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ORIGINAL ARTICLE

Outcomes in infants with prenatally diagnosed gastroschisis and planned preterm delivery

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Abstract
Background The timing and mode of delivery of pregnancies with prenatally diagnosed gastroschisis remains controversial.
Aim To evaluate the outcome of patients with gastroschisis managed during two time periods: 2006–2009 and 2010–2014, with planned elective cesarean delivery at 37 versus 35 gestational weeks (gw). A secondary aim was to analyze the outcome in relation to the gestational age at birth.
Material and methods Retrospective review of all cases with gastroschisis managed at our institution between 2006 and 2014.
Results Fifty-two patients were identified, 24 during the initial period, and 28 during the second. There were a significantly higher number of emergency cesarean deliveries in the first period. There were no differences between groups with regard to the use of preformed silo, need of parenteral nutrition or length of hospital stay. When analyzing the outcome in relation to the gw the patients actually were born, we observed that patients delivered between 35 and 36.9 gw were primary closed in 88.5 % of cases, with shorter time on mechanical ventilation, parenteral nutrition and hospital stay.
Conclusion Planned caesarian section at 35 completed gestational weeks for fetuses with prenatally diagnosed gastroschisis is safe. We observe the best outcome for patients born between 35 and 36.9 gw.

Keywords Gastroschisis · Abdominal wall defects · Caesarean section · Short bowel syndrome · Intestinal failure · Small bowel atresia · Colon atresia · Preterm delivery

Introduction

Gastroschisis is an abdominal wall defect with a reported increasing incidence of 4 in 10,000 births [1–3]. The etiology is unknown. During the course of pregnancy the bowel usually becomes coated in inflammatory fibrin peels, resulting in thickening of the intestinal wall, decreased motility and potential obstruction of the lumen [4–6].

Gastroschisis may cause prenatal as well as postnatal complications, including small bowel and colon atresias, volvulus with necrosis of the bowel with subsequent short bowel syndrome and postnatal bowel dysfunction [7, 8].

Postnatally, gastroschisis may be classified into two separate groups, simple (2/3 of the cases) and complex cases (1/3). Complex cases usually have associated gastrointestinal pathology that may contribute to short bowel syndrome and intestinal failure [9]. Complex gastroschisis is associated with both prolonged parenteral nutrition and hospital stay [9].

The mortality rate in the complex group may be as high as 28 %, whereas the survival rate in the simple category approaches 100 % [10, 11].

Controversy still exists regarding the obstetrical management of pregnancies with gastroschisis, including fetal monitoring [10, 12, 13], timing and mode of delivery [14–26]. When some centers advocate for delivery by elective

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cesarean section [22, 26, 27] others opt for vaginal delivery [15, 28, 29] without any differences in outcomes for the infants being observed [15, 25, 30]. Contradictory results have also been reported regarding the gestational age at induced delivery, preterm vs term. Preterm delivery has been associated with more complications, longer hospital stay and longer time to full enteral feeds, [31, 32]. At the same time, others advocate for early deliver to ameliorate damage to the bowel due to the prolonged exposure to toxic substances in the amniotic fluid as well as mechanical obstruction secondary to the inflammatory ongoing process [26, 29, 33]. However, there is consensus that delivery at a perinatal center is a significant factor for better outcome in infants born with gastroschisis [34, 35], with the potential advantage of coordinating obstetrical, neonatal, anesthesiological and pediatric surgery care.

Cesarean section has not been demonstrated to be superior, to vaginal delivery. At our institution the policy is to deliver infants with gastroschisis by planned elective caesarean section, in order to better optimize the resources for peri- and postnatal care. In 2006, our management was elective caesarian section at 37 weeks gestational age (GA), but due to a high number of emergency caesarean sections, this policy was changed in 2010 to elective caesarean delivery at 35 completed weeks, as we could observe that the median gestational age at delivery was approximately 35 gestational weeks (GA). We assumed this change in policy to be a good compromise between the risks related to prematurity and the complications related to intestinal peel and progressive bowel dilatation causing iatrogenic premature deliveries. The main aim of this study was to evaluate and compare the outcomes of pregnancies with prenatally diagnosed gastroschisis at our institution during these two time periods and to evaluate if this change of policy had resulted in differences in outcomes for patients with gastroschisis. A secondary aim was to analyze their outcome in relation to the gestational age at birth.

Materials and methods

Medical records, including ultrasound reports, from all pregnancies with gastroschisis monitored and managed at our institution between 2006 and March 2014 were reviewed.

Data on patient demographics, prenatal imaging, gestational age at birth, mode of delivery, surgical management, associated gastrointestinal anomalies, postoperative short and long-term complications, time to full enteral feeding and length of hospital stay were collected from patient records. The surgical approach in our institution did not change during the study period. We attempted primary closure if possible and the use of preformed silo bag when this was not possible. The feeding strategy did not change during the study period other than that home parenteral nutrition (PN) was introduced during the second study period. The patient material was divided into two groups: group 1 born during 2006–2009 and group 2 born in 2010–2014. A sub-analysis of the study material was also performed after dividing the pregnancies into three different groups according to the actual gestational age when the child was delivered: before 35A.

Statistical analysis was performed using Fisher's exact test for categorical variables, and Mann–Whitney or Kruskal–Wallis test for continuous variables, and linear regression analysis, with p values <0.05 considered as significant. All data analysis was conducted using GraphPad Prism 6.0 (La Jolla, CA, USA).

The study was approved by the regional ethical board, local committee of North Stockholm, Dnr 2014/1519/-31/3.

Results

A total of 52 patients were identified. The first group, i.e., patients who were diagnosed and managed during 2006–2009, consisted of 24 patients, and the second group (2010–2014) was comprised of 28 patients. The follow-up period varied from 3 months to 8 years postnatally. In three pregnancies, there was not a prenatal diagnosis made two during the first study period and one case during the second time period.

The maternal age, gestational age at delivery, gender of the fetus, Apgar score and birth weight were found to be similar in both groups. There were a significantly higher number of emergency caesarean sections during the first period compared to the second (75 vs 44 %) (Fig. 1). During the second study period, the main indication for emergency caesarean section was fetal (92 %; suspicion of bowel ischemia, progressive bowel dilation, decreased peristalsis, gastric dilatation, CTG-changes, changes in

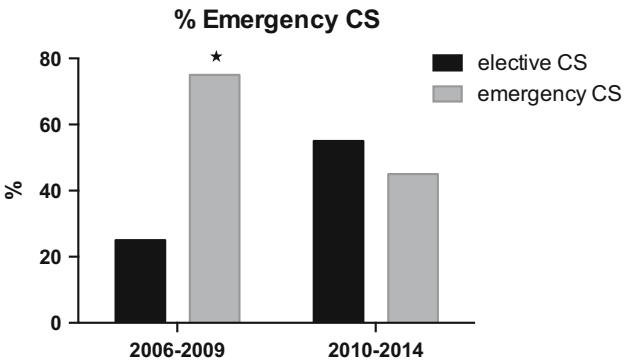

Fig. 1 Emergency vs elective cesarian-section rates during the two study periods (2006–2009, 2010–2014). *$p < 0.05$

umbilical artery flow or bradycardia) (Table 1). Time to primary closure, duration of mechanical ventilation, use of preformed silo, need of prolonged parenteral nutrition or length of hospital stay were observed to be similar in the two groups. Twenty-five percent were complex gastroschisis cases, 29 % in the first period and 21 % in the second. These cases had associated gastrointestinal anomalies such as prenatal volvulus and bowel ischemia, which were observed more commonly in the first period. Bowel atresias and stenosis occurred, more commonly occurring during the second period. Complications such as short bowel syndrome and catheter-related septicemia were more common during the first period, whereas wound infection, postnatal volvulus and bowel obstruction were more common during the second period (Table 2). The perinatal and late mortality rate was 5.8 % (three patients) in the complete study group. There was one case of intrauterine demise in the first period due to severe fetal distress secondary to bowel necrosis, and also two cases of late mortality, one in each period (Table 2).

Of the children with postnatal demise, two were complex cases, and one observed in the non-complex gastroschisis group.

Furthermore, the study material was analyzed according to gestational age at the time of delivery. The patients were divided into three groups: delivery before 35 GA ($n = 18$), between 35 and 36 + 6 weeks GA ($n = 27$) and term delivery (after 37 completed weeks; $n = 7$). The rate of emergency caesarean sections was significantly lower in the subgroup of patients born between 35 and 36 + 6 GA (37 %) compared to those born before 35 GA. Indication for emergency caesarian section before 35 GA was fetal in all cases. In the other two subgroups, the indications for emergency caesarian section were evenly distributed between maternal and fetal indications.

Patients born between 35 and 36.9 GA had significantly better Apgar scores after 1 min and also a significantly reduced need of silo treatment with a primary closure rate of 88 % (24/27) as compared to those born before 35 weeks (44 %, 6/18). We also observed a shorter time on mechanical ventilation, need for parenteral nutrition for a significantly shorter time, as well as reduced length of hospital stay in the subgroup delivered between 35 and 36 + 6 GA. In the subgroup of patients with gastroschisis delivered before 35 weeks, 50 % were complex gastroschisis with associated gastrointestinal anomalies, predominantly volvulus, with 22 % developing short bowel syndrome (Table 3; Fig. 2). Despite being a small group, patients born after 37 GA have a trend towards longer time on PN compared to those born between 35 and 36.9 weeks.

Table 1 Perinatal outcomes

	2006–2009	2010–2014	*p* values
Total	24	28	
Maternal age (years)	24.95 ± 5.8	26 ± 5	
PV	1	1	
Emergency CS	75 % (18)*	44 % (12)	0.04
No prenatal dx	8 % (2)	4 % (1)	
GA (weeks)	35.61 ± 1.69	34.9 ± 1.08	
Indication for emergency CS			
Maternal	28 % (5)	8 % (1)	
Fetal	72 % (13)	92 % (11)	
APGAR 5	8.3 ± 2.37	9.15 ± 1.75	
Birth weight (g)	2323 ± 547	2441 ± 455	
Complex gastroschisis	29 % (7)	21 % (6)	
Atresia	8 % (2)	15 % (4)	
Stenosis	4 % (1)	4 % (1)	
Bowel ischemia	8 % (2)	4 % (1)	
Volvulus	8 % (2)	0	

* $p < 0.05$, Fischer's and Chi-square test for categorical variables, Mann–Whitney for numerical variables

Discussion

Changing strategy to elective caesarean section after 35 completed GA has resulted in fewer emergency procedures maintaining similar outcomes for patients with prenatally diagnosed gastroschisis. We find that a planned delivery with caesarean section at this time point is a good compromise between the risks related to prematurity and the complications secondary to intestinal peel and progressive bowel injury. Furthermore, the time window between 35 and 36.9 GA seems to be an optimal gestational age for delivery of pregnancies with gastroschisis, resulting in higher rates of primary closure and a shorter stay in hospital and need for PN.

Planned delivery by C-section allows us for better planning and optimization of surgical resources. But even after the change of policy, we still had a fairly high number of emergency caesarean sections due to fetal indications which were unavoidable mainly due to signs of bowel complications or asphyxia at the time of prenatal evaluation. The optimal timing for and mode of delivery still remain controversial, with contradictory results advocating both caesarean section and vaginal delivery. Some studies, including one systematic review, have shown that elective caesarian section does not improve outcome in patients with prenatally diagnosed gastroschisis [15, 36], whereas others have shown more favorable results [22, 37].

However, delivery with elective caesarean section, in contrast to vaginal delivery, allows for better planning and optimization of surgical resources with the aim to reintroduce the baby's bowels into the abdominal cavity

Table 2 Postnatal outcomes

	2006–2009	2010–2014	*p* values
Total	24	28	
Silo	29 % (7)	36 % (10)	ns
Patch	8 % (2)	7 % (2)	ns
Age at primary closure (mean ± SD) (days)	2.6 ± 3.4	3.6 ± 3.9	ns
Mechanical ventilation (mean ± SD) (days)	2.78 ± 1.9	3.9 ± 3.7	ns
Time with PN median (days)	17	21	ns
PN <1 month	79 % (19)	75 % (21)	ns
LOS median (days)	23	32	ns
Mortality	8 % (2)	4 % (1)	ns
Complications			
SBS	12 % (3)	7 % (2)	ns
Bowel obstruction	4 % (1)	11 % (3)	ns

* $p < 0.05$, Fischer's and Chi-square test for categorical variables, Mann–Whitney for numerical variables

Table 3 Prenatal and postnatal outcomes for patients delivered before 35 GA, 35–36.9 GA and after 37 GA

	<35 GA	35–36.9 GA	>37 GA	*p* values
Total	35 % (18)	52 % (27)	13 % (7)	
Emergency CS	94 % (17)	37 % (10)	57 % (4)	0.0001
GA (mean ± SD) (weeks)	33.7 ± 0.87	35.7 ± 0.6	37.4 ± 0.54	
Fetal indication	100 % (17)	60 % (6)	50 % (2)	
APGAR 1	7.5	8.24	6.8	
APGAR 5	8.5	8.92	8.5	
APGAR 10	9.22	9.08	9.5	
Birth weight (g)	2036.8	2554	2750	
Complex gastroschisis	50 % (9)	7 % (2)	14 % (1)	
Silo	66 % (12)	11 % (3)	28 % (2)	0.0001
Patch	17 % (3)	0	43 % (3)	
Age at primary closure (mean ± SD) (days)	5.06 ± 3.95	1.75 ± 2.61	3.83 ± 4.6	0.0012
Mechanical ventilation (mean ± SD) (days)	4.89 ± 3.8	2.48 ± 2.38	3.5 ± 2.8	0.0055
Time with PN (median) (days)	26	23	25	0.0005
PN <1 month	61 % (11)	89 % (24)	71 % (5)	
LOS (median) (days)	45	14	27	0.0035
Mortality	5 % (1)	4 % (1)	14 % (1)	

* $p < 0.05$, Kruskal–Wallis test for numerical variables and Fischer's and Chi-square test for categorical variables

immediately post partum. We believe that our surgical approach of attempting to reintroduce the herniated bowel primarily without the need for silo is beneficial for the infant, reducing the number of days on mechanical ventilation and subsequent risk for infection. On the other hand, mothers to gastroschisis babies are often young primiparas, and delivery by a planned caesarean section may lead to an increased frequency of subsequent CS in future pregnancies and are also more costly. At the same time, the rate of emergency C-section following a trial of labor with vaginal delivery has been found to be as high as 37–51 % in previous studies mainly due to fetal distress [38]. Typically, spontaneous onset of labour in a pregnancy complicated with gastroschisis in the fetus will occur by 36 GA [39], which also supports the time for delivery chosen by our institution.

Several studies have advocated early delivery, based either on the ambition to prevent bowel ischemia and avoid peel formation, reporting shorter time to full enteral feeding, decreased need of prosthetic patches at the time of repair as well as reduced number of repeated surgeries due to intestinal obstruction. All these positive effects resulted in a shorter hospital stay [26, 29, 33]. However, other reports have indicated an improved outcome following term delivery (at or after 37 completed GA), with early closure of the abdominal wall defect and less time to full

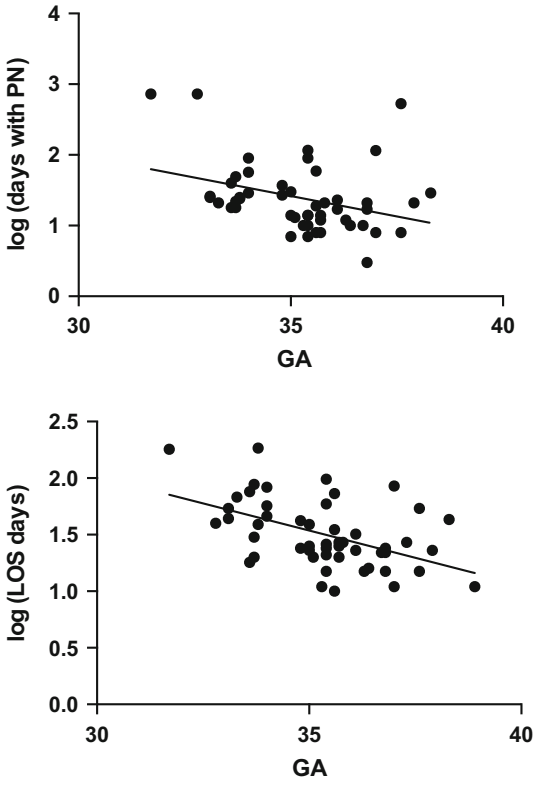

Fig. 2 Need for parenteral nutrition (**a**) and hospital stay (**b**) in the three subgroups (<35 GA, 35–36.9 GA or >37 GA)

feedings [40, 41], as well as a lower rate of co-morbidities [24]. One of the problems when trying to compare results from several institutions is their definition of prematurity that varies among the different studies ranging from <34 to 37 GA. Most of these studies divided the patients more crudely into those born before or after 37 GA, without stratifying the degree of prematurity. Lastly, several studies have failed to demonstrate any difference in outcome between preterm and term delivery [32, 42]. These include a small randomized controlled trial [23] and a recently published Cochrane review [14].

The underlying cause of injury to the bowel is not entirely understood. As the pregnancy with gastroschisis progresses, the bowel usually becomes coated in an inflammatory fibrinous peel, resulting in thickening of the bowel wall, decreased bowel motility and possible luminal obstruction [4–6]. Several studies have demonstrated neuronal immaturity in animal models of gastroschisis that might explain the postnatal dysmotility observed in some of the patients with gastroschisis [43–45].

Furthermore, inflammatory cells and significantly elevated levels of pro-inflammatory cytokines have been described in the amniotic fluid in gastroschisis pregnancies compared to controls [46, 47]. There have been unsuccessful attempts to dilute and remove toxic inflammatory substances from the amniotic fluid by repeated amnioexchange procedures performed during the third trimester [48].

If the inflammatory injury to the bowel seen in some patients with gastroschisis is progressive, this will imply that early delivery may suspend this process and improve the short-term and possibly also long-term results. However, it is crucial to avoid co-morbidity caused by preterm delivery, which makes the timing important.

In this study, we have demonstrated significantly better outcomes in newborns with gastroschisis delivered preterm after 35 GA, compared to term delivery, leading to higher rates of primary closure, shorter time on ventilation, hospital stay and time on PN. Early delivery between 35 and 36 + 6 gestational weeks was correlated with better outcomes as compared to the other groups. There was a significantly higher rate of primary closure, i.e., reduced need of preformed silos, dependence on parenteral nutrition for a significantly shorter time, as well as a reduced hospital stay. Patients born after 37 weeks, had a longer time on PN, which would support the hypothesis of progressive bowel dysfunction occurring in pregnancies continuing to term. We suggest that timing of delivery may influence the outcome in patients with gastroschisis.

Limitations of the results in this study are the retrospective nature of analysis, the small number of cases in the different groups as well as observations in the subanalysis are based on when delivery actually took place. Also the relatively high occurence of complex gastroschisis may have had an effect on our results due to many cases being delivered preterm secondary to bowel complications and fetal distress.

In conclusion, the change of strategy with a planned caesarian section at 35 completed gestational weeks for pregnancies with gastroschisis has led to a reduction in the number of emergency caesarean sections for fetal indications. In this study, delivery between 35 and 36 + 6 gestational weeks resulted in a better short-term outcome with the majority of cases undergoing primary closure. Moreover, the patients were dependent on parenteral nutrition for a significantly shorter time and the mean hospital stay was <1 month in the majority of infants. Most importantly, we were able to show that planned caesarian section at 35 weeks was safe and did not lead to an increased morbidity or mortality in neither the mother nor the child.

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