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Impact and effectiveness of pentavalent rotavirus vaccine in children <5 years of age in Burkina Faso☆

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☆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 (CDC) or the World Health Organization (WHO).

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Appendix A
See Appendix Table 1.

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Abstract

Background: Burkina Faso was one of the first African nations to introduce pentavalent rotavirus vaccine (RV5, RotaTeq) into its national immunization program in October 2013. We describe the impact and effectiveness of rotavirus vaccine on acute gastroenteritis (AGE) hospitalizations among Burkinabe children.

Methods: Sentinel hospital-based surveillance for AGE was conducted at four hospitals during December 2013 – February 2017. Demographic, clinical, and vaccination information was collected and stool specimens were tested by EIA. Trends in rotavirus AGE hospitalizations and changes in the proportion of AGE hospitalizations due to rotavirus were examined at two sentinel sites from January 2014 – December 2016. Unconditional logistic regression models using data from all 4 surveillance sites were used to calculate vaccine effectiveness (VE, defined as 1-odds ratio) by comparing the odds of vaccination among rotavirus AGE (cases) and non-rotavirus AGE (controls) patients, controlling for age, season, hospital site and socioeconomic factors.

Results: The proportion of AGE hospitalizations that tested positive for rotavirus declined significantly among children <5 years of age, from 36% (154/422) in 2014 to 22% (71/323, 40% reduction, $p < .01$) in 2015 and 20% (61/298, 44% reduction, $p < .01$) in 2016. Among infants, the percentage of AGE admissions due to rotavirus fell significantly from 38% (94/250) in 2014 to 21% (32/153, 44% reduction, $p < .01$) in 2015 and 17% (26/149, 54% reduction, $p < .01$) in 2016. The adjusted VE for full 3-dose series of RV5 against rotavirus hospitalization was 58% (95% [CI], 10%, 81%) in children 6–11 months of age and 19% (−78%, 63%) in children ≥12 months.

Conclusion: Rotavirus hospitalizations declined after introduction of pentavalent rotavirus vaccine in children, particularly among infants. RV5 significantly protected against severe rotavirus gastroenteritis in infants, but effectiveness decreased in older children.

Keywords

Rotavirus; Acute gastroenteritis; Hospitalization; Burkina Faso; Vaccine effectiveness

1. Introduction

Rotavirus is the leading cause of severe and fatal diarrhea among children <5 years of age globally [1]. Prior to rotavirus vaccine introduction in Burkina Faso, rotavirus gastroenteritis was the leading cause of diarrhea-associated hospitalizations, accounting for 34% of AGE admissions, with peak activity during the dry season, from December to April [2–4]. In 2009, the World Health Organization (WHO) recommended that all countries, particularly

those with high diarrhea mortality rates among children, introduce rotavirus vaccines into their national immunization programs [5].

Two live attenuated oral rotavirus vaccines, a monovalent human vaccine (RV1; Rotarix, GlaxoSmithKline Biologics) and a pentavalent bovine-human reassortant vaccine (RV5; Rotateq, Merck Vaccines), are licensed and available for use in routine childhood immunization programs worldwide [6]. For both vaccines, clinical trials and post licensure evaluations have demonstrated varying performance, with vaccine efficacy ranging from approximately 70–100% in high-and upper-middle-income countries and approximately 50–70% in lower-income settings in Africa and Asia, and vaccine effectiveness demonstrating similar variation depending on setting [7,8]. Reasons for this discrepancy are not fully understood and many factors—such as interference by maternal antibodies, concurrent oral polio vaccine administration, prevalent viral and bacterial gut infections, and malnutrition—might adversely affect the performance of these vaccines among children in low-income settings [9,10]. Despite the lower efficacy and effectiveness of rotavirus vaccines observed in lower income settings, rotavirus vaccines have substantially reduced severe morbidity and mortality in these populations because of the high rotavirus disease burden [11–15].

Only 5 countries in the World Health Organization (WHO) Africa region had introduced RV5 into their national immunization program by 2017 [16,17]. Burkina Faso was one of these countries, introducing RV5 into the routine immunization program, with doses to be given at 2, 3 and 4 months of age, in October 2013. We assessed the impact and effectiveness of RV5 in routine use in Burkina Faso.

2. Methods

2.1. Setting and participants

Burkina Faso is a landlocked country located in the middle of West African countries with a total population of 19,173,317 and an annual birth cohort of 741,830 in 2017 [18]. Routine vaccinations are provided free of charge two times per week in health centres and one time per month in villages located >5 km from the health centres.

In December 2012, active hospital-based AGE surveillance was initiated 24 h per day in the pediatric emergency department (ED) and wards among children <2 years of age at a single hospital, Hôpital du District de Bogodogo (HBD), in Ouagadougou. In December 2013, surveillance was expanded to children <5 years of age and 3 additional hospitals (2 urban hospitals in the capital, Ouagadougou: Centre Hospitalier Yalgado Ouédraogo (CHU-YO), Centre Hospitalier Pédiatrique Charles De Gaulle (CHUP-CDG) and 1 rural hospital in Gaoua, South-Western Region; Centre Hospitalier Régional de Gaoua (CHRG)) initiated surveillance. Surveillance continued at all 4 hospitals through February 2017. Children who were admitted for severe AGE, defined as requiring hospital admission or intravenous fluid rehydration were enrolled. Additionally, nurses and physicians in the wards were encouraged to notify the surveillance coordinator when treating children with diarrhea. The ED and hospital admission log was used to further identify any child presenting with diarrhea with or without vomiting at the sentinel sites. Children identified >48 h after admission were not enrolled because of the risk of including nosocomial infections. AGE

was defined as ≥3 looser-than-normal stools in a 24-h period with or without vomiting occurring for ≤7 days duration upon presentation to the hospital, as per the WHO generic protocol [19].

To assess vaccine effectiveness (VE), a case-control evaluation was performed using a test-negative design [20]. Cases were defined as children with AGE, who were at least 6 months of age and were age-eligible to have received rotavirus vaccine (i.e., born on or after July 1st, 2013), and who had laboratory-confirmed rotavirus infection by enzyme immunoassay. Test-negative controls were similarly aged children with AGE who tested negative for rotavirus infection.

2.2. Data collection

Following parent/guardian consent, demographic, socioeconomic, immunization history and clinical data were obtained. The medical chart was used to obtain height, weight and midarm circumference measures. AGE severity was scored using a modified 20-point Vesikari scale [21]. A photocopy of the child's immunization card was obtained to confirm information on vaccination dates.

2.3. Laboratory testing

Stool specimens were collected within 48 h of admission and stored at 2–8 °C (if tested within one week) or at −20 °C (if tested >1 week) prior to transfer to the national public health reference laboratory, where rotavirus testing was conducted. Specimens were tested using a commercially available enzyme immunoassay (EIA; ProSpecT, Oxoid, Cambridge, United Kingdom). Specimens were stored at −70 °C at the national public health laboratory in Burkina Faso.

2.4. Ethical approval

This study received ethical clearance from the Burkina Faso Ministry of Health. Study personnel obtained informed consent from the parents or legal guardian of the child prior to enrollment.

2.5. Analysis

2.5.1. Vaccine impact—The impact of RV5 was evaluated using two approaches. First, we examined data from sites that consistently reported every month during January 2014–December 2016. Surveillance years were defined as January–December calendar years. Two sites (HBD and CHRG) were included as they did not experience any surveillance interruptions during this period. We calculated the annual proportion of children who tested positive for rotavirus in the baseline (2014) year and each post- vaccine year (2015, 2016), as well as reductions from the baseline in the proportion positive for each post-vaccine year. We used 2014 data for baseline disease burden assessment despite vaccine introduction in October 2013 because surveillance data had not been collected from both sites prior to vaccine introduction and only children <6 months of age would have been vaccine eligible during January–March of the 2014 rotavirus season. Results are reported for all children <5 years and separately, for those <1 year, 1 year and 2–4 years of age.

Second, we examined data from HBD alone, which had ongoing surveillance from December 2012, prior to vaccine introduction. Given that HBD had enrolled only children <2 years of age in the pre-vaccine period, we limited the single site impact analysis to children <2 years. Results are reported for all children <2 years and separately, for those <1 year and 1 year of age. For both analyses, chi-square testing was used to determine statistical significance. P-values < .05 were considered significant.

2.5.2. Vaccine effectiveness—We determined the VE of RV5 against hospitalizations for severe AGE. We calculated the effectiveness of 3-dose, 2-dose, 1-dose and any-dose (defined as 1 or more doses) RV5 as compared to zero doses. Assuming 80% coverage and a 2:1 control:case ratio, we required a sample size of at least 126 cases and 252 controls to detect a VE of 50% with 80% power and a type 1 error rate of 5%.

We included enrolled children who were age-eligible to receive rotavirus vaccination (born on or after 1 July 2013) as part of their routine childhood immunizations at all four surveillance sites. We excluded children from enrollment when we were unable to contact a parent or caretaker to obtain consent and from the analysis when we were unable to verify vaccination status with a copy of the immunization card or vaccination registry. A verified RV5 dose was included if it had been administered ≥14 days before the date of hospitalization for AGE. Bivariate analysis was used to compare characteristics of rotavirus-positive and negative children. Unconditional logistic regression was used to determine the odds ratio (OR) and 95% confidence intervals (CI) for rotavirus vaccination among cases versus controls. RV5 VE was calculated as (1 − odds ratio) × 100%. We adjusted the crude model *a priori* for birth month, birth year, admission month, admission year and site of enrolment. We tested for sociodemographic confounders by including in the initial model all characteristics with $p < .05$ in the bivariate analyses. We then used backwards elimination, removing variables that did not change the VE estimate by >10% of our original estimate, to arrive at the most parsimonious model. Separate multivariable models were used for all children ≥6 months, children aged 6–11 months, children ≥12 months, and by Vesikari score.

3. Results

In our population of enrolled infants age-eligible to receive rotavirus vaccine, 35% received at least 1 dose of RV5 in 2014. This proportion rose to 70% and 76% in 2015 and 2016, respectively.

3.1. Vaccine impact

3.1.1. HBD and CHRG—From January 2014 through December 2016, 1043 children <5 years of age were enrolled and tested in the HBD and CHRG surveillance sites. Of these, 286 (27%) tested positive for rotavirus (Fig. 1a). The number and proportion of rotavirus positive children peaked during January – March of each year with blunted peaks seen in 2015 and 2016. A similar trend was seen among infants and children 1 year of age (Fig. 1b and c), while no decline was noted among 2–4 year olds (Fig. 1d).

The impact of rotavirus vaccination was seen most clearly when data were stratified by specific age groups (Table 1). Among all children <5 years of age, the percentage of hospital admissions positive for rotavirus fell significantly ($p < .001$) from 36% (154/422) in 2014 to 22% (71/323) (40% reduction) in 2015 and 20% (61/298) (44% reduction) in 2016. Both sites, one of which was urban and the other rural, saw significant reductions (data not shown). Among infants, the percentage of AGE admissions for rotavirus fell significantly ($p < .001$) from 38% (94/250) in 2014 to 21% (32/153) (44% reduction) in 2015 and 17% (26/149) (54% reduction) in 2016. Smaller declines in the total number of children enrolled and the number of rotavirus positive and the percentage of rotavirus positive were observed in children 1 year of age. No declines were observed in children 2–4 years of age.

3.1.2. HBD alone—From January 2013–December 2016, 588 children <2 years of age were enrolled and tested in the HBD surveillance site. Of these, 180 (31%) tested positive for rotavirus (Fig. 2). A similar blunting of peaks was seen in the post-vaccine years as was seen in the two site impact analysis. Among all children under 2 years of age, 47% tested positive for rotavirus in the 2013 pre vaccine year, this fell to 13% and 21% in 2015 and 2016, representing declines of 71% and 56% respectively (Table 2). Infants were 51% rotavirus positive in the 2013 pre vaccine year, falling by 75–13% positive in 2015 and falling by 61–20% positive in 2016. Older children did not see as dramatic a decline.

3.2. Vaccine effectiveness

During December 2013 – February 2017, 988 children met the eligibility criteria for inclusion in the VE analysis (Table 3). Of these, 227 (23%) were rotavirus-positive cases and 761 (77%) were rotavirus-negative AGE controls. The median age of cases was 2 months older than controls (12 months vs. 10 months, $p < .005$), and cases weighed slightly more (8.0 kg vs. 7.0 kg, $p < .001$) and were taller (74 cm vs. 72 cm, $p < .001$). Cases were also more often from homes with electricity as compared to controls (64% vs. 50%, $p < .001$). The parents of cases had attained more years of education as compared to controls ($p = .04$ for maternal education, $p = .007$ for paternal education). There was no difference in mother's age, marital status, source of drinking water for the child, or the number of total individuals or children in the child's household between cases and controls (Appendix Table 1). Of these vaccine-eligible children, documented RV5 status (from a vaccine card or clinic record) was available for 204 (96%) of the cases and 678 (95%) of the controls (Table 4). Thirty-nine (19%) cases and 94 (14%) controls had not initiated RV5; while 133 (65%) cases and 488 (72%) controls had completed the full 3-dose series. Apart from a small difference noted for pneumococcal conjugate vaccine (PCV), the groups were similar with regards to vaccination coverage for other standard EPI vaccines.

The adjusted VE for full 3-dose series of RV5 against rotavirus hospitalization was 35% (95% CI: −15%, 63%) among all children 6 months of age and older, and 58% (95% CI: 10%, 81%) in those 6–11 months of age (Table 5). Among the children 12 months and older, VE for 3-doses of RV5 was 19% (95% CI: −78%, 63%). Results for any-dose VE against rotavirus hospitalizations was similar. We stratified the analysis by Vesikari score and found 3-dose VE against hospitalization with severe diarrhea, with a Vesikari score greater than or equal to 15, to be 38% (95% CI: −165%, 86%).

4. Discussion

Introduction of pentavalent rotavirus vaccine demonstrated a significant impact on AGE hospitalizations among children in Burkina Faso. By 2016, two years after RV5 introduction, our analyses demonstrated a 54–61% decline in infants hospitalized for rotavirus gastroenteritis. Additionally, the peaks in the proportion of rotavirus positive children seen during the dry season/months and relatively cool and cold nights of the year decreased in amplitude. The greater declines were consistent with increasing vaccine coverage from 35% in 2014 to 76% in 2016, further implicating rotavirus vaccines as the main driver in this decreased disease burden. The findings outlined in this study are consistent with hospitalization trends documented in Zambia after the introduction of RV1 and Rwanda after introduction of RV5 [22,23]. However, we did not see any evidence of indirect effects among children too old to have been eligible for RV5 during the surveillance period, unlike what has been reported with RV5 use in Rwanda[14]. Reasons for the lack of indirect effects are unknown and should be explored further.

A full course of RV5 was 58% effective in preventing rotavirus hospitalizations among children 6–11 months of age in Burkina Faso. This VE is similar to that for monovalent rotavirus vaccine effectiveness (60%) in Ghana which is a close neighbor of Burkina Faso [24] and in other low-income settings in Africa including Zambia and Botswana [25,26]. However, our VE is lower than that noted for Rwanda, the only other African country with published data on RV5 in routine use, which demonstrated 80% VE for full course RV5 among hospitalized children, and 65% VE among children aged 6–12 months of age, though this latter estimate was not statistically significant [23].

We found reduced vaccine effectiveness among children in the second year of life. Reduced effectiveness in the second year of life was not observed in Rwanda [23], the US [27], or among Bedouin children in Israel [28]. However, decreased vaccine effectiveness and efficacy in the second year of life have been documented in other low-income settings, including in Africa [29]. In the RV5 clinical trials from 3 low-income African settings conducted before routine use, a 64% vaccine efficacy was reported among infants, dropping to 20% in the second year of life [30].

This analysis was subject to several limitations. In our impact analysis, we did not have pre-vaccine data available from all sites as only one site was conducting rotavirus surveillance prior to vaccine introduction and only two sites had uninterrupted surveillance during the study period from January 2014 to December 2016. The use of 2014 as a baseline year when children <6 months of age were eligible for rotavirus vaccine likely biases the observed impact of rotavirus vaccine downward. However, despite this tempering of impact, we were able to observe a significant reduction in rotavirus hospitalizations between 2014 and 2015–2016. Similarly, our single site analysis which included pre-vaccine data from 2013 also demonstrated similar reductions in rotavirus hospitalizations.

5. Conclusions

The introduction of RV5 into the national immunization program of Burkina Faso resulted in significant reductions in rotavirus-gastroenteritis hospitalizations among children in both urban and rural settings. Additionally, a full course of RV5 protected 6–11 month old children against rotavirus hospitalization. Reduced effectiveness may be an issue for protection against these hospitalizations among children 12 months and older. As older children who have received RV5 accumulate, ongoing studies are necessary to further test for factors associated with decreasing effectiveness in our population.

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Appendix Table 1: Sociodemographic and clinical characteristics of children ≥6 months of age and age eligible to receive rotavirus vaccine by rotavirus test result, December 2013 – February 2017.

Sociodemographic characteristics	Rotavirus positive n = 227 (%)	Rotavirus negative n = 761 (%)	p-value
Mother's marital status			0.79
Married	97/216 (45%)	353/744 (47%)	
Single	6/216 (3%)	31/744 (4%)	
Divorced	2/216 (1%)	5/744 (1%)	
Co-habitation	110/216 (51%)	351/744 (47%)	
Widowed	1/216 (1%)	4/744 (1%)	
Source of drinking water in child's household			0.19
Tap to house	104/214 (49%)	312/741 (42%)	
Shared community tap	62/214 (29%)	213/741 (29%)	
Bore hole	41/214 (19%)	165/741 (22%)	
Covered well	1/214 (0.5%)	17/741 (2%)	
Open well	5/214 (2%)	20/741 (3%)	
Lake/river/spring	1/214 (0.5%)	14/741 (2%)	
Median number of people in household (range)	4[g] (1–20)	4[h] (0–30)	0.92
Median number of children in household (range)	1[i] (0–10)	1[j] (0–10)	0.48
Possessions in child's household (% yes)			
Radio	180/216 (83%)	574/739 (78%)	0.07
Television	148/216 (69%)	413/740 (44%)	<0.001
Refrigerator	83/215 (39%)	205/741 (28%)	0.002
Mattress	184/216 (85%)	586/740 (79%)	0.05

Sociodemographic characteristics	Rotavirus positive n = 227 (%)	Rotavirus negative n = 761 (%)	p-value
Mobile phone	210/216 (97%)	706/739 (96%)	0.27
Computer	70/215 (33%)	180/736 (24%)	0.02
Car	47/216 (22%)	131/738 (18%)	0.18
Bicycle	164/215 (76%)	590/740 (77%)	0.27
Motorcycle	190/216 (88%)	612/740 (83%)	0.06
Clinical characteristics			
Duration of diarrhea			0.004
1–4 days	198 (87%)	586 (77%)	
5 days	10 (4%)	67 (9%)	
≥6 days	19 (8%)	108 (14%)	
Max number of diarrhea episodes in 24 h			0.03
0 episodes	16 (7%)	44 (6%)	
1–3 episodes	43 (19%)	90 (12%)	
4–5 episodes	98 (43%)	357 (47%)	
≥6 episodes	70 (31%)	270 (35%)	
If yes, duration of vomiting			0.04
0 days	12 (6%)	31 (6%)	
1 day	65 (32%)	123 (23%)	
2 days	48 (24%)	117 (22%)	
≥3 days	76 (38%)	257 (49%)	
If yes, max number of vomiting episodes in 24 h			<0.001
0 episodes	1 (1%)	0 (0%)	
1 episode	3 (2%)	28 (5%)	
2–4 episodes	86 (43%)	315 (60%)	
≥5 episodes	111 (55%)	185 (35%)	
Fever (% yes)	179/222 (81%)	661/744 (89%)	0.006
Temperature			<0.001
<37 °C	7/227 (3%)	23/761 (3%)	
37–38.5 °C	92/227 (41%)	199/761 (26%)	
38.5-<39 °C	43/227 (19%)	178/761 (23%)	
≥39 °C	85/227 (37%)	361/761 (47%)	
Received ORS before admission (% yes)	67/221 (30%)	193/744 (26%)	0.41
Condition on arrival			0.78
Well, alert	130/221 (59%)	406/739 (55%)	
Restless, irritable	56/221 (25%)	203/739 (27%)	
Lethargic or unconscious	35/221 (16%)	130/739 (18%)	
Sunken eyes (% yes)	65/213 (31%)	219/721 (30%)	0.87
Child’s thirst status at admission			0.83
Drank normally, not thirsty	122/222 (55%)	394/742 (53%)	
Thirsty, drank eagerly	79/222 (36%)	262/742 (35%)	
Drank poorly, not able to drink	21/222 (9%)	86/742 (12%)	

Sociodemographic characteristics	Rotavirus positive n = 227 (%)	Rotavirus negative n = 761 (%)	p-value
Child's skin turgor at admission			0.81
Goes back quickly (immediately)	137/217 (63%)	433/725 (60%)	
Goes back slowly (1–2 s)	60/217 (28%)	213/725 (29%)	
Goes back very slowly (>2 s)	20/217 (9%)	79/725 (11%)	
Received IV fluids during hospital stay (% yes)	139/223 (62%)	516/749 (69%)	0.18
Received ORT during hospital stay (% yes)	184/219 (84%)	584/734 (80%)	0.34
Hospitalized	180/227 (79%)	612/761 (80%)	0.71

[g] n = 212.

[h] n = 731.

[i] n = 222.

[j] n = 73.

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Fig. 1.

(a) Rotavirus testing, CHRG HBD, <5 yo 2014–2016. (b) Rotavirus testing, CHRG HBD, <1 yo 2014–2016. (c) Rotavirus testing, CHRG HBD, 1 yo 2014–2016. (d) Rotavirus testing, CHRG HBD, 2–4 yo 2014–2016.

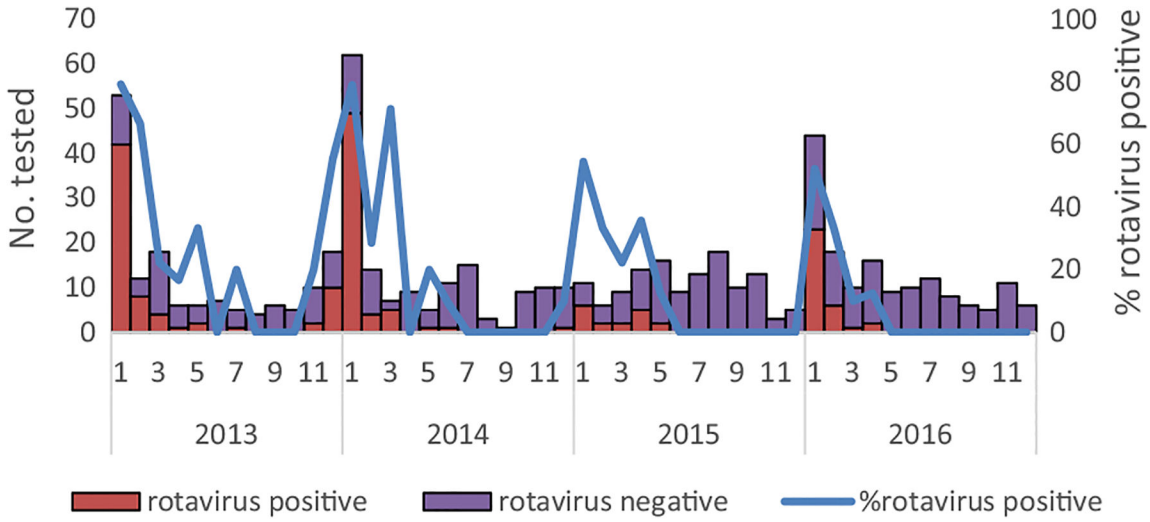

Fig. 2.
Rotavirus positive, negative and % rotavirus positive, all children <2 yrs, HBD 2013–2016.

Table 1

Number and proportion rotavirus positive cases by age and reductions in the number and proportion of rotavirus positive cases, two sites HBD and CHRG, 2014–2016.

Age group	N Total	N Rotavirus positive	% Rotavirus positive	% Reduction in number positive from 2014	% Reduction in %p ositive from 2014	P-value*
2014						
<1 year	250	94	38%	–	Reference	–
1 year	146	57	39%	–	Reference	–
2–4 years	26	3	12%	–	Reference	–
All <5 years	422	154	36%	–	Reference	–
2015						
<1 year	153	32	21%	66%	44%	<.01
1 year	121	33	27%	42%	30%	.04
2–4 years	48	6	13%	−100%	−8%	.9
All <5 years	323	71	22%	54%	40%	<.01
2016						
<1 year	149	26	17%	72%	54%	<.01
1 year	115	26	23%	54%	42%	<.01
2–4 years	32	8	25%	−167%	−117%	.2
All <5 years	298	61	20%	60%	44%	<.01

*P-value is for % reduction in % positive compared to the 2014 reference year.

Table 2

Number and proportion rotavirus positive cases by age and reductions in the number and proportion of rotavirus positive cases, one site HBD, 2013–2016.

Age group	N total	N Rotavirus positive	% Rotavirus positive	% Reduction in number positive from 2013	% Reduction in % positive from 2013	P-value*
2013						
<1 year	121	62	51%	–	Reference	–
1 year	29	8	28%	–	Reference	–
All <2 years	150	70	47%	–	Reference	–
2014						
<1year	97	35	36%	44%	30%	.03
1 year	59	26	44%	−225%	−60%	.1
All <2 years	156	61	39%	13%	16%	.2
2015						
<1year	77	10	13%	84%	75%	<.01
1 year	50	7	14%	13%	49%	.1
All <2 years	127	17	13%	76%	71%	<.01
2016						
<1year	95	19	20%	69%	61%	<.01
1 year	60	13	22%	−63%	21%	.5
All <2 years	155	32	21%	54%	56%	<.01

*P-value is for % reduction in % positive compared to the 2013 reference year.

Table 3

Sociodemographic and clinical characteristics of children ≥6 months of age and age eligible to receive rotavirus vaccine by rotavirus test result, December 2013 – February 2017 (N = 988).

Sociodemographic characteristics	**Rotavirus positive n = 227 (%)**	**Rotavirus negative n = 761 (%)**	**p-value**
Median age in months (range)	12 (6–28)	10 (6–40)	.005
Male	138 (61%)	437 (57%)	.37
Median weight (in kg) (range)	8.0 (0.02–87.0)	7.0 (0–98.0)	<.001
Median height (in cm) (range)	74 (50–92)[a]	72 (12–735)[b]	<.001
Median mid arm circumference (in cm) (range)	13.0 (0.03–18.0)[c]	13.0 (0–40.0)[d]	.01
Chronic medical condition (% yes)	7/215 (3%)	40/719 (6%)	.40
Median maternal age (range)	28 (16–45)[e]	26 (14–55)[f]	.05
Mother's education			.04
None	70/216 (32%)	326/742 (44%)	
Primary	47/216 (22%)	149/742 (20%)	
Secondary	56/216 (26%)	152/742 (21%)	
Post-secondary	18/216 (8%)	47/742 (6%)	
University or above	25/216 (12%)	68/742 (9%)	
Father's education			.007
None	65/216 (30%)	309/740 (42%)	
Primary	42/216 (19%)	129/740 (17%)	
Secondary	44/216 (20%)	133/740 (18%)	
Post-secondary	26/216 (12%)	47/740 (6%)	
University or above	39/216 (18%)	122/740 (16%)	
Child lives in house with electricity (% yes)	135/212 (64%)	370/738 (50%)	<.001
Clinical characteristics			
Diarrhea (% yes)	227 (100%)	760 (99.9%)	
Vomiting (% yes)	201/226 (89%)	528/749 (70%)	<.001
Vesikari score			0.03
≤10 (mild)	61/227 (27%)	245/761 (32%)	
11–14 (moderate)	124/227 (55%)	338/761 (44%)	

Sociodemographic characteristics	Rotavirus positive n = 227 (%)	Rotavirus negative n = 761 (%)	p-value
≥15 (severe)	42/227 (19%)	178/761 (23%)	

[a] n = 209.

[b] n = 694.

[c] n = 189.

[d] n = 598.

[e] n = 203.

[f] n = 704.

Table 4

Vaccine coverage of children ≥6 months of age and age eligible to receive rotavirus vaccine by rotavirus test result, November 2013 – February 2017.

	Rotavirus positive n = 227 (%)	**Rotavirus negative n = 761 (%)**	**p-value**
Verified vaccination Status			.74
Card	204 (90%)	678 (89%)	
Not verified/verbal	23 (10%)	83 (11%)	
Coverage among children with verified vaccination status			
	n = 204	n = 678	
Rotavirus vaccine			.17
0 Doses	39 (19%)	94 (14%)	
1 Dose	9 (4%)	29 (4%)	
2 Doses	22 (11%)	56 (8%)	
3 Doses	133 (66%)	488 (73%)	
Missing	1	11	
Pentavalent vaccine *			.97
0 Doses	6 (3%)	18 (3%)	
1 Dose	4 (2%)	13 (2%)	
2 Doses	8 (4%)	31 (5%)	
3 Doses	168 (90%)	543 (90%)	
Missing	18	73	
Oral polio vaccine (Birth dose)	182 (99%)	624 (98%)	.34
Missing	20	40	
Oral polio vaccine			.62
0 Doses	2 (1%)	5 (1%)	
1 Dose	8 (4%)	15 (3%)	
2 Doses	9 (5%)	23 (4%)	
3 Doses	174 (90%)	555 (93%)	
Missing	11	80	
Pneumococcal vaccine			.03
0 Doses	14 (8%)	49 (8%)	
1 Dose	8 (5%)	29 (5%)	

	Rotavirus positive n = 227 (%)	Rotavirus negative n = 761 (%)	p-value
2 Doses	23 (13%)	37 (6%)	
3 Doses	130 (74%)	476 (81%)	
Missing	29	87	
Measles vaccine	123 (68%)	341 (61%)	.09
Missing	22	116	

*Pentavalent vaccine is a combination vaccine against diphtheria, pertussis, tetanus (DTP), hepatitis B and Haemophilus influenzae type B (Hib).

Table 5

Rotavirus vaccine effectiveness among children ≥6 months of age and age eligible to receive rotavirus vaccine by rotavirus test result, November 2013 – February 2017.

	Rota+ n = 203 (%)	Rota− N = 667 (%)	Unadjusted VE (95% CI)	Adjusted VE[a] (95% CI)
All children ≥ 6 months				
0 doses	39 (19%)	94 (14%)	Ref.	Ref.
1 dose	9 (4%)	29 (4%)	25% (−73%, 68%)	36% (−73%, 76%)
2 doses	22 (11%)	56 (8%)	5 (−76%, 49%)	−16% (−148%, 45%)
3 doses	133 (66%)	488 (73%)	34% (0%, 57%)	35% (−15%, 63%)
Any dose	164 (81%)	573 (86%)	31% (−4%, 54%)	27% (−24%, 57%)
Children ≥6 and <12 months				
0 doses	23 (23%)	57 (13%)	Ref.	Ref.
1 dose	5 (5%)	21 (5%)	41% (−75%, 80%)	59% (−50%, 89%)
2 doses	11 (11%)	39 (9%)	30% (−60%, 69%)	−5% (−192%, 62%)
3 doses	59 (60%)	323 (73%)	55% (21%, 74%)	58% (10%, 81%)
Any dose	75 (77%)	383 (87%)	52% (16%, 72%)	50% (−3%, 76%)
Children ≥12 months				
0 doses	20 (17%)	44 (16%)	Ref.	Ref.
1 dose	5 (4%)	9 (3%)	−22% (−312%, 64%)	−7% (−370%, 76%)
2 doses	11 (10%)	22 (8%)	−10% (−170%, 55%)	−6% (−219%, 65%)
3 doses	79 (69%)	207 (73%)	16% (−51%, 53%)	19% (−78%, 63%)
Any dose	95 (83%)	238 (84%)	12% (−57%, 51%)	13% (−85%, 59%)
Children with Vesikari ≥11				
0 doses	30 (20%)	60 (13%)	Ref.	Ref.
1 dose	8 (5%)	22 (5%)	27% (−83%, 71%)	39% (−81%, 79%)
2 doses	14 (9%)	41 (9%)	32% (−44%, 68%)	13% (−115%, 65%)
3 doses	101 (66%)	331 (73%)	39% (0%, 63%)	39% (−18%, 68%)
Any dose	123 (80%)	394 (87%)	38% (−1%, 62%)	35% (−22%, 65%)
Children with Vesikari ≥15				
0 doses	8 (22%)	19 (12%)	Ref.	Ref.
1 dose	2 (6%)	6 (4%)	21% (−379%, 87%)	38% (−482%, 94%)

	Rota+ n = 203 (%)	Rota− N = 667 (%)	Unadjusted VE (95% CI)	Adjusted VE[a] (95% CI)
2 doses	5 (14%)	15 (10%)	21% (−192%, 79%)	−13% (−492%, 79%)
3 doses	21 (58%)	113 (74%)	56% (−14%, 83%)	38% (−165%, 86%)
Any dose	28 (78%)	134 (88%)	50% (−25%, 80%)	37% (−177%, 81%)

[a] Adjusted for month and year of birth, month and year of admission, and whether the child's household has electricity.