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A health surveillance data-based assessment of the impact of routine paediatric rotavirus vaccination on all-cause acute childhood diarrhoea

Brainard A ASARE ^{1*}, Grace ASARE ²¹ Department of Statistics, Kwaebibirem Municipal Health Directorate, Ghana Health Service, Kade, Ghana; ² Department of Child Health, Kade Government Hospital, Ghana Health Service, Kade, Ghana.

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Abstract

Background: To improve the fight against faecal-orally transmitted rotavirus infection, which is the leading cause of severe diarrhoea among children aged < 5 years, Ghana has incorporated rotavirus vaccination into its expanded programme of immunization. Rotavirus diarrhoea constitutes a significant portion of all-cause acute childhood diarrhoea (ACD) in children.

Objective: This study was designed to investigate the impact of routine rotavirus vaccination on ACD cases.

Methods: The study was completed through a cross-sectional review of health institutional childhood diarrhoea surveillance data from 2012 to 2021, which includes the year when rotavirus vaccination was introduced. The study dataset was abstracted from the DHIMS-2 internet-based health data repository and was descriptively analyzed by administrative regions using Epi Info™ version 3.5.1 (CDC, USA).

Results: The burden of ACD in terms of both absolute and mean values remained the lowest among infants aged under 28 days across all regions, as they had not yet received rotavirus vaccination. In contrast, children aged 1 to 4 years, who are typically exposed to rotavirus serotypes 1 and 2, consistently experienced the highest burden of ACD. With increasing rotavirus vaccination coverage, children aged 1 month to 4 years recorded a marginal, but sustained decline in mean ACD cases from 2016 to 2021. The ACD also similarly declined slowly among the rotavirus vaccine naïve infants aged < 28 days. Despite a spike in 2017, the burden of ACD was low in the Ahafo administrative region. However, increasing rotavirus vaccination coverage did not appear to have a significant impact on reducing ACD in the Ashanti, Bono, Bono East, Eastern, and Northeast administrative regions. From 2012 to 2021, the Central, Greater Accra, Oti, Upper East, Volta, and Western administrative regions recorded a marginal decline in the burden of ACD among children aged 1 to 4 years, and this was accompanied by an increase in rotavirus vaccination coverage. The ACD cases rose as rotavirus vaccination coverage decreased in the Western North Region between 2015 and 2019.

Conclusion: Routine rotavirus vaccination may have contributed to a reduction in severe childhood ACD cases even though this study cannot exclude the impact of other anti-diarrhoeal interventions. To evaluate the population effectiveness of rotavirus vaccines, it is recommended to widely promote routine rotavirus disease surveys, which can be nested within ACD surveillance.

Keywords: Rotavirus, vaccination, effectiveness, diarrhoea, under 5 years

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INTRODUCTION

A significant proportion of children aged < 5 years continue to experience morbidity and mortality associated with diarrhoeal diseases, which are largely preventable. Globally, the number of affected children surpasses the combined number of those affected by

HIV/AIDS, malaria, and measles [1,2]. In 2015, more than 50% of mortality estimates among children aged < 5 years were accounted for by 55 out of 782 African states, provinces, and regions [2]. Poor access to healthcare, safe water, and childhood undernutrition are established risk factors for diarrhoea and its associated adverse outcomes among children aged < 5 years [3]. Faeco-orally transmitted rotavirus acute gastroenteritis, which is caused by a genus of double-stranded Reoviridae RNA viruses, is the commonest cause of severe diarrhoea among children of

* Corresponding author

Email: brainardasare@gmail.com

this age group [4]. Globally, all children aged < 5 years have been exposed to rotavirus infection at least once, with some immunity developed after each infection. This post-primary rotavirus infection-induced immunity significantly lessens the severity of all subsequent infections. Adults are rarely affected [4]. Despite accounting for 50% of childhood severe diarrhoea-related hospitalizations, the public health importance of rotavirus infection remains unknown in developing countries [5]. Rotavirus infection accounts for 500,000 deaths among children aged < 5 years globally with at least, two million severe cases among children of this age group [5]. Severe rotavirus diarrhoea (RVD) is more prevalent among boys than girls and about 42% of diarrhoea-associated mortality among children aged < 5 years occur in the WHO Africa region [5,6].

Ghana's all-cause acute childhood diarrhoea (ACD)-associated mortality remains significantly high proportionately accounting for 10% of all childhood deaths [6]. The 2017 prevalence estimates of Ghana indicate that childhood diarrhoea differentially affects urban (10.5%) and rural (12.8%) residents, affecting males (13.1%) more than females (10.2%) and has a peak prevalence of 15.4 to 16.8% among children aged 12 to 23 months [7,8,9]. Ghana, incorporated rotavirus vaccination, into its expanded program of immunization in May 2012 [6]. Studies, before the introduction, indicated that rotavirus vaccines were safe, effective, and comprised a cost-effective intervention against severe rotavirus acute gastroenteritis [6]. The monovalent rotavirus vaccine, given orally to infants in two doses at 6 and 10 weeks, aimed to reduce diarrhoea morbidity, mortality, and hospitalizations in children aged < 5 years [6,8]. Rotavirus strain G1P, the major circulating strain during the pre-rotavirus vaccination era, was replaced by strain G12P as the most predominant strain post-introduction of the vaccine [8]. This strain replacement was deemed possibly temporary at the time of the introduction of the vaccine but an increase in the prevalence of the G12P strain was later observed in other countries yet to introduce the vaccine in West Africa [8]. Continuous surveillance for characteristics of the pathogen and associated morbidity and mortality patterns in this post-rotavirus vaccination era is recommended for monitoring circulating rotavirus strains [8].

Fiji, the first independent Pacific island country to introduce the rotavirus vaccine in 2012, described the vaccine's impact on all-cause diarrhoea in all ages, and on RVD in children aged < 5 years. The ACD significantly declined among all age groups except infants aged ≤ 2 months and adults aged ≥ 55 years and reduced by 39% among children aged < 5 years. The RVD admissions at the largest hospital declined among children aged < 5 years by 87% while RVD and ACD mortality in Fiji declined among children aged 2 months to adults aged 54 years post-rotavirus vaccination [10]. This study aimed to observe whether there has been a decrease in the burden of RVD and its proportionate contribution to the burden of ACD from 2012 (the year when rotavirus vaccination was introduced) to 2021. This hypothetical premise posits that

continued rotavirus vaccination will effectively reduce RVD incidence and vividly impact the ACD trends. Therefore, this study analyzed the trends of ACD for routine rotavirus vaccination coverage among children aged < 5 years, who are the target population for this intervention against childhood diarrhoea.

MATERIALS AND METHODS

This health facility surveillance data-based cross-sectional study was completed through a review of health institutional ACD surveillance data on childhood diarrhoea morbidity from 2012 to 2021. The information for children aged < 5 years, who reported to outpatient departments (OPD) in different hospitals, was extracted from the District Health Information Management System (DHIMS-2), an internet-based health dataset repository of the Ghana Health Service, under the Ministry of Health. The data followed established age group categorizations. Information abstracted for analyses included the overall burden of ACD morbidity among children aged < 5 years in Ghana and rotavirus vaccination coverage for the first and second doses of the monovalent vaccine given at 6 and 10 weeks of age. Pre-existing age groups from the DHIMS-2 datasets repository were analyzed by regional ACD case burdens and rotavirus vaccination coverage.

We aimed to observe prior correlations between rising trends of rotavirus vaccination and the hypothetically expected commensurate declines in incidence patterns of childhood ACD cases from 2012 to 2021. Data abstraction was fundamentally premised on a research assumption that all institutional childhood ACD-specific morbidity was consistent with the clinical spectrum of moderate and severe disease. This was based on a preceding assumption that mild ACD cases would not likely be brought to health facilities but be remedied at home by caregivers of children aged < 5 years. These assumptions also posited that mild cases would resolve spontaneously without any interventions and would therefore not likely account for ACD surveillance data.

In line with existing evidence, it is hypothetically estimated that the RVD may be responsible for up to 50% of the childhood ACD burden [5]. The hypothetical premise of the study is therefore linked to the research assumption that continued routine administration of efficacious rotavirus vaccines should translate into observable reductions in ACD morbidity burdens. This is linked to established evidence that a significant proportion of childhood ACD cases constitutes RVD, whose incidence, when averted, will generally impact the ACD burden. Data were analyzed descriptively and predominantly through graphical presentations of study findings by administrative regions of Ghana. Data were retrieved from the DHIMS-2 internet-based general health and surveillance dataset repository for all 16 administrative regions in Ghana. In 2018, Ghana had 10 administrative regions when the rotavirus vaccine was introduced. Subsequently, the number of administrative regions grew from 10 to 16.

Table 1: Mean all-cause acute childhood diarrhoea cases among children aged < 5 years, 2012-2021

| Region | Mean diarrhoea cases (±SD) by age group, 2012-2021 | | | | | | Mean Rotavirus vaccination coverage, 2012-2022 | |
|---------------|--|---------------------------|-------------|---------------------------|-----------|--------------------------|--|-------------|
| | < 28 days | Standard Deviation (± SD) | 1-11 months | Standard Deviation (± SD) | 1-4 years | Standard Deviation (±SD) | Mean Rota 1 | Mean Rota 2 |
| Ahafo | 152 | 64 | 4708.1 | 816 | 14168.9 | 3201.2 | 82.2 | 77.1 |
| Ashanti | 852.2 | 386 | 19585 | 1437 | 48284.2 | 3578.9 | 97.8 | 91.7 |
| Bono | 322.3 | 89.2 | 9024.6 | 1015.9 | 28921.6 | 3527.7 | 82.1 | 77.1 |
| Bono East | 468.1 | 277.8 | 10993.8 | 1555.2 | 28935.5 | 3781.3 | 90.3 | 87.1 |
| Central | 558.6 | 127.9 | 12431 | 1493.8 | 30213 | 4319.1 | 74.5 | 70.1 |
| Eastern | 507.8 | 232.7 | 16318.3 | 2018.4 | 46525.8 | 4993.6 | 82.7 | 78.5 |
| Greater Accra | 542.3 | 116.4 | 10270.6 | 2354.9 | 25170.6 | 4557.7 | 74.4 | 73.7 |
| North East | 298.2 | 67.6 | 7299.9 | 1465.7 | 15752.8 | 2213.5 | 105.1 | 98.6 |
| Northern | 659.2 | 250.6 | 16448.4 | 2823.5 | 44132.3 | 8049.9 | 115.8 | 109.2 |
| Oti | 278 | 73.5 | 7146.8 | 994.4 | 17980.9 | 4175.9 | 91.8 | 86.5 |
| Savannah | 295 | 141.8 | 5840.2 | 961.6 | 13753.5 | 2872.5 | 117.1 | 110.2 |
| Upper East | 385.7 | 229 | 14191.9 | 1721.4 | 30010.3 | 4973.5 | 79.8 | 78.6 |
| Upper West | 228.1 | 112.1 | 9712.2 | 1290.7 | 21096.9 | 2368.2 | 75.3 | 74.8 |
| Volta | 339.2 | 76.6 | 10139.6 | 1596.4 | 25392.1 | 4581.6 | 68.3 | 67.9 |
| Western | 496.1 | 238.2 | 12982.2 | 1840.5 | 36087.8 | 4253.9 | 77.8 | 74.4 |
| Western North | 1542.8 | 1283.7 | 6418.6 | 1768.4 | 17654.2 | 2625.3 | 75.7 | 73.3 |

*SD, standard deviation

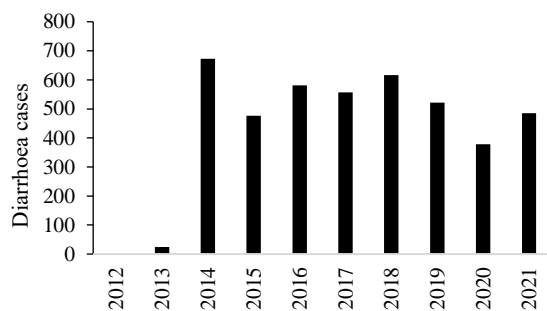


Figure 1: Overall mean all-cause acute childhood diarrhoea cases among neonates aged < 28 days, 2012-2021

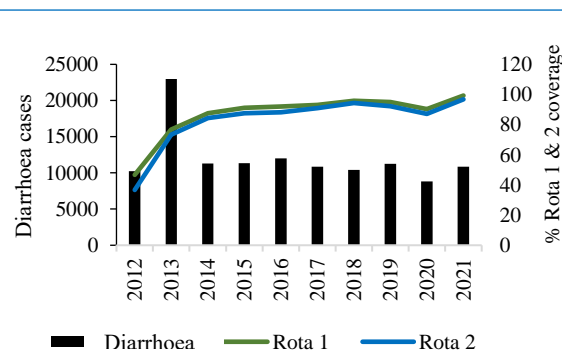


Figure 2: Overall mean all-cause acute childhood diarrhoea cases among infants aged 1 to 11 months, analysed by Rota 1 and 2 vaccination coverage, 2012-2021

The ACD surveillance data were therefore abstracted from the administrative regions which existed before the rotavirus vaccination campaign in 2012. The ACD data for all 16 administrative regions in Ghana were analyzed for the years 2012-2021. Permission to access the ACD surveillance data was granted by the hospital’s medical superintendent, through the office of the Regional Director of Health Services.

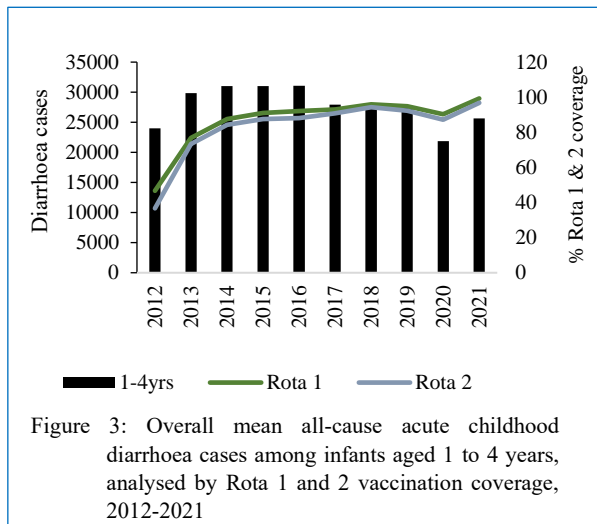
Statistical analysis

Abstracted data were organized and analyzed with the Epi Info™ version 3.5.1 software (CDC, USA). Means and their associated standard deviations (SD) were presented for the various age groups by administrative region and compared with mean rotavirus vaccination coverage over the same period. The ACD among children aged < 5 years were analyzed in absolute figures and not in percentage terms as the ACD surveillance DHIMS-2 dataset is devoid of the total population of children out of whom the absolute figures comprise a proportionate fraction. The age groups available in the DHIMS-2 database are children aged < 28 days, 1 to 11 months, and 1 to 4 years. Findings were mainly presented in tabular and graphical formats by administrative regions. Key study limitations comprised the inherently limited capacity for robust age group analyses using disaggregated age groups of childhood ACD. The dataset did not also facilitate analyses by sex.

RESULTS

The average burden of region-specific ACD continued to be the lowest for neonates below 28 days old, who have not yet received rotavirus vaccination. On the other hand, the number of ACD cases seen was significantly higher among

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children aged 1 to 4 years, regardless of the average rotavirus vaccination coverage in the region (Table 1). Overall, age-specific mean ACD cases from 2012 to 2021 remained lowest among neonates aged < 28 days. This was characterized by a gradual increase from 2012 to 2018 after which a slow decline is observed. Children aged 1 to 11 months recorded a marginal, but sustained decline in mean ACD cases from 2016 to 2021 with increasing RV vaccination coverage. A similar trend was also observed among the age group 1 to 4 years (Figures 1-3).

Overall, the incidence of ACD cases in the Ahafo region was relatively low across all age groups. However, there was a noticeable increase in cases among children aged 1 to 4 years in 2017, regardless of the region's rotavirus vaccination coverage. Ashanti, Bono, Bono East, Eastern, and the North East regions showed childhood ACD trends that were not amenable to increasing rotavirus vaccination coverage. The Central, Greater Accra, Oti, Upper East, Volta, and Western regions experienced a slight decrease in Acute Cholecystitis and Cholangitis Disease (ACD) cases among children aged 1 to 4 years. This decrease coincided with an increase in rotavirus vaccination coverage among children aged 1 month to less than 5 years in those regions. There was a noticeable increase in ACD cases in the Western North Region among all children aged < 5 years as rotavirus vaccination coverage decreased from 2015 to 2019. However, as vaccination coverage increased, there was a decreasing trend in ACD cases (Figures 4 and 5).

DISCUSSION

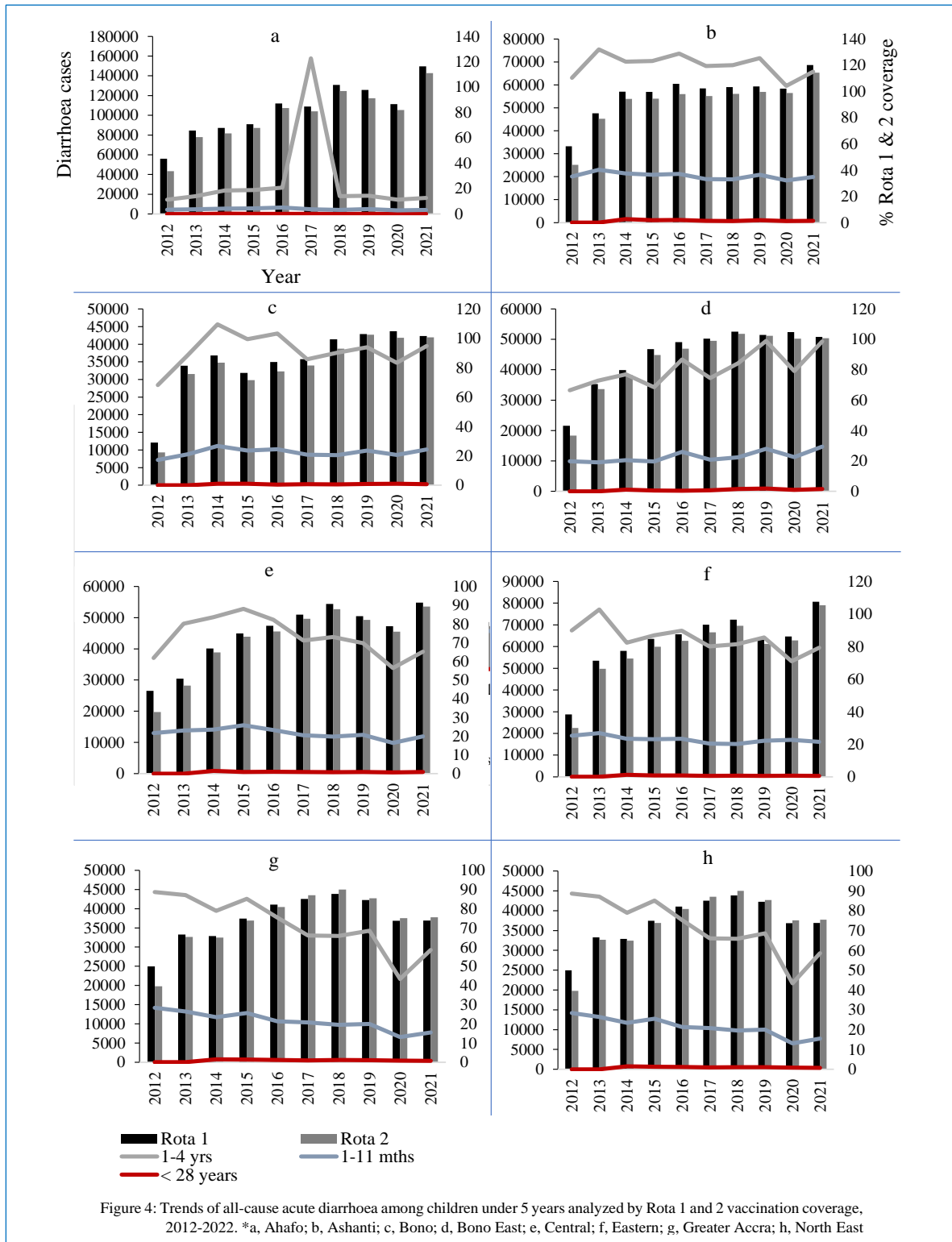
This study aimed to investigate the impact of routine pediatric rotavirus vaccination on the burden of childhood ACD which comprises both RVD and diarrhoea of other causes. The research study assumed that all estimates of diarrhoea obtained from health facility-based surveillance data were indicative of moderate and/or severe acute childhood ACD. The study's assumption further held that

the health facility-based ACD surveillance dataset was devoid of mild diarrhoea cases because such cases would likely be managed at home by caregivers and not brought to health facilities. Studies, published between 1986 and 1999 indicate that RVD accounts for an estimated 22% (defined by an uncertainty interval of 17–28%) of childhood ACD hospitalizations which increased from 2000 to 2004 to 39%, (range, 29 to 45%) [11,12]. A study on childhood ACD in Hanoi, Vietnam, pointed to an RVD case burden of 56% reported among children hospitalized with diarrhoea [12,13]. The RVD is defined as the most common diarrheal disease worldwide accounting for an estimated 33% of ACD-associated hospitalizations and 800,000 deaths annually [14]. Samples from eligible subjects with acute diarrhoea in Nigeria yielded a 55.9% positivity rate and an 80% positivity rate among infants aged < 24 months [15]. This study reported the highest prevalence of ACD among children aged 1 to 4 years as compared with neonates aged < 28 days who consistently recorded a markedly lower prevalence. Confirmation of RVD status to determine the proportionate composition of childhood ACD by administrative regions was however beyond the scope of this study.

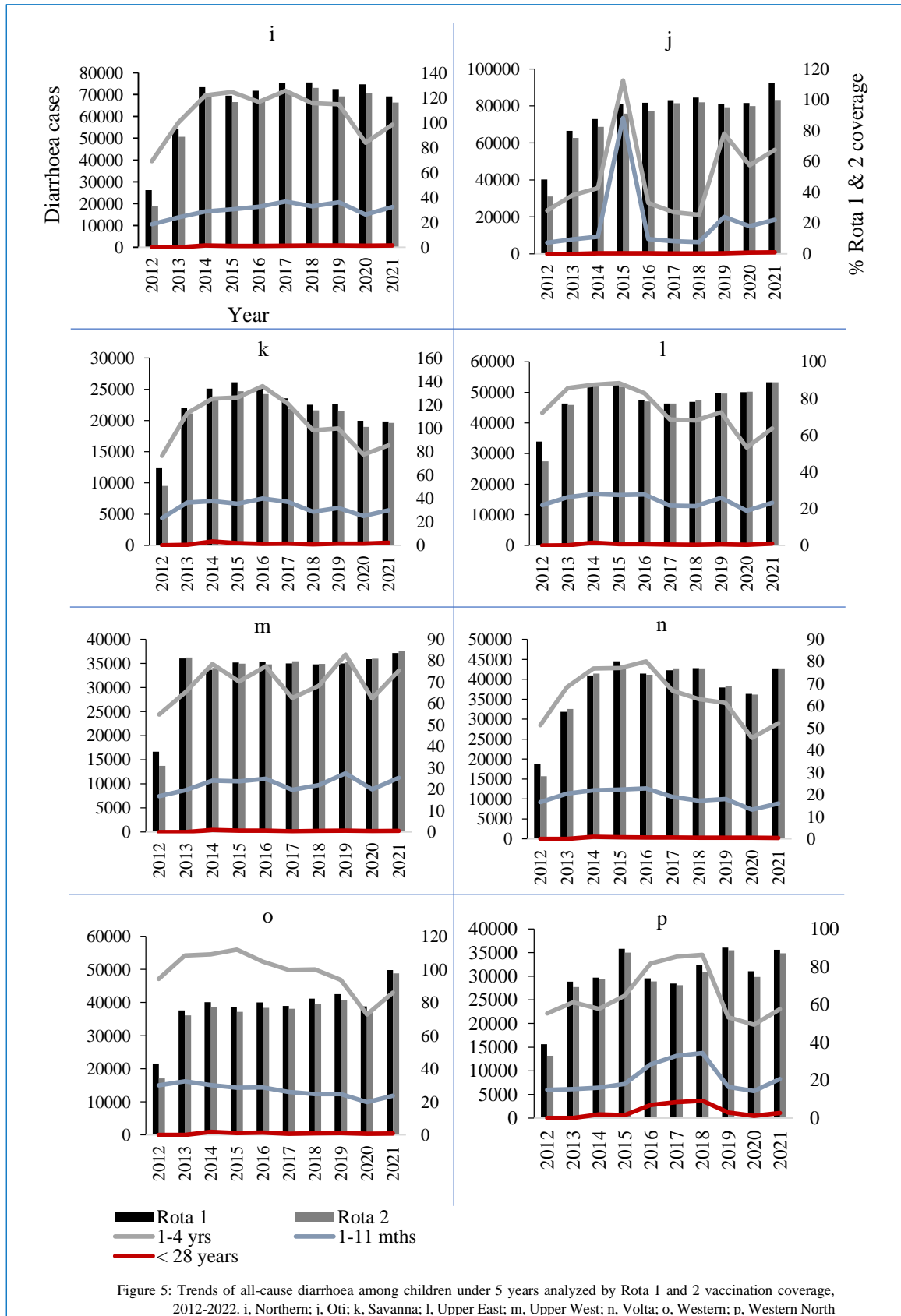
A study in Enugu, Nigeria indicated an RVD prevalence of 31.5% among children with acute gastroenteritis and 25.7% prevalence in the general population [16]. A study reported a high prevalence of RVD (60.9%) among children aged 0 to 12 months in Enugu, which decreased with increasing age. Also, RVD prevalence in Nigeria was significantly higher in bottle-fed children than in exclusively breastfed children [16]. Nigeria, therefore, remains an important zone for RVD with an estimated overall prevalence of 56% of ACD [12]. A study indicated a 60.8% prevalence of RVD in children between the ages of 0 to 12 months, 19.5% in children aged 13 to 24 months, 8.8% in children aged 25 to 36 months, and 2.19% in children between the ages of 49 and 60 months [16]. A study in Ghana reported an RVD prevalence of 68.7%, while another study attributed 49% of childhood all-cause diarrhoea to RVD. Additionally, during peak diarrhoea months, RVD positivity rates exceeded 60% [17,18]. A study conducted over a period of 13 months in Ghana revealed that 34% of childhood ACD cases were attributed to RVD. Based on this established prevalence, it can be inferred in our current study that RVD significantly contributes to ACD among children aged < 5 years. Therefore, it is hypothesized that increasing the coverage of routine rotavirus vaccination, which is known to significantly reduce RVD incidence, would lead to a noticeable decrease in the incidence of childhood ACD. The effectiveness of rotavirus vaccination in preventing childhood diarrhoea varies significantly between countries. In low child mortality countries, such as developed countries, it is known to prevent up to 90% of cases, while in high child mortality countries, mainly developing countries, it is only effective in preventing up to 50% of cases. This difference in effectiveness has been a topical issue in current literature, highlighting the disparities between countries. [20,21,22,23].

In the context of this study, a decrease in the incidence of childhood ACD could be partially indicative of the population-level effectiveness of rotavirus vaccination. Fiji became the first independent Pacific Island country to introduce routine rotavirus vaccination. A post-introduction

assessment described the impact of the vaccination on ACD hospitalizations in all ages and RVD in children aged < 5 years [10]. The ACD hospitalization in Fiji, post-vaccination, declined among all age groups except among infants aged ≤ 2 months and adults aged ≥ 55 years.



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For children aged < 5 years, ACD hospitalization declined by 39%. There was an 81% reduction in mortality among ACD hospitalizations in children aged < 5 years [10]. The RVD hospitalization at the largest hospital, among children aged < 5 years, declined by 87% in Fiji [10]. The proportion of RVD cases among childhood ACD cases seen at the OPD has significantly decreased, and there has been a decline in RVD-specific morbidity and mortality in Fiji among infants aged 2 months to 54 years since the introduction of the rotavirus vaccine [10]. Rahajamanana et al. analyzed trends of childhood ACD and RVD hospitalization in children aged < 5 years before and after the introduction of rotavirus vaccination in Madagascar [24]. They observed that ACD hospitalizations decreased after the introduction of rotavirus vaccination. The median proportion of annual hospitalizations due to childhood ACD reduced from 26%, before vaccine introduction to 25% the year of vaccine introduction, to 17% in 2015 and 16% in 2016 [24]. Following the introduction of rotavirus vaccination, childhood ACD and RVD-specific hospitalizations declined dramatically [24]. Our recent study indicates that there has been a limited impact of the increasing coverage of rotavirus vaccines 1 and 2 from 2012 to 2021 on ACD among children aged < 5 years. Although there were some isolated and inconsistent declines in the trends of childhood ACD cases during the studied period, it is not feasible to attribute these declines solely to rotavirus vaccination. This is because it is purely speculative to attribute any reduction in childhood ACD cases to a specific intervention against childhood diarrhoea. Such an attribution, regardless of the magnitude of the reduction, would be purely hypothetical. Studies conducted after vaccine introduction should focus on examining the population-level effectiveness of rotavirus vaccines in developing countries. Numerous studies have indicated that the effectiveness of these vaccines is significantly lower in developing countries with high mortality rates, where they are most needed [26-31].

In our current study, the level of ACD cases remained remarkably low among infants aged < 28 days who were naïve to rotavirus vaccination in all administrative regions. It is worth noting that the slow decline of childhood ACD cases observed among the age groups of 1 month to 4 years who were exposed to the rotavirus vaccine was also observed in the age group of infants aged < 28 days who were naïve to vaccination. We recommend that, following the introduction of routine rotavirus vaccination, it is crucial to prioritize research on the impact of all other interventions for preventing childhood diarrhoea. This can help monitor the characteristics of other diarrhoea-causing pathogens in the current context of routine rotavirus vaccination.

Conclusion

The implementation of routine rotavirus vaccination may have resulted in some level of reduction of severe childhood ACD cases, although this study cannot rule out the impact of other ongoing ACD prevention interventions. It would be of great public health importance to establish the

relationship between ACD, RVD, and all other anti-diarrhoeal interventions.

DECLARATIONS

Ethical considerations

Raw data were generated at the District Health Information Management System (DHIMS-2), an internet-based health dataset repository of the Ghana Health Service, under the Ministry of Health.

Consent to publish

All authors agreed to the content of the final paper.

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Competing Interests

No potential conflict of interest was reported by the authors.

Author contributions

BAA, GA developed the concept, assisted with data collection, analysed the survey data, and wrote the manuscript.

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Availability of data

Data for this work is available upon reasonable request from the corresponding author.

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