OUTCOMES OF THE INJURED OESOPHAGUS IN CHILDREN MANAGED AT CHARLOTTE MAXEKE JOHANNESBURG ACADEMIC HOSPITAL.

By

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A research report compiled by Dr. M.M. Kopolo in fulfilment of the requirements for the degree Master of Medicine in Paediatric Surgery. Submitted to Faculty of Health Sciences University of Witwatersrand, Johannesburg.

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DECLARATION

I, Matongo Mfuneko Kopolo, student number 587856, declare that the research report titled "OUTCOMES OF THE INJURED OESOPHAGUS IN CHILDREN MANAGED AT CHARLOTTE MAXEKE JOHANNESBURG ACADEMIC HOSPITAL" is my original work. It is submitted for the fulfilment of the requirements for the degree Master of Medicine in Paediatric Surgery at the University of Witwatersrand, Johannesburg.

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Dr. M.M. Kopolo

DEDICATION

This work is dedicated to my wife Lonwabo Pearl Zilungile Khanyie Kopolo and to my parents Victor Sonwabo Kopolo and Thenoria Nodumo Mzembeta, who had supported and encouraged me during my studies.

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ABSTRACT

BACKGROUND

Caustic and foreign body related oesophageal injuries impose a significant burden of disease amongst children in developing countries.

OBJECTIVES

To determine outcomes and complications of caustic and foreign body ingestion in the study setting.

METHODS.

A retrospective record-based review of all children under 16 years of age admitted to Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) from June 2010 to June 2016 with a history of caustic or foreign body ingestion was performed. Statistical analysis was performed using the Chi-squared and Fischer's Exact tests where appropriate. Data was analysed using SAS software. Ethics clearance was obtained (M1660660).

RESULTS.

188 patients with caustic or foreign body ingestion were identified. Of these, 10 patients (10/188, 5.3%) were excluded as their records were lost. The majority of foreign bodies ingested were coins (55.1%, 98/178), followed by button batteries (13.5%, 24/178). Approximately one quarter of patients (24.2%, 43/178) presented with caustic ingestion. The majority of patients (81%, 144/178) suffered no complications, with 11.2% (20/178) suffering early complications. Patients with caustic and button battery ingestion were significantly more likely to experience early complications than those with coin and other foreign body ingestion (p=0.002). Early complications in the caustic and button battery ingestion group made up 85% (17/20) of all early complications and included laryngospasm, prolonged dysphagia, and lower respiratory tract infection. The only late complication in the study population was oesophageal stricture. Further, late complications (8.4%, 15/178) were only noted in the caustic and button battery ingestion group.

Conclusions

Foreign body and caustic ingestion are a common occurrence in children in our population. Prevention and early management strategies should be prioritised in order to decrease the complications associated with these avoidable injuries.

INTRODUCTION

Oesophageal injuries from ingestion of caustic substances, button batteries and foreign bodies may result in severe injuries to the oesophagus, upper airway and stomach, and have a potential to cause severe acute and long-term complications. Ingestion of caustic agents is known to be more pronounced in less developed countries (LDCs) especially in children under the age of six years (1). Poor socio-economic status and lower level of education of parents contribute to accidental ingestion caustic agents by children (2). In developed countries, legislation to control sales, distribution, packaging and labelling caustic substances have reduced the incidence of caustic ingestions in children (3). In South Africa, the Hazardous Substance Act of 1973 aims to control importation, sale, labelling, use, disposal and modification of corrosive substances and other hazardous substances including electronic devices, but caustic substances are easily found in South African households (4). The act does not provide for child-resistant packaging. In contrast to developed countries the reduction in corrosive substances has not been observed in developing countries (5). The most commonly ingested materials are household cleaning agents or chemicals that have been mistakenly ingested as being a drinkable beverage (6). Caustic soda has been reported to be the most commonly ingested caustic agent resulting in oesophageal strictures in South Africa, Sierra Leone and Nigeria and potash as the most common corrosive in Egypt (7)(8)(9)(10). Beverage bottles are routinely used for storage of caustic substances and other toxic substances in these developing countries.

Initial management of caustic ingestions includes resuscitation followed by endoscopy within 24-48 hours to assess the extent of the injury and to assess the risk of developing oesophageal strictures (11–13). Symptomatic patients or even asymptomatic patients that have ingested a known strong caustic agent should undergo endoscopy within 24-48 hours (5). Depending on the severity of the injury, adjunctive measures include placement of a nasogastric tube to provide access for feeding and access for future dilatations and placement of gastrostomy tubes to provide nutritional support (7,14).

Oesophageal strictures are the most common late complication associated with ingestion of caustic agents and endoscopic guided dilatation is the first line of management (10). The aim of oesophageal dilatation is to establish an adequate oesophageal lumen to relieve symptoms. Internationally, serial oesophageal dilation results are associated with a 60% - 80% success rate (10). However, this is not the case in some developing countries where delayed treatment and defaulting treatment of oesophageal strictures leads to formation of refractory strictures and

less success with oesophageal dilatation (7,14). Most authors agree that efforts should be made to preserve the patient's own oesophagus when patients develop oesophageal strictures. This comes with the repeated number of hospital visits, general anaesthesia and complications of oesophageal dilatations e.g. oesophageal perforations. Within the literature, there is no consensus on the limits of oesophageal dilatation and treatment failure. However, the predictors for oesophageal replacement have been identified, these include delayed presentation, defaulting treatment, poor follow, the requirement of more than ten sessions of dilatations and long tortuous strictures (7,10,14). If efforts to preserve the native oesophagus fail, then oesophageal replacement, using stomach, colon or small bowel is required. However, this option carries a risk of complications including leakage, strictures, graft necrosis and death (10).

Coins are the most ingested foreign bodies by children (15). Complications due coin ingestions are rare and when they happen, they are mainly caused by prolonged oesophageal impaction (16). Severe complications like oesophageal strictures and oesophago-aortic fistula strictures have been reported (17,18).

Pointed foreign bodies like pins, needles, toothpicks and nails are also among commonly ingested substances by children (19). Delayed diagnosis and management increase the risk of complications (20). Complications depend on the site of impaction. In the chest they can penetrate through the oesophagus into the pleura, lungs, aorta and heart leading to mediastinitis, empyema, lung abscesses and aorto-oesophageal fistula (19).

Button battery ingestion accompanied by major complications and fatalities are on the rise globally especially in children less than six years of age (21). This is attributed to widespread use of powerful Lithium batteries particularly the 3V 20mm for toys and household electronic devices (21). Complications include oesophageal perforations, tracheo-oesophageal fistula, fistula into a major vessel, oesophageal strictures, vocal cord paralysis, spondylodiscitis and death. Children may need major surgeries and prolonged intensive care unit admissions to treat these complications (21,22). Unwitnessed ingestions leads to delayed diagnosis because signs symptoms are non-specific and that can lead to misdiagnosis by clinicians (21,23). Missed diagnosis contributes to morbidity and mortality from accidental battery ingestions (21,23).

To reduce battery associated injuries the US government passed the Consumer Product safety Improvement Act of 2008 which required that the batteries must be inaccessible in all toys for use by children under the age of 3 years (21). This resulted in a moderate reduction of battery ingestion, but complications and fatalities were on the rise due to the use of Lithium batteries (21,24). Accidental ingestion of button batteries especially Lithium cells is also a problem in

developing countries. Umana A. et al reported a series of six patients with Lithium button battery ingestion from Nigeria in which 5 had severe complications on presentation including tracheo-oesophageal fistula and oesophago-pleural fistula with hydrothorax (25). Time to presentation ranged from three days to seven weeks (25). Although this study was limited by the small number of patients, it highlighted the problem of delayed presentation of patients in LDCs.

Urgent endoscopic removal is paramount in the management of impacted button batteries because oesophageal damage with major complications can happen within two hours of ingestion (26). Acute complications are severe injuries to the oesophagus which can progress to neighbouring tissues including the trachea resulting in a trachea-oesophageal fistula, or major vessels like aorta resulting in oesophago-aortic fistula (26). The most common late complications are the development of oesophageal strictures, although other complications such as tracheo-oesophageal fistula, laryngeal stenosis, fistula into the major vessel are also observed (26).

Oesophageal strictures resulting from ingestion of caustic substances and button batteries are a significant problem in children, and can result in malnutrition, food impaction and pulmonary aspiration (27). At Charlotte Maxeke Johannesburg Academic Hospital (CMJAH), a significant number of children are treated for oesophageal injuries and related complications due to caustic ingestions, button batteries, coins and other foreign bodies. Currently there is no data regarding the outcomes of management of children presenting to CMJAH with ingestion of caustic substances, button batteries, coins and other foreign bodies. In order to identify patients at risk of developing severe complications from these ingestions and to improve our outcomes, we aimed to describe the population of patients with the ingestion of caustic substances, button batteries, coins and other foreign bodies treated at CMJAH and to describe complications associated with them in our patients. We also aimed to establish if delayed referral for dilatation and poor compliance to dilatation programme contributes to development of refractory oesophageal strictures.

METHODS

Study design and patients.

This is a descriptive, retrospective cross-sectional study carried out at Charlotte Maxeke Johannesburg Academic Hospital, a University of Witwatersrand teaching hospital in Johannesburg. Electronic medical records and patient files of children between ages of 0 to 16 years with ingestion of coins, button batteries, foreign bodies and caustic agents from 01 January 2010 until 24 June 2016 was reviewed. Patients were identified by reviewing ward and theatre records as well as Paediatric Surgery database. The patient files were obtained from CMJAH records department, after ethics approval by Wits Health Science Ethics Review Committee (M160660) on 24 June 2016. Data was captured by the principal investigator and entered to a Redcap database.

Patients older than sixteen years, asymptomatic patients with foreign bodies that have passed the oesophagus at the time of imaging, and patients that were not admitted to hospital were excluded. Children with oesophageal injuries due to gastro-oesophageal reflux were also excluded.

For patients that presented with caustic ingestion, if they presented within 72 hours of ingestion, an endoscopy was performed under general anaesthesia. Endoscopic findings were graded according to Zagar's modified endoscopic classification (28). In patients that presented after 72 hours of ingestion, an oesophagoscopy was not performed because of a high risk of perforating the oesophagus. In symptomatic patients an upper GIT contrast study was done after 2 weeks and if an evidence of oesophageal stricture was found then oesophageal dilatations were started three weeks after the injury.

Patients that presented with coin ingestions, button battery ingestions, or foreign bodies underwent rigid esophagoscopy under general anaesthesia if foreign body was still in the oesophagus. Some patients with coins in the oesophagus underwent balloon catheter removal. Patients that ingested a button battery who remained symptomatic after button battery removal had an upper GIT contrast study and if a stricture was identified then oesophageal dilatations were commenced after three weeks.

Definitions

Ingestions were classified into four groups: caustic agents, button batteries coins and other foreign bodies. For each group we analysed the age of the child, the gender, the time at presentation after the foreign body or caustic ingestion, and the incidence of no complications, early complications and late complications.

Early complications were defined as adverse events that occurred within two weeks of ingestion, either due to ingestion or treatment. Oesophageal perforations, hospital acquired infections, complications related to gastrostomy, and complications related to anaesthesia to perform the endoscopy belonged to this group. Late complications were described as adverse events that occurred after two weeks from the ingestion and included stricture formation and complications related to management of oesophageal strictures. No complications were defined as patients that had an uneventful hospital stay with no adverse events related to the

ingestion or the management of the ingestion. Other factors that were measured include the number of dilatations, the outcome of management of strictures and the need for oesophageal replacement surgery.

In button battery, coins and other foreign bodies if patients presented to CMJAH within 24 hours were classified as early referrals and the patients that presented beyond 24 hours were classified as delayed referrals. However, in patients with caustic ingestions if patients presented within 3 weeks to CMJAH they were classified as early referrals and if patients presented beyond 3 weeks they were classified as delayed referrals. This is because emergency management of caustic ingestions does not have any correlation with long term complications like development of oesophageal strictures.

The oesophageal stricture was defined as radiological or endoscopic evidence of oesophageal narrowing accompanying dysphagia. A refractory stricture was defined according to Kochman criteria, as a stricture that could not be dilated to an adequate oesophageal calibre to allow normal ingestion of food after five sessions of endoscopy or an inability to maintain the targeted oesophageal calibre after four weeks (29). Poor follow up was defined as those patients that defaulted follow up on their own. Resolution of the strictures was defined by a patient being asymptomatic with no need for further dilatations. After discharge, patients were followed in the outpatient clinic for at least 6 months or until they were asymptomatic.

STATISTICAL ANALYSIS

Categorical variables were analysed using proportions and frequency tables. Mean, standard deviation, median and interquartile range were used to analyse continuous variables. Chi-squared test was used to determine the association between a cause of injury and early complications, need for early gastrostomy, late complications and refractory stricture. Fisher's exact test was used if the requirements for the Chi-squared test were not be met. The Cramer's V and the phi coefficient were used to assess the strength of the relationship between the variables. The scale of interpretation was: 0.50 and above showed a strong association, 0.30 to 0.49 moderate association, 0.10 to 0.29 weak association, and below 0.10 little if any association. A binomial regression was used to determine the association between the presence of refractory strictures and delay in admission, a cause of injury, disturbance in dilatation. Data were analysed by SAS (version 9.4 for Windows). The 5% significance level was used.

RESULTS

DEMOGRAPHIC PROFILE

During the considered period 188 patients met the inclusion criteria but 10 files in the coin ingestion group could not be retrieved in both electronic and medical records. Therefore 178 children were included in the study. One hundred and fourteen patients (64 %) were male and 64 (36%) were female.

The median age at presentation was 31 months (range 7-180months). The predominant reason for admission was coin ingestion (n= 98;55,1%), followed by caustics (n= 43; 24,2%), then button batteries (n=24; 13,5%) (Figure1) and other foreign bodies (n=13;7,3%) which were, broken glass in three patients, sewing needle, chicken bone, paper pin, safety pin, marble, pen, pencil, plastic object, screw and the spring of a clothing peg

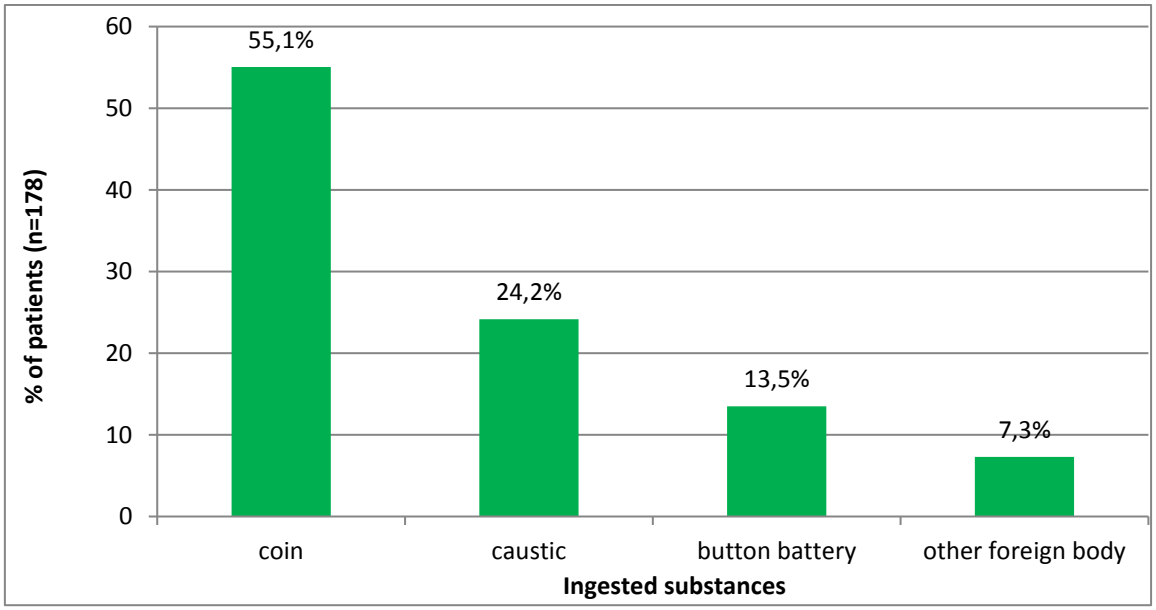

Figure 1. Reasons for admission.

Patients were predominantly local (n=95 ;53.4%) within CMJAH drainage area and referrals by local clinics but also came from other countries which were Zimbabwe, Democratic Republic of Congo and Mozambique (figure 2.)

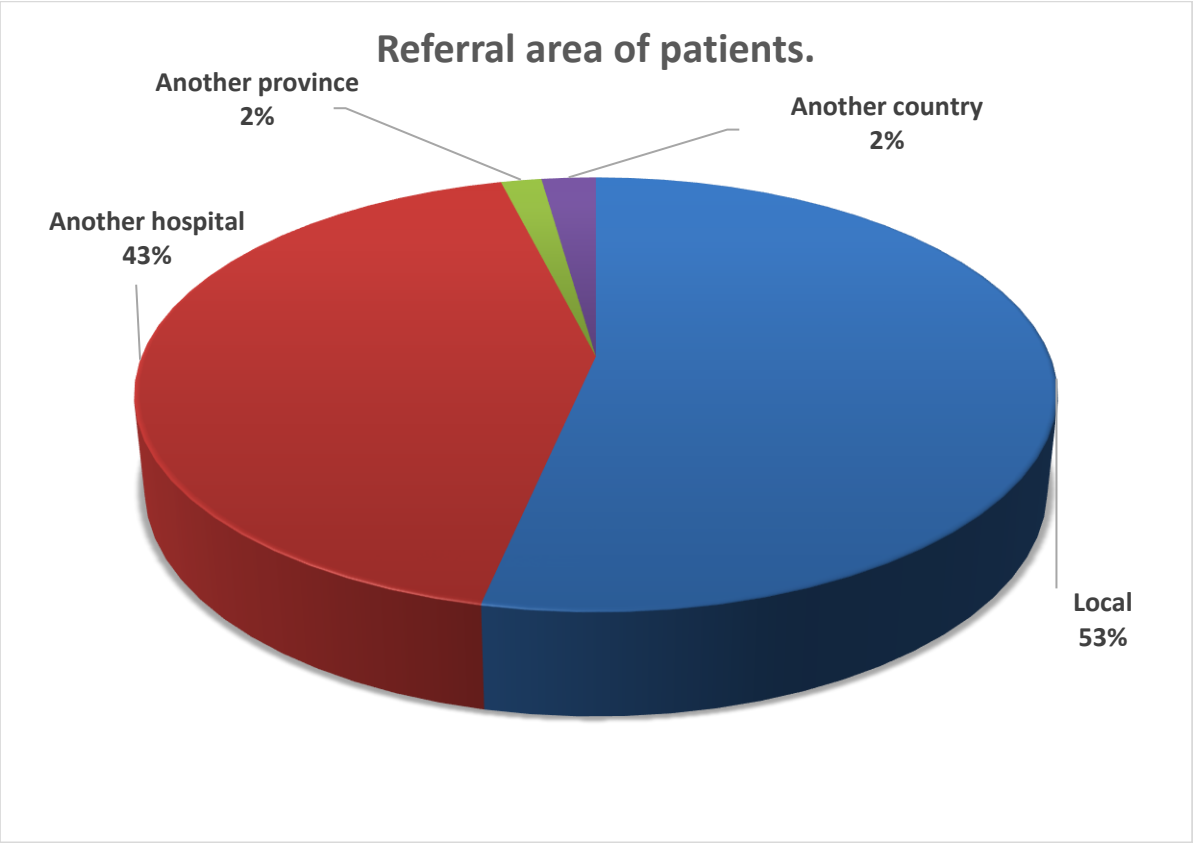

Figure 2**.** Referral area of patients admitted at CMJAH

COINS

Within the 98 patients who had ingested coins, 60 (61.2%) were male and 38 (38.8%) were females. Median age was 36 months (range 7- 105 months). Ninety-four (96%) had ingested only one coin and four (4%) ingested more than one coin. Seventy-one patients (72.4%) presented within 24 hours and 27 (27.5%) patients presented after 24 hours. Predominantly, 2-rand coins (n=29; 29,6%) and 5 cent coins (n=17, 17,34%) were ingested. Methods of removal of coins is summarised in table 1.

Method of removal of coins	**n**	**%**
Rigid endoscopic removal	82	83.6%
Foley catheter balloon removal	4	4%
Accidentally pushed to the stomach.	2	2%
Removed by an anaesthetist.	1	1%
Passed the oesophagus at the time of endoscopy.	9	9.1%

Table 1. Method of removal of ingested coins.

Two patients (2%) had underlying oesophageal abnormalities, one patient previously had an oesophageal atresia repair and another patient had gastro-oesophageal reflux stricture.

OUTCOMES

No complications

Ninety-five patients (97%) were managed successfully with no early or late complications. Majority of these patients with no complications presented within 24 hours (n=69; 70.4%) and had mainly rigid endoscopic removal (n=79; 83.2%) of coins done.

Early complications

Three patients (3%) had early complications that happened during induction of anaesthesia. These were laryngospasms in two patients and a cyanotic spell in one patient with a Tetralogy of Fallot. Of these three patients, one had a delay in presentation.

Late complications

None.

CAUSTIC INGESTION

Within the 43 patients who ingested caustic substances, 30 (70%) were male and thirteen (30%) were females. Median age was 33 months (range 12-180 months). Thirty-two patients (74.4%) presented within 24 hours and eleven patients (25.5%) presented after 24 hours. 39 ingestions (90.7%) were accidental and the median age was 29 months in the accidental ingestions group, and four (9.3%) were intentional and in older children with a median age of 168 months (14 years). Figure 4 shows a variety of caustic substances agents were ingested.

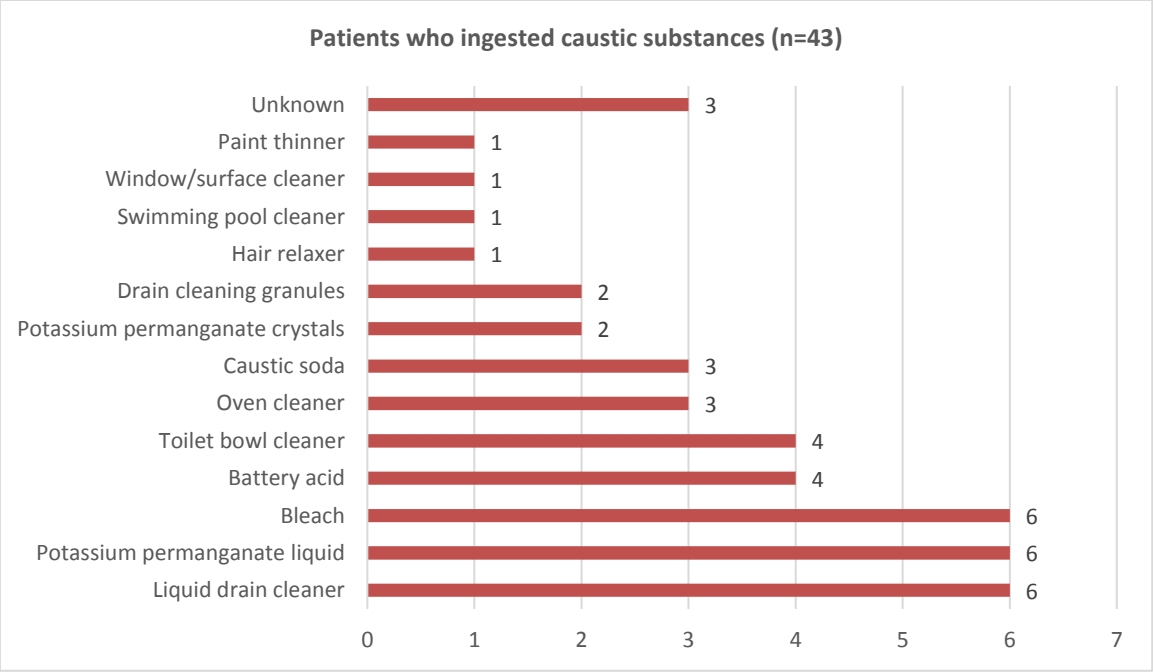

Figure 3. Variety of ingested caustic materials.

Liquid drain cleaner, potassium permanganate and bleach cleaner were the most commonly ingested caustic substances but, in some patients, the ingested caustic substance was unknown.

Most patients ingested the caustic substance from its original container 80.6% (n=29), and the 16.7% (n=6) ingested it from beverage containers, and 2.8% (n=1) ingested it from street vendor repackaging. Endoscopy on admission was done in 18 patients and the findings are summarised in table 1.

Endoscopic findings caustic ingestions	n=18	%
Grade 0 (Normal mucosa)	5	27.8%
Grade 1 (Erythema and oedema of the mucosa)	5	27.8%
Grade 2A (Superficial ulceration, erosions)	4	22.2%
Grade 2B, circumferencial lesions,	4	22.2%

Table 2. Endoscopic findings in patients that ingested caustic substances and had an oesophagoscopy done.

A Stamm gastrostomy was done in six patients (13.9%) during initial oesophagoscopy due to the severity of oesophageal injuries.

OUTCOMES

No complications

Twenty-four patients (56%) had no early or late complications during management.

Early complications

Seven patients (16%) had early complications. These were upper airway obstruction in three patients with two patients requiring tracheostomy, two patients had early dislodgement of the gastrostomy and required laparotomy and redo gastrostomy, one patient who ingested battery acid had gastric outlet obstruction that required parenteral nutrition and pyloroplasty. One patient had early stricture seen on a contrast study with prolonged dysphagia. These patients with early complications had ingested battery acid (n=1), liquid drain cleaner (n=1), toilet bowl cleaner (n=1), oven cleaner (n=1) and unknown caustic agents in three patients.

Late complications

Twelve patients (28%) developed oesophageal strictures as late complications of caustic ingestion and were started on oesophageal dilatation programme. Two strictures were due to drain cleaner, two from caustic soda, and one stricture each from battery acid, swimming pool cleaner, window cleaner, hair relaxer and paint thinner. The ingested caustic substance could

not be identified in three patients. The characteristics of strictures are summarised in Table 2. The mean number of dilatations was eight (range 1- 26). One patient (8.3%) had an oesophageal perforation during dilatation and another patient developed a refeeding syndrome after dilatation. Eight patients (66.6%) had a disturbance of the scheduled dilatation. The reasons for disturbance were lost to follow up in six patients (50%), not coming to the hospital on the scheduled day in one patient (12.5%), and unknown reason in one patient. Four patients (33.3%) required oesophageal replacement, three had a gastric pull-up procedure and one patient that had a colonic interposition which was done in another institution. The mean period from injury to oesophageal replacement was 17.8 months (range 2 to 26 months).

Inadvertent removal of gastrostomy was the common late gastrostomy complication seen in all six patients (100%) that required gastrostomy due to caustic ingestion.

Location stricture		%
upper oesophagus	5	41.6%
middle oesophagus	5	41.6%
distal oesophagus	1	8.3%
entire oesophagus	1	8.3%
Number of strictures		%
Single	9	92.86
Multiple	3	7.14
Nature of stricture		%
Short	7	58.3%
Long	3	25%
short and tortuous	1	8.3%
long and tortuous	1	8.3%

Table 3. Characteristics of oesophageal strictures due to caustic ingestion.

BUTTON BATTERY INGESTIONS

Twenty-four patients ingested button batteries, sixteen (66.6%) were male and eight (33.3%) were females. Median age was 17 months (range 10-84 months). Twelve patients (50%) were local and eleven (46%) patients were referred from other hospitals, one patient (4%) was referred from another country. Fifteen patients (62.5%) presented to CMJAH within 24 hours and nine patients (37.5%) presented after 24 hours. The chief causes of delayed transfer to CMJAH were due to a missed diagnosis by referring facilities (n=4; 16.6%) and initial management at another facility (n=4; 16.6%), failure to seek medical attention early in was seen in one patient (4%) (Figure 5.).

The initial diagnoses in patients with missed diagnoses were asthma, recurrent chest infections, upper respiratory tract infection, and feeding intolerance with failure to thrive.

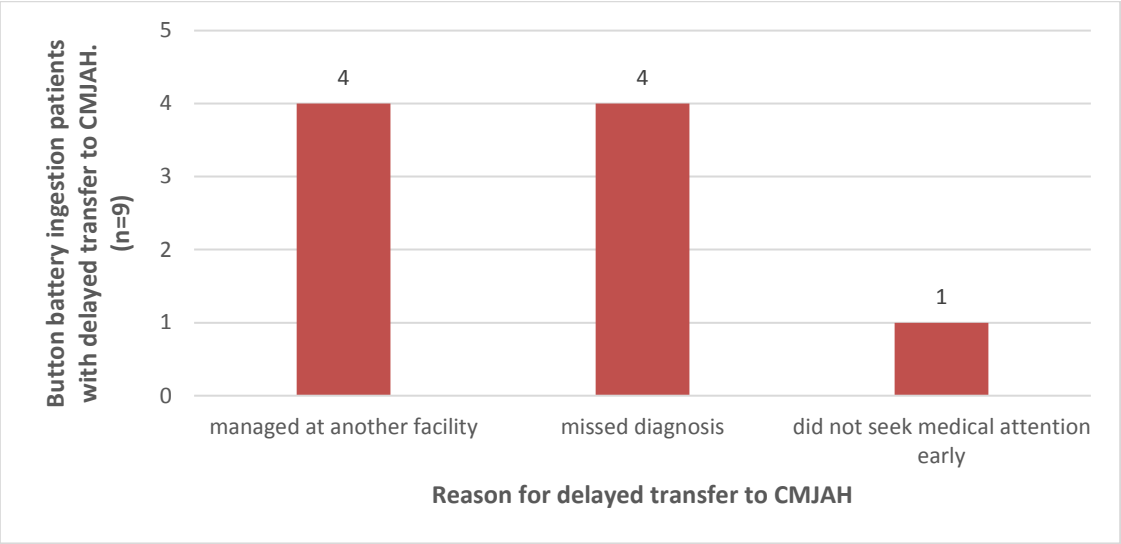

Figure 4. Patients with button battery ingestions with delayed referral to CMJAH

Majority of button batteries were in the cricopharyngeus (n=18; 75%), and four (16.6%) were at the aortic arch and right main bronchus, and two (8%) were in the stomach at the time of imaging.

Endoscopic retrieval of the button batteries was successful in 83% (n=20), three patients (12.5%) had an oesophagotomy done due to failed endoscopic retrieval, and of those three patients, one patient had oesophagostomy done in addition to oesophagotomy. Endoscopic findings in patients with button battery ingestions are summarised in Table 3. The button battery had already passed the oesophagus in one patient (4%) at the time of endoscopy

Endoscopy findings of ingested button batteries	n=24.	%
No injury	1	4.1%
Superficial mucosal injury	13	54.1%
Deep oesophageal injury	8	33.3%
No endoscopy done (battery already in the stomach)	2	8.3%

Table 4. Endoscopic findings in patients with button battery ingestion.

OUTCOMES

No complications

Sixteen patients (66.6%) with button battery ingestions did not have any complication during management. Twelve (75%) of these patients with no complications presented within 24 hours and all had endoscopic removal of button batteries done except for one patient in which the button battery was on the stomach.

Early complications

Eight patients (33.3%) had early complications. These complications were pneumonia in three patients requiring intensive care unit (ICU) admission and mechanical ventilation, hospital-acquired infection requiring ICU admission and in one patient, upper airway obstruction in two patients and prolonged dysphagia without an oesophageal stricture in one patient and an oesophageal leak from an oesophagostomy one patient.

Four patients (16.6%) had a Stamm gastrostomy on the first admission. Three of the four gastrostomies got dislodged and required laparotomy for peritoneal contamination and gastrostomies were revised. Five (62.5%) of these eight patients with early complications presented more than twenty-four hours of ingestion.

Late complications

Three patients (12.5%) developed oesophageal strictures and were started on the dilatation programme. These three patients with late complications were transferred to CMJAH more than 24 hours after battery ingestion. Two of these three patients had a resolution of the strictures after eight and sixteen oesophageal dilatation sessions. Two patients (8.3%) required oesophageal surgery, a gastric pull-up was done for the patient that had an oesophagostomy and a localised stricture resection and primary anastomosis was done in one patient whose stricture did not resolve after eleven dilatation sessions. These patients had oesophageal surgery done after seven and twenty-two months after oesophageal injury respectively. Table 6. shows the dilatation outcomes of all the strictures.

OTHER FOREIGN BODIES

Thirteen patients (7.3%) ingested a variety of other foreign bodies was ingested, table 5 summarise these foreign bodies and their method of removal.

Foreign body	**Number of patients**	**Method of removal**
Broken glass	3	Endoscopic
Sewing needle	1	Laparotomy
Marble	1	Pushed down to the stomach
Chicken bone	1	Endoscopic
Screw	1	Already passed the oesophagus
Paper pins	1	Endoscopic
Safety pin	1	Endoscopic
Pen	1	Endoscopic
Pencil	1	Already passed oesophagus
Plastic object,	1	Passed the stomach
Spring of a clothing peg	1	Endoscopic

Table 5. Other ingested foreign bodies and their method of retrieval

OUTCOMES

No complications

Eleven patients (84.6%) with ingestion of other foreign bodies were managed successfully with no complications. Ten (91%) of these eleven patients with no complications presented within 24 hours.

Early complications

Two patients (15.4%) had early complications during initial management. An oesophageal perforation accompanied by an empyema was seen in a patient that ingested a safety pin. A colonic perforation that required a laparotomy for removal because of a sewing needle ingestion. These two patients presented to CMJAH more than 24 hours after ingestion.

Late complications

None of the patients suffered late complications.

Summary of all oesophageal strictures.

A total of 15 patients developed oesophageal strictures as a result of button battery (n=3) and caustic ingestion (n=12). No patients developed strictures from coins and foreign bodies. These patients were started on oesophageal dilatation programme and the final outcomes of dilatation are summarised in table 6.

Oesophageal stricture dilatation outcome	n= 15	%
Resolution	2	13,3%
Required oesophageal surgery/ replacement (done)	5	33.3%
Awaiting surgery oesophageal surgery/ replacement	2	13,3%
Lost to follow up	2	13.3%
Still on dilatation programme	3	20%
Requires further surgery but refusing surgery	1	6,7%

Table 6. Features of the strictures and outcomes of dilatations in the 15 patients with oesophageal strictures due to caustic ingestion and button batteries.

Of these fifteen patients that developed oesophageal strictures due to caustics and button batteries, nine (60%) of the strictures became refractory strictures. Two (13.3%) patients from the button battery group had complete resolution of the strictures.

Summary of all gastrostomy complications

Thirteen patients (7.3%) had a laparotomy done for a Stamm gastrostomy during initial admission to CMJAH due to the severity of the oesophageal injuries, four patients in the button battery group and nine patients in the caustic ingestion group. The complications related to gastrostomy are summarised in Table 7. Early dislodgement of the gastrostomy necessitating a laparotomy and a redo gastrostomy was the most common early gastrostomy seen in five patients (38.5%). And the most common late gastrostomy complication was inadvertent removal of gastrostomy seen in 10 patients (76.9%).

Required gastrostomy on admission		N=13	7.3%
Gastrostomy: Early complications	Yes	6	46,2 %
	No	7	53,9%
Gastrostomy: Early complication- type	Dislodged	*5*	
	wound infection	*1*	
Gastrostomy: Early Complication-Management	laparotomy and redo gastrostomy	*5*	
	non-operative management	*1*	
Gastrostomy: Late complications	yes (inadvertent removal of gastrostomy)	10	76,9%
	No	3	23,1%

Table 7. Complications related to feeding gastrostomy.

Association between the cause of injury and the following outcomes: early complications, need for early gastrostomy and refractory strictures.

The incidence of early complications was higher following the ingestion of button batteries and caustic substances, compared to coins and other foreign objects (p=0.0002; phi coefficient=0.34)

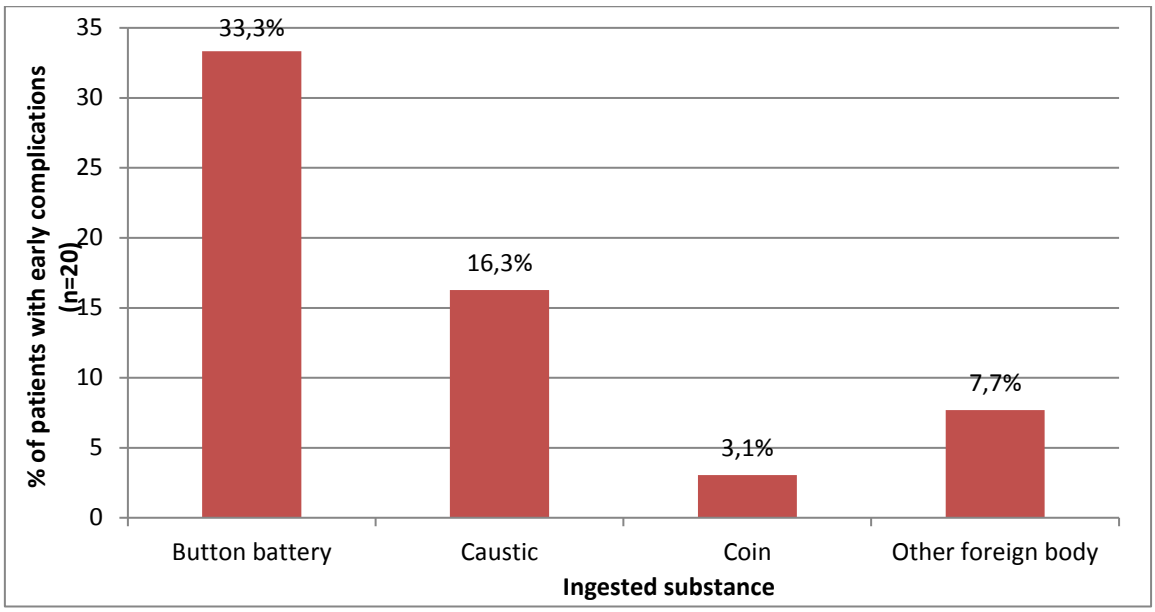

Figure 5. Association between the cause of injury to early complications**.**

Similarly, the requirement for early gastrostomy was higher following the ingestion of button batteries and caustic substances, compared to coins and other foreign objects ($p<0.0001$; phi coefficient=0.36).

The incidence of refractory strictures was higher following the ingestion of button batteries and caustic substances, compared to coins and other foreign objects ($p<0.0001$; phi coefficient=0.40).

The association between the presence of refractory strictures and the following and disturbance in dilatation.

The sample size was small analyse of the role of disturbance in dilatation and development of refractory strictures.

DISCUSSION

Early and late complications were more likely to occur due to caustic and button battery ingestions in comparison to coins and other foreign body ingestions. Foreign bodies including button batteries are likely to be impacted in the oesophagus because its anatomical constrictions and when button batteries get stuck in the oesophagus, they can cause oesophageal damage by three mechanisms, generation of an electric current between the battery and the oesophageal tissue, leakage of alkaline material and to a lesser extent by pressure necrosis (30). Experimental data have demonstrated that adherence of the button battery to the oesophageal mucosa with progression to mucosal necrosis can occur within 15 minutes of oesophageal impaction (31). Prolonged duration of contact of the button battery to the oesophagus leads to further tissue damage which can lead to major complications including oesophageal perforations, trachea-oesophageal fistulae and fistulisation to major vessels within two hours of ingestion (21). In our study, more than a third of patients with button battery ingestion (37.5%) presented to CMJAH more than 24 hours of ingestion and both early and late complications were more common on the patients that presented more than 24 hours. Delayed referral due to a missed diagnosis and initial management at other health facilities without the expertise to manage button batteries was the major cause of delayed presentation to CMJAH. The delay in the referral of patients to CMJAH ranged from 48 hours to 7 months. Three patients in our study who presented more than 24 hours required oesophagostomy to remove the impacted button batteries after failed endoscopic retrieval attempts. Two of these three patients were symptomatic for 3 months and 7 months and were treated as asthma and recurrent chest infections, with no radiographs done during that period. Majority of the ingestions are unwitnessed and have non-specific symptoms, therefore a high index of suspicion and an active investigation is important to diagnose and remove the batteries urgently (21). There is a need to educate health care practitioners in community health centres, district hospitals and the community members on the potential for harm of button batteries as part of prevention of morbidity associated with button batteries.

The majority of ingestions of the caustic substances were mainly accidental in our study, this is in keeping with other published studies in literature(10,14). More concerning though was that the majority ingested caustic substances were drunk directly from their original containers which suggest that the containers are not childproof. Another important finding was the storage of caustic substances on beverage containers which can lead to accidental ingestion thinking that it is a drinkable beverage (32). Acute complications usually result from ingestion of strong

alkali which causes liquefactive necrosis of the tissues or strong acids that can cause coagulative necrosis (11,33). Depending on the amount ingested and the duration of contact, these ingestions can result in injuries to the lips, oral mucosa upper airway, oesophagus and the stomach (11). In our study seven patients (16%) had acute complications due to caustic ingestions, some of the complications were upper airway obstruction in three patients with two of them requiring tracheostomy, one patient had gastric outlet obstruction that required pyloroplasty and severe oesophageal injuries. Drain cleaner and potassium permanganate were the ingested substances in patients that had severe upper airway obstruction necessitating tracheostomy. Drain cleaner is made from sodium hydroxide which is a very strong alkali that is known to cause severe tissue damage (7,14,34). Potassium permanganate is mainly used as a household cleaner, antiseptic, antifungal and available over the counter. In the mucous membranes after contact with water it forms potassium hydroxide which is a caustic substance (35). Most solutions are dilute but strong concentrations can be found and they can cause severe tissue damage. Gastric outlet obstruction resulted from ingestion of battery acid which supports the that strong acids are likely to injure the stomach (33).

Even though coins constituted most of the ingestions with few complications, coin ingestions are not always harmless. Patients have suffered complications ranging from oesophageal perforation to death from coin ingestions (17,36). In our study, complications due to coin ingestions were limited to anaesthetic complications only, with no long-term complications. Within the patients that ingested other foreign bodies with oesophageal and colonic perforations, both these patients were delayed referrals to CMJAH. This indicates the importance of early extraction of sharp foreign bodies as they can lead to perforation if their removal is delayed (20).

Fifteen patients developed oesophageal strictures from caustic and button batteries ingestions. Among the patients that developed strictures from caustic ingestion, the causative substances were strong alkali and strong acids like drain cleaners, caustic soda and battery acid (sulphuric acid). None of the strictures resulted from bleach ingestion or potassium permanganate even though these were among the most commonly ingested substances in our patients. Resolution of oesophageal strictures from dilatation was seen in two patients (13.3%) at the conclusion of the study but three patients (20%) were still on the dilatation programme and two patients (13%) got lost to follow up. Therefore, the final dilatation outcomes could not be assessed in our study. In contrast to 60% - 80% success rate quoted in international literature, the outcomes of oesophageal dilatation in studies done in developing countries differ considerably. In a study done in Cape Town, the success rate of oesophageal dilatation was 41%, and the Contini et al's

in Sierra Leone, success with oesophageal dilatation was 16% (7,14). The common causes for these lessor outcomes are delayed management of strictures, defaulting treatment, severe burns requiring tracheostomy, oesophageal perforations and complex strictures (7,14). Given the high rate of loss to follow up and variable presentation of patients, it is not possible to analyse and compare dilatation outcomes in this study. These deficiencies may be accounted for in future prospective studies examining caustic and foreign body ingestion in our setting.

In our study, six patients required oesophageal surgery, four gastric pull-ups, one colonic interposition (done at another institution), and one stricture resection and anastomosis. At CMJAH, gastric pull-up is the oesophageal replacement surgery of choice if the stomach is not severely damaged. Some perceived advantages are that the stomach is a well-perfused organ, therefore graft necrosis is rare, there is a single anastomosis in the neck and a relatively low leak rate (37). The choice of oesophageal replacement graft is based on institutional preferences, as there are no randomised controlled trials comparing different oesophageal replacement operations.

Feeding gastrostomy is a necessary adjunct in the management of patients with caustic ingestion and oesophageal strictures to prevent malnutrition and to aid in dilatation of difficult strictures (14). In our study, a total of 13 patients (7.3%) required a feeding gastrostomy during initial admission. Unfortunately, we observed multiple complications arising from gastrostomy tubes. Early inadvertent gastrostomy removal before the gastrostomy tract was mature was the most common early gastrostomy complication with up to five patients (5/13; 38%) needing laparotomies and revisions of their gastrostomy's. This complication was common in patients with severe oesophageal injuries that were admitted to the intensive care unit. In most patients with early displacement of the gastrostomy tube, the exact reasons were unknown but, among the reasons that we identified were patients pulling their gastrostomy tubes out and inappropriate use of gastrostomy tubes where the balloon port would be used for feeding or medication resulting in rupture of the balloon leading to early dislodgment and peritoneal contamination with gastric contents. Within the literature, gastrostomy complications rates are reported to be at 16%- 70%, with most complications being reported as minor (38). One of the risk factors for gastrostomy tube displacement are confused and combative patients (38). This indicates that gastrostomy tubes are not without complications. Late accidental removal of gastrostomy was also another common late gastrostomy complication. This indicates that staff and parents need to be educated on the safe use of feeding tubes. Such education may take the form of in-service training and appropriate

counselling on gastrostomy usage and care for the families of and patients in whom such intervention is necessary.

Limitations

The limitations of this study include its retrospective nature, reporting data only from a single hospital, and the inability to retrieve ten files in the coin's groups, where we might have missed some complications. Some patients were managed in other institutions before being sent to CMJAH. The role of disturbance to dilatation and refractory strictures could not be ascertained due to small sample size, therefore a prospective study looking at the role and reasons for disturbances in the dilatation programme is recommended.

Conclusions

Foreign body ingestions especially button batteries and caustic ingestions are a common cause of injury in children in our population. A high index of suspicion, early diagnosis and immediate removal of button batteries is recommended to reduce the complications associated with button battery ingestion. Early referral to centres with experience and expertise in the management of oesophageal strictures is also recommended as delayed dilatation of oesophageal strictures can contribute to the failure of dilatations. Even though gastrostomies are a useful adjunct in the management of severe oesophageal injuries, they have complications associated with its use. Prevention through education of health-care professionals and communities should be prioritised in order to prevent these injuries and reduce the complications related to these avoidable injuries.

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APPENDICES

APPENDIX A: RESEARCH PROTOCOL

1. BACKGROUND

Ingestion of foreign bodies and caustic substances is a common condition in children globally. These may result in significant injuries of the oesophagus, upper airway and the stomach and have a potential to cause acute and long term complications. The most common late complication after caustic ingestion or button battery ingestion is the development of oesophageal strictures (1,16). Other complications like the development of trachea-oesophageal fistula, laryngeal stenosis and cervical spondylosis are seen with button battery ingestions. Oesophageal strictures from caustic and button cell battery ingestion are a significant problem in these children. Children with oesophageal strictures suffer from morbidity with severe consequences, such as failure to thrive, food impaction, and pulmonary aspiration [2].

Ingestion of caustic agents accompanied by refractory oesophageal strictures is particularly pronounced in less developed countries (LDCs) especially in children between the ages of 2 and 6[3]. Delayed presentation after caustic ingestion and poor follow up has been shown to be a predictor of development of refractory stricture in LDCs[6]. Poor socio-economic status and lower level of education of parents have been identified as contributing factors in accidental ingestion caustic materials [5].Significantly, the majority of caustic ingestion related oesophageal injuries are preventable [3]. In developed countries, there are legislations passed to control sales, distribution, packaging and labelling caustic substances. This has significantly lowered the incidence of caustic ingestions in these countries [4]. In South Africa, there is Hazardous Substance Act of 1973 which aims to control

importation, sale, labelling, use, disposal and modification of corrosive substances and other hazardous substances including electronic devices, but caustic substances are still readily available in households [13]. The act does not provide for child-resistant packaging. In South Africa, household caustic agents are for sale in major retail supermarkets without child-resistant packaging. In contrast to developed countries the reduction in corrosive substances has not been observed in developing countries [3]. In South Africa, there is no data indicating that the Hazardous Substance act has led to the reduction of caustic injuries. The most commonly ingested materials are house-hold cleaning agents or chemicals that have been mistakenly ingested as being a drinkable beverage [5]. Caustic soda is reported to be the most commonly ingested caustic agent in Sierra Leone, Nigeria and other developing countries where it is used to make soap and potash as the most common corrosive in Egypt[3][5][10].

Button battery ingestion, accompanied by major complications or even a fatal outcome is a global problem and is on the rise especially in children less than 6 years of age [7].This is due to the availability of batteries from toys and house- hold electronic devices. Data from The National Poison Data System shows that major complications and fatal outcomes are on the rise even though there is no demonstrated increase in battery ingestions [14].This is attributed to widespread marketing and use of more powerful Lithium batteries especially the 3V 20mm[7]. Major complications include oesophageal perforations, trachea-oesophageal fistula, fistula into a major vessel, oesophageal strictures vocal cord paralysis, spondylodicitis and death. These children will often need major surgeries and prolonged intensive care unit admissions to treat these complications [15]. Delayed diagnosis from non-specific symptoms and signs and misdiagnosis by clinicians are

also some of the major contributing factors in morbidity and mortality from accidental battery ingestions [8] [9].

The main mechanism of injury is from the generation of hydrogen ions at the negative pole of the battery caused by current created through the adjacent tissue [12]. The other mechanism is the leakage of alkaline substance from the battery and to a lesser extent pressure effect. In an effort to reduce battery associated injuries the US government passed the Consumer Product safety Improvement Act of 2008 which required that the batteries must be inaccessible in all toys for use by children under the age of 3 years [7]. This resulted in a moderate reduction of battery ingestion from 3461 in 2009 and 3366 in 2013[14]. Accidental ingestion of button batteries especially Lithium cells is also a problem in developing countries. Umana A.et al reported a series of 6 patients with Lithium button battery ingestion from Nigeria in which 5 had severe complications on presentation. Time to presentation ranged from 3days to 7 weeks [9]. This study was limited by a very small number of patients but highlights the problem of delayed presentation of patients in LDCs.

Primary treatment of oesophageal strictures irrespective of aetiology is endoscopically guided dilatation. The aim of oesophageal dilatation is to establish an adequate oesophageal lumen to relieve symptoms. Serial oesophageal dilation results are associated with a 60% - 80% success rate [10]. Most authors agree that every effort should be made to preserve the patient's own oesophagus irrespective of the cause of the stricture. This comes with repeated number of hospital visits, general anaesthesia and complications of oesophageal dilatations. Within the literature, there is no clear consensus on the limits of oesophageal dilatation and treatment failure. However, requirement of more than ten sessions of dilatations has

been identified as one of the predictors of the need for oesophageal replacement surgery [10].

Delayed presentation, patient default and poor follow up have also been shown to be an independent predictor for requirement of oesophageal replacement [6].

If preservation of the native oesophagus is not successful, then oesophageal replacement is the next step. These are massive operations that carry a significant risk of complications including leakage, strictures, graft necrosis and death [10].

A significant number of children are treated annually for recurrent oesophageal strictures resulting from caustic substances, button cell battery and other foreign bodies in our hospital. There is no data regarding the causes of recurrent oesophageal strictures, management, and outcomes for these children in our hospital.

This study aims to establish if delayed presentation and poor compliance to dilatation programme is the major cause of refractory strictures in children treated at Charlotte Maxeke Johannesburg Academic Hospital. Data obtained from this study will also help us identify children at risk for developing refractory strictures so that we can devise short and long term management plans for these patients.

2. OBJECTIVES

1. To describe the demographic profile of patients treated for oesophageal injuries at the Charlotte Maxeke Johannesburg Academic Hospital from 01 January 2010 until 24 June 2016.

2. To describe the relationship between causes of oesophageal injuries and outcomes of treatment in paediatric patients treated at Charlotte Maxeke Johannesburg Academic Hospital.

3. To determine the factors associated with refractory strictures during management of oesophageal injuries in children at CMJAH.

2. METHODS

This study is going to be a retrospective cross-sectional study carried out at Charlotte Maxeke Johannesburg Academic Hospital department of Paediatric Surgery. Patient information will be obtained from the paediatric surgery patient database and patient's medical records from Charlotte Maxeke Johannesburg Academic Hospital [CMJAH] records department.

Inclusion criteria: all patients that have been treated for confirmed oesophageal injuries under the age of 16 years from 01 January 2010 until 24 June 2016 will be included. Injury to the oesophagus could have happened before the start of the study but if the first admission to CMJAH is during the study period then patients will be included.

Exclusion criteria: Children with oesophageal injuries due to GERD and congenital causes are excluded. Children with an uncomplicated foreign body or caustic ingestions will also be excluded.

SAMPLE SIZE: At 95% confidence interval and 5% accepted margin of error a minimum sample size of 111 files/ records is required. This is based from Epi Info sample size calculator software. Proportion of caustic and foreign bodies estimated at 8% of all paediatric surgical admissions.

3. DATA MANAGEMENT.

Collected data will be entered into Redcap electronic database. Data management and analysis will be performed using Redcap electronic database and Stata software. Data will be kept and used strictly confidential. No names and direct personal information will be linked to collected data. Access to Redcap database will be controlled by a use of a username and a password that will only be available to primary researcher and the supervisors.

4. DATA ANALYSIS

a) Objective 1: a descriptive analysis of continuous variables will be analysed using summary measures such as means and standard deviations if the data follows a normal distribution, otherwise median and IQR will be used. Categorical variables will be analysed using proportions and frequency tables.
b) Objective 2: descriptive outcomes will be analysed by frequency tables. A Chi-square test will be used for categorical variables to analyse the association between the causes of oesophageal injuries and outcomes.
c) Objective 3: a multiple regression analysis will be used to determine the factors associated with refractory oesophageal strictures.

5. ETHICS

The research protocol has been submitted to the University of the Witwatersrand Human Research Ethics Committee for review and ethics have been granted. Permission to access medical records have also been Granted by the superintendent and CEO of CMJAH (permission letter attached).

6. POSSIBLE CONSTRAINTS

Inability to obtain all the files and if there is any missing important information from the file will be a possible constraint. Paediatric Surgery database will be used to get any missing information and if there is still important missing information then patient will be excluded on the basis of missing data and this will be recorded.

7. BUDGET

No funding is required for this study.

8. TIMELINE

2016- 2017	May-June	June - Jul	Aug- Sept	Oct-Jan
Protocol Development	**X**			
Ethics		**X**		
Data collection			**X**	
Data analysis and write up				**X**

9. OUTPUT

Study findings will be submitted for publication in local and international peer-reviewed journals. Findings will also be submitted for presentation at the Bert Myburgh research symposium. The research findings will also be shared with agencies concerned with the welfare of children in South Africa like Childsafe.

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APPENDIX B. DATA COLLECTION FORM.

Confidential

Outcomes of Oesophageal injuries in Children Treated at Charlotte Maxeke Johannesburg Academic hospital

Participant id	_____
age at presentation	_____
gender	○ male ○ female ○ other
refferal infomation	○ local ○ referred from another hospital ○ referred from another province ○ self-referral ○ other ○ reffered from another country
other, Specify	_____
Province	○ Mpumalanga ○ Northwest ○ Limpopo ○ Free State ○ Eastern Cape ○ Northen Cape ○ Western Cape
Time from ingestion to admission at Charlotte Maxeke	○ within 24 hours ○ more than 24 hours ○ unknown
reason for delayed transfer	○ managed at another facility ○ did not seek medical attention early ○ missed diagnosis ○ other reasons
Other reason for delay	_____
cause of injury	○ button battery ○ caustic ○ coin ○ other foreign bodies
other foreign bodies	_____
underlying oesophageal abnormality	○ Yes ○ No
specify underlying	_____

coin value	○ 5 cent ○ 10 cent ○ 20 cent ○ 50 cent ○ 1 rand ○ 2rand ○ 5 rand ○ not specified ○ other
number of coins	○ one coin ○ more than one
Ingestion intent	○ accidental ○ non accidental ○ intentional as suicide / parasuicide ○ other
other intentions	_____
caustic agent	○ liquid drain cleaner ○ oven cleaner ○ battery acid ○ caustic soda ○ hair relaxer ○ potassium permanganate liquid ○ potassium permanganate crystals ○ dishwasher detergents ○ bleach ○ swimming pool cleaner ○ toilet bowl cleaner ○ rust remover ○ other
other caustics	_____
button battery source	○ directly from the device ○ loose ○ unknown ○ other
type of device	_____
container of caustic substance obtained	○ original container ○ beverage container ○ unknown ○ other
specify other container	_____

symptoms at presentation	☐ asymptomatic ☐ dysphagia ☐ refusing feeds ☐ mucosal burns ☐ drooling saliva ☐ odynophagia ☐ retrosternal pain ☐ abdominal pain, ☐ nausea, ☐ vomiting, ☐ hematemesis ☐ stridor ☐ hoarseness ☐ cough ☐ recurrent respiratory infections ☐ wight loss/ failure to thrive ☐ other ☐ respiratory distress
other symptoms at presentation	_____
radiology findings button battery/coin/other	○ cricopharyngeus ○ aortic arch/ left main bronchus ○ gastro-oesophageal junction ○ stomach ○ other
other radiology findings	_____
initial endoscopy done	○ yes ○ no
endoscopy findings caustic injury	○ grade 0 ○ grade 1 ○ grade 2A ○ grade 2B ○ grade 3A ○ grade 3B ○ grade 4
endoscopy findings battery/coin/other fb	○ no injury ○ superficial mucosal injury ○ deep oesophageal injury ○ oesophageal perforation ○ tracheo-oesophageal fistula ○ edema ○ other
other endoscopy findings	_____

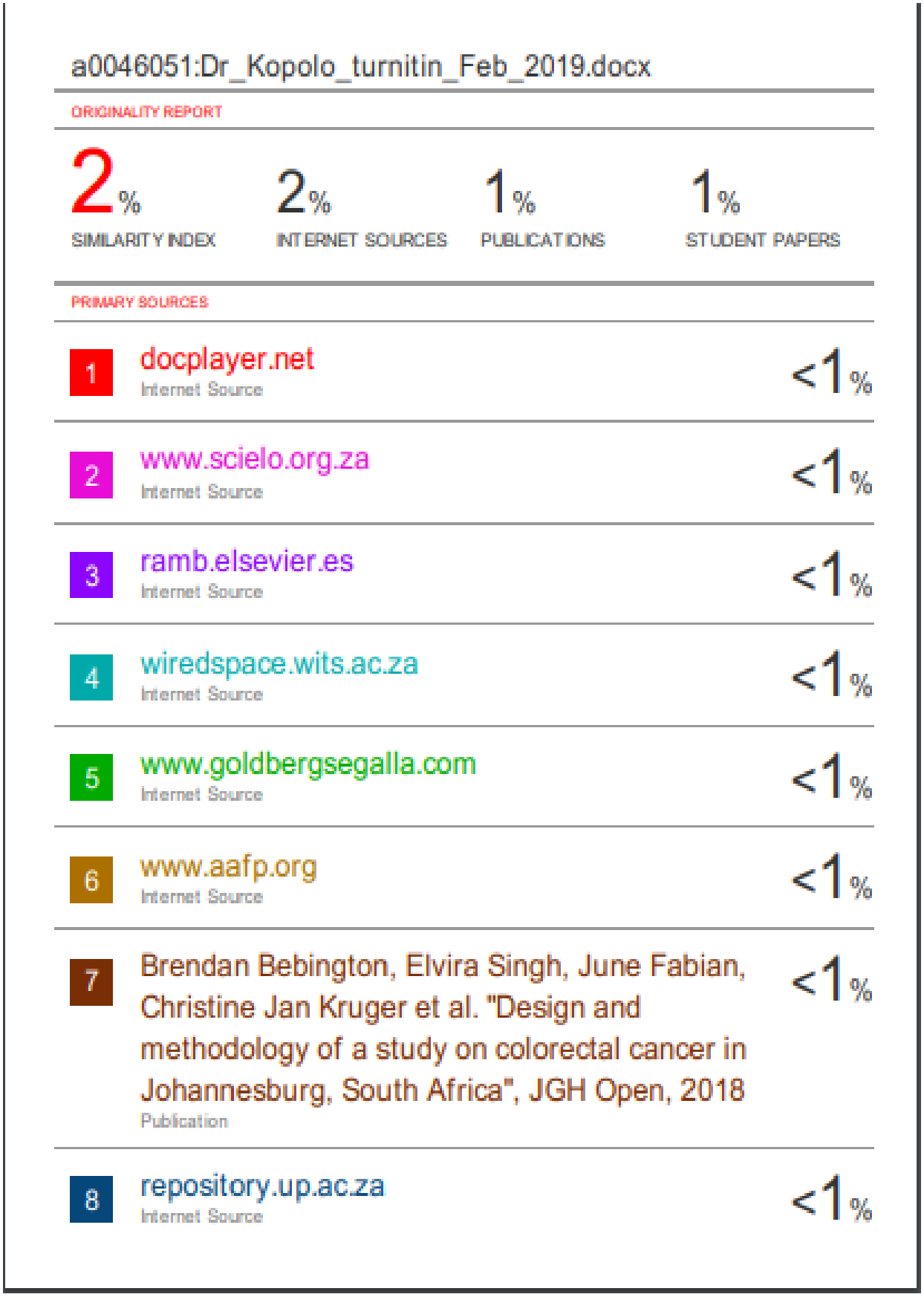
Method of removal	○ endoscopic retrieval ○ pushed down to the stomach intentionally ○ pushed to the stomach accidentally ○ foley catheter removal ○ already passed the oesophagus ○ removed surgically ○ removed by anaesthetist ○ other ○ oesophagotomy and esophagostomy
surgical procedure	_____
other method of removal	_____
complications during initial management	○ Yes ○ No
early complications specified	○ upper airway obstruction ○ developed a leak on the oesophagus ○ tracheo-oesophageal fistula ○ empyema/ chest collections ○ pneumonia ○ hospital-acquired infection ○ death ○ other complications ○ gastrostomy complications
other early complications	_____
management early complication	○ non-operative management ○ antibiotics in the ward ○ antibiotics and ICU admission ○ tracheostomy ○ thoracotomy ○ laparotomy ○ other
other management	_____
need for early gastrostomy	○ yes ○ no
type of gastrostomy	○ PEG ○ Stamm gastrostomy ○ laparoscopic assisted gastrostomy
early gastrostomy complications	○ none ○ dislodged ○ wound infection ○ bleeding ○ gastric outlet obstruction ○ gastro-colic fistula

management gastrostomy complications	○ non-operative management ○ laparotomy and redo gastrostomy ○ other
late complications	○ Yes ○ No
specific late complications	○ none ○ oesophageal stricture ○ failure to thrive ○ other late complications
other late complications	_____
number of strictures	○ single ○ multiple
location of stricture	○ upper oesophagus ○ middle oesophagus ○ distal oesphagus ○ entire oesophagus
nature of the stricture	○ short ○ long ○ short and tortuous ○ long and tortuous
number of dilatations	_____
any disturbance in the dilatation programe	○ yes ○ no
reason	☐ did not come on his/her own ☐ cancellation due to time ☐ cancellation due emergencies ☐ cancellation due to hospital/equipment problems ☐ cancellation due to ill health ☐ unknown reason for cancellation ☐ other reasons for cancellation ☐ lost to follow up
late gastrostomy complications	○ none ○ Inadvertent removal of gastrostomy ○ Wound infection ○ blocked tube ○ migration ○ other complications
complications during dilatation programe	○ Yes ○ No
complications during dilatations	○ perforation ○ pneumonia ○ bacteremia ○ chest pain ○ other

other complications during dilatation	_____
management of complications	○ operative ○ nonoperative
operative management of complication specify	_____
outcomes after management of complications	○ resolved ○ died ○ other
other outcomes	_____
did patient develop refractory/ recurrent stricture	○ yes ○ no
refractory stricture management	○ further dilatations only ○ further dilatation and steroid injections ○ further dilatation and mitomycin C application ○ stent placement ○ other
other refractory stricture management	_____
outcomes dilatation	○ resolution ○ lost to follow up ○ still on dilation program ○ required oesophageal surgery / replacement ○ awaiting oesophageal replacement ○ died ○ other outcomes ○ required futher surgey but refusing surgery
further surgery	○ gastric pull-up up ○ colonic interposition ○ stricture resection and primary anastomosis ○ other
other outcomes	_____
time period from diagnosis of stricture to resolution	_____
time period in months from from injury to oesophageal surgery	_____
outcomes post oesophageal surgery	○ surgery successful ○ surgery abandoned ○ died on the table ○ died postoperatively ○ other

overall outcome of management	○ succesfull ○ still undergoing treatment ○ awaiting definitive surgery ○ died ○ lost to follow up

APPENDIX C: TURNITIN REPORT



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APPENDIX D. ETHICS CLEARANCE CERTIFICATE.

R14/49 Dr Matongo Mfuneko Kopolo

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M160660

NAME: (Principal Investigator)	Dr Matongo Mfuneko Kopolo
DEPARTMENT:	Paediatric Surgery Charlotte Maxeke Johannesburg Academic Hospital
PROJECT TITLE:	Management of Oesophageal Strictures in Children: Charlotte Maxeke Johannesburg Academic Hospital Experience
DATE CONSIDERED:	24/06/2016
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Dr Ellen Mapunda
APPROVED BY:	Professor P. Cleaton-Jones, Chairperson, HREC (Medical)
DATE OF APPROVAL:	08/07/2016

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary in Room 10004,10th floor, Senate House/2nd floor, Phillip Tobias Building, Parktown, University of the Witwatersrand. I/We fully understand the the conditions under which I am/we are authorised to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated,from the research protocol as approved, I/we undertake to resubmit to the Committee. **I agree to submit a yearly progress report**. The date for annual re-certification will be one year after the date of convened meeting where the study was initially reviewed. in this case, the study was initially review in June and will therefore be due in the month of June each year.

Principal Investigator Signature Date

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES