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## Intussusception Cases Among Children Admitted to Referral Hospitals in Kenya, 2002–2013: Implications for Monitoring Postlicensure Safety of Rotavirus Vaccines in Africa

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### Abstract

To describe the epidemiology of intussusception before introduction of the rotavirus vaccine, we reviewed the records of 280 patients younger than 5 years who were hospitalized in Kenya between 2002 and 2013. The patients who died (18 [6.4%]) had sought care later after symptom onset than the patients who survived (median, 5 vs 3 days, respectively;  $P = .04$ ). Seeking prompt care may improve therapeutic outcomes.

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## Keywords

childhood mortality; intussusception; Kenya; risk factors

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Intussusception is a rare, life-threatening, acute intestinal obstruction with which a segment of the bowel prolapses into a more distal segment. Its causes are usually unknown, and the disease has no clear seasonality [1, 2]. Intussusception is the most common abdominal complication in infants and children younger than 2 years [3].

Both internationally recommended rotavirus vaccines have been associated with a low risk of intussusception, but the benefits of vaccination, including decreases in mortality and hospitalization rates, outweigh the risk [4]. The World Health Organization therefore recommends the global use of rotavirus vaccine [5]. As rotavirus vaccines are introduced in low- and middle-income countries, we urgently need to understand the prevaccine epidemiology and clinical characteristics of intussusception and establish surveillance to monitor the rates of intussusception prospectively [5-7].

Kenya introduced rotavirus (Rotarix; GlaxoSmithKline Biologicals) vaccine in the routine immunization program in July 2014. However, background data on intussusception in Kenya and the sub-saharan African region are limited. Here, we describe the pre-rotavirus vaccine epidemiology and risk factors for intussusception-related mortality among Kenyan children younger than 5 years who were hospitalized between 2002 and 2013.

## METHODS

### Study Design and Setting

We retrospectively reviewed medical records to identify pediatric patients hospitalized with intussusception at 12 geographically dispersed referral hospitals in Kenya from January 2002 to November 2013. The exact review period varied by hospital depending on the availability of patient records.

### Data Collection

In each study hospital, pediatric surgeons systematically reviewed hospital logbooks and treatment and discharge records to identify all pediatric patients clinically diagnosed with intussusception and confirmed the diagnosis by using Brighton Collaboration level 1 criteria [3] during the time period in which records were available at the hospital.

Demographic and clinical characteristics, type of surgery, and outcome information were abstracted by using standard case-report forms.

### Statistical Analysis

Fisher's exact test was used to compare characteristics of the patients who died and those of the patients who survived. Medians were compared by using the Wilcoxon rank-sum test. For all statistical tests, a 2-sided *P* value of <.05 was considered statistically significant. Data were entered into a Microsoft Access database and analyzed by using SAS version 9.4 (SAS

Institute, Inc, Cary, NC). The study protocol was reviewed and approved by the Kenyatta National Hospital (KNH) Ethics Review Committee (protocol number P514/09/2012). Approval from the US Centers for Disease Control and Prevention Institutional Review Board (protocol number 6513) relied on KNH approval.

## RESULTS

Of the 305 records for children treated for intussusception at the 12 referral hospitals during the study period, 25 (8.2%) were excluded from further analysis because of missing age ( $n = 12$ ), because the age was  $>60$  months ( $n = 12$ ), or because the episode occurred before 2002 ( $n = 1$ ); thus, 280 (91.8%) patients were included. The majority of these patients were  $<1$  year of age (192 [68.6%]), male (186 [66.4%]), and referred from another district-level hospital (165 [58.9%]). None of the referrals were from any of the 12 participating hospitals to another. Intussusception cases were diagnosed throughout the year in October to December (81 [28.9%]), July to September (75 [26.8%]), January to March (65 [23.2%]), or April to June (59 [21.1%]), and no seasonal pattern was detected. During the time period when all hospitals had records available (2010–2013), 31 to 48 cases were identified annually.

Vomiting (88.2%), blood detected in stool or gross rectal bleeding (81.1%), abdominal distension (75%), and diarrhea (74.6%) were the most common clinical symptoms (Table 1). The overall median time to seeking care was 3 days (interquartile range, 2–6 days) after illness onset. Overall, 97 (35%) of the patients underwent abdominal radiography only, 36 (13%) underwent ultrasonography only, and 55 (20%) underwent both ultrasonography and abdominal radiography, whereas 92 (33%) underwent neither ultrasonography nor abdominal radiography. Overall, surgery was the most common treatment (73.2%); nonoperative reduction was uncommon (only 5 [1.8%] patients were treated with contrast-fluid enema). For 26.1% of the patients, the type of treatment was unknown.

Eighteen (6.4%) patients died during hospitalization while undergoing treatment. Compared with the patients who survived, those who died were more likely to be younger (7.0 vs 5.5 months, respectively;  $P = .04$ ), to have sought care late after symptom onset (median, 3 vs 5 days, respectively;  $P = .04$ ), to have had fever on admission ( $P = .004$ ), and to have been treated by bowel resection ( $P = .003$ ) (Table 1).

## DISCUSSION

We describe here characteristics of patients with intussusception who presented for care at Kenya's main referral hospitals before the national rotavirus vaccine introduction. Compared with patients who survived, those who died were younger and were more likely to have sought care late after symptom onset (as characterized by the presence of fever at admission) and to have undergone bowel resection. However, these observations need to be interpreted with caution, because the study was not designed to assess prognosis, and the results may simply reflect differences in age, gender, or severity at presentation among those who sought care. In Kenya, most district- or lower-level hospitals do not have specialized pediatric care for diagnosing or treating intussusception. More than half of the cases were referrals to

provincial or higher-level hospitals from district-level hospitals, which is comparable with findings from another study conducted at Moi Teaching and Referral Hospital in Kenya [8].

Consistent with results from previous studies in Africa [7], surgery was the most common treatment of intussusception in our study. However, nonoperative treatment of intussusception by using ultrasound-guided reduction causes no radiation exposure and has been shown to result in better success rates than surgery. Furthermore, nonsurgical treatment methods are safe, painless, and quicker than surgery and have not been associated with complications or recurrence of intussusception [9, 10].

However, in our study, late care seeking may have been associated with the use of surgery because patients may have had progressive disease, as evidenced by the presence of fever, a classical sign of severe disease. Our finding that patients who died were more likely to have been treated through bowel resection than manual reduction may also have been a consequence of late presentation to a facility where intussusception could be managed. Although referral was appropriate, it may have led to further delays in appropriate management, potentially leading to fatal outcomes. Prompt care seeking by the patient and early detection and treatment of intussusception at a primary- or secondary-level facility could lead to better outcomes, as observed elsewhere [11, 12]. Children with symptoms lasting >1 day before seeking care have been shown to be at increased risk for requiring surgery [11]. Creating awareness among parents and healthcare workers to recognize the signs and symptoms associated with intussusception could help to improve early care seeking, diagnosis, and treatment [13].

The case-fatality rate in our study was low compared with 14% reported from other regions in Kenya [8], 28% in Rwanda [14], and ~13% reported from other African countries [7]. Although the in-hospital case-fatality rate in our study was similar to that (4.2%) reported from a multicountry surveillance study in Egypt, Kenya, India, and Brazil [15], the difference in this rate may be a result of methodological differences, because we were not able to ascertain disease outcomes after discharge and records of the children who died may have been less accessible.

Our findings are comparable with those of other studies in which intussusception was reported to be more common among patients aged 0 to 11 months [7] and among boys [14]. The incidence of naturally occurring intussusception is normally low in the first 3 months of life, as observed in other countries such as Bangladesh [16]. Intussusception among Kenyan children peaked at 4 to 6 months of age. The higher occurrence of intussusception among children 4 to 6 months of age is important when interpreting trends in intussusception after the introduction of rotavirus vaccine. The lack of information about the epidemiology of intussusception in young children could lead some to suggest a link to vaccination rather than a natural increase in cases coinciding with the time period when vaccine is typically given.

This study had limitations. First, given that intussusception is rare and the availability of records varied over the almost 11 years of our retrospective study period, we were unable to systematically monitor trends in intussusception over time. Furthermore, we

may have underestimated the number of intussusception cases, particularly in the early years of the study when record keeping may not have been as complete as in later years. Second, our study methodology did not allow an observation window beyond hospital discharge, possibly leading to an underestimation of the case-fatality rate. Third, we did not have baseline population data for the catchment area of participating hospitals given the large number of patient referrals, which made the calculation of population-based baseline incidence rates for intussusception impossible. Finally, the method of treatment was not recorded in approximately one quarter of the cases. Although surgeons reported that these cases met the Brighton Collaboration criteria for confirmed intussusception, we were not able to verify this confirmation, which may have led to an over-estimate of the number of cases that met the level 1 criteria for intussusception.

Despite these limitations, we made key observations in this study that are important for setting up prospective surveillance of intussusception in Kenya. First, we were able to identify the hospitals with the highest numbers of intussusception cases to be targeted as sentinel sites for postlicensure monitoring of rotavirus vaccine effects. Second, understanding where and how intussusception cases present and referral patterns will help us to identify cases more efficiently.

Continued monitoring of intussusception in Kenyan children and scaling up efforts targeted at reducing delays in seeking care for intussusception may contribute to early diagnosis and appropriate treatment for better outcomes in this setting.

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### Disclaimer.

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the US Centers for Disease Control and Prevention.

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**Table 1.** Comparing Characteristics of Children Aged 0 to 59 Months Who Died Versus Those Who Survived After Treatment for Intussusception at Referral Hospitals in Kenya, 2002–2013

<b>Background Characteristic</b>	<b>All (N = 280)</b>	<b>Died (n = 18)</b>	<b>Survived (n = 262)</b>	<b>P<sup>a</sup></b>
Demographic characteristics (n [%])				
Child age				
0–5 mo	81 (28.9)	9 (50)	72 (27.4)	.195
6–11 mo	11 (39.3)	6 (33.3)	105 (40.1)	
12–23 mo	43 (15.4)	2 (11.1)	41 (15.7)	
24–59 mo	45 (16.1)	1 (5.6)	44 (16.8)	
Median (IQR) age of patients (mo)	7.0 (5–14)	5.5 (4.0–9.0)	7.0 (5.0–14.0)	<b>.04</b>
Gender (n [%]) <sup>b</sup>				
Male	186 (66.4)	11 (61.1)	175 (67)	.611
Female	93 (33.2)	7 (38.9)	86 (33)	
Days before seeking care (median [IQR])	3 (2–6)	5 (3–9)	3 (2–5)	<b>.04</b>
Days to death/discharge upon recovery after admission (median [IQR])	5 (3–8)	2 (1–6)	6 (4–8)	<b>.01</b>
Clinical features (n [%])				
Fever	177 (63.2)	17 (94.4)	160 (61.4)	<b>&lt;.01</b>
Temperature <sup>c</sup>				
<37.0	38 (17)	1 (6.2)	37 (17.9)	<b>.01</b>
37.0–38.4	125 (56.1)	5 (31.2)	120 (58)	
38.5–38.9	21 (9.4)	3 (18.8)	18 (8.7)	
39.0	39 (17.5)	7 (43.8)	32 (15.4)	
Vomiting	247 (88.2)	17 (94.4)	230 (87.8)	.71
Diarrhea	209 (74.6)	13 (72.2)	196 (74.8)	.78
Blood in stool	227 (81.1)	13 (72.2)	214 (81.7)	.35
Abdominal pain	178 (63.6)	10 (55.6)	168 (64.1)	.46
Abdominal distension	210(75)	16 (88.9)	194 (74)	.26
Abdominal mass	111 (39.6)	5 (27.8)	106 (40.5)	.33
Rectal mass	80 (28.6)	4 (22.2)	76 (29)	.79
Type of intussusception (n [%])				

Background Characteristic	All (N = 280)	Died (n = 18)	Survived (n = 262)	<i>P</i> <sup>a</sup>
Ileocolic	132 (47.1)	10 (55.6)	122 (46.6)	.76
Colocolic	40 (14.3)	5 (27.8)	35 (13.4)	
Ileoileal	22 (7.9)	2 (11.1)	20 (7.6)	
Diagnosis method (n [%]) <sup>d</sup>				
Ultrasound	91 (32.5)	10 (55.6)	81 (30.9)	<b>.04</b>
Abdominal radiograph	152 (54.3)	14 (77.8)	138 (52.7)	<b>&lt;.05</b>
Treatment method (n [%]) <sup>e</sup>				
Operative				
Bowel resection	91 (32.5)	12 (66.7)	79 (30.2)	<b>&lt;.01</b>
Manual reduction	128 (45.7)	4 (22.2)	124 (47.3)	<b>&lt;.05</b>
Ileostomy	5 (1.8)	1 (5.6)	4 (1.5)	.28
Nonoperative				
Air reduction	0 (0)	0 (0)	0 (0)	NA
Contrast-fluid enema	5 (1.8)	0 (0)	5 (1.9)	>.1
Unknown	73 (26.1)	1 (5.6)	72 (27.5)	.049

Abbreviations: IQR, interquartile range; NA, not applicable.

<sup>a</sup>Significant *P* values are indicated with bold type.

<sup>b</sup>Gender information was missing for 1 child.

<sup>c</sup>The total number was 223. Died was 16. Survived was 207.

<sup>d</sup>Multiple diagnosis methods were possible.

<sup>e</sup>Multiple treatment methods possible.