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OBSERVATIONAL STUDY

# Neonatal gastric perforation: A single center experience

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### Abstract

**AIM:** To determine the etiology and prognostic factors for neonatal gastric perforation (NGP), a rare but life-threatening disease.

**METHODS:** Between 1980 and 2011, nine patients underwent surgical intervention for NGP at Seoul National University Children's Hospital. The characteristics and prognosis of the patients were retrospectively analyzed.

**RESULTS:** Among the nine patients, three (33.3%) were preterm babies and five (55.5%) had associated anomalies, which included diaphragmatic eventration (n = 2), congenital diaphragmatic hernia, esophageal atresia with tracheoesophageal fistula, and antral web. Three (33.3%) patients were born before 1990 and three (33.3%) had a birth weight < 2500 g. Pneumoperitoneum was found on preoperative images in six (66.7%) patients. Surgery was performed within 24 h after the onset of symptoms in seven (77.8%) patients. The overall mortality rate was 22.2% (2/9). The time between symptoms and surgical intervention was the only prognostic factor for survival, whereas premature birth and birth weight were not.

**CONCLUSION:** Early detection and advances in neonatal intensive care may improve the prognosis of NGP.

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**Key words:** Neonate; Gastric perforation; Etiology; Prognosis; Surgical intervention

**Core tip:** Neonatal gastric perforation (NGP) is an extremely rare condition and very few cases have been reported to date. We determined the etiology and prognostic factors for NGP in nine cases who were treated at a single center. Early detection and prompt surgical intervention are essential to improve the outcomes of NGP.

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### INTRODUCTION

Neonatal gastric perforation (NGP) accounts for approximately 7% of all gastrointestinal perforations in neonates, and has a poor prognosis with a high mortality rate<sup>[1,2]</sup>. Factors associated with NGP include prematurity, asphyxia, congenital anomalies, stress at birth, vigorous respiratory resuscitative measures, increased intragastric pressure caused by distal obstruction, and anatomic abnormalities of the stomach<sup>[3-7]</sup>. Male gender, metabolic acidosis, premature birth, and low birth weight are associated with worse outcomes<sup>[8,9]</sup>. However, the etiology and prognostic factors of NGP are still widely debated. Here, we describe our experience of treating nine patients with NGP at a single center. The aim of this study was to review patients with NGP and discuss its etiology and



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| Table 1      Patient characteristics |        |               |                  |           |        |          |                   |                                   |       |         |
|--------------------------------------|--------|---------------|------------------|-----------|--------|----------|-------------------|-----------------------------------|-------|---------|
| Patient                              | Gender | Date of birth | GA (wk)          | Term      | BW (g) | Delivery | Symptom onset (d) | Time from symptoms to surgery (d) | pН    | NG tube |
| А                                    | F      | 1983-02-24    | 40+2             | Full term | 3500   | Natural  | 5                 | 1                                 | N.D.  | Yes     |
| В                                    | F      | 1987-07-09    | 40               | Full term | 2950   | Natural  | 2                 | 2                                 | 7.13  | Yes     |
| С                                    | М      | 1990-09-05    | 35               | Preterm   | 2190   | Natural  | 2                 | 2                                 | 7.03  | Yes     |
| D                                    | М      | 1993-06-03    | 38+4             | Full term | 2950   | C-sec    | 4                 | 0                                 | 7.19  | No      |
| Е                                    | М      | 1999-05-13    | 36+3             | Full term | 2860   | Natural  | 2                 | 0                                 | 7.43  | No      |
| F                                    | F      | 2003-05-10    | 32+6             | Preterm   | 1960   | C-sec    | 2                 | 0                                 | N.D.  | Yes     |
| G                                    | М      | 2009-02-03    | 38               | Full term | 3620   | Natural  | 0                 | 1                                 | 7.086 | Yes     |
| Н                                    | М      | 2011-08-03    | 24               | Preterm   | 730    | Natural  | 4                 | 1                                 | 7.058 | Yes     |
| Ι                                    | F      | 2011-12-27    | 39 <sup>+3</sup> | Full term | 4040   | Natural  | 2                 | 0                                 | 7.391 | Yes     |

GA: Gestational age; BW: Birth weight; F: Female; M: Male; NG: Nasogastric; C-sec: Cesarean section.

#### Table 2 Preoperative conditions

| Initial symptom                | Diet | Ventilator | O <sub>2</sub> therapy | Pneumoperitoneum on X-ray | Associated anomaly        | Maternal problem |
|--------------------------------|------|------------|------------------------|---------------------------|---------------------------|------------------|
| High fever, vomiting, dyspnea  | Yes  | Yes        | Yes                    | No                        | Diaphragmatic eventration | None             |
| Vomiting dyspnea               | Yes  | Yes        | Yes                    | No                        | Diaphragmatic eventration | None             |
| Hematemesis                    | Yes  | No         | Yes                    | No                        |                           | PROM             |
| Abd. dist, vomiting, fever     | Yes  | No         | No                     | Yes                       |                           | None             |
| Abd. dist                      | Yes  | No         | No                     | Yes                       |                           | None             |
| Abd. dist                      | No   | No         | No                     | Yes                       | TEF                       | None             |
| Abd. dist                      | No   | Yes        | Yes                    | Yes                       | CDH                       | None             |
| Metabolic acidosis, abd. dist, | No   | Yes        | Yes                    | Yes                       | Antral web                | PROM             |
| Abd. dist                      | Yes  | No         | No                     | Yes                       |                           | None             |

PROM: Premature rupture of membranes.

prognosis, in order to improve patient outcomes.

### MATERIALS AND METHODS

#### Data collection

Between 1983 and 2011, nine neonates (five males and four females) who underwent surgical treatment for NGP at a single center were identified using written and electronic medical records.

#### Variables

We focused on preoperative and intraoperative characteristics that are known or thought to be prognostic factors for NGP. The characteristics retrieved from medical records included gender, year of birth, gestational age, birth weight, method of delivery, maternal gestational problems, maternal age at delivery, Apgar score, initial symptoms, time from birth to initial symptoms after birth, time between symptom onset and surgery, serum pH, serum pCO<sub>2</sub>, use of a nasogastric tube, ventilator therapy, O<sub>2</sub> therapy, diagnostic method, associated anomalies, site of perforation, length of perforation, type of surgical procedure, and postoperative complications.

#### Statistical analysis

Statistical analyses were performed using SPSS 19.0 software for Windows (IBM Inc., Armonk, NY, United States). Descriptive data are reported as percentage of patients or as mean (range). The  $\chi^2$  test was used to identify possible prognostic factors.

### RESULTS

The clinical features of the nine patients are described in Table 1. There were five boys and four girls; three were born before 1990 and six after 1991. The mean gestational age was  $38^{+0}$  wk (range,  $24^{+0}-40^{+2}$  wk) and the mean birth weight was 2950 g (range, 730-4040 g). Three patients were preterm and six were full term. Two patients had a low birth weight (LBW; < 2500 g) and one had an extremely LBW (ELBW; < 1000 g). Seven were born *via* natural delivery and two *via* cesarean section. Two patients were born after premature rupture of the membranes, of whom one was a twin. The mean maternal age at delivery was 32 years (range, 25-32 years). In one patient, Apgar score was 1 and 4 at 1 and 5 min, respectively. In another patient, Apgar score was 2 and 7 at 1 and 5 min, respectively.

Preoperative conditions are described in Table 2. Preoperative serum pH was < 7.30 in five patients and > 7.30in two patients, and was not determined in the other two patients. A nasogastric tube was used preoperatively in seven patients. Six were on a specialist diet, four were on ventilators, and six received supplemental O<sub>2</sub>.

All nine patients presented with mild to severe abdominal distension. Patient A initially presented with high fever, vomiting, and dyspnea. Congenital diaphragmatic hernia was initially suspected, but the final diagnosis was diaphragmatic eventration. Gastric perforation was found during surgery. Patient B initially presented with vomiting and dyspnea. Abdominal exploration was performed because of suspected congenital diaphragmatic hernia,



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| Table 3 Intraoperative and postoperative outcomes |                    |                     |             |     |               |                   |          |  |
|---|--------------------|---------------------|-------------|-----|---------------|-------------------|----------|--|
| Patient   | Surgical procedure | Perforated site     | Length (cm) | NEC | Complications | Hospital stay (d) | Survival |  |
| А   | RA                 | Body, LC, PW        | 4           | Yes | Wound problem | 18                | Alive    |  |
| В   | RA                 | Body, PW            | 2.5         | No  | Sepsis        | 4                 | Deceased |  |
| С   | Primary repair     | Whole, GC           | 10          | Yes | Sepsis        | 46                | Deceased |  |
| D   | Primary repair     | Whole, GC           | 10          | No  |               | 11                | Alive    |  |
| Е   | RA                 | Body, GC            | 5           | Yes |               | 28                | Alive    |  |
| F   | Primary repair     | LC                  | 3           | No  |               | 40                | Alive    |  |
| G   | Primary repair     | Body, GC            | 1           | No  |               | 24                | Alive    |  |
| Н   | Primary repair     | (1) LC (2) body, AW | 5           | No  |               | 131               | Alive    |  |
| Ι   | Primary repair     | Antrum, AW          | 0.5         | No  | Wound problem | 11                | Alive    |  |

NEC: Necrotizing enterocolitis; RA: Resection and anastomosis; LC: Lesser curvature; PW: Posterior wall; GC: Greater curvature; AW: Anterior wall.

which was ultimately diagnosed as diaphragmatic eventration. Gastric perforation was also found intraoperatively. Patient C initially presented with dyspnea and was intubated at birth. At 3 d of age, the patient exhibited hematemesis and severe abdominal distension. Paracentesis revealed bloody ascites, and explorative surgery was performed 2 d after the onset of symptoms. All of the patients, except for Patients B and C, underwent surgery within 24 h of the onset of symptoms. The mean age of symptom onset was 3 d (range, 0-5 d). Five patients had associated anomalies, which included diaphragmatic eventration, congenital diaphragmatic hernia, esophageal atresia with a tracheoesophageal fistula, and antral web.

The intraoperative and postoperative findings are summarized in Table 3. The mean size of the perforation was 4.5 cm (0.5-10 cm). The body (n = 5, 55.5%) of the stomach was the most common site of perforation. The perforation was located in the greater curvature in four patients and in the lesser curvature in three patients. Primary repair was performed in six patients, while resection and anastomosis were performed in three patients (55.6%), which included wound problems in two patients and recurrence in one patient. The other four patients were discharged without any complications.

Patient H, who had recurrence, was male and was born at a gestational age of 24 wk with a birth weight of 730 g. He presented with pneumoperitoneum on infantogram and underwent surgery at 5 d old. A 5 cm long laceration on the lesser curvature and pyloric thickening were found during explorative surgery. Therefore, primary repair was done. However, the postoperative infantogram and sonogram revealed an increase in free air. Small bowel series suggested obstruction of the gastric outlet. Three days after initial surgery, the patient underwent a second operation that revealed another perforation of the upper body of the anterior wall and prepyloric antral web. Primary repair and Heineke-Mikulicz pyloroplasty were performed, and an ileostomy was formed because of enteritis of the entire small bowel. Ileostomy repair was done 3 mo after surgery.

The overall mortality rate was 22.2% (2/9). Patient B was born at a gestational age of 40 wk and the birth weight was 2950 g. The patient was diagnosed with Bo-

chdalek hernia at another hospital and was transferred to our institute for surgery. On surgical exploration, the anterolateral portion of the diaphragm was eventrated, and a 2.5 cm long laceration was found in the posterior wall of the stomach. Diaphragm repair and primary suturing of the stomach were done. The patient died 5 d after surgery because of septic shock. Patient C was born at a gestational age of 35 wk and with a birth weight of 2190 g. Hematemesis and hematochezia were found at 3 d of age. The patient received conservative therapies, including transfusion for 24 h. Diagnostic paracentesis performed at 4 d of age revealed bloody ascites. Explorative laparotomy was done to evaluate the patient's hemoperitoneum and gastrointestinal bleeding. On exploration, a 10 cm long laceration with a necrotic margin was found on the greater curvature of the stomach, and primary repair was performed. Fifteen days later, the patient suffered from abrupt onset of abdominal distension and vomiting, and an erythematous discoloration was found on the left flank. Necrotizing enterocolitis was suspected based on infantogram, and the patient underwent surgery to repair multiple small bowel perforations. Gross fecal spillage into the abdominal cavity and multiple perforations of the small bowel were found, and approximately 20 cm of the ileum was resected. Despite intensive postoperative care, the patient's septic condition, hepatic dysfunction, and renal dysfunction resulted in death 29 d after the second surgery.

When we performed analyses to identify factors associated with survival, the time between symptoms and surgical intervention was the only prognostic factor for survival (P < 0.05) (Table 4). However, factors that appeared to show some association with survival included the presence of pneumoperitoneum on preoperative imaging (P = 0.083) and the year of birth (P = 0.083). Prematurity and birth weight were not associated with survival (P = 1.000 for both).

### DISCUSSION

Since Herbut first suggested that the congenital absence of muscular structures of the stomach may result in perforation<sup>[10]</sup>, multiple theories have been proposed to describe the etiology of NGP. High gastric acid produc-

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| Table 4 Prognostic factor analysis |                    |                    |                 |  |  |  |  |  |
|------------------------------------|--------------------|--------------------|-----------------|--|--|--|--|--|
|                                    | Survival $(n = 7)$ | Deceased $(n = 2)$ | <b>P</b> -value |  |  |  |  |  |
| Male                               | 4                  | 1                  | 1.000           |  |  |  |  |  |
| Birth before 1990                  | 1                  | 2                  | 0.083           |  |  |  |  |  |
| Birth before 2000                  | 3                  | 2                  | 0.444           |  |  |  |  |  |
| Preterm                            | 2                  | 1                  | 1.000           |  |  |  |  |  |
| BW < 2500 g                        | 2                  | 1                  | 1.000           |  |  |  |  |  |
| pH < 7.30                          | 3                  | 2                  | 1.000           |  |  |  |  |  |
| NG tube                            | 5                  | 2                  | 1.000           |  |  |  |  |  |
| Diet                               | 4                  | 2                  | 0.500           |  |  |  |  |  |
| Ventilator                         | 3                  | 1                  | 1.000           |  |  |  |  |  |
| O2 therapy                         | 3                  | 2                  | 0.464           |  |  |  |  |  |
| Pneumoperitoneum                   | 6                  | 0                  | 0.083           |  |  |  |  |  |
| Associated anomaly                 | 5                  | 1                  | 1.000           |  |  |  |  |  |
| Time from symptom                  | 0                  | 2                  | < 0.001         |  |  |  |  |  |
| onset to surgery > 24 h            |                    |                    |                 |  |  |  |  |  |
| Length > 2 cm                      | 5                  | 2                  | 1.000           |  |  |  |  |  |
| Primary repair                     | 5                  | 1                  | 1.000           |  |  |  |  |  |
| NEC                                | 2                  | 1                  | 1.000           |  |  |  |  |  |

BW: Body weight; NG: Nasogastric; NEC: Necrotizing enterocolitis.

tion and stress ulceration<sup>[11]</sup>, abdominal trauma<sup>[12]</sup>, ischemia of the stomach wall due to asphyxia<sup>[13]</sup> or vascular shunting<sup>[14]</sup>, lack of intestinal pacemaker cells<sup>[15]</sup>, and lack of C-KIT mast cells<sup>[16]</sup> have all been proposed as possible causes of NGP. NGP was historically thought to occur spontaneously<sup>[10,17-19]</sup> without any association with distal obstruction or other gastrointestinal conditions. However, since Shaw *et al*<sup>[20]</sup> reported perforation of the stomach after tying both ends of the stomach and insufflating it with air, mechanical pneumatic rupture has been proposed as a possible etiologic factor<sup>[6,7,14]</sup>. Gryboski<sup>[21]</sup> investigated the mechanism involved in neonatal swallowing, and reported that esophageal peristalsis was not coordinated until 3 d after birth. Jones et al<sup>[22]</sup> suggested that neonatal immaturity of the vomiting mechanism made it possible to increase the intragastric pressure to its limit.

Irrespective of the etiology, NGP mostly occurs between 2 and 7 d of age<sup>[23]</sup>. Indeed, all of the patients in the present series presented with symptoms by 7 d of age. Some authors have noted that premature birth is a common finding in patients with NGP<sup>[24,25]</sup>. In our study, 33.3% (3/9) of patients were preterm, which is higher than the normal rate. O2 supplementation and hypoxic stress were also reported as etiologic factors for NGP<sup>[26]</sup>, and 55.6% (5/9) received supplemental O2 in our study and the initial symptom was dyspnea in 22.2% (2/9). None of the patients in our series had trauma, but intragastric acidity was not assessed. Leone et al<sup>6</sup> suggested that NGP is not spontaneous and most patients have accompanying anomalies, including tracheoesophageal fistula or duodenal strictures, which may lead to intestinal obstruction and increased intragastric pressure. In fact, 55.6% (5/9) of patients in our series had an associated anomaly and one patient with NGP and accompanying antral web experienced disease recurrence. This finding supports the theory that distal obstruction is a common cause of NGP. Thus, in patients with suspected NGP, the consultant should consider the likelihood of accompanying disorders, especially disorders that may increase intragastric pressure. Although the greater curvature is thought to be the most common site of perforation<sup>[6,20]</sup>, the distribution of perforation sites was fairly even.

Factors predicting the survival of NGP have not been extensively examined. Lin *et al*<sup>p</sup> reported that the mortality rate was significantly higher in premature infants and in those with a low birth weight. Chung et  $al^{[8]}$  reported that male gender and metabolic acidosis (pH < 7.3) were associated with poor prognosis. In the present patients, prematurity was not associated with survival; of three premature patients, only one died (because of septic shock) and the  $\chi^2$  test yielded a *P*-value of 1.000. Likewise, low birth weight was not associated with survival. There were two LBW and one ELBW patients, and only one LBW patient died. Furthermore, male gender was not associated with survival. There were five boys and four girls, and gender was not associated with survival. Five patients had preoperative metabolic acidosis, of whom two died because of postoperative septic shock. In both of these patients, the preoperative serum pH was < 7.30, but the association between preoperative pH and survival was not significant.

The time between symptoms and surgical intervention was the only prognostic factor for survival, with a P-value of < 0.05. However, because the study group was small, involving just nine patients, there is the possibility of type II error. We considered the *P*-value as a factor of relativity and extended its interpretation criteria. Even though several other factors were not statistically significant, they may be clinically relevant in terms of survival outcomes. The factor with the lowest *P*-value was the year of birth. Of note, two of three patients born before 1990 died. There is a great difference between the clinical and mechanical environments of the neonatal intensive care unit in the 1980s compared with those today. It is likely that clinical and technical developments in pre- and postoperative intensive care have improved the survival outcome of NGP patients. Another factor with a low P-value was preoperative pneumoperitoneum on plain X-ray. Notably, two of three patients who did not undergo preoperative infantography died. Had intestinal perforation been detected or suspected based on preoperative radiographs, earlier intervention may have been possible, increasing the likelihood of survival. Interestingly, all three patients who did not undergo infantography were treated before 1990. Thus, the lack of a diagnostic protocol and diagnostic tools probably contributed to the poor prognosis before 1990 in particular.

Limitations of our paper are that it was performed retrospectively and the number of patients was too small to achieve statistical significance. However, NGP is extremely rare and very few cases have been reported to date. Therefore, our findings should help clinicians and surgeons with their decisions.

In conclusion, early detection and prompt surgical intervention are essential to improve the outcomes of infants with NGP. The survival outcomes of preterm



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infants or LBW infants were not inferior to those of other patients. NGP can accompany other significant anomalies. Therefore, careful examination of the patient, together with imaging studies, may lead to early detection and improve the outcomes of NGP.

### COMMENTS

### Background

Neonatal gastric perforation (NGP) is a very rare but life-threatening disease. **Research frontiers** 

Because of its rarity, the etiology and prognostic factors of NGP are debated. *Innovations and breakthroughs* 

The time between symptoms and surgical intervention was the only prognostic factor for survival; premature birth and birth weight were not associated with the survival of patients with NGP.

#### Applications

Early detection and advances in neonatal intensive care may improve the prognosis of NGP.

### Terminology

NGP: Neonatal gastric perforation; LBW: Low birth weight; ELBW: Extremely low birth weight.

#### Peer review

This is an important case series to publish as it deals with a rare but important neonatal emergent disorder. The abstract, introduction, methods and results are all well written.

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