

CLINICAL SCIENCE

Evolution of critically ill patients with gastroschisis from three tertiary centers

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OBJECTIVES AND INTRODUCTION: Gastroschisis is a congenital abdominal wall defect with increasing occurrence worldwide over the past 20–30 years. Our aim was to analyze the morbidity of newborns after gastroschisis closure, with emphasis on metabolic and hydroelectrolyte disturbances in patients at three tertiary university centers.

METHODS: From January 2003 to June 2009, the following patient data were collected retrospectively: (A) *Background maternal and neonatal data:* maternal age, prenatal diagnosis, type of delivery, Apgar scores, birth weight, gestational age and sex; (B) *Surgical modalities:* primary or staged closure; and (C) *Hospital course:* levels of serum sodium and levels of serum albumin in the two first postoperative days, number of ventilation days, other postoperative variables and survival. Statistical analyses were used to examine the associations between some variables.

RESULTS: 163 newborns were included in the study. Primary closure of the abdominal defect was performed in 111 cases (68.1%). The mean serum sodium level was 127.4 ± 6.7 mEq/L, and the mean serum albumin level was 2.35 ± 0.5 g/dL. Among the correlations between variables, it was verified that hyponatremia and hypoalbuminemia correlated with the number of days on the ventilator but not with the number of days on total parenteral nutrition (TPN); mortality rate correlated with infection. The final survival rate was 85.9%.

CONCLUSION: In newborns with gastroschisis, more aggressive attention to hyponatremia and hypoalbuminemia would improve the outcome.

KEYWORDS: Gastroschisis; Gastroschisis repair; Preterm; Morbidities; Neonates; Body wall defects.

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INTRODUCTION

Gastroschisis is a congenital defect of the abdominal wall, and its cause is unknown.¹ A trend towards increasing occurrence of gastroschisis has been reported worldwide over the past 20–30 years.^{2–4}

Despite a reported survival rate typically above 90% for neonates with gastroschisis,⁵ there is a large subset of infants with significant short- and long-term morbidities, generally associated with prolonged gastrointestinal dysfunction, sepsis and prolonged hospital stay.⁶ Although extensive investigations have been performed, there is still no consensus on the risk factors for morbidities.

Surgical management of gastroschisis consists basically in safely reducing the evisceration and closing the defect in one or two stages, depending on the viscero-abdominal disproportion.⁷ However, there is always a variable amount of abdominal tension after closure.

Abdominal tension, associated with the serositis of the previously exposed bowel, may be responsible for some early postoperative complications, such as oliguria, anasarca, metabolic and hydroelectrolyte disturbances. There are no reports in the literature concerning these complications, their possible causes or consequences for the prognosis.

Our aim was to analyze the morbidity of a large series of newborns with gastroschisis, with emphasis on metabolic and hydroelectrolyte disturbances. The final aim was to evaluate whether there is any association between these metabolic disturbances and the time period during which the newborn is submitted to mechanical ventilation and the time on total parenteral feeding.

MATERIALS AND METHODS

This study was carried out at three tertiary university centers of pediatric surgery that routinely perform neonatal surgery in the state of São Paulo, Brazil: the School of Medicine – University of São Paulo (FM-USP), the School of Medical Sciences – State University of Campinas (FCM-UNICAMP) and the School of Medicine of Ribeirão Preto – University of São Paulo, (FMRP-USP). The study protocol was approved by the ethics committee at each of the three institutions.

From January 2003 to June 2009, patient data were retrospectively collected and analyzed from medical records at these institutions. Medical records were collected for all the newborns with gastroschisis who were born at the three institutions. All the patients were followed from birth until hospital discharge.

The following data were analyzed: (A) *Background maternal and neonatal data*: maternal age, prenatal diagnosis, type of delivery, Apgar scores, birth weight, gestational age measured by the Capurro method and sex; (B) *Surgical modalities*: primary or staged closure (silo was used only when primary closure was considered unsafe); and (C) *Hospital course*: serum sodium and serum albumin levels in the first two postoperative days, number of ventilation days, time to initiation of enteral feeding, time to full enteral feeding, length of parenteral nutrition (TPN), length of hospital stay, complications (infection/sepsis, oliguria/anuria, defined as urinary output <1 mL/kg/h and no diuresis respectively), necrotizing enterocolitis and survival.

Hyponatremia was defined as sodium serum levels <135 mEq/L and hypoalbuminemia as albumin serum levels <3 g/dL. No patient was receiving loop diuretics in the study period. The diagnosis of infection was based on the presence of clinical signs and confirmed by leukocyte counts. No severity score was used.

Statistical analyses

The results were expressed as mean \pm standard deviation (SD). Linear regression analyses were used to examine the associations between total number of days on the ventilator, TPN days, serum albumin level and sodium level. Comparisons between unpaired groups with respect to continuous variables that were normally distributed were performed with the Student's t-test; if variables were not normally distributed, the Mann-Whitney test was performed. The chi-square method was used to compare groups of infected and non-infected patients as to the incidences of deaths. The level of significance was $p \leq 0.05$.

RESULTS

A total of 163 newborns were included in the study. Diagnosis of fetal gastroschisis was made by prenatal ultrasound in 134 (82.2%) cases. The mean maternal age was 20.1 ± 4.5 years. Birth was via cesarean delivery in 138 cases (84.7%) and via vaginal delivery in the rest. Median Apgar scores at 1 and 5 min were 7 and 9 respectively. The average birth weight was 2.2 ± 2.1 kg, and the average gestational age at birth was 36.1 ± 0.17 weeks. Among the newborns, 89 (54.6%) were female and 74 (45.4%) were male. There were 22 (13.5%) complex cases, associated with intestinal atresias or perforations.

Table 1 - Variables studied in the newborns with gastroschisis.

Variable	Mean \pm SD (median)
No. of days on ventilator	4.9 ± 7.6 (4.0)
No. of days to the first enteral feeding	24.7 ± 19.1 (18.0)
No. of days to full enteral feedings	37.6 ± 39.5 (14.0)
No. of days on TPN	33.2 ± 29.3 (26.0)
No. of days in hospital	41.2 ± 35.7 (31.0)

TPN, total parenteral nutrition.

Table 2 - Statistical correlations between the variables.

Correlated variables	p value
Natremia variation \times no. of days on ventilator	0.03
Albuminemia variation \times no. of days on ventilator	0.01
Natremia variation \times no. of days on TPN	0.07
Albuminemia variation \times no. of days on TPN	0.82
Infection \times mortality	0.005

TPN, total parenteral nutrition.

Primary closure of the abdominal defect was performed in 111 cases (68.1%). The mean serum sodium level was 127.4 ± 6.7 mEq/L and the mean serum albumin level was 2.35 ± 0.5 g/dL. The number of ventilation days, time to first and full enteral feeds, number of days on TPN and hospital stay are shown in Table 1.

The correlated variables and the values of p are presented in Table 2. There was a strong correlation between number of days on the ventilator and lower levels of serum sodium and albumin, as demonstrated in linear regression graphics (Figures 1 and 2). However, natremia and albuminemia variation did not influence the number of days on TPN (Table 2).

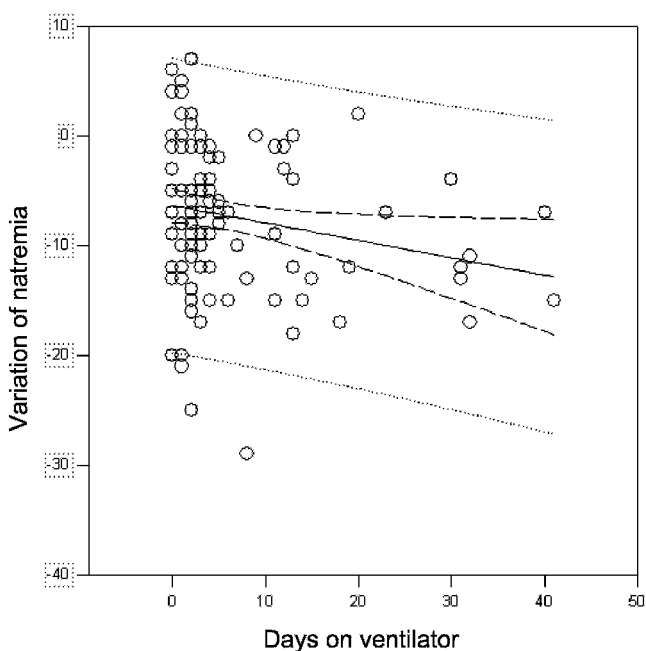


Figure 1 - Linear regression of variation in natremia and days on the ventilator ($r = -0.2108$).

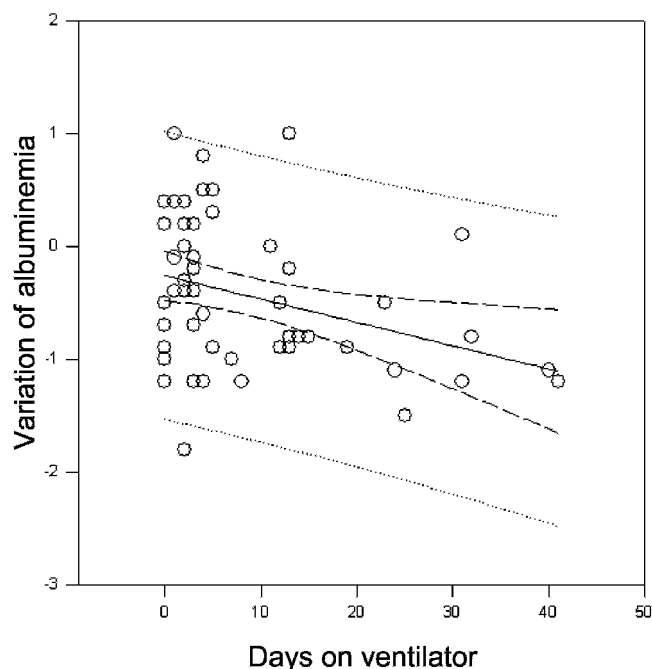


Figure 2 - Linear regression of variation in albuminemia and days on the ventilator ($r = -0.1246$).

We observed oligoanuria in 33 (20.2%) newborns, in association with hyponatremia ($p = 0.05$). All were managed with administration of colloids and loop diuretics. There was no need for urgent opening of the abdominal wall to release abdominal compartment syndrome in any case.

The incidence of infection in our series was 40.5% (66 patients). However, the mortality rate was related to infection ($p = 0.005$). Finally, necrotizing enterocolitis occurred in 5 cases (3.0%).

Overall, 140 patients survived (85.9%). Causes of death are summarized in Table 3.

DISCUSSION

Although gastroschisis is a congenital anomaly with a high and increasing frequency, its management is still a challenge for neonatologists and pediatric surgeons, because of considerable morbidity and prolonged hospital stay.⁸

This is the largest series of gastroschisis described in our country, from three tertiary referral centers covering a large geographical area of the State of São Paulo (Brazil), home to approximately 30 million inhabitants. Improved prenatal diagnosis (82.2%) and selective referral may have contributed to the number of cases. Our results are in agreement with other published series in which fetal gastroschisis occurred mostly in young mothers.¹ The high percentage of

cesarean deliveries reflects the marked preference for this kind of delivery in our country.

The average low birth weight and borderline prematurity, which are in agreement with the literature,¹ emphasize the probable link between gastroschisis and growth retardation. Carroll et al. demonstrated that fetuses with gastroschisis have lower serum protein concentrations and higher amniotic fluid total protein than do cases of exomphalos or control subjects, reflecting malabsorption or loss of protein from the exposed viscera, which can lead to growth retardation.⁹

The results of our study demonstrate that, in fact, newborns operated on for gastroschisis repair have hyponatremia and hypoalbuminemia, and these alterations in critically postoperative patients may result from several factors such as fluid retention, oliguria and fluid administration. In addition, experimental investigations from our laboratory¹⁰ and others have demonstrated that fetuses with iatrogenic gastroschisis are smaller compared with control subjects, have lower serum sodium and chloride levels, have reduced uptake of amino acids and glucose and reduced expression of genes involved in nutrient absorption within the enterocyte.^{11,12}

There is continuing controversy as to how the herniated bowel should be managed.⁸ Our approach has been primary closure within 6 h of delivery whenever possible. Silo placement is chosen only if viscerio-abdominal disproportion impedes the safe reduction of eviscerated intestines. There is some evidence indicating no difference between the two forms of surgical treatment in terms of days to first and full feeds and hospitalization,⁷ although some authors observed a reduction in days on the ventilator when silo was used.¹³⁻¹⁵ In a previous report, we proved that mortality rate is not correlated with the type of abdominal closure.¹⁶

The low levels of serum sodium and albumin may be associated with exudative losses from the serosal surface of previously exposed bowel.⁹ Furthermore, an increased intraabdominal pressure caused by the closure of a wall defect could lead to a decrease in renal perfusion and a tendency to oliguria and liquid retention. Kidney immaturity with impairment of the capacity for sodium retention exacerbates the problem in the context of premature birth.¹⁷

The most important result of this large series refers to the correlations between number of days on the ventilator and lower levels of serum sodium and albumin. In addition, on account of the large number of patients studied, we were able to demonstrate a correlation between mortality rate and infection ($p = 0.005$).

Lower levels of serum sodium and albumin should lead to reduced colloid osmotic pressure in the plasma, and consequent leak of liquid to the interstitium and anasarca. This phenomenon may involve the lungs and ventilatory mechanics, which are already impaired by the increased abdominal pressure. This chain of events could explain the increase in ventilation time seen in newborns with hyponatremia and hypoalbuminemia. Eventual fluid repositions with crystalloids in an attempt to increase kidney perfusion and diuresis could even worsen this problem.

The other important result of this series was that hyponatremia and hypoalbuminemia did not influence intestinal function, as these alterations were not correlated with the number of days on TPN. In fact, the intestinal dysfunction and the need for long periods of parenteral nutritional support result from delay in the maturation of the enteric nervous plexus and not the presence of intestinal

Table 3 - Comorbidities of newborns with gastroschisis.

Causes of death	No. of patients (% of deaths)
Sepsis	16 (69.5)
Associated malformations	2 (8.6)
Respiratory distress	1 (4.3)
Intestinal perforation	1 (4.3)
Others	3 (13.0)

serositis.¹⁰ As a consequence, there is no benefit in performing preterm cesarean section in the treatment of patients with gastroschisis in an effort to reduce the incidence of serositis, as advocated by some authors.¹⁸

Compared with other large series^{1,19} we found a high percentage of infections (40.5%) and a relatively low incidence of necrotizing enterocolitis (3.0%). This may reflect a very careful approach to the initiation of infant feeding at our institutions. The mean time to first feed is reported to be between 14 and 21 days,^{1,20} whereas our result was 24.7 ± 19.1 days (Table 1). The prolonged fasting period with consequent impairment of intestinal immunity is associated with bacterial overgrowth and translocation, which could explain the high incidence of sepsis in our cases. On the other hand, the delayed introduction of an enteral diet should work as a "protection factor" against necrotizing enterocolitis.

Despite morbidity and prolonged hospital stays, our survival indexes were high, comparable to those from centers in developed countries.^{8,19}

In conclusion, our study shows that low serum levels of sodium and albumin observed in newborns operated upon for gastroschisis are significantly correlated with a greater period of time on the ventilator. It might be that more aggressive attention to these parameters would improve the outcome. In addition, these disturbances are not related to the time on parenteral nutrition.

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