

Advanced Medical Science (AMS)

Research Report

***Correlating sonographic findings
with postnatal outcome in neonates
with gastroschisis.***

**Supervisor: Dr Louise Kornman,
The Royal Women's Hospital, Melbourne**

AMS Unit: 00357 Maternal & Fetal Medicine

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Abstract

Objective

The purpose of this study was to assess whether there are sonographic findings that are useful in prenatally predicting the postnatal outcome and appropriate time for delivery of fetuses with gastroschisis. This was performed with a view to updating the information available to clinicians managing, and parents being counselled regarding, a gastroschisis-affected pregnancy.

Study design

A retrospective review was conducted of 53 gastroschisis cases followed in The Royal Women's Hospital (RWH) (Melbourne) Ultrasound Department between August 1991 and September 2001. Maternal and ultrasound scan (USS) data was gathered from RWH maternal histories. Postnatal outcome data was from neonatal histories held at The Royal Children's Hospital (Melbourne), where the 48 liveborn cases underwent surgical repair of their gastroschisis hernia.

Results

The relationship between maximal bowel luminal diameter on antenatal USS and duration of Total Parenteral Nutrition (TPN) was assessed in 36 cases. Fetuses with maximal bowel luminal diameter ≥ 17 mm had significantly longer durations of TPN (Chi-Square 10.784, $p = 0.005$; Spearman's rho 0.526, $p = 0.001$; Mann-Whitney U 78.5, $p = 0.008$). The association between polyhydramnios on USS (amniotic fluid index ≥ 20) and the presence of atresia at surgery was examined in 46 cases. The results were statistically significant (Yates' corrected Chi-Square 7.74, $p = 0.005$), the high negative predictive value (92.3%) suggesting that the absence of polyhydramnios on USS signifies increased likelihood of finding no atresia postnatally.

Conclusion

We conclude that there is an increased probability of gastrointestinal morbidity with increasing maximal bowel luminal diameter. However, this does not prove that preterm delivery lessens the development of gastrointestinal damage causing that morbidity. Furthermore, preterm delivery introduces multiple risks associated with prematurity. Thus, we recommend only term delivery (> 37 weeks) in the absence of other indications. The finding of lengthier TPN durations among babies with larger bowel diameters can at best currently be used to update the information given to parents being counselled about the postnatal course of their child with gastroschisis.

The relationship between polyhydramnios and atresia warrants further research to observe whether the (positive) predictive value of polyhydramnios for atresia improves with increased subject numbers. In the meantime, surgeons could be informed of the likelihood of increased chance of atresia in babies with polyhydramnios.

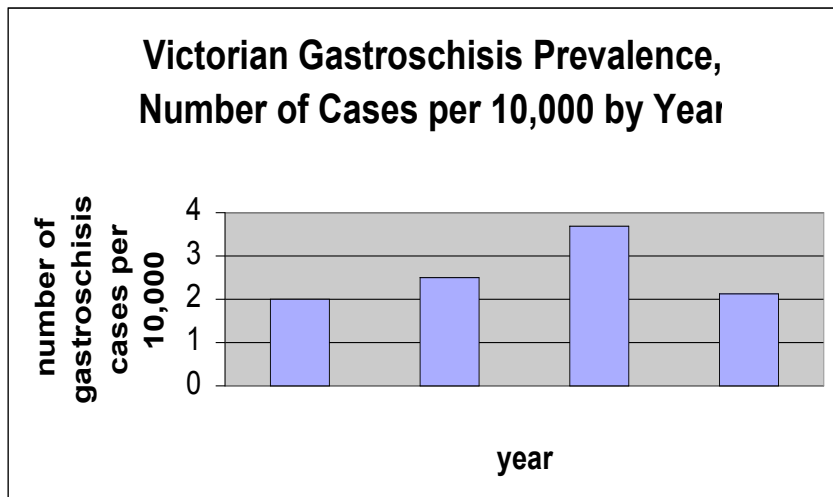
Introduction and background

Gastroschisis is a congenital abnormality where abdominal contents herniate through a defect in the anterior abdominal wall. Usually, the defect is to the right of the umbilicus and the hernia contains small and large bowel.

Prevalence

The mean gastroschisis prevalence in Victoria from 1995-98 was 2.6 per 10,000 livebirths, ranging from 2.0-3.7 per 10,000 livebirths (**Figure 1**) (Riley et al., 2000, pp. 91).

Figure 1



(Riley et al., 2000, pp. 91)

These figures mirror those in other western societies. The UK gastroschisis prevalence in 2000 was 2-3 per 10,000 births (Curry et al., 2000). Gastroschisis is observed at an increased rate of 7 per 10,000 births in first time teenage mothers (Torfs et al., 1990).

Embryology

The small intestine is derived from the midgut, which begins rapid growth in length after 5 embryonic weeks. Midgut growth exceeds that of the embryonic body, causing it to herniate through the coelom of the body stalk by the 6th embryonic week. The midgut

then continues to grow extensively outside the abdominal cavity before returning to the abdomen by the 10th week (Gray et al., 1972, pp. 130).

Failure of this process can lead to exomphalos, where the physiological hernia described above persists in the umbilical cord (Warner & Ziegler, 1993). This hernia is membrane-bound and distinct from gastroschisis. In gastroschisis, the growing abdominal organs protrude through an abdominal wall defect when the free space in the abdominal cavity decreases. The hernia is not membrane-bound and may contain small and large bowel, stomach, spleen, bladder, liver and genital organs (Callen, 2000, pp. 492).

Normally, in the process of returning to the abdominal cavity, the midgut rotates and becomes fixed to the posterior abdominal wall. Gastroschisis disrupts these events and a midgut volvulus may develop with twisting of the intestines upon their mesentery. This may result in intestinal ischaemia and lead to necrosis of the entire midgut. In such cases, surgery to resect necrotic intestine is often so extensive that Short Bowel Syndrome (SBS) is observed in the neonate. Insufficient gastrointestinal absorption necessitates aggressive nutritional support, medical and surgical intervention (Warner & Ziegler, 1993).

Aetiology

The abdominal wall defect in gastroschisis is thought to arise during organogenesis, the period from 5-10 menstrual weeks when all major internal and external structures develop (Callen, 2000, pp. 489). Some researchers suggest it arises from incomplete lateral infolding of the embryonic disc, disrupting closure of the anterior abdominal wall (McCollum & Thigpen, 1993, pp. 459). Most researchers support Hoyme's (1981) proposal that a vascular event causes occlusion or regression of the omphalomesenteric artery (vitelline artery), which arises from the aorta and branches over the yolk sac to

supply the anterior abdominal wall (Hoyme et al., 1981). Tissue ischaemia and necrosis, or failed fusion of abdominal wall layers, at the region of disrupted vascular supply creates a defect through which bowel can eviscerate (*Omphalomesenteric artery, 2001*).

A possible aetiological factor in such vascular events is exposure to vasoactive drugs (like cocaine and tobacco smoke). This may explain the increased prevalence of gastroschisis among teenage women, researchers suggesting they are more likely to have been in contact with these agents during pregnancy than older women (Howell, 1998).

Unlike other anterior abdominal wall defects, gastroschisis is not usually associated with chromosome anomalies and is often an isolated finding (**Table 1**). As a result, obstetricians frequently do not counsel in favour of karyotyping for fetuses with gastroschisis (*Gastroschisis: Evaluation & Treatment Options, 2001*).

Table 1 *Victorian gastroschisis patterns, 1983-1998*

Type	Number	Percentage
Isolated anomaly*	111	67.3
Other associations:		
Chromosomal	3	1.8
Other same system (musculoskeletal)	1	0.6
Other different systems	50	30.3

* Isolated cases may include cases with undescended testes.

(Riley et al., 2000, pp. 92)

Diagnosis, pregnancy management and delivery

Diagnosis of gastroschisis typically follows detection on the routine 18-week ultrasound scan (USS) (*Gastroschisis: Evaluation & Treatment Options*, 2001). Referral to a tertiary institution usually ensues, where specialist ultrasonologists and obstetricians may further monitor the pregnancy.

Infants with gastroschisis commonly deliver early, either in spontaneous labour or induced labour (or Caesarean section) secondary to fetal distress. In 1978, Seashore reported a spontaneous preterm (< 37 weeks gestation) delivery rate of 58% for gastroschisis babies in his study (Seashore, 1978). Intrauterine growth restriction (IUGR) also occurs more commonly in fetuses with gastroschisis, necessitating serial growth assessment on ultrasound.

Obstetricians currently advocate spontaneous vaginal delivery of neonates with gastroschisis in the absence of some other indication for Caesarean section. In a 1999 study involving 42 babies, Kumar et al. found no statistically significant difference between babies born by Caesarean section and by vaginal delivery, in relation to commencement of feeds, attainment of full feeds and length of hospital stay. They concluded there was no justification for performing an elective Caesarean section for gastroschisis unless indicated for some other reason, especially given that “Caesarean section involves morbidity and stress on the family already facing the birth of a baby with a defect” (Kumar et al., 1999).

Correcting the defect

Surgical repair occurs shortly after birth. Usually, primary closure is successful, where eviscerated organs are returned into the abdominal cavity and the abdominal wall closed in

layers (*Gastroschisis: Evaluation & Treatment Options*, 2001). Where there is a large or complicated hernia, however, a Silastic silo is used for gradual reduction of the hernia with daily manual compression (Cox, 1999). This is secondary closure, with final surgery usually occurring after 1 week.

During surgery, the infant is artificially ventilated and shortly thereafter commences intravenous nutrition (Total Parenteral Nutrition, TPN). Enteral feeding is only possible when intestinal function is restored. This can take days to months. Complications that sometimes prolong TPN or hospital stay include intestinal atresia, motility dysfunction and necrotizing enterocolitis (NEC) (Tawil & Gillam, 1995), or more generally, the effects of premature delivery and IUGR (Nichols et al., 1997). Nevertheless, a survival rate of more than 95% typically exists for infants with gastroschisis, being largely due to the absence of associated anomalies and the quality of neonatal care (Sleurs & Valero, 2000).

Ultrasound features

Several features in externalised bowel can be observed on ultrasound, including wall thickening and matting (Langer et al., 1993). Some researchers believe these features result from direct exposure of herniated bowel to amniotic fluid in utero (Cox, 1999). In 1986, Tibboel et al. suggested that chemical irritation by amniotic fluid caused peritonitis, progressive fibrosis and other changes in the intestinal serosa (Tibboel et al., 1986). In 1996, Simmons and others proposed an association between “bowel fibrosis” on ultrasound and reduced intestinal enzyme production and delayed return of gastrointestinal motility at delivery. Based on their results, they recommended early delivery for fetuses with gastroschisis to minimise these adverse influences on abdominal viscera and thereby improve neonatal outcome (Simmons et al., 1996).

More recent results are contradictory, suggesting that prolonged amniotic fluid exposure plays only a minimal role in the development of bowel changes (Deans et al., 1999). An alternative explanation is that intestinal wall thickening and matting results from venous and lymphatic obstruction. This is supported by the observation that the intra-abdominal peritoneum, although always exposed to amniotic fluid, does not always demonstrate matting or fibrous peel. On these grounds, there is no evidence that early delivery, which would decrease exposure to amniotic fluid, improves neonatal outcome (Crabbe et al., 1991).

Another feature on USS is maximal bowel luminal diameter. Bond et al. reviewed 11 pregnancies with prenatally detected gastroschisis, in which 5 fetuses had bowel dilatation and thickening. These fetuses subsequently had an increased incidence of intestinal atresia, necrosis and poor clinical outcome (lengthy duration of hospital stay and TPN). Bond's conclusions, however, were based on subjective descriptions of bowel appearance rather than more objective bowel lumen diameter measures (Bond et al., 1988).

Recognising this limitation, Adra and colleagues attempted to develop objective sonographic criteria for predicting postnatal outcome. They defined bowel dilatation as luminal diameter ≥ 10 mm. The 12 fetuses with "dilated" bowel had significantly more bowel oedema at birth ($p = 0.038$), longer operative time ($p = 0.013$) and higher overall rate of post-operative complications ($p = 0.037$) compared to the 15 cases with "normal" bowel. However, dilated bowel did not correlate significantly with rate of primary closure ($p = 1.000$), incidence of bowel ischaemia or atresia necessitating bowel resection ($p = 0.590$), days of parenteral nutrition ($p = 0.393$) and time from delivery to oral feeding ($p = 0.274$). Adra et al. also noted that ultrasound involved significant inter-observer and intra-observer variability, difficulty differentiating large bowel from severely dilated small

bowel and inaccuracy in measuring bowel. They recommended caution when interpreting such findings in terms of postnatal outcome and concluded little prognostic value of the sonographic appearance of fetal bowel, other than more difficult surgical repair and a higher overall incidence of post-operative complications (Adra et al., 1996).

In their retrospective review of 30 consecutive gastroschisis-affected pregnancies and their outcomes, Pryde and others used a less conservative measurement of maximal bowel luminal diameter ≥ 17 mm to define intestinal dilatation. Bowel dilatation was significantly associated with more “short-term complications” (44% in “dilated” group versus 14% in “undilated” group, $p < 0.05$) and fewer good “long-term outcomes” (45% in “dilated” group versus 86% in “undilated” group, $p < 0.05$). Short-term complications included secondary surgery, NEC and bowel obstruction, and lengthy hospital stay. Long-term infant outcomes were based on the paediatric surgeon’s impression in ongoing outpatient evaluations of weight gain and cognitive development (Pryde et al., 1994).

These and other like findings led some researchers to argue that if prenatal markers for complications were detectable on ultrasound, they should be used as an indication for early intervention that could decrease the severity of these complications and improve clinical outcome (Tawil & Gillam, 1995). For example, Swift et al. advocated Caesarean section at 37-38 weeks gestation. They suggested that at this age the risk of complications owing to premature delivery was reduced whilst the chance of achieving primary repair (the “best surgical outcome”) was improved, through preventing further exposure to whatever “factor” was causing bowel dilatation in utero (Swift et al., 1992). In reality, however, Swift’s recommendation is redundant among the many infants with gastroschisis born preterm (58% in Seashore’s study) who fail to reach his gestation “cut-off” for delivery.

A more recent report involved detection of acute bowel perforation on ultrasound at 34 weeks gestation in a fetus with gastroschisis. Immediate delivery by Caesarean section was performed, preventing further bowel injury, and the defect repaired by primary closure. Ultrasound findings used to identify acute bowel perforation were a dilated bowel mass that decreased in size and peristaltic activity over 2 days, and spillage of echogenic material from a bowel loop near the abdominal wall defect. Postnatal findings were consistent with the diagnosis. Haberman and colleagues suggested that prenatal diagnosis of this complication and acting on it improved the chance of successful repair by primary closure, leading to more favourable neonatal outcome (Haberman et al., 2000). However, this was a single and isolated case and, as such, is not appropriate to use as evidence in support of preterm delivery by Caesarean section for all babies with gastroschisis.

Furthermore, researchers and obstetricians alike recognise that whilst preterm delivery may be advantageous for preventing ongoing bowel damage, it adds the multiple risks of prematurity (Langer et al., 1993). Simmons and colleagues conducted a 6-year retrospective review to assess the influence of gestational age at delivery on morbidity in babies with gastroschisis. Early delivery did not decrease the need for silo closure, time until full enteral feeding or hospitalisation period. Whilst preterm elective Caesarean section shortened exposure of abdominal viscera to the possible “noxious effects of amniotic fluid and mesenteric constriction”, *longer* hospital stays were observed for these infants compared with those delivered because of preterm labour and at term (> 37 weeks). Thus, Simmons et al. recommended term delivery wherever possible (Simmons et al., 1996).

Clearly, no study has provided conclusive evidence to support early delivery of babies with gastroschisis via Caesarean section in the absence of other maternal or obstetric indications. Yet, the numerous reports documenting some correlation between ultrasound features and neonatal outcome cannot be ignored. Further review of gastroschisis cases is required to address the trade-off between preventing ongoing bowel damage and the multiple risks of premature delivery.

This study is a review of gastroschisis cases to address the research question: Are there sonographic findings that are useful in prenatally predicting the postnatal outcome and appropriate time for delivery of fetuses with gastroschisis? In particular, we aimed to determine the relationship between maximal bowel luminal diameter and TPN duration, to assess whether this could justify preterm delivery by obstetricians.

In addition, we aimed to identify features on antenatal USS that could be prospectively collected for future investigation of their relationship with postnatal outcome measures.

Materials and methods

A retrospective review was conducted of all gastroschisis cases followed in the Ultrasound Department at The Royal Women's Hospital (RWH), Melbourne, from August 1991 to September 2001. This was a quality assurance study, an audit of outcome, performed with a view to improving and updating the information available to clinicians, and to parents being counselled, regarding gastroschisis-affected pregnancies. Ethical approval was not required.

All surviving neonates were transported after birth to The Royal Children's Hospital (RCH), Melbourne, for surgery. Because prime interest was in correlating antenatal USS findings with postnatal outcomes, the inclusion criterion was antenatal diagnosis of gastroschisis paired with adequate attendance in clinic to provide antenatal scan data. Fifty-three cases fulfilled this requirement. Inferences and generalisations based on findings in this study can be applied to this group only and not the general population of gastroschisis cases.

Data sheets (**Appendix 1**) were created to collect information from RWH maternal histories and RCH neonatal histories. USS reports, held on file in the RWH Ultrasound Department, were reviewed in cases where scan data was missing from maternal histories.

Maternal, fetal and neonatal factors recorded included age, parity, gravidity, previous medical and obstetric history, smoking history and recreational drug use, gestation at diagnosis of gastroschisis, karyotype, delivery mode (vaginal versus Caesarean section; spontaneous, induced or no labour), gestation at delivery, use of antenatal steroids, liquor quality at birth, 1-minute and 5-minute Apgar scores and birthweight.

For each antenatal ultrasound performed at RWH, the following were noted: gestational age (dated by last known menstrual period or earliest USS), fetal biometry measures (biparietal diameter, head circumference, femur length and estimated fetal weight; abdominal circumference gives a poor growth estimate with the externalisation of abdominal contents and was excluded), amniotic fluid index, the side and size of the abdominal wall defect, hernia contents and aspects of bowel character (presence of matting, peristaltic activity or echogenicity, maximum bowel wall thickness, maximum bowel luminal diameter). Any additional abnormalities noted during USS were also recorded.

Neonatal data gathered included sex and birthdate, hernia contents and bowel character on observation at surgery, type of surgery (primary versus secondary; duration of silo usage in secondary closure), surgical findings (intestinal necrosis, atresia, perforation), additional surgical procedures and their indications (eg. bowel resection for intestinal necrosis), post-operative complications (sepsis, NEC, bowel obstruction), duration of ventilatory support and TPN, date of commencement of full enteral feeding and enteral nutrition source, and date and weight at discharge home.

Statistical analysis was performed with the Statistical Package for the Social Sciences for Windows (SPSS, Version 11). For continuous variables like maternal age, results were presented as mean \pm standard deviation, whilst discrete data like surgery type were expressed in raw numbers and percentages.

Comparison of maternal age and gravidity with those of the Victorian birthing population in 1999-2000 was undertaken using Yates' corrected Chi-Square analysis and the 2-tailed

Fisher exact test, where appropriate. Five-minute Apgar Scores were also compared with those of all babies born in Victoria in 1999-2000 and analysis performed using the 2-tailed Fisher exact test. This test was also used to assess the relationship between surgery type and sepsis rate.

The relationship between maximal bowel luminal diameter and gestation at its measurement was assessed using Rank Correlation (Spearman's rho). Rank correlation involved transforming the data to ranks which allowed for it not following a normal distribution (**Appendix 2**). Relationships between polyhydramnios on USS and atresia at surgery, polyhydramnios and duration of TPN, and maximal bowel luminal diameter and atresia, were investigated using Yates' corrected Chi-Square analysis, the 2-sided Fisher exact test (where expected cell counts < 5), and through calculating positive and negative predictive values.

The cases for which maximal bowel luminal diameter was recorded on antenatal USS were divided into 2 groups using a 17 mm threshold (**Table 1**). The threshold was decided after performing a literature review. This highlighted the downfalls of subjective description of bowel dilatation on USS, including intra- and inter-observer variability (Bond et al., 1988), and that objective measurement of maximal bowel luminal diameter was necessary. Researchers' trials of a range of "cut-off" values for identifying cases as "dilated" versus "normal" revealed 17 mm as a clinically and statistically viable measure. Thus, 17 mm appeared appropriate for use in this study.

The relationship between maximal bowel luminal diameter and TPN duration was then assessed using 3 statistical methodologies that took into account the outlying TPN duration values. Chi-Square analysis was used to assess the relationship between

categories of maximal bowel diameter and categories of TPN duration (**Table 2**). The decision about categorisation of TPN values took into account what parents are currently told during antenatal counselling about the possible postnatal course of their baby. Three weeks is used as a “yard-stick” of postnatal stay and this was supported by our observation that nearly two-thirds of babies in the sample had ceased TPN by that time. We also observed that one-third of babies fair very well, ceasing TPN within the first 2 weeks of postnatal life.

Table 2

		TPN duration categories		
		TPN < 14 days	$14 \leq \text{TPN} < 21$ days	TPN ≥ 21 days
Maximal bowel luminal diameter categories	“Undilated” group (bowel diameter < 17 mm)	<i>a</i>	<i>b</i>	<i>c</i>
	“Dilated” group (bowel diameter ≥ 17 mm)	<i>d</i>	<i>e</i>	<i>f</i>

The second method of analysis was to apply Rank Correlation, where transformation of the data to ranks compensated for outlying TPN values.

Finally, the Mann-Whitney U test was performed. The procedure was to convert TPN duration values to a rank order and then calculate the *t* statistic using these ranks rather than the original TPN values.

The results were considered statistically significant when $p < 0.05$.

Results

Most data points were available for all 53 cases. However, where some data points are missing, data totals do not equal 53.

For all 53 gastroschisis cases, mean maternal age was 23.2 ± 3.1 years (20.8% teenage mothers). **Table 3** compares this data to figures for all Victorian births in 1999-2000.

The 2-tailed Fisher exact test demonstrated that the proportion of teenage mothers in the study sample was significantly larger than the proportion of teenage mothers in the Victorian population ($p = 0.0000007$).

Table 3

	Teenage	Not teenage	Total
RWH study sample mothers	11 (20.8%)	42 (79.2%)	53
Victorian mothers*	4036 (3.2%)	123156 (96.8%)	127192
Total	4047	123198	127245

*Victorian data from Riley et al, 2001, pp. 20.

Median gravidity was 1 (range 1-5) and 27 mothers (50.9%) were primigravidae. This rate of primigravidity was not found to be significantly different from the rate for all Victorian births in 1999-2000 (Yates' corrected Chi-Square 1.59, $p = 0.21$ **Table 4**).

Table 4

	Primigravida	Not primigravida	Total
RWH study sample mothers	27 (50.9%)	26 (49.1%)	53
Victorian mothers*	51072 (41.5%)	72084 (58.5%)	123156
Total	51099	72110	123209

* Victorian data from Riley et al., 2001, pp. 29.

Fifteen (31.9%) of the 47 mothers questioned regarding smoking habits at their first RWH antenatal visit identified themselves as cigarette smokers. **Table 5** contains other medical and obstetric characteristics.

Table 5

Subject	Age	Medical/Obstetric History
1	20	Carbamazepine overdose (1 year before pregnancy)
2	24	Thalassaemia minor
4	20	Irritable bowel syndrome
12	19	Cousin had "mild gastroschisis"
16	24	Heroin user, on Methadone throughout pregnancy
18	23	Postnatal depression (previous pregnancy). Cervical dysplasia
23	21	Asthma
33	19	Recurrent bleeding per the vagina throughout first trimester
34	16	Anaemia. Recurrent bleeding per the vagina throughout first trimester
36	24	Epilepsy: treatment clonazepam
38	19	Endometriosis. Cervical warts
39	24	Cervical carcinoma insitu. Past intravenous drug and amphetamine use
40	28	Ovarian cyst
43	27	Second trimester bleeding
47	24	Postnatal depression (previous pregnancy)
50	22	Asthma
51	27	Mild asthma
52	21	Herpes Simplex Virus (type 2)

Mean gestational age at diagnosis of gastroschisis (first visualisation of the anomaly, at RWH or referring hospital) was 18.8 ± 4.1 weeks (**Table 6**). 56.6% were diagnosed by 18 weeks and 79.2% by 19 weeks. Only 9.5% remained undiagnosed by 22 weeks.

Table 6

Gestation (weeks) at diagnosis	Frequency	Percentage diagnosed	Cumulative % diagnosed
10	1	1.9	1.9
12	2	3.8	5.7
13	1	1.9	7.6
15	1	1.9	9.5
16	3	5.6	15.1
17	5	9.4	24.5
18	17	32.1	56.6
19	12	22.6	79.2
20	4	7.5	86.7
21	1	1.9	88.6
22	1	1.9	90.5
23	1	1.9	92.4
24	1	1.9	94.3
27	1	1.9	96.2
32	1	1.9	98.1
36	1	1.9	100.0
Total	53	100.0	

Amniocentesis was performed in 25 cases. Twenty-two karyotypes were normal and results could not be obtained in 2 cases. One case (1.9%) had an abnormal karyotype of 46XY with a Robertsonian translocation on chromosome 21 and the baby was stillborn at 28 weeks gestation.

There were 2 other stillbirths (total 3 cases, 5.7%) at 26 and 30 weeks gestation, and 2 terminations (3.8%) at 14 and 19 weeks gestation. For the 48 cases that survived to delivery, mean gestational age at delivery was 36.7 ± 1.7 weeks. **Table 7** describes the delivery characteristics.

Table 7

Mode of delivery	Labour onset	Frequency	%	Gestation (weeks) at delivery (median & range)	Indication
Vaginal	Spontaneous	25	52.0	36, 32-39	N/A
Vaginal	Induced	8	16.7	37, 35-41	Fetal distress (1), IUGR (1) PROM** (1), gastroschisis (2) fetal tachycardia (2), gestation > 40 weeks (1)
EmCS*	Spontaneous	8	16.7	37, 34-40	Fetal distress (6), breech (2)
EmCS*	Induced	2	4.2	37, 36-38	Fetal distress (2)
EmCS*	No labour	5	10.4	36, 33-37	Fetal distress (5)

* EmCS = Emergency Caesarean section

** PROM = premature rupture of the membranes

Table 8 displays the number of RWH USSs performed during each gastroschisis-affected pregnancy.

Table 8

Number of RWH ultrasound scans	Frequency (%) of subjects
1	11 (20.8%)*
2	9 (17.0%)
3	13 (24.5%)
4	12 (22.6%)
5	5 (9.4%)
6	2 (3.8%)
7	1 (1.9%)

* includes 2 stillborn & 2 terminated cases

Liquor character was assessed at the time of membrane rupture in 44 deliveries.

Meconium was said to be present in 28 cases (63.7%), bile in 2 (4.5%), meconium and bile in 1 case (2.3%) and liquor was normal in 13 cases (29.5%).

Apgar scores were recorded for all 48 livebirths. Most babies (29.2%) scored 8 at 1 minute, improving to a score of 9 (56.3%) at 5 minutes. When these infants were compared with all Victorian babies born in 1999-2000, the proportion of study sample infants scoring a 5-minute Apgar of 9 or 10 was significantly lower (2-tailed Fisher exact p -value: 0.00001 **Table 9**).

Table 9

	Apgar Score 9 or 10	Apgar Score 1-8	Total
RWH study sample babies	30 (62.5%)	18 (37.5%)	48
All Victorian babies born 1999-2000*	115156 (92.6%)	9205 (7.4%)	124361
Total	115186	9223	124409

* Victorian data from Riley et al., 2001, pp. 50.

Mean birthweight for all 48 livebirths was 2566.3 ± 617.1 grams, with 50.0% of neonates less than 2500 grams at birth and 20 (41.7%) identified as small for gestational age (less than 10th percentile weight range). Nine (18.8%) were below the 3rd percentile weight range, making them cases of severe IUGR. **Figure 2** demonstrates birthweight for all 48 liveborn cases.

Figure 2 a.

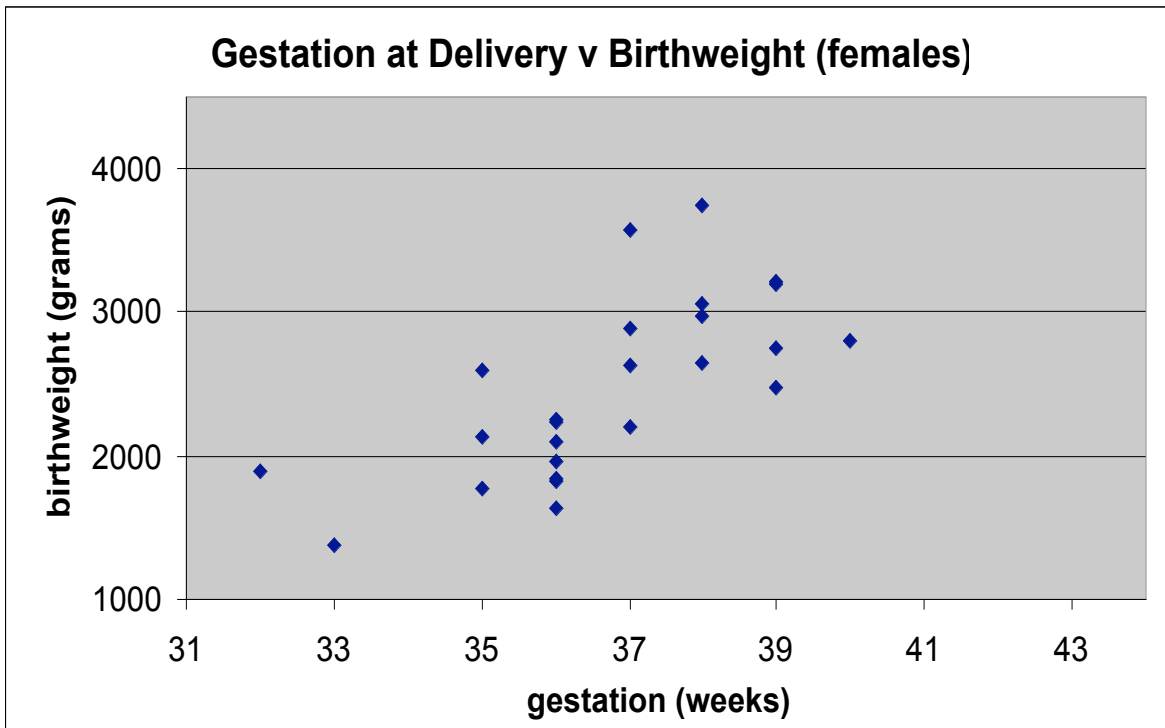
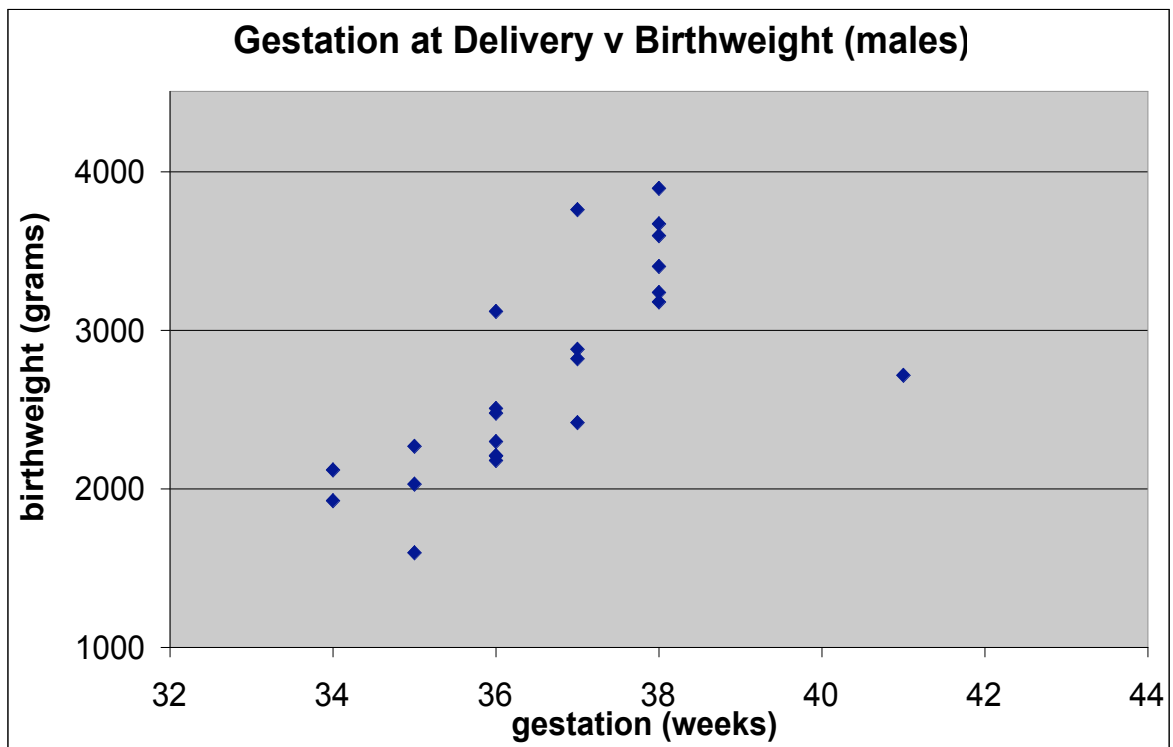


Figure 2 b.



Of the 48 liveborn, 42 (87.5%) underwent primary surgical closure. For the 6 babies requiring secondary closure, median duration of Silastic silo usage was 8 days with range 4-10 days. Nine (18.8%) infants required small bowel resection (caused by intestinal necrosis in 2, and intestinal atresia in 7, one of which also had small intestinal perforation). Post-operative complications included 4 cases of bowel obstruction, 3 requiring repeat surgery and ultimately resulting in SBS; 3 cases of NEC and 21 (43.8%) cases of sepsis. All neonates survived to discharge home.

Analysis of the relationship between surgery type and the likelihood of developing sepsis was performed using the 2-tailed Fisher exact test (**Table 10**). No statistically significant association was found ($p = 0.39$).

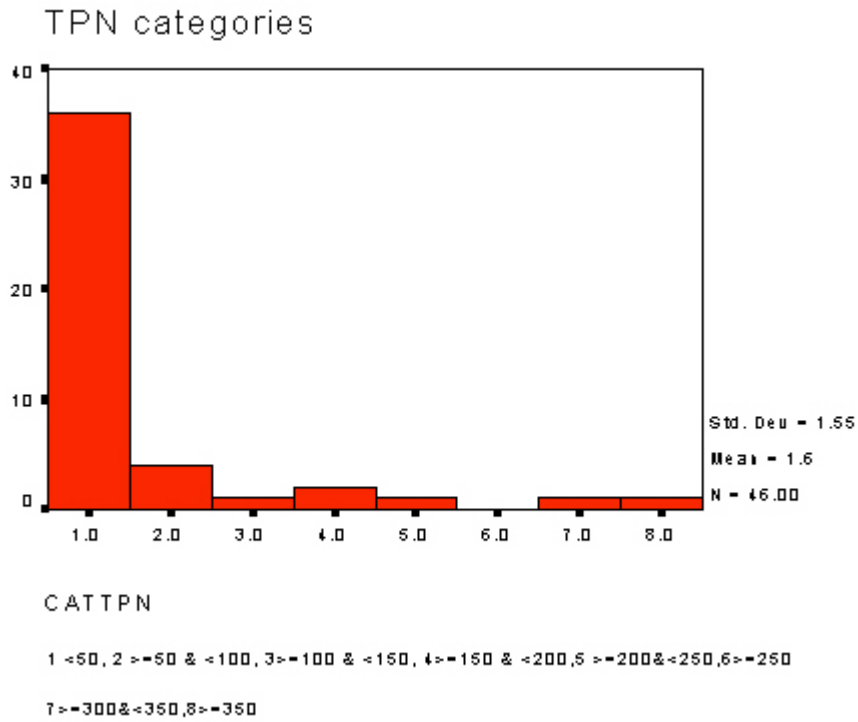
Table 10

	Sepsis	No sepsis	Total
Secondary surgery	4	2	6
Primary surgery	17	24	41
Total	21	26	47

Duration of TPN was recorded in 46 cases, with mean 49.2 ± 80.3 days (median 16.5, range 7 to 365 days). **Figure 3** demonstrates that TPN values were not normally distributed.

Figure 3

Distribution of TPN duration values



Categories of TPN duration

Category	Range of max bowel luminal diameter measures
1	0 – 49 days
2	50 – 99 days
3	100 – 149 days
4	150 – 199 days
5	200 – 249 days
6	250 – 299 days
7	300 – 349 days
8	≥ 350 days

Table 11 demonstrates the distribution of TPN values. Approximately one-third of cases ceased TPN within 2 postnatal weeks, another third within the 3rd postnatal week and the remaining one-third ceased TPN after 3 or more weeks.

Mean age at discharge for the 48 liveborn infants was 71.0 ± 113.2 days (median 25, range 12 to 587 days). Comparison of these figures within infants showed that 53.3% of babies had been discharged 1 week after ceasing TPN (**Table 12**).

Table 11

Days of TPN	Frequency	%	Cumulative %
7	1	2.2	2.2
9	5	10.9	13.0
10	2	4.3	17.4
11	2	4.3	21.7
12	2	4.3	26.1
14 (2 weeks)	5	10.9	37.0 (~ 1/3)
15	1	2.2	39.1
16	5	10.9	50.0
17	2	4.3	54.3
19	3	6.5	60.9
22 (~3 weeks)	1	2.2	63.0 (~ 2/3)
25	3	6.5	69.6
28	1	2.2	71.7
33	1	2.2	73.9
42	1	2.2	76.1
48	1	2.2	78.3
54	1	2.2	80.4
61	1	2.2	82.6
62	1	2.2	84.8
63	1	2.2	87.0
126	1	2.2	89.1
173	1	2.2	91.3
181	1	2.2	93.5
221	1	2.2	95.7
336	1	2.2	97.8
365	1	2.2	100.0
Total	46	100.0	

Table 12 *Days between TPN cessation and discharge home*

Days	Frequency	%	Cumulative %
1	1	2.2	2.2
2	3	6.7	8.9
3	5	11.1	20.0
4	2	4.4	24.4
5	7	15.6	40.0
6	1	2.2	42.2
7	5	11.1	53.3
8	2	4.4	57.8
9	3	6.7	64.4
10	4	8.9	73.3
11	2	4.4	77.8
12	1	2.2	80.0
15	2	4.4	84.4
16	2	4.4	88.9
19	1	2.2	91.1
23	1	2.2	93.3
28	1	2.2	95.6
46	2	4.4	100.0
Total	45	100.0	

Defect side was reported on antenatal USS in 41 of 53 cases. Thirty-seven (90.3%) were right-sided, 2 (4.9%) were left-sided, 1 defect (2.4%) was “above” the umbilicus and 1 was “below” the umbilicus. Defect size was not consistently or clearly reported on USS and as such is not included among results. Amniotic fluid index (AFI) at any stage in pregnancy was assessed in 50 cases, oligohydramnios (AFI < 5) being noted in 2 (4%) and polyhydramnios (AFI ≥ 20) in 7 pregnancies (14%). Matting was detected in 9 of 53 cases (17%). A measure of bowel wall thickness was recorded in only 13 cases, with mean value 3.0 ± 1.4 mm (median 2.8, range 0.9 to 6 mm).

Mean gestation at which maximal bowel luminal diameter on USS was reached was 32.6 ± 3.1 weeks (median 32, range 19 to 38 weeks). The relationship was assessed between maximal bowel luminal diameter and gestation at its measurement. The association was not statistically significant at the 5% level (Spearman’s rho 0.435, $p = 0.06$). However, as $p = 0.06$, it is likely that a statistically significant relationship would be shown if the sample size was larger.

The association between polyhydramnios on antenatal USS and the presence of atresia at surgery was examined for 46 cases. The relationship was statistically significant (Yates’ corrected Chi-Square 7.74, $p = 0.005$ **Table 13**).

Table 13

	Atresia	No atresia	Total
Polyhydramnios	4	3	7
No polyhydramnios	3	36	39
Total	7	39	46

Because one cell had an expected count less than 5, the 2-sided Fisher exact test was performed and again the result was significant ($p = 0.006$). Positive predictive value was 57.1%, as 4 of the 7 babies with polyhydramnios also had atresia. Negative predictive value was 92.3%, with 36 of the 39 without polyhydramnios having no atresia. Of the 3 cases with polyhydramnios but no atresia, one baby was suspected of having atresia on 32-week USS when “kinked” small intestine was detected, and another had multiple bowel resections resulting in SBS postnatally.

The association between polyhydramnios on antenatal USS and duration of TPN was also assessed (**Table 14**). A TPN duration “cut-off” of 21 days was selected because this is the time period RWH obstetricians currently suggest (to parents) a baby with gastroschisis will remain on TPN in the absence of other complicating factors.

Table 14

	TPN \geq 21 days	TPN < 21 days	Total
Polyhydramnios	4	1	5
No polyhydramnios	14	25	39
Total	18	26	44

The results were not statistically significant at the 5% level (Yates’ corrected Chi-Square 1.97, $p = 0.16$). The 2-sided Fisher exact test was performed as 2 cells had expected counts < 5. Again, the results were not statistically significant ($p = 0.14$). However, positive predictive value was 80.0%, with 4 of 5 cases of polyhydramnios remaining on TPN for 3 weeks or more. The single case with polyhydramnios and TPN < 21 days had TPN for 19 days. Negative predictive value was 64.1%, with 25 of 39 cases without polyhydramnios also having TPN duration less than 3 weeks.

The association was examined between maximal bowel luminal diameter on antenatal USS and finding atresia at surgery. A 17 mm “cut-off” was used, as shown in **Table 15**.

Table 15

	Atresia	No atresia	Total
Bowel diameter \geq 17 mm	6	15	21
Bowel diameter $<$ 17 mm	1	16	17
Total	7	31	38

Analysis revealed a result that was not statistically significant at the 5% level (Yates’ corrected Chi-Square 1.89, $p = 0.17$). However, as in Table 14, there was the case of 2 cells with expected counts < 5 . The 2-sided Fisher exact test also yielded a result that did not achieve statistical significance ($p = 0.10$). Positive predictive value was calculated to be 28.6%, as only 6 out of 21 cases with maximal bowel luminal diameter ≥ 17 mm had atresia. Negative predictive value was high at 94.1%, with 16 of 17 cases with bowel diameter < 17 mm having no atresia at surgery. The single fetus with atresia and bowel diameter < 17 mm had maximal bowel luminal diameter 16 mm. Thus, had the cut-off been slightly modified, all babies with atresia would have had dilated bowel on USS.

Of primary interest was to examine the relationship between maximal bowel luminal diameter and duration of TPN. Thirty-six cases were suitable for analysis, which revealed that antenatal ultrasonographic evidence of bowel dilatation was significantly associated with TPN duration (Chi-Square 10.784, $p = 0.005$ **Table 16**).

Table 16

	TPN $<$ 14 days	$14 \leq$ TPN $<$ 21 days	TPN \geq 21 days	Total
Bowel diameter $<$ 17 mm	9	3	5	17
Bowel diameter \geq 17 mm	1	10	8	19
Total	10	13	13	36

When the 5 cases with maximal bowel luminal diameter < 17 mm and TPN \geq 21 days were reviewed, one had omental bleeding and suspected SI perforation that was never isolated; one developed NEC and meningitis in hospital; another had a narrow stenotic region of mid-colon necessitating additional surgery and bowel diameter measure 15 mm; one baby had atresia at surgery and bowel diameter measure 16 mm; the remaining baby had a comparatively uncomplicated postnatal course.

The relationship was also assessed using Rank Correlation and again a statistically significant association was identified (Spearman's rho 0.526, $p = 0.001$ **Table 17**).

Table 17

	Max diameter	TPN duration
Spearman's rho	1.000	0.526**
Max diameter		
Correlation coefficient	0.001	0.001
Sig. (2-tailed)		
Number	39	36
TPN duration	0.526**	1.000
Correlation coefficient	0.001	
Sig. (2-tailed)		
Number	36	42

** Correlation is significant at the 0.01 level (2-tailed).

Finally, the Mann-Whitney U test was performed on the ranked data and again the result was statistically significant (Mann-Whitney U 78.5, $p = 0.008$ **Table 18**).

Table 18

	Maximal bowel diameter category	Number	Mean Rank	Sum of Ranks
TPN duration rank	Bowel diameter < 17 mm	17	13.62	231.50
TPN duration rank	Bowel diameter \geq 17 mm	19	22.87	434.50
	Total	36		

Discussion and conclusion

The mean maternal age of 23.2 ± 3.1 years for the sample of 53 mothers supports the proposed trend that gastroschisis is more common among younger women. Furthermore, it was demonstrated that the percentage of teenage mothers in the sample (20.8%) is significantly larger than the percentage of teenage mothers in Victoria in 1999-2000 (3.3%).

Interestingly, the difference between the proportion of primigravidae women in the sample (50.9%) and that of all Victorian women giving birth in 1999-2000 (41.7%) is not statistically significant at the 5% level. This suggests that the risk of gastroschisis is related more closely to maternal age than to gravidity.

The self-reported smoking incidence (31.9%) among mothers in the sample is very similar to the percentage of self-reported smokers (28%) at the time they became pregnant in a 1999 study by Panjari et al. (Panjari et al., 1999). This lends no support to the aetiological theories linking tobacco smoke, a vasoactive agent, with gastroschisis. However, 31.9% is unlikely to be the true percentage of smokers in the sample, but merely the number that chose to admit to smoking when questioned. The role of tobacco in the aetiology of gastroschisis might be more accurately assessed in a future RWH study through the measurement of urinary cotinine levels. Cotinine is the major metabolite of nicotine, has a long endogenous half-life and is exclusively derived from nicotine intake (Panjari et al., 1997).

The range of medical or obstetric problems among mothers in the sample fits the picture of young maternal age. There are 2 cases of a sexually transmitted disease (STD) and 2 of

cervical dysplasia, possibly linked with the sexually transmitted Human Papilloma Virus. A higher incidence of STDs is expected within a younger female population, given the larger number of sexual partners usually associated with younger age. One mother was receiving methadone during pregnancy and used heroin at the time of conception.

Another reported past intravenous drug and amphetamine use. It is possible that the use of drugs, in particular vasoactive agents, played an aetiological role in their babies' gastroschisis. However, without prevalence data for the above conditions in a control population, and the timing of the ingestion of these drugs, it is impossible to interpret their relevance to the aetiology of gastroschisis. Also, as with self-reporting of smoking, information about use of vasoactive drugs in very early pregnancy may not have been volunteered or recorded.

The mean gestational age at diagnosis, 18.8 ± 4.1 weeks, is typical of gastroschisis. Eighteen weeks is the time at which the "routine" morphology USS is usually performed. The single case (1.9% of sample) with an abnormal karyotype mirrors the 1.8% of gastroschisis cases associated with chromosomal anomalies in Victoria from 1983-98 (Riley et al., 2000, pp.10). Interestingly, karyotypes were available for 47.2% of the sample, indicating that obstetricians were offering (and patients accepting) genetic testing in almost half of cases. This behaviour seems contrary to the widely accepted "low" association rate of gastroschisis with chromosomal anomalies. However, it is not at all surprising when the association rate is considered in context. That is, 1.8% risk of genetic association in gastroschisis is relatively high compared to risks for other anomalies where genetic testing is routinely offered. For example, karyotyping for trisomy 21 (Down syndrome, DS) is offered to all women over 35 years at RWH, the risk of DS being approximately 1 in 200 (0.5%) in women 35-39 years (Riley et al., 2000, pp. 94). On the

basis of such figures, many RWH obstetricians obviously felt compelled to offer karyotyping to mothers with gastroschisis-affected pregnancies.

The frequency of stillbirth in the sample (5.7%) is less than the 13.8% recorded among Victorian gastroschisis cases from 1995-98. Similarly, only 3.8% of pregnancies in the study were terminated, compared with 7.7% of Victorian 1995-98 gastroschisis cases (Riley et al., 2000, pp. 92). These figures are difficult to interpret, however, as the RWH study population actually comprises a large percentage of the reported Victorian gastroschisis cases. Nevertheless, it is *expected* that the study sample would include more cases where there was a desire to continue pregnancy (fewer terminations), as RWH is the primary referral centre for management and monitoring of gastroschisis-affected fetuses. Furthermore, we would also expect termination rate to fluctuate between study populations and over time. In Victoria from 1983-1994, 11.0% of gastroschisis cases ended in termination compared with the 1995-98 figure of 7.7%. Such variation is often a function of the nature of counselling, that is, the way the anomaly is first described to the parents and the degree of optimism expressed by the management team in terms of prognosis. In this respect, the proportion of parents deciding to terminate their gastroschisis-affected pregnancy increases or decreases according to changes in the approach of the management team. Such changes in approach are both necessary and appropriate, reflecting the improved understanding of the condition through observation of the general outcome of gastroschisis babies over time.

Mean gestational age at delivery, 36.7 ± 1.7 weeks, with 50.0% of all liveborn cases delivered before 37 weeks, echoes the spontaneous preterm delivery rate of 58% for gastroschisis babies reported in 1978 (Seashore, 1978). In line with current obstetric

management preferences, Caesarean section was performed only when indicated for an obstetric reason other than the presence of gastroschisis.

The presence of meconium in the liquor is said to be indicative of fetal distress (Impey, 1999). Thus, the high proportion of cases with meconium reported at the time of membrane rupture suggests that gastroschisis babies are prone to fetal distress at delivery. Bile in the liquor is postulated to be associated with intestinal perforation or atresia, yet neither of these was detected in the 3 cases with suspected bile-staining. This reminds us that visual liquor quality assessment at membrane rupture is by no means objective and data collected must always be interpreted with caution.

There is marked improvement in Apgar Scores at 5 minutes (62.6% scoring 9 or 10) compared with those at 1 minute (29.2% scoring 9 or 10). This is a predictable and expected change observed in most babies as they achieve respiratory stability, not just a finding among neonates with gastroschisis. However, a statistically significant difference is apparent between gastroschisis babies in the sample and all babies born in Victoria in 1999-2000 in relation to 5-minute Apgar Scores. That is, the percentage of gastroschisis babies scoring 9 or 10 at 5 minutes (62.6%) is significantly smaller than that in Victorian babies (92.6%). This reinforces the notion that babies with gastroschisis are born with morbidity that extends beyond the mere presence of an extra-abdominal hernia.

The finding of birthweight < 2500 grams in 50.0% of liveborn cases is very similar to the Victorian 1983-98 figures for gastroschisis cases with 56% < 2500 grams at birth (Riley et al., 2000, pp. 91). However, it is difficult to interpret this similarity as again the RWH sample comprises a large proportion of the Victorian gastroschisis cases. Nevertheless, 83.4% of all low birthweight babies in the sample (41.7% of entire liveborn sample) were

also small for gestational age. This highlights the importance of serial growth assessment on USS for detection of IUGR in fetuses with gastroschisis. However, it must be admitted that this is difficult, given the inability of accurately measuring the abdominal circumference in these fetuses, a dimension that is useful when estimating fetal weight.

The high rate of primary surgical closure (87.5%) also mirrors current gastroschisis trends. Interestingly, a high rate of sepsis followed surgery, developing in almost half of all babies (43.8%). This is not unusual; a study by Adra et al. involved 46.6% cases of sepsis (Adra et al., 1996). These infections frequently result from resistant bacterial strains located in hospital. Babies with gastroschisis often remain inpatients for long periods, up to 587 days in the RWH sample, increasing exposure to drug-resistant microorganisms and therefore the risk of sepsis. Statistical analysis suggests that the risk of developing sepsis is not significantly associated with surgery type. That is, in spite of increased exposure of abdominal organs to microorganisms during secondary surgical closure, by virtue of these organs being extra-abdominal for days as they are eased into the abdominal cavity, babies undergoing secondary closure in the sample were *not* significantly more likely to develop sepsis. However, the frequency of secondary closure is small so it is difficult to establish a difference in the rates of infection between the groups undergoing primary and secondary closure. At best, the high sepsis rate observed can serve as a reminder to counsel parents antenatally about this particular complication in babies with gastroschisis. It can, however, be optimistically followed by description of favourable survival rates (usually about 95%), as demonstrated in the sample with all neonates surviving to discharge home.

Duration of TPN is clearly not normally distributed, with mean 49.2 days and standard deviation 80.3 days. This has implications for the method of statistical analysis of TPN.

The spread of TPN values falls into 3 roughly equal groups. Interpreting this distribution, one-third of babies with gastroschisis received TPN for up to 2 weeks, another third ceased TPN within their 3rd postnatal week, and the remaining third received intravenous nutrition for 3 weeks or more. Whilst inferences about this pattern of TPN duration cannot be generalised to the general population of gastroschisis cases, the distribution clearly demonstrates that a vast range of outcomes is apparent for babies with gastroschisis. This is important to consider when counselling parents about the postnatal course of their baby, as duration of TPN is frequently something parents are keen to know. This keenness is well founded in light of the duration between ceasing TPN and discharge home. Within the sample, over 50% of babies had been discharged 1 week after establishing full enteral feeding. Whilst the extreme cases (the infant remaining in hospital for 46 days after ceasing TPN) reinforce the fact that caution must be exercised when predicting postnatal course, this data nevertheless suggests that ceasing TPN is a reasonably good indicator that a baby is fairing well.

As is common, defect side was described as right-sided on antenatal USS in the majority of cases (90.3%). The fact that defect size was not consistently or clearly reported suggests that ultrasonologists attribute little significance to its value, or that measurement is too difficult to reliably obtain given the dynamic nature of the hernia. Certainly, review of the literature reveals no reporting of defect size and no attempts to examine its significance in terms of prognosis. However, if it is indeed possible to reliably measure defect size, its relationship with intestinal necrosis or perforation discovered at surgery might prove interesting for analysis. A smaller defect might constrict herniating bowel, leading to necrosis with the local occlusion of blood supply, or to dilatation and rupture when bowel contents cannot pass through the narrowed lumen at that point. RWH

ultrasonologists could prospectively measure abdominal wall defect size to determine whether it can be related to the postnatal outcome of babies with gastroschisis.

Reporting of bowel wall thickness on antenatal USS was also poor, with measures recorded in only 13 out of 53 cases (24.5%). Whether ultrasonologists deemed unmeasured cases “unthickened”, or whether they failed to recognise bowel wall thickness as a finding worth measuring on USS, is unknown. Review of the literature reveals that past researchers have attempted to investigate the role of bowel wall thickness, although this has usually been a secondary focus. Langer et al. defined “thickening” as a bowel wall measure > 3 mm and analysed its association with days to full oral feeds. Although they noted a trend toward shorter time to feeding in babies with antenatal maximal bowel wall thickness of 3 mm or less, this was not statistically significant at the 5% level (Langer et al., 1993). No such analysis can be reliably performed in this study owing to the small number of reported measures described above.

The occurrence of matting in only 17% of cases does not support the “irritation by amniotic fluid” theory, popular from 1986-1996. Matting should occur in a much larger proportion of cases if amniotic fluid exposure is important, as all gastroschisis hernias bathe in amniotic fluid for the duration of the pregnancy (Dean et al., 1999). Clearly, many questions remain regarding the aetiology and significance of matting.

A statistically significant relationship exists between polyhydramnios on antenatal USS and atresia at surgery. The positive predictive value of 57.1% (4 out of 7 cases) suggests that detecting polyhydramnios is only moderately predictive of having atresia. However, 2 of the 3 cases with polyhydramnios and no atresia had findings that suggest atresia may indeed have been present but “missed” by surgeons (“kinked small intestine” detected on

32-week USS; multiple bowel resections postnatally). This highlights the possible error involved in atresia detection and warns that the positive predictive value may underestimate the strength of the relationship between polyhydramnios and atresia. The high negative predictive value (92.3%) suggests that not having polyhydramnios is highly predictive of having no atresia. The apparent relationship between these parameters fits the physiological theory regarding the aetiology of polyhydramnios in gastroschisis. That is, a blockage in the gastrointestinal tract (such as intestinal atresia) impairs the passage of amniotic fluid through the fetus, increasing the volume of amniotic fluid surrounding it, defined as polyhydramnios when $AFI \geq 20$.

Diagnosis of polyhydramnios involves either the measurement of the single deepest “pocket” of amniotic fluid within the amniotic cavity or the 4-quadrant deepest pocket, procedures that are subject to moderate intra- or inter-observer variability. Thus, it is possible that additional cases of polyhydramnios in the sample may have been missed. Regardless, in spite of the small number of cases with diagnosed polyhydramnios and atresia, the relationship between polyhydramnios and atresia is statistically significant and thus worthy of consideration when managing the fetus with gastroschisis.

The relationship between polyhydramnios and duration of TPN is not statistically significant at the 5% level using Yates’ corrected Chi-Square analysis and the 2-sided Fisher exact test. However, the positive predictive value is high at 80.0% (4 out of 5 cases with polyhydramnios also had $TPN > 21$ days). If the TPN “cut-off” measure of 21 days was lowered slightly to include the single case with polyhydramnios and TPN for 19 days, positive predictive value would improve to 100%. This highlights the major limitation of a categorical approach utilising “cut-off” values. It must be admitted, however, that it is

difficult to analyse such a relationship without categorising data and this may undermine future investigations.

The association between maximal bowel luminal diameter on antenatal USS and finding atresia at surgery is not statistically significant at the 5% level using Yates' corrected Chi-Square and the 2-sided Fisher exact test. However, the negative predictive value is high at 94.1%, with 16 out of 17 "undilated" cases (maximal bowel luminal diameter < 17 mm) having no atresia. Furthermore, the single "undilated" case with atresia has a "borderline" bowel diameter measurement of 16 mm. If the 17 mm "cut-off" was slightly lowered, all cases with atresia would have "dilated" bowel, making bowel diameter a very *sensitive* "test" for the prediction of atresia. Sensitive tests have a high detection rate of cases with a given condition. However, bowel diameter ≥ 17 mm on USS is not a particularly *specific* "test" for atresia, as 71.4% of cases without atresia fall into the "dilated" bowel category (moderately high "false positive" rate). Nevertheless, the findings warrant future investigation of the relationship between bowel dilatation and atresia. Furthermore, polyhydramnios may also be present in cases with "dilated" bowel and atresia, blocked and dilated bowel possibly impairing amniotic fluid transfer to the placenta and thereby increasing AFI.

The relationship between maximal bowel luminal diameter and gestation at its measurement narrowly "misses" statistical significance at the 5% level ($p = 0.06$). This is probably due to small sample size, as a statistically significant relationship would be in agreement with the literature. In 1993, Langer et al. suggested that gestational age influences the degree of bowel dilatation in fetuses with gastroschisis (Langer et al., 1993). Ideally, further investigation with more subjects could be performed to more reliably analyse the relationship. In particular, calculation of the mean gestational age at

which “bowel dilatation” is observed, as well as analysis of patterns of bowel luminal diameter changes over time, could assist obstetricians in their decisions regarding when to deliver these babies.

Before even *considering* early delivery on the basis of “bowel dilatation”, the ultimate significance or definition of such bowel findings on USS, in relation to postnatal outcome, should be determined. In this study, the relationship between maximal bowel luminal diameter on antenatal USS and duration of TPN (a measure of postnatal outcome) was analysed using 3 different statistical methodologies.

The “categorical” approach involved separating cases into “dilated” versus “normal” maximal bowel luminal diameter groups, according to the “17 mm parameter”. As previously explained, 17 mm was identified as a suitable “cut-off” measure on the basis of thorough literature review. Two groups of roughly equal size resulted that were then each further separated according to TPN duration. As described earlier, the decision about TPN categorisation took into account the current RWH advice given to parents regarding TPN duration, as well as the distribution of TPN values in the sample. TPN duration is clearly not normally distributed, as demonstrated in **Figure 3**. Babies were thus categorised according to TPN duration < 14 days, $TPN \geq 14$ days but < 21 days, and TPN duration ≥ 21 days.

Chi-Square analysis suggested that a statistically significant relationship exists between maximal bowel luminal diameter and TPN duration in the sample. That is, babies with bowel diameter measures of ≥ 17 mm were more likely to receive TPN for long periods than were babies with bowel diameter measure of < 17 mm.

Rank Correlation and the Mann-Whitney U test confirm the significance of this relationship. Each takes into account the outlying TPN duration values, a crucial feature to remember when choosing an appropriate statistical test. In fact, findings of non-significance by past researchers analysing similar relationships may be a function of poor selection of statistical tests.

Another downfall in previous attempts to analyse the relationship between bowel dilatation in utero and TPN duration has been small sample size, translating into lack of adequate statistical power. This study compares favourably, with 36 cases eligible for statistical analysis. In fact, it has the largest sample size to date for the analysis of this particular relationship, involving 9 cases more than Adra's 1996 study which has been the forerunner until now, with 27 cases.

Thus, we conclude that antenatal ultrasound scan does offer insight into the prognosis of fetuses with gastroschisis. The results of this study suggest that as the maximal bowel luminal diameter increases above 17 mm, there is trend towards increased duration of TPN. Unfortunately, there is no definitive measurement above which postnatal morbidity can be confidently predicted, or below which parents can be assured of minimal risk. For example, one baby was found to have a maximal bowel luminal diameter of 25 mm yet required TPN for only 12 days. At the opposite extreme, another fetus with maximal bowel luminal diameter of 5 mm subsequently received TPN for 181 days.

On this basis, the significance of these findings alone is not sufficient to warrant preterm (< 37 weeks gestation) delivery of fetuses purely because of "dilated" bowel on antenatal USS. This is contrary to recommendations by researchers such as Haberman, who reported "more favourable outcome" in a fetus delivered prematurely upon detection of

dilated bowel in utero. Whilst the results of our study demonstrate an increased probability of gastrointestinal morbidity with increasing bowel luminal diameter, this does not *prove* that preterm delivery necessarily influences the evolution of the gastrointestinal damage causing that morbidity. Only the results of a randomised controlled trial investigating the impact of preterm delivery on postnatal outcome in fetuses with “dilated” bowel on antenatal USS, could reliably assist obstetricians in the management of gastroschisis-affected pregnancies. As highlighted by Langer et al., premature delivery *might* be advantageous for preventing ongoing bowel damage in utero, but it does introduce the multiple risks associated with prematurity.

However, this does not rule out delivery of fetuses beyond 37 weeks in whom lung maturity has been demonstrated. As documented by Swift et al., delivery at 37-38 weeks gestation carries a reduced risk of complications compared with preterm delivery, as well as reducing exposure to whatever “factor” might be responsible for causing bowel dilatation in utero. Preterm (spontaneous) birth rates of up to 58% remind us, however, that such a recommendation could be redundant among a large proportion of babies with gastroschisis, as many will have already spontaneously delivered by 37 weeks gestation.

Therefore, until further study can demonstrate that preterm delivery decreases the rate of gastrointestinal changes associated with increasing bowel luminal diameter, delivery before 37 weeks is recommended *only* for other indications. At best, the finding of lengthier TPN durations among babies with larger bowel luminal diameters can currently be used to update the information told to parents during antenatal counselling regarding the possible postnatal course of their baby with gastroschisis.

In addition, the statistically significant relationship between polyhydramnios on antenatal USS and finding atresia at surgery warrants further research in this area. In the meantime, surgeons could be informed of the likelihood of increased chance of atresia in babies demonstrating polyhydramnios on antenatal USS and encouraged to look carefully for atresia in these cases.

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Appendix 1

GASTROSCHISIS DELIVERY & NEONATAL OUTCOME DATA SHEET

UR
Mother's Surname
First name
DOB
Address

Study number _____
Baby's name _____ UR _____ Sex M / F
Place of delivery The Royal Women's Hospital, Melbourne, Victoria
Date of delivery ___ / ___ / ___ Gestation _____ weeks
Antenatal complications _____
Antenatal steroids Y / N No. doses _____ Gestation(s) _____

Labour: Spontaneous / Induced (indication) _____
Abnormalities Y / N (details) _____

Delivery: Vaginal Y / N
Additional obstetric tools eg. forceps (details) _____
Elective caesarean (indication) _____
Emergency caesarean (indication) _____
Meconium Y / N Apgars 1min ___ 5min ___ 10min ___ 15min ___
Bile Y / N Intubated at delivery Y / N
Cord blood gas pH _____ pCO₂ _____ pO₂ _____ HCO₃ _____ BE +/- _____
Birth weight _____ g Head circumference _____ cm Length _____ cm

Surgery:

Place of surgery The Royal Children's Hospital, Melbourne, Victoria
Contents of hernia small bowel / large bowel / stomach / gonads / other _____
Character of bowel eg. dilated, thickened, matted, adherent, independent loops

Age at initial surgery _____ hours
Initial surgery type:
Primary closure Y / N If yes, tight or loose closure? _____

Secondary closure Y / N If silo used, for how long? _____
Tight or loose closure? _____
Surgical complications _____

Other anomalies found eg. atresia Y / N (details) _____

Post-operative complications eg. sepsis Y / N If yes, details _____

Additional surgery Y / N If yes, details (age, type, indication) _____

Length of stay in level 3 nursery _____ days
Ventilation Y / N Duration _____ days
Total parenteral nutrition Y / N Duration _____ days
Date commenced total enteral feeding ___ / ___ / ___
Enteral nutrition source eg. formula, breast milk _____
Death within 28 days Y / N If yes, date ___ / ___ / ___
Postmortem Y / N If yes, please attach report
Date of discharge home ___ / ___ / ___ Weight at discharge _____ g

Appendix 1 cont.

**GASTROSCHISIS OBSTETRIC
DATA SHEET**

UR Mother's Surname First name DOB Address
--

Study number _____

Maternal details

Nationality: Caucasian / Asian / Aboriginal / European / African / Other _____

Gravida _____ Para _____ Miscarriages _____ Terminations _____

Previous caesarean section Y / N

Significant obstetric history _____

Significant medical history _____

Smoker Y / N

Vasoconstrictor use eg. ephedrine, cocaine (details) _____

Other drugs (details) _____

Current pregnancy

Date of first antenatal visit ___ / ___ / _____ Gestation _____ weeks

Date of first antenatal ultrasound ___ / ___ / _____ Gestation _____ weeks

Gastroschisis first detected _____ weeks

Date of first RWH antenatal ultrasound ___ / ___ / ___ Gestation _____ weeks

Karyotype: Amniocentesis / CVS / cordocentesis / nil Result _____

Other associated anomalies Y / N (details) _____

Pregnancy termination Y / N

Gestation _____ weeks

Indication _____

Method _____

Complications _____

Post mortem Y / N (if yes, please attach report)

Appendix 1 cont.

**FETAL GASTROSCHISIS
ANTENATAL ULTRASOUND
DATA SHEET**

UR Mother's Surname First name DOB Address
--

Study number _____

Scan number _____

Ultrasound date __/__/____ Gestation _____ weeks EDD __/__/____

Biometry

BPD _____ mm HC _____ mm AC _____ mm FL _____ mm

AFI _____ cm EFW _____ g UA S/D _____

Hernia

Side left / right Defect size _____ mm

Contents small bowel / large bowel / stomach / liver / other _____

Appearance of bowel

Matted Y / N

Thickened wall Y / N (measurement of maximal thickening) _____ mm

Dilated lumen (maximal measurement) _____ mm

Peristalsis Y / N (details) _____

Echogenic bowel Y / N

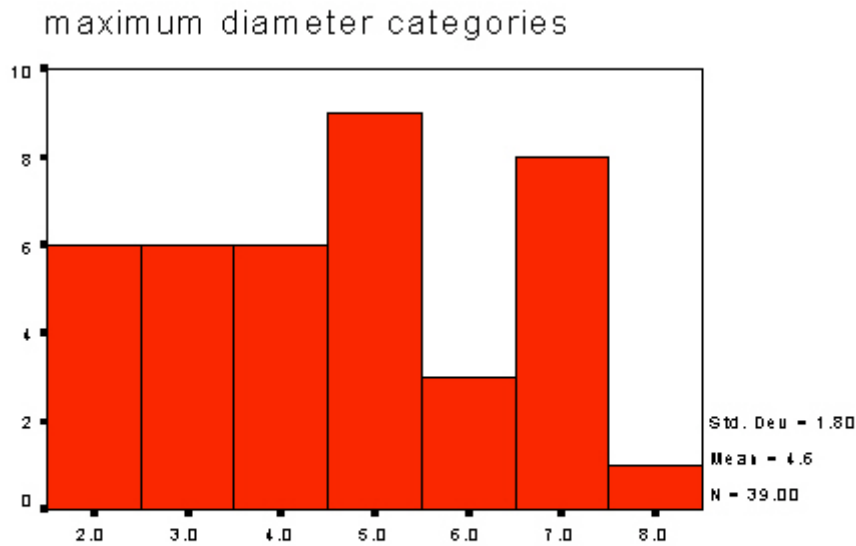
Echogenic material in amniotic fluid Y / N (details) _____

Impending rupture Y / N (details) _____

Other abnormalities

Appendix 2

Distribution of maximal bowel luminal diameter measures



V2MAXCAT

cat1 <=4, cat2 5<=8, cat3 9<=12, cat4 13<=16

cat5 17<=20, cat6 21<=24, cat7 25<=28, cat8 >28

Categories of maximal bowel luminal diameter

Category	Range of max bowel luminal diameter measures
1	0 – 4 mm (no cases)
2	5 – 8 mm
3	9 – 12 mm
4	13 – 16 mm
5	17 – 20 mm
6	21 – 24 mm
7	25 – 28 mm
8	> 28 mm