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Pediatric intussusception in Uganda: differences in management and outcomes with high-income countries

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ABSTRACT

Purpose: In high-income countries the presentation and treatment of intussusception is relatively rapid, and most cases are correctable with radiographically-guided reduction. In low-income countries, many delays affect outcomes and surgical intervention is required. This study characterizes the burden and outcome of pediatric intussusception in Uganda.
Methods: Prospective case series of intussusception cases from May 2015 to July 2016 at a tertiary referral hospital in Uganda.
Results: Forty patients were included in the study. Male to female ratio was 3:2. Average duration of symptoms before presentation was 4.5 days. Median duration of symptoms in referred patients was 4 days and 2 days in non-referred patients (P value 0.0009). All 40 patients underwent surgical treatment: 25% had resection and enterostomy, 15% had resection and primary anastomosis, 2.5% had resection, primary anastomosis and enterostomy and 57.5% underwent manual reduction. Mortality was 32% and febrile patients on admission were 20 times more likely to die (P value 0.040).
Conclusion: Intussusception carries a high operative and mortality rate in Uganda. Referred patients presented later than non-referred patients to health facilities. Fever on examination at admission was positively associated with mortality. This disease remains a target for quality metrics in global pediatric surgery.
Type of study: Diagnostic study.
Level of Evidence: III

Pediatric intussusception results from invagination of one part of the bowel into another, ultimately causing bowel obstruction, necrosis, and perforation [1]. At Mulago National Referral Hospital (MNRH), review of operative theater records between January 2015 and September 2015 showed that intussusception accounted for approximately 46% of all cases of intestinal obstruction in children. Children with intussusception are typically previously healthy before developing sudden onset of colicky abdominal pain and emesis which progresses to bilious emesis [2]. Passage of red currant-jelly stools (due to mucosal necrosis) with progressive abdominal distention are indicative of advanced disease[3]. Ultimately, the blood supply is compromised and intestinal ischemia and perforation result from bowel wall gangrene [4]. In Sub Saharan Africa early intussusception has a broad differential diagnosis including malaria, gastroenteritis, and dysentery—all of which are more prevalent than intussusception, complicating the diagnosis and early treatment [5].

Delayed presentation after 24 h of onset of symptoms predisposes to bowel complications and increased need for primary surgical intervention and has been shown to be associated with higher mortality rates [4,6–8]. Delay in access to care is reported by studies especially in low and middle income countries [9]. This delay has been attributed to lack of diagnostic capabilities, delayed referrals to definitive care centers and lack of medical expertise outside tertiary centers [10,11].

Intussusception may be treated via pneumatic or hydrostatic enema reductions, laparoscopic reductions or laparotomy. For ill-defined reasons in African studies, laparotomy including manual reduction, intestinal resection with anastomosis or enterostomy continues to be the procedure of choice [12,13]. Other African countries report mortality rates ranging from 8.4% to 28% [8,12,14], a sharp contrast to high-income countries where mortality is less than 1%[8]. This difference highlights the consequence of late diagnosis and prompted the current study, which aims to characterize the presentation, treatment, and

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outcomes of pediatric intussusception in Mulago National Referral Hospital where the disease contributes to a substantial burden of pediatric morbidity.

1. Method

Following approval from the Makerere University College of Health Sciences School of Medicine Research and Ethics Committee, all patients presenting to the pediatric surgery service at Mulago Hospital in Kampala with suspected intussusception from history, clinical examination and /or abdominal ultrasound from May 2015 to July 2016 were prospectively selected for inclusion in the study. Follow up clinical data was recorded up to 14 days from the time of surgery.

Patients greater than 12 years of age (the cutoff for admission to the pediatric surgery ward) and those with post-operative intussusception following other procedures were excluded from the study. Informed consent was obtained from the parents and guardians of all participants. Detailed clinical information including weight, clinical presentation, duration of symptoms prior to presentation, distance from hospital, state of bowel at laparotomy, and outcomes including recurrence, length of stay, and mortality were gathered. The operative procedures were carried out by the General Surgery resident on call supervised by the consultant on call. Data was entered using Epidata version 3.1 and validated manually before analysis using STATA version 12.1 for analysis. Descriptive univariate statistics were obtained and reported as frequency and proportions for participant characteristics, clinical presentation, and outcomes. Differences between two groups on continuous parametric variables were estimated using the t-test for the difference in means while that for non-parametric continuous variables were estimated using the Mann–Whitney U test (difference in medians).Bivariate and multivariate analysis was performed using a logistic regression model to determine clinical factors associated with mortality. P-values less than 0.05 were considered statistically significant. Patients were followed up through Out Patients Clinics and by phone up to 2 weeks following hospital discharge. If phone contacts failed, home visits were scheduled.

2. Results

A total of 43 children suspected to have intussusception presented to the emergency wards during the period of study (May 2015–July 2016). Three children died preoperatively during resuscitation no post mortem was done to confirm a diagnosis of pediatric intussusception and so where excluded from analysis. Therefore the remaining 40 participants were included in this study.

2.1. Demographic characteristics

The male to female ratio in this study was 3:2 and the children were between the ages of two to 74 months, with a mean age of 8.3 months (SD 11.39). The weight on admission ranged from 4.5 kg to 13kgs. Most of the children presented as referrals from peripheral sites (62.5%) traveling from between 0.5 km to 294 km to access the hospital.

Abdominal pain, vomiting, and passage of blood stained stools were the most common presenting complaints in over 90% of children. On clinical examination, the most common signs were dehydration and abdominal distention. However none of the children had been exposed to Rotavirus vaccine in the last month since this study was done in the Rotavirus vaccine pre public hospital licensure era.

The demographic characteristics and clinical presentation of the participants are elaborated in Table Error! Reference source not found..The median duration of symptoms before presentation for referred children was four days; this was two days for non-referred children. This difference in the median was statistically significant after a two sample Mann Whitney test was done with a P value of 0.0009.

Table 1.

Table 1
Demographic and clinical characteristics of the children.

Patient Characteristics		N	%
Gender	Female	16	40.0%
	Male	24	60.0%
Age	< 3 months	2	5.0%
	3–9 months	33	82.5%
	> 9 months	5	12.5%
Referral	Yes	25	62.5%
	No	15	37.5%
		Mean	**SD**
Weight		7.7 kg	1.85
Distance traveled to hospital		22 km	48.93
		Duration of Symptoms before presentation	
Referral Status		**Median(Days)**	**Interquartile range(Days)**
Not referred		2	2
Referred		4	4
Clinical Presentation		**N**	**%**
Abdominal pain		37	92.7%
Vomiting		37	92.7%
Blood stained stools		36	90.0%
Abdominal swelling		26	65.0%
Fever		14	35.0%
Classical triad (Colicky abdominal pain, red currant stools and palpable abdominal mass)		30	75.0%
Associated Signs			
Dehydration		33	82.5%
Abdominal distention		31	77.5%
History of cough		16	42.1%
Abdominal mass		15	37.5%
History of diarrhea		9	22.5%
Raised temperature		8	20.0%
Digital rectal exam findings			
Red currant stool		20	50.0%
Palpable mass		7	17.5%
Not done		13	32.5%

Fig. 1 illustrates the duration of symptoms of intussusception before presentation to hospital of the study participants. The average duration of symptoms of pediatric intussusception before presentation was 4.5 days (SD 4.55) with a range of less than 1 day to 21 days. 22% of children presented to hospital in less than 24 h of onset while about half presented after 72 h of onset of symptoms.

Fig. 1

2.2. Operative interventions and findings

All forty patients underwent laparotomy. Of these 38 had ileo-colic intussusception, one patient had an ileo-ileal intussusception and one other had colo-colic intussusception. Resection rates at laparotomy were 44%. Twenty three (57.5%) had manual reduction of the bowel,

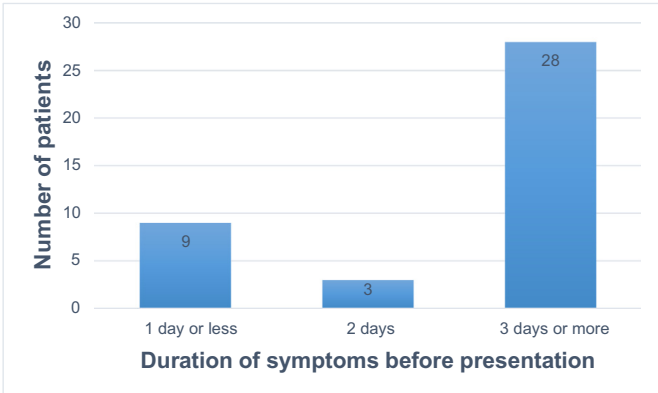

Fig. 1. Duration of Symptoms before presentation to hospital.

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10 (25%) had bowel resection and enterostomy creation, six (15.0%) had resection and primary anastomosis, and one (2.5%) had both resection with primary anastomosis and a diverting stoma. At laparotomy four children had bowel perforations, eight had gangrenous bowel, five had both bowel perforations and gangrene and the rest (23) had viable bowel.

2.3. Outcomes

Two patients required re-laparotomy. Both presented four days after discharge with features of peritonitis. At the initial operations, one of the children had a manual reduction done and the other had a bowel resection and anastomosis. Both cases required resection and enterostomy creation at re-laparotomy. Both patients recovered after treatment and were subsequently discharged.

Out of the 40 patients, 13 (32%) died in the post-operative period with all deaths occurring within four days of surgery. Five occurred within the first post-operative day, six on the second post-operative day, and two on the fourth post-operative day.

One patient (2.5%) developed a recurrence of intussusception following manual reduction for an ileo-colic intussusception. On the 9th postoperative day, the child had a second manual reduction done for an ileo-ileal intussusception. He subsequently recovered and was discharged.

The average length of hospital stay was 4.0 days (SD 2.48) with a range of one to 11 days.

2.4. Factors associated with mortality

Bivariate analysis of the factors associated with mortality in children who presented with pediatric intussusception is shown in Table 2.

Variables with a P value of 0.05 or less after univariate analysis where included in the multivariate logistic regression analysis model. We adjusted for symptom of abdominal swelling, signs of palpable abdominal mass and fever on examination, duration of symptoms less than 72 h before presentation, and lastly surgical findings of gangrenous bowel and viable bowel. These findings are shown in Table 3. Fever on examination was statistically significant with a P value of 0.040.

Table 2.

Table 3.

3. Discussions

The disparities in presentation, management, and outcomes of intussusception, one of the most common pediatric surgical emergencies in children, remain substantial between high and low-income countries. While death from intussusception is rare in high-income countries, case mortality rate in this study was 32% and 38.5% of the deaths occurred within 24 h of the surgery. These findings are in keeping with a report that states that children undergoing emergency surgery in low income countries were found to have high 24 h mortality rates[9]. Due to the high mortality, intussusception is thought to be underreported in Africa especially for deaths that occur out of hospital [15]. This finding is supported by our investigation in which three children died before a definitive intervention was done however post mortem studies was not done to confirm that these children had pediatric intussusception Mortality rates of up to 33.7% have been reported in African studies and these are the highest in comparison to other regions[11,16].

As this study site is a tertiary facility, the referral rate from other health facilities was high (62.5%), with 77.5% of patients presenting after 24 h from the onset of symptoms. Referred patient presented most commonly four days after onset of symptoms as opposed to non-referred patient who came two days earlier. This finding was statistically significant(P value of 0.0009).Previous studies have shown that although patients may present early to primary health care facilities, referrals were delayed[17–19]. The delay at primary health care centers is

Table 2
Cross tabulation of presence of risk/survival factors with mortality in children with pediatric intussusception.

Predictor of Outcome	Category	Death status	Non Adjusted Odds ratio (95% CI)	P-Value
		Alive Died		
		(n = 27) (n = 13)		
Sex	**Male**	**15 (55.6) 9 (69.2)**	**0.55(0.14–2.26)**	**0.411**
	Female	**12 (44.4) 4 (30.8)**		
Abdominal pain	**No**	**1 (3.7) 1 (7.7)**	**0.42(0.02–7.39)**	**0.556**
	Yes	**26 (96.3) 11 (84.6)**		
Vomiting	**No**	**1 (3.7) 2 (15.4)**	**0.21(0.02–2.58)**	**0.224**
	Yes	**26 (96.3) 11 (84.6)**		
Abdominal swelling(Symptom)	**No**	**13 (48.1) 1(7.8)**	**11.14(1.27–98.10)**	**0.030**
	Yes	**14 (51.9) 12(92.3)**		
Fever(symptom)	**No**	**18 (66.7) 7 (53.8)**	**1.04(0.52–8.00)**	**0.308**
	Yes	**8 (29.6) 6 (46.2)**		
Febrile(sign)	**No**	**25 (92.6) 7 (53.8)**	**10.71(1.76–65.24)**	**0.010**
	Yes	**2 (7.4) 6 (46.2)**		
Palpable abdominal mass		**13 (48.1) 12 (92.3)**	**0.08(0.01–0.68)**	**0.021**
	No			
	Yes	**14 (51.9) 1 (7.7)**		
Gut perforations	**No**	**22 (81.5) 9 (69.2)**	**1.96(0.42–9.00)**	**0.389**
	Yes	**5 (18.5) 4 (30.8)**		
Gut gangrene	**No**	**22 (81.5) 5 (38.5)**	**7.04(1.60–30.94)**	**0.010**
	Yes	**5 (18.5) 8 (61.5)**		
Viable bowel	**No**	**8 (29.6) 9 (69.2)**	**0.19(0.44–0.79)**	**0.022**
	Yes	**19 (70.4) 4 (30.8)**		
Manual Reduction	**No**	**8 (29.6) 9 (69.2)**	**0.19(0.44–0.79)**	**0.022**
	Yes	**19 (70.4) 4 (30.8)**		
Enterostomy	**No**	**23 (85.2) 6 (46.2)**	**6.70(1.46–30.73)**	**0.014**
	Yes	**4 (14.8) 7 (53.8)**		
Anastomosis	**No**	**23 (85.2) 10 (76.9)**	**1.70(0.32–9.17)**	**0.522**
	Yes	**4 (14.8) 3 (23.1)**		
Duration of symptom less than 72 h		**17 (63.0) 4 (30.8)**	**0.30(0.04–0.80)**	**0.024**
	Yes			
	No	**10 (37.0) 9 (69.2)**		
Referral	**No**	**11 (40.7) 4 (30.8)**	**1.5(0.38–6.31)**	**0.543**
	Yes	**16 (49.3) 9 (69.2)**		

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Table 3
Multivariate analysis of factors associated with mortality in children with intussusception.

Predictor of Outcome	Adjusted Odds Ratio	P value
Duration of symptoms less than 72 h	0.28(0.03–2.93)	0.286
Abdominal swelling	9.58(0.51–179.86)	0.131
Palpable abdominal mass	0.35(0.02–6.42)	0.477
Febrile	**19.50(1.14–333.56)**	**0.040**
Gut gangrene	10.46(0.42–261.36)	0.153
Viable bowel	0.56(0.03–13.21)	0.746

further worsened by the absence of streamlined free or subsidized ambulance services for referral of patients in majority of public health facilities in Uganda. Patients are usually expected to cater for the referral costs despite the fact that the cost of health care in public hospitals is covered by the government of Uganda. These seemingly low costs can be a substantial financial burden as approximately one third of the population in Uganda lives below the international extreme poverty line of USD$ 1.90 a day[20].

The average duration of symptoms before presentation in this study was 4.5 days. This is similar to an Ethiopian study, but longer than many studies in the region which found average duration of symptoms of 3 days[5,21,22]. Children who presented 72 h after onset of symptoms were more likely to die than children who presented earlier; this however did not attain statistical significance in this study. This finding is similar to reports from other parts of Sub-Saharan Africa [9,23]. Studies have shown that duration of symptoms and delays in initiating treatment were associated with increased mortality [8,11,14]. Timely access to care is imperative due to the emergent nature of many surgical conditions like pediatric intussusception and can have significant outcomes morbidity and mortality [24].

Fever on examination (P value 0.040) was associated significantly with an increased risk of mortality in this study. Similar findings were made by a study done in Kenya were fever on admission was associated with a higher risk of death[23].

The clinical signs and symptoms at presentation further demonstrate advanced disease such as red currant stools seen in 90% of patients, the classical triad (colicky abdominal pain, red currant stool, and palpable abdominal mass) in 75% of the patients, and a resection rate of 44% due to devitalized bowel**.** These resection rates are similar to other African studies where resection rates were up to 48.4% following surgical management[22,25]. Previous studies have showed that mortality and devitalized bowel tends to occur commonly in patients who present to hospital after 24 h from onset of symptoms [7].

The procedures performed included manual reduction (57.5%), resection and enterostomy creation (25%), resection and primary anastomosis (15%) and resection, primary anastomosis and enterostomy creation (2.5%). In contrast to other studies in the region were resection and anastomosis was commonly performed, there seemed to be a preference for enterostomy creation in our study[22,25]. This could be attributed to surgeon perception of the patient's overall stability as sicker children are more likely to have stoma placement due to the possible risk of anastomotic leak. Our study did not capture some of the more specific variables that would quantify this higher risk such as ASA status, presence of sepsis and need for transfusion. This would be a focus for future study. Once again, these findings underscore the substantial disparity with high income settings, where these patients can be successfully treated non-operatively with enema reduction in 60–80% of cases. In fact, the majority of protocols in high-income countries even support discharge from the emergency room in stable patients after enema reduction.

Our average length of hospital stay of 4.0 days was similar to 5.2 days reported in Ethiopia and slightly lower than in Nigeria where the average length of hospital stay was 12 days[12,21]. This study included patients who died (most deaths occurred within 48 h post-operatively) which could account for the low length of hospital stay and differences in management protocols.

Rota Shield, rotavirus vaccine launched in 1998 was associated with an increase the incidence of intussusception and had to be withdrawn from the market[26]. Though the current vaccines have not been associated with intussusception, limited post-licensure studies have been carried out in low income countries[27]. To fill this gap, intussusception surveillance is being carried out in African countries[16,27]. In this study, none of the children had been exposed to the Rotavirus vaccine in the two weeks before developing intussusception.

Though distance from health care facility and absence of referral transportation from peripheral health units could have impacted significantly on delayed presentation, other factors like poor health seeking behavior of parents and misdiagnosis may have contributed as well. Sensitization of parents, health workers especially low cadre health workers about the symptoms and signs of pediatric intussusception and the urgency of referral of these children would reduce the duration of symptoms before presentation. Since over half of the patients in the study had contact with a health worker before presentation to hospital. Improving transfer from primary health care facilities to higher-level centers for definitive treatment by putting in place pediatric referral ambulance systems, preferably at subsidized cost to the patients will decrease the time to presentation and subsequently mortality rates of pediatric intussusception in Uganda. We advocate that the government of Uganda puts in place a reliable ambulance system especially at district hospitals to aid safe transfer of not only pediatric patients but other patients groups to regional referral and national referral hospitals which have surgeons and other specialists on staff.

In addition, radiology services have not developed adequately to treat children with intussusception. While some pilot efforts, mostly led by surgeons, have been described in other similar settings without routine access to fluoroscopy, such as ultrasound guided reduction, this has not yet gained widespread traction in Uganda. In an Ethiopian study, introduction of Ultrasound guided hydrostatic enema reductions as the initial treatment successfully led to a drastic decrease in the number of laparotomies performed for pediatric intussusception[28]. This was performed in patients presenting up to 4 days from onset of symptoms similar to majority of patients in our study[28]. We therefore advocate that the government should avail ultrasound machines to national and regional referral hospital theaters as well as training of personal to be able to safely perform enema reductions and also have a radiologist on staff in these centers.

Limitations of this study included it being a single tertiary center study. However, we feel confident that we captured a representative sample of infants and young children with intussusception. The breakdown of surgical options may not be generalizable to the Ugandan population as the choice of procedure is dependent on the availability of equipment and surgeon preference. More detailed patient data was not available due to poor reliability of paper charts in our health system, as has been reported in other studies.

4. Conclusions

Pediatric intussusception in Uganda remains a major challenge, with a mortality rate of 32% and the majority of children requiring laparotomy with resection. This represents substantial disparity with management in high-income countries where treatment is generally non-operative and mortality rates negligible. Duration of symptoms before presentation was significantly higher in children who were referred as opposed to children who were not referred. Sensitization of parents and health workers about pediatric intussusception and development of pediatric ambulance systems for expeditious transfer of patients to points of definitive care will have a positive impact on mortality.

Conflict of Interest

The authors declare that they have no conflicts of interest.

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Ethical Approval

Approval for this study was obtained from Makerere University College of Health Sciences Ethics and Research Committee.

Informed Consent

Informed consent was obtained from all individual participants included in the study.

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