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Impact of rotavirus vaccine on acute gastroenteritis in children under 5 years in Senegal: Experience of sentinel site of the Albert Royer Children’s Hospital in Dakar

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Abstract

Background—Acute gastroenteritis (AGE) is a leading cause of morbidity and mortality among children <5 years of age in developing countries, with rotavirus being the most common infectious etiology. In November 2014, monovalent rotavirus vaccine was introduced in Senegal. We determined the impact of rotavirus vaccine on hospitalizations for all-cause and rotavirus related AGE in children <60 months of age.

Methods—We examined two data sources from the national referral hospital. Using sentinel surveillance data from March 2011 to February 2017, we examined the proportion of AGE hospitalizations among children <60 months of age attributable to rotavirus, stratified by age groups (0–11, 12–23 and 24–59 months). Using pediatric logbook data from March 2010 to February 2017, we examined the proportion of all childhood hospitalizations attributable to AGE, among the same age groups.

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Potential conflicts of interest

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Results—In sentinel surveillance, 673 patients <60 months were hospitalized for AGE, with 30% (203/673) due to rotavirus. In pre-vaccine years, the median proportion of rotavirus-positive hospitalizations was 42%; this proportion declined by 76% to 10% rotavirus positive in 2015–2016 ($p < .001$) and by 59% to 17% in 2016–2017 ($p < .001$). From the logbook data, among all children <60 months, a median of 11% of all hospitalizations in the pre-vaccine period were due to AGE, with 2015–2016 seeing a 16% decline ($p < .001$), to 9% of all hospitalizations, and 2016–2017 seeing a 39% decline ($p < .001$), to 7% of all hospitalizations. Declines in both rotavirus-associated and all-cause AGE hospitalizations were most marked among infants, with a suggestion of herd effect among older children seen in the surveillance data.

Conclusion—Rotavirus vaccine demonstrated a significant impact on rotavirus-associated hospitalizations and all-cause AGE hospitalizations in the first two seasons after vaccine introduction in Senegal. Our data support the continued use of this vaccine in national immunization program.

Keywords

Acute gastroenteritis; Rotavirus; Monovalent rotavirus vaccine; Senegal

1. Introduction

Acute gastroenteritis (AGE) is one of the leading causes of morbidity and mortality among children under 5 years of age in developing countries, with rotavirus as the most common etiology [1]. Complications of AGE include electrolyte disorders and malnutrition, often necessitating hospitalization. In November 2014, the Senegalese Ministry of Health and Social Action, with assistance from Gavi, the Vaccine Alliance, introduced the 2-dose monovalent rotavirus vaccine, RV1 (Rotarix, GlaxoSmithKline Biologicals), in the national immunization program. RV1 is administered to children at 6 and 10 weeks of age. The vaccine effectiveness (VE) of RV1 against hospitalization for rotavirus diarrhea in the African setting is 57–60% [2–4], which is lower than the >90% described in more developed settings [5,6]. Despite this lower VE, data demonstrating the impact of rotavirus vaccines in reducing the burden of diarrheal disease are starting to emerge from African countries [7,8]. The purpose of this evaluation is to examine the impact of rotavirus vaccine on AGE and rotavirus hospitalizations in children under 60 months of age in Senegal.

2. Methods

We evaluated children under 60 months of age admitted to the National Children’s Hospital of Albert Royer (Centre Hospitalier National d’Enfants Albert Royer, CHNEAR) in Dakar, Senegal before and after vaccine introduction. CHNEAR is a national and sub-regional tertiary referral centre as well as a sentinel site for rotavirus surveillance since 2011. We used data derived from two sources: active surveillance for rotavirus in children hospitalized with AGE and AGE hospitalization data from pediatric ward logbooks. Surveillance years were defined as March of one year through February of the following year. Given that vaccine introduction occurred in November 2014, March 2014–February 2015 was considered a transitional period, and not considered in the analysis.

2.1. Surveillance data

Using the standard World Health Organization (WHO) rotavirus surveillance protocol [9], we prospectively enrolled children under 60 months of age meeting the case definition for AGE from March 2011 to February 2017. AGE is defined as three or more watery stools per 24 h period, lasting for a period of 7 days or less. Upon enrolment into sentinel rotavirus surveillance, parental consent was obtained, a questionnaire was administered to obtain demographic and clinical information, and 5–10 g of stool was collected and transported to the CHNEAR laboratory for analysis. This analysis was conducted within the routine public health surveillance system in Senegal. Detection of group A rotaviruses was performed by ELISA (ProSpect Rotavirus, OXOID).

2.2. Pediatric ward logbook data

We conducted a retrospective review of children under 60 months of age hospitalized with AGE in the four pediatric wards of CHNEAR during March 2010 – February 2017. For March – November 2010, one ward register was missing, and individual medical charts were obtained from the hospital archives and abstracted for this period. AGE was defined as any discharge diagnosis that included one of the following key words: gastroenteritis, AGE, enteritis, or diarrhea. We excluded chronic diarrhea, bloody diarrhea, dysentery and related diagnoses. In the instances where discharge diagnosis was missing, we used the admission diagnosis. We attempted to use toxic ingestions as a control condition to demonstrate stability of hospitalizations over time, however these data were sparse and were not suitable for analysis and are not included.

3. Analysis

3.1. Surveillance data

Using the sentinel site surveillance data, we compared the proportion of rotavirus-associated AGE before and after the introduction of rotavirus vaccine. The pre-vaccine period was defined as March 2011 – February 2014, while the post vaccine period spanned March 2015 – February 2017. Data were stratified by the following age groups: 0–11 months, 12–23 months and 24–59 months. We also calculated the percent reduction in the proportion of rotavirus positive tests in post vaccine periods, compared to the median for the pre-vaccine period. Fisher's exact testing was used to determine the statistical significance of the changes in proportion rotavirus positivity before and after vaccine introduction.

3.2. Pediatric ward logbook data

Using the pediatric ward logbook data, we tallied the number of all-cause hospitalizations and AGE hospitalizations among children <60 months of age. We calculated the proportion of all-cause hospitalizations due to AGE by year stratified by the same age groups as the surveillance data. We also calculated the percent reduction in the proportion of AGE-hospitalizations. We used Fisher's exact test to determine statistical significance in the change in the proportion of all-cause hospitalizations due to AGE before and after rotavirus vaccine introduction. The pre-vaccine period was defined as March 2010 – February 2014, while the post vaccine period spanned March 2015 – February 2017.

P-values < .05 were considered statistically significant. Data were entered and analyzed using Epi Info 3.5.4, SAS 9.4, and Microsoft Excel.

4. Results

4.1. Surveillance data

Over the entire surveillance period from March 2011 to February 2017, 673 patients met the case definition for AGE, were enrolled, and of which, 30% (203/673) tested positive for rotavirus. The median age of patients was 10 months (IQR: 25% 4, 75% 21), and 57% (386/673) were male. Infants < 12 months of age accounted for 60% (121/203) of all rotavirus positive hospitalizations. Rotavirus-positive cases peaked in January, with post-vaccine introduction years maintaining this seasonality, though with a blunted peak (Fig. 1).

In the pre-vaccine years, among all children < 60 month olds, the median number of all-cause AGE hospitalizations was 106 per year, with a median of 44 (41.5%) being rotavirus-positive. This fell significantly to 9.8% rotavirus-positive in the 2015–2016 surveillance year, representing a 76.3% reduction ($p < .01$) in rotavirus-associated hospitalizations as compared to the pre-vaccine period, and subsequently, to 17.0% in the 2016–2017 surveillance year, representing a 59.0% reduction ($p < .01$) (Table 1).

We also stratified the analysis by age groups, and saw reductions in rotavirus associated hospitalizations across all ages (Table 1, Fig. 2a–d). In the pre-vaccine years, the median proportion of rotavirus positive hospitalizations was 44.3% among 0–11 month olds, 48.1% among 12–23 month olds and 23.8% among 24–59 month olds. After vaccine introduction, in 2015–2016, among 0–11 month olds, there was an 81.5% reduction ($p < .01$) compared to pre-vaccine years, followed by a 45.0% reduction ($p < .01$) in 2016–2017. Among 12–23 month olds, there was a 68.5% reduction ($p < .01$) in 2015–2016, compared to the pre-vaccine period and a 73.2% reduction ($p < .01$) in 2016–2017. The 24–59 month olds also saw declines, with a 70% reduction ($p = .12$) in 2015–2016 compared to pre-vaccine years, and a 55% decline ($p = 0.25$) in 2016–2017 (Fig. 2a–d).

4.2. Pediatric ward logbook data

Among all children < 60 months, a median of 12.9% of all hospitalizations in the pre-vaccine period were due to AGE, with 2015–2016 seeing a 29.8% decline ($p < .01$), to 9.1% of all hospitalizations, and 2016–2017 seeing a 39.2% decline ($p < .01$), to 7.9% of all hospitalizations (Table 2). The infant age group saw significant reductions ($p < .01$) in the proportion of AGE admissions, falling from a median of 12.4% for the pre-vaccine years to 8.0% and 6.3% in the following post vaccine years, respectively, representing declines of 35.6% ($p < .01$) and 48.7% ($p < .01$), respectively. Significant reductions were not seen among the older age groups.

In terms of seasonality, peaks in AGE hospitalizations were recorded in January and February among all age groups (Fig. 3a–d). After vaccine introduction this seasonality was maintained, though winter peaks were blunted.

5. Discussion

Laboratory-diagnosed rotavirus AGE hospitalizations and all-cause AGE-hospitalizations, particularly among younger children, substantially declined following rotavirus vaccine introduction in Senegal. Rotavirus vaccine was introduced in November 2014, and rapidly reached 89% 2-dose coverage by the end of 2015, and 83% by 2016 [10]. We are unaware of any other nationally implemented interventions to target diarrheal diseases that occurred simultaneously. Infants were the first to benefit from vaccine. The 45–82% reductions in the proportion of AGE hospitalizations due to rotavirus that were observed in the post-vaccine years in this age group reflect this high reported coverage and that this age group had the greatest burden of rotavirus disease accounting for 60% of all rotavirus hospitalizations prior to vaccine introduction. Among 12–23 year olds, who also had opportunity for vaccination by the 2015–2016 season, sustained declines in rotavirus positivity were also seen in the sentinel site surveillance data.

A suggestion of herd immunity was gleaned through our data. Older children 24–59 months of age did not have the opportunity to receive rotavirus vaccine, as they were too old for rotavirus vaccine routine administration, and no catch-up program exists. This age group also witnessed 55–70% declines in the proportion rotavirus positive, possibly indicating indirect or herd-effects of the infant immunization program. Findings reported from other sub-Saharan African countries, have shown significant declines of 33–51% in the proportion of rotavirus-positive hospitalizations were seen in infants, but not older children, in the first post-vaccine seasons [7,8,11]. These data are reported from countries who, like Senegal, introduced rotavirus vaccine in 2013 or later. Data from Rwanda, where vaccine was introduced in 2012, demonstrated herd protection of children both too young and too old to have received vaccine [12]. As surveillance continues, and vaccine coverage includes children in the older age group, we anticipate seeing similar effects in our population in the coming years.

This analysis was subject to several limitations. Using retrospective logbook data is inherently imprecise, and, while we distinguished AGE from bloody, chronic and dysentery-related diarrhea, we were unable to distinguish hospital-acquired diarrhea from AGE as this information was not documented in the ward registers. While using admission diagnoses would have overcome this obstacle, discharge diagnoses provide more precise estimates of AGE, as admission diagnoses often include lists of symptoms rather than a diagnosis, which is often available only after diagnostic work-up during the course of hospitalization. Another limitation of this analysis is that we were unable to identify a suitable control condition with enough data to analyze trends over time, as a reliable diagnosis with adequate data could not be identified. Finally, the few number of post-vaccine introduction seasons limited interpretation of this data. It is too early to determine what the longer-term impact of rotavirus vaccine will be in Senegal. Though we saw significant annual reductions in all age groups in the rotavirus positive hospitalizations, there was a slight increase in the proportion of rotavirus positive hospitalizations in the surveillance data during the March 2016 to February 2017 rotavirus season, and it is too soon to tell if these are reflective of an emerging biennial seasonal pattern as that seen elsewhere [13]. Two one month interruptions in surveillance occurred in May 2011 in the pre-vaccine period and October 2015 in the

post-vaccine period. While interruptions in surveillance can make the analysis of trends challenging, these interruptions were brief and limited to non-rotavirus seasons, and therefore minimally impacted our findings.

6. Conclusion

Childhood diarrhea remains a public health problem with significant morbidity and mortality. The post-vaccine introduction decrease in the proportion AGE hospitalizations attributed to rotavirus, accompanied by the decrease in total hospitalizations due to all-cause AGE over the same period likely reflects the impact of rotavirus vaccine on the main cause of infectious diarrhea in children under 5 years of age in Senegal. Vaccination against rotavirus is an effective means of preventing severe forms of rotavirus AGE and our findings support the continued use of rotavirus vaccine as well as continued surveillance to demonstrate the longer term impact of rotavirus vaccine in Senegalese children.

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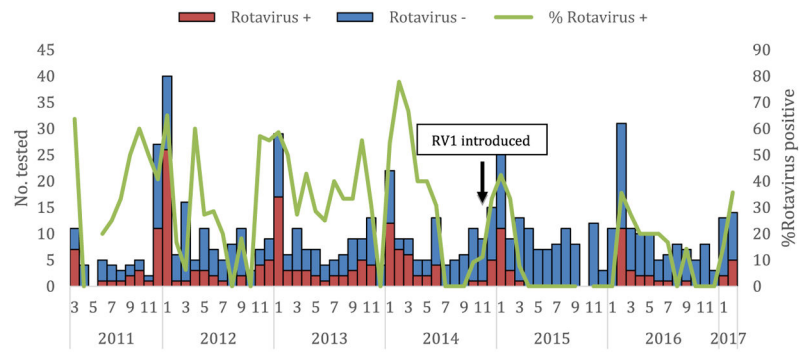


Fig. 1. Trends in rotavirus testing and positivity, children <60 months, Centre Hospitalier National d’Enfants Albert Royer –2011–2017. *Surveillance year defined as March of one year to February of the following year; RV1 introduced November 2014; surveillance interrupted in May of 2011–2012 surveillance year and October of 2015–2016 surveillance year.

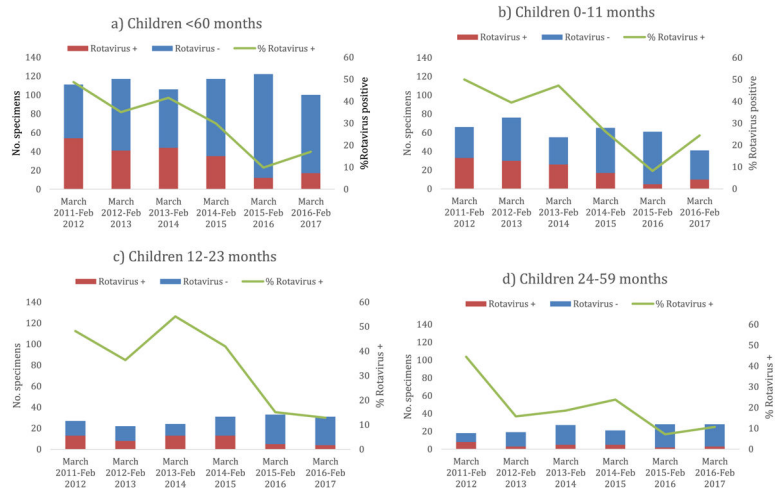


Fig. 2. (a–d) Annual hospitalizations for all-cause and rotavirus-associated AGE in children <60 months by age group, Centre Hospitalier National d’Enfants Albert Royer –2011–2017. *Surveillance year defined as March of one year to February of the following year; RV1 introduced November 2014; surveillance interrupted in May 2011 and October 2015. March 2014–February 2015 considered transitional year and excluded from pre/post vaccine introduction analyzes.

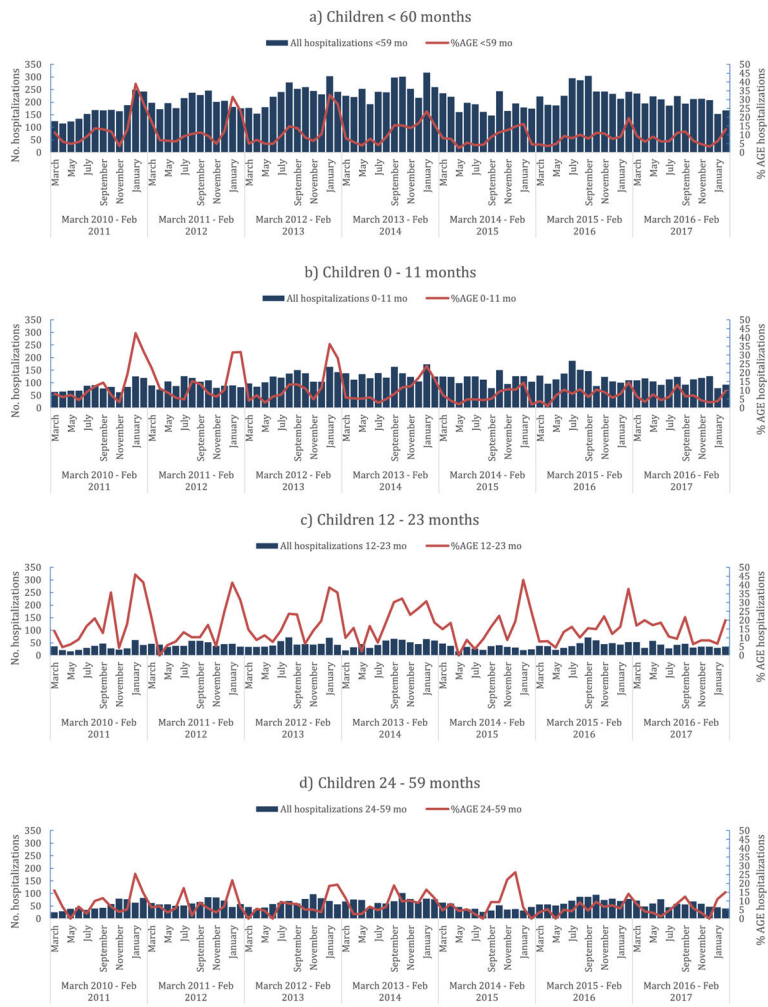


Fig. 3. (a–d) All cause hospitalizations and AGE hospitalizations among children by age group, Centre Hospitalier National d’Enfants Albert Royer, 2011–2017.

Table 1

Rotavirus positive, percent rotavirus positive and reductions in rotavirus positivity by surveillance period, children <60 months, Centre Hospitalier National d'Enfants Albert Royer, Senegal– 2011–2017.

| Surveillance period ^a | No. rotavirus positive/total (%rotavirus positive) | % Reduction rotavirus positive | % Reduction % rotavirus positive | p-value ^b |
|----------------------------------|--|--------------------------------|----------------------------------|----------------------|
| <i>All <60 months</i> | | | | |
| Median 2011–2014 | 44/106 (41.5%) | Reference | Reference | – |
| March 2015–February 2016 | 12/122 (9.8%) | 72.7 | 76.3 | <0.01 |
| March 2016–February 2017 | 17/100 (17.0%) | 61.4 | 59.0 | <0.01 |
| <i>0–11 months</i> | | | | |
| Median 2011–2014 | 31.5/71 (44.3%) | Reference | Reference | – |
| March 2015–February 2016 | 5/61 (8.2%) | 84.1 | 81.5 | <0.01 |
| March 2016–February 2017 | 10/41 (24.4%) | 68.3 | 45.0 | 0.03 |
| <i>12–23 months</i> | | | | |
| Median 2011–2014 | 13/27 (48.1%) | Reference | Reference | – |
| March 2015–February 2016 | 5/33 (15.2%) | 61.5 | 68.5 | <0.01 |
| March 2016–February 2017 | 4/31 (12.9%) | 69.2 | 73.2 | <0.01 |
| <i>24–59 months</i> | | | | |
| Median 2011–2014 | 5/21 (23.8%) | Reference | Reference | – |
| March 2015–February 2016 | 2/28 (7.1%) | 60.0 | 70.0 | 0.12 |
| March 2016–February 2017 | 3/28 (10.7%) | 40.0 | 55.0 | 0.25 |

^aSurveillance year defined as March of one year to February of the following year; surveillance interrupted in May 2011 and October 2015; March 2014–February 2015 considered transitional year and excluded from analyzes. RV1 introduced November 2014.

^bp-value is for % Reduction in % rotavirus positive.

Table 2

Acute gastroenteritis hospitalizations and percent acute gastroenteritis hospitalizations and reductions by surveillance period, children <60 months, Centre Hospitalier National d'Enfants Albert Royer, Senegal–2011–2017.

| Surveillance period ^a | No. AGE ^b /total (% AGE) | % reduction no. AGE | % reduction % AGE | P-value ^c |
|----------------------------------|-------------------------------------|---------------------|-------------------|----------------------|
| <i>All <60 months</i> | | | | |
| Median 2010–2014 | 336.5/2606 (12.9%) | Reference | Reference | – |
| March 2015–February 2016 | 261/2880 (9.1%) | 22.4 | 29.8 | <0.01 |
| March 2016–February 2017 | 190/2420 (7.9%) | 43.5 | 39.2 | <0.01 |
| <i>0–11 months</i> | | | | |
| Median 2010–2014 | 161.5/1306 (12.4%) | Reference | Reference | – |
| March 2015–February 2016 | 118/1482 (8.0%) | 26.9 | 35.6 | <0.01 |
| March 2016–February 2017 | 81/1278 (6.3%) | 49.8 | 48.7 | <0.01 |
| <i>12–23 months</i> | | | | |
| Median 2010–2014 | 99.5/545.5 (18.2%) | Reference | Reference | – |
| March 2015–February 2016 | 85/534 (15.9%) | 1.2 | 12.7 | 0.29 |
| March 2016–February 2017 | 67/466 (14.4%) | 32.7 | 21.2 | 0.09 |
| <i>24–59 months</i> | | | | |
| Median 2010–2014 | 58/755 (7.7%) | Reference | Reference | – |
| March 2015–February 2016 | 58/864 (6.7%) | 0 | 12.6 | 0.45 |
| March 2016–February 2017 | 42/676 (6.2%) | 27.6 | 19.1 | 0.28 |

^aSurveillance year defined as March of one year to February of the following year; March 2014–February 2015 considered transitional year and excluded from analyses. RV1 introduced November 2014.

^bAcute gastroenteritis.

^cp-value is for % reduction in %AGE.