GASTROSCHISIS IN KWAZULU NATAL

By

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DECLARATION

This is my original work and has not been submitted previously to the University of KwaZulu-Natal or any other University.

Name: J. Sekabira

Signature: _____

DEDICATION

To my dear wife Mariam for her moral support and encouragement.

To my children Kenneth, Keith, Brianna and Bertha for enduring my absence.

To my parents for the prayers and constant encouragement.

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I am deeply grateful to the entire department of Paediatric Surgery for the support, and wise counsel during my training and facilitating completion of this dissertation.

I thank:

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LIST OF ABBREVIATIONS

ABC of resuscitation	Airway, breathing and circulation
AFP	Alpha-feto-protein
ASP	Atrial septal defect
C-section	Caesarian section
GIT	Gastro intestinal tract
IALCH	Inkosi Albert Luthuli Central Hospital
ICU	Intensive Care Unit
NICU	Neonatal intensive care unit
IUGR	Inter uterine growth retardation
NVD	Normal vaginal delivery
PDA	Patent ductus arteriosus
TPN	Total parentral nutrition
TBA	Traditional birth attendant
UDT	Undescended testis

ABSTRACT

Gastroschisis is a full thickness abdominal wall defect, usually to the right of the umbilicus, through which a variable amount of viscera herniates, without a covering membrane. Newborns with gastroschisis present challenging problems to paediatric surgeons. The incidence of gastroschisis is rising worldwide. In developed countries, advances in neonatal intensive care have improved survival of patients with gastroschisis. In the few reported studies from Africa, mortality rates of patients with gastroschisis are high. The aim of this study was to evaluate outcome of gastroschisis from a centre in Africa with modern neonatal intensive care facilities.

Methods: A retrospective analysis of all neonates admitted with the diagnosis of gastroschisis at Inkosi Albert Luthuli Central Hospital (IALCH) over a 6-year period (2002-2007). Proportions in percentages were used for categorical variables. For continuous variables the mean with standard deviation (SD) were derived. Two sampled t-test was used to show the p-value for the time to reduction between the non-survivors and survivors with a 95% confidence interval.

Results: There was a significant increase in the prevalence of gastroschisis among neonatal surgical admissions from 6.2% in 2003 to 15.2% in 2007. There were more females 53.4%, the majority (71.7% had low birth weight and 64.2% were born prematurely. Although 75% (n=79) of the mothers attended antenatal clinic, antenatal diagnosis by ultrasound was made in only 13 (n=12%)). Most of the babies 90.6% were out-born, with 70.8% delivered by normal vaginal delivery (NVD), and 57.4% of the mothers were primiparous. Primary closure was achieved in 73.5% of the patients. The overall mean (SD) time from birth to primary surgical intervention

was 16 (13.04) hours and was higher 17(9.1) hours in those who died compared to survivors 15 (16.0), but the difference was not statistically significant, p=0.4465 and mortality was 43% with sepsis as the leading cause. Staged closure with a plastic silo bag was associated with more than double the mortality as compared to primary closure.

Conclusion: The prevalence of gastroschisis among neonatal surgical admissions has increased in accordance with international trends. Due to lack of antenatal diagnosis, most of the babies were out-born resulting into delay in offering surgical treatment. Mortality is still high despite the presence of modern intensive care.

CHAPTER 1

INTRODUCTION, BACKGROUND , AIMS , OBJECTIVES AND JUSTIFICATION

1.1 INTRODUCTION AND BACKGROUND

A newborn with an abdominal wall defect is one of the most dramatic presentations in medicine and offers challenging problems to the Paediatric Surgeon. Gastroschisis, as one of the presentations of anterior abdominal wall defects, offers even more challenges. Newborns with this condition are usually of low birth weight.[1] The eviscerated bowel, already inflamed by the action of amniotic fluid on the serosa, immensely increases the surface area for fluid losses. There is increased heat loss due to radiation and convection. The bowel, coming out of the abdomen through a narrow defect, is in danger of becoming ischaemic due to oedema and kinking of the mesenteric vessels.

The incidence of gastroschisis has been noted to be increasing worldwide. The cause of this trend is not yet known.[2-8]

The survival rate for gastroschisis has improved markedly in the past 20 years in the developed world. This is attributed to good antenatal services, improved perinatal care of these children, and improvements in post-operative care and life support.[2,4,9-11]

In most of the developing countries, especially in Africa, the mortality associated with gastroschisis remains very high. In some reported series in South Africa, it ranges from 30-

40%. In the rest of Africa mortality can be as high as 100%.[8,12] This is attributed to poor antenatal care whereby the condition is not diagnosed during pregnancy, most of the babies with gastroschisis are delivered outside tertiary hospitals, in some instances by traditional birth attendants (TBAs), they present late and are often hypothermic and electrolyte, and fluid depleted after having been transported to hospital, frequently over long distances without adequate bowel protection. Some patients are septic at presentation and exposed bowel often contaminated.[12]

KwaZulu-Natal Province is home to 10.03 million people and is serviced by 65 State-funded Hospitals (a map of Kwazulu Natal Province with the Health Districts is shown in Figure 5.5). Inkosi Albert Luthuli Central Hospital (IALCH) is the tertiary referral centre for the Province. It was opened in June 2002. Most of the children requiring specialized paediatric care from other hospitals in the Province are referred to IALCH. One study showed that transfer of neonates with surgical emergencies in this region is inefficient and preparation is poor.[13]

The aim of this study was to analyse data sets of neonates who presented with gastroschisis and managed at IALCH between June 2002 and December 2007 (dates inclusive) with the objectives

1. To review the epidemiological characteristics of children with gastroschisis in KwaZulu-Natal.
2 To review the surgical and post operative management of gastroschisis at IALCH.
3. To measure the outcome of gastroschisis at Inkosi Albert Luthuli Central Hospital.

1.2 JUSTIFICATIONS OF THE STUDY

1. The incidence of gastroschisis is increasing worldwide.
2. The out come of children with gastroschisis has improved markedly in the developed world, while it remains poor in the developing countries.
3. There is no published study on the subject from KwaZulu-Natal.
4. Findings of this study might be used in formulating intervention strategies to improve the outcome of children with gastroschisis in KwaZulu-Natal.

CHAPTER 2

LITERATURE REVIEW

Gastroschisis is a full thickness defect in the abdominal wall usually just to the right of a normal insertion of the umbilical cord into the body wall. Rarely is it located in a mirror image position to the left of the umbilicus. A variable amount of intestine and occasionally parts of other abdominal organs are herniated outside through the defect without covering membrane or sac.[2,14,15]

Unlike most other birth defects, reported rates of gastroschisis have increased over the past 25 years from 0.1-1.0 per 10,000 births to 3.0-5.0 per 10,000 births in many developed and developing countries.[3,5,6,16,17] However, this increase is not universal with regional differences in the incidence noted in some regions.[5,18] For example in Italy the rates have remained stable at under 1.0 per 10,000.[18] Furthermore, on the British Isles, the incidence of gastroschisis is markedly higher in the northern regions of the United Kingdom(1.55 per 10,000 total births) than the Southeast (0.72 per 10,000) total births and highest in Wales (6.2 per 10,000 total births.[5,19,20]

In South Africa the incidence of gastroschisis in one series was shown to have increased by 35-fold in the past 20 years.[8]

The speed at which the increase has occurred and the regional differences suggests environmental rather than genetic factors.[18]

The cause of gastroschisis is not known but there is evidence to suggest that it results from an ischaemic insult to the developing abdominal wall.[2,15,21] Another hypothesis that may account for some cases of gastroschisis is that the defect results from an early rupture of a hernia of the umbilical cord.[2,21] All together, the embryological hypotheses that have been proposed are;

1. Failure of the mesoderm to form the body wall.
2. Rupture of the amnion around the umbilical ring with subsequent herniation of bowel.
3. Abnormal involution of the right umbilical vein leading to weakening of the body wall and gut herniation.
4. Disruption of the right vetelline (yolk sac) artery with subsequent body wall damage and gut herniation.
5. Abnormal folding of the body wall resulting in a ventral body wall defect through which the gut herniates, and
6. Escape of the yolk sac and related vetelline structures to be incorporated in the yolk stalk.[22,23]

Gastroschisis has a very strong association with young maternal age, with most of these mothers being aged 20 years or younger.[24-27] In addition, gastroschisis has been linked to maternal exposure to cigarette smoking, illicit drugs and environmental toxins.[15,24-28] These associations are consistent with the vascular insufficiency of the abdominal wall theories for the aetiology of gastroschisis. The most likely cause is early interruption of the fetal omphalo-mesenteric arterial blood supply.[5] A recent large population based case-control study in the United Kingdom found significant adjusted odds ratios for the use of aspirin, vasoconstrictive drugs (ecstasy, amphetamine, and cocaine), history gynecological infection, use of any recreational drug, low body mass index, unmarried status and cigarette smoking.[16]

The overall pattern of findings from all these studies suggests that the risk for having a newborn with gastroschisis is highest in young women, mainly teenagers, with one or more of the following characteristics- have low social economic status, smoke cigarettes, eat too little, drink alcohol, use illicit drugs, have an early unprotected sexual intercourse, and have genital urinary infection.[16,29]

However, recent studies have shown a multifactorial aetiology of gastroschisis involving both genes and environmental factors. A polymorphism of 32 genes representing enzymes involved in angiogenesis, blood vessel integrity, inflammation, wound repair and dermal or epidermal strength has shown to be associated with an increased risk of gastroschisis. Variations, especially of endothelial nitric oxide synthase (eNOS) gene and endothelial cell growth factor (VEGF) gene, have been shown to have a very strong association.[30,31]

The relative risk and pattern of associated anomalies is one of the major differences between gastroschisis and exomphalos.[2,28] Patients with omphalocoele have a very high (up to 50-70%) risk of associated abnormalities. Most of these abnormalities are chromosomal and cardiac. In gastroschisis, the incidence of associated anomalies is between 10-20% and most of the significant anomalies are in the gastro-intestinal tract. About 10% of babies who have gastroschisis have intestinal stenosis or atresia that results from vascular insufficiency to the bowel at the time of gastroschisis development, or more commonly, from later volvulus or compression of the mesenteric vascular pedicle by the narrowing abdominal wall ring. Associated anomalies outside the abdomen or gastro-intestinal tract, such as chromosomal abnormalities, are unusual.[2,32]

2.1 PRENATAL DIAGNOSIS

Abdominal wall defects are often diagnosed by prenatal ultrasound done for routine screening or for obstetric indications such as evaluation of an elevated maternal serum alpha-feto-protein (AFP). Prenatal ultrasound is done for almost all pregnancies in the developed world. It identifies the majority of abdominal wall defects and accurately distinguishes gastroschisis from exomphalos. The identification presents an opportunity to counsel and prepare optimum perinatal and postnatal care.[2,33]

The accuracy of prenatal ultrasound in diagnosing anterior abdominal wall defects is affected by the timing and goals of study, foetal position and the experience and expertise of the operator. The specificity is high (>95%) but sensitivity is only 60–75% for identifying gastroschisis and exomphalos.[34]

Diagnostic error may result because of:

1. Confusion with other rare abdominal wall defects.
2. Ruptured exomphalos that mimic gastroschisis.[34,35]

Serial Ultrasound scans have also been found useful in follow up of foetuses already diagnosed with gastroschisis to determine the timing and mode of delivery. Preterm delivery can be indicated in cases of excessive peel formation to prevent further bowel injury.[36]

2.2 PRENATAL MANAGEMENT

A foetus with an abdominal wall defect is a high risk pregnancy on many levels. For gastroschisis there is an increased risk of intra-uterine growth retardation (IUGR), foetal death and premature delivery, so careful obstetric follow-up is indicated.[2,37] There is still some

controversy regarding the timing and mode of delivery, but it is generally agreed that mothers with a prenatal diagnosis of anterior abdominal wall defect should deliver in a tertiary care facility which can handle the delivery and manage the newborn as appropriate, including surgery.[2,33,36,37]

2.3 NEWBORN MANAGEMENT

The initial management of newborns with gastroschisis starts with the ABC of resuscitation, after which attention is turned to the abdominal wall defect.[2,33,38] These babies in particular have high fluid losses from evaporation and third space losses and may require twice the maintenance volumes of fluids to maintain an adequate intravascular volume. A bladder catheter is passed to closely monitor urine output and guide the resuscitation. A nasogastric tube is passed for gastric decompression. Serum glucose levels are checked and maintained. Broad spectrum prophylactic antibiotics are started.[2,37]

When the ABCs have been accomplished the abdominal wall defect can be assessed and treated. The exposed viscera are inspected avoiding twisting of the mesenteric vascular pedicle and then covered, or wrapped with plastic. The entire mass is stabilized by placing the baby with its right side down to prevent kinking of the mesenteric pedicle.[2]

2.4 SURGICAL MANAGEMENT

In gastroschisis, the ongoing fluid and heat losses of exposed bowel and the subsequent metabolic derangements make rapid coverage a high priority.[39]

In many centers in Europe and North America, during the initial resuscitation at delivery or as soon as possible thereafter, a prefabricated spring-loaded silastic silo is placed in the defect to cover the exposed bowel. This minimizes evaporative losses, prevents additional trauma and allows for on-going assessment of bowel perfusion.[2,9]

Abdominal wall closure can be done by primary or staged repair with a silastic silo.

Immediate primary repair without anaesthesia has been reported for selected cases.[38] There also are reports of using plastic haemoderivative bags in the treatment of gastroschisis.[39] With spontaneous diuresis, gastrointestinal tract decompression from above and below and resolution of bowel wall oedema, the volume of the exposed bowel in the bag markedly reduces in a short period of time.

When the baby is otherwise stable and the spontaneous reduction of bowel into the abdomen has reached a plateau, the baby is taken to theatre for an attempt at delayed primary closure.[2,10,11] The decision whether a baby can tolerate reduction and repair can be aided by measuring the intra-gastric pressure, changes in the central venous pressure, in ventilatory pressures, intravesical pressure and end tidal CO_2.[2,40,41]

In cases of associated intestinal atresia, the first priority is to close the abdomen by primary, delayed primary or staged silo repair. The baby is maintained with gastric decompression and TPN for several weeks until repeat laparotomy and repair of the intestinal atresia.[2]

2.5 OUTCOMES

The outcome of patients who have gastroschisis depends largely on the condition of the vulnerable bowel and to some extent on the condition of the child. Overall, patients who have gastroschisis have an excellent prognosis – survival reaching 90-95% in the Western World.[2,10,33,38]

In the developing countries the prognosis varies. In some countries mortality can be as high as 100%. This is mainly due to the absence of prenatal diagnostic facilities leading to births with unrecognized gastroschisis and late presentation of patients with gastroschisis to a tertiary health facility, or, on the other hand, there are no intensive care facilities like TPN and ventilation, which are necessary for proper management of these patients.[8, 12]

CHAPTER 3

MATERIALS AND METHODS

3.1 STUDY DESIGN

This was a retrospective analytical study of consecutive data sets of patients admitted to Inkosi Albert Luthuli Central Hospital with gastroschisis.

3.2 STUDY POPULATION

All children admitted to IALCH with gastroschisis were included in the study.

3.3 STUDY VARIABLES

Children and mothers' epidemiological characteristics, place and mode of delivery, associated abnormalities, surgical procedure, mortality and causes of death thereof.

3.4 DATA COLLECTION AND STATISTICAL ANALYSIS

IALCH is a fully computerized hospital .All patients records are entered on the computer and the department of paediatric surgery maintains a database of all patients admitted and managed by the department. From this database records of patients with gastroschisis were retrieved and entered into a structured questionnaire and then captured into dataset with the help of a statistician using a foxpro software, and was cleaned for consistency. Continuous variables were categorized into two or more levels for easier analysis obtaining mean with standard deviation and median. For categorical variables, proportions were calculated and expressed in percentages. Two sampled t-test with unequal variances was used to calculate the p- value between the time

to reduction for those who died and the survivors and was considered significant when the p-value was less than 0.010 with 95% confidence interval.

3.5 STUDY LOCATION

The study site was in The Department of Paediatric Surgery, IALCH.

3.6 LIMITATIONS OF THE STUDY

As in all retrospective studies, not all the necessary information was available in all the patient records retrieved.

3.7 ETHICAL CONSIDERATIONS

1. Names of patients did not appear on the data sheet.
2. Permission to carry out the study was first sought from the Faculty of Health Sciences, University of KwaZulu-Natal Ethics Committee.
3. Co-operation from colleagues in NICU.

CHAPTER 4

RESULTS

Records of 106 patients admitted with gastroschisis over a six year period (2002-2007) were retrieved.

Table 4.1. Surgical neonatal admissions and patients with gastroschisis seen by year (2002-2007) at IALCH.

Year	Neonatal admissions	Patients with gastroschisis
2002	97	8
2003	191	12
2004	209	18
2005	189	14
2006	194	21
2007	217	33

From 2002 to 2007, there was a gradual increase in neonatal surgical admissions and the number of patients with gastroschisis seen.

There were fewer neonatal admissions in 2002 as the hospital opened in the middle of the year.

Table 4.2. Epidemiological characteristics of children seen with gastroschisis.

Children characteristics	Number	Proportions (%)
Sex		
Female	57/106	53.4
Male	49/106	46.6
Birth weight (kg)		
Normal (> or = 2.5)	30/106	28.3
Low (<2.5)	76/106	71.7
Mean (SD)	2.24 (0.41)	
Median (IQR)	2.2 (2.0-2.5)	
Gestation age (weeks)		64.2
<37	68/106	35.8
37-40	38/106	
Mean (SD)	36.4 (2.76)	

There were more female babies with gastroschisis (53.4 %). 71.7% of the babies were of low birth weight (less than 2.5 kg), mean (SD) 2.24 (0.41), and 64.2% were of low gestation age, less than 37 weeks, mean (SD) 36.4 (2.76).

Table 4.3. Delivery.

	Number	Proportion (%)
Place of Delivery		
Outborn	96/106	90.6
In-house	10/106	9.4
Mode of delivery		
C-section	31/106	29.2
NVD	75/106	70.8
Distance to IALCH		
Within 2 hours	35	39.8
More than 2 hours	53	60.2

Majority of the patients with gastroschisis n= 96 (90.6%) were born outside IALCH before referral. Only 10 (9.4%) were born in-house.

Majority n=75 (70.8%) were by NVD. There were no indications in the records for the C-section. Out of 96 babies born outside IALCH, the approximate time taken from respective places of delivery was obtained for 88 patients from the Ambulance services. Distances were given by approximate time it takes by road for the ambulance crew to reach IALCH from the respective referring hospital. The distance was categorized into 2 groups; within 2 hours and more than 2 hours. Majority of the babies n=53 (60.2%) were born at distances of more than 2 hours.

Table 4.4. Mothers' characteristics.

Mothers' characteristics	Number	Proportions (%)
Age in years		
Less than 19	23/68	22.8
20-24	30/68	44.1
24-40	15/68	22.1
Parity		
Primiparous	39/68	57.4
Multiparous	29/68	42.7

Records on mothers' characteristics could be obtained from 68 files.

The s light m ajority n =30 (44.1%) w ere i n t he a ge br acket 20 -24 years. A lso pr imiparous (57.4%) were more than multiparous (42.7%).

Table 4.5. Associated Abnormalities.

Associated anomaly	Number of cases
Cardiac	
PDA	4
ASD	5
Dextrocardia	1
Chromosomal	
Downs	8
Trisomy-18	2
Trisomy-13	1
Genito-urinary	
Bladder exstrophy	1
Bifid scrotum	3
UDT	3
Hydronephrosis	1
GIT	
Small bowel atresia	4
Small bowel volvulus	3
Skeletal	
Microcephaly	1

There were 37 associated anomalies recorded in 32 patients. Some of the patients had more than one anomaly. Extra GIT anomalies were found in 25 patients (23.5%).

Chromosomal abnormalities were n=11 (9.4%) with 8 having Down's syndrome, 2 trisomy-18 and one with trisomy 13. Of the 8 patients with Down's syndrome, one had a PDA, one had ASD and another one had hydronephrosis. One with Trisomy-13 had PDA plus ASD and dextrocardia. Treatment was discontinued in the 3 patients with trisomy 18 and 13.

GIT anomalies were recorded in 7 patients (6.6%). All those babies with small bowel volvulus the bowel was necrotic by the time of admission. One died before surgical intervention, two had bowel resection but treatment was withdrawn as the remaining bowel was too short to sustain life.

Table 4.6. Antenatal diagnosis.

	Number	Proportions (%)
Antenatal clinic		
Attendance	79/106	75
More than once	20/106	18
Antenatal ultrasound scan		
Done	22/106	21
Diagnostic	13/106	12
Antenatal diagnosis and in-house delivery	9/10	90
Antenatal diagnosis and Caesarean section	9/13	69

Seventy nine (75%) of the mothers attended antenatal clinic with n=20 (18%) attending more than once.

Ultrasound scan was done in n-22 (21%) of the mothers and was only diagnostic in n=13 (12%).

Nine out of the ten in-born babies (90%) had antenatal diagnosis with ultrasound and all of them were delivered by Caesarean section, contributing 69% of all the Caesarean sections.

The indications for Caesarean section was recorded in only 4 cases: placenta praevia in 3 and foetal distress in 1.

Table 4.7. Surgical procedure.

Procedure	Number	Proportions (%)
Primary closure	67/102	65
Staged repair with a silo	30/102	28.3
Ward reduction	9/102	8.5

Primary closure was achieved in n=67+9 (73.5%) of the cases. Staged repair with initial plastic silo was done in n=30 (65%) of the patients. This was when safe primary closure was possible in those newborns because of the disproportion between the volume of exposed viscera and the size of abdominal cavity. The defect is extended both cranially and caudally and the intravenous fluid bag is fixed with a continuous suture on the muscle-aponeurotic plane. The skin is left intact and umbilicus preserved. The infant is then transferred to ICU on ventilatory support and TPN. Serial reduction by gentle compression on the bag, a rolling fixed spatulas is started on day 2 post-surgery, allowing the viscera into the abdominal cavity. After 5 to 7 days, the baby is taken back to theatre for abdominal wall closure. In some cases it is not possible to close the abdomen and a decision is made to apply a goretex patch.

Nine of the patients had primary closure in the ward (in ICU, high care and obstetric theatre) under local anaesthesia. No mention in the records of whether sedation was used but all had a nasal gastric tube and the bowel evacuated before reduction.

Four out of the 106 patients did not require surgery: 1 had Trisomy 18 and it was decided to withdraw treatment, 3 had already necrotic bowel on arrival (1 of whom had primary surgery from a peripheral hospital).

4.1 MORTALITY

Overall mortality was n= 46 patients out of the 106 patients (43%).

Table 4.8. Causes of death.

Condition	Number of cases	Proportion dead (%)
Sepsis	22/46	48.0
Necrotic bowel	9/46	19.5
Abdominal compartment	3/46	6.5
Chromosomal anomalies	3/46	6.5
Intractable hypothermia	2/46	4.7
No cause found in records	7/46	15.0

The commonest recorded cause of death was sepsis in n=22 (48%) out of which 7 died from TPN-related sepsis.

Necrotic small bowel was the cause of death in 9 patients, 3 of whom arrived with already necrotic bowel and no surgical treatment was given, 2 died on the table during surgery and 3 were sent back to the original hospitals after extensive resection of the dead bowel.

Abdominal compartment syndrome and chromosomal anomalies were recorded in 3 cases respectively.

In 7 of the cases (15%), no cause was found in the records.

Three out of the five babies who developed abdominal compartment syndrome after abdominal wall closure were taken back to theatre and a silo plastic bag was stitched to the fascia to relieve the pressure. They developed sepsis after and died.

Table 4.9. Surgical procedure and mortality.

Procedure	Number	Death	Mortality rate (%)
Primary closure	63	18	28
Staged repair	30	18	63
Ward reduction	9	5	55.5
Total	102	42	100

Mortality was highest among babies who underwent staged repair (63%), more than double the mortality for primary closure (28%). Also, those babies who underwent ward reduction had a higher rate of mortality (55.5%).

Table 4.10. Comparison of birth weight and gestation age for dead and survivors with a positive antenatal ultrasound.

Total (n=13)	Dead (n=7, 54%)	Survivors (n=6, 46%)
Mean birth weight (kg) Mean gestation age in weeks	1.98 33.7	2.37 37.0

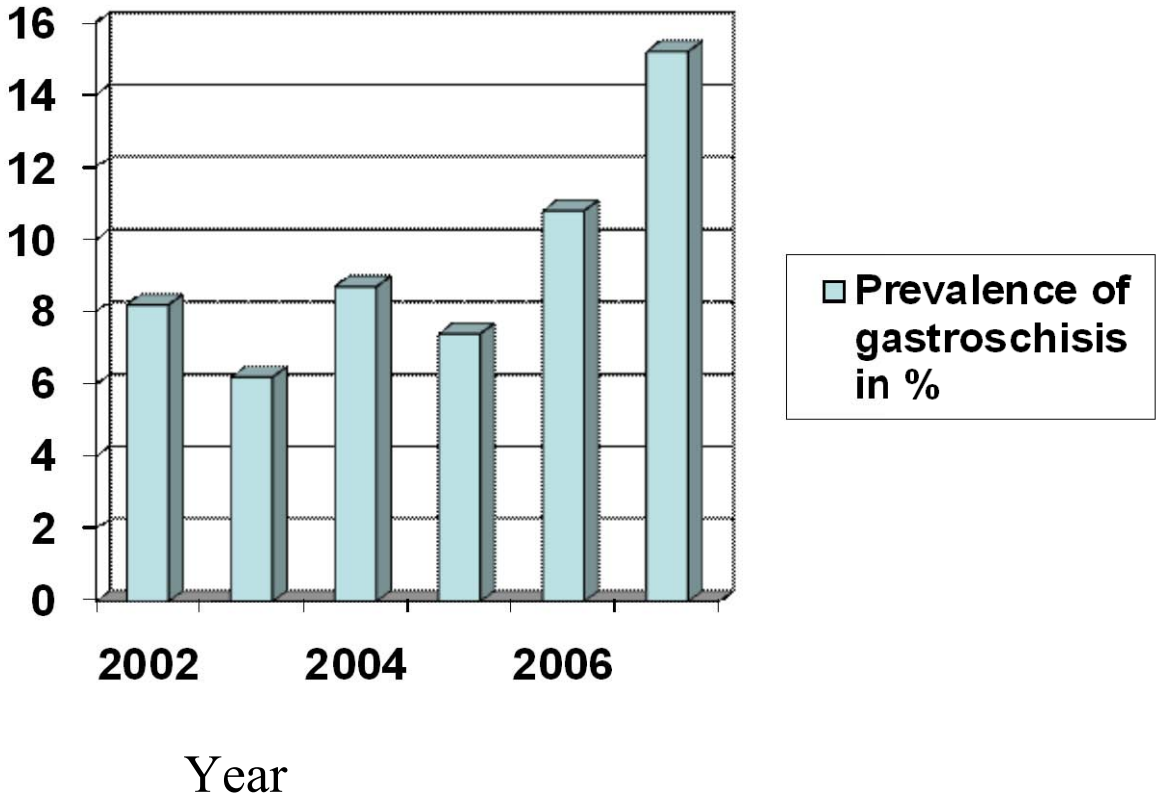
Seven out of the 13 patients (54%) with a positive antenatal ultrasound died. All were in-born and were delivered by Caesarean section with a mean birth weight of 1.98 kg and mean gestation age of 33.7 weeks as compared to the survivors (n=46%) with mean birth weight of 2.37 kg and gestation age of 37 weeks.

Table 4.11 Comparison of time to reduction (ie. time from birth to primary surgery) for dead and survivor patients.

Group	Number	Mean Time to reduction	Standard Deviation(SD)
Alive	57	14.94	16.0
Dead	40	16.98	9.14
Combined	97	15.95	13.04

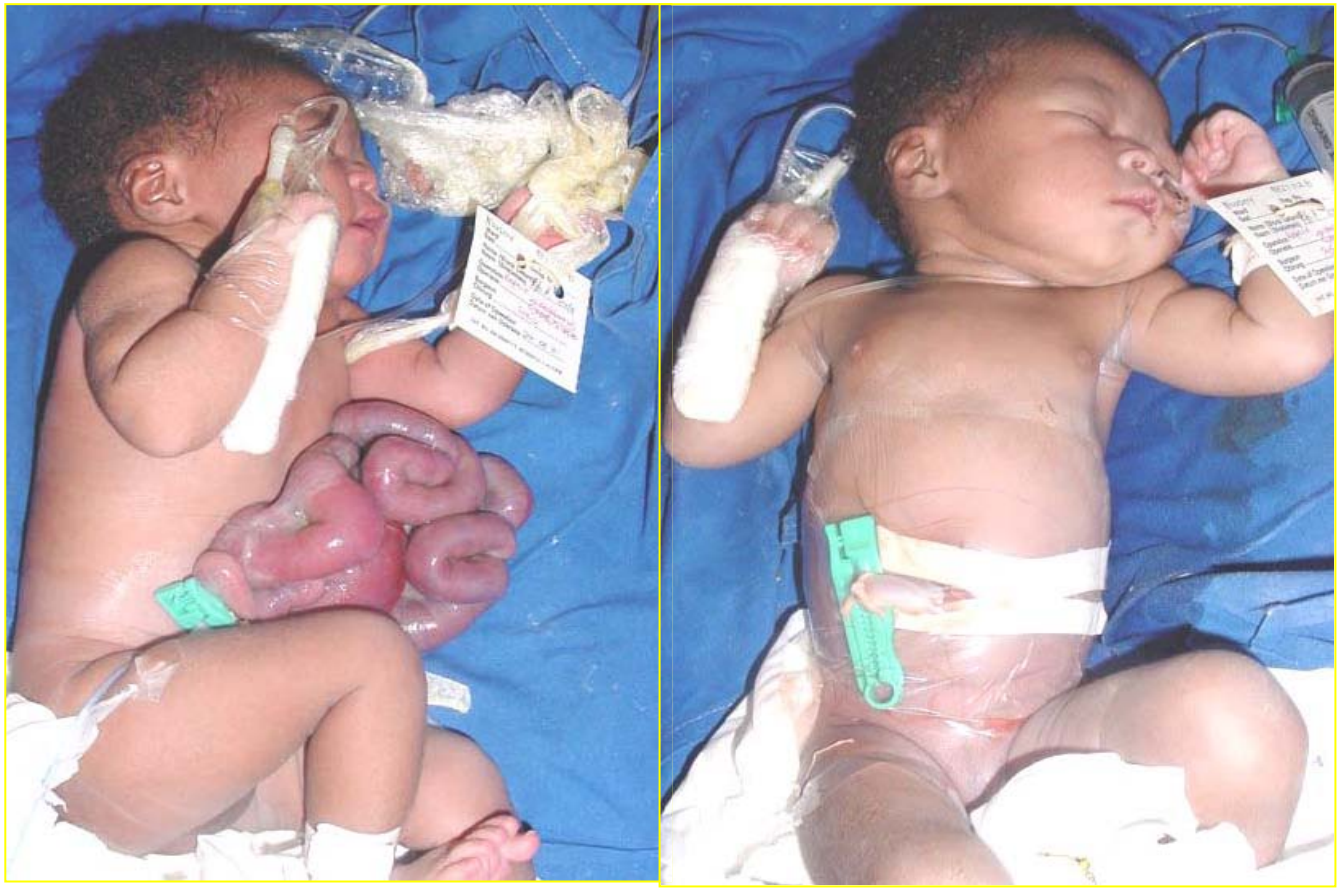
The overall mean (SD) time to reduction i.e. time form birth to primary surgical intervention, was about 16 hours (13.04). It was higher among those who died 17 (9.1) compared to the survivors 15 (16), but the difference was not statistically significant, p=0.4465.

Figure 4.1. Prevalence of gastroschisis among neonatal surgical admissions.



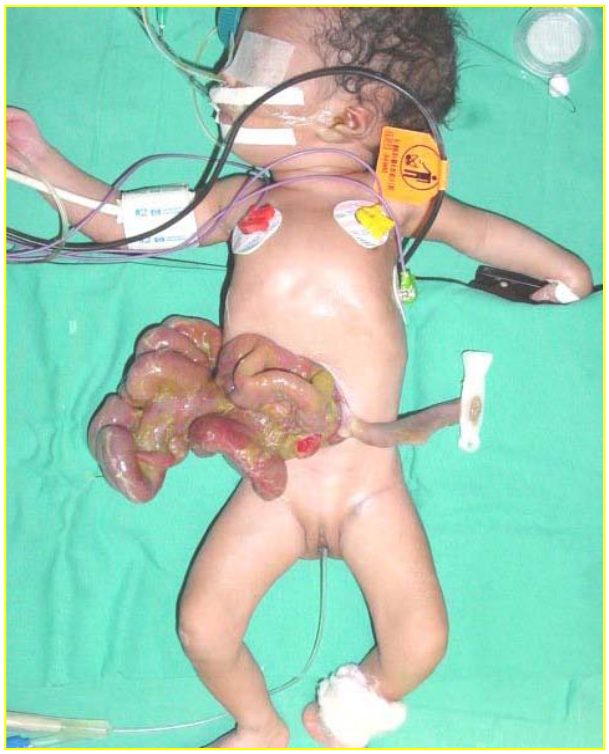
The prevalence of gastroschisis among neonatal surgical admissions more than doubled from 6.2% in 2003 to 15.2% in 2007. It was not possible to get the prevalence of gastroschisis per live births as it would require collecting data of all births from the entire province.

Figure 4.2 Newborn with gastroschisis before and after primary reduction.



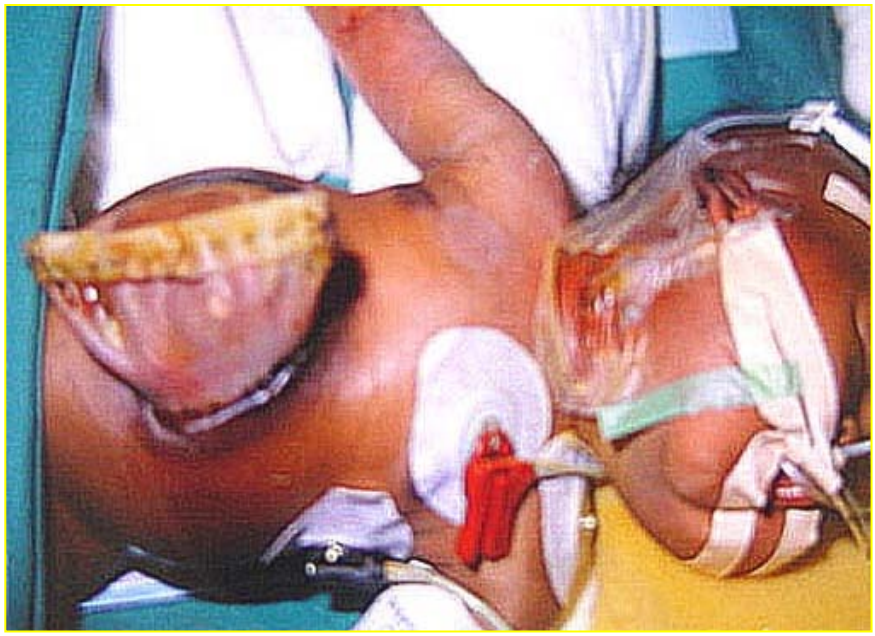
A baby with gastroschisis, in-born, birth weight 3.2 kg. The bowel loops were dilated but not thickened.

Figure 4.3 Picture of another newborn with gastroschisis before undergoing staged reduction.



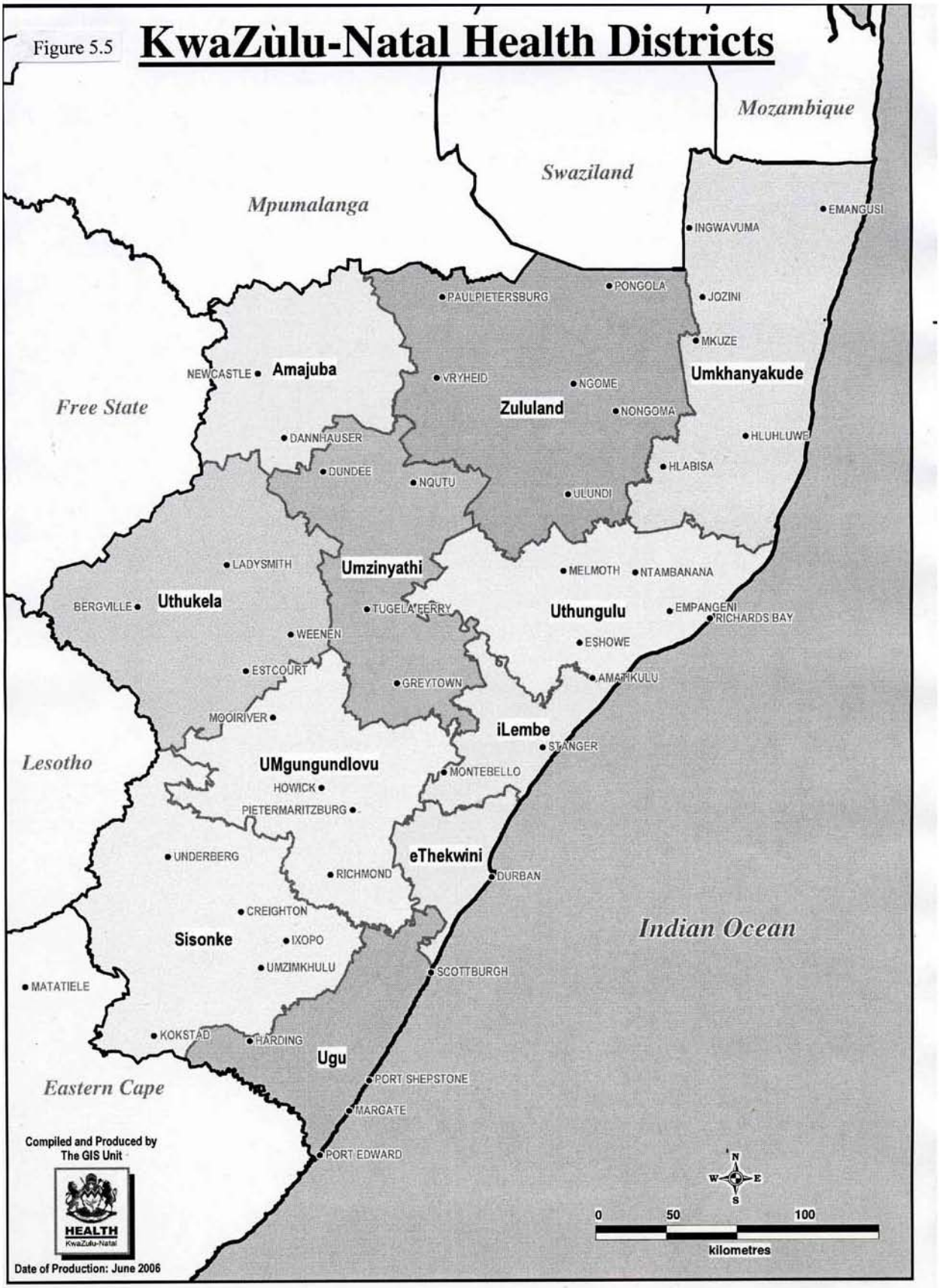
Another baby with gastroschisis, out-born, birth weight 2.25 kg. Note the thickened bowel, covered with a peel. Primary reduction was not possible.

Figure 4.4 Picture of a baby with gastroschisis with a plastic silo almost ready for secondary closure.



A baby with gastroschisis who underwent staged repair with a plastic silo bag. The bowel in the bag was gradually reduced by serial tightening on the bag, then after secondary repair was done.

Figure 5.5


KwaZùlu-Natal Health Districts
Mozambique
Swaziland
Mpumalanga
Free State
Lesotho
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Indian Ocean
EMANGUSI
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PAULPIETERSBURG
JOZINI
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NEWCASTLE
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VRYHEID
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DANNHAUSER
DUNDEE
NQUTU
HLABISA
ULUNDI
LADYSMITH
Umzinyathi
MELMOTH
NTAMBANANA
BERGVILLE
Uthukela
TUGELA FERRY
Uthungulu
EMPANGENI
RICHARDS BAY
WEENEN
ESHOWE
ESTCOURT
GREYTOWN
AMATIKULU
MOOIRIVER
iLembe
STANGER
UMgungundlovu
MONTEBELLO
HOWICK
PIETERMARITZBURG
UNDERBERG
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RICHMOND
DURBAN
CREIGHTON
Sisonke
IXOPO
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SCOTTBURGH
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CHAPTER 5

DISCUSSION

Worldwide, there has been a rising incidence of gastroschisis over the last 2 decades.

In this study, there was a four fold increase in the number of patients with gastroschisis at IALCH during the six year period (2002-2007) from 8 to 31 patients and the prevalence of gastroschisis among neonatal admissions more than doubled from 6.2% in 2003 to 15.2% in 2007. Although this is not a population based study to analyse the true prevalence per live births, it reflects an increase in the incidence of gastroschisis in the babies referred from the province to IALCH with surgical conditions. Amongst other factors which could have contributed to this increase could be improved awareness, better transport and referral systems. Nonetheless, several studies have noted an increase in the incidence of gastroschisis among surgical admissions.

Sharp *et al* [4] in Western Australia showed that the incidence of gastroschisis doubled for the period 1986-1988 and 1995-1996.

In the United States, Jona *et al*[10] reported a mini epidemic in their centre with an 8-fold increase in the incidence of gastroschisis in one year and pointed out that it is the observation throughout the rest of the country.

In Europe, Colzorali *et al* [42] Eurocat working group, in a survey of three million 1980-1990, reported an increased incidence of gastroschisis.

The International Clearing House of Birth Defects Surveillance and Research (ICBDSR) reported that fourteen registries showed a significant increasing temporal trend of gastroschisis worldwide. This trend is however not universal. For example, in Italy four regional birth registries have not seen any increase in the incidence of gastroschisis in the past 25 years.[17]

Baerg *et al*[6] reported an increase in the incidence of gastroschisis from 1.85 in 1985-1990 to 3.60 in 1991-1995 to 4.06 in 1996-2000.

The UK chief medical officer has expressed concern about the rising incidence of gastroschisis and has highlighted the importance to public health of rigorously compiled and centrally funded regional registries in providing information on congenital anomalies.[3]

Recent data from the British Isles Network of Congenital Anomaly Registries (BINOCAR) confirm the increasing incidence of gastroschisis from 2.5 per 10,000 total births in 1994 to 4.4 per 10,000 in 2004, with Welsh register indicating an incidence of 6.2 per 10,000 total births.[5]

The increased prevalence is unlikely to be explained by a systematic shift in the classification of abdominal wall defects.[5] The speed at which the increase has occurred and the observed regional differences suggests environmental rather than genetic risk factors.[18]

However most studies, like some quoted above do consider the prevalence of gastroschisis among live births, not considering still births which could probably show a higher figure.

As mentioned above, this study only considered the incidence of gastroschisis among neonatal surgical admissions. A prospective population based study to analyse the prevalence among the live births and still births is therefore recommended.

In this present study, there were more females, 53% (n=57), compared to males. Other studies have reported no universal sex predilection, with some reporting more males, while others reporting more females. In all, the difference is not high. In Zaria Teaching Hospital, Nigeria, Ameh *et al*[12] reported a M:F = 1.8:1. Novotny *et al*,[9] Northern Ohio Universities College of Medicine, Akron, reported no sex predilection, while in the series reported by Jona *et al*[10], majority of the babies were boys. Olisevich *et al*,[41] in Cleveland, US in their series reported a female preponderance with 62% females and 38% males.

Majority of the babies with gastroschisis 71.7% (n=76) were of low birth weight (less than 2.5kg, mean-2.24). Most studies report a similar observation.[10,12,32,33,42,43] This is attributed to prematurity of most of the patients and the intrauterine growth retardation. Worse outcomes can be anticipated in low-birth weight and preterm neonates with gastroschisis.

Most of the babies in this study, 64.2% (n=68) ,were of low gestation age, less than 37 weeks, mean (SD) 36.4 (2.76). Ameh[12] in Nigeria had a series of 16 infants with gastroschisis and none was a premature, but had low birth weight (mean of 2.1 kg). In their series, Zamakhary *et al*[44] reported 59% of the children with gastroschisis having a mean gestation age 36.2, and this was associated with complications. In Illinois US, Jona *et al*[10] reported a mean gestation age of 37 weeks in a series of 16 babies with gastroschisis. The problems associated with prematurity are many, and when this is in a baby with gastroschisis further compounds the grim picture. Most prematures have pulmonary hypoplasia and are prone to hypoglyceamia and hypothermia. All

these factors put the baby at a higher risk and management of gastroschisis more difficult with poorer outcome.

A body of medical literature suggests that prenatal diagnosis, antenatal transfer, and delivery in a regional centre favourably impacts on the postnatal outcome of babies with gastroschisis.[45,46] In this study, only 10 babies (9.4%) with gastroschisis were born in-house, while the majority n=96, 90.6% were born outside IALCH. The distance in the majority of the cases n=53 (60.2%), was more than 2 hours to the referral centre. This is the trend in most of the developing countries and has a big bearing on outcome.

In the series of 16 patients, in Nigeria reported by Ameh *et al*, [12] most the deliveries were done by traditional birth attendants (TBA) in rural areas, very far from the referral centre. They presented late, and were often hypothermic and electrolyte- and fluid-depleted after having been transported to hospital, frequently over long distances with inadequate protection. Some patients were septic at presentation and exposed bowel was often contaminated. The median time at presentation was 24 hours (range 7 hours to 5 days).The situation is not different in most of tropical Africa.

In developed countries the picture is different. Most of the patients with gastroschisis are in-born and neonatal transport and referral to a tertiary hospital are avoided.

Driver *et al,*[40] in Manchester St. Mary's hospital while analyzing the influence of delay in closure of abdominal wall on out come in gastroschisis, in a series of 91 patients an antenatal

diagnosis of gastroschisis was made in 89 (97%) of cases, 81 (89%) were delivered "in house", and surgical intervention occurred at a median of 4.0 hours post delivery.

In Illinois US, in the series of 16 patients reported by Jona *et al*,[10] only 2 babies were out born.

Most of the babies n=75 (70.8%) were delivered by normal vaginal delivery (NVD) and only 29.2% were by C-section. Most studies report a similar observation. There is no reported benefit of delivery by C-section. Quirk *et al*[11] observed that C-section is associated with poor outcome. Preterm C-section is only indicated when "peel" formation is confirmed on follow up US scans antenatally after ensuring lung maturity.[36]

In the present study only 33.8% (n=23) were under 19 years, majority 44.1% (n=30) being in the 20 -24 years age bracket, although majority (57%) were pr imiparous. This is s lightly different from what is reported in studies from developed countries, where majority of the mothers are young, below 19 years.[6,20,21,44] The consistent risk factors shown, in all the epidemiological studies, for having a child with gastroschisis, is young maternal age. One European study found that compared to with mothers aged 25-29, the relative risk was 7.0 (95% confidence interval 5.6 to 8.7) for mothers under 20 and 2.4 (2.0 to 3.0) for mothers aged 20-24 years.[27]

Other characteristics mentioned are; low social economic status, cigarette smoking low body mass index, alcohol consumption, use of illicit drugs, having early unprotected sex and genitourinary infection especially Chlamydia trachomatis.[16,29] The correlation with young

maternal age and these risk factors, perhaps in combination with other environmental exposure and genetic susceptibility may explain the increased frequency of the defect in many countries.

Although n= 79 (75%) of the mothers attended antenatal clinic, with records showing 18 % attending more than once, antenatal ultrasound was recorded as having been done in only 21% 22 (21%) of the expectant mothers and was diagnostic in a mere 13 (12%).

Antenatal ultrasound scan can potentially identify majority of anterior abdominal wall defects and distinguish omphalocoele from gastroschisis. This identification would permit an opportunity to counsel the family and prepare optimal postnatal care.[2] It is unfortunate however that it is user-dependant and is affected by the timing of the study and experience of the operator. It has a high specificity (>90%) but the sensitivity is only 60-70%.[2,46] Despite that most studies in Europe report a correct antenatal diagnosis of gastroschisis by ultrasound in 90-100% of cases.[9,40,47] It is evident that there is a potential for improvement of the learning curve by the technician in this region so that more antenatal ultrasound scans are diagnostic to plan optimal delivery. Retraining workshops and apprenticeship under experienced sonographic technicians can be of help in this aspect.

Unlike most of studies, where only gastrointestinal anomalies are reported to be associated with gastroschisis, in this study a number of extra gastrointestinal anomalies were found as seen in Table V. In the series by Murphy *et al*,[43] and Ameh *et al*,[12] all the children with gastroschisis had no extra GIT anomalies. In Thailand, Surasak Sangkhathat *et al*.[48] reported 16 cases (23.5%) with associated congenital anomalies, among these, 7 were confined to the gastrointestinal tract. There was no mention what extra gastrointestinal anomalies the rest of the 9 cases had. Novotny

et al[9] reported associated anomalies in 26% of the series of 69 patients, majority were intestinal atresia, volvulus and/or undescended testis.

The incidence of associated anomalies in gastroschisis is reported to be 10-20%, and most of them are in the GIT. Serious associated anomalies outside the abdomen, such as chromosomal abnormalities are unusual.[2] In this study however, serious cardiac and chromosomal anomalies were encountered, which had a bearing on outcome. A baby with a dextrocardia plus ASD died, and treatment was withdrawn in those with trisomy 18 and 13, they were sent back to the respective referring hospitals to die near home.

Primary closure of the abdominal wall is the treatment of choice in the management of gastroschisis.[47] However, due to the disproportion between the herniated bowel and abdominal cavity, in some patients primary closure is not always possible. In such cases an option of staged repair with a silo fixed to the fascia is taken.[2,39] This prevents development of abdominal compartment syndrome. The decision of whether a baby can tolerate reduction and primary repair can be taken by measuring intragastric or intravesical pressures, mean air pressure, or end tidal CO_2.[2,41]

Staged repair with a silo is associated with numerous complications. Babies managed by this procedure spend longer periods on ventilatory support and TPN and are more prone to developing septic complications. In this study primary closure was achieved in 73.5% of patients (including those who had ward reduction. Most studies report similar primary closure rates.[10,40,41,47] Unfortunately, some patients developed abdominal compartment syndrome and had to be taken back to theatre to open up the abdomen.

The overall morality was 45 out of 106 patients (43%). This high mortality is typical for most of Africa. For example, Arnold *et al*.[8] reported a mortality rate of 38.7% and in Nigeria Ameh *et al*.[12] had a mortality of 71.4%. In contrast, researchers from developed countries all report comparatively very low mortality. In the United Kingdom, Driver *et al*.[40] reported a 7.7% mortality in a series of 91 patients, while Baerg *et al*.[6] reported a survival rate of 93% in 71 patients, and Novotny *et al*.[9] reported mortality of 4.3% in 69 patients.

Most of the improvement in outcome of patients in developed countries is attributed to antenatal diagnosis, *in utero* transfer to a tertiary centre, planned in-house delivery, early referral and proper neonatal transport for out-born babies, refinement in surgical techniques and advances in intensive care and TPN.[2,12,47] In this study, antenatal diagnosis was only made in 12% of the patients. In Nigeria only 2 mothers out of 14 ever attended antenatal clinics. Most of the babies were delivered at home by TBA's, while in the United Kingdom, Driver *et al*.[40] reported that antenatal diagnosis was made in 97% of cases and 89% were delivered in-house with a subsequent mortality of 7.7%.

Another observation made in this study is that in those 13 patients where an antenatal ultrasound was diagnostic, 7 (54%) died and 6 (46%) survived. All those who died were delivered by Caesarean section with a mean birth weight of 1.98 kg and mean gestation age of 33.7 weeks as compared to the survivors with mean birth weight of 2.3 kg and gestation age of 37 weeks. This implies that there was a tendency for preterm Caesarean section after an antenatal diagnosis of gastroschisis. There were earlier reports suggesting that preterm Caesarean section minimizes the effects of amniotic fluid on bowel serosa with less peel formation.[49] However, recent studies have shown no benefit from preterm delivery.[36] The complications of prematurity far

outweigh the presumed benefits. It is now common practice to deliver all those babies with antenatal diagnosis of gastroschisis at term. There is a need for collaboration between the obstetricians and the paediatric surgeons to decide the timing and mode of delivery.

Sepsis in this study was found to be the commonest cause of death n=20 (50%), of which 7 succumbed to TPN related sepsis. Other causes recorded were small bowel necrosis, abdominal compartment syndrome and chromosomal anomalies. It is evident that mortality can be reduced by taking up measures to control sepsis. Most of the babies with gastroschisis in this study were outborn, and referred late, having been transported to IALCH over long distances with inadequate bowel protection. Some babies were fluid- and electrolyte-depleted and septic at presentation and the exposed bowel heavily contaminated and grossly thickened. Such babies had to undergo staged repair with a silo, with longer times on TPN, hence ended up developing sepsis. It is prudent that the realistic way of reducing sepsis is to improve antenatal services, have most mothers deliver in-house, for earlier surgical intervention, improve bowel protection to prevent contamination and instituting strict measures of reducing TPN-related sepsis. Aseptic protocols and hand washing techniques are paramount in this aspect. A strict microbiological protocol based on sound knowledge of organisms most likely to cause infections in our ICU's is important in deciding initial antibiotic therapy. Early trophic feeds may be beneficial in preventing translocation of enteric organisms. Other studies from even developed countries reports epsis as the leading cause of death in children with gastroschisis. Bianchi *et al*[47] reported overwhelming sepsis causing 71% of the deaths. Surasak Sungkathat *et al*[48] reported infectious complications in 65% of patients with gastroschisis.

Other preventable causes of death seen in this study are abdominal compartment syndrome, which was seen in n=5 (12.5%) and bowel necrosis seen in n=6 (15%) of the death. Olesevich *et al,*[41] while studying the role of intraoperative measurement of abdominal pressure concluded that intravesical pressure monitoring can be used to improve safety of primary closure to avoid bowel ischeamia. Other methods reported to help in the decision to close or not to close are measuring changes in central venous pressure, in ventilatory pressures and in end tidal carbon dioxide. Bowel necrosis can be prevented by placing the baby with its right side down to prevent kinking of the mesenteric pedicle, after covering the exposed bowel.

On analysing the relative contribution to mortality for each of the surgical procedures in this study, staged repair with a silo carried the highest mortality rate of 63%, more than double the mortality rate for primary closure (28%). This is explained by the fact that patients who undergo staged repair spend longer periods on ventilation and TPN, require routine change of dressings, and the presence of a plastic prosthesis – all these predispose these infants to septic complications.

It is also interesting to note that 5 out of the nine children 55.5% of the children who underwent ward reduction died. It was not clear in the records how they were selected but all underwent the standard surgical procedure under local anaesthesia. It is difficult to identify what contributed to the higher mortality among this group. Probably more time for stabilisation after birth is needed before one embarks on surgical management of newborns with gastroschisis.

In this study, time to reduction was considered separately as it has been found, by previous studies to have a big bearing on outcome. Longer time reduction is a result of late presentation,

which was noted in this study. The exposed bowel is in danger of secondary injury and infection. It has been observed that the risk of mortality doubles every after 12 hours. In the developed countries, most children with gastroschisis get surgery within the first hours of life after birth. Initially, immediately after birth, usually in the labour suite, a spring loaded silo is applied to protect the bowel. Driver *et al*,[40] reported in their study that surgical intervention occurred in 90 babies, out of the 91(99%) at a median of 4.0 hours post delivery and in 72 (80%) cases primary abdominal wall closure was achieved. While Weinsheimer *et al*[50] reported 90% successful primary closure, in less than 6 hours post delivery in the series of 99 patients.

The overall mean (SD) time to reduction in this study was about 16 hours (13.4). This had a bearing on survival. It was higher among those who died 17 hours (9.1), compared to the survivors 15 (16). In order to improve on outcome, it is evident from this study that efforts have to be taken to reduce the time to reduction. The most effective way is to have mothers expecting babies with gastroschisis delivering "in house", thus overcoming the delay during referral and transport. Hadley *et al*[13] have showed that transfer of neonates with surgical emergencies in this region is inefficient and preparation is poor. In developed countries postnatal transfer of neonates is often performed to a suboptimal level, despite reports and guidelines.[51,52] Prenatal transfer of a fetus therefore caries less risk than transfer of a newborn infant. It also avoids the need for separation of the child and its mother and facilitates communication between parents and medical staff at the time of significant parental anxiety.[53] Furthermore, delivery in a regional unit allows the obstetric and surgical paediatric teams to co-ordinate optimum perinatal management. It is important to sensitise doctors and other health care providers in district hospitals on this aspect.

CHAPTER 6

CONCLUSIONS

From this study it can be concluded that;

1. The incidence of gastroschisis among neonatal surgical admissions increased during the period 2002-2007 .
2. Most babies were born outside, by NVD, and were of low birth weight with a slight increase in risk of death.
3. There were a number of associated extra GIT abnormalities, some of them serious, which impacted on survival.
4. Mortality among babies with gastroschisis in this study was high 43 %.
5. Staged closure of the abdominal wall was associated with increased risk of death.
6. Longer time to reduction was associated with slightly increased risk of mortality
7. Sepsis was the most leading cause of death.

CHAPTER 7

RECOMMENDATIONS

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1. To initiate a comprehensive program for antenatal diagnosis of congenital abnormalities like gastroschisis by measuring serum AFP in all expectant mothers followed by serial ultrasound scans.
2. Antenatal transfer of all mothers with congenital abnormalities like gastroschisis to IALCH for delivery to avoid the delicate transport of the vulnerable babies and delay in surgical management.
3. Institute measures of reducing TPN related sepsis and other forms of sepsis.
4. To carry out a prospective, population based study for gastroschisis in KwaZulu-Natal province.

CHAPTER 8

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