Male	27 + 2	565	30	35	8 cm of necrotic ileum	Bowel resection and primary ileoileal anastomosis
Female	24 + 0	590	7	42	10 cm of necrotic terminal ileum	Bowel resection, proximal loop ileostomy and mucous fistula
Male	23 + 5	593	6	17	35 cm of necrotic small bowel and 6 cm necrotic transverse colon	Bowel resection proximal ileostomy and 3 × mucous fistulas
Female	28 + 3	640	49	52	10 cm of necrotic ileum	Bowel resection, proximal ileostomy and mucous fistula
Female	27 + 5	660	31	31	Necrosis totalis	Open and close
Female	27 + 2	670	33	41	4 cm of necrotic terminal ileum and 2 cm of ascending colon	Bowel resection (including ICV), proximal ileostomy and mucous fistula
Male	24 + 3	685	14	14	Necrosis totalis	Open and close
Male	24 + 2	700	28	43	Extensive necrosis from terminal ileum to sigmoid colon and single perforation 40 cm from DJF	Subtotal colectomy, proximal ileostomy, mucous fistula and perforation oversewn
Male	24 + 2	720	22	23	Necrosis totalis	Open and close
Male	24 + 2	729	37	46	50 cm of necrotic small bowel	Bowel resection, proximal ileostomy and mucous fistula
Male	27 + 2	750	3	5	15 cm of necrotic ileum and single perforation 1 cm from ICV	Bowel resection, proximal ileostomy and mucous fistula
Male	26 + 3	800	22	25	Patchy necrosis throughout bowel, ascending colon containing 2 × perforations	Diverting jejunostomy and perforations oversewn
Female	28 + 1	890	4	16	15 cm of necrotic ileum (90 cm from DJF)	Bowel resection, proximal ileostomy and mucous fistula
Female	26 + 2	915	1	8	1 cm of necrotic ileum and single distal perforation	Bowel resection, primary anastomosis and perforation oversewn
Female	26 + 6	920	13	13	Partial gut necrosis of the distal ileum, ICV sparing and patchy necrosis of the ascending colon	Bowel resection, ileoileal anastomosis, ileostomy, mucous fistula and subtotal colectomy
Male	27 + 0	975	6	7	14 cm of necrotic ileum plus multiple perforations 38 cm from DJF	Bowel resection, double-barrelled ileostomy and perforations oversewn
Male	27 + 0	1020	7	17	20 cm of necrotic ileum and caecum with 2 × perforations seen 10 and 20 cm from DJF	Bowel resection, proximal ileostomy and mucous fistula and perforations oversewn
Male	32 + 6	1580	21	21	Necrosis totalis	Open and close
Female	39 + 1	3510	1	1	Patchy gut necrosis of the transverse colon	Transverse colectomy, end ileostomy and colostomy

DJF, duodenojejunal flexure; ICV, ileocaecal valve; NEC, necrotizing enterocolitis.

Table 3 Postoperative sequelae

Postoperative morbidity	Patients [*n* (%)]
Sepsis	11 (52)
Metabolic acidosis	5 (24)
Short bowel syndrome	5 (24)
Delayed growth	4 (19)
Relaparotomy (stricture, perforation, intraperitoneal pus)	4 (19)
Hypoglycaemia	3 (14)
Neurodevelopmental impairment	2 (10)
Intra-abdominal abscess	2 (10)
Disseminated intravascular coagulopathy	1 (5)
Intestinal obstruction	1 (5)
Stricture	1 (5)
Wound dehiscence	1 (5)
Suspected (Bell's stage 1) NEC	1 (5)
Total	40

NEC, necrotizing enterocolitis.

IUGR ($n = 5$) or a gestational birth weight between 501 and 750 g ($n = 9$) (Table 4), although none of these factors reached statistical significance ($P > 0.05$); probably due to the small size of our cohort. In the infants who survived ($n = 9$), the median length of hospital stay was 134 days (87–190 days). One patient was lost to follow-up.

Discussion

Despite advances in neonatal intensive care, the surgical morbidity and mortality from NEC still remain a concern. Infants born prematurely and those of lower birth weights [2,3] are considered at risk. Term infants who develop NEC often have additional comorbidities such as congenital heart disease [10]. In our study, most infants with surgical NEC had extreme prematurity or VLBW. Only one pregnancy reached term gestation, and this infant had no comorbidities.

Large population-based studies have evaluated perinatal risk factors for developing NEC, although limited data are available for infants requiring surgery [11–14]. Guthrie *et al.* [13] reported that mechanical ventilation on the first day of life and exposure to both glucocorticoids and indomethacin during the first week of life increased the risk for surgical NEC. The same authors found no significant association between birth weight or gestational age and the need for surgery. In our study, around 95% of neonates who required laparotomy were mechanically ventilated on the 1st day of life because of respiratory distress syndrome, but less than 20% of infants diagnosed with patent ductus arteriosus were treated with indomethacin before developing NEC. Our analysis also appears to show that most infants operated on had VLBW, with the majority weighing between 501 and 750 g at birth ($P = 0.08$).

Studies have shown that up to 50% of infants with NEC require surgery [15]. Our findings were similar to this, with 45% of patients with suspected stage 2–3 NEC taken to theatre. Overall, 30% had surgically or histologically proven NEC and 19% had NEC totalis at initial

Table 4 Mortality and gestational birth weight

Birth weight (g)	Patients	Deaths	*P*-value
≤ 500	1	1	1.00
501–750	12	9	0.08
751–1000	5	1	0.11
1001–1250	1	0	NA
1251–1500	0	0	NA
≥ 1501	2	1	0.55

NA, not available.

laparotomy. In all these patients NEC had been suspected within 24 h of surgery. It is not surprising that the most common reasons for surgery were suspected perforation or pneumatosis intestinalis; however, interestingly, 29% of patients developed severe thrombocytopenia, which has previously been linked to the severity of NEC [16,17].

In our study, laparotomy occurred following a median of 1 week after NEC was initially suspected. The majority of patients (76%) had focal NEC confined to the ileum and/or ascending colon (Table 1). Bowel perforations occurred infrequently ($n = 7$) and were more likely to be single perforations (57%). Importantly, all perforations were confined to an area of necrotic bowel. Intestinal resection of the affected bowel and enterostomy formation were the mainstay of treatment, which was usually performed in neonates who needed rapid and effective surgical defunctioning.

It is widely accepted that infants with surgical NEC have higher morbidity and longer hospital stay compared with those treated nonsurgically [18,19]. In our study, postoperative sequelae were frequently encountered, with the most common complication being sepsis from coagulase-negative Staphylococcus. Early complications such as metabolic acidosis and disseminated intravascular coagulopathy were rare; however intermediate sequelae such as intestinal stricture, short gut syndrome and neurodevelopmental delay were more frequently observed. In the surviving infants the median length of postoperative hospital stay exceeded 3 months. All affected neonates with suspected NEC were managed initially with gut rest, drainage of aspirates and intravenous antibiotics. However, despite maximal medical management and adequate resuscitation, a failure to demonstrate clinical improvement was considered an indication for surgery in our centre. Our findings further emphasize the delayed morbidity associated with surgical NEC and the importance of having a high threshold for surgical intervention in such cases.

In the UK, the number of deaths attributable to NEC has increased in recent years [7,20]. It has been suggested that an increase in the number of births and an increase in the survival of preterm infants has lead to larger numbers of children at higher risk of developing NEC. In contrast, recent data from the US suggest that the mortality trend of NEC remains relatively constant [21]. In our study the mortality rate of confirmed NEC was 57%. Interestingly, if the number of deaths for infants with SIP ($n = 0$) is included in our analysis, the total mortality for babies with clinical, laboratory and/or radiographic signs of Bell's stage 2–3 NEC who underwent laparotomy would be 38%. These results suggest that further research is needed to stratify infants on the basis of underlying intra-abdominal pathology to optimize surgical care.

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Conflicts of interest

There are no conflicts of interest.

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