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Neonatal Gastric Perforation: Report of 15 Cases and Review of the Literature

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Background: Gastric perforation among neonates is a rare but frequently fatal condition of uncertain etiology. The aim of this study was to review the clinical course of neonatal gastric perforation and to evaluate possible prognostic factors.
Methods: We retrospectively analyzed the medical records of 15 patients with neonatal gastric perforation over a 19-year period. Another 97 patients described in the medical literature, for whom the gestational ages and birth weights were clearly stated, were also reviewed.
Results: In our series, there were three girls and 12 boys, nine of whom were full-term infants and six preterm infants. The most common initial manifestations were poor activity, abdominal distension, and respiratory distress. The overall mortality was 47% (7/15). Prematurity was the only statistically significant risk factor; 83% (5/6) of premature infants died compared with 22% (2/9) of term babies ($p<0.05$). Combining our series with the patients reported in the literature, there were a total of 50 premature infants and 62 term infants. Gastric perforation occurred on postnatal days 2–7 and presented with nonspecific manifestations. The mortality was significantly higher in premature than in term infants (31/50, 62% *vs.* 16/62, 26%; $p<0.001$). A trend towards higher mortality in infants with lower birth weights was observed (>2500 g, 28%; 1501–2500 g, 52%; 1000–1500 g, 60%; <1000 g, 100%). Infants with birth weights <2500 g had a significantly higher mortality than infants with birth weights >2500 g (32/58, 55% *vs.* 15/54, 28%; $p<0.05$).
Conclusion: Neonatal gastric perforation is associated with high mortality, particularly in premature infants. There is also a trend towards higher mortality in lower-birth-weight infants.

1. Introduction

Neonatal gastric perforation is a rare but life-threatening condition. It often occurs without any apparent precipitating event, after which patients deteriorate rapidly. Siebold first reported a case of neonatal spontaneous gastric perforation in 1825.[1] The first successful surgical repair was reported by

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Leger et al in 1950,[2] and several subsequent reports of successful repair have since been reported and improved survival rates have been documented.[3,4] Many theories have been proposed for the pathogenesis of gastric perforation, but the etiology is still unknown. Male gender, hyponatremia (serum sodium <130 mEq/L) and metabolic acidosis (pH< 7.3) have been suggested to be poor prognostic factors for survival.[5] Here, we present 15 patients with neonatal gastric perforation treated in our hospital, and review another 97 cases reported in the literature, with the aim of clarifying the prognostic factors and so improving the outcome.

2. Methods

Fifteen neonates with gastric perforation were admitted to Mackay Memorial Hospital from January 1984 to December 2002, and their records were retrospectively analyzed. Gastric perforation was diagnosed at operation. The data reviewed included birth weight, gestational age at birth, mode of delivery, age at presentation, clinical manifestations, initial laboratory studies, pathologic findings and outcome. Using MEDLINE, we also identified papers published from 1965 to the present, and earlier published papers that were cited as references in these. Another 97 patients for whom the gestational ages and birth weights were documented were reviewed from these papers. Statistical analysis was performed using Chi-squared and Fisher's exact tests. A p value of less than 0.05 was considered to be statistically significant.

3. Results

Fourteen of the 15 babies treated in our hospital were not born in the hospital, but were referred to our hospital for further management because of worsening of their clinical conditions. The clinical data are summarized in Table 1. There were three girls and 12 boys, nine of whom were full-term infants and six preterm infants. Of the latter, one was born at 32 weeks, two at 35 weeks, and three at 36 weeks of gestation. The average birth weight was 2982 g (range, 2100–3600 g). The prenatal courses were all uneventful except for two mothers, one of whom had poorly controlled pregnancy-induced hypertension and the other had a low-grade fever and diarrhea 1 day before delivery. The delivery in all cases was uneventful. All patients had Apgar scores >8 at 1 and 5 minutes.

No positive pressure ventilation was required for the preterm babies. Patient 7 had congenital heart disease with a single atrium and ventricle. However,

Table 1 Clinical data from 15 neonates with gastric perforation

	Case														
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Sex	M	M	M	F	M	M	M	M	M	F	M	M	M	F	M
Gestational age (wk)	T	T	T	T	T	T	T	36	T	35	36	35	36	T	32
Birth weight (g)	3600	3500	3400	3250	3000	3000	2900	2780	3600	3300	3200	2600	2520	2100	2000
Age at perforation (d)	4	3	3	5	3	4	3	2	4	2	7	3	4	4	2
Maternal complications†	–	–	–	–	–	–	–	–	–	HT	–	–	Fv	–	–
Associated disorders‡	–	DE	–	–	–	–	CHD	–	–	–	MMIHS	–	–	–	–
WBC count (/mm^3)	4800	10,100	2900	2900	2800	5600	12,200	13,700	1900	910	16,500	2050	4790	3600	2700
pH	7.29	7.33	7.33	7.25	7.26	7.131	NA	7.56	7.17	7.06	7.38	7.27	7.31	6.97	7.1
Sodium (mEq/L)	137	147	135	147	137	133	133	138	143	143	143	148	144	136	135
Bacteremia	×	×	K	×	×	×	K	×	E	×	×	E+K	×	E	×
Operation	G	P	P	P	G	P	P	P	G	P	P	P	P	S	B
Outcome	S	S	S	S	S	S	S	S	D	D	D	D	D	D	D

M = male; F = female; T = term; – = none; HT = hypertension; Fv = maternal fever; DE = diaphragmatic eventration; CHD = congenital heart disease (single atrium and single ventricle); MMIHS = megacystis-microcolon-intestinal hypoperistalsis syndrome; WBC = white blood cell; NA = not available; × = no growth; K = *Klebsiella pneumonia*; E = *Escherichia coli*; G = partial gastrectomy and primary repair; P = primary repair; S = primary repair and splenectomy; B = primary repair and partial bowel resection; S = survived; D = died.

Table 2 Initial manifestations in 15 neonates with gastric perforation

	n (%)
Poor activity	15 (100)
Abdominal distension	14 (93)
Respiratory distress	8 (53)
Cyanosis	6 (40)
Fever	4 (27)
Vomiting	3 (20)
Bloody stool	2 (13)

he had no apparent respiratory symptoms or cyanosis before the onset of gastric perforation. Patient 2 had left diaphragmatic eventration, noted incidentally during the repair of the gastric perforation, during which diaphragm plication was performed. A cystic lesion in the abdomen had been identified by prenatal ultrasound in patient 11. After birth, he had mild abdominal distension that improved after decompression by a nasogastric tube. On the seventh day of life, he developed significant abdominal distension, and gastric perforation was found at surgery. He was finally found to have an association of megacystis-microcolon-intestinal hypoperistalsis syndrome. With the exception of this infant, all the others tolerated oral feeding well and had an uneventful course prior to the onset of gastric perforation, which occurred from 2–7 days after birth. The most common presenting manifestations of the perforation included the abrupt onset of abdominal distension, poor activity, and respiratory distress (Table 2).

Massive pneumoperitoneum was a consistent radiographic finding, leading to a preoperative diagnosis of perforated hollow viscus. Eight patients had perforations in the greater curvature of the stomach, five in the anterior wall, and two in the posterior wall. Simple primary repair was performed in 10 patients, partial gastrectomy in three, splenectomy in one who had splenic necrosis, and resection of 10 cm of gangrenous bowel in one.

Metabolic acidosis was a common feature of gastric perforation. The arterial blood pH ranged from 6.97 to 7.56, with a median of 7.26. Five patients had marked metabolic acidosis with a pH $<$ 7.20 and four of them died, although pH was not statistically associated with death (Table 3). Leukopenia was also common; the median blood white cell count was 3600/mm^3. The overall mortality in our series was 47% (7/15). It was significantly higher for premature babies than term infants (5/6, 83% *vs.* 2/9, 22%; $p<0.05$). Prematurity was the only factor in our series that was significantly associated with death (Table 3).

Table 3 Prognostic factors in 15 neonates with gastric perforation*

	Nonsurvival (n=7)	Survival (n=8)	$p^\dagger$
Male	5	7	0.5
Low birth weight	2	0	0.2
Prematurity	5	1	0.03
Cesarean section	3	3	0.76
Outborn	6	8	0.46
Sodium $<$ 130 mEq/L	0	0	1
pH $<$ 7.30	5 of 7	4 of 7	0.5
pH $<$ 7.25	4 of 7	1 of 7	0.13
WBC $<$ 5000/mm^3	6	4	0.18
Sepsis	3	2	0.42

*Data are presented as *n*; †Fisher's exact test, one-tailed. WBC = white cell count.

3.1. Previously reported series

We found 10 published reports involving a total of 97 patients for whom gestational ages and birth weights were clearly documented.[3,5–12] Combining these 97 with our 15 cases gave a total of 112 cases of neonatal gastric perforation. Among these patients, there were 43 females and 69 males. Fifty patients were delivered before 37 weeks and 62 at term. The mortality among premature infants was 62% (31/50) and among term infants 26% (16/62) ($p<0.001$; Table 4). Mortality was inversely associated with birth weight: for infants $>$2500 g, it was 28%; 1501–2500 g, 52%; 1000–1500 g, 60%; and $<$1000 g, 100% (Table 5). More than one-half of the patients with neonatal gastric perforation (58/112) were low-birth-weight (LBW; $<$2500 g) neonates. The mortality among LBW neonates was higher than that among those with a birth weight $>$2500 g (32/58, 55% *vs.* 15/54, 28%; $p<0.05$).

4. Discussion

We found that the mortality of infants with gastric perforation was higher among premature and LBW neonates than in full-term babies. Only 6–14% of all infants are LBW,[13] but they accounted for 52% of all patients with gastric perforation in the 112 cases we reviewed. There is possibly a higher incidence of gastric perforation in LBW neonates than in term neonates. Death was also more likely to occur in LBW than in normal-weight neonates (55% *vs.* 28%; $p<0.05$), and in premature rather than in full-term neonates (62% *vs.* 26%; $p<0.001$). Although mortality was inversely associated with birth weight, there was no particular predilection for gastric perforation in extremely-low-birth-weight neonates (birth

Table 4 Mortality in premature and term infants with gastric perforation ($n=112$)

Authors	Premature infant, *n*		Term infant, *n*		Total
	Died	Total	Died	Total	
Amadeo et al[6]	2	2	1	1	3
Wilson[1]	1	1	1	1	2
Shashikumar et al[7]	4	5	4	14	19
Jones et al[8]	3	4	0	0	4
Houck and Griffin[9]	0	1	0	2	3
Holgersen[10]	7	16	2	12	28
Hwang et al[11]	0	1	0	2	3
Rosser et al[12]	3	6	1	10	16
Chung et al[5]	3	4	4	8	12
Leone and Krasna[3]	3	4	1	3	7
Present series	5	6	2	9	15
Total	31	50	16	62	112
Mortality (%)*	62		26		42

*$p<0.001$ by Fisher's exact test, comparing premature with term neonates.

Table 5 Mortality in neonates with gastric perforation by birth weight ($n=112$)*

Authors	Birth weight <1000 g		Birth weight 1000–1500 g		Birth weight 1501–2500 g		Birth weight >2500 g		Total
	Died	Total	Died	Total	Died	Total	Died	Total	
Amadeo et al[6]	0	0	0	0	3	3	0	0	3
Wilson[1]	0	0	0	0	2	2	0	0	2
Shashikumar et al[7]	0	0	0	1	6	11	2	7	19
Jones et al[8]	0	0	2	3	1	1	0	0	4
Houck and Griffin[9]	0	0	0	0	0	1	0	2	3
Holgersen[10]	0	0	4	5	3	11	2	12	28
Hwang et al[11]	0	0	0	1	0	0	0	2	3
Rosser et al[12]	0	0	0	0	3	8	1	8	16
Chung et al[5]	0	0	0	0	2	3	5	9	12
Leone and Krasna[3]	2	2	0	0	2	4	0	1	7
Present series	0	0	0	0	2	2	5	13	15
Total	2	2	6	10	24	46	15	54	112
Mortality (%)†	100		60		52		28		42
	←		55		→				

*Data are presented as *n*. †$p<0.05$ by Fisher's exact test, comparing low-birth-weight neonates (birth weight <2500 g) with those with a birth weight >2500 g (32/58, 55% *vs.* 15/54, 28%).

weight <1000 g), who account for around 2% of the general population,[13] and a similar percentage of the 112 patients with gastric perforation (2/112, 2%). This is unlike the situation with necrotizing enterocolitis, which is more common among extremely-low-birth-weight neonates.

There were two LBW neonates with gastric perforation in the present study, both of whom died. LBW was not a significant prognostic factor in the present study, but it was statistically significant in the analysis of the total 112 cases. This apparent discrepancy is likely due to the fact that the number of cases in the present study was small, and was not sufficient to show a statistical difference.

The etiology of neonatal gastric perforation is still unclear. Several possibilities have been discussed, including congenital defects of the gastric muscle wall,[6,14] mechanical disruption[10] stress ulceration secondary to neurogenic disorders,[4] and ischemia of the gastric wall secondary to vascular shunting.[15]

In 1943, Herbut[14] reported a case of gastric perforation with a demonstrable congenital defect of

the musculature of the stomach wall. Histologically, the wall had a complete, abrupt termination of the musculature with an intact serosa. Shaw et al[16] conducted experiments in which they mechanically induced pneumatic perforation of the stomach in animals. When the perforations were examined microscopically, the musculature was lacking in the perforated areas. They suggested, however, that this may have resulted from retraction of the muscle after perforation rather than being a true congenital defect. The greater curvature was the usual site of perforation in these experiments, which was also the most common site in our patients.

Anatomic defects of the gastric muscular wall have been suggested to potentiate perforation of the stomach among neonates, especially in prematurity. The circular muscle layer of the newborn stomach normally contains several gaps, most prominently in the fundus, near the greater curvature. These gaps are more common in premature infants.[11] Under normal circumstances, such gaps may have little clinical significance, but they are potential weak points in the stomach wall that might be susceptible to rupture if intragastric pressure increases.

Gryboski[17] investigated swallowing in neonates and found that peristalsis in the esophagus was uncoordinated until the third day of life. Normal gastric motility does not occur until the third month of life. Increased intragastric pressure may, therefore, result from the lack of coordination and the immaturity of the vomiting mechanism.[8] Some authors have suggested that sudden gastric distension may result in angulation at the hiatus, causing some degree of proximal gastric obstruction, thus predisposing to perforation.[17]

The peak incidence of gastric perforation is reported to be from the second to the seventh day of life,[18–20] similar to that observed in our series. Miller[21] found that gastric acidity in the newborn child was equal to that of an adult and was maximal at 24 hours of age. The acidity decreased over the following 9 days, by which point it approached the normal level for a child.[21] Thus, the gastric acidity is exceptionally high during the first week of life, which is the period in which the incidence of gastric perforation peaks. While this temporal association does not prove causality, it is possible that high gastric acidity in the early newborn period contributes to gastric perforation.

The timing of initiation and amount of enteral feeding may influence the intragastric load and pressure. Necrotizing enterocolitis occurs more frequently in premature infants whose enteral intake is being aggressively increased. Because of a variety of disorders commonly associated with prematurity, the initiation and advancement of enteral feeding among these infants is usually conservative and minimal or even delayed for a few days. Because intravenous fluids can be given as needed to assure adequate hydration, the amount of enteral feeding can be adjusted according to the digestive condition, in which case the gastric load during the first week of life would be relatively low. In neonates with respiratory distress, gastric lavage is often used to decompress the stomach to relieve pressure on the lungs, again a factor that may reduce intragastric pressure. Acutely ill neonates are generally managed in intensive care units and are carefully monitored, so it is less likely that they would have substantial elevations of intragastric pressure. Our patients, however, as well as those reported by Chung et al,[5] appeared normal at birth and were fed normally from the beginning, with normal stools produced during the first few days of life. This observation of perforation occurring in normally-fed infants appears to support the hypothesis that gastric load may contribute to perforation.

Anatomic immaturity and impaired motility are characteristic of premature neonates but may also be present in term infants, especially within the first 7 days of life. While some of these factors may be an underlying cause of neonatal gastric perforation, it is surprising that extremely-low-birth-weight neonates are apparently not at significantly increased risk of gastric perforation. However, these neonates tend to have a higher gastric pH[22] and are usually cared for in an intensive care unit, where the monitoring is intense, feeding is delayed and gastric distension is decompressed.

Metabolic acidosis ($pH < 7.30$) has been proposed as a poor prognostic factor,[5] although we were unable to demonstrate this in our small series. The two patients with more complicated problems (splenic and intestinal necrosis) died. It is possible that delayed surgery is associated with a poorer prognosis.

While the pathogenesis of gastric perforation remains obscure, it seems likely that enteral load may be a significant factor. However, because enteral nutrition is still the optimal physiological nutrition for neonates, it is not reasonable to use intravenous fluids for support and delay feeding neonates, regardless of gestational age.

In summary, the mortality associated with neonatal gastric perforation is high, particularly in premature, LBW neonates. Mortality is inversely related to birth weight. It is hoped that early diagnosis and early intervention may improve the prognosis.

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