Original Article

Neonatal Gastrointestinal Perforations: A 4-year Experience in a Single Centre

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Abstract

Background: Gastrointestinal perforation (GIP) during the neonatal period is still a significant problem despite improved neonatal care. The study aimed to report on incidence, management, morbidity and mortality. **Material and Methods:** Records of neonates with GIPs between October 2018 and November 2022 were retrospectively analysed. **Results:** There were 47 patients, 22 (46.8%) males and 25 (53.2%) females. The incidence of neonatal GIP was 0.39% amongst all newborns treated in the neonatal intensive care unit. The mean gestational age was 30.4 ± 4.5 (23–38) weeks, and the mean birth weight was 1493.08 ± 753 (580–2940) g. Of 47 neonates, 5 (10.6%) were full term and 42 (89.4%) were preterm. The mean age of surgery was 12.25 ± 9.89 (0–41) days. A laparotomy was performed in 43 (91.4%) of 47 neonates, while seven of the patients underwent surgical intervention after decompression by percutaneous drainage. Four patients were managed with peritoneal drainage alone due to poor general condition. The pathologies unrelated to necrotising enterocolitis (NEC) were the most common cause of GIPs (55.3%) and included spontaneous intestinal perforation ($n = 18$), stomach perforation ($n = 4$), segmental volvulus ($n = 2$), acute mesenteric ischaemia ($n = 1$) and meconium peritonitis ($n = 1$). Overall survival was 55.4%. **Conclusion:** GIPs are one of the most significant causes of mortality in newborns. The most common cause of perforations is non-NEC entities and can be seen in the entire intestinal system from the stomach to the colon. Surgical exploration is still the primary management model.

Keywords: Gastrointestinal perforation, necrotising enterocolitis, newborn, premature infant

Introduction

Despite the improvements in intensive care and developing medical devices, gastrointestinal perforation (GIP) is frequently seen in premature and low birth weight (LBW) infants hospitalised in the neonatal intensive care unit (NICU) and is one of the leading life-threatening complications.[1-3] Although a prevalence of 0.6%–1.3% has been reported in the literature, mortality has a very high rate of 15%–70%.[3-5]

The aetiology of GIP includes immaturity, microbial dysbiosis, enteral nutrition, hypoxia, ischaemia, inflammation, drugs and maternal causes.[6-9] The most frequent causes of GIP include necrotising enterocolitis (NEC), sepsis, intestinal obstructions, iatrogenic traumas due to irrigation of nasogastric or rectal catheters, Hirschsprung's disease and spontaneous intestinal perforation (SIP). The frequency of GIP increases as the patient's birth weight and week of birth decrease. However, depending on the underlying cause, it can be seen in any segment of the gastrointestinal (GI) tract from the stomach to the rectum.[1,2]

Abdominal distension, discolouration of the abdominal skin, increased infection parameters in the blood, biliary vomiting and the absence of stool output might be warning symptoms for GIP.[10,11] Intra-abdominal free air is the most definitive indicator of GIP. However, the absence of free air in the abdomen does not rule out perforation. The perforation area is surrounded by inflammation, fibrin tissues, surrounding intestinal loops and omental tissue, which may prevent free air development.[12] The indications for surgical intervention and

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the treatment methods to be applied are decided specifically for the patient.

In this study, we aimed to present our 4 years of single-centre experience on neonates with GIPs and evaluate the patient's characteristics and the factors that affect the treatment and outcome.

Material and Methods

A retrospective analysis of patient files and operative logs was done for all patients diagnosed with GIP admitted to the NICU between 1 October 2018 and 1 November 2022.

The patients' demographic data (age, gender and weight), underlying disease, surgery indications, surgery timing, surgical technique, outcome, complications and mortality rates were evaluated. According to the surgical findings, the patients were divided into Group 1, GIP related to NEC; Group 2, GIP unrelated to NEC and Group 3, patients with unknown aetiology.

The diagnosis was based on operative and histopathological findings. A small isolated gut perforation in an otherwise non-diseased bowel with histology confirming isolated mucosal and serosal inflammation was accepted as SIP. Multiple areas of coagulative and haemorrhagic transmural necrosis were consistent with NEC.

All procedures performed were by the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1964 and later versions. This study was approved by the Institutional Review Board of Harran University (approval number 2022/08), and written informed consent for surgery was obtained from all patients' parents.

The statistical analysis was performed using the IBM SPSS Statistics for Windows, Version 22.0. (Armonk, NY, USA: IBM Corp.) The demographic and clinical characteristics of the patients were analysed descriptively.

Results

During the 4 years evaluated, a total of 11794 neonates were admitted to our NICU. Amongst these, GIP was detected in 47 (0.39%) neonates. There were 22 (46.8%) males and 25 (53.2%) females. Of 47 neonates, 5 (10.6%) were full term and 42 (89.4%) were preterm. The mean gestational age was 30.4 ± 4.5 (23–38) weeks, and the mean birth weight was 1493.08 ± 753 (580–2940) g. According to the birth weights, 8 (17.1%) were normal birth weight (between 2500 and 4000 g), 11 (23.4%) were (LBW, <2500 g), 9 (19.1%) were very LBW (<1500 g) and 19 (40.4%) were extremely LBW (ELBW, <1000 g). No patient had a high birth weight (>4000 g).

Twenty-seven of the patients were delivered by caesarean section (C/S), and 20 by normal spontaneous vaginal delivery (NSVD). All patients born by C/S were premature. The mean gestational age of C/S patients was 29 ± 3.47 (25–37) weeks, and the mean birth weight was 1199.8 ± 553.5 (700–2600) g. Of the patients born by NSVD, 15 were premature, and five were full term. The mean gestational age of NSVD patients was 32.3 ± 5.2 (23–38) weeks, and the mean birth weight was 1889 ± 808.3 (580–2940) g.

The primary diagnoses were prematurity and respiratory distress syndrome (n = 34, 72.4%), asphyxia (n = 4, 8.5%), poor feeding (n = 4, 8.5%), tachypneic breathing (n = 3, 6.4%), COVID-19 positive mother's baby (n = 1, 2.1%) and complicated meconium peritonitis with antenatal diagnosis (n = 1, 2.1%). Additional congenital anomalies were present in seven patients. These were Adam's Oliver syndrome, congenital hypothyroidism, neonatal purpura fulminans, cystic fibrosis, hydrocephalus, twin-to-twin transfusion syndrome, congenital heart disease and unilateral renal agenesis. Four of these patients were diagnosed antenatally.

All of the patients had abdominal distension on physical examination. Biliary drainage from the nasogastric tube accompanied 37 (78.7%) patients. Of 47 neonates, 45 (95.7%) had free intraabdominal air on standing direct abdominal X-ray. One of the patients who did not detect free intraabdominal air had a preliminary diagnosis of antenatal bowel perforation. On postnatal physical examination, the abdominal skin was hyperemic and compatible with the acute abdomen [Figure 1]. The other patient had a persistent bowel loop on direct abdominal X-ray.

Complete blood count, biochemistry tests, C-reactive protein and blood gas values were studied preoperatively, and blood culture was taken from all patients. Laboratory test results are given in Table 1. Blood culture was negative on 31 (65.9%) patients. Gram-positive bacteria growth was detected in eight patients, Gram-negative bacteria in seven, and fungus in one.

The mean age of surgery was 12.25 ± 9.89 (0–41) days. A laparotomy was performed in 43 (91.4%) of 47 neonates.



Figure 1: (a) Direct X-ray image of the patient with the diagnosis of antenatal bowel perforation, (b) The view of abdominal distension and hyperaemic abdominal skin

Due to the poor general condition of 11 neonates, temporary peritoneal drainage catheters were placed as a bedside procedure first. After recovering the general condition, 7 of them were taken to laparotomy. Four of them died before laparotomy could be done.

According to the surgical findings, the patients were divided into three groups: Group 1, GIP related to NEC (n = 17); Group 2, GIP unrelated to NEC (n = 26) and Group 3, patients with unknown aetiology (n = 4). Patients who did not undergo laparotomy were grouped as unknown aetiology.

There were 7 (41.1%) males and 10 (58.9%) females in Group 1. The mean gestational age was 29.8 ± 4.5 (25–38) weeks, and the mean birth weight was 1400 ± 746 (580–2940) g. The mean age of surgery was 14.5 ± 9.47 (1–34) days. Peritoneal drainage catheter was placed in six patients primarily because of poor general condition. The mean time to surgery after drainage catheter insertion was 5.5 ± 3.01 (2–16) days. Perforations were observed in the small intestine (n = 10), colon (n = 4) and small intestine and colon (n = 3) [Figure 2]. The areas of perforation described during surgical exploration are presented in Table 2. An intestinal diversion with necrotic bowel segment resection was performed in 16 patients, and ileal resection and anastomosis were performed in one. On the follow-up, nine patients died. Stoma closure was performed in five patients before discharge. Two patients were lost to follow-up. Follow-up of other discharged patients is uneventful.

The pathologies unrelated to NEC were the most common cause of GIPs (55.3%) and included SIP (n = 18), stomach perforation (n = 4), segmental volvulus (n = 2), acute mesenteric ischaemia (n = 1) and meconium peritonitis (n = 1). Of 18 patients diagnosed with SIP, nine were female, and nine were male. The mean gestational age was 30.2 ± 4.55 (26–38) weeks, and the mean birth weight was 1442 ± 749 (700–2930) g. The mean age of surgery was 11.6 ± 9.89 (2–32) days. Perforations were observed in the small intestine (n = 11) and colon (n = 7) [Figure 3]. An intestinal diversion (ileostomy n = 14, colostomy n = 2) was performed in 16 patients, ileal resection and anastomosis in one and primary repair of the perforation area in one. Biopsy was taken from the perforation areas, and appendectomy was done for ganglion cell evaluation in all SIP patients. The biopsy result of the patient with perforation in the transverse colon was evaluated as ganglion negative. Ganglion cells were detected on the other biopsy specimens. On the follow-up, seven patients died. Stoma closure was performed in two patients before discharge. Seven patients were lost to follow-up. Follow-up of other discharged patients is uneventful.

The mean birth weight of four patients with gastric perforation was 2155 ± 738 (970–2900) g. The mean gestational age was 33.2 ± 4.67 (26–38) weeks. Primary repair was done in gastric perforation patients. All patients with gastric perforation survived.

Segmentary volvulus was detected in two patients at laparotomy. In the terminal ileum, it was observed that necrosis developed due to segmental ileal volvulus and perforated from this area. In both patients, the necrotic bowel segment was resected, and the ileostomy was opened. The stomas of patients were closed in the 2nd and 6th months postoperatively. Follow-up is uneventful.

The patient with the diagnosis of acute mesenteric ischaemia, with a birth weight of 2050 g, was delivered at 34 weeks of gestation from a COVID-19-infected mother. On the postnatal 3rd day, the patient suddenly had tachycardia and abdominal tension. Moreover, there was intraabdominal free air. On laparotomy, necrotic small bowel and colon starting from 20 cm of ligament of Treitz to the middle part of the transverse colon. Ileostomy and resection of necrotic bowel segments were done. The patient died 1 day after surgery due to cardiorespiratory arrest and multiorgan failure.

Table 1: Laboratory test parameters of patients

Parameter	Range	Mean±SD
Haemoglobin (g/dL)	14.2–24.6	13.2±3.08
White blood cell (×10^3/uL)	5–21	12.7±11.1
Platelets count (×10^3/uL)	150–450	151.7±106.6
CRP (mg/L)	0–5	63.8±64.8
pH	7.35–7.45	7.24±1.56
Lactate (mmol/L)	0.5–1.6	3.78±2.27

SD: Standard deviation, CRP: C-reactive protein

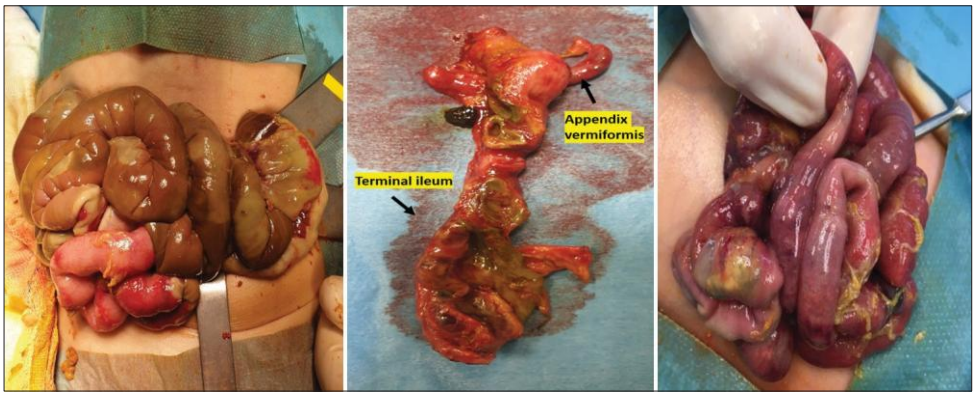


Figure 2: The surgical findings of some patients diagnosed with perforation due to necrotising enterocolitis (arrows: terminal ileum, appendix vermiformis)

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

Area of perforation	Group 1	Group 2	Number of deaths	Mortality (%)
Stomach	0	4	0	0
Small bowel	10	11	8	38
Jejunum	2	0	1	50
Ileum	8	11	7	36.8
Colorectal	4	7	6	54.5
Multiple (small bowel+colorectal)	3	0	3	100
Undefined	4		4	100

Table 3: Relationship between the mortality according to birth weights and gastrointestinal perforation aetiology

Reasons for mortality	HBW (*n*)	NBW (*n*)	LBW (*n*)	VLBW (*n*)	ELBW (*n*)	Total (*n*)
GIP related to NEC	0	1	2	1	5	9
GIP unrelated to NEC	0	1	1	0	6	8
Unknown aetiology	0	0	0	1	3	4
Total	0	2 (9.6)	3 (14.2)	2 (9.6)	14 (66.6)	21 (100)

HBW: High birth weight, NBW: Normal birth weight, LBW: Low birth weight, VLBW: Very LBW, ELBW: Extremely LBW, NEC: Necrotising enterocolitis, GIP: Gastrointestinal perforation



Figure 3: The surgical findings of spontaneous intestinal perforation; perforation area in the terminal ileum

A female patient with a diagnosis of antenatal bowel perforation, born at 37 weeks and 1750 g, was operated on with a preliminary diagnosis of complicated meconium peritonitis. Small bowel perforation was detected in the patient, and ileostomy was opened. The stoma was closed before discharge. The follow-up of the patient, who was subsequently diagnosed with cystic fibrosis, was uneventful.

Laparotomy could not be performed in four patients in whom a peritoneal drainage catheter was placed because their general condition was very poor. The mean birth weight of the patients was 932.5 ± 779 (600–1350) g. The mean gestational age of the patients was 25.7 ± 4.91 (23–29) weeks. The patients died an average of 2 ± 1.4 (1–4) days after the procedure.

Amongst the 47 patients, 21 (44.6%) died, and 26 (55.4%) survived. The relationship between mortality according to birth weights and GIP aetiology is given in Table 3. There were significant differences in the gestational ages and the birth weights concerning mortality rate.

Discussion

As the technological and medical infrastructures of NICUs develop, the number of premature and LBW patients who are treated is increasing day by day.[1,2,13] Secondary to this increase, the incidence of respiratory, neurological and GI system-related diseases frequently encountered in this patient group is also increasing. GIPs are a serious complication of digestive system diseases, and their mortality is quite high.[14]

The causes of GIP can be roughly divided into two groups: NEC and non-NEC pathologies. The two most common causes of pneumoperitoneum have been described in the literature as NEC and SIP.[15,16] Although NEC is usually seen in the terminal ileum, it is a progressing disease that can affect all intestinal segments, resulting in full-thickness necrosis of the intestinal wall. On the other hand, SIP is characterised by isolated bowel perforation, especially in low birth weight newborns, and it was reported in about 1%–2% of low birth weight newborns.[17-19] In this study, 74.3% of the patients' diagnoses were NEC and SIP. GIP can also be caused by many diseases, such as bowel atresia, Hirschsprung disease, gastric perforation, midgut volvulus, mesenteric ischaemia, meconium ileus, incarcerated inguinal hernia and complicated meconium peritonitis.[14,16,20,21] This wide range of diagnoses shows that the aetiology of GIP can originate from any part of the GI tract, from the stomach to the rectum. About 17% of the study group had GIP due to pathologies, except for the NEC and SIP. Since only an intraperitoneal drain was placed in four patients and the location and aetiology of the perforation could not be diagnosed, they could not be grouped. Since levelling biopsies are not routinely taken for ganglion investigation, except for the bowel resection materials sent from the patients, a definitive interpretation of the rate of Hirschsprung's disease cannot be made in this series. This may cause a difference in the diagnosis percentages of the aetiology of GIP compared to the literature.

The incidence of SIP and NEC is expected to increase as the birth weight and week decrease in the newborn.[22] The fact that one newborn with a diagnosis of NEC and two newborns with a diagnosis of SIP had a term birth week that indicates the week of birth is not the only effective factor in the pathogenesis. However, detecting SIP in 42% of patients with ELBW in the study is consistent with the literature.[18,19] In aetiology, apart from prematurity, LBW and high-osmolality nutrition, another reason accused is the use of drugs such as indomethacin, ibuprofen and steroids.[23-25] The lack of knowledge of drug use histories in this retrospective study is one of the limitations of the study.

Although there is no clear consensus in the literature on the effect of bowel perforation sites on mortality, publications suggest that colon perforation has higher mortality.[15,26] In this series, the mortality of patients with colon perforation was 54.5% (6/11), jejunoileal perforations was 38% (8/21) and multiple perforations (small bowel and colorectal) was 100% (3/3). Mortality was found to be higher in colon perforation in accordance with the literature.

The incidence of gastric perforations, especially in very LBW infants treated in the NICU, has been reported as 0.4%–0.5%, and mortality rates between 21% and 30%.[25,27,28] In the aetiology, it is argued that it may be due to stress ulcers and iatrogenic development, especially during nasogastric or orogastric insertion in low birth weight infants.[16,28] The reason for the 8.5% gastric perforation rate detected in the study, which is a very high rate compared to the literature, is unknown. The absence of mortality can be explained by the fact that the patients' gestational weeks and birth weights are higher than the literature. However, the limitation of the study is the need for more information about whether gastric perforations are iatrogenic or secondary to an underlying pathology.

The most appropriate treatment for GIP still needs to be clarified. Many factors, such as the patient's general condition, gestational age, weight, cause of perforation, length and localisation of the affected bowel segment, guide the planned treatment. The general approach is to remove necrotic areas from the body and to ensure the continuity of the GI passage. In the literature, it is still controversial which treatment method will be applied according to the general condition of the patient after primary anastomosis after resection of the perforated necrotic segment, stoma opening before the perforated bowel segment or application of a peritoneal drain.[4,29-31]

The newborn's immune system is immature.[7,10] Especially considering that the majority of those with GIP are premature and low birth weight newborns, we should eliminate intraabdominal stool and bile contamination as quickly as possible in these patients, and the main target is to ensure that they might be fed as soon as possible. In the study, one of the intestinal diversion methods was used in 36 (92.3%) of 39 patients, except those with gastric perforation and peritoneal drainage catheters. None of the patients developed complications secondary to the surgical technique. Although there are publications in the literature advocating that primary anastomosis can be performed in GIP independent of the patient's birth week and weight, we thought that delayed anastomosis function in a contaminated abdomen, delayed enteral feeding of the patient or complications that may develop may impose additional major morbidity on the patient. For this reason, we primarily preferred one of the temporary intestinal diversion methods.

Peritoneal drainage is recommended to reduce mortality in patients with poor general conditions and unsuitable for laparotomy.[14,32-34] In this study, temporary peritoneal drainage catheters were placed in 11 patients as a bedside procedure first. After recovering the general condition, seven of them were taken to laparotomy. Four of them died before laparotomy could be done. Of the seven patients who underwent laparotomy, three were discharged without any problem. Mortality was quite high in patients who underwent peritoneal drainage, but it should not be forgotten that the general condition of these patients before the procedure was very poor. Therefore, temporary peritoneal drainage may be life-saving in the selected patient group.

Conclusion

GIPs are one of the most significant causes of mortality in newborns. In this study, the most common cause of perforations was non-NEC entities, seen in the entire intestinal system from the stomach to the colon. Although the placement of a temporary peritoneal drainage catheter can be a time-saver in patients with poor general condition, laparotomy is still the primary procedure since the extent of the affected bowel segment in the abdomen is unknown.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient (s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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