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Sustained impact of rotavirus vaccine introduction on rotavirus gastroenteritis hospitalizations in children <5 years of age, Ghana, 2009–2016

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Abstract

Introduction: Ghana introduced monovalent rotavirus vaccine in April 2012. We sought to determine the long-term impact of routine rotavirus vaccination on rotavirus gastroenteritis hospitalizations in Ghana during the first 4 years following rotavirus vaccine introduction.

Methods: Active sentinel surveillance for acute gastroenteritis hospitalizations among children <5 years of age was conducted at two sites from July 2009 through June 2016. Stool specimens were collected from enrolled children and tested by enzyme immunoassay. Changes in the proportion of all-cause gastroenteritis hospitalizations due to rotavirus pre- (July 2009–June 2012) and post-vaccine introduction (July 2012–June 2016) were compared using chi-square test.

Results: The proportion of acute gastroenteritis hospitalizations due to rotavirus among children <5 years of age significantly declined by 42% from a pre-vaccine median of 50% (343/684) to a post-vaccine median of 29% (118/396) ($p < 0.001$). The age distribution of rotavirus hospitalizations shifted toward older ages with 64% (759/1197) of rotavirus hospitalizations occurring in children <12 months of age pre-vaccine introduction to 47% (212/453) occurring in children <12 months of age post-vaccine introduction ($p < 0.001$).

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Discussion: The decline in rotavirus hospitalizations following rotavirus vaccine introduction have been sustained over the first 4 years of the vaccination program in Ghana. Continued vaccination against rotavirus will ensure that this burden remains low.

Keywords

Rotavirus; Rotavirus vaccine; Ghana

1. Introduction

Ghana became the first country in sub-Saharan Africa to introduce rotavirus vaccine with support from Gavi when it introduced monovalent rotavirus vaccine (Rotarix; GlaxoSmithKline Biologicals, Rixensart, Belgium) in April 2012. A previous study during the first 31 months post-rotavirus vaccine introduction in Ghana showed that the vaccine was 60% effective against rotavirus hospitalizations and resulted in a 49% decline in rotavirus hospital admissions among children <5 years of age [1]. Rotavirus vaccine administration was timely and coverage was high with over 93% of age-eligible children fully vaccinated during this 31 month period [1]. These findings are in line with those from other early introducing countries in sub-Saharan Africa which also showed substantial reductions in diarrhea hospitalizations following rotavirus vaccine introduction [2–9]. However, several countries in the region also showed lower protection of the vaccine in the second year of life and a shifting of the disease burden to older ages [1,5,7]. Thus, understanding the long-term impact of rotavirus vaccination on the burden of severe rotavirus disease is important.

As Ghana approaches graduation from Gavi support, fully documenting the impact of the rotavirus vaccination program is important to ensuring the country's continued investment in the vaccination program. We sought to determine the long-term impact of routine rotavirus vaccination on rotavirus gastroenteritis hospitalizations in Ghana during the first 4 years following rotavirus vaccine introduction.

2. Methods

Active sentinel surveillance for acute gastroenteritis has been ongoing in Ghana at two large tertiary care hospitals, Korle Bu Teaching Hospital (KBTH) in Accra and Komfo Anokye Teaching Hospital (KATH) in Kumasi since January 2009, as described previously [1]. Briefly, children were enrolled following the World Health Organization-recommended protocol for hospital-based surveillance for rotavirus gastroenteritis [10]. Children <5 years of age admitted for diarrhea, defined as ≥3 loose stools in a 24 h period, and/or vomiting of ≤7 days duration were approached for enrollment in the surveillance platform. Surveillance was conducted 24 h per day in the emergency department and inpatient wards to identify all children <5 years of age with acute gastroenteritis who required hospital admission. Because of the possibility of nosocomial infection, children identified >48 h after admission were excluded from enrollment.

Stool specimens were collected from enrolled children within 48 h of admission and stored at 2–8 °C until testing at the medical virology laboratory of the two surveillance hospitals.

Specimens were tested by a commercially available enzyme immunoassay (EIA) (ProSpecT; Oxoid, Cambridge, United Kingdom).

Given the seasonal nature of rotavirus disease in Ghana, we defined year-long periods from July of one year to June of the following year to ensure that we captured each entire rotavirus season in a single 12 month period. The pre-rotavirus vaccine introduction period was defined as July 2009 to June 2012 and the post-vaccine introduction period was defined as July 2012 to June 2016. Changes in the proportion of all-cause gastroenteritis hospitalizations due to rotavirus and the age distribution of rotavirus hospitalizations pre- and post-vaccine introduction were compared using chi-square tests with $p < 0.05$ considered as significant. Analyses were also stratified by age group (<12 months, 12–23 months, and 24–59 months of age).

3. Results

During the pre-vaccine period from July 2009 to June 2012, 2473 children with acute gastroenteritis were enrolled in the two surveillance facilities (2086 from KBTH and 387 from KATH) and of which, 1192 (48%) (1001 (48%) from KBTH and 191 (49%) from KATH) tested positive for rotavirus by EIA. Annual fluctuations in the percent of acute gastroenteritis hospitalizations due to rotavirus in the pre-vaccine period were small and ranged from 43% to 51% (Fig. 1). Following rotavirus vaccine introduction, 1593 children with acute gastroenteritis were enrolled from July 2012 through June 2016 (1340 from KBTH and 253 from KATH) and of which, 453 (28%) (363 (27%) from KBTH and 70 (28%) from KATH) tested rotavirus positive. The annual proportion of acute gastroenteritis hospitalizations due to rotavirus among children <5 years of age was stable (median: 29%; range: 23–32%) during the post-vaccine period and significantly lower than the pre-vaccine period ($p < 0.001$) (Table 1). Comparable trends over time were observed in both sites. Similarly, rotavirus positivity significantly declined by 49% among children <12 months of age from a pre-vaccine median of 54% (range: 46–54%) to 27% (range: 23–29%) post-vaccine introduction. Among children 12–23 months of age, rotavirus positivity declined 27% overall ($p = 0.02$) from a pre-vaccine median of 47% (range: 41–54%) to 35% (range: 19–41%) post-vaccine introduction but was only significantly lower than the pre-vaccine baseline in 2 of the 4 post-vaccine years. No significant change in positivity ($p = 0.33$) was observed in children 24–59 months of age from pre-vaccine (median: 34%; range: 33–37%) to post-vaccine introduction (median: 26%; range: 22–27%) but the total number of enrolled children and the number of rotavirus positive was small in this age group.

Prior to rotavirus vaccine introduction, the greatest burden of rotavirus disease was among children <12 months of age, who accounted for 64% (759/1192) of all rotavirus hospitalizations among children <5 years of age (Table 2). Only 8% (93/1192) of rotavirus hospitalizations occurred in children 24–59 months of age. The burden of rotavirus hospitalizations significantly shifted toward older children during the post-vaccine period ($p < 0.001$). The proportion of rotavirus hospitalizations that occurred in children <12 months of age declined from 64% (759/1192) in the pre-vaccine era to 47% (212/453) in the post-vaccine era. Conversely, the proportion of rotavirus hospitalizations that occurred in children 12–23 months of age increased from 29% (340/1192) to 39% (177/453) and

the proportion among children 24–59 months of age increased from 8% (93/1192) to 14% (64/453). Despite the shift in proportion of rotavirus hospitalizations toward older children, the number of rotavirus hospitalizations in all age groups during the post-vaccine period remained below the pre-vaccine baseline.

4. Discussion

The reduction in rotavirus hospitalizations following the introduction of rotavirus vaccine into the routine immunization program in Ghana in 2012 was sustained over the first four years of the vaccination program. The median annual proportion of acute gastroenteritis hospitalizations due to rotavirus declined by 42% resulting in fewer numbers of children being hospitalized for rotavirus gastroenteritis and subsequently an overall decline in the number of acute gastroenteritis hospitalizations among children <5 years of age. These findings are consistent with findings of sustained impact in high-income countries [11–15] and should provide reassurance of the long-term benefits of rotavirus vaccine to other countries in sub-Saharan Africa that have subsequently introduced the vaccine. By December 2016, 31 sub-Saharan African countries had introduced rotavirus vaccine into their routine childhood immunization programs [16].

The age distribution of rotavirus hospitalizations in Ghana has shifted to older children following the introduction of rotavirus vaccine. This phenomenon has been observed in other early introducing countries [5,6]. Some countries have shown lower vaccine effectiveness in older age children compared to the first year of life. Additionally, there is no catch-up campaign for rotavirus vaccine so older children are initially not directly protected by rotavirus vaccination because they are too old to receive the vaccine at the time of introduction. In Ghana, there may not be significant indirect protection in older children as declines in rotavirus positivity for diarrhea hospitalization among children 24–59 months of age were not observed in the first few years following vaccine introduction when these children were not age-eligible to receive vaccine although few rotavirus hospitalizations occurred in this age group. Despite this age shift in rotavirus hospitalizations, the overall number of rotavirus hospitalizations is lower compared to the pre-vaccine baseline resulting in a substantially lower burden of rotavirus hospitalizations.

This evaluation has several limitations. First, although rotavirus vaccine was introduced in Ghana in April 2012, we included data from April 2012 through June 2012 in our pre-vaccine baseline period. Given that vaccine introduction occurred immediately after the period of peak rotavirus circulation when detection of rotavirus was traditionally low and few children were age-eligible to receive rotavirus vaccine during this period, inclusion of these three months in the pre-vaccine baseline would have minimal effect on overall vaccine impact. Second, we only included two hospitals from Ghana in this evaluation. However, a previous rotavirus vaccine effectiveness analysis used data from 8 hospitals around the country and showed that the vaccine was 60% effective against rotavirus hospitalizations [1]. Thus, we would expect the impact seen in these two hospitals to be broadly representative of the impact of rotavirus vaccine on severe rotavirus disease in Ghana.

The dramatic declines in rotavirus hospitalizations following rotavirus vaccine introduction have been sustained over the first 4 years of the vaccination program in Ghana. Furthermore, the rotavirus vaccine program has been shown to be cost-effective in reducing the rotavirus disease burden [17]. Continued vaccination against rotavirus will ensure that this burden remains low. Ongoing surveillance including testing for other diarrhea pathogens will help identify additional ways that Ghana can reduce the burden of diarrheal disease in young children.

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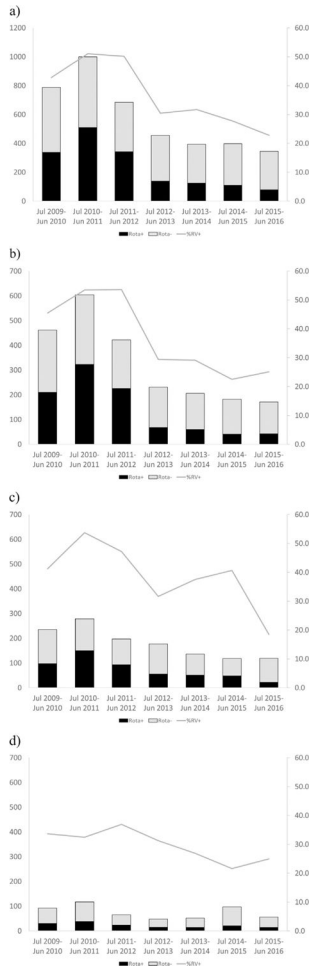

Fig. 1.

Trends in number of rotavirus positive and negative children enrolled in the active surveillance and the proportion rotavirus positive among children (a) <5 years of age, (b) <12 months of age, (c) 12–23 months of age, and (d) 24–59 months of age, from two hospitals in Ghana, July 2009–June 2016. Rotavirus vaccine was introduced in April 2012.

Table 1

Number of total and rotavirus positive children enrolled and the percent rotavirus positive pre- and post-rotavirus vaccine introduction by age from two hospitals in Ghana, July 2009-June 2016.

	N Enrolled	N RV+	% RV+	% Reduction in% RV+	p-value
<12 months					
Jul 09- Jun 10	462	210	45.5%	–	–
Jul 10- Jun 11	604	323	53.5%	–	–
Jul 11- Jun 12	422	226	53.6%	–	–
Pre-vaccine median	**462**	**226**	**53.5%**	**ref**	**–**
Jul 12- Jun 13	231	68	29.4%	45.0%	<0.001
Jul 13- Jun 14	206	60	29.1%	45.5%	<0.001
Jul 14- Jun 15	182	41	22.5%	57.9%	<0.001
Jul 15- Jun 16	171	43	25.1%	53.0%	<0.002
Post-vaccine median	**194**	**52**	**27.1%**	**49.3%**	**<0.001**
12–23 months					
Jul 09- Jun 10	235	97	41.3%	–	–
Jul 10- Jun 11	279	150	53.8%	–	–
Jul 11- Jun 12	197	93	47.2%	–	–
Pre-vaccine median	**235**	**97**	**47.2%**	**ref**	**–**
Jul 12- Jun 13	177	56	31.6%	33.0%	0.002
Jul 13- Jun 14	136	51	37.5%	20.6%	0.07
Jul 14- Jun 15	118	48	40.7%	13.8%	0.25
Jul 15- Jun 16	119	22	18.5%	60.8%	<0.001
Post-vaccine median	**128**	**50**	**34.6%**	**26.8%**	**0.02**
24–59 months					
Jul 09- Jun 10	92	31	33.7%	–	–
Jul 10- Jun 11	117	38	32.5%	–	–
Jul 11- Jun 12	65	24	36.9%	–	–
Pre-vaccine median	**92**	**31**	**33.7%**	**ref**	**–**
Jul 12- Jun 13	48	15	31.3%	7%	0.77
Jul 13- Jun 14	52	14	26.9%	20.1%	0.40

	N Enrolled	N RV+	% RV+	% Reduction in% RV+	p-value
Jul 14- Jun 15	97	21	21.6%	35.7%	0.07
Jul 15- Jun 16	56	14	25.0%	25.8%	0.27
Post-vaccine median	**54**	**15**	**26.0%**	**23.0%**	**0.33**
<5 years					
Jul 09- Jun 10	789	338	42.8%	–	–
Jul 10- Jun 11	1000	511	51.1%	–	–
Jul 11- Jun 12	684	343	50.1%	–	–
Pre-vaccine median	**789**	**343**	**50.1%**	**ref**	**–**
Jul 12- Jun 13	456	139	30.5%	39.2%	<0.001
Jul 13- Jun 14	394	125	31.7%	36.7%	<0.001
Jul 14- Jun 15	397	110	27.7%	44.7%	<0.001
Jul 15- Jun 16	346	79	22.8%	54.5%	<0.001
Post-vaccine median	**396**	**118**	**29.1%**	**42.0%**	**<0.001**

ref = reference.

Bold values indicate median data for the period before and period after rotavirus vacccine introduction.

Table 2

Distribution of rotavirus positive cases by age pre- and post-rotavirus vaccine introduction by age from two hospitals in Ghana, July 2009-June 2016.

	Pre-vaccine introduction (July 2009–June 2012) n = 1192 (%)	**Post-vaccine introduction (July 2012–June 2016) n = 453 (%)**
<12 months of age	759 (64%)	212 (47%)
12–23 months of age	340 (29%)	177 (39%)
24–59 months of age	93 (8%)	64 (14%)