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# Is early delivery beneficial in gastroschisis?



Helen Carnaghan <sup>a</sup>, Susana Pereira <sup>b</sup>, Catherine P. James <sup>c</sup>, Paul B. Charlesworth <sup>d</sup>, Marco Ghionzoli <sup>a</sup>, Elkhouli Mohamed <sup>c</sup>, Kate M.K. Cross <sup>a</sup>, Edward Kiely <sup>a</sup>, Shailesh Patel <sup>d</sup>, Ashish Desai <sup>d</sup>, Kypros Nicolaides <sup>b</sup>, Joseph I. Curry <sup>a</sup>, Niyi Ade-Ajayi <sup>d</sup>, Paolo De Coppi <sup>a</sup>, Mark Davenport <sup>d</sup>, Anna L. David <sup>c</sup>, Agostino Pierro <sup>e</sup>, Simon Eaton <sup>a,\*</sup>

- a UCL Institute of Child Health and Great Ormond Street Hospital for Children, London, UK
- <sup>b</sup> The Harris Birthright Centre for Fetal Medicine, King's College Hospital, London, UK
- <sup>c</sup> Fetal Medicine Unit, University College London Hospital, London, UK
- <sup>d</sup> Paediatric Surgery Unit, King's College Hospital, London, UK
- <sup>e</sup> Division of General and Thoracic Surgery, The Hospital for Sick Children, Toronto, Ontario, Canada

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### ABSTRACT

*Purpose*: Gastroschisis neonates have delayed time to full enteral feeds (ENT), possibly due to bowel exposure to amniotic fluid. We investigated whether delivery at <37 weeks improves neonatal outcomes of gastroschisis and impact of intra/extra-abdominal bowel dilatation (IABD/EABD).

Methods: A retrospective review of gastroschisis (1992–2012) linked fetal/neonatal data at 2 tertiary referral centers was performed. Primary outcomes were ENT and length of hospital stay (LOS). Data (median [range]) were analyzed using parametric/non-parametric tests, positive/negative predictive values, and regression analysis. Results: Two hundred forty-six patients were included. Thirty-two were complex (atresia/necrosis/perforation/stenosis). ENT (p < 0.0001) and LOS (p < 0.0001) were reduced with increasing gestational age. IABD persisted to last scan in 92 patients, 68 (74%) simple (intact/uncompromised bowel), 24 (26%) complex. IABD or EABD diameter in complex patients was not significantly greater than simple gastroschisis. Combined IABD/EABD was present in 22 patients (14 simple, 8 complex). When present at <30 weeks, the positive predictive value for complex gastroschisis was 75%. Two patients with necrosis and one atresia had IABD and collapsed extraabdominal bowel from <30 weeks.

Conclusion: Early delivery is associated with prolonged ENT/LOS, suggesting elective delivery at <37 weeks is not beneficial. Combined IABD/EABD or IABD/collapsed extra-abdominal bowel is suggestive of complex gastroschisis. © 2014 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY-NC-SA license (http://creativecommons.org/licenses/by-nc-sa/3.0/).

Gut dysfunction is a major morbidity in infants born with gastroschisis resulting in prolonged time to reach full enteral feeds (24 days in simple gastroschisis and 47 days in complex in a recent national UK study) [1]. There have been no advances in the treatment of gut dysfunction since the advent of parenteral nutrition. Optimizing antenatal management of gastroschisis may improve neonatal outcomes. There has been much debate as to whether early delivery of gastroschisis would improve gut function and if antenatal intraabdominal or extra-abdominal bowel dilatation could predict patients that would benefit from early delivery. However, studies to date have included small numbers and no clear consensus has been reached for either issue. Our aim is to evaluate the clinical significance of both these issues.

E-mail address: s.eaton@ucl.ac.uk (S. Eaton).

### 1. Background

Nearly half of all infants with gastroschisis have type 2 intestinal failure (>28 days of parenteral nutrition) [1]. It has been hypothesized that gestational age (GA) at delivery and intra-abdominal bowel dilatation (IABD) could play a significant role in the development of pathological post-natal bowel function [2,3]. Changes in the composition of the amniotic fluid in the third trimester may lead to inflammation of the exposed bowel and gut dysfunction [4,5]. Currently, many centers electively deliver women whose fetus has gastroschisis at 37 to 38 weeks gestation due to concerns about unexpected fetal death in later gestation [6–9]. It is unclear whether delivery at less than 37 weeks and as early as 34 weeks gestation would reduce the bowel inflammation that is secondary to amniotic fluid exposure and thence improve gut function after birth. A number of studies present conflicting evidence both for [2,10-13] and against [14-16] delivery at less than 37 weeks gestation. The majority of these studies have small numbers of patients.

<sup>\*</sup> Corresponding author at: Unit of Paediatric Surgery, UCL Institute of Child Health, 30 Guilford Street, London WC1N 1EH, UK. Tel.: + 44 20 7905 2158; fax: +44 20 7404 6181.

 Table 1

 Presence of intra-abdominal bowel dilatation (IABD), extra-abdominal bowel dilatation (EABD) and both IABD/EABD (combined) at different stages during pregnancy by gastroschisis complexity group. Positive predictive value and negative predictive value are for complex gastroschisis.

All intra-abdominal bowel dilatation (	IABD)				
Complexity group (n = total in group)	IABD at last scan Number (% of complexity group)	IABD at ≥30 weeks to ≤34 GA Number (% of complexity group)	IABD at <30 weeks GA Number (% of complexity group)	Resolved IABD Number (% of complexity group)	Never had IABD Number (% of complexity group)
Simple n = 214	68 (32%)	47 (22%)	21 (10%)	16 (7%)	130 (61%)
Complex $n = 32$	24 (75%)	21 (66%)	13 (41%)	2 (6%)	6 (19%)
Positive or negative	26%	31%	38%	89%	96%
predictive value	PPV	PPV	PPV	NPV	NPV
(PPV or NPV)					
All extra-abdominal bowel dilatation (	EABD)				
Complexity group	EABD at last scan	EABD at $\geq$ 30 weeks to $\leq$ 34 GA	EABD at <30 weeks GA	Resolved EABD	Never had EABD
(n = total in group)	Number (% of complexity group)	Number (% of complexity group)	Number (% of complexity group)	Number (% of complexity group)	Number (% of complexity group)
Simple $n = 214$	46 (21%)	28 (13%)	4 (2%)	6 (3%)	162 (76%)
Complex $n = 32$	12 (38%)	11 (0.34%)	7 (22%)	1 (3%)	19 (59%)
Positive or negative predictive value	21%	28%	64%	86%	90%
(PPV or NPV)	PPV	PPV	PPV	NPV	NPV
Combined intra and extra-abdominal b	powel dilatation (combined)				
Complexity group	Combined at last scan	Combined at $\geq$ 30 weeks to $\leq$ 34 GA.	Combined at <30 weeks GA	Resolved combined	Never had combined
(n = total in group)	Number (% of complexity group)	Number (% of complexity group)	Number (% of complexity group)	Number (% of complexity group)	Number (% of complexity group)
Simple $n = 214$	14 (26%)	13 (6%)	1 (0.5%)	1 (0.5%)	200 (93%)
Complex $n = 32$	8 (25%)	8 (25%)	3 (9%)	1 (3%)	24 (75%)
Positive or negative predictive value	36%	38%	75%	50%	89%
(PPV or NPV)	PPV	PPV	PPV	NPV	NPV

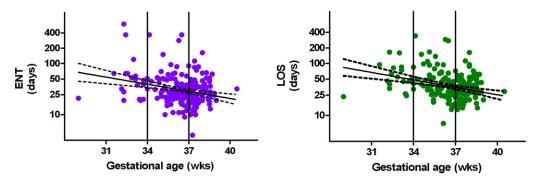


Fig. 1. Effect of gestational age at birth on length of stay (LOS) (A) and time to full enteral feeds (ENT) (B). Linear regression of log data with 95% confidence interval.

A further concern is that some fetuses may have a tight or closing abdominal wall defect causing compression of the bowel resulting in atresia or ischemic/necrotic bowel. Several studies have found an association between antenatally detected IABD with complicated gastroschisis [3,17-19]. Others hypothesize that the presence of dilatation in simple gastroschisis (continuous, uncompromised bowel) could also represent poorly functioning bowel resulting in prolonged time to full enteral feeds (ENT) and length of stay (LOS) [20]. However, extra-abdominal bowel dilatation (EABD) is considered by some as a normal phenomenon in gastroschisis [3,21] and thought not to be predictive of outcomes [22,23]. Some clinicians therefore advocate early delivery based on IABD in order to prevent development of bowel necrosis secondary to closing gastroschisis. However, most studies on bowel dilatation are limited due to small numbers and there is a paucity of data evaluating the predictive value of combined IABD and EABD.

The aim of this study was to investigate whether elective preterm delivery at <37 weeks is associated with improved neonatal outcome of gastroschisis pregnancies and if bowel dilatation is a reliable predictor of poor outcome indicating the need for early delivery.

## 2. Methods

With institutional approval we performed a retrospective study of all live-born gastroschisis neonates treated both antenatally and neonatally at two tertiary referral centers (University College London Hospital/Great Ormond Street and King's College Hospital) between 1992 and 2012. This extensive original series includes data from 38 infants who were included in a previous study on the impact of GA on outcomes [16] and 47 infants included in a bowel dilatation paper [18]. Women whose fetus is affected by gastroschisis are referred from district general hospitals to these tertiary centers where pregnancies are usually monitored at 4 weekly intervals up until 30 weeks of gestation and 2 weekly thereafter. More frequent monitoring is usually instigated for findings suggestive of fetal compromise including IABD, growth restriction or abnormal amniotic fluid volume. Women are electively delivered vaginally at the tertiary center by induction of labor at 37-38 weeks gestation unless obstetric reasons necessitate caesarean section. Earlier delivery is performed if there is suspicion of fetal compromise (severe fetal growth restriction, abnormal umbilical artery Doppler or sudden onset of polyhydramnios), maternal concerns or as a result of spontaneous labor. Throughout pregnancy the bowel is routinely evaluated and the presence or absence of IABD/EABD documented throughout the study period, although the dimensions of the bowel dilatation was not always assessed.

Fetal gastroschisis cases were identified through interrogation of the computerized fetal database (Viewpoint). All obstetric notes, antenatal ultrasound reports and neonatal notes were reviewed. Linked fetal and neonatal data were collected. Women and neonates treated at neonatal centers other than the study centers were

excluded from the study. For all antenatal ultrasounds, data were collected on gestational age at time of ultrasound, presence or absence of IABD/EABD and size (mm) of IABD/EABD (if documented).

Antenatal data on concomitant fetal abnormalities, labor onset, mode of delivery, indication for premature delivery (if applicable), gestational age at delivery (GA), and birth weight were also collected. Our postnatal primary outcome measures were ENT and LOS. Additional neonatal data included appearance of bowel at birth, bowel complications (atresia, necrosis, perforation, stenosis, volvulus and necrotizing enterocolitis) and death.

Data median [range] were analyzed using Mann-Whitney tests (for non-normally distributed data) or t-tests (for normally distributed data) as appropriate, positive and negative predictive values and Fisher's exact test were used for proportion data, linear regression and multiple regression analysis for log-transformed ENT and LOS.

### 3. Results

Two hundred forty-six patients were included (n = 143 and n = 143) 103 from each center) of which 32 were complex (24 atresias, 6 necrosis, 1 stenosis and 1 perforation). Twenty-three otherwise simple cases had either dusky bowel or required widening of a tight defect at birth. One hundred thirty-five patients were delivered at <37 weeks GA for the following reasons; 56 spontaneous deliveries/ premature rupture of membranes, 11 elective normal planned induction of labor at 36 + 6, 20 IABD (11 simple, 8 atresia and 1 necrosis), 28 suspicion of fetal compromise (13 healthy at birth, 3 compromised at birth and 12 unknown, based on APGAR scores and cord blood pH), 20 unknown. One hundred eleven patients were delivered at  $\geq$  37 weeks GA for the following reasons; 26 spontaneous deliveries, 80 planned induction of labor, 5 suspicion of fetal compromise (2 healthy at birth, 3 unknown, based on APGAR scores and cord blood pH). Overall there were 8 deaths; sepsis in 1 atresia patient, unknown cause in 1 atresia patient, 1 volvulus at birth (with no antenatal IABD), 1 volvulus following primary closure at day 10 of life, 1 respiratory failure, 2 unexpected infant deaths following discharge and 1 unknown cause in a patient with Pierre Robin sequence.

LOS (Fig. 1A, P < 0.0001) and ENT (Fig. 1B p < 0.0001) were significantly increased at lower birth GA. Analysis showed that an infant delivered at 34 weeks instead of 37 weeks resulted in an increased time to ENT by 10.8 days (p = <0.0001) and LOS by 13.4 days (p = <0.0001). These results were unchanged if the three infants delivered early for suspected fetal compromise who had documented low APGAR scores or cord blood pHs were removed from the analysis. To remove the effect of extreme prematurity, we repeated the analysis with all patients born  $\geq 34$  weeks (n = 224) and the relationship remained significant for both ENT (p = 0.047) and LOS (p = 0.0004). In addition, the relationship remained significant following multiple regression analysis taking into account the source

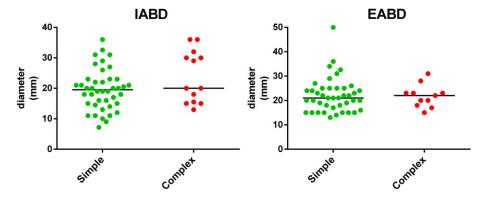


Fig. 2. Correlation of intra-abdominal bowel dilatation (IABD) and extra-abdominal bowel dilatation (EABD) with complex and simple gastroschisis.

hospital, complex gastroschisis and use of antenatal steroids (p=0.015 for LOS, p=0.04 for ENT). Additionally, with the inclusion of necrotizing enterocolitis (n=21) LOS remained significant (p=0.021) but ENT did not (p=0.66). Lower birth weight was only weakly associated with longer LOS (p=0.04) and not with longer ENT (p=0.27). Analysis of atresia patients showed that GA at birth did not significantly affect ENT (p=0.35) or LOS (p=0.19).

Later GA at delivery has been hypothesized to be associated with bowel inflammation. Bowel appearance at birth was documented in 209 (85%) patients. Bowel inflammation/peel was reported in 61 (29%) patients. There was no significant difference in GA between infants with inflammation/peel (GA 36.5 [32.3–38.7] weeks) and those without inflammation/peel (GA 36.9 [31.8–39.0] weeks, p = 0.13). In addition, there was no significant difference between the inflammatory and non-inflammatory patients in ENT (29 [14–590] days vs. 27 [4–365] days respectively, p = 0.35) or LOS (33 [10–340] days vs. 36 [9–290] days respectively, p = 0.90).

Antenatal IABD (including stomach dilatation) was detected at any time during pregnancy in 110 patients, resolving in 18 after 1 [1–3] ultrasound scans. In the remaining 92 patients IABD persisted until the last scan of whom 68 (74%) were simple and 24 (26%) complex (positive predictive value [PPV] for complex gastroschisis 26%, Table 1). Of these 92 patients, IABD was present at <30 weeks in both simple and complex gastroschisis (Table 1). IABD was never present in 130 simple cases, and in 6 complex cases (3 atresia, 2 necrosis and 1 perforation, negative predictive value [NPV] for complex gastroschisis 96%, Table 1).

EABD was detected at anytime in 65 patients, which resolved in 7 after 1 [1–3] scans and was present at the last scan in 58 patients (46 simple, 9 atresia, 2 necrosis, 1 stenosis, Table 1). PPV of EABD for complex gastroschisis was low at >30 weeks GA but higher (64%) at

**Table 2**Categorization of diameter of intra-abdominal bowel dilatation (IABD) and extra-abdominal bowel dilatation (EABD) for both complex and simple gastroschisis groups.

Degree of intra-abdominal bowel dilatation (IABD)					
IABD diameter (mm)	Complex gastroschisis, n = 13 Number (% in group)	Simple gastroschisis, n = 42 Number (% in group)	Positive predicative value		
<10 10 to <18 ≥18 Degree of extra-	0 4 (31%) 9 (69%) -abdominal bowel dilatat	2 (5%) 13 (31%) 27 (64%) ion (EABD)	0% 24% 25%		
EABD diameter (mm)	Complex gastroschisis n = 11 Number (% in group)	Simple gastroschisis n = 40. Number (% in group)	Positive predicative value		
<10 10 to <18 ≥18	0 2 (18%) 9 (82%)	0 11 (28%) 29 (72%)	0% 15% 24%		

<30 weeks GA (Table 1). EABD was never present in 19 (59%) of complex gastroschisis (NPV 90%).

Both IABD and EABD (combined BD) were present in 22 cases (14 simple, 7 atresia, 1 necrosis) and when present at <30 weeks GA the PPV for complex gastroschisis was high at 75% (Table 1). Furthermore, 3 patients had IABD with collapsed extra-abdominal bowel loops from <30 weeks all were complex (1 atresia, 2 necrosis).

In simple gastroschisis, the presence of dusky bowel or the need for widening of a tight defect at birth was considered a marker of impending closing gastroschisis. Within this cohort there were 23 patients that fulfilled these criteria of whom 5 (22%) had persistent IABD (combined with EABD from > 30 weeks GA in 2 cases), 5 (22%) had resolved IABD, 4 had persistent EABD and 8 (36%) never had IABD or EABD.

IABD diameter was documented in 55 patients. There was a tendency towards greater dilatation in complex (20 [13-36] mm) vs. simple gastroschisis patients (19 [7.2–36.0], p = 0.064), but there was only a difference of 1 mm in median diameter (Fig. 2). An IABD diameter  $\geq$  18 mm was present in 64% of simple and 69% of complex gastroschisis cases with measured dilatation (PPV 25% for complex patients, Table 2). Overall, there was no correlation between degree of dilatation and ENT (p = 0.33) but there was a weakly significant association between bowel dilatation and LOS (p = 0.049). This was not present when LOS for simple (p = 0.26) and complex (p = 0.42) gastroschisis were analyzed separately. Within the simple gastroschisis group, there was no significant difference between those patients with IABD and without IABD in ENT (24.5 [11–112] days vs. 26.0 [4–365] days, p = 0.65) or LOS (32.0 [15–94] days vs. 29.0 [7–167] days p = 0.13).

EABD diameter was documented in 51 patients with no significant difference between complex (22 [15–31] mm) and simple gastroschisis (21 [13–50], p=0.91, Fig. 2). A diameter  $\geq$ 18 mm was present in 72% of simple and 82% of complex cases with measured EABD (PPV for complex gastroschisis 24%, Table 2). There was no correlation between degree of EABD and ENT (p=0.50) or LOS (p=0.47). Patients with combined IABD/EABD had longer ENT

**Table 3**Diameter of dilatation and proportion of complex patients within the planned early delivery for IABD group verses no early delivery for IABD present at any time.

	Planned early delivery for IABD (n = 20)	IABD at any time but no early delivery $(n = 90)$	p-value
IABD Diameter (mm) Patients with bowel necrosis Number (% in group)	20 [12–36] 1 (5%)	19.0 [7.2–36] 3 (3%)	0.17 0.56
Patients with atresia Number (% in group)	8 (40%)	13 (14%)	0.023

(30 [15–365] days vs. 26.5 [4–365] days, p = 0.14) and LOS (37 [16–273] vs. 32 [7–300] days, p = 0.17) but neither reached significance.

Twenty patients were delivered early due to persistent/static dimension of IABD (5 simple, 3 atresia, 1 necrosis), sudden onset of large IABD in the 3rd trimester (6 simple, 1 atresia), increasing IABD throughout pregnancy (3 atresia) raising concerns of closing gastroschisis. Of these patients, one had necrosis and 8 atresia (Table 3); one atresia patient died aged 5 months. There was no difference in the proportion of patients with necrosis in the early delivery and nonearly delivery groups (Table 3). Of the patients delivered early who had simple gastroschisis, only one was reported to have dusky bowel. Overall, 59 patients had persistent/static IABD (45 simple, 11 atresia, 3 necrosis), 27 sudden (21 simple, 5 atresia, 1 necrosis) and 6 increasing (2 simple, 4 atresia).

### 4. Discussion

Our large cohort shows a highly significant association with early delivery and prolonged ENT and LOS. This was independent of confounding factors such as source hospital, complexity of gastroschisis and antenatal steroid use. Low birth weight only had a weak relationship with neonatal outcomes. In addition, bowel inflammation or peel at birth was not associated with later GA or to be predictive of ENT/LOS. Furthermore, our series included 110 patients who had IABD and 65 who had EABD at any time point during pregnancy. Analysis of IABD and EABD individually yielded mixed results. Many complex patients had IABD but the PPV was low. In contrast the NPV is high at 96% but this also equates to 19% of complex patients in this cohort without IABD. Generally the PPV of EABD was low except when present at <30 weeks GA. However, when IABD and EABD are considered together our data revealed a 75% PPV for complex gastroschisis if both were present from <30 weeks GA. Additionally, 2 necrosis, 1 atresia and no simple gastroschisis had IABD with collapsed extra-abdominal bowel from <30 weeks GA onwards. Finally, patients with signs of impending closing gastroschisis at birth infrequently presented with antenatal bowel dilatation.

There has been much unresolved debate as to the benefit of elective early delivery (<37 weeks) for all gastroschisis patients. Previous studies have included retrospective studies [10,15,16], prospective studies [2,13] and one randomized controlled trial [14]. The two prospective studies delivered patients at 34-35 weeks gestation and compared outcomes with retrospective controls. These included 32 [2] and 23 [13] patients with both showing a reduction in ENT and LOS within the early delivery group; however all early delivery patients were treated with antenatal corticosteroids to improve lung maturation. Animal studies have shown antenatal steroids reduce bowel inflammation in gastroschisis [24,25] and a human study showed improved gut function in otherwise normal premature neonates who received antenatal steroids [26]. Thus, these apparent benefits of early delivery could actually be due to a therapeutic or maturational effect of corticosteroids on the bowel. The only randomized control trial [14] included 42 cases in which patients were randomly allocated to either delivery prior to 36 weeks or continuation of pregnancy to full term. Although the study showed no benefit from early delivery, there was little difference in GA at birth between the early delivery group (35.8 weeks) and controls (36.7 weeks). A previous retrospective study from one of our study centers [16] included 110 patients and showed that although there was no advantage to early delivery in terms of ENT, low birth weight was a predictor of delayed ENT.

Our data suggest that preterm delivery is detrimental to neonatal gut function resulting in prolonged dysfunction. Hence, bowel dysfunction in gastroschisis is more multifactorial than simple duration of bowel exposure to amniotic fluid or overt evidence of bowel inflammation. These data suggest that the positive effect of fetal bowel maturation in the latter stages of pregnancy has a stronger

influence on bowel motility and neonatal outcomes than the negative effects of prolonged amniotic fluid exposure. This may be due to the continued maturation of the interstitial cells of Cajal (the pacemaker of the gut) through the later stages of the third trimester [27].

It has been hypothesized that antenatal bowel dilatation and in particular IABD is prognostically useful for detection of impending necrosis, atresia or other patients who would have poorer outcome, thus selecting a group of patients who would benefit from early delivery and salvage of bowel before further deterioration [17]. One study [3] investigated IABD alone and found an association with prolonged ENT and LOS. These results are not supported by our data or a systematic review of isolated gastroschisis, which shows that independently of each other IABD or EABD are not associated with increased adverse neonatal outcomes [28]. A previous study from one of our study centers found that the absence of bowel dilation excludes atresia [18]. This to a certain extent is true given the high NPV (96%) of IABD for complex gastroschisis, however, it is important to note that in the series presented here 6 (19%) complex patients never had IABD and 24 (75%) never had EABD therefore the absence of bowel dilatation cannot fully exclude complex patients. Finally, a study from Vanderbilt concluded that second trimester IABD predicts atresia and potentially may form the basis for early delivery to prevent ongoing damage [19]. To a certain extent our data disagrees with this finding given the PPV of IABD <30 weeks GA for complex gastroschisis was only 38%. However, what appears to be more predictive of complex gastroschisis is the presence of both IABD and EABD at <30 weeks GA giving in this series a PPV of 75%.

In terms of identifying cases of closing gastroschisis it appears basing a clinical decision solely on the presence or progression of IABD is inaccurate for detecting necrosis or impending closing gastroschisis. These data suggest a combined approach taking into account both IABD and EABD seems more appropriate. Previous case reports have noted necrotic bowel to be associated with shrinkage of extra-abdominal bowel and intra-abdominal bowel dilatation [29,30]. Our cohort has revealed three similar cases whereby IABD was associated with collapsed extra-abdominal bowel from <30 weeks GA persisting through until the last ultrasound scan in two cases of necrosis and one of atresia. In addition, one of the 11 cases with both IABD and EABD also had necrosis, the remaining 10 included 4 simple and 6 atresia patients.

These data were from two tertiary referral centers with a relatively high number of gastroschisis patients. The data therefore includes variation in terms of antenatal and neonatal management improving the generalisability of the study to other centers. Multiple regression analysis showed this variation did not affect the primary outcomes measures of ENT or LOS. Reasons for early delivery did include signs of reduced fetal movements, poor cardiotocography and fetal distress, which may have impacted on neonatal outcomes. However, only three of the infants delivered at <37 weeks had documented evidence of fetal compromise (low APGAR scores, abnormal cord blood pH). In addition, LOS could be affected by socio-economic factors surrounding young maternal age and both the definition of ENT and bowel dilatation were non-protocolized. IABD and EABD were classified based on whether they were documented in the fetal medicine notes, and so is open to interobserver variability. Although we were unable to apply a threshold level for determination of bowel dilatation given only 55 of the 110 patients with IABD and 51 of 65 patients with EABD had bowel diameter measurements, there was no difference in diameter between those infants born with simple and those born with complex gastroschisis. However, a previous study associated a threshold bowel diameter of >18 mm with significantly longer time to ENT and greater need for bowel resection [20]. However, our results do not support that those patients with IABD > 18 mm have worse neonatal outcomes. Finally, this is a retrospective series with the inherent restrictions associated with this study type.

We have investigated two frequently debated topics in the antenatal management of gastroschisis. These data have shown that early delivery is associated with prolonged ENT and LOS. As a result, it would seem inadvisable to deliver before 37 weeks as a strategy to improve gut function and enteral tolerance as indeed an opposite relationship may exist. Assessment of IABD and EABD independently of each other leads to inaccurate prediction of those patients who would benefit early delivery given the lack of effect of presence of IABD on ENT and LOS, the lack of difference of degree of dilation between simple and complex gastroschisis patients, and the failure to reliably detect patients with necrosis or ischemia based solely on one parameter. However, the presence of both IABD/EABD or IABD and collapsed extra-abdominal bowel at <30 weeks GA proved to be a more accurate predictor of poor outcome in this cohort. Although, these antenatal findings may indicate that the bowel damage has already occurred it may be prudent in the presence of such findings to consider early delivery with the aim to salvage necrotic bowel.

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#### References

- [1] Bradnock TJ, Marven S, Owen A, et al. BAPS-CASS. Gastroschisis: one year outcome from national cohort study. BMJ 2011;343:d6749.
- [2] Moir CR, Ramsey PS, Ogurn PL, et al. A prospective trial of elective preterm delivery for fetal gastroschisis. Am J Perinatol 2004;21:289–94.
- [3] Huh NG, Hirose S, Goldstein RB. Prenatal intraabdominal bowel dilatation is associated with postnatal gastrointestinal complications in fetuses with gastroschisis. Am J Obstet Gynecol 2010;202:396.31–6.
- [4] Morrison JJ, Klein N, Chitty LS, et al. Intra-amniotic inflammation in human gastroschisis: possible aetiology of postnatal bowel dysfunction. Br J Obstet Gynaecol 1998:105:1200–4.
- [5] Api A, Olguner M, Hakguder G, et al. Intestinal damage in gastroschisis correlated with the concentration of intraamniotic meconium. J Pediatr Surg 2001;36:1811–5.
- [6] Burge DM, Ade-Ajayi N. Adverse outcome after prenatal diagnosis of gastroschisis: the role of fetal monitoring. J Pediatr Surg 1997;32:441–4.
- [7] Crawford RA, Ryan G, Wright VM, et al. The importance of serial biophysical assessment of fetal wellbeing in gastroschisis. Br J Obstet Gynaecol 1992;99: 899-902
- [8] Baud D, Lausman A, Malikah A, et al. Expectant management compared with elective delivery at 37 weeks for gastroschisis. Obstet Gynaecol 2013;121:990–8.
- [9] David AL, Tan A, Curry J. Gastroschisis: sonographic diagnosis, associations, management and outcome. Prenat Diagn 2008;28:633–44.
- [10] Gelas T, Gorduza D, Devonee S, et al. Scheduled preterm delivery for gastroschisis improves postoperative outcome. Pediatr Surg Int 2008;24:1023–9.
- [11] Martinez CY, Millian LA, Tuduri LI. Modifiable prognostic factors in the morbiditymortality of gastrochisis. Cir Pediatr 2012;25:66–8.
- [12] Moore TC, Collins DL, Catanzarite V, et al. Pre-term and particularly pre-labor cesarean section to avoid complications of gastroschisis. Pediatr Surg Int 1999;15:97–104.
- [13] Serra A, Fitze G, Kamin G, et al. Preliminary report on elective preterm delivery at 34 weeks and primary abdominal closure for the management of gastroschisis. Eur J Pediatr Surg 2008;18:32–7.
- [14] Logghe HL, Gerald CM, Thornton JG, et al. A randomized controlled trial of elective preterm delivery of fetuses with gastroschisis. J Pediatr Surg 2005;40:1726–31.
- [15] Simmons M, Georgeson KE. The effect of gestational age at birth on morbidity in patients with gastroschisis. J Pediatr Surg 1996;31:1060–2.
- [16] Charlesworth P, Njere I, Allotey J, et al. Postnatal outcome in gastroschisis: effect of birth weight and gestational age. J Pediatr Surg 2007;42:815–8.

- [17] Houben C, Davenport M, Ade-Ajayi N, et al. Closing gastroschisis: diagnosis, management, and outcomes. J Pediatr Surg 2009;44:343-7.
- [18] Ghionzoli M, James CP, David AL, et al. Gastroschisis with intestinal atresia predictive value of antenatal diagnosis and outcome of postnatal treatement. J Pediatr Surg 2012;47:322–8.
- [19] Nick AM, Bruner JP, Moses R, et al. Second-trimester intra-abdominal bowel dilation in fetuses with gastroschisis predicts neonatal bowel atresia. Ultrasound Obstet Gynecol 2006;28:821–5.
- [20] Langer JC, Khanna J, Caco C, et al. Prenatal diagnosis of gastroschisis: development of objective sonographic criteria for predicting outcome. Obstet Gynecol 1993;81:53–6.
- [21] Contro E, Fratelli N, Okoye B, et al. Prenatal ultrasound in the prediction of bowel obstruction in infants with gastroschisis. Ultrasound Obstet Gynecol 2010;35: 702–7.
- [22] Badillo AT, Hedrick HL, Wilson RD, et al. Prenatal ultrasonographic gastrointestinal abnormalities in fetuses with gastroschisis do not correlate with postnatal outcomes. J Pediatr Surg 2008;43:647–53.
- [23] Mears AL, Sadiq JM, Impey L, et al. Antenatal bowel dilatation in gastroschisis: a bad sign? Pediatr Surg Int 2010;26:581–8.
- [24] Bittencourt DG, Barreto MWG, Franca WMG, et al. Impact of corticosteroid on intestinal injury in a gastroschisis rat model: morphometric analysis. J Pediatr Surg 2006;41:547–53.
- [25] Yu J, Gonzaalez-Reyes A, Diez-Pardo JA, et al. Local dexamethasone improves the intestinal lesions of gastroschisis in chick embryos. Pediatr Surg Int 2004;9:780–4.
- [26] Morriss FH, Moore M, Weisbrodt NW, et al. Ontogenic development of gastrointestinal motility: IV. Duodenal contractions in preterm infants. Pediatrics 1986;78:1106–13.
- [27] Faussone-Pellegrini MS, Vannucchi MG, Alaggio R, et al. Morphology of the interstitial cells of Cajal of the human ileum from foetal to neonatal life. J Cell Mol Med 2007;11:482–94.
- [28] Tower C, Ong SSC, Ewer AK, et al. Prognosis in isolated gastroschisis with bowel dilatation: a systematic review. Arch Dis Child Fetal Neonatal Ed 2009;94: F268-74.
- [29] Winter LW, Giuseppetti M, Breuer CK. A case report of midgut atresia and spontaneous closure of gastroschisis. Pediatr Surg Int 2005;21:415–6.
- [30] Anveden-Hertzberg L, Gauderer MWL. Paraumbilical intestinal remnant, closed abdominal wall, and midgut loss in a neonate. J Pediatr Surg 1996;31:862–3.

### Discussion

- Discussant: Dr. Kenneth Gow; Seattle, Wa: Are you able to tell the folks who is delivering these babies, and how do you organize this to make this a reality?
- Response: Dr. Carnaghan: We currently deliver electively. We aim for 37 to 38 weeks. Some deliver spontaneously early, and others we delivered at 36 plus 6 weeks probably based on the fact it was a Friday rather than a Saturday at 37 weeks. We don't believe that delivering early would actually be beneficial to these patients. Obviously some were delivered early because the obstetricians had concerns that the patient may be compromised, but actually when they were born, most of them were absolutely fine, so I think just aiming for 37 weeks would be a good approach.
- Discussant: Dr. Tippy Mackenzie, Md; San Francisco, CA Congratulations on a beautiful study. Did you have any patients with vanishing gastroschisis, as that would be one small subset who might be anticipated to improve outcomes with early delivery?
- Response: Dr. Carnaghan: Vanishing gastroschisis cases were included within the necrosis patients, and we had possibly one that was vanishing, but that was included within our six necrosis patients. Of those, three were detected by combined dilatation, but the other three, two had dilatation at the last scan, and no other time, and the other one didn't have any dilatation at all.