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Gastroschisis Treatment: What are the Causes of High Morbidity and Mortality Rates?

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Rezumat

Tratamentul laparschizisului: care sunt cauzele morbidității și mortalității crescute?

Introducere: Laparoschizisul este unul dintre cele mai frecvent întâlnite defecte congenitale ale peretelui abdominal anterior, în ultimele decenii observându-se o creştere spectaculoasă a supraviețuirii copiilor cu o astfel de afecțiune. Studiul de față își propune a descoperi cauzele morbidității şi a mortalității perinatale crescute în cazul laparoschizisului în țara noastră.
Metode: Am efectuat un studiu retrospectiv pe 54 nou-născuți cu laparoschizis, datele pacienților fiind prelucrate statistic şi analizându-se caracteristicile demografice, diagnosticul antenatal, prezența anomaliilor asociate, metoda de tratament chirurgical, complicațiile post-operatorii, numărul de zile de spitalizare şi rata supraviețuirii.
Rezultate: Majoritatea datelor demografice precum şi rata asocierilor malformative ale pacienților analizați sunt în perfectă concordanță cu datele din literatura de specialitate, mai puțin rata diagnosticului antenatal (16,7% vs 68-88%), rapiditatea transportului (4,8 ore) şi a intervenției chirurgicale, şi cel mai grav, rata mare a infecțiilor (68,5%) şi implicit a mortalității (63% vs 6-7%).
Concluzii: Deşi conduita terapeutică adoptată în clinica noastră este conformă cu trendul internațional, totuşi rata mortalității este încă foarte mare, cauza principală a mortalității în cadrul lotului studiat demonstrându-se a fi sepsisul prelungit şi insuficiența multiplă de organ, favorizate probabil de rata scăzută a diagnosticului antenatal care duce la rândul ei la întârzierea tratamentului chirurgical adecvat.

Cuvinte cheie: laparoschizis, atrezii intestinale, închidere primară, durata spitalizării

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Abstract

Introduction: Gastroschisis is one of the most common birth defects of the anterior abdominal wall, in recent decades being witnessed a significant increase in the survival of children with such a condition. This study aims to discover the causes of the increased perinatal morbidity and mortality rates from gastroschisis in our country.
Methods: Retrospective study on 54 infants with gastroschisis. Patient data were statistically processed and the demographic characteristics, antenatal diagnosis, presence of associated anomalies, method of surgical treatment, postoperative complications, number of hospital stay days and survival rate were analysed.
Results: Most demographic data and associated malformation rate in the study patients are in agreement with the data in the literature, except for prenatal diagnosis rate (16.7% vs 68-88%), rapid hospital arrival and surgery (6.8 vs 4.3 hours), and the worst, the high rate of infections (68.5%) and hence mortality rate (63% vs. 6-7%).
Conclusions: Although the therapeutic approach in our clinic complies with the international trend, the mortality rate is still very high, its main cause in the study group proving to be prolonged sepsis and multiple organ failure, probably favored by

the low rate of antenatal diagnosis leading to delay in the appropriate surgical management.

Key words: gastroschisis, intestinal atresia, primary closure, hospital stay

Introduction

Omphalocele and gastroschisis are the most common birth defects of the anterior abdominal wall and it seems that their incidence is increasing worldwide (1). In recent decades, in civilized countries there was a dramatic increase in the survival of children with these conditions, from 10% in 1960 to about 90% in 1980-1990 (2), due to several factors. Unfortunately, in Romania the survival rate is still very low, at least in the region of Moldavia, accounted for by the lack of a consensus on treatment and a nationwide centralized database. In the literature there are still many controversies regarding optimal therapeutic approach of a newborn with omphalocele or gastroschisis, especially if complicated or very large. We conducted this study aimed at finding the causes and further reducing the high rate of perinatal morbidity and mortality associated with gastroschisis in our country.

Material and Methods

We conducted a retrospective study on 54 neonates with gastroschisis admitted to and treated in the Pediatric Surgery Clinic of the "Sfânta Maria" Emergency Children Hospital in the interval 2001-2010. Patient data extracted from case report forms were processed statistically, and the demographic data, prenatal diagnosis, presence of associated anomalies, surgical method, postoperative complications, number of hospital stay days, and survival rate were analysed. Data were processed using Microsoft Excel Data Analysis.

Patients came from seven Moldavian counties, being referred immediately after birth for specialized treatment in our clinic. Obstetric practice in our country is spontaneous vaginal delivery, cesarean delivery being used only in high-risk pregnancies. The most commonly performed routine newborn baby care procedures are suctioning, cord clamping, vitamin K injection, antibiotic prophylaxis, vaccination according to the schedule, and the herniated abdominal viscera are covered with sterile saline-soaked dressing. In the intensive care unit of our hospital the newborn undergoes rapid reassessment and the hemodynamic, cardiorespiratory, and thermal statuses are rebalanced. Then surgery is performed in all cases under general anesthesia. In the operating room eviscerated bowel loops are abundantly washed with disinfectants and saline solution and a careful inspection is made to detect any associated stenosis or atresia. Primary closure of the anterior abdominal wall defect was performed whenever possible, depending on the ease of returning the eviscerated intestinal loops to the peritoneal cavity, subjectively estimated by the surgeon, arterial oxygen saturation and the need for increased ventilation pressures, objectively assessed by the anesthetist.

Results

Demographic data

During the study interval 54 patients with gastroschisis were admitted to our clinic (*Table 1*). The male/female ratio was 1.07, mean gestational age at birth was 37 weeks, and mean birth weight 2409 grams (ranges 1480-3300 grams). Forty-one patients (75.9%). had normal vaginal delivery The average age of mothers was 20.4 ± 3.6 years, with 31.5% of them aged under 19 years; 53.7% were single mothers and 66.6% first time pregnant. Prenatal diagnosis of gastroschisis was known in only 9 cases (16.7%), 5 diagnosed in Iassy town. County distribution of newborns with gastroschisis enrolled in this study is shown in *Fig. 1*. Associated anomalies, the bowel ones excepted, were present in 16 patients (29.6%, the most common being heart defects (6 patients). Chromosomal abnormalities were found in only one patient, trisomy 21 respectively, with favorable outcome. The mean age of patients at the time of admission to our hospital was 4.8 hours, and

Table 1. *Characteristics of the gastroschisis patients*

Gender	28 M/26 F
Average age of the mother (years)	20.4 (13 – 31)
First pregnancy	66.6% (n = 36)
Prenatal diagnosis	16.7% (n = 9)
Natural delivery	75.9% (n = 41)
Average gestational age (weeks)	37 (30 – 41)
Average birth weight (grams)	2409 (1480 – 3300)
Associated anomalies	29.6% (n = 16)
Trisomy 21	n = 1
Heart anomalies	n = 6 (3 PCA, 2 CMH, 1 CoAo)
Intestinal pseudo-obstruction	n = 2
Congenital megacolon	n = 1
Congenital undescended testis	n = 2
Hydrocephalus	n = 1
Congenital hip dislocation	n = 1
Pielouretheral duplicity	n = 1
Hemangioma	n = 1
Intestinal anomalies	16.6% (n = 9)
Severe bowel involvement (necrosis, perforation)	n = 2
Intestinal atresia (ileal and/or colonic)	n = 6
Mean age at admission (hours)	4.8 (0.5 – 12)
Mean age at the time of surgery (hours)	6.8 (0.5 – 20)
Primary closure of the abdominal wall defect	81.5% (n = 44)
Fufezan procedure (umbilical cord patch)	n = 11
Gross procedure	n = 2
Closure through Schuster procedure	18.5% (n = 10)
Concomitant interventions (intestinal resections, anastomoses, interventions for atresias)	13% (n = 7)
Average time until total enteral nutrition (days)	26.8 (15 – 59)
Average hospital stay of survivors (days)	45.3 (16 – 140)
Simple gastroschisis (days)	36 (16 – 72)
Complex gastroschisis (days)	73.4 (38 – 140)
Mean age at death (days)	15.4 (1 - 63)
Survival rate	37%

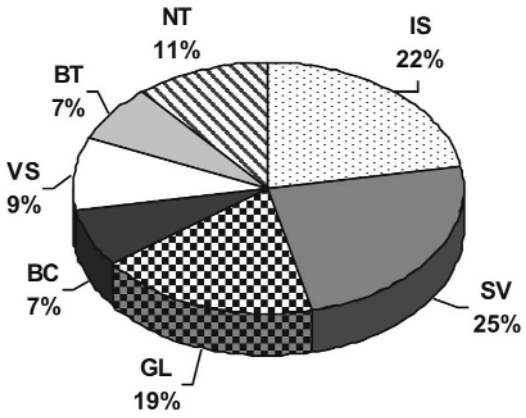


Figure 1. *Geographic distribution of the newborns with gastroschisis*



Figure 2. *Umbilical cord patch*

preoperative preparation in the newborn intensive care unit lasted on average 2 hours. Primary closure of the abdominal wall defect was possible in 31 cases, in 11 cases the gastroschisis was repaired using umbilical cord as a patch (*Fig. 2*), in 2 cases the defect was covered by skin (Gross method), in the remaining patients the Schuster procedure of gradual closure of the abdominal wall being used. In our clinic "silo bag" not being available, it was replaced with prolene mesh, sterile surgical gloves or plastic sterile collection bags. The average number of days until total enteral nutrition was 26.8, range 15- 59 days. The average hospital stay of surviving patients was 45.3 days, with the mention that in three patients hospital stay days for two successive admissions, required to solve the basic surgical disease, were considered.

Complications

Nine patients (16.6%) had associated intestinal abnormalities: severe ischemia and bowel necrosis (*Fig. 3*), ileal atresia, colonic atresia, and ileal atresia associated with colonic atresia were present in 2 cases each, the remaining case presenting persistence of the omphaloenteric duct for which resection and primary anastomosis were performed. In 7 of the 9 patients, concomitant with primary closure surgical interventions were performed: two absolutely necessary due to ileal necrosis and perforations, one resection and primary anastomosis for persistence of the omphaloenteric duct, the other four being resections, intestinal anastomoses, and enterostomies for intestinal atresias. Mortality rate in gastroschisis patients with associated intestinal abnormalities was 44.4%, and in patients with simple gastroschisis 66.6%. Thirteen patients (24%) had an unfavorable postoperative course, requiring one or more additional surgeries for intestinal occlusion, anastomotic disruption or loop perforation, evisceration (*Table 2*). In 10 of the 13 patients with surgical reinterventions, primary closure of the abdominal wall defect was attempted. Four patients who underwent bowel resection developed short bowel syndrome; only two of them survived without requiring intestinal transplantation. At one year of age both children with short bowel syndrome were underweight, one of them being also neurologicaly impaired. In only one of the six children with simple gastroschisis who developed abdominal compartment syndrome surgical reintervention was timely and the outcome favorable. None of the patients with complex gastroschisis developed

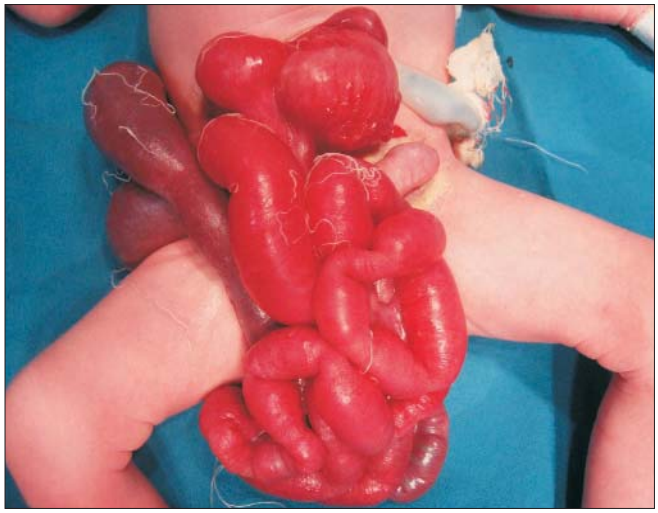


Figure 3. *Ileal ischemia*

Table 2. *Complications in the patients with gastroschisis (%)*

Postoperative complications	13 (24%)
Evisceration	10 (18.5%)
Intestinal occlusion requiring surgical reintervention	9 (16.6%)
Anastomotic disruption requiring surgical reintervention	5 (9.2%)
Surgical wound suppuration	4 (7.4%)
Abdominal compartment syndrome	6 (11.1%)
Short bowel syndrome	4 (7.4%)
Athrepsia	16 (29.6%)
Enterocolitis	22 (40.7%)
Sepsis	37 (68.5%)
Mortality	34 (63%)
Severe sepsis and multiple organ failure	27 (79.4%)
Bronchopneumonia with severe respiratory failure	3 (8.8%)
Ventricular hemorrhage, septic meningitis	3 (8.8%)
Ulceronecrotic enterocolitis	1 (3%)

abdominal compartment syndrome, mainly due to bowel resections. Many newborns developed sepsis, in 27 of the 37 such patients sepsis being the cause of death. Mortality rate in our study group was 63%, in almost 80% the cause of death being severe sepsis and multiple organ failure. Thirty-four patients had positive cultures, the most common isolated germs being Candida spp, Klebsiella pneumoniae, Escherichia coli, Pseudomonas aeruginosa (*Fig. 4*). On average, death occurred on the 15th day of life (range 1-63 days). At one year of age, four of the 20 survivors were underweight, three children were suffering from repeated subocclusions, and two were neurologicaly impaired.

Discussions

Most features in the study gastroschisis patients are in agreement with the data in the literature. The slight male predominance was demonstrated by Blakelock in 1997, with a maximum of 1.68 found by Torfs in 1994 (3,4). In our study, the average age of gastroschisis children' mothers was 20.4 ± 3.6 years, similar to that in a study conducted in 2000 by Suita who found a mean age of 20.6 ± 4.9 years (5), most authors stating that maternal age under 20 is an associated risk factor for gastroschisis (6). The average gestational age at birth of 37 weeks (versus 259 days, 37 weeks, respectively), average birth weight of 2409 grams (versus 2490 grams), frequency of joint malformation, 75.9% vaginal births (versus 74%), and even the treatment modalities, use of the Schuster method in 18.5% of the cases (versus 19%) are similar to a Dutch study conducted in 2007 by Jager (7), but prenatal diagnosis rate (16.7% versus 68%), rapid hospital arrival and surgery (6.8 versus 4.3 hours), and worst of all, the high infection rate, and therefore death, are quite different. It is clear from many studies published in recent years that the mortality rate for congenital anomalies of the anterior abdominal wall has declined to 6-7% for gastroschisis, being closely related to the association of atresia and intestinal complications, but these good results are recorded in developed countries, where over 60% of the cases are prenatally diagnosed (69% for omphalocele and 88% for gastroschisis in Germany), allowing birth planning and optimal medical and surgical management (8). Over a period of 10 years in the entire Moldavia region a prenatal diagnosis of gastroschisis was made in only 9 cases (16.7%), and it seems that in the rest of the country the situation is the same (9). An explanation could be that mothers do not go to the doctor, come from disadvantaged backgrounds, are very young (one third of them aged under 19) and more than half unmarried. In most developing countries, mortality rates remain high, reaching 80% for gastroschisis (10).

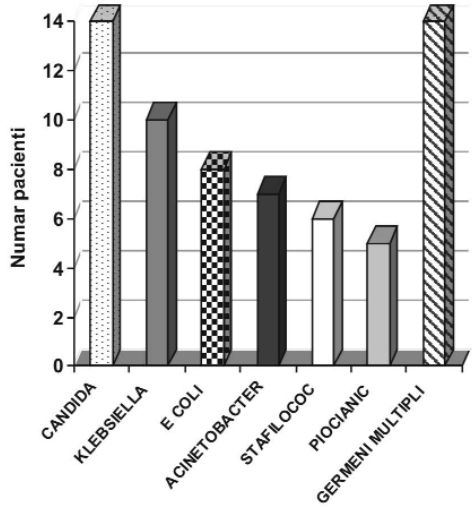


Figure 4. *Nosocomial infections*

In the literature, morbidity and mortality are even higher for complex gastroschisis, according to Molik's classification, associated with intestinal atresia, volvulus, intestinal perforation or necrosis due to intra-abdominal infections and sepsis, gastrointestinal bleeding, abdominal compartment syndrome, and respiratory distress (11). An interesting finding in our study was the higher mortality rate in the group of newborns with simple gastroschisis compared to those with complex gastroschisis, 66.6% versus 44.4%, respectively, one possible explanation being that for complex gastroschisis some degree of visceral reduction through intestinal resections was required for atresias or necrosis, this surgical gesture protecting against abdominal compartment syndrome, one major cause of death in patients with gastroschisis. However, the overall mortality rate was extremely high, 63%, almost 80% of the patients dying from severe sepsis and multiorgan failure. It is known that the most common complications in the management of anterior abdominal wall defects are infections, which can occur both locally and generally. Neonates with gastroschisis make up an increasing proportion of prolonged neonatal ICU admissions, on average 45.3 days in our study group.

Infectious complications are responsible for increased morbidity and mortality rates in these patients; however, they are not closely related with patient initial status or therapeutic method used. It seems that while demographic data, surgical management and postoperative complication rate in our study are similar to other studies (7), mortality rate was very high due to nosocomial infections, favored by the long distance ambulance transportation, thus prolonging the birth-to-surgery period (6.8 hours on average). A recent study on a series of 395 gastroschisis cases reported surgical wound infections in 12.6% and catheter infections in 14.9%, particularly due to a coagulase-negative staphylococci species. The authors have demonstrated the importance of early abdominal wall defect closure on the infectious complications rate: 21.2% in patients with late surgery versus 8.2% in patients in which the abdominal closure took place within 6 hours of birth (12). In 1976, in a series of 55 omphocele and gastroschisis cases treated by Schuster method, Rubin reported an infection rate of 60% with a mortality rate of 28%, especially due to Candida, closely related to how long the prosthetic material stayed in place, but also to the long-term central venous catheterization for parenteral nutrition (13). Based on the need for close monitoring of antibiotic treatment and proper assessment of patients with sepsis, procalcitonina as biological

marker appears to have significant value, being proposed for detection and evaluation of bacterial infection and antibiotic management (14). Many of these infections can be avoided by strictly observing the rules of perioperative asepsis and antisepsis and by systematic antibiotic therapy, initially broad-spectrum and subsequently targeted, under antifungal protection when antibiotics are administered for a long time.

Long term outcome of patients with gastroschisis is closely related to the presence of intestinal atresia, which is one of the most important prognostic factors of unfavorable progression. The presence of multiple intestinal atresia with proximal intestinal loop damage requiring extensive resection or loss of ileocecal valve may further predispose the patients to develop short bowel syndrome and malabsorption. Numerous authors recommend that resection and primary anastomosis be a delayed reoperation a few weeks later after primary closure. Although in our study in 4 of 6 patients with intestinal atresia resection, primary anastomosis or enterostomies were also performed per primam, the postoperative complications rate was similar to other reports in the literature. The most common complication was evisceration due to tension suture closure of the abdominal wall (18.5%). In our study group the frequency of abdominal compartment syndrome after primary closure of the abdominal wall was high; moreover, 5 of the 6 patients who developed this complication died. Primary closure-related complications can be minimized by objective perioperative measurement of intra-abdominal pressure. According to Olesevich, intra-operative measurement of bladder pressure improves primary closure safety, prevents intestinal ischemia, and these patients have a faster return to full feed and a significantly shorter hospital length of stay (15).

Obviously, length of hospital stay, as well as all other parameters commonly monitored in the management of anterior abdominal wall defects, depends on the type of gastroschisis: simple or complex. According to various authors, time and place of study, length of hospital stay ranges between 10 and 50 days for simple gastroschisis and about 162 days for complex gastroschisis, an overall mean of approximately 42 days (16). A recent study in the UK reported a mean length of hospital stay of 36 days for simple gastroschisis and 84 days for complex gastroschisis (17), similar to our data: 36 and 73.4 days, respectively.

Conclusions

Although the demographic data of our study patients are largely in line with those in the literature, and despite the fact that the therapeutic approach in our clinic complies with the international trend, the mortality rate from gastroschisis in still very high in Moldavia. The main cause of death in our patients was prolonged sepsis and multiple organ failure, probably favored by the low prenatal diagnosis rate, which in turn leads to delayed access to a specialized unit for adequate surgical treatment and further monitoring in a neonatal intensive care unit. More studies on congenital malformations are needed because they still are an important contributor to neonatal deaths in our country. We believe that by the publication of these studies in medical journals GPs will become aware of the importance of a closer follow-up of mothers, so that these women to be provided with documented information and referred to an obstetrician familiar with the role of prenatal diagnosis of some congenital malformations that are repairable immediately after birth (18) and to a neonatologist able to organize immediate and adequate transportation of the newborn to a pediatric surgery center.

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