Childhood Intussusception after Introduction of Indigenous Rotavirus Vaccine: Hospital-Based Surveillance Study from Odisha, India

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Abstract

Objective To study the epidemiology of intussusception in children < 2 y of age, post-introduction of Rotavac® (an indigenous oral rotavirus vaccine).

Methods A multicenter hospital-based surveillance was conducted in Odisha from February 2016 to June 2019. The cases were diagnosed according to Brighton level-1 criteria. Data were collected regarding the time of onset, signs and symptoms, radiological diagnosis, management, complications, and outcome (discharged/died).

Results One hundred and twenty children < 2 y of age were enrolled. The median age was 7 mo (M:F ratio = 2:1). The most common clinical feature was abdominal distention and blood in stool. The most common method for treatment was hydrostatic/pneumatic reduction. Median time (days) between symptom onset and admission was 2. Median (IQR) duration (days) of hospitalization was 5. Most common location of intussusceptions was ileo-colic.

Conclusions Hydrostatic/pneumatic reduction was possible in the majority presenting ≤ 48 h of symptom onset, and those presenting > 48 h mostly required surgical reduction. Intestinal resection was required in some cases presenting on day 5 of symptom onset. Majority of cases were managed by surgical reduction in Government facility.

Keywords Pain abdomen · Bloody stool · Epidemiology · Rotavac · Intussusception

Introduction

In young children, commonest cause of acute intestinal obstruction is intussusception, which is idiopathic in > 90% of the cases [1]. While spontaneous resolution may occur [2, 3], failure to relieve the obstruction may cause complications with fatal outcome. WHO estimated the burden of intussusceptions (from year 1960–2002) to be at 5 to 43 cases per 10,000 live births (7.4 to 12 cases per 10,000 live births in infants) with peak incidence among 5–7 mo old [4, 5]. In some countries, there is a low risk of intussusception (1–2 excess cases per 100,000 rotavirus immunizations), as per the post-licensure safety data [6].

There have been various publications regarding burden of intussusceptions from different parts of India. In a study from...
southern India (from 2012 to 2013), 205 children < 5 y of age were diagnosed with intussusceptions [1]. In a study from north India (from 2009 to 2015), 277 children of < 5 y of age were diagnosed with intussusceptions (estimated incidence of 20 per 100,000 infants; and 5 per 100,000 children of < 5 y of age per year) [7]. There have been many other studies estimating the burden of childhood intussusceptions since 1966 [8]. However, no study till date has estimated the burden of childhood intussusceptions in Eastern Indian states including Odisha.

Over the past two decades, major efforts have been put in developing countries for an effective as well as safe rotavirus vaccine to prevent morbidity and mortality [9, 10]. Rotavirus vaccines have been shown to reduce rotavirus hospitalizations (49% to 92%), all-cause diarrhea hospitalizations (17% to 55%), and mortality (22% and 50%) [10]. The first vaccine “Rotashield” was associated with a very high-risk of intussusception (3 to 14 d after the first dose), and was withdrawn immediately from the market [11]. In a meta-analysis, the authors found an increased risk of intussusception (initial 7 d of administration of first dose) with currently used rotavirus vaccines [12]. In a USA study, increase rates of hospitalization in infants (due to intussusception) were observed, when pre- and post-rotavirus-vaccine-introduction data were compared [13]. This emphasizes the need of an effective surveillance system in countries that have introduced rotavirus vaccine recently [14]. In Odisha, Rotavac® was incorporated in the immunization programme in March 2016. The present study was carried out after this time period to understand the epidemiology of intussusceptions in children < 2 y of age.

Material and Methods

This prospective hospital-based surveillance study was conducted from February 2016 to June 2019 (post-rotavirus-vaccine-introduction phase), and included children admitted with a diagnosis of intussusception at the pediatrics wards of four tertiary care teaching hospitals from Odisha [SVP Post Graduate Institute of Pediatrics, Cuttack; Institute of Medical Sciences (IMS) and SUM, Bhubaneswar; KIMS, Bhubaneswar; and Hi-tech medical college, Bhubaneswar]. Of the four hospitals; only SVPPGIP, Cuttack was the Government facility. Having dedicated departments of pediatric surgery, intussusception cases are usually referred to these hospitals from various parts of Odisha. Consecutive children < 2 y of age were taken as cases if they met the Brighton collaboration working group diagnostic certainty criteria [15]. There are: (i) surgical criteria (presence of intestinal invagination at surgery); (ii) radiological criteria (demonstration of intestinal invagination by contrast enema, and reduction of an intra-abdominal mass with characteristic features of intussusception on ultrasound by hydrostatic enema); and (iii) autopsy criteria (demonstration of invagination of the intestine at autopsy).

Patients who denied admission were excluded. Data were recorded on a pre-designed data collection form. The details regarding time of onset, signs and symptoms, radiological diagnosis, management, complications, and outcome (discharged/died) were collected. Institutional ethical committee approval was obtained from the respective study sites. Written and informed consent was obtained from the parents/legal guardians of included children. Patients were managed as per the protocol described previously [16].

For all statistical analysis, STATA version 13 (StataCorp LCC, College station, Texas, USA) was used. Descriptive statistics are used to express the numbers with proportions. Continuous variables including age (years), duration of symptoms (days) and hospital stay (days) are presented as mean (±SD) or median (IQR).

Results

A total of 123 Intussusception cases were included. Majority of the children were < 1 y (n = 90, 73%) of age with the median age being 7 (4–12) mo (Fig. 1). Male:female (M:F) ratio was 2:1 (Table 1). The details of clinical course have been described in Table 2. The most common presentations were abdominal pain/distension (n = 104, 85%), blood in stool (n = 104, 85%), and vomiting (n = 98, 80%).

The most common method for treatment was surgical resection (N = 85, 69%), followed by hydrostatic/pneumatic reduction (N = 35, 29%). Surgical resection was required in a very small number of cases (N = 3, 2%). An abdominal mass could not be palpated in any of the patient. The classical triad (pain abdomen, blood in stool, and vomiting) was present in 27 (22%) patients. Diarrhea secondary to enteritis was present in a good number of patients (N = 76, 62%). None of those presenting with diarrhea reported spontaneous resolution of their intussusceptions. Median (IQR) time between symptom onset and admission was 2 (1, 3) d. Median (IQR) duration of hospitalization was 5 (4, 6) d. Most common location of intussusceptions was ileo-colic.
The most common complication noted was peritonitis. There was no secondary intestinal obstruction. There was no mortality. Seasonal trend was noted with two peaks: Winter (November to January), and Summer (March to June) (Fig. 2). For unknown reasons, years 2017 and 2019 reported more number of cases compared to years 2016 and 2018.

Table 1  Characteristics of children with intussusception

| Clinical course | SVPPGIP, Cuttack (N=80) | SUM & IMS, Bhubaneswar (N=27) | KIMS, Bhubaneswar (N=11) | HI-TECH, Bhubaneswar (N=5) | Total (N=123) |
|-----------------|--------------------------|-------------------------------|--------------------------|----------------------------|----------------|
| Age in months, median (IQR) | 6 (4, 9.5) | 10 (6, 16) | 7 (5, 12) | 13 (9, 15) | 7 (4, 12) |
| Age | < 1 y | 65 (81%) | 15 (56%) | 8 (73%) | 2 (40%) | 90 (73%) |
|      | 1–2 y | 15 (19%) | 12 (44%) | 3 (27%) | 3 (60%) | 33 (27%) |
| Sex | Male | 48 (60%) | 19 (70%) | 8 (73%) | 5 (100%) | 80 (65%) |
|    | Female | 32 (40%) | 8 (30%) | 3 (27%) | – | 43 (35%) |

The trend of treatment modality according to the day on which the cases presented to the hospital showed that hydrostatic/pneumatic reduction was possible in the majority presenting within 48 h of symptom onset (Fig. 3). Those presenting after 48 h mostly required surgical reduction. In 5 cases, the per-operative findings included malrotation (n =

Table 2  Clinical course (symptoms, treatment, complication, and outcome) of infants with intussusception

| Clinical course | SVPPGIP, Cuttack (N=80) | SUM & IMS, Bhubaneswar (N=27) | KIMS, Bhubaneswar (N=11) | HI-TECH, Bhubaneswar (N=5) | Total (N=123) |
|-----------------|--------------------------|-------------------------------|--------------------------|----------------------------|----------------|
| Clinical symptoms | Diarrhea | 64 (80%) | 8 (30%) | 4 (36%) | 0 | 76 (62%) |
|                  | Vomiting | 64 (80%) | 21 (78%) | 10 (91%) | 3 (60%) | 98 (80%) |
|                  | Fever | 28 (29%) | 13 (48%) | 7 (64%) | 1 (20%) | 49 (36%) |
|                  | Blood in stool | 74 (93%) | 20 (74%) | 7 (64%) | 3 (60%) | 104 (85%) |
|                  | Abdominal distension | 69 (86%) | 25 (93%) | 5 (45%) | 5 (100%) | 104 (85%) |
| Treatment method | Hydrostatic/pneumatic reduction | 0 | 23 (85%) | 7 (64%) | 5 (100%) | 35 (29%) |
|                  | Surgery without resection | 79 (99%) | 2 (7.5%) | 4 (36%) | 0 | 85 (69%) |
|                  | Surgery with resection | 1 (1%) | 2 (7.5%) | 0 | 0 | 3 (2%) |
| Outcome | Discharged home | 80 (100%) | 27 (100%) | 11 (100%) | 5 (100%) | 123 (100%) |
|        | Died | 0 | 0 | 0 | 0 | 0 |
| Interval (days) between symptom onset and admission, median (IQR) | 3 (2, 3) | 1 (0, 2) | 4 (1, 7) | 1 (1, 1) | 2 (1, 3) |
| Duration of hospitalization (days), median (IQR) | 6 (5, 7) | 3 (3, 4) | 5 (4, 8) | 3 (3, 3) | 5 (4, 6) |
| Location of intussusception | Ileo-colic | 77 (96%) | 25 (92%) | 8 (73%) | 5 (100%) | 115 (93%) |
|                        | Colo-colic | 2 (3%) | 1 (4%) | 1 (9%) | 0 | 4 (3%) |
|                        | Ileo-ileo | 1 (1%) | 1 (4%) | 1 (9%) | 0 | 2 (2%) |
|                        | Compound | 0 | 0 | 0 | 0 | 1 (1%) |
|                        | Unknown | 0 | 0 | 1 (9%) | 0 | 1 (1%) |
| Complication | Wound infection | 0 | 1 (100%) | 0 | 0 | 1 (100%) |
|               | Wound dehiscence | 0 | 1 (100%) | 0 | 0 | 1 (100%) |
|               | Peritonitis | 5 (100%) | 0 | 0 | 0 | 5 (100%) |
2), an inflamed appendix (n = 1), a Meckel’s diverticulum (n = 1), and a duplication cyst (n = 1). Intestinal resection was required in some cases presenting on day 5 of symptom onset. Hydrostatic/pneumatic reduction was possible in a good number of cases presenting even after 5 d of symptom onset.

No recurrence was observed following surgical reduction. The recurrence rates after first, second, and third hydrostatic/pneumatic reduction was 16%, 23%, and 29%, respectively. Those having recurrence after third attempt underwent surgery without any major complications.

The authors compared the age of presentation (completed months), duration of symptoms (days), and duration of hospitalization (days) in the two treatment groups. No significant difference in the mean age of presentation (8.3 in nonsurgical vs 10.7 in surgical reduction, \( p = 0.34 \)), and mean duration of symptom (1.8 in nonsurgical vs 2.8 in surgical reduction, \( p = 0.24 \)) was observed. However, a significant difference in the mean duration of hospitalization (3.1 in nonsurgical vs 7.8 in surgical reduction) was observed between the two groups.

A comparison of treatment types was done between government and private facilities, which showed that majority of cases were managed by surgical reduction in government facility (99% vs 14%) (Fig. 4).

### Discussion

The present study provided the epidemiological pattern of intussusception immediately after the rotavirus vaccine introduction for the first time in the National Immunization Schedule (NIS) of Odisha.

During the study period, mean number of intussusception cases reported was 41 per year. The M:F ratio was 2:1, which is in accordance with previously published studies from other parts of the world and India. However, the ratio varies widely across the world ranging from 1.3:1 (Singapore) to 9:1 (India) [7, 17]. Though there is no definitive reason behind the same, sex-linked (sons over daughters) preferential treatment could be a reason particularly in Indian subcontinent [7]. Median age of the cases was 7 mo with 73% being < 12 mo, which is like previously published Indian [7, 17] and Western [18, 19] studies. In the present study, the classic triad of intussusception (pain abdomen, vomiting, and blood in stool) was reported in 22% cases, which is higher than previous studies from India (from 6.4% to 18.7%) [7, 17, 20], except the one from South India [16]. Moreover, abdominal distention and blood stool was common than vomiting in contrast to other published studies from India [7, 17, 20]. Surprisingly, diarrhea was the presenting complaint in 62% cases, which was much higher than that reported in any of the previously published Indian or Western studies. The cause may be an active infection causing lymphoid hyperplasia forming the lead point for intussusception. However, there was no report of any spontaneous reduction of intussusceptions in these patients in contrast to a previously published study from South India that showed 22% spontaneous reduction in those having diarrhea/enteritis [16].

A seasonality trend was noted in the present study. Seasonal peaks were noted during winter (November to January) and summer (April to June). Two previous studies from India have reported seasonality trends in rotavirus diarrhea cases [7, 17]. However, in another study from South
India, seasonality was not observed [20]. This is an interesting observation as rotavirus causes diarrhea mostly during winter, and has been implicated as the cause of “winter diarrhea”.

Surgical reduction (69%) was the commonest method employed in the present study, which is much higher than two South Indian studies [1, 16] but similar to other studies (varied from 61.7 to 71%) [7, 17]. Hydrostatic/pneumatic reduction was achieved in 29% cases in the present study, which was lower than two South Indian studies [1, 20], but similar to other studies [7, 17]. Hydrostatic/pneumatic reduction was possible in the majority presenting within 48 h of symptom onset. There was not a single case of recurrence following any of the methods of intussusception reduction. In the present study, a higher rate of hydrostatic/pneumatic reduction was employed in private facility, and a higher rate of surgical reduction was employed in government facility. The surgical resection rate was much higher (5 times more) in private facilities. The reason for the same is not clear, though one possibility might be the less chance of availing the operation theater during emergency (in case of failure of hydrostatic/pneumatic reduction) in government facility because of heavy patient load.

In those undergoing nonsurgical reduction, the recurrent intussusception reported rate in the literature is up to 20%, and in those undergoing surgical reduction as 1% to 3% [21, 22]. These figures were nearly similar to the present study. The authors followed the suggestion given previously for surgical reduction (after third attempt), as the probability of recurrence may increase following fourth attempt of hydrostatic/pneumatic reduction. However, a South Indian study found 66% cure rate of nonsurgical reduction even after fourth recurrence.

The strengths of the present study are prospective designing of the surveillance, employment of standard case definition, and rigorous case documentation. The cases were confirmed by a dedicated team (pediatric surgeons, and radiologists) in ruling out any miss-classification error. The limitation include an inability to estimate the intussusception incidence rate (because of difficulty in defining the catchment area, and chance of mild to moderate cases being missed as severe cases usually get referred to these tertiary care hospitals).

**Conclusions**

Hydrostatic/pneumatic reduction was treatment of choice in the majority of patients presenting ≤ 48 h of symptom onset, and those presenting > 48 h mostly required surgical reduction. Intestinal resection was required in some cases presenting on day 5 of symptom onset. Majority of cases were managed by surgical reduction in government facility.

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**Compliance with Ethical Standards**

**Conflict of Interest** None.

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