

## Research Article

# Sustained Impact of Rotavirus Vaccine on Childhood Acute Gastroenteritis Hospitalization in Togo

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## Keywords

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## Abstract

**Background:** Monovalent rotavirus vaccine (Rotarix), was introduced in the immunization schedule of Togo in June 2014. We evaluated the sustained impact of the vaccine on acute gastroenteritis (AGE), and rotavirus-associated hospitalizations in Togolese children.

**Methods:** Sentinel surveillance for AGE hospitalizations among children <5 years of age was conducted in two sites in the capital city, Lome. ELISA was used for diagnosis of rotavirus infection in children with AGE. For the vaccine impact analysis, the pre-vaccine period was defined as July 2010-June 2014 and the post-vaccine period was July 2014-June 2018.

**Results:** During the pre-vaccine period, sentinel surveillance showed that 1,017 patients were enrolled and 57% (range, 53%-62%), tested positive for rotavirus, declining to an annual median of 34% (range, 26 - 42%), in the post-vaccine years. The median reduction was 38% (range, 24 - 53%). Declines were most marked among infants

**Conclusions:** We report sustained reduction in the number of AGE hospitalizations and the proportion of AGE hospitalizations attributable to rotavirus in the first four years post- Rotarix implementation in Togo. It is necessary to monitor long-term vaccine impact on death and change in rotavirus strains through continued surveillance.

## INTRODUCTION

Diarrhea was responsible for 11% of deaths among children <5 years of age worldwide [1]. Globally, rotavirus is the leading cause of severe acute gastroenteritis (AGE), in infants and young children, and the mortality is particularly high in sub-Saharan Africa. Of the 215 000 global childhood deaths from rotavirus disease, 121 000 occur in sub-Saharan Africa [2]. Licensed vaccines against rotavirus have been available since 2006 worldwide, and have been recommended by the World Health Organization (WHO), for incorporation into routine immunization programs since 2009 [3,4]. These vaccines have been shown to be effective both in developed and developing countries [5-8]. Many countries in sub-Saharan Africa, including Togo, have introduced rotavirus vaccines in their routine immunization schedule [9-13]. Togo introduced monovalent rotavirus vaccine (RV1), Rotarix<sup>®</sup>

in June 2014. The availability of baseline data on rotavirus gastroenteritis disease in Togo prior to RV1 introduction enables the early impact of the vaccine to be examined [14-16]. Previous reports demonstrated evidence vaccine impact observed through significant reduction in rotavirus-associated hospitalizations [15,16]. To evaluate long term vaccine impact, we compared all-cause acute gastroenteritis (AGE), hospitalizations and rotavirus-associated hospitalizations during the pre- and post-vaccine periods from the routine sentinel surveillance system.

## METHODS

Since February 2008, sentinel active surveillance for AGE and rotavirus-associated hospitalizations among children <5 years of age has been conducted in two sites in the capital city, Lome (Sylvanus Olympio Teaching Hospital and Be Hospital), using the World Health Organization (WHO), generic protocol [17].

Children aged <5 years, who were examined at the emergency department for AGE (defined as  $\geq 3$  liquid or semi-liquid stools/24 hours lasting <7 days), were included. After written parental consent was granted, a stool sample was collected. An ELISA (Enzyme Linked Immunosorbent Assay; IDEIA™ Rotavirus OXOID), was used for diagnosis of rotavirus infection according to the manufacturer's specifications. Batch testing was conducted monthly at the sentinel laboratory of Sylvanus Olympio Teaching Hospital.

For the vaccine impact analysis, we considered the period from July 2010-June 2014 as the pre-vaccine period and July 2014-June 2018 as the post-vaccine period. Data analysis was stratified by age-group: all children <5 years, <1 year and 1-4 years. To determine reductions in rotavirus-associated hospitalizations during four post-vaccine years, we compared the median annual proportion of rotavirus-associated hospitalizations in post-vaccine years to the median annual proportion of rotavirus-associated hospitalizations in four years pre-vaccine period. Statistical analysis was performed by Epi info.  $\chi^2$  test was used to compare some variables. A value mid-P exact <0.05 was significant.

## RESULTS

During the 4-year pre-vaccine period from July 2010 to June 2014, 1,017 children <5 years of age with AGE were enrolled, of whom 578 (57%), were positive for rotavirus. The median annual numbers of AGE and rotavirus-associated hospitalizations were 258 and 142 respectively; and the proportion of AGE hospitalizations attributable to rotavirus ranged from 53% to 62% (median 55%). In the 4-year post-vaccine period from July 2014 to June 2018, a total number of 680 cases with AGE were enrolled among children <5 years of age and 239 (35%), cases were positive for rotavirus (Figure 1A). The median annual proportion of rotavirus positive cases was 34% (range, 26-42%). Compared with the median annual proportion of rotavirus positive cases in the pre-vaccine years, this reflects a median reduction of 38% (range, 24-53%), in the proportion of rotavirus positive cases during the post-vaccine period (mid-P exact <0.001).

Among infants <1 year of age, the proportion of rotavirus-positive hospitalizations declined by a median of 51% during the post-vaccine introduction years compared with the median in pre-vaccine years (Figure 1B, Mid-P exact <0.001). A median decline of 40% was observed among children in the 1-4 year age-group during the post-vaccine years compared with the median in pre-vaccine years (Figure 1C, mid-P exact <0.001).

During the pre-vaccine period, the majority of AGE cases (71%), were observed during the period from November to March and 73% of rotavirus-associated hospitalizations occurred in these months (Figure 2A). Among all children <5 years, a 43% reduction in rotavirus-positive hospitalizations was observed during both the first and the second post-vaccine introduction rotavirus seasons from November to March compared with the median proportion during pre-vaccine November to March

rotavirus seasons. Again, reductions (59%), during the rotavirus season in the first post-vaccine year were most marked among infants aged <1 year, than 1-4 year old children (28%). Reductions during the rotavirus season in the second post-vaccine year were observed among both infants aged <1 year (45%), and 1-4 year children (40%, Figure 2B, C). In the third and fourth years post vaccine introduction the peak of rotavirus season disappeared.

## DISCUSSION

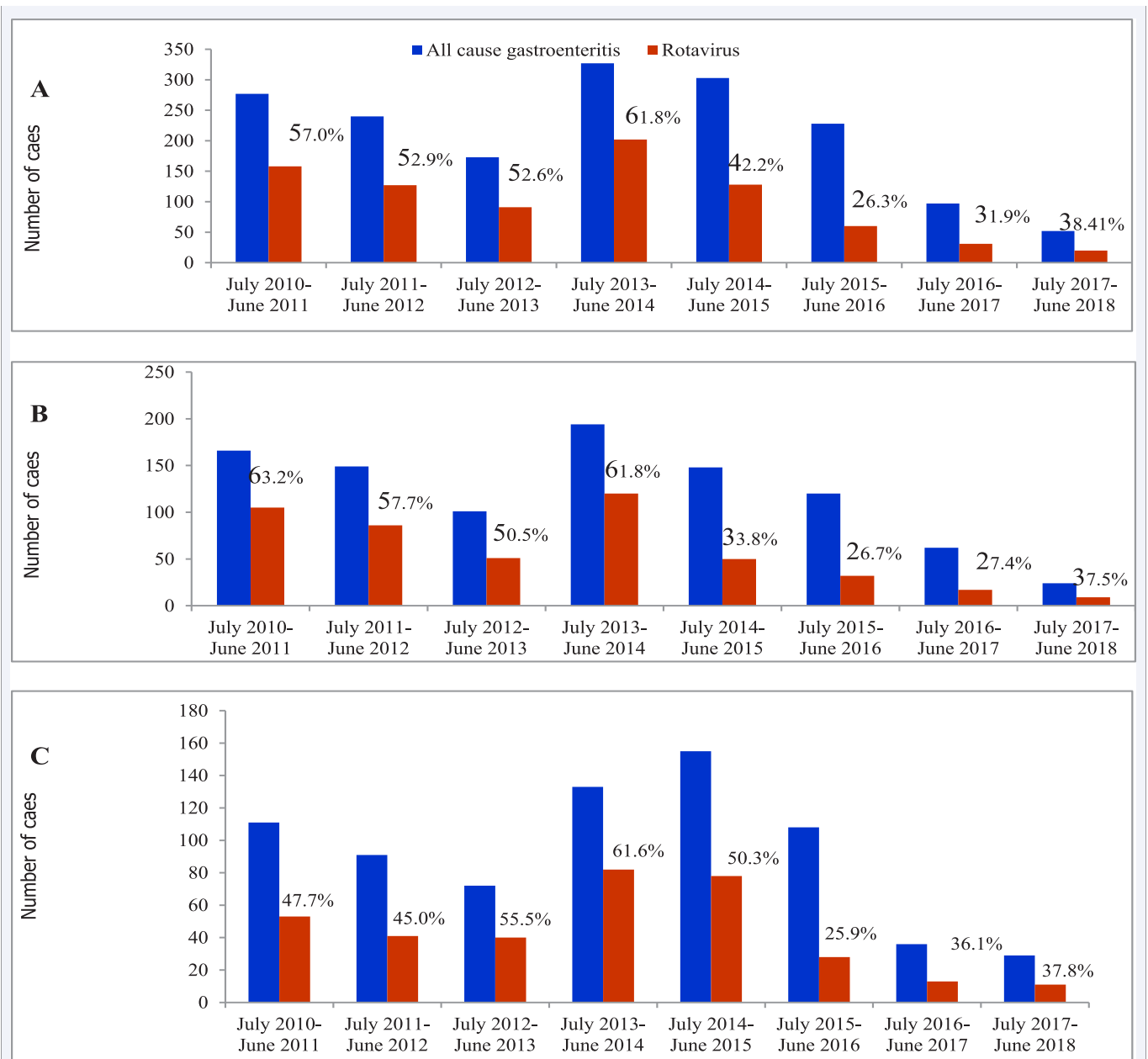
Togo is one of the few francophone countries in Africa that has introduced Rotarix® in its routine immunization schedule. We evaluated rotavirus vaccine sustained impact through active sentinel surveillance for AGE. Overall, active surveillance in children <5 years of age showed a median reduction of 38% in the proportion of rotavirus positive cases during the first four post-vaccine years, compared with pre-vaccine years. Our current findings demonstrate rapid and sustained reductions in all-cause diarrhea hospitalizations and rotavirus-associated hospitalizations among Togolese children <5 years of age during the first four years following vaccine implementation.

Few studies are available in Africa on rotavirus vaccine impact, but all of them have confirmed a post-vaccine reduction in all-cause diarrhea hospitalizations and rotavirus-associated hospitalizations. In Rwanda, 61% - 70% reduction in rotavirus-associated hospitalizations was greater than the reduction rates observed in our study [9]. In Ghana, Malawi, and Botswana, the 43% - 52% reduction rates were similar to our findings [10,12,18]. Two studies in South Africa showed 45% - 65% reduction [19,20]. In the pre-vaccine period in Togo, rotavirus-associated AGE prevalence was high and ranged from 53% to 62%. The high pre-vaccine prevalence in rotavirus positive cases among Togolese children likely contributed to the significant early post-vaccine impact demonstration. Overall, our findings demonstrated sustained vaccine impact observation in the first four years post-vaccine implementation similar to findings in Africa and elsewhere [20-26].

Worldwide, many studies have showed rotavirus vaccine impact on rotavirus-associated hospitalizations among children [27-33].

The observed reductions in the proportion of hospitalizations due to AGE were greater during the rotavirus season and were greater among infants <1 year of age who were vaccine age-eligible in the first and second years, corroborating that vaccination was likely responsible for the declines. These observations and also the fact that the peak of diarrhea cases disappeared in the third and fourth post-rotavirus years highlighted the fact that rotavirus was the leading cause of childhood diarrhea before rotavirus vaccine implementation [14-16].

Some limitations should be noted. The active surveillance was only conducted in the capital city area. Despite the consistency of the evidence of rotavirus vaccine impact that was observed, these data may not be representative of rotavirus vaccine impact in rural areas or other urban areas of the country.



**Figure 1** Annual number of all-cause gastroenteritis hospitalizations and rotavirus-associated hospitalizations by hospitalization year and patient age, July 2010 –June 2019, sentinel surveillance hospitals. The proportion of rotavirus positive cases is noted. (A) All children <5 years of age. (B) Children aged <1 year. (C) children aged 1-4 years.

**CONCLUSIONS**

Our findings support continued use of rotavirus vaccination in Togolese children. It is necessary to monitor a long-term evaluation of the impact of the vaccine on epidemiology including the effect on reduction of deaths associated with gastroenteritis and the effect on circulating rotavirus strains through continue surveillance.

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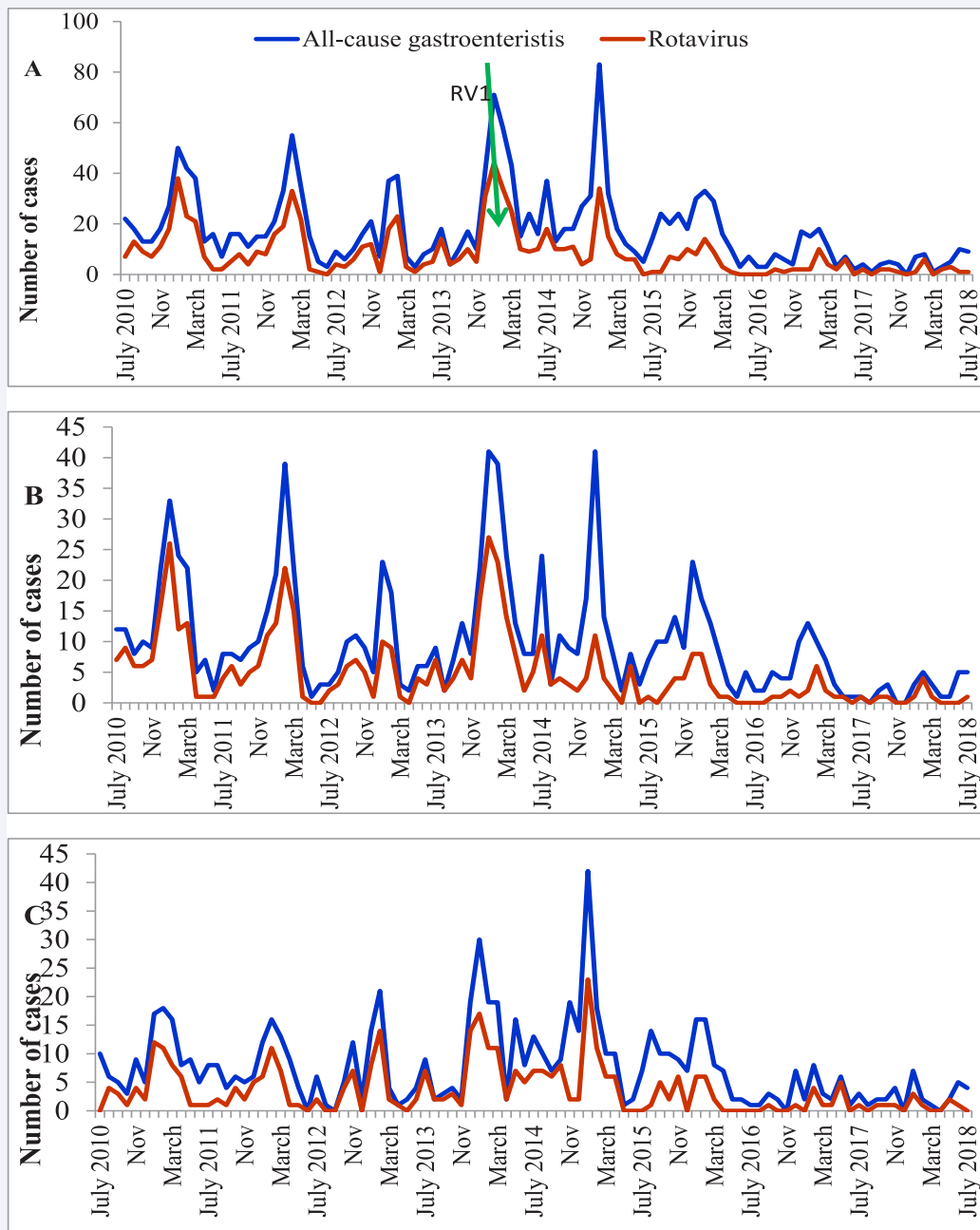
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**DISCLAIMER**

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of



**Figure 2** Monthly trends of all-cause gastroenteritis hospitalizations and rotavirus-associated hospitalizations by age group, July 2010 –June 2016, sentinel surveillance hospitals. (A) All children <5 years of age. ((B) Children aged <1 year. (C) children aged 1-4 years.

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