An analysis of **neonatal mortality** following gastro-intestinal and/or abdominal surgery in a tertiary hospital in South Africa

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by

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Contents

Declaration

I, *Thozama Violet Siyotula* hereby declare that the work on which this dissertation/thesis is based is my original work (except where acknowledgements indicate otherwise) and that neither the whole work nor any part of it has been, is being, or is to be submitted for another degree in this or any other university.

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Abstract

Background: The World Health Organisation estimates approximately 10% of neonatal deaths in sub-Saharan Africa and South Asia are due to congenital malformations. Neonatal mortality in the Republic of South Africa needs to be benchmarked against high income countries' (HIC) standard of care to identify means to reduce infant mortality, much of which is due to congenital anomalies amenable to surgical correction.

Objectives: (1) Assess 30-day, 6-month and 12-month post-operative mortality for neonates operated for gastrointestinal and abdominal wall defects at a tertiary free-standing paediatric hospital in Western Cape, South Africa, over a 12-year period. (2) Ascertain the causes and risk factors associated with 30-day post-operative mortality.

Method: A retrospective folder audit of all neonates that underwent gastrointestinal & abdominal wall surgery within the neonatal period at Red Cross War Memorial Children's Hospital (RCWMCH) during the 12-year period from 1 January 2007 to 31 December 2018.

Results: The 30-day post-operative mortality rate was 73/762 (11%). Mortality was found in 9 conditions. An additional 57/762 patients (7%) died post-surgery between 30 days from surgery and 6 months of age. A further 34 patients (4%) died between 6 and 12 months of age. Mortality resulted from: sepsis (74%), palliation due to ultra-short bowel length (12%); in patients with necrotizing enterocolitis, intestinal atresia and malrotation with volvulus, ventilation associated pneumonia (10%), associated congenital cardiac lesions (3%) and intestinal failure associated liver disease (1%). Most neonates (69%) who died were prematurely born. Mean age at surgery was 10 days (median 6 days; interquartile range (IQR) 3-16) and mean age at death was 6 days (median 5 days; IQR 2-12; range 1-30). Nearly all patients who died were managed in the intensive care unit post-operatively (97%), with a median stay of 7 days (IQR 1-10) and overall hospital stay of 8 days (IQR2-12). Mortality in patients from referral hospitals more than an hour drive

from RCWMCH was high (15/39, 38%). The odds ratio for death for patients with travel time over one hour from the referral hospital was 3.6 [95% confidence interval 1.8 to 7.3; z-statistic 3.6; p=0.0003]. The majority of surgical procedures in patients who died were for abdominal surgery 70/73 (96%). Surgery for necrotizing enterocolitis (NEC) had the greatest mortality (38%), followed by spontaneous intestinal perforation at (29%), gastroschisis (18%). Thirty-day mortality for oesophageal atresia, congenital diaphragmatic hernia and malrotation with volvulus was 9% each, followed by intestinal atresia at 8%, anorectal malformation (5%) and inguinal hernia (3%). No post-operative mortality was reported for Hirschsprung disease, choledochal malformation, hypertrophic pyloric stenosis, biliary atresia and omphalocele. Relook procedures were conducted for 37%, with the highest percentage of revision surgery for necrotizing enterocolitis at 42%. Abdominal compartment syndrome was noted post operatively in 15% patients. Significant modifiable risk factors for sepsis in patients who died were central line-associated bloodstream infections (65%), respiratory tract infections (41%) and surgical complications [anastomotic breakdown (7%) and wound infection (24%)].

Conclusion: The 30-day post-operative mortality rate in this middle-income setting is similar to the overall mortality rate in HIC, despite excluding pre-operative mortality in this study. Prevention and improvement strategies for infection control are imperative to improve outcomes in surgical neonates, including optimizing timing of surgical intervention for bowel perforation or obstruction through timeous patient transfer for definite management and intensive care unit capacity optimization, central line care and post-operative infection surveillance. Liberal abdominal compartment pressure monitoring and delayed abdominal closure in selected patients may further reduce mortality. Addressing modifiable factors for morbidity and mortality in this vulnerable patient group is required for comparable outcomes to HIC.

Abbreviations

ARM	-anorectal malformation
BA	-biliary atresia
CDM	-choledochal malformation
CDH	-congenital diaphragmatic defects
ELBW	-extremely low birth weight
GS	-gastroschisis
HPS	-hypertrophic pyloric stenosis
HIC	-high income countries
HD	-Hirschsprung disease
IH	-inguinal hernia
IA	-intestinal atresia
LBW	-low birth weight
LMIC	-low- and middle-income countries
MV	-malrotation with volvulus
NEC	-necrotizing enterocolitis
OA/TOF	-oesophageal atresia +/trachea-oesophageal fistula
OMPH	-omphalocoele
RCWMCH	-Red Cross War Memorial Children's Hospital
VLBW	-very low birth weight

Chapter 1

Introduction and literature review

1.1 Incidence of neonatal mortality

Bringing down infant mortality rate is a major goal for low- and middle-income countries including South Africa. In low- and middle-income countries (LMIC) there are multiple problems still faced causing high morbidity and mortality. Neonatal mortality was reported between 16-40% in these countries (1). South Africa has implemented strategies to reduce under-five mortality and stabilize infant mortality, but more research is needed to identify areas for further improvement (2,3).

Congenital malformations are the fifth leading cause of death in children under five years of age globally (4). This equates to approximately half a million deaths from congenital anomalies each year, 97% of which occur in low- and middle-income countries (LMIC) (4).

A significant proportion of Infant mortality occurs in the neonatal period. Mortality due to congenital abnormalities is estimated at 10% of the overall neonatal mortality rate according to the UNICEF data from South Africa in 2016 (5). In 2019, overall neonatal mortality rate for South Africa was 11.5 deaths per 1,000 live births (6). The World Health Organisation estimates approximately 10% of neonatal deaths in sub-Saharan Africa and South Asia are due to congenital malformations (7). Many of these require appropriate surgical management to ensure survival.

Congenital and acquired gastrointestinal and abdominal wall conditions make up a large portion of surgical burden in Africa (8,9). Incidence per live birth for the most common of these conditions is shown in Table 1. A high mortality of more than 40% has been reported for diseases such as oesophageal atresia, diaphragmatic hernia, omphalocele, and gastroschisis, and intestinal atresia in LMIC (1,2,3,9). Although the conditions are not common individually, collectively they contribute significantly to neonatal mortality as indicated by the high associated mortality rates.

Table 1: Reported Incidence of common congenital and acquired neonatal surgical conditions

No.	Condition	Incidence (per live births) 4,10,11,12,13
1	**ARM**	1/ 2500-5000
2	**BA**	1/10000-16700
3	**CDM**	1/100,000-150,000
4	**CDH**	1/2000-5000
5	**Gastroschisis**	1/4000-10,000
6	**Hirschsprung**	1/5000
7	**Intestinal malrotation**	1/6000
8	**Spontaneous intestinal perforation**	1/6000- 1/10 000
9	**Inguinal hernia**	0.8- 4.4/1000
10	**Intestinal atresia**	1/6000-10000
11	**Necrotizing enterocolitis**	1-3/1000
12	**Oesophageal atresia**	1/3500
13	**Pyloric stenosis**	1.5-4.0/1000
14	**Omphalocoele**	1-2.5/5000

There are several challenging aspects of the surgical management of neonates. Neonates have unique differences in physiology, such as a vulnerability to electrolyte and fluid imbalances, compared to older children and adults. They also have a different disease profile affecting them, and often have associated congenital anomalies, as well as increased risk for sepsis due to an immature immune system. They therefor have different care needs.

Mortality in neonatal surgery in high income countries has decreased more than 50% since the 1990's, this to a figure of less than 5% in recent years (1,14). This is due to improvements in surgical techniques, better intensive care facilities, anaesthesia and a

broader concept and clarity of embryology, neonatal physiology, improvement in diagnostic technologies and better nutritional support. These are a result of better training, research and increased health care sector funding (15,16). Significant differences still exist between HIC and LMICs in terms of neonatal surgical outcomes (17,18). Literature outcomes in most African countries indicate neonatal surgery has challenges with regards to neonatal intensive care facilities, surgical training, and support personnel just to mention a few, resulting in a high rate of morbidity and mortality following neonatal surgery (19).

1.2 Factors which influence neonatal mortality

Many possible factors are potentially responsible for mortality in neonates. Reported mortality rates vary widely between hospitals as well as different countries. Factors that impact neonatal surgical outcomes can be grouped as pre-operative, intra-operative and post-operative. The factors related to mortality can also be identified as modifiable or non-modifiable. Defining these assists addressing the concerns at different points of care for these surgical neonates in an attempt to improve outcome. There is an overlap between modifiable and non-modifiable factors, for example prolonged time from patient presentation to definitive tertiary care which can be due to infrastructure problems, personnel problems as well as distant referral site.

1.2.1 Non-modifiable factors associated with neonatal mortality

Table 2 displays non-modifiable factors that contribute to neonatal mortality. These have been described in LMIC and are well-described in the South African setting (7,19,20).

Table 2: Non-modifiable risk factors associated with 30-day post-operative mortality

Pre-operative factors	Intra-operative factors	Post-operative factors
Distance and other causes for delay in transfer from primary care centre to definitive care institution	Urgency of surgical procedure: *Emergency (e.g. bowel perforation) or urgent procedure (e.g. bowel obstruction without perforation)*	Organ failure: renal, respiratory, cardiac
Gestational age		
Associated congenital anomalies		
Pre-operative haemodynamic instability		
Pre-operative respiratory failure		
HIV exposure		

1.2.1.1 Health-care system/ infra-structure factors

This can contribute to delayed presentation as above as well as to poor management for the following reasons:

1. **Personnel**

   Adult and paediatric studies show that hospital and surgeon characteristics and level of care are associated with patients' outcomes after surgery. The experience with very low birth weight neonates and presence of a neonatal intensive care unit at the delivery hospital also influence a neonate's risk of mortality and morbidity (21,9). The following factors also play a role:

   - Limited workforce for large neonatal surgical workload
   - Skill limitations/ unavailability of trained personnel in neonatal surgery and anaesthesia

- Lack of multidisciplinary care e.g., in complex patient pathology

2. **Facilities and material resources**

    - Lack of neonatal intensive care units
    - Lack of equipped operating theatres for neonatal surgery
    - Need for transportation to a referral centre influences neonatal surgical outcomes (17).

1.2.1.2 Patient-related factors

1. **Demographics**

Prematurity and low birth weight are associated with poor prognosis in neonates (1,14,22,23,24). A multivariate analysis presented gestational age and birth weight as significant independent predictors of mortality, owing to immaturity in immune system and organ system function in preterm neonates (25).

2. **Comorbid conditions**

Patient's structural anomalies of the respiratory and cardiovascular system influence their survival and post-surgery outcomes, especially when complicated by sepsis and organ system failure. Patient factors that predict the risk of death within 30 days of surgery include the presence of associated life-threatening anomalies (cardiac and central nervous system anomalies) which may be a significant predictor of death unrelated to the pathology for which the neonate undergoes a surgical procedure (17).

Other patient factors that increase risk of death include conditions such as acute renal failure, bleeding disorders, haematological disorders, pneumonia, bronchopulmonary dysplasia and HIV exposure. Neonates who required medical interventions or treatment prior to surgery were noted to have significant risk of death. Many authors have reported increased probability of death for neonates that were haemodynamically unstable, in

shock or septic and those requiring ventilatory support or oxygen therapy, blood transfusion, nutritional or inotropic support (17,21,26). These presenting features may reflect late presentation in many cases, inadequate resuscitation at the primary health care level or inadequate definitive care at the receiving hospital (25). While these may be regarded as factors amenable to modification at referring hospital level, they were regarded as non-modifiable factors for the purposes of this study, which focuses on care at the institution where definitive surgical care was provided (RCWMCH).

3. **Specific surgical conditions**

Postoperative neonatal surgical outcomes were reported from a large national database in the United States of America, a high-income country (HIC), from 2012 to 2014, where mortality was incurred after the following procedures: exploratory laparotomy, bowel resection with anastomosis or stoma creation, congenital diaphragmatic hernia repair, repair of large omphalocoele or gastroschisis and drainage of peritoneal abscess (21). A high mortality of more than 40% has been reported particularly for diseases such as oesophageal atresia, diaphragmatic hernia, omphalocele, gastroschisis, and intestinal atresia in LMICs (9,14,27,28). The mortality rates were substantially higher compared to the 10% mortality reported from HICs during the same period (1,14,27,28).

Life-threatening conditions that require early neonatal interventions like necrotizing enterocolitis, oesophageal atresia and congenital diaphragmatic hernia are infrequently treated in some African countries as a result of high prehospital mortality as opposed to a true low incidence of the conditions (14). Mortality rate from the reviewed publications on neonatal surgery in Africa showed reported overall averages between 29.1-36.9 (14).

4. **Urgency of surgical procedure**

Elective or emergent operative case status influences the outcome of surgical intervention in neonates (17). Septic conditions or conditions where hollow visceral perforation is imminent require emergency surgery as opposed to other conditions such as congenital diaphragmatic hernia and oesophageal atresia where short-term delays in surgery until

specialists are available for the procedure may be preferable, provided there is appropriate interim care.

5. **Poor follow-up after surgical intervention**

Cultural, educational and socio-economic factors as well as infrastructure can affect health-seeking behaviour and can impact on follow up care and resultant outcomes(17).

1.2.2. Modifiable risk factors for mortality

Modifiable risk factors for neonatal mortality shown in Table 3.

Table 3: Modifiable risk factors associated with 30-day post-operative mortality

1. Pre-operative factors	2. Intra-operative factors	3. Post-operative factors
Anaemia, coagulopathy due to progression of disease resulting from delays in care	Type of surgical procedure, *especially those involving bowel resection, bowel anastomosis and large abdominal wall defect repair*	Systemic sepsis due to CLABSI, anastomotic breakdown or wound infection
Delayed transfer to definitive care e.g. due to lack of intensive care bed capacity	Duration of surgical procedure	Surgical site infection
	Experience level of personnel performing the surgery	Abdominal compartment syndrome
		Need for revision surgery

1. **Pre-operative factors: delayed presentation**

Delayed presentation is an independent risk factor that predicts the mortality for neonates who have undergone surgical intervention (25). Time to arrival at the institution where definitive care takes place i.e., tertiary care centre, also impacts age at surgery. Early referral and surgery have been advised to avoid morbidity and mortality (7,14,9,29,30).

Neonates born outside the tertiary center's where definitive management is undertaken have a worse reported outcome in some low-income African countries (1,9,14,22,23,24,30,31). This is exacerbated by very distant referral sites as well as underdeveloped transport systems e.g., poor road infrastructure.

Healthcare system factors causing delayed presentation for neonatal surgical conditions include availability of antenatal diagnosis, resources at primary health-care facility, delayed presentation, transport facilities and systems for referral (32). Delays in transfer may also be affected by limited intensive care unit facilities at the receiving hospital (14). Healthcare worker education also plays a role. A low index of suspicion of these disorders among the healthcare professionals in the primary and secondary care facilities leads to delays in initial diagnosis and referral to the appropriate centres (1,14,22,23,31).

Socio-economic contributors to morbidity and mortality include poverty e.g., lack of financial means to travel to clinic (14). Culture and education influence health-seeking behaviour patterns.

2. Intra-operative factors

Appropriate initial treatment strategies need to be implemented to improve outcome by advances in diagnostic techniques and perioperative care have greatly improved the outcome of neonatal surgery. Neonatal surgery studies from HICs show advances in availability of trained personnel, early diagnosis, peri-operative support, surgical technique, anaesthesia and integration of multidisciplinary care (14,19). Early diagnosis, improved operative techniques and better perioperative management have improved outcomes and reduced mortality rate in HIC (19). The challenges implicated in outcomes of LMICs included inadequate theatre facilities, limited trained personnel and absence of neonatal intensive care (14). Paediatric abdominal surgical emergencies in LMIC settings have high morbidity and mortality. Efforts to improve diagnosis and perioperative care resulting in better outcomes need to be undertaken(25). Surgical techniques and comprehensive understanding of age-dependent variables, effects of anaesthetic drugs and surgical techniques on the neonate present many challenges for paediatric surgeons

and anaesthesiologists. Thorough preoperative evaluation and open communication between team members is essential in minimizing perioperative morbidity and mortality (22,23,33).

3. **Post-operative factors**

Poor prognosis and outcomes may potentially be a result of sepsis and shock among other factors. Strategies which may be put in place to reduce mortality from sepsis include but are not limited to hand-washing and aseptic technique, central line care and early detection of sepsis with appropriate antibiotic treatment (7,14,29,34,35,36,37). Sepsis outbreaks are frequent with under-reporting noted and predominance of Gram-negative bacteria documented. Literature reviewing sepsis in African neonates reported 50% of outbreaks were caused by extended-spectrum β-lactamase-producing Klebsiella pneumoniae. Commonly implicated are breaches in infection prevention practices. Programmes in African neonatal units are urgently required to improve sepsis prevention, early septic shock recognition and treatment to reduce hospital mortality (34,35,26,38,).

1.3. Purpose of the study

This study aims to assess the above factors and their influence on neonatal mortality in a South African tertiary hospital setting to identify problems underlying poor outcomes that can be rectified to improve care. Only post-operative mortality was analyzed at in this study, to evaluate how the RCWMCH mortality rate compared to other LMIC and HIC. Factors affecting pre-operative mortality are largely due to factors surrounding care at referral hospitals and transport infrastructure as well as comorbid conditions such as other congenital anomalies. By focusing on cases operated on, factors directly affecting surgical care at RCWMCH can be identified for improvement.

Chapter 2

Methods

2.1 Objective

The primary objective was to assess post-operative mortality for neonates operated under general anaesthesia for gastrointestinal and abdominal wall defects at a single free-standing tertiary paediatric hospital (Red Cross War Memorial Children's Hospital; RCWMCH) over a 12-year period. One-month, 6-month and 12-month post-operative mortality were evaluated.

The secondary objective was to identify causes and modifiable risk factors for 30-day post-operative mortality.

2.2 Study Design

The study was a retrospective audit of patient records over a 12-year period from 1 January 2007- 31 December 2018.

Source of Data

- Patient medical record review
- Paediatric Surgery Department operative database (names, dates of birth, folder numbers, operation dates, type of operation)
- Patient medical records (demographics, clinical risk factors for death e.g., gestational age, sepsis, comorbidities, late presentation, cause of death)
- Red Cross War Memorial Children's Hospital Intensive Care Unit- discharge summaries
- Referring Neonatal Intensive Care Units- records
- National Health Laboratory Service (NHLS) records (histological records of resected surgical specimens, evidence for sepsis)

- Picture Archive and Communication System ("PACS") Radiological database (radiological evidence of bowel obstruction or perforation)
- Department of Western Cape Clinicom administrative database (date of demise if not at RCWMCH)

Data analysis

Data was anonymized for analysis. Descriptive statistics were generated using Excel (Windows Vista) including mean, median and interquartile range.

Data on the following were assessed:

Cause of death

Risk factors for death (modifiable and non-modifiable) including:

- Presenting Surgical condition
- Demographics
- Date of birth
- Date of demise
- Age at demise
- Sex
- Birth weight
- Gestational Age
- Ante-natal history
- Mode of delivery
- Referring Hospital
- Distance of transferring hospital from RCWMCH
- Human Immune Virus exposure and PCR results
- Anti-retroviral drug prophylaxis
- Comorbidity
- Tracheal Aspirates
- Wound Swab culture < and equal 30-days post Index procedure
- Score for neonatal Acute Physiology and prenatal extension (SNAPPEII)

- Clinical Risk for Babies (CRIB II) Scores
- Age at index surgical procedure
- Type surgical procedure performed
- Surgeon performing the procedure
- Emergency or elective procedure
- Complications related to the surgery
- Anaemia: Hb <7 transfusion
- Sepsis within the 30-days post-operative period
- Wound Infection within the 30-day post-operative period
- Organ failure
    - Post-operative respiratory support days within the first 30-days post index procedure
    - Inotropic support within 30-days post-operatively

Inclusion criteria:

All patients operated at RCWMCH for gastrointestinal or abdominal wall conditions were included if they were under 28 days old for term infants or under 44 weeks corrected gestational age for premature neonates.

The following index 14 neonatal congenital gastrointestinal conditions were evaluated: anorectal malformation (ARM), biliary atresia (BA), choledochal malformation (CM), congenital diaphragmatic defects (CDH), spontaneous intestinal perforation (SIP), gastroschisis (GS), Hirschsprung disease (HD), inguinal hernia (IH), malrotation with volvulus (MV), necrotizing enterocolitis (NE), oesophageal atresia +/trachea-oesophageal fistula (OA±TOF), omphalocoele (OMPH), hypertrophic pyloric stenosis (HPS) and intestinal atresia (IA)

Exclusion criteria:

Patients were excluded where there was inadequate information e.g., missing medical records. Those patients that demised prior to receiving surgery were also excluded from the study.

Patient were excluded from the study if operated for one of the study conditions outside the neonatal period or if they received their index surgery at another institution i.e., at a hospital other than RCWMCH. Those who did not have complete information with regards to weight or gestational age were excluded from the analysis. Neonates not operated by the division of paediatric surgery at RCWMCH were not included in the study i.e., thoracic surgery other than for oesophageal atresia, central line insertions, and surgery for ear, nose and throat, neurosurgical or urologic conditions.

Data collection and storage:

Retrospective data was collected and stored electronically in a password-protected database. Data was anonymized, with each patient assigned a study number, and no identifying data e.g., name and surname or hospital number. All data used was routinely collected information used in the management of these patients. Access to information was restricted to study personnel.

Statistical Data Analysis:

Descriptive statistics was generated using Microsoft Excel ®.

Sample size: An estimated 100 neonates are operated at RCWMCH annually for general surgical conditions, giving an estimated population size of 1000 over 10 years. Assuming a mortality of 10%, a study population of 100 patients was estimated. It was then estimated that due to the retrospective nature of the study and lack of availability of medical records, approximately 50% of the medical records may not be available, reducing the potential study population to 50 patients with adequate information to confirm death and determine the cause of mortality.

Ethical considerations

This research protocol was submitted and approved by the Committee for Human Research at the University of Cape Town and was carried out according to internationally accepted ethical standards and guidelines.

Human Research Ethics Committee (HREC) approval was granted for the project (University of Cape Town HREC approval number **036/2019**).

Motivation for waiver of informed consent from patients

As this was routinely collected data needed for patient management, no parent/patient interaction was necessary for data collection. All information extracted was stored in a excel database and access restricted to the investigators and password protected. Once relevant data was extracted it was anonymized for analysis. Because of the routine nature of the data under investigation, and anonymous handling of extracted data, informed consent was thus not considered necessary for this retrospective review. Consent for collecting the data was obtained from the medical manager and RCWMCH research and ethics committee after ethical approval to carry out the study.

Privacy and confidentiality

Data was held securely with access restricted to study investigators only, and anonymization of data to protect patient confidentiality. A study number connecting data to the relevant patient folder numbers was stored separately from the database under password protection.

Definitions, terms and parameters:

Listed below are explanations of various parameters used to define comorbid conditions or morbidities as well as definitions of terms used within the text.

Terms and Parameters

Bradycardia: Mean heart rate <10th percentile for age (34,38,39,).

Cardiovascular: Hypotension, or reliance on a vasoactive drug to maintain blood pressure, metabolic acidosis, elevated arterial lactate, oliguria, or prolonged capillary refill (34,39).

Core temperature: Measured by rectal, bladder, oral, or central probe of >38.5°C or <36°C (34,39,40,41).

Extremely low birth weight: ≤1000g (33)

Haematologic: Platelet count <80,000/10^{9}/L or a decline of 50 percent from highest value. Disseminated intravascular coagulation (34,39).

Hepatic: Total bilirubin ≥4 umol/L or alanine aminotransferase (ALT) >2 times upper limit of normal for age (34,39).

High income country (HIC): Those with a gross national income per capita, calculated using the World Bank Atlas method of US$12,736 (42).

Leukocyte count: elevated or depressed for age, or >10 percent immature neutrophils (34,39).

Low and middle income (LMIC): Countries with a gross net income (GNI) per capita, calculated using the World Bank Atlas method of more than US$1045 but less than $4,125 (42)

Low birth weight: ≤ 2500g (29).

Neonate: The World Health Organization defines it as a child under 28 days of age(35).

Neurologic: Glasgow coma score ≤11, or acute change in mental status (34,38,39,).

Mean respiratory rate: More than two standard deviations above normal for age(34,38,39).

Renal: Serum creatinine ≥2 times upper limit of normal for age or twofold increase in baseline creatinine (40,41,43).

Respiratory: Arterial oxygen tension/fraction of inspired oxygen (PaO_2/FiO_2) <300, arterial carbon dioxide tension ($PaCO_2$) >65 mmHg over baseline $PaCO_2$, need for >50 percent FiO_2 to maintain oxygen saturation ≥92 percent, or need for nonelective mechanical ventilation (34,38,39,).

Tachycardia: Heart rate more than two standard deviations above normal for age, or for children younger than one year of age (34,38,39).

Very low birth weight: ≤1500g (29)

Definitions

Modifiable risk factors: Features that may be adjusted at RCWMCH level to improve patient outcomes.

Sepsis: Systemic inflammatory response syndrome in the presence of suspected or proven infection constitutes sepsis (34,38,39).

Septic shock: Septic shock is sepsis with cardiovascular dysfunction that persists despite a ≥40 mL/kg of isotonic fluid administration in one hour (34,38,39).

Severe sepsis: Associated cardiovascular dysfunction, acute respiratory distress syndrome, or dysfunction in two or more other organ (34,39,44).

Short bowel syndrome (SBS): Massive surgical bowel resection resulting in impaired capacity for nutritional absorption relative to growth and development needs requiring parenteral nutritional support and/or other dietary adjustment to meet nutritional requirements; ultra-short SBS with

expected fatal outcome defined as <15cm small bowel with intact colon or <40cm without colon (45) or <10% expected small bowel length for age (46).

Systemic inflammatory response syndrome:

Widespread inflammatory response that may or may not be associated with infection. Two or more of the following criteria and one of which must be abnormal temperature or leukocyte count (34,39,39).

Chapter 3:

Results

3.1 Neonatal surgical case volume

Neonates accounted for ten percent of the patients operated by the Division of Paediatric Surgery at RCWMCH over the 10-year period between 2007 and 2018, totaling 1130 neonates. Seven hundred and sixty-two of these had gastro-intestinal (GIT) or abdominal wall conditions (67%).

3.2 Mortality rate

Eighty-three out of the 762 neonates who underwent GIT surgery demised (11%). Table 3 shows the surgical conditions and mortality rates for these 83 patients. The overall 30-day post-operative neonatal mortality rate was 83/762 (11%). Mortality was found in 9 of the 14 index neonatal conditions analysed. An additional 57/762 patients (7%) died between 30 days from surgery and 6 months of age. A further 34/762 patients (4%) died between 6 and 12 months of age. Overall mortality at one year of age for the 10-year period was thus 174/762 (23%) for neonates undergoing GIT surgery.

3.3 Exclusions

There were incomplete records for 12 cases who died who were thus excluded from detailed analysis of cause of death. Ten of these excluded patients died within 30 days of surgery for necrotizing enterocolitis, and two had biliary atresia, of which one died within 6 months and one within 12 months post-operatively. This left 73 cases for whom detailed records of the cause of thirty-day post-operative mortality were available.

Table 4: **Neonatal mortality according to surgical condition at thirty days post-operatively, at six months and at one year**

Condition	Patients operated	30-day mortality n (%)	Additional mortality at 6 months n (%)	Additional mortality at 12 months n (%)	Total (cumulative) mortality at 12 months n (%)
Necrotising enterocolitis	137	38 (28%)	26 (19%)	16 (12%)	**80 (58%)**
Spontaneous intestinal perforation	17	5 (29%)	2 (12%)	-	**7 (41%)**
Gastroschisis	50	9 (18%)	2 (4%)	3 (6%)	**14 (28%)**
Oesophageal atresia	35	3 (9%)	5 (14%)	2 (6%)	**10 (29%)**
Malrotation	67	6 (9%)	4 (6%)	1 (1%)	**11 (16%)**
Congenital diaphragmatic hernia	32	3 (9%)	2 (6%)	-	**5 (16%)**
Intestinal atresia	137	11 (8%)	4 (3%)	7 (5%)	**22 (16%)**
Anorectal malformation	94	5 (5%)	6 (6%)	3 (3%)	**14 (15%)**
Inguinal hernia	116	3 (3%)	1(1%)	-	**4 (3%)**
Omphalocele	31	-	4 (13%)	1 (3%)	**5 (16%)**
Biliary atresia	5	-	1 (20%)	1 (20%)	**2 (40%)**
Hypertrophic pyloric stenosis	25	-	-	-	-
Hirschsprung disease	15	-	-	-	-
Choledochal malformation	1	-	-	-	-
Total	**762**	**83 (11%)**	**57 (7%)**	**34 (4%)**	**174 (23%)**

3.4 Causes of early (30-day) post-operative mortality

Mortality resulted from the following:

- Sepsis in 54/73 (74%)
- Ventilation-associated pneumonia in 7/73 (10%)
- Palliation for intestinal failure due to pan-intestinal necrosis and/ atresia with ultra-short bowel syndrome in 9/73 (12%)
- Associated congenital cardiac lesions in 2/73 (3%)
- Liver failure in 1/74 (1%) as a result of liver cirrhosis (intestinal failure associated liver disease)

3.5 Risk factors for mortality

3.5.1. Demographics

1. Age and weight

Gestational age and weight were available for 71/73 of the infants who died within 30 days post-operatively. Mean gestational age and weight for individual conditions are shown on **Table 5** on page 29.

The majority of patients were born at a gestation less than 37 weeks (49/71; 69%), with a mean gestational age of 33 weeks. The gestational ages for patients ranged between 25 to 40 weeks.

Three patients had no documented weight. A total of 59/70 neonates (81%) had a birthweight below 2500g. Birthweight sets were categorised as follows:

- 9/70 (12%) extremely low birth weight
- 19/70 (25%) very low birth weight
- 31/70 (43%) low birth weight
- 11/70 (12%) normal birth weight

Most patients died within the first week after birth with a mean of 9 days and range of (1-30). Age at admission to RCWMCH, surgery and death is shown on **Table 6** on page 30.

Table 5. **Demographics of patients who died: Gestational age and weight stratified by surgical condition**

Condition	Birth weight (g) Mean (Range)	Gestational age (days) Mean (Range)
Necrotising enterocolitis	1476 (840-3750)	31 (25-40)
Intestinal atresia	1789 (1100-3030)	31 (29-40)
Gastroschisis	2141 (1750-2590)	36 (35-38)
Malrotation	2296 (1300-3400)	36 (34-40)
Anorectal malformation	2296 (985-3100)	38 (30-40)
Spontaneous intestinal perforation	1355 (940-2980)	30 (29-40)
Inguinal hernia	2180 (2000-2360)	38 (36-40)
Oesophageal atresia	1155 (910-1400)	33 (28-40)
Congenital diaphragmatic hernia	1933 (1000-2500)	33 (35-40)
OVERALL	**1737** (840-3750)	**33** (25-40)

Table 6. **Demographics of patients who died: Age at admission, operation and death**

Condition	Age at admission (days) Mean (Range)	Age at operation (days) Mean (Range)	Age at death (days) Mean (Range)
Necrotising enterocolitis	17 (3-30)	17 (7-29)	9 (7-30)
Intestinal atresia	2 (1--4)	3 (1-5)	13 (1-30)
Gastroschisis	1 (1-2)	4 (1-9)	10 (1-18)
Malrotation	9 (1-28)	9 (1-28)	6 (2-17)
Anorectal malformation	2 (1-4)	3 (1-4)	8 (1-29)
Spontaneous intestinal perforation	5 (1-7)	5 (2-7)	7 (2-11)
Inguinal hernia	19 (17-21)	20 (10-21)	1 (18-23)
Oesophageal atresia	1 (1-2)	2 (1-3)	7 (3-12)
Congenital diaphragmatic hernia	2 (1-3)	7 (1-16)	10 (5-13)
OVERALL	4 (1-30)	10 (1-29)	6 (1-30

2. Sex

Males accounted for 58/73 (80%) of the overall cohort of patients who died. Patients with NEC had a similar male to female distribution with 13/28 females and 15/28 males. All patients with anorectal malformation and inguinal hernia were males.

3. Mode of delivery

Mode of delivery included normal vertex delivery in 32/73 (44%) and caesarian section in 19/73 (26%) but was unknown for 22/73 (30%). This was not further analyzed due to lack of antenatal information.

3.5.2. Co-morbidities

Thirty-seven (51%) of the 73 patients who died had associated comorbidities at presentation as shown in **Table 7**.

Table 7: Co-morbidities associated with mortality (as per parameters defined in chapter 2)

Associated condition	Comorbidity present	Comorbidity contributed to death
Respiratory	22 (30%)	7/22 (32%)
Cardiac	21 (29%)	2/7 (29%)
Chromosomal	7 (10%)	-
Liver failure	2 (3%)	1/2 (50%)
Central nervous system	10 (14%)	-
Total	**48/73 (66 %)**	**10/73 (14%)**

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3.5.3. Congenital anomalies

1. Cardiovascular

Cardiac lesions 21/73 (29%) included patent ductus arteriosus in 8, ventricular septal defect in 4, atrioventricular septal defect in 5, Tetralogy of Fallot in 2, mitral regurgitation in 1 and interrupted aortic arch in 1. Two patients died from congenital cardiac disease (ventricular septum defect with aortic override and Tetralogy of Fallot).

2. Chromosomal

Chromosomal conditions were present in 7/73 patients (10%). Death was not associated with any of these chromosomal conditions.

3. Human Immunodeficiency Virus exposure

There were 20/73 (27%) patients who were Human Immunodeficiency Virus exposed with mothers having received prevention of mother to child transmission protocol. Low risk exposure accounted for 17/73 (23%) of the patients and 3/73 (4%) had high risk exposure as evidenced by neonates being on two-drug prophylaxis (Zidovudine and Nevirapine). Thirty-three (45%) were documented as not exposed and 20 (27%) patients did not have information available regarding HIV exposure. Polymerase Chain Reaction (PCR) testing was conducted for 52/73 (72%). All of these HIV PCR results were negative.

3.5.4. Acquired comorbidities

1. Respiratory failure

Pre-operative respiratory failure was present in 22/73 (30%) as a result of lung prematurity and hyaline membrane disease, neonatal respiratory distress syndrome, pulmonary haemorrhage, acute respiratory distress syndrome and pulmonary effusion.

This contributed to post-operative mortality in 7/73 (10%). A total of 7/22 (32%) of patients with necrotizing enterocolitis had underlying respiratory disease, leading to death in 2/22 (12%) of these patients.

2. Central nervous system conditions

Ten patients had central nervous system pathology which included intraventricular bleed 8/73 (11%) and hypoxic brain injury 2/73 (3%), but this did not lead to death in these patients.

3. Haemodynamic impairment

Fifty-seven neonates received inotropic support, 21/73 (29%) pre-operatively and 36//73 (78%) post operatively. Pre-operative inotropic support was given most commonly in 14/73 (19%) of neonates with necrotizing enterocolitis, who also had the highest mortality rate. This was followed by patients with malrotation and volvulus 2/73 (3%). Other patients on preoperative inotropes included patients with spontaneous intestinal perforation, inguinal hernia, oesophageal atresia, anorectal malformation and congenital diaphragmatic hernia.

4. Anaemia

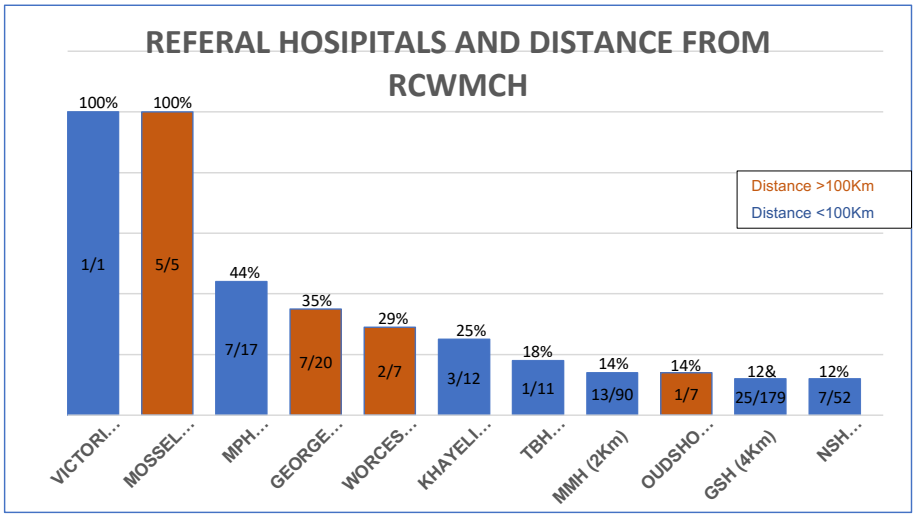
For this study we used a blood haemoglobin level of ≤ 7g/dL to define anaemia. Overall, blood transfusion was given in 33/73 (46%) patients. A total of 31/73 (43%) patients had a haemoglobin level less than 7g/dL. Pre-operative transfusion was given in 13/73 (18%) and post-operative transfusion in 20/73 (27%) patients.

3.5.5. Distance from referral hospital

Four referral hospitals are more than 100km from RCWMCH, requiring more than an hour for transfer. These centres are George Regional, Worcester, Oudtshoorn and Mossel Bay Hospitals. All referral hospitals and their associated distance from RCWMCH are shown in **Figure 1**, together with their respective contribution to referral volume and the absolute numbers and percentages of patients who died.

For patients whose transfer took over an hour of travel time, 15 out of 39 (38%) died. Patients in this group had necrotizing enterocolitis, spontaneous intestinal perforation, gastroschisis, oesophageal atresia, congenital diaphragmatic hernia. Where transfer took less than one hour, 58/335 patients (17%) died; these patients died from the following conditions: necrotizing enterocolitis and spontaneous intestinal perforation in addition to intestinal atresia, anorectal malformation and inguinal hernia. The odds ratio for death for patients with travel time over one hour from the referral hospital was 3.6 [95% confidence interval 1.8 to 7.3; z-statistic 3.6; p=0.0003].

Figure 1. Distance from referral hospital in kilometres and number of neonates and corresponding referral volume with one-month post-operative mortality from each referral hospital (distance to Red Cross War Memorial Children's Hospital (RCWMCH) shown in brackets; centres over 100km away are highlighted in bold);



MMH-Mowbray Maternity Hospital, **GSH**- Groote Schuur Hospital, **NSH**- New Somerset Hospital, **TBH**- Tygerberg Hospital, **MPH** Mitchells Plain Hospital

3.5.6 Length of intensive care unit (ICU) stay

Ninety-seven percent of patients who died were admitted post-operatively into the ICU with an average ICU stay of 5 days (median 7 days; interquartile range 1-10; absolute range 1-30 days). There were two patients not admitted to ICU, both due to a decision for palliative care following surgery.

3.6 Detailed analysis of mortality cases

3.6.1 Type of surgery

The majority of surgical procedures in patients who died were for abdominal surgery 70/73 (96%). This included laparotomy with bowel resection (45), stoma creation(7), primary anastomosis(6), damage control surgery(15), inguinal hernia repair(3) and abdominal wall closure(5). The remaining procedures were thoracotomies for oesophageal atresia repair. There was no mortality reported for patients with Hirschsprung disease, choledochal malformation, hypertrophic pyloric stenosis, biliary atresia and omphalocele. Surgery for NEC had the greatest mortality 28/73 (38%), followed by gastroschisis and intestinal atresia 11/73 (15%) each), malrotation with volvulus 6/73 (8%) and anorectal malformation 5/73 (7%).
The remaining conditions had 30-day mortality rates below 5% (oesophageal atresia, inguinal hernia, congenital diaphragmatic hernia).

3.6.2 Disease condition

Specific causes of deaths for each disease condition are itemized below.

1. Necrotizing enterocolitis (NEC)

Patients with NEC 28/73 (38%) had resection of necrotic bowel and primary anastomosis 3/28 (11%) with only a few having stomas created 9/28 (32%), while others had no intervention due to NEC totalis 4/28 (14%). A quarter 7/28 (25%) had resection leading to very short bowel while the rest of the patients with NEC had a damage control procedure 5/28 (18%) and died of sepsis before a definitive procedure could be performed. Abdominal compartment syndrome 4/28 (14%) and underlying respiratory pathology with respiratory failure was also associated with mortality in patients with NEC.

2 Spontaneous intestinal perforation (SIP)

Patients who SIP 6/73 (8%) all had a laparotomy with bowel resection and primary anastomosis. All died of sepsis which was associated with an anastomotic leak in two patients. Five of the patients had a gestational age less than 30 weeks and also very low birth weights.

3 Malrotation with volvulus (MV)

For patients with MV 6/73 (8%), one had total midgut necrosis at initial laparotomy leading to palliation. Two had damage control surgery but died before relook surgery. The remaining three had resection and primary anastomosis. All three of these patients died within the first week post-surgery from sepsis; two of these were palliated as a result of severe sepsis and short bowel syndrome.

4 Inguinal hernia (IH)

Three out of seventy-three patients who died had an incarcerated and strangulated IH; operative information was available for two patients. One patient had a laparotomy due to bowel perforation at the initial surgery which resulted in sepsis from intra-abdominal soiling; the other patient had an herniotomy via inguinal incision. Both had resection of necrotic bowel and primary anastomosis. Demise for all three patients was associated with sepsis more than a week post-surgery.

5 Anorectal malformation (ARM)

The neonates with ARM who died 5/73 (7%) all had a divided sigmoid colostomy. One died of cardiac failure as a result Tetralogy of Fallot. Three of the patients developed sepsis of which two had associated multi organ failure. One of the patients had sepsis that was complicated by abdominal compartment syndrome. No surgical information was available for one of the patients. Mean age at arrival was 2 days with a range (1-4). The mean age at surgery was 3 days with a range of (1-4). Of the five patients, two were operated day 1 and two of life. The other two were 3 days old at surgery and one was 4 days old at surgery. Delay in recognition in the last patient resulted in one of the patients arriving day four of life in septic shock, patient had surgery on the day of arrival and complicated further with abdominal compartment syndrome 24 hours later requiring decompressive laparotomy. Four of the five patients died in the first week while the other demised at twenty-nine days post-surgery as a result of complex cardia lesion.

6 Oesophageal atresia and trachea oesophageal fistula (OA/TOF)

Patients with OA/TOF 3/73 (4%), had thoracotomy and repair of atresia in two cases and gastrostomy for long gap OA/TOF in one case, which was complicated by gastric perforation and sepsis. One of the patients who had a primary oesophageal repair developed an anastomotic leak associated with pneumonia and then died as a result of sepsis. Information for the other patient who had a thoracotomy and primary repair was not available.

7 Intestinal atresia (INT)

Intestinal atresia 10/73 (14%) patients included 3/10 who had duodenal atresia and 7 with jejunal atresia. One patient had an open and close laparotomy procedure as a result of total midgut necrosis, due to antenatal volvulus. One patient with 3b jejunal atresia had a damage control procedure due to ischaemic bowel and seven of the patients had anastomotic repair of the bowel atresia. Two patients had anastomotic leaks with one complicated by ACS which was a patient with jejunal atresia; the other patient had a

duodedudenostomy for duodenal atresia. Seven had associated sepsis and multi organ failure of which three had short bowel syndrome resulting in palliation.

8 Gastroschisis (GS)

The patients with GS 9/73 (12%) with a mean gestational age of 36 weeks (range 35-38). The surgical procedures included one who had an "open-and-close" non-therapeutic exploratory laparotomy procedure as a result of necrotic bowel, and seven who had closure of abdominal wall defect with one patient having jejunal atresia not corrected at the closure of abdominal wall surgery. The average time to closure was 4 days (range 1-9). The remaining patient with complicated gastroschisis requiring bowel resection and primary anastomosis with application of a silo bag in theatre.

9 Congenital diaphragmatic hernia (CDH)

Laparotomy with repair of CDH 3/73 (4%) was performed in all three patients and one had the abdomen left open due to increased intra-abdominal pressures and inability to close the abdomen. Three patients had pulmonary hypoplasia of these, two had comorbid pulmonary hypertension and respiratory sepsis.

3.6.2 Post-operative complications

1. Short bowel syndrome

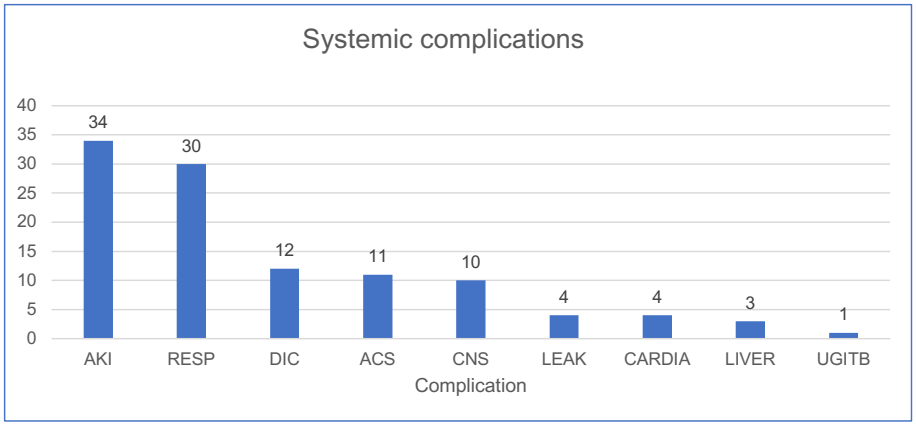
A total of 21 patients at 29% had short bowel syndrome. Causes of short bowel included intestinal atresia (7/21) and necrotizing enterocolitis (7/21), gastroschisis (5/21) and malrotation with volvulus (2/21). Of these patients (9/21) 43% had ultrashort bowel resulting in these patients being palliated. This included patients with NEC (4/9), intestinal atresia (3/9) and MV (2/9). Half of the patients with SBS died from sepsis and multi organ failure and one patient with NEC had intestinal failure associated liver disease.

2. Systemic complications

Seventy four percent (54/73) of patients who died had post-operative had associated complications(see figure 2). This included: respiratory failure; acute kidney injury, disseminated intravascular coagulation, upper gastrointestinal bleeding, liver failure; anastomotic leak and abdominal compartment syndrome.

Common post-operative organ dysfunction included acute kidney injury in 34/73, (47%); respiratory failure (requiring respiratory support of various forms) in 30/73, (41%), and disseminated intravascular coagulopathy in 12/73, (16%).

Figure 2: Post-operative complications associated with mortality



RESP-respiratory,AKI-acutekidneyinjury,**DIC**-disseminatedintravascular coagulation-central nervous system, **ACS**-abdominal compartment syndrome

3. Surgery-related complications

3.1. Anastomotic leak

Anastomosis leaks occurred in 5/73 (7%) of patients who had primary anastomosis of the following conditions:

- Jejunal atresia(1)
- Duodenal atresia(1)
- SIP(2)
- Oesophageal atresia(1)

Anastomotic leak resulted in gram negative sepsis following intraabdominal soiling from site of anastomosis and development of multi organ failure in 4/5 patients. Sepsis was associated with death except for 1/5 who developed respiratory failure with pulmonary haemorrhage as the associated cause of death complicated by intraventricular bleed. In the group with intestinal atresia patients one of the patients developed abdominal compartment syndrome, which caused further compromise to the bowel. Of the 5 patients with anastomotic leaks three of them had revision of the anastomosis and one had stoma formation (SIP) post the anastomotic leak. The patient with oesophageal atresia demised due to sepsis-related respiratory failure prior to revision of the anastomosis.

3.2. Respiratory failure requiring support

Pre-operative respiratory support was required in 40/73, (54%) of patients, continuous positive airway pressure therapy 8/73 (11%), nasal prongs oxygen 2/73 (3%) and conventional ventilation 30/73, (41%). Respiratory failure requiring respiratory support developed post-operatively in 67/73, (92%) patients, high frequency oscillator 32/73, (44%) and conventional ventilation 35/73, (48%).

3.3. Surgical procedure

Ninety five percent of operations in those who died (69/73) were conducted as emergency procedures and 4/73, (5%) were planned elective procedures, the latter being mostly in the gastroschisis group.

3.4. Relook procedure

Certain patients needed more than one procedure. Twenty-six out of the 73 patients who died required relook surgery (37%). This was common among patients with necrotizing enterocolitis, intestinal atresia, malrotation and spontaneous intestinal perforation. The groups with the highest percentage of revision surgery were necrotizing enterocolitis 11/26, (42%) and intestinal atresia at 6/26, (23%). Reasons for repeat laparotomy procedures were abdominal compartment syndrome 11/26, (42%,) initial damage control surgery 7/26, (27%), anastomotic leak 5/26, (19%), colonic perforation with evolving NEC 2/26, (8%) and adhesive bowel obstruction 1/26, (4%).

3.5. Abdominal compartment syndrome

Abdominal compartment syndrome was noted post operatively in 11/73 patients who died (15%). Nine out of 11 of these patients received inotropic support following index surgery (82%). Out of the eleven patients who developed abdominal compartment syndrome, six were complicated by sepsis and multi- organ failure, and 3/11 patients had organ failure without sepsis. There were two patients who died due to short bowel syndrome as a result of extensive ischaemic bowel. The various diagnoses were as follows:

- Necrotizing enterocolitis (4/11) of whom three had bowel resection with primary anastomosis and closure of the abdomen. One of these patients was left with an open abdomen after damage control surgery, despite which abdominal compartment syndrome developed.
- Incarcerated inguinal hernia (1/11) complicated by bowel ischaemia post resection and primary anastomosis.
- Anorectal malformation (1/11) presenting at 3 days old in whom dilated and oedematous large bowel was noted at divided colostomy.
- Long gap oesophageal atresia and no distal fistula (1/11) complicated by gastric perforation following gastrostomy
- Gastroschisis (1/11) post-surgical abdominal wall closed after staged reduction with silo bag.

- Congenital diaphragmatic (1/11) hernia reported to have difficult initial reduction and closure.
- Intestinal atresia (2/11) with anastomotic leaks.

3.6. Sepsis

Sixty-seven out of 73 (92%) of patients who died were clinically septic leading up to death. Fifty-four out of 73 (74%) had an identified source of sepsis. Sources of sepsis included central line associated sepsis 35/54, (65%), wound sepsis 13/54, (24%), infective endocarditis 2/54, (4%) and anastomotic leaks 4/54, (7%). No source of infection was identified in 13/73 (18%).

Specific organisms were cultured from blood in 45/73 (62%) of the patients who died of sepsis, with Enterococcus species 10/45, (14%), Klebsiella pneumonia 14/45, (19%), Actinobacteria baumannii 9/45, 1(2%) and Candida species 3/45, (7%) being the most common organisms cultured. The remaining cultures were other Gram-negative organisms (5/45; 11 %) and Gram-positive organisms 4/45, (9%).

Positive blood cultures were associated with the following causes of sepsis:

- There were 36/73 (49%) patients who had sepsis related to **underlying surgical pathology**. This included intestinal perforation and intra-abdominal soiling (13/36; 36%), ischaemic bowel 11/36, (31%) and necrotic diseased bowel 12/36, (33%).
- Positive blood cultures were associated with **central venous catheters** in (33/73) 45%. All organisms cultured were Gram-stain negative. Sixty-five out of 73 (89%) of patients who died had central venous access catheters. This included umbilical catheters, peripherally inserted central catheters, and mostly percutaneously inserted central venous catheters (placed with ultrasound guidance).
- There was a total of 45/73 with clinical features of wound infection who were swabbed yielding 19/45 (42%) culture-positive **wound infections**. Cultures yielded Gram negative organisms in 15/19; Streptococcus epidermis in 6/19 and Staphylococcus aureus in 3/19.

- All patients who were septic and ventilated had a **tracheal aspirate** performed 22/73, (30%); 15/73 cultured organisms (21%). Organisms identified included Acinebacter baumannii (8/15), extended spectrum beta-lactamase Klebseilla (2/15), staphylococcus aureus (2/15), one Candida species and one viral infection.

Sepsis was associated with organ failure, particularly acute kidney injury and pneumonia, these being contributors to but not direct causes of mortality. Respiratory dysfunction occurred in 30/73 (41%) and acute kidney injury in 30/73 (47%). Forty-one percent of patients who died were ventilated pre-operatively increasing to 92% in the post-operative period. This increased the risk of ventilator associated pneumonia with 10% of patients who died succumbing to this.

3.7 Physiological prognostic scoring systems

The scores for neonatal Acute Physiology and prenatal extension (SNAPPEII) and clinical Risk for Babies (CRIB II) Scores were unobtainable due to missing information from the retrospective nature of study and poor data keeping with respect to variables to calculate these scores.

Chapter 4:

Discussion

4.1 Neonatal surgical mortality compared to other settings

The overall 30-day post-operative mortality rate for neonatal surgical conditions examined in this study was 11%. This study's neonatal post-surgery 30-day mortality for commonly encountered gastrointestinal and abdominal wall conditions requiring surgery is shown in comparison to other reported HIC and LMIC mortality rates in Table 8. There are few publications on neonatal mortality in Africa but the post-operative mortality in this study compares favourably to other African countries as well as the limited reports from other South African centres ((24,30). It also underscores the significant differences that still exist between neonatal post-operative mortality rates in HIC and LMIC (17).

In addition, one-year post-natal survival in neonates receiving gastro-intestinal/ abdominal surgery in this study cohort is 77%, highlighting the need for further evaluation beyond the 30-day post-operative period of cause of mortality.

Table 8: Comparison of neonatal mortality between study cohort and other settings for various surgical conditions

[LMIC= low-to-middle income countries; HIC= high income countries; N=number; ARM= anorectal

Condition	Study cohort	LIC (4,9,10,11,12,47)	MIC (4,7,9,10,11,24,30)	HIC (4,10,11,31,48)
Necrotising enterocolitis	28%	19-53	32-50%	15-30%
Spontaneous intestinal perforation	29%	15-70%	22-32%	19%
Gastroschisis	18%	90-63%	31-42%	1-4%
Oesophageal atresia	9%	20-80%	15-10%	3%
Malrotation	9%	50%	37%	3-9%
Congenital diaphragmatic hernia	9%	20-60%	42-50%	10-30%
Intestinal atresia	8%	50%	47%	3%
Anorectal malformation	5%	31%	11-20%	3-10%
Inguinal hernia	3%	5%	0.2%	0%
Total	**83 (11%)**			

4.1.1 Study outcomes compared to HIC

The overall 30-day post-operative mortality rate for neonatal surgical conditions examined in this study was 11% which is double the rate in HIC over the same period for all neonates with surgical conditions. In addition, one-year post-natal survival in neonates receiving gastro-intestinal/ abdominal surgery in this study cohort is 77% which is much lower than HIC at 95% (49). High income countries have mortality rates lower than 10% for most conditions (4). For the high-income countries this comparison is made for all patients, operated and not operated, indicative of an even lower post-operative mortality rate.

4.1.2 Study outcomes compared to other South African settings

A large paediatric surgical centre in South Africa reported their overall 30-day neonatal patient mortality to be 22%. This was largely due to sepsis which contributed to death in over 80% of their cohort. Surgical complications occurred in over 18% of patients who had morbidities, with morbidity in nearly 60% of the cohort (30). Forty percent of this cohort had NEC, a higher proportion than in our study (30). Another study at a different tertiary hospital in South Africa showed a 66% overall mortality for surgical patients admitted to their ICU and a 35% post- surgical mortality. Eighty-three percent of procedures were abdominal, and sepsis as well as low birth weight and gestational age were major predictors of poor outcome (24). Patients with NEC patients made up 39% of admissions with an overall mortality of 56% and post-surgical mortality of 53% (24).

The 30-day post-operative mortality of 11% as a MIC hospital compared better to countries on the African continent who were LIC, where mortality rates are between 30-40% (4,7). Disease-specific mortality was similar to MIC on the continent such as Egypt (50), which reports post-operative mortality ranging from 6 to 45% for various conditions (8,50,51)·

4.1.3 Study outcomes compared to other African settings

Comparison from low-income countries is for those that were operated. It is evident from this that RCWMCH has post-operative mortality rates that are lower in comparison to LIC but worse than HIC. The mortality rate of necrotizing enterocolitis was lower in comparison to other centres in South Africa and LIC on the African continent.

4.1.4 Study outcomes compared to other MIC settings

On comparison for neonatal mortality with middle income countries for overall surgical conditions (operated and those not operated) such as Egypt, Indonesia and the Philippines, our neonatal mortality rates were found to be similar (6).

4.2 Non-modifiable factors associated with 30-day post-operative mortality

Pre-operative risk factors:

These risk factors for mortality related to delays in patient arrival to the hospital where definitive care would take place (RCWMCH) or otherwise have impact on patient clinical condition at time of surgery.

4.2.1 Distance from referral centre

Delayed presentation is an independent risk factor that predicts the mortality for neonates who have undergone surgical intervention (9,25). Early referral and surgery are advised to avoid morbidity and mortality. The odds ratio for death for patients with travel time over one hour from the referral hospital was 3.6 (95% confidence interval). Patients who were more than one hour away from the receiving institution (RCWMCH) experienced a higher mortality, indicating that distance travelled from referral hospital negatively impacts patient outcome. Resultant delays to definitive care may contribute to increased rates of morbidity and mortality in neonates reliant on surgical intervention for survival. The only distant hospital with a mortality comparable to hospitals close to RCWMCH was Oudtshoorn Hospital, which refers very ill patients to nearby George Regional Hospital for stabilization prior to transfer to RCWMCH for definitive surgical care. This may then give the impression of slightly lower numbers. Patient pathology from this distance of more than 100 km included necrotizing enterocolitis, spontaneous intestinal perforation and gastroschisis which were conditions among the top 5 causes of mortality. It stands to reason that distance and primary pathology both impact on survival outcomes post-surgery. This may be evident by significant increase in development of morbidities as a result of delayed transfer receiving patients who are critically ill at time of admission Efficient referrals and neonatal transport systems are essential interventions to reduce neonatal mortality (9,24,31). Paediatric surgical services, with early referral and improvement of neonatal transport systems need to be prioritized.

4.2.2 Presenting comorbidities

Prematurity, low birth weight, respiratory failure, sepsis and shock at presentation are amongst many factors potentially responsible for poor prognosis in neonates (1,13,22,23,24). Preterm birth, low birth weight, chromosomal defects, genetic anomalies and multiple organ dysfunction may require intensive specialized management (15,51).

- Gestational age has a contribution to mortality. Most of our neonates were born prematurely and the cohort of patients who died had a mean gestational age in the cohort of 33 weeks. Prematurity is known to have significant influence on outcome. Most premature neonates were noted in the necrotizing enterocolitis and spontaneous intestinal perforation group. These are among the same two groups with the highest mortality.

The majority of the patients who died were males at 80%. This is explained by sex differences in genetic and biological makeup, with boys being biologically weaker and more susceptible to diseases and premature death (29). Certain conditions such as anorectal malformations with recto-urethral fistulae occur uniquely in males, of which there were 5 in our mortality cohort, where lack of timeous intervention may be more lethal than in girls where fistulous decompression of obstructed bowel is more likely.

Congenital Anomalies: Ten percent of patients who died had an underlying congenital cardiac lesion with this contributing to mortality in 2 cases 2/73, (3%).

Other comorbid (acquired) conditions:

1. Patients with underlying **respiratory conditions** contributed to mortality, these were patients with hyaline membrane disease and neonatal respiratory distress syndrome. Respiratory failure occurred as a result of underlying respiratory pathology, infection, pulmonary oedema or pulmonary haemorrhage. Factors responsible may be divided into patient factors from underlying respiratory disease, while others are procedure-related factors from surgery or sepsis that have impact on outcome.

- Patients with NEC accounted for 32% of patients with underlying respiratory disease, leading to death in 12% of these patients. This reflecting pan systemic inflammation and sepsis associated with severe NEC. Respiratory failure or compromise may affect surgical patients' outcomes resulting in prolonged stay in ICU and ventilation. It is important to recognize patients at increased risk of respiratory complications.

- **Sepsis**: Patients who had initial perforated bowel, necrotic or ischaemic bowel which resulted in early sepsis with influence on mortality were 49% of the cohort who died. This included intestinal perforation and intra-abdominal soiling (36%), ischaemic bowel (31%) and necrotic diseased bowel (33%).

These presenting comorbidities may reflect delays in transfer and presentation in many cases and inadequate resuscitation at the primary health care level. Therefore efficient transfer systems, availability of intensive care facilities at receiving definitive care hospitals are important factors to improving neonatal surgical outcome

4.3 Modifiable factors associated with 30-day post-operative mortality

4.3.1 Intra-operative factors

The volume of neonatal operative work load at this study hospital (averaging 10 cases a month) is similar to another large tertiary institution in the country (52). The study did not look at level of surgical or anaesthetic training or experience although procedures were performed at a training institution. Further prospective work is required to look at the impact of surgical experience and intra- operative technique.

4.3.2 Post-operative factors

A major factor directly related to the cause of short-term mortality included ultra-short bowel length for which there are limited resources to manage severe intestinal failure with a poor prognosis hence early decision made to palliate these cases·

1. Intensive care

There is an increased burden placed on paediatric surgical services at referral hospital in South Africa (24). The experience with very low birth weight neonates and presence of a neonatal intensive care unit at the delivery hospital also influences neonate's risk of mortality and morbidity (21). Neonates with major surgical conditions accounted for a significant burden on ICU admissions at RCWMCH with 97% of patients admitted post operatively and an average stay of 5 days. Two patients were not admitted into the ICU, for the NEC group, as no further intervention was planned for these patients due to a decision for palliative care. The limitation in bed availability related to demand has always been a challenging problem, especially in the ICU. This resulting in delays in transfer and definite management of neonates who are already critically ill. This further affected by associated life-threatening anomalies (cardiac and central nervous system anomalies) which may be a significant predictor of death unrelated to the pathology for which the neonate undergoes a surgical procedure (17). Inotropic support increased considerably from pre- to post-operative, especially among the necrotizing enterocolitis group.

Health system infrastructure and planning to increase bed availability needs to be prioritized as a healthcare intervention to reduce neonatal mortality in LMIC.

2. Post-operative surgical complications

Seventy four percent (54/73) of patients had post-operative complications. These include but not limited to abdominal compartment syndrome, anastomotic leak, and sepsis. This may be related to the extremist condition that some of these patients arrived in, related to primary pathology, associated comorbidity, and delays in transfer for definitive are as

a result of transport or ICU space limitations. Neonates born outside the tertiary center's where definitive management is undertaken have a worse reported outcome in LMIC (1,14,22,23,24,30). Delayed presentation is an independent risk factor that predicts the morbidity and mortality.

- ***Abdominal compartment syndrome*** was mostly encountered in patients with necrotizing enterocolitis requiring re operation. Consideration should be made at initial surgery if patients' abdomen should have been left open, especially patients with necrotizing enterocolitis who ended up with necrotic bowel on the second look procedure as a result of abdominal compartment syndrome. Acute abdominal risk factors especially in NEC, perforation, strangulated inguinal hernia, ileus and volvulus; this group of patients being at increased risk of ACS because of distended oedematous bowel associated with systemic inflammatory response syndrome and organ dysfunction (30).

  Careful patient selection and intra operative decision-making regarding patients who should be left with an open abdomen and planned review procedure with optimal conditions and patient factors to close the abdomen to ensure better outcomes and avoid ACS. Abdominal pressure monitoring should be done for patients of concern or at risk of ACS with a low threshold for re-exploration in such patients. There needs to be increased awareness problem of intra-abdominal hypertension that result from an operative closure of congenital abdominal wall defect such as gastroschisis or Omphalocoel. Considerations for staged procedures in particular patients with abdominal wall defects and specific abdominal surgery, organ dysfunction, cardiac insufficiency as well as hepatic and renal dysfunction, capillary leak syndrome, continuous positive airway pressure and systemic inflammatory response syndrome to eliminate deleterious consequences of increase intra-abdominal pressure and progression to abdominal compartment syndrome (30).

  Identifying at risk groups which may be divided into congenital or acquired causes with abdominal wall defects and NEC mostly involved. Instituting continuous or

intermittent measurement methods of intra-abdominal pressure either via bladder or stomach. The patients who are potentially at high risk of ACS would need close monitoring for acidosis or high gastric residuals. Monitoring in the ICU for high lactate values with onset of distension may assist determine timing of early surgical intervention. Implementation of strategies to allow early recognition and reduce the deleterious consequences of ACS need to be addressed (53).

- ***Anastomotic leaks*** were observed mostly in patients with intestinal atresia. Better selection of patients for primary anastomosis and those that would have had a better outcome with stoma formation needs to be held in balance with the poor outcome of especially premature neonates with proximal stomas due to high intestinal losses and fluid/electrolyte replacement in context with high rates of CLABSI. Patients in the study had systemic sepsis, inotropic support with organ system failure. There were multiple confounding factors to their break down. Anastomosis leaks may be reduced by opting either for abbreviated surgery with planned relook surgery at a later stage when patient has been optimized or the formation of stomas. There would be less chance of anastomotic leak whether intra-abdominal or intra thoracic if consideration for staged procedures in patients with sepsis and organ support was instituted.

3. Sepsis

Sepsis is an important cause of death in neonates and children under 5 years of age globally at 7% (54). Fifteen percent of our patients died, due to sepsis, a frequency at least 2–3 times higher in LMIC than HIC. Infection causes 4–56% of all neonatal mortality in LMICs (24,27,54). In South African literature frequent organisms cultured in neonatal ICUs were predominantly Group B Streptococcus, Staphylococcus aureus, Serratia marcescens, Acinetobacter baumani, Vancomycin Resistant Enterococcus , Pseodomonas aeruginosa, Escherichia coli, Candida albicans, and Klebsiella pneumoniae with fungal sepsis less common (24,30,40,55,56), similar to the organisms

cultured from patients in this study, reflecting the enteric source of the sepsis in most cases and the similarity with other ICU in the country

- ***Pre-operative risk factors for sepsis***

Neonates requiring surgery are more often premature or have very low birth weight (VLBW) and require interventions such as central venous catheterisation more frequently. They also have prolonged hospital stay due to underlying congenital anomalies or prematurity, which may further predispose to development of morbidity, especially nosocomial sepsis. There were 41% of patients in the cohort with respiratory failure requiring intubation and ventilation, and 10% of these complicated by ventilator associated pneumonia resulting in death. Prolonged ventilation being another cause of sepsis.

- ***Intra-operative risk factors for sepsis***

Factors such as intra-operative hypothermia could not be assessed in this retrospective study. Surgical experience may reduce subsequent complications such as anastomotic leak and wound dehiscence but could not be satisfactorily evaluated in this retrospective study due to incomplete or missing information for a large number of patients. Further study is needed to see if intra-operative factors resulting in sepsis could be reduced. Demise from sepsis in cases such as bowel perforation due to incarcerated inguinal hernia might have been related to inadequate sepsis source control at the index procedure as well as sepsis-related organ complications such as respiratory failure and acute kidney injury. This might also hold true for the other abdominal surgery's such as intestinal atresia, volvulus, NEC, and spontaneous intestinal perforation if intra-abdominal contamination is not controlled.

- ***Post-operative risk factors for sepsis***

Mortality was caused by sepsis in 74% with these organisms cultured: Enterococcus spp., Klebsiella pneumoniae, Acinebacter baumaniae and Candida albicans. Culture-proven wound infection was accounted for by Streptococcus

pneumoniae and Staphylococcus aureus. Sources of sepsis included line sepsis with the highest percentage followed wound sepsis from surgical sites, infective endocarditis and anastomotic leak. Early identification of at-risk patients for wound break down and anastomotic leak by setting in place monitoring and intervention strategies is required. This may also include decision making intra operatively decision making regarding stoma creation or versus primary anastomosis. Programs to improve infection prevention, stringent transmission-based precaution, education and adjustments or modifications to clinical practice is required to address post-surgical sepsis in neonates (40).

- *Central lines and sepsis:* Central lines were inserted in 89% of patients, putting these patients at increased risk of CLABSI, especially in patients with ultra-short bowel syndrome who needed long term total parenteral nutrition (such as intestinal atresia, necrotizing enterocolitis, gastroschisis with atresia and malrotation with volvulus). Forty eight percent of patients had culture-proven sepsis from the central line.
- *Surgical site infection:* This is higher in neonates due to underlying co-morbidities, prematurity, prolonged requirements for total parenteral nutrition and immature immune system of neonates (41). Improvement in prevention of sepsis and improved infection control are therefore an absolute necessity if we are to improve outcomes in surgical neonates.

Sepsis was associated with organ failure in particular acute kidney injury and pneumonia, these being contributors to but not direct causes of mortality. Post-operative organ dysfunction included respiratory failure, acute kidney injury, disseminated intravascular coagulation and abdominal compartment syndrome. Most patients who died 34/73, (46%) had sepsis related to underlying surgical pathology despite comprehensive intensive care support and surgical source control of sepsis, indicating the need for earlier surgical intervention through timeous transfer and speedy access to intensive care support and emergency operative theatre to curb inflammatory response to compromised bowel in many

patients, although notable preventable surgical complications are discussed above.

4.4 Disease-specific mortality

Patients with NEC, SIP and gastroschisis were associated with higher mortality rates compared to the rest of the conditions. The rest of the other conditions had significantly lower comparative mortality rates. Sepsis was the largest contributor to mortality in NEC, SIP and gastroschisis, and typically complicated with anastomotic leaks and organ failure. Abdominal compartment syndrome resulting in patient deterioration and in some instances bowel ischaemia, anastomotic leak and central line sepsis had a contribution to mortality. Early recognition of ACS having options to perform abbreviated surgery and leaving abdomen open for planned relook surgery and closure when patient condition has been optimized needs to be considered.

1.Necrotizing enterocolitis

Predominantly affecting premature infants, this had the highest mortality. South Africa has shown a high prevalence of surgical necrotizing enterocolitis (1,16,18,26,30,). Those requiring surgery had perforation, ischaemic bowel that needed resection or mechanical bowel obstruction. This condition is associated with shock, sepsis and organ failure, having a high mortality of 19-50% in LIC. In this study the NEC group was associated with longer ICU stays and more inotropic requirement than other patients who died and most of the patients were ventilated pre and post operatively complicated by pneumonia. Relook surgery at 46% was required mostly due to open abdomen or ACS. Systemic and central line sepsis was also highest in patients with NEC. In the United States the mortality ranged from 15-30%, especially in low birth weight neonates with extensive disease requiring surgery (10,11). RCWMCH mortality rate of 38% for those operated likely reflects delayed surgical source control with timeous surgery constrained by lack of in-house ICU beds. This leading to delays in transfer from neonatal units, as RCWMCH is not attached to the obstetric units, so all referrals are out born.

2.Intestinal atresia

This condition had the second highest mortality rate. Death was related to sepsis, **anastomotic leak requiring relook surgery (in 25%)** and ultra-short **bowel length** leading to palliation. Survival has increased in high income countries from 45% to 95% over the years. Survival rates between 80-90% are a result of advances in neonatal intensive care units, ventilation management, sepsis control and parenteral nutrition. The most common cause of death internationally is sepsis (10,11). Eighty nine percent of patients in the study had a central line placed, 8/73 (10%) did not have a central line placed and 1% of patients had no information available regarding line placement. Patients with intestinal atresia (2/10) did not have central lines placed. The one patient had total midgut necrosis with a decision made for no further intervention. The second patient had an abbreviated procedure due to haemodynamic instability and a line was not placed at the first operation. Unfortunately, the patient demised prior to relook, so no line was ever placed for the patient. Sepsis as a result of **CLABSI** occurred in 48% of patients post operatively.

3.Gastroschisis

Although the group with the third highest cause of mortality among our patient groups, mortality was lower compared to other LMIC. These patients with anterior abdominal wall defects pose challenges with fluid under- or over-hydration which impacts on bowel distension and delays closure, while dehydration and bowel obstruction are associated with electrolyte deficits. The practice in our institution is application of preformed silo bag at the bedside, despite several advantages there are potential complications which may include bowel ischemia, dislodgement and difficulties with final closure (31,57).

- ***Delay in referral:*** **Distance from receiving hospital** impacts survival (1,14,22,23,24,30,31). A study in 2015 looking at early primary repair of gastroschisis without general anaesthesia were noted to established full enteral feeding and discharge earlier from hospital compared to those treated by primary closure under anaesthesia or by staged repair (58) The

average time to surgery of the patients at RCWMCH was as 3 days, with five patients closed at the original surgery. Gastroschisis patients in this study were mostly referred from hospitals located at distances more than 100km from RCWMCH. Predictor of mortality in gastroschisis may be related to time from birth to first surgical consultation. This may further be affected by deficiencies in the neonatal transfer system which impacts outcomes for this particular group of patients (59). This especially for patients born outside the definite care centre, which may be the reasons for high mortality in our patients transferred more than 100km from RCWMCH. This does need to be investigated further as to underlying reason so we may implement strategies to improve outcome.

- Sepsis was common, mostly as a result of **CLABSI** due to delays with progression to full feeds. Central-line associated blood stream infection (CLABSI) is a strong predictor of outcome for patients with gastroschisis (57). One of the patients developed ACS post closure in theatre which was only on day 9 of life. This patient arrived day one of life but had a delayed closure. Closure of the defect at an older age, longer mechanical ventilation, CLABSI and necrotizing enterocolitis have been associated with longer hospital stays and parenteral nutrition (57). Infection prevention practices especially with central line care bundles need to be set in place and attempts for early closure. This has implication on outcome for patients with gastroschisis that is why it's important to evaluate current management strategies.

- ***Prematurity and low birth weight****:* These adversely affect morbidity and mortality, reflecting the need for improved antenatal care in these patients. Five of the nine patients with gastroschisis were born preterm with a gestation age below 36 weeks. In this cohort only one patient had a birthweight above 2500g, all the other patients fitting into LBW or VLBW categories, both of these factors impacting patient outcome.

4.Anorectal malformations

Electrolyte derangements, sepsis, compartment syndrome of the abdomen or perforation has resulted in most associated morbidity and mortality. Mortality in the literature ranges from 4-10% mostly related to the delayed presentation of cases and reflects the importance of early diagnosis and treatment of ARMs (10,11,60). In our cohort, distance from referring institutions to RCWMCH was less than 100km, so distance was not a factor.

- ***Delayed recognition*** of the congenital anomaly resulted in adverse outcomes, nevertheless, as reflected by the mean age of 3 in for the patients in this study. It was evident from this group of patients that delayed referral and time to surgery impacted patients. These patients had organ system dysfunction, especially acute kidney injury, on arrival.
- One patient with delayed presentation developed **abdominal compartment** syndrome following stoma formation requiring decompressive. There needs to be particular attention to abdominal pressure monitoring with low threshold for surgical re-exploration in such delayed presentation.

4.5 Long-term outcomes for neonatal surgery

Overall RCWMCH neonatal post-operative mortality at 30 days post-surgery was 11% with an increase to 23% by 12 months. This late doubling of mortality requires further investigation to see if it is related to poor follow-up or other underlying conditions or comorbidities such as chromosomal abnormalities or other organ dysfunction such as the poor neurological outcomes frequently seen following surgical management of necrotizing enterocolitis for example (17,21,26). This was not assessed as part of the study.

Chapter 5

Conclusion

5.1 Summary of key findings

This study identified the 30-day neonatal post-operative mortality rate at RCWMCH, a MIC free-standing tertiary paediatric hospital, to be 11% which was lower compared to LIC post-surgery outcomes but inferior to other MIC for some disease conditions, and higher than HIC mortality. Limited post-surgical disease specific data restricted direct comparison of outcomes. Mortality in patients with necrotizing enterocolitis and intestinal atresia was the highest. Gram-negative sepsis was a major contributing factor in the development of morbidity and mortality in our cohort, with sepsis accounting for 74% of deaths, often associated with anastomosis leak, as well as CLABSI. Abdominal compartment syndrome was another significant preventable cause of death. A list of recommendations for service improvement to assist in improved acre and outcome for our patients is discussed below.

The factors related to mortality were identified as modifiable or non-modifiable. Defining this would assist to address the concerns and issues at different points of care for these surgical neonates in an attempt to improve outcome. Improvement have been achieved in outcomes of neonatal surgery in Africa. Adaptations of neonatal intensive care, coordinated acute initial management of patients and timeous transfer surgical patients for definite management are potential interventions that could help to address the challenges and further improve outcome. Addressing modifiable or non-modifiable Morbidity and mortality related factors of this vulnerable patient group needs to be improved to improve outcome and have comparable outcomes to HIC.

5.2 Limitations of this study

The retrospective nature of the study affected availability of information from files which was often poor due to quality of record-keeping. There was difficulty in acquiring some patient records at the hospital limiting variables that could be collected, this included operative surgeon seniority details or level of training and duration of surgical procedure.

This study analyzed at post-operative mortality. Patients who did not survive to surgery were not included. Risk factors for pre- and post-operative mortality overlap but there may be a few differences. However, further prospective multi centre studies will be required investigation at the overall neonatal mortality for the various surgical conditions.

5.3 Recommendations

There need to be ongoing efforts to improve the quality of surgical care for children in low and middle-income countries to prevent mortality and morbidity across multiple congenital and infection-related neonatal conditions.

1. Prevention and improvement strategies for infection control are imperative if we are to improve outcomes in our surgical neonates. Better central line venous care needs to be instituted as this is a contributor to sepsis. Programmes to improve infection prevention practice in African neonatal units are urgently required. Implementation of transmission-based precautions, health care worker education, and changes to clinical practices could potentially contain infection outbreaks.
2. Considerations need to be made to reduce ACS by leaving the abdomen open after laparotomy for peritonitis with planned relook for definitive closure.
3. Early referral and definitive management to allow a better prognosis. This was evident in those patients who were transferred from areas more than an hour away.

4. We need improvements in timeous transfer for definite surgical procedure through infrastructural and organizational logistics.
5. Addressing intensive care bed capacity for regional hospital transfer.
6. Recognize specific group of patient's pathologies at increased risk for mortality with early intervention and sepsis control measures in place. This is especially the case for patients with necrotizing enterocolitis and gastroschisis.
7. Improved surgical technique
8. Improved communication with the multidisciplinary team, including with paediatricians, fetal medicine specialist and obstetricians. This resulting in coordinated delivery and transfer of patients timeously for their definitive intervention
9. The mortality at 6 and 12 months was significant and would need to be assessed in detail in future further studies to define the cause and associated factors.

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