Epidemiology of Intussusception Hospitalizations in Children Under 2 Years of Age Post Rotavirus Vaccine Introduction in Tamil Nadu and Puducherry, India

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Abstract

Objective High burden of rotavirus associated diarrhea has been documented among Indian children. The phased introduction of an indigenous rotavirus vaccine ‘ROTAVAC’ in India’s national immunization programme began in 2017. Phase-III trial showed the vaccine to have a low-intussusception-risk profile. However, evaluation of post-licensure trends of intussusception is necessary to assess potential vaccine-associated intussusception risk. This study’s objective was to describe the epidemiology of intussusception hospitalizations in children under two years of age in Tamil Nadu and Puducherry following ROTAVAC introduction.

Methods A cross-sectional surveillance was established in six hospitals in Tamil Nadu and Puducherry. Children under two years of age with intussusception fulfilling Brighton Collaboration’s criteria for level 1 diagnostic certainty were enrolled. Patient and disease characteristics were captured using a standardized questionnaire. Descriptive and inferential statistical analyses were performed using Stata Version 13.

Results Overall, 287 cases were enrolled and had a median age of seven months. Frequently presenting symptoms were vomiting (78%), abdominal pain (76%), and blood in stool (71%). Abdominal ultrasonography or radiography confirmed diagnosis in 65% of cases and managed by nonoperative measures. Remaining 35% of cases were diagnosed and managed with surgery. Over 98% of the cases had positive treatment outcomes. Age less than five months (OR = 4.36), and hospitalization at a state government health facility (OR = 5.01) were significant predictors for children to receive surgical management.

Conclusions The present study documents the epidemiology of intussusceptions immediately after the rollout of rotavirus vaccine in Tamil Nadu and Puducherry. No appreciable increase in intussusception hospitalizations was seen in the study hospitals after vaccine introduction.

Keywords India · Intussusception · Puducherry · Rotavirus vaccination · ROTAVAC · Tamil nadu
Introduction

Intussusception is a common cause of intestinal obstruction in infancy and childhood; the majority of cases being idiopathic [1]. Diagnosis of intussusception is made by ultrasonography, radiology or at surgery, and cases are mostly managed with nonoperative techniques of pneumatic or hydrostatic reductions. However, in complicated cases or on the failure of nonoperative reduction, surgery is usually required and may involve either manual reduction or intestinal resection in patients presenting with vascular compromise or perforation or pathological lead point [1, 2]. The estimated median annual incidence of intussusception globally ranges from 34 (African region) to 90 (Western Pacific region) per 100,000 children aged less than one year [3]. In South-East Asia, the estimated incidence is 90 per 100,000 children aged <1 y and 52 per 100,000 children aged <5 y. There is a paucity of intussusception incidence data in India. Studies from Delhi and Chandigarh have reported an estimated 17.7 and 20 cases, respectively per 100,000 infant-years [4, 5].

Rotavirus is a major cause of severe diarrhea requiring hospitalization in young children worldwide [6]. The first licenced rotavirus vaccine ‘Rotashield®’ was withdrawn in the USA, following its association with an increased incidence of intussusception among vaccinated children [7]. Consequently, the association of intussusception with rotavirus vaccines was closely studied, when newer rotavirus vaccines - Rotarix® and Rotateq® were introduced in several countries [7]. In India, data on the high burden of rotavirus-associated diarrhea in children under 5 y of age was generated between 2005 and 2016 by several studies including two rounds of national-level multi-centric rotavirus surveillance [8, 9]. Availability of robust data on rotavirus-associated diarrhea contributed to the introduction of an indigenously developed monovalent rotavirus vaccine, ROTAVAC® in the national immunization programme in select states and union territories of India including Tamil Nadu and Puducherry [10, 11].

Despite the low intussusception risk demonstrated by the vaccine in trial settings, it was essential to monitor the level of intussusception, post-vaccine introduction. For evaluating post-licensure trends of intussusception and assessing any potential vaccine-associated risk, geographically representative baseline data on intussusception were necessary. Towards generating this data, prospective surveillance of intussusception was established in six hospitals in Tamil Nadu and Puducherry. In this report, the authors describe the epidemiologic features of intussusception among under two-year-old children following the introduction of the rotavirus vaccine in Tamil Nadu and Puducherry, South India.

Material and Methods

This is a prospective, cross-sectional multi-site evaluation of intussusception conducted between June 2017 and September 2019 at five sentinel hospitals in Tamil Nadu (Christian Medical College and Hospital, Vellore; Institute of Child Health and Hospital for Children, Chennai; Kanchi Kamakoti Childs Trust Hospital, Chennai; Government Medical College, Madurai and Government Medical College, Coimbatore) and one in Puducherry (Jawaharlal Institute of Post-Graduate Medical Education & Research) (Fig. 1). Details of site selection and surveillance initiation has been previously published [12].

Children under two years of age with suspected intussusception admitted to the participating sentinel hospitals were eligible for enrollment into surveillance. Inclusion criteria for case enrollment were i) age below 2 y, and ii) fulfilling Brighton collaboration criteria for level 1 diagnostic certainty for intussusception i.e., confirmation during surgery and/or by specific radiologic findings (reduction by pneumatic/hydrostatic/contrast enema) or specific characteristics on sonography or at autopsy [13].

Surveillance staff identified hospitalized intussusception cases by visiting pediatric in-patient wards and reviewing admission and surgical theatre logs. The eligibility of each case was ascertained by the study physician prior to enrollment. For each enrolled child, a case report form was filled and a copy of the ultrasound report along with image, hospital procedure/treatment notes, and a copy of the vaccination record were collected. The enrolment activity was carried out in close coordination with the pediatric surgeons and radiologists in the participating hospitals. Monitoring of surveillance activity at each sentinel site was carried out once in 3 mo, and performance was evaluated using a monitoring checklist.

All statistical analyses were performed using Stata Version 13 (StataCorp, College Station, TX, USA). Descriptive analyses of demographic, clinical, and treatment characteristics were carried out. The median [with interquartile range (IQR)] was calculated for continuous variables whereas proportions and frequency tables were used to summarize categorical variables. Univariate logistic regression analysis followed by multivariable logistic regression model was adopted to identify predictors of different treatment modalities. Variables of known clinical or contextual importance were used for the multivariable regression model.

The study was approved by the institutional review boards/ethics committees of each participating hospital/institution. Written informed consent was obtained from parents/guardians of eligible children prior to enrollment in the surveillance.

Results

During the period of surveillance, 287 intussusception cases matching the Brighton’s collaboration level-I diagnostic
certainty was admitted and managed at the participating hospitals. Median age (IQR) of cases was 7 (6–12) and 74% of them were aged < 1 y (Table 1). The authors found a unimodal age distribution with a peak in children aged 4–10 mo (Fig. 2). The male-to-female ratio was 2.8:1 and ranged between 1:1 in Vellore and 2.8:1 in Madurai. Intussusception hospitalizations were seen throughout the year in all participating hospitals. About 50% of cases had received one or more doses of rotavirus vaccination.

The most frequent presenting symptoms were vomiting (78%), abdominal pain (76%), and blood in stool (71%) (Table 1). The classic triad of bloody stool, vomiting, and abdominal pain was found in 125 (43.6%) patients. The median duration between onset of the symptom(s) and admission to any of the surveillance hospitals was 1 d (IQR, 1–2), with 42% of the cases being referrals from other hospitals. There was no significant association of the presence of classical triad among cases with either time to hospitalization from symptom(s) onset (p = 0.703) or duration of hospitalization (p = 0.061). Abdominal ultrasonography or radiography confirmed diagnosis in 65% of cases whereas, in 36% cases, intussusception was diagnosed on surgery. The frequency of using radiography and/or ultrasonography procedures did not differ among the study hospitals except in Madurai and Chennai where a large proportion of cases were diagnosed at surgery. A reduction of intussusception by nonoperative measures was possible in 65% of cases. In the remaining 35% of cases, surgical procedure i.e., manual reduction (30%) or resection (5%) was performed. There was no significant association between the type of treatment received and the day of presentation to the hospital (Fig. 3).

The most common location of intussusception was ileocolic (88%), followed by ileoileal (2%), colocolic (1%), and compound (6%). In 3% of cases, information on the location was not available. In 3.5% of cases, complications such as wound infection (2.5%), secondary intestinal obstruction (0.7%) and peritonitis (0.3%) was seen. Overall, the median duration of hospital stay was 2 d (IQR 1–6) but it was higher in Madurai, Chennai, and Coimbatore (Table 1). Except for five cases, all other children (98%) had good outcomes and were discharged. Three of the deaths were from Madurai whereas the remaining two were from the public sector hospital in Chennai. Among the five cases, four were male children and the median time to hospitalization for the five cases was 3 days whereas the median length of hospitalization was 13 d. All five cases had either surgical reduction or resection and two of them had peritonitis (n=1) and wound infection (n=2).
The authors also investigated predictors of treatment (surgery vs nonsurgical intervention) using Univariate and multivariable logistic regression analysis (Table 2). Age 0–5 mo [OR = 4.36, CI = (1.46–13.05)] and hospitalization at a state government health facility [OR = 5.01, CI = (2.29–10.98)] were the significant predictors for children to receive surgical management (Fig. 3).

Discussion

Initiation of the phased introduction of the rotavirus vaccine in 2016 was an important milestone in the national immunization program in India. As part of the efforts that were made to study the impact of the rotavirus vaccine rollout, active hospital-based surveillance for intussusception was established in many of the vaccine introducer states including Tamil Nadu and Puducherry. The authors describe the findings of over two years of intussusception surveillance involving five sentinel hospitals in Tamil Nadu and Puducherry. Intussusception is known to occur more commonly among males. The proportion of males diagnosed with intussusception in the present study was higher than that of females, which is consistent with previous reports from India [14–17]. The classical triad of abdominal pain, vomiting, and blood in stools was seen only in 44% of the total cases.

Table 1  Patient characteristics and clinical course of intussusception cases, 2016–2019

| Clinical course         | CMC VEL | GMC CBE | GMC MDU | ICH CHE | JIPMER PY | KKCTH CHE | Total |
|-------------------------|---------|---------|---------|---------|-----------|-----------|-------|
| Number (%)              |         |         |         |         |           |           | 287 (100) |
| Age (mo)                |         |         |         |         |           |           |       |
| 0–2                     | 38 (13) | 18 (6)  | 23 (8)  | 93 (33) | 38 (13)   | 77 (27)   |       |
| 3–5                     | 0       | 0       | 0       | 1 (1.1) | 0         | 1 (1.3)   | 2 (0.7) |
| 6–11                    | 5 (13)  | 5 (28)  | 8 (35)  | 17 (18) | 11 (29)   | 21 (27)   | 67 (23) |
| 12–23                   | 27 (71) | 7 (39)  | 9 (39)  | 39 (42) | 19 (50)   | 41 (53)   | 142 (49) |
| Age in mo, median (IQR) | 7 (5–10)| 7 (5–14)| 6 (4–10)| 7 (5–10)| 7 (5–11)| 6 (4–10)| 7 (6–12)|
| Sex                     |         |         |         |         |           |           |       |
| Male                    | 19 (50) | 12 (67) | 17 (74) | 62 (67) | 23 (61)   | 47 (61)   | 180 (63) |
| Female                  | 19 (50) | 6 (33)  | 6 (26)  | 31 (33) | 15 (39)   | 30 (39)   | 107 (37) |
| Clinical symptoms       |         |         |         |         |           |           |       |
| Diarrhea                | 15 (39) | 6 (33)  | 9 (39)  | 26 (28) | 26 (68)   | 22 (29)   | 104 (36) |
| Vomiting                | 35 (92) | 10 (56) | 18 (78) | 77 (83) | 30 (79)   | 54 (70)   | 224 (78) |
| Fever                   | 6 (16)  | 2 (11)  | 8 (35)  | 23 (25) | 7 (18)    | 12 (16)   | 58 (20)  |
| Blood in stool          | 31 (82)| 8 (44)  | 18 (78) | 73 (79) | 29 (76)   | 46 (60)   | 205 (71) |
| Abdominal pain          | 19 (50) | 12 (67) | 19 (83) | 64 (69) | 38 (100)  | 66 (86)   | 218 (76) |
| Classical triad         | 14 (37)| 4 (22)  | 12 (52) | 43 (46) | 23 (61)   | 29 (38)   | 125 (44) |
| Diagnosis level of criteria |      |         |         |         |           |           |       |
| Radiological 1          | 6 (16)  | 0       | 0       | 6 (7)   | 2 (5)     | 8 (10)    | 22 (8)  |
| Radiological-USG        | 23 (60)| 14 (78)| 1 (5)   | 41 (44) | 26 (68)   | 58 (75)   | 163 (57) |
| Surgical                | 9 (24)  | 4 (22)  | 22 (95) | 46 (49) | 10 (27)   | 11 (15)   | 102 (35) |
| Treatment method        |         |         |         |         |           |           |       |
| Pneumatic/Hydrostatic reduction | 29 (76)| 14 (78)| 1 (5)   | 47 (51) | 28 (74)   | 66 (86)   | 185 (65) |
| Surgery without resection | 9 (24)| 3 (17)  | 18 (78) | 41 (44) | 5 (13)    | 11 (14)   | 87 (30)  |
| Surgery with resection  | 0       | 1 (5)   | 4 (17)  | 5 (5)   | 5 (13)    | 0 (0)     | 15 (5)   |
| Outcome                 |         |         |         |         |           |           |       |
| Discharged home         | 38 (100)| 18 (100)| 20 (87) | 91 (98) | 38 (100)  | 77 (100)  | 282 (98) |
| Died                    | 0 (0)   | 0       | 3 (13) | 2 (2)   | 0         | 5 (2)     | 18 (6)   |
| Duration of hospitalization in days, median (IQR) | 1 (1–3)| 3 (2–5)| 10 (7–13)| 4 (2–6)| 1 (1–4)| 2 (1–2)| 2 (1–6)|
| Time between onset of symptoms and admission (Treating Hospital) in d, median (IQR) | 1 (1–2)| 1 (0–1)| 2 (0–3)| 1 (1–2)| 1 (0–2)| 1 (1–2) | 1 (1–2)|
| No. of referral presentations | 31 (82)| 0     | 18 (78)| 28 (30)| 2 (5)     | 40 (52)   | 119 (42) |
| Location of intussusception |      |         |         |         |           |           |       |
| Ileocolic               | 30 (79)| 18 (100)| 22 (96)| 80 (86) | 31 (82)   | 71 (92)   | 252 (88) |
| Colo-colic              | 1 (3)  | 2 (2)   | 0       | 1 (1)   | 1 (4)     | 4 (1)     | 6 (2)    |
| Ileo-ileoal            | 2 (5)  | 1 (4)   | 2 (2)   | 1 (1)   | 5 (2)     | 17 (6)    | 8 (3)    |
| Compound               | 2 (5)  | 8 (9)   | 7 (18)  | 4 (6)   | 0         | 7 (2.5)   | 1 (0.3)  |
| Unknown                | 3 (8)  | 1 (1)   | 3 (8)   | 0       | 0         | 7 (2.5)   | 2 (0.7)  |
| Complication            |         |         |         |         |           |           |       |
| Wound infection         | 2 (5)  | 0       | 1 (4)   | 1 (1)   | 3 (8)     | 0         | 7 (2.5)  |
| Peritonitis             |         |         |         | 1 (1)   | 3 (8)     | 0         | 7 (2.5)  |
| Secondary intestinal obstruction | 2 (11)|       |        |        |           |           |        |

CBE Coimbatore; CHE Chennai; MDU Madurai; PY Puducherry; VEL Vellore
This was higher than 6.4%–29.6% seen in recent reports from India [14, 16–18].

In this study, intussusception was commonly seen during the first year of life, with a higher proportion of cases 6–12 mo age category. The number of cases rose from 3 mo of age and peaked at around 6 mo before decreasing gradually. Similar age trends were documented in previous studies from India [14–17]. Admissions of intussusception cases were seen throughout the year in all participating hospitals without any appreciable seasonality. A similar trend in the occurrence of intussusception cases has been documented in other studies in India [14, 15, 17].

A review of studies reporting intussusception between 2002 and 2012 showed a low rate of surgical management
The rotavirus vaccine is permitted until one year of age [20]. Currently, in the vaccination programme, administration of Tyloha in India is at ages 6, 10, and 14 wk [20]. In this study, very few cases were seen among under three-mo olds whereas about one-fourth of the cases were in 3–6 mo age category. However, in the present study, the median time to hospitalization was short and hence there may be other factors such as nonavailability of radiologists/sonologists 24×7 etc., that needs to further analyzed to enable nonsurgical management to be attempted in all eligible cases. This will reduce surgery associated morbidity and complications as well as avert prolonged hospital stays, all of which impose a considerable economic burden on the patients and the health system provided infrastructure and expertise for nonoperative reduction is available. The low proportion of deaths in the present study is comparable to previous reports from India and Asia [15–17, 19].

The current recommendation of rotavirus vaccination in India is at ages 6, 10, and 14 wk [20]. In this study, very few cases were seen among under three-mo olds whereas about one-fourth of the cases were in 3–6 mo age category. Currently, in the vaccination programme, administration of the rotavirus vaccine is permitted until one year of age [20]. Continued monitoring of trends in intussusception case burden across the country with a larger sample is necessary to document the impact of rotavirus vaccination on background rates of intussusception in India. The current study was limited only to intussusception cases admitted to select hospitals, most of which were tertiary level hospitals. Thus, not all cases in the study population/region were captured in this surveillance and the catchment population of the study hospitals could also not be defined, making incidence rate estimation not possible.

The present study is one of the early reports on epidemiology of intussusception hospitalizations in post-rotavirus vaccine introduction scenario in India and the first report from Tamil Nadu and Puducherry.

### Table 2 Logistic regression model for predictors of treatment type among children under two years of age admitted with intussusception

| Variables | Category             | Hy/Py reduction n (%) | Surgical procedure n (%) | Odds ratio (95% CI) | p value | AOR (95% CI) | p value |
|-----------|----------------------|-----------------------|--------------------------|---------------------|---------|--------------|---------|
| Age       | 0–5 mo               | 32 (46%)              | 37 (54%)                 | 2.49 (1.38–4.5)     | 0.002   | 4.36 (1.46–13.05)* | 0.009   |
|           | 6–11 mo              | 97 (68%)              | 45 (32%)                 | Ref                 | Ref     | Ref          | Ref     |
|           | 12–23 mo             | 56 (74%)              | 20 (26%)                 | 0.77 (0.41–1.43)    | 0.409   | 0.79 (0.29–2.14) | 0.643   |
| Blood in stools | No                  | 61 (75%)              | 20 (25%)                 | Ref                 | Ref     | Ref          | Ref     |
|           | Yes                  | 124 (60%)             | 81 (40%)                 | 1.99 (1.12–3.55)    | 0.019   | 1.3 (0.44–3.79) | 0.642   |
| Classical triad | No                  | 113 (70)              | 49 (30)                  | Ref                 | Ref     | Ref          | Ref     |
|           | Yes                  | 72 (58)               | 53 (42)                  | 1.69 (1.04–2.77)    | 0.034   | 1.09 (0.44–2.72) | 0.849   |
| Treatment facility | Private              | 95 (83%)              | 20 (17%)                 | Ref                 | Ref     | Ref          | Ref     |
|           | Govt-state           | 62 (46%)              | 72 (54%)                 | 5.52 (3.06–9.95)    | <0.001  | 5.01 (2.29–10.98)* | <0.001  |
|           | Central institutes   | 28 (74%)              | 10 (26%)                 | 1.7 (0.71–4.04)     | 0.233   | 0.77 (0.14–4.35) | 0.765   |
| Age at start of other milk (n=172) | 1–3 mo               | 15 (43%)              | 20 (57%)                 | 5.09 (1.98–13.07)   | 0.001   | 1.77 (0.53–5.88) | 0.353   |
|           | 4–6 mo               | 48 (67%)              | 24 (33%)                 | 1.91 (0.84–4.36)    | 0.125   | 1.08 (0.42–2.79) | 0.875   |
|           | 7–9 mo               | 42 (79%)              | 11 (21%)                 | Ref                 | Ref     | Ref          | Ref     |
|           | >9 mo                | 11 (92%)              | 1 (8%)                   | 0.35 (0.04–2.99)    | 0.335   | 0.35 (0.04–3.48) | 0.372   |

**Govt** Government; **Hy/Py** Hydrostatic/Pneumatic reduction; *p value < 0.05

Statistically significant predictors of treatment type are shown in bold

from studies in Asia [19]. One-third of cases in the present study undergoing surgical intervention and this finding is comparable with more recent studies in India wherein higher surgical rates (39%–72%) are reported. Delay in seeking medical attention or delay in referral to an appropriate health facility is usually considered the reason for severe cases requiring surgical intervention. However, in the present study, the median time to hospitalization was short and hence there may be other factors such as nonavailability of radiologists/sonologists 24×7 etc., that needs to further analyzed to enable nonsurgical management to be attempted in all eligible cases. This will reduce surgery associated morbidity and complications as well as avert prolonged hospital stays, all of which impose a considerable economic burden on the patients and the health system provided infrastructure and expertise for nonoperative reduction is available. The low proportion of deaths in the present study is comparable to previous reports from India and Asia [15–17, 19]. The current recommendation of rotavirus vaccination in India is at ages 6, 10, and 14 wk [20]. In this study, very few cases were seen among under three-mo olds whereas about one-fourth of the cases were in 3–6 mo age category. Currently, in the vaccination programme, administration of the rotavirus vaccine is permitted until one year of age [20]. Continued monitoring of trends in intussusception case burden across the country with a larger sample is necessary to document the impact of rotavirus vaccination on background rates of intussusception in India. The current study was limited only to intussusception cases admitted to select hospitals, most of which were tertiary level hospitals. Thus, not all cases in the study population/region were captured in this surveillance and the catchment population of the study hospitals could also not be defined, making incidence rate estimation not possible.

The present study is one of the early reports on epidemiology of intussusception hospitalizations in post-rotavirus vaccine introduction scenario in India and the first report from Tamil Nadu and Puducherry.

### Conclusion

The present study documents the epidemiology of intussusceptions immediately after the rollout of rotavirus vaccine in Tamil Nadu and Puducherry. Though no appreciable increase in intussusception hospitalizations was seen in the study hospitals after vaccine introduction, continued monitoring of intussusception rates is necessary to monitor safety profiles of the current as well as newer rotavirus vaccines in the national immunization programme.

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Compliance with Ethical Standards

Ethics Approval Ethical clearance has been obtained by each of the
participating institutes from their respective ethical clearance
committees/institute review boards.

Conflict of Interest None.

Consent to participate and Consent for publication Consent for partic-
ipation and for publication and sharing of data have been obtained from
the guardians of each of the participants (cases and controls) prior to
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References

1. World Health Organization. Vaccines and Biologicals: Acute intussus-
ception in infants and children: incidence, clinical representation
and management: a global perspective. Available at: https://vaccine-
safety-training.org/tl_files/vs/pdf/acute-intussusception-
infants-children.pdf. Accessed 20th Jan 2020.
2. Stringer MD, Pablot SM, Brereton RJ. Paediatric intussusception.
Br J Surg. 1992;79:867–76.
3. Clark A, Tate J, Parashar U, et al. Mortality reduction benefits and
intussusception risks of rotavirus vaccination in 135 low-income
and middle-income countries: a modelling analysis of current and
alternative schedules. Lancet Glob Health. 2019;7:e1541-52.
4. Bahl R, Saxena M, Bhandari N, et al. Population-based incidence of intussusception and a
case-control study to examine the association of intussusception with natural rotavirus infection among Indian children. J Infect Dis.
2009;200:5277–81.
5. Gupta M, Kanojia R, Singha R, et al. Intussusception rate among
under-five-children before introduction of rotavirus vaccine in North India. J Trop Pediatr. 2018;64:326–35.
6. World Health Organization. Rotavirus. Available at: https://www.
who.int/immunization/diseases/rotavirus/en/. Accessed 11th
Jan 2020.
7. World Health Organization. Rotavirus vaccines WHO position pa-
paper: January 2013 – recommendations. Vaccine. 2013;31(52):
6170–1 Available at: https://www.who.int/wer/2013/wer8805.
pdf?ua=1. Accessed 11th Jan 2020.
8. Kang G, Desai R, Arora R, et al. Diversity of circulating rotavirus
strains in children hospitalized with diarrhea in India, 2005–2009.
Vaccine. 2013;31:2879–83.
9. Kumar CP, Venkatasubramanian S, Kang G, et al. Profile and
trends of rotavirus gastroenteritis in under 5 children in India,
2012–2014, preliminary report of the Indian national rotavirus sur-
veillance network. Indian Pediatr. 2016;53:619–22.
10. Shri J P Nadda launches Rotavirus vaccine as part of Universal
Immunization Programme; terms it a “historic moment”. Available at: http://pib.nic.in/newsite/PrintRelease.aspx?relid=138342. Accessed 11th Jan 2020.
11. Shri JP Nadda launches expansion of rotavirus vaccine under uni-
iversal immunization Programme. http://pib.nic.in/newsite/
PrintRelease.aspx?relid=158549. Accessed 11th Jan 2020.
12. Reddy S, Nair NP, Giri S, et al. Indian Intussusception Surveillance
Network. Safety monitoring of ROTAVAC vaccine and etiological
investigation of intussusception in India: study protocol. BMC
Public Health. 2018;18:898.
13. Bines JE, Kohl KS, Forster J, et al. Brighton Collaboration
Intussusception Working Group. Acute intussusception in infants
and children as an adverse event following immunization: case
definition and guidelines of data collection, analysis, and presenta-
tion. Vaccine. 2004;22:569–74.
14. Singh JV, Kamath V, Shetty R, et al. Retrospective surveillance for
intussusception in children aged less than five years at two tertiary
care centers in India. Vaccine. 2014;32:A95-8.
15. Bhowmick K, Kang G, Bose A, et al. Retrospective surveillance for
intussusception in children aged less than five years in a South
Indian tertiary-care hospital. J Health PopulNutr. 2009;27:660–5.
16. Mehendale S, Kumar CPg, Venkatasubramanian S, Prasanna T.
Intussusception in children aged less than five years. Indian J
Pediatr. 2016;83:1087–92.
17. Srinivasan R, Girish Kumar CP, Naaraayan SA, et al. Intussusception hospitalizations before rotavirus vaccine introduc-
tion: retrospective data from two referral hospitals in Tamil Nadu,
India. Vaccine. 2018;36:7820–5.
18. Simon NM, Joseph J, Philip RR, Sukumaran TU, Philip R.
Intussusception: single center experience of 10 years. Indian
Pediatr. 2019;56:29–32.
19. Jiang J, Jiang B, Parashar U, Nguyen T, Bines J, Patel MM.
Childhood intussusception: a literature review. PLoSOne. 2013;8:
e68482.
20. National Immunization Schedule (NIS) for Infants, Children and
Pregnant Women. Ministry of Health and Family Welfare,
Government of India. Available at: https://mohfw.gov.in/sites/
default/files/245453521061489663873.pdf. Accessed 14th
Jan 2020.

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