

Isolated prenatal ultrasound findings predict the postnatal course in gastroschisis

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Abstract

Purpose The aim of the study was to identify which prenatal ultrasonographic findings in fetuses with gastroschisis correlate with complicated postnatal outcome.

Methods Ultrasound findings at the 30th week of pregnancy and medical reports were statistically analyzed to identify independent prenatal ultrasonographic predictors of postnatal outcome.

Results Completed prenatal data were gathered from 64 pregnancies. Prenatal intra-abdominal bowel dilatation (cutoff 10 mm) correlated with the presence of atresia ($p < 0.01$), longer administration of parenteral nutrition, extended hospital stay (median 53 vs. 21 days; 68 vs. 36 days, both $p < 0.05$), and greater number of additional surgical procedures ($p < 0.05$). Infants with antenatal presence of thickened bowel wall (greater than or equal to 3 mm) required longer administration of parenteral nutrition (median 34 vs. 20 days; $p < 0.01$) and prolonged stay (median 44 vs. 37 days; $p < 0.05$). Presence of oligohydramnion (amniotic fluid index below 8 cm) was

connected with longer administration of parenteral nutrition in newborns (median 30 vs. 16 days; $p < 0.05$).

Conclusion The isolated presence of oligohydramnion with amniotic fluid index below 8 cm, thickened bowel wall equal to or more than 3 mm and the prenatal intra-abdominal dilatation with 10 mm cutoff had significant predictive value for the adverse postnatal outcome of patients with gastroschisis.

Keywords Gastroschisis · Prenatal ultrasonographic findings · Intestinal atresia · Intra-abdominal dilatation · Oligohydramnion · Thickened bowel wall

Introduction

Gastroschisis, one of the most common prenatally diagnosed congenital malformations, is characterized by eventration of intestinal loops through the abdominal wall defect. The bowel wall is edematous, with inflammatory infiltration and covered with fibrin coatings. The total length of the intestines might be shortened; intestinal atresia is present in 10–15 % [1, 2]. The motility and absorption capacity of a prenatally affected intestine is postnatally reduced [3]. Restoration of full bowel function after birth is crucial for nutrition, development, immune response and defensive capacity of infants and prevention of life-threatening postnatal complications. The survival of neonates with gastroschisis is currently over 90 % [4].

Gastroschisis is not a lethal malformation; prenatal diagnosis has, therefore, focused on optimizing the management of pregnancies, preventing serious complications and reducing the overall stress in newborns with a congenital defect. Prenatal ultrasound findings suggest, in some fetuses with gastroschisis, that there is a

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significant damage to the intestine [5, 6], but objective parameters of ultrasound findings have not been established yet [3, 7].

It remains unclear whether ultrasound prenatal findings such as intra-abdominal bowel dilatation, thickened bowel wall, abdominal defect size or herniation of stomach could help us to predict the outcome of our patients and prevent some of the serious complications during their treatment [3]. The aim of the present study was to find relevant ultrasound markers that could predict the outcome in fetuses with gastroschisis.

Materials and methods

Medical records of consecutive 64 neonates with gastroschisis who were prenatally examined and postnatally treated in a single tertiary referral center from 2004 to 2013 were retrospectively reviewed. The predictive value of the prenatal ultrasonography findings and the presence of intestinal atresia on postnatal outcome were analyzed. The demographic data of the study group are shown in Table 1.

Prenatal management and delivery

All patients with prenatally diagnosed gastroschisis were sent to the reference center to confirm the diagnosis and determine the next prenatal course of action. Ultrasound evaluation of fetal growth, amniotic fluid amount and individual ultrasound markers associated with the gastroschisis in 30th week of gestation was mandatory, standardized and performed in all patients. In the 36th week of gestation (36+) all patients were preventively admitted to the hospital for labor induction using locally administered prostaglandins. The actual finding of congenital defect was not considered as an absolute indication for Cesarean section. Operative delivery was indicated, when obstetric indication was present, depending on the clinical condition of the mother and fetus and with respect to the mother's preference.

Prenatal ultrasonography study design

Completed prenatal data and ultrasound parameters assessed in the 30th week of gestation (30+) were gathered from 64 pregnancies. Examinations were carried out using the Toshiba Xario XT and Toshiba Aplio 500 ultrasound machines. All examinations were performed by one sonographer/specialist in fetomaternal medicine. In addition to the growth of the fetus and the amount of amniotic fluid, we measured the size of the defect in the abdominal wall (Fig. 1), the maximum level of intra-abdominal bowel dilatation, the wall thickness of everted bowel loops (Fig. 2), and the presence of colon eventration and stomach herniation. Abdominal wall defects were evaluated in transverse diameter at the level of insertion of the umbilical cord with cutoff value defined at 20 mm. The choice of such measurement plane allowed inter-examination reproducibility and evaluation regardless of current gestational age. A cutoff value of 20 mm was set by a statistician based on a distribution curve of defects measured in gestational week 30. The threshold value for the presence of dilatation of the intra-abdominal bowel loops was set to 10 mm, the width of wall thickness of extra-abdominal bowel loops was set to 3 mm. The amount of amniotic fluid was evaluated using the amniotic fluid index (AFI): oligohydramnion was defined with the AFI value below 8 cm, euhydramnion 8–18 cm, polyhydramnion over 18 cm [8]. All parameters were recorded and later independently compared with postnatal data.

Postnatal gastroschisis management protocol

All neonates with gastroschisis were admitted to the Neonatal Intensive Care Unit (NICU). One team of attending pediatric surgeons and neonatologists directed the management of all patients. The management protocol was identical for all neonates. A nasogastric tube was placed and antibiotic prophylaxis and parenteral fluids were given. Haemodynamic stability was monitored, in case of instability volume expansion and inotropic drugs were used. The patients underwent surgery within 6 h after admission

Table 1 Characteristics of the study population

Mean birth weight (g)	2,270 (range 1,110–3,790)
Gestational age at delivery (weeks)	35.9 (range 28.5–38.4)
Maternal age (years)	25 (range 15–38)
Cesarean section (<i>n</i>)	30
Mean no. of days to achievement of oral feeding 20 ml/kg/day (days)	19 (range 4–216)
Mean no. of days on parenteral nutrition (days)	26 (range 7–123)
Mean length of hospital stay (days)	41 (range 13–241)
Bacteremic episode (<i>n</i>)	23
Neonatal death (<i>n</i>)	3



Fig. 1 Measurement of the abdominal wall defect



Fig. 2 Measurement of the thickened bowel wall of extra-abdominal bowel loops >3 mm

and after preoperative stabilization, when the clinical condition had been optimized. Antibiotic prophylaxis was given before surgery and stopped 48 h after surgery. The repair of the abdominal wall defect was performed under general anesthesia in the operating theater. Primary closure was performed with an interrupted absorbable suture with attention to preserving the umbilicus. Gore-Tex silo (1 mm Dual Gore-Tex patch) was only used when primary closure was not possible, according to the attending surgeon, or when attempt of primary closure deteriorated cardiorespiratory function. Synchronized Intermittent Mechanical Ventilation (SIMV) mode, with pressure support was used during and after surgery in all patients. Weaning of ventilation started according to improving of patients' own respiratory effort. Total parenteral nutrition (TPN) was started within 24 h via a central venous catheter, parenteral nutrition discontinued after full enteral feeding was reached. Enteral feeding was introduced once postoperative ileus had been resolved. Neonates received mother's milk or bank milk continuously via nasogastric tube. Feeding was increased gradually according to tolerance and measurement of gastric residua.

Postnatal outcome study design

The records of 64 neonates were reviewed. Birth weight, gestational age at delivery, age of mothers, type of defect closure and number of surgeries, length of hospital stay, the beginning of minimal enteral feeding and achievement of full enteral nutrition were evaluated. The beginning of minimal enteral feeding was defined as 20 ml/kg/day tolerated for at least 24 h.

Data analysis

The correlation of prenatal ultrasonography parameters with the data of postnatal outcomes was analyzed. Continuous data are presented as the median (range). Discrete data are provided as number of cases and percentages. The outcome of infants with intestinal atresia was compared with the data of newborns without atresia. The data were analyzed using a statistical Student's t-test and the Mann-Whitney test where appropriate. *P* values of <0.05 were considered statistically significant. The study design was approved by the Ethical Committee of the 2nd Medical Faculty Charles University in Prague.

Results

64 patients with complete prenatal data were analyzed. Maternal age ranged from 15 to 38 years with a mean age of 25 years. The mean gestational age at delivery was 35.9 weeks with a mean weight of 2,270 g (1,110–3,790 g). 30 neonates were delivered via Cesarean section. The mode of delivery did not have any correlation with the manifestation of complications from gastroschisis. 43 pregnancies had associated oligohydramnion. The mean time from surgical closure to the achievement of minimal enteral feeding was 19 days. The mean duration of parenteral nutrition and the mean length of stay were 26 and 41 days, respectively. 23 patients had at least one bacteremic episode. The patient characteristics are presented in Table 1.

Prenatal findings

The prenatal intra-abdominal bowel dilatation was related to longer administration of parenteral nutrition, extended hospital stay (median 53 vs. 21 days; 68 vs. 36 days, both *p* < 0.05), and greater number of additional surgical procedures (*p* < 0.05). The intra-abdominal bowel dilatation correlated with the presence of atresia (*p* < 0.01), 5 of our 6 patients with atresia had prenatally diagnosed the intra-

abdominal dilatation. Sensitivity of intra-abdominal dilatation to predict atresia was 83 %, specificity was 93 %, positive predictive value was 50 %, negative predictive value 97 %. Infants with antenatal presence of thickened bowel wall (greater than or equal to 3 mm) required longer administration of parenteral nutrition (median 34 vs. 20 days; $p < 0.01$) and prolonged stay (median 44 vs. 37 days; $p < 0.05$). Presence of oligohydramnion (AFI below 8 cm) was connected with longer administration of parenteral nutrition in newborns (median 30 vs. 16 days; $p < 0.05$), whilst the length of stay did not differ significantly (44 vs. 31 days, $p > 0.05$).

The multivariate analysis of these three markers did not reveal any statistically significant correlations. However, colon eventration, stomach herniation, and the size of the defect of the abdominal wall measured at 30th week of pregnancy did not correlate with adverse outcome. Table 2 provides a summary of the measured prenatal ultrasound parameters.

Surgical treatment

Surgical treatment consisted of primary closure in 52 patients, the rest of the patients (12) were treated by Gore-Tex silo placement. 20 of patients passed through more than one operation (silo removal, intestinal obstruction, stoma closure, etc.). Ten patients underwent reoperation for various form of intestinal obstruction. Eight of these were reoperated for prolonged disorder of intestinal motility and intolerance of enteral feeding of duration more than 4 weeks after delivery. Peroperatively, we found adhesions or the sharp bend of the bowel. One patient who developed NEC was reoperated later for two small-intestinal strictures that were the cause of the ileus. One patient with unrecognized atresia at the time of primary closure was operated on 14 days later for the ileus. An overview of surgical treatment is depicted in Table 3.

Table 2 Prenatal ultrasound findings at the 30th week of gestation

	N	% ^a
Colon eventration	42	66
Oligohydramnion	43	67
Intra-abdominal bowel dilatation ≥ 10 mm	10	16
Thickened bowel wall ≥ 3 mm	20	31
Herniation of stomach	5	8
Wall defect >20 mm	29	45

N number of patients with ultrasound finding

^a Result is expressed as a percentage of the total number of patients

Intestinal atresia

There were six atresias in study group. Five of them were revealed at the birth or during the first operation. Temporary ileostomy was performed in four cases and the stoma was closed after 4–12 weeks. Anastomosis of the bowel and primary closure of the abdominal defect was performed in one patient. The only patient with unrecognized atresia at the time of primary closure was operated on 14 days later for ileus. Jejunostomy was performed and the stoma was closed after 7 weeks. Neonates who had postnatally diagnosed intestinal atresia were compared with neonates without atresia detected. A significant difference in adverse neonatal outcome in the group of patients with atresia was found. Both the median length of TPN (74 days) and the length of hospitalization (86 days) for patients with atresia were prolonged compared to the neonates without atresia (22 days and 36 days) with the p -values $p < 0.05$ and $p < 0.01$.

The mean number of days to first feeding was clearly higher in the group with atresia (59 vs. 16 days, $p < 0.05$). The comparison of outcomes for patients with and without intestinal atresia is summarized in Table 4.

Outcome

Four patients developed NEC during hospitalization. All of them were cured conservatively in acute phase. One of them required surgery later for ileus caused by two strictures on the small intestine. Three patients from the study developed short bowel syndrome and they were discharged home on parenteral nutrition. Long-term follow-up of presented gastroschisis patients shows that they are well-integrated into their children's collectives.

Neonatal deaths

Three neonatal deaths occurred in our study population (mortality 5 %). One girl died of MODS on the 5th day after surgery. Another patient died after multiple laparotomies and fulminant sepsis on the 76th day of hospitalization. The third neonate died on the 4th day after primary suture due to pericardial tamponade as a complication of a central venous catheter malposition. The analysis did not reveal any correlation of the deaths with prenatal ultrasonographic findings.

Discussion

Damage to the intestinal wall in each neonate with gastroschisis varies from a minimum swelling of the intestinal wall, over solid convolute of intestinal loops and

Table 3 Surgical treatment of GS

	<i>N</i>	% ^a
Primary closure	52	81
Silo	12	19
Multiple surgery	20	31
Intestinal atresia	6	9

Multiple surgery = number of patients who passed through more than one operation (silo removal, intestinal obstruction, stoma closure, etc.)

N number of patients

^a Result is expressed as a percentage of the total number of patients

mesentery, to intestinal atresia in the advanced stages of the disease [1, 9]. In our study, we were looking for prenatal ultrasound parameters suggestive of intestinal atresia and severe intestinal damage in terms of postnatal function, which may predispose the development of future postoperative complications [9–11].

Our data have shown that the presence of each isolated ultrasound finding such as presence of intra-abdominal bowel dilatation with more than 10 mm, thickened bowel wall of extra-abdominal herniated bowel loops equal to or more than 3 mm and oligohydramnion with AFI below 8 cm predict a worse outcome. All examinations were performed by one sonographer/specialist in fetomaternal medicine in the 30th week of gestation; predefined parameters were recorded at the same time and later independently compared with postnatal data. Our study design seems to be superior to data obtained from retrospective analysis of USG records or photographs [6]. In contrast to a multicentre study, the result of single center study is not flawed by case selection bias and different therapeutic approaches. One team of attending neonatologists, obstetricians and pediatric surgeons directed the management of all patients in our study, and all patients with prenatal data were included into statistical analysis. Regrettably, we were not able to collect representative series of pathological findings from other gestational weeks and the absence of serial ultrasound information is the main weakness of our limited single center study.

A standard quantitative method of ultrasound assessment of the intestinal damage in gastroschisis has not been established yet and the gestational age at examination,

ultrasound parameters, cutoff value and published results seem to vary among different authors [5–7, 9, 11–14]. Both intra-abdominal [9, 12, 14, 15] and extra-abdominal bowel dilatation [6, 11] have been evaluated as prognostic factors in recent literature. Cutoff values of extra-abdominal bowel dilatation are arbitrarily set within a limited series of individual authors [6, 11]. However, cutoff value of intra-abdominal dilatation can be derived from the reference size of the fetal intestine in normal pregnancy [16, 17] and thus seems to be a more objective parameter. The diameter of the lumen of the small bowel and colon increases with gestational age. Nevertheless, the fetal small bowel lumen rarely exceeds 6 mm in diameter, and the fetal colon lumen diameter rarely exceeds 23 mm [16, 17]. Thus, the presence of intra-abdominal dilatation could be the most promising ultrasound parameter predicting intestinal atresia and the adverse postnatal course [9, 12, 14, 15].

The results of our study could be compared with the study by Ghionzioli et al. [5]. They published a retrospective study of 130 neonates with gastroschisis and intestinal atresia was found in 14 (11 %) of them. We had 64 patients and 6 intestinal atresias were found (9 %). We are in agreement with Ghionzioli’s declaration that infants from his group with atresia had longer duration of parenteral nutrition compared with infants with no atresia; the presence of atresia did not increase the mortality of the group. As we had already concluded, intra-abdominal dilatation is a strong predictor for the presence of intestinal atresia and so is the predictor for a worse postnatal outcome. This statement is supported by the results of the study by Nick et al. [14], in which they suggested that intra-abdominal bowel dilatation in the second trimester predicts neonatal bowel atresia in fetuses with gastroschisis. Ten of the 58 fetuses had intra-abdominal bowel dilatation and all had bowel atresia at birth. The number of patients with intestinal atresia in our retrospective study is limited, yet, we can report that the associated morbidity in this subgroup is substantial: 36 days of hospitalization for patients without atresia, 86 days for those who had intestinal atresia. Our results are consistent with the study reported by Nick et al.: Neonates with small bowel atresia spent a median of 84.0 days in hospital compared with 26.5 days for those without atresia [14]. Even in the study by Huh et al. [12], the presence of intra-abdominal

Table 4 Comparison of patients with and without atresia

	Atresia absent	Atresia present	<i>p</i> value
Mean no. of days to achievement of minimal enteral feeding (20 ml/kg/day)	16	59	<i>p</i> < 0.05
Mean no. of days on parenteral nutrition (days)	22	74	<i>p</i> < 0.05
Mean length of hospital stay (days)	36	86	<i>p</i> < 0.01
Mean no. of surgical procedures (<i>n</i>)	1.3	2.3	<i>p</i> < 0.01

dilatation is associated with increased time to full enteral feeding and length of hospital stay. Corresponding findings to our study were also reported by Janoo et al. [15], and by Kuleva et al. [9]. They suggested that intra-abdominal bowel dilatation is a strong predictor for morbidity in the post delivery period. On the contrary, the recommendations for prenatal surveillance of Cohen-Overbeek et al. [10] denied correlation between prenatal bowel dilatation and the outcome of patients. They admitted that the only prognostic factor which could influence morbidity was the presence of intestinal atresia in their limited series of 24 fetuses.

In our study, 67 % of mothers had oligohydramnion and this fact had a positive predictive value for future complications. However, none of our pregnant women of neonates with gastroschisis had associated polyhydramnion in the 30th week of pregnancy. Chan et al. [17] published in their study that fetuses with gastroschisis had a noticeably higher incidence of oligohydramnion [18]. The length of stay and time to full enteral feeding were longer if oligohydramnion was present in the study by Capelle et al. [19]. It is a question how much the volume of amniotic fluid can affect the outcome of patients with gastroschisis. Further work on this topic is needed.

Not all gastroschisis experts believe in the isolated prenatal ultrasound findings. Badillo et al. [7], in a retrospective review, compared postnatal outcomes between newborns who had a qualitative description of at least one additional sonographic gastrointestinal abnormality on prenatal ultrasound and those without secondary changes to the bowel appearance. Their study design was based on uniting various ultrasound parameters according to qualitative descriptions and simplified statistical analysis seems to be a weakness of their study. There were no significant differences found between groups with respect to the time to initial and full enteral nutrition, total hospital stay, central line infection rates, reoperation rates or mortality. They came to the conclusion that isolated findings of gastrointestinal abnormalities on prenatal ultrasound do not correlate with adverse postnatal outcome, although they admitted that all 3 patients who died during their study had an additional prenatal gastrointestinal ultrasound finding. Also Japaraj et al., Durfee et al. and Alsulyman et al. [6, 11, 20] were quite skeptical while looking for ultrasound predictors of postnatal outcomes. They concluded that there was no statistically significant correlation between ultrasound findings (bowel wall thickness, extracorporeal bowel dilatation) and adverse neonatal outcome.

The supplemental value of prenatal diagnosis to the outcome of infants with gastroschisis may be in the prevention of fetal distress, unnecessary intrauterine death and reduction of intestinal complications [1, 10, 21, 22]. Progression of intestinal damage could be limited by early

induction of labor [23], amnioinfusion or exchange of amniotic fluid in fetuses with gastroschisis [24, 25]. Nevertheless, these methods have not been generally accepted because of associated risk and lack of indication criteria. Beneficial effect of early delivery for less severe damage of the intestine must balance the risk of complications due to lung immaturity before 35 weeks of gestation [26–28]. Beneficial effect of amnioinfusion for correction of oligohydramnion must balance the invasivity of procedure [24, 29]. Fetal surgery itself (fetoscopic enlargement of the defect, return of herniated abdominal viscera followed by abdominal closure) remains currently as a learning process in experimental animal model [30].

Considering our results and a review of the above-mentioned literature, we presume that isolated prenatal ultrasound findings can predict intestinal damage and outcome. Prediction of the severity of intestinal damage is currently important in informing parents and evaluating the prognosis of pregnancy with congenital malformation [1, 31]. Its usefulness as an individual decision-making criterion for prenatal therapy, early induction of labor and surgical technique (primary repair vs. silo) is doubtful at present, as this will certainly continue to be a subjective decision of the attending team in years to come.

Further study is needed to set the “gold standard” for ultrasound examination of the intestine in gastroschisis and to identify pathological “cutoff” values for a gestational week. Our proposal is that the first examination will take place after inclusion in prenatal care at the time of diagnosis at 20–24 gestational weeks. Further examination (depending on the course of pregnancy) will be carried out at 28 weeks and every 2 weeks following (i.e. 28–30–32–34–36th week). Ongoing investigations will focus on the dynamics of pathological findings. Prenatal ultrasound examination of the fetus will target for evidence of intestinal damage (maximum dilatation of bowel loops, the maximum thickness of the intestinal wall, abdominal wall defect size in the transverse diameter, the presence of intra-abdominal dilatation of bowel loops, evaluation of fetal growth using biometric desired parameters (BPD, AC, HC, FL), assessment of the status of the fetus by measuring the amount of amniotic fluid (AFI, DVP) and monitoring functions of the placenta (grading, flow measurement of UA, MCA).

Conclusion

Our study has shown that the isolated presence of oligohydramnion with AFI below 8 cm, thickened bowel wall equal to or more than 3 mm, and prenatal intra-abdominal dilatation with more than 10 mm had significant predictive value for the adverse postnatal outcome of patients with

gastroschisis. Prenatal ultrasound findings should warn us to be more cautious in prenatal counseling of parents and during postnatal intensive care.

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Conflict of interest The authors declare that they have no conflict of interest.

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