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Research Article

NEONATAL GASTROINTESTINAL PERFORATIONS: A 7-YEAR SINGLE CENTER EXPERIENCE AT A TERTIARY NEONATAL INTENSIVE CARE UNIT IN TURKEY

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ABSTRACT

We aimed to present our experience on the gastrointestinal (GI) perforations and the factors affecting the outcome. A retrospective study carried out at a tertiary neonatal intensive care unit. A total of 38 neonates with GI perforation managed in our neonatal intensive care unit during 2005 to 2011 were included into the study. The patients were grouped as necrotizing enterocolitis (NEC) and non-NEC patients. Twenty four of 38 infants (63.2%) were premature. Non-NEC conditions were most common cause of the perforation (57.9%). Twelve cases were managed with peritoneal drainage alone. Surgical repair without conservative approach was performed in 19 patients, while seven of the patients underwent to surgical intervention after decompression by the percutaneous drainage. The overall mortality rate was 28.9%. It were 43.7% and 18.1% in NEC and non-NEC group, respectively ($p>0.05$). The mortality rate in small bowel perforation and colorectal perforation was 30.7% and 22.2%, respectively ($p>0.05$). All patients with gastric perforation survived. Non-NEC conditions were common cause of GI perforations. Although some patients could be managed with conservative approach, surgical exploration is still the main management model. The prognosis of the gastric perforation was good; however, the prognosis of small bowel and colorectal perforation was poor.

Key Words: *Etiology, Gastrointestinal Perforation, Necrotizing Enterocolitis, Percutaneous Drainage, Surgical Repair, Mortality, Morbidity, Newborn*

INTRODUCTION

Despite the recent progress in the neonatal intensive care such as the ventilator management, the availability of the antibiotics and other medicines, and the operative and anesthetic techniques, the gastrointestinal (GI) perforation during the neonatal period is still a major problem regarding the neonatal morbidity and mortality (Takamatsu *et al*., 1997; Nakamura *et al.*, 2003; St-Vil *et al.*, 1992; Al-Qahtani *et al.*, 2001; Sakellaris *et al.*, 2012). Neonatal GI perforations consist of a heterogeneous group of patients ranging from very sick premature babies to healthy full-term babies (Weinberg *et al.*, 1989). Co-morbid factors, mainly the prematurity and the low birth weight, have a negative impact on the outcome (Kuremu *et al.*, 2007). In the past, their poor prognosis was more related to the common acute event, the intraperitoneal perforation and its ensuing surgical management than to the underlying cause (Borzotta and Groff, 1988).

The aim of this study was to analyze the clinical presentation, etiology, management, outcome, and short-term prognosis of the neonatal GI tract perforations, and also to investigate the factors affecting the outcome in a single tertiary neonatal intensive care unit (NICU).

MATERIALS AND METHODS

Our NICU with a capacity of 72 beds is a tertiary reference center for the patients from all parts of Turkey, especially the Central Anatolian region. The medical records of the newborn infants with the GI perforation between January 2005 and December 2011 were reviewed retrospectively. The diagnosis of the GI perforation was made by clinical and radiological findings that is free air on the abdominal radiography and/or confirmed during the operation. The diagnosis of necrotizing enterocolitis (NEC) was made by clinically and radiologically according to the modified Bell criteria (Walsh and Kliegman, 1986). The patients were grouped as NEC and non-NEC patients. The

demographic characteristics (gestational age, birth weight, mode of delivery, sex, postnatal day of perforation) and the clinical data (underlying cause, site of perforation, co-morbid factors, operation details, treatment, complications related to the operation, and clinical outcomes) of the patients were recorded from the medical files. Student's and two-sample t tests were used for the statistical analysis. A value of $p<0.05$ was considered as statistically significant.

RESULTS AND DISCUSSION

There were 38 infants (20 boys, 18 girls) with a mean gestational age of 34.2±4.4 (25-42) weeks and a birth weight of 2.0±0.7 (0.98-3.5) kg (Table 1). Twenty three (60.5%) of them were born by caesarian section, and 24 newborn (63.2%) were preterm. Perforation was caused by NEC in 16 patients (42.1%) while the non-NEC-related conditions were responsible for the perforation in 22 patients (57.9%). The gestational age and birth weight of the NEC patients were significantly lower than the non-NEC patients ($p<0.05$) (Table 1). Perforation was observed from birth to 60th postnatal day (mean 10.3 ± 12.3 days).

Non-NEC-related Perforations

Non-NEC-related perforations were idiopathic or secondary. Secondary perforations due to any underlying pathology occurred in 13 patients (34.2%), whereas in nine patients (23.7%) spontaneous perforation occurred in an apparently normal bowel without any evident cause (idiopathic perforation). Underlying pathology in secondary perforations included ileal atresia (n: 4), jejunal atresia (n:1), esophageal atresia/tracheo-esophageal fistula (n:1), volvulus (n:2), total colonic duplication (n:1), peptic ulcer (n:1), multiple colonic atresia (n:1), meconium ileus (n:1), and incarcerated inguinal hernia (n:1).

Clinical Presentation and co-morbid Conditions

Abdominal distension was the most common finding (74%) of the perforation. The free intraperitoneal air and/or the calcification were observed on the abdominal radiography of 31 patients (81.5%). Sixteen patients (42.1%) were given mechanical ventilatory support before GI perforation occurred. Accompanying co-morbid factors were prematurity (n: 24), respiratory problems (n:15), major cardiac anomaly (n:4), malrotation (n:3), gastroschisis (n:2), Hirschsprung's disease (n:1), arthrogryposis multiplex (n:1), and cystic fibrosis (n:1). The perinatal asphyxia, intrauterine growth retardation, and obstetrical complications (premature rupture of membranes, preeclampsia, chorioamnionitis, maternal diabetes, placental abruption, and fetopelvic disproportion) were more common accompanied factors of perforation in the NEC group.

Site of the Perforation

The anatomical location of the perforation sites were shown in Table 2. Four patients had multiple perforation sites. Of those, one had NEC, one with gastroschisis; one had jejunal atresia, and the other with colonic atresia.

Gastric perforation was defined in five patients (13%). While secondary perforations due to underlying pathology occurred in two patients, idiopathic perforations occurred in three patients. The primary pathologies for secondary perforations were tracheo-oesophageal atresia with tracheo-oesophageal fistula and peptic ulcer.

The perforation was seen in small bowel of the 13 patients (34.2%), and most common site of perforation was the terminal ileum (n:8). Secondary perforations occurred in seven patients, idiopathic in two patients, and the NEC related perforation in four. Primary pathologies in secondary perforations were as follows: ileal atresia (n:4), jejunal atresia (n:1), and volvulus (n:2).

The colorectal region was involved in nine out of 38 patients (23.6%) and the caecum was most common site in three cases. In the remaining six patients, involved sites were as follows: sigmoid colon (n:2), rectum (n:2), and descending colon (n:2). Idiopathic and secondary perforations were observed in either four patients. In addition, NEC was considered as the main cause of perforation in one patient. Underlying pathologies for secondary perforation were colonic atresia (n:1), colonic duplication (n:1), incarcerated hernia (n:1), and meconium ileus (n:1).

Managements, Complications, and Mortality

Twelve cases were conservatively managed only with decompression by percutaneous drainage. Especially, among them, the isolated gastric perforation in a premature infant improved with

percutaneous peritoneal drainage without primary surgical repair. Laparotomy without the conservative approach was performed for 19 patients. Seven patients underwent laparotomy after decompression by percutaneous drainage. Debridement, repair or limited resection and primary anastomosis were performed in 11 out of 26 cases, and enterostomias were performed in 15 cases. Seven patients managed with percutaneous drainage survived while five patients died. There was no difference in mortality among patients who underwent only percutaneous drainage or laparotomy, or laparotomy after the percutaneous drainage ($p>0.05$).

The re-laparotomy was required in 14 patients (53.8%). Of those, one had intestinal obstruction because of brid, one developed a new perforation in the small bowel, two had anastomotic leakage (converted to enterostomies), one had gastroschisis (related to a new perforation in the small bowel), and nine had early closure of enterostomias.

Post-operative complications were septicemia (n:9, 34.6%), respiratory failure (n:7, 26.9%), leakage in anastomosis area (n:2, 7.7%), renal failure (n:1, 3.8%), and short bowel syndrome (n:1, 3.8%). The overall mortality rate of all patients was 28.9% (11/38).

Mortality rates related to underlying causes were shown in Table 3. The difference in the mortality rate between NEC and non-NEC patients was not statistically significant ($p>0.05$). Mortality rates per perforation site were shown in Table 2. There was an insignificant difference in the mortality rate between colonic and small bowel perforations ($p>0.05$).

Deaths were caused by the septicemia (n:6, 54.5%), intraventricular hemorrhage (n:3, 27.2%), and multiple organ dysfunction syndrome (n:2, 18.1%). The relationship among the mortality, the gestational age and birth weight was given in Table 4. Mortality rate of low birth weight infants (less than 1500g) and preterm infants less than 30^{th} week's gestation were 42.8% and 50%, respectively ($p>0.05$).

The gastrointestinal perforation is a dramatic event for a neonate and has significant morbidity and mortality rate despite the advances in perinatal care (Tan *et al.,* 1989; Meyer *et al.,* 1991; Bell, 1985; Chirdan and Ameh, 2001). The prognosis of an infant with a perforated viscus depends on the underlying pathology, the type and severity of associated conditions, level of the perioperative care, degree of the prematurity, and birth weight. The mortality rates are reported between 30% and 50% (Tan *et al.,* 1989; Meyer *et al.,* 1991; Bell, 1985; Chirdan and Ameh, 2001). The overall mortality rate of infants with GI perforation in the present series was 28.9%, and this rate was accordance with the results of other groups. Some researchers have found an increasing incidence of NEC related perforation, as very low birth weight infants survived because of improved perinatal care (St-Vil *et al.,* 1992; Tan *et al.,* 1989). Indeed, NEC was underlying etiology in 42.1% of all our cases while Asabe *et al.,* (2009) found a rate of 29.4% between the years of 1974 and 1997.

In contrast to other studies, in this study, the predominant cause of the perforation was non-NEC conditions in 38 patients. The reason of this result was unclear but it may be due the improvement in the level of medical care over time. In addition, it would be due to the fact that our hospital being a tertiary reference center. Further studies are needed to confirm this result.

Like to other studies (St-Vil *et al.,* 1992), the infants with NEC related perforation were also significantly more premature than the non-NEC group in our study. In other studies, the infants with NEC related perforation had worse prognosis than the non-NEC group (St-Vil *et al.,* 1992). However, we could not find any difference between the NEC and non-NEC patients' mortality rate. This finding may be related to the size of our patient group. In 1980, the mortality rate due to NEC related perforations was uniformly high. Since then, the risk inherent to laparotomy in a small infant has been decreased (St-Vil, 1992). In other studies, with regard to the prognostic factors, the gestational age and birth weight were significantly lower in non-survivals (Nakamura *et al.,* 2003; Asabe *et al.,* 2009). Akatsuka *et al.,* (1994) also reported that the mortality rate of premature babies less than 28 week's gestational age was 80%. Nakamura *et al.,* (2003) revealed no survival for those less than 25 week's gestational age, and a mortality rate of 84.6% under 30 week's gestational age. However, in the present study, the mortality rate was 50% in newborns under 30^{th} week's gestational age. There is a narrowing of the mortality gap between infants above and under 30^{th} week's gestational age in our study. This condition could be explained by the improvement in surgical outcome and the neonatal intensive care over time.

According to the national survey on neonatal surgery up to 1983 in Japan, the most commonly perforated site was stomach (from 50% to 75%) followed by the small intestine and colon. However, the small intestine became the most frequent site (about 50%) after 1988, followed by the stomach and colon (Ohota, 1980; The Committee on Academic Survey and Advanced Medical Science, the Japanese Society of Pediatrie Surgeons, 2004; The Committee on Academic Survey and Advanced Medical Science, the Japanese Society of Pediatrie Surgeons, 1999). Accordingly, the most common site of the GI perforation in our series was also the small intestine.

The site of the perforation may be more important prognostic factor. According to the national survey on neonatal surgery in 2003 in Japan, mortality rates related to the perforation site were as follows: stomach 42.9%, small intestine 50% and colon 33.3% (Ohota *et al.*, 1980). In our series, all patients with gastric perforations survived. The mortality rate related to the perforation site was 30.7% in the small intestine, and 22% in the colon (including 2 rectal cases). In contrast to the high mortality rate of other reports, all the patients in our study with the spontaneous gastric perforation, this is usually related with the selective ischemia during periods of perinatal asphyxia, survived. This was most likely due to the fact that many of these patients were healthy full-term newborns. But, only one baby with gastric perforation was premature with a 28 weeks' gestational age. In this patient, the isolated gastric perforation occurred at the 30th hour of the life. When the baby's clinical status worsened, a Penrose drain was inserted. The surgical repair was planned when the patient's general status does permit it. During the follow-up, the complete resolution of the free air with presence of gastric gas shadow was observed. Without requirement for primary surgical repair, percutaneous drainage was terminated on the 27th postnatal day (Aydin *et al.*, 2011).

Table 1: Gestational age and birth weight of infants with GI[£] perforation

	NEC*	Non-NEC**	p value
Number of patients	16	22	
Gestational age (week)	31±3.5	36.5±3.4	<0.05
Birth weight (kg)	1.6±0.7	2.3±0.6	<0.05

*£: Gastrointestinal, ***:** Necrotizing enterocolitis*
*****:** Idiopathic and secondary perforations*

Table 2: Incidence of mortality according to location of the perforation sites

Site of perforation	Number of patients	Number of deaths	Mortality (%)
Stomach	5	0	0
Small bowel	13	4	30.7
Ileum	8	2	25
Jejunum	5	2	40
Colorectal	9	2	22
Undefined	11	5	45.4

Table 3: Relationship between diagnosis and mortality

Diagnosis		Mortality/Total (%)
*NEC[¥]		7/16 (43.7)
*Non-NEC	**Secondary perforations	3/13 (23)
	**Idiopathic perforations	1/9 (11)
Total		11/38 (28.9)

*[¥]: Necrotizing enterocolitis, *p>0.05, **p>0.05*

Table 4: Relationship among mortality, and gestational age and birth weight

	Mortality (n)		
	NEC	**Non-NEC**	**Mortality/Total (%)**
Gestational age*			
≤30 wk	5	0	5/10 (50)
>30 wk	2	4	6/28 (21.4)
Birth weight[¥]			
≤1.500 g	6	0	6/14 (42.8)
>1.500 g	1	4	5/24 (20.8)

**: p>0.05; [¥]: p>0.05*

The abdominal distension was most common feature of perforation in our series. The abdominal distension caused the respiratory distress by splinting the diaphragm. The decompression of the pneumoperitoneum by percutaneous drainage relieves the respiratory distress and also decreases the progression of peritoneal contamination and subsequent septicemia (Rao *et al.,* 2011; Sola *et al.,* 2010; Resch *et al.,* 1998; Ricketts, 1990). In our study, 12 patients were managed with the decompression by percutaneous drainage without an open surgery. The drainage may be curative as seen in seven of our patients.

Gastrointestinal perforations in the newborn infants are still important in terms of postoperative complications and mortality. The most important main cause of the high mortality rate seen in the GI perforations was preoperative or postoperative septicemia (Rao *et al.,* 2011; Wang *et al.,* 1994). The sepsis occurred in 34.6% of our cases during the postoperative period. Episodes of the sepsis were accounted for 54.5% of the mortality.

Tan *et al.,* (1989) reported in their series that the main cause of deaths was mainly due to the ongoing septicemia. An appropriate antibiotic therapy including the anaerobes was very important for these patients together with the supportive care.

Conclusion

At the present time, neonatal GI perforations are still a major concern for pediatric surgeons and neonatologist in our institution. Non-NEC conditions were common cause of the GI perforation. Although peritoneal drainage is an alternative management model in some patients whose clinical condition does not permit surgical repair, the surgical exploration is still remaining the main management model.

The prognosis of the GI perforation was less related to the birth weight and gestational age. The gastric perforations had an excellent prognosis, while the prognosis of the small bowel and colorectal perforations were poor. The mortality rate of the GI perforations was still high even though a significant improvement in the neonatal intensive care. The sepsis accounted for many of deaths in these patients group.

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