

Effect of pentavalent rotavirus vaccine introduction on hospital admissions for diarrhoea and rotavirus in children in Rwanda: a time-series analysis



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Summary

Background In May, 2012, Rwanda became the first low-income African country to introduce pentavalent rotavirus vaccine into its routine national immunisation programme. Although the potential health benefits of rotavirus vaccination are huge in low-income African countries that account for more than half the global deaths from rotavirus, concerns remain about the performance of oral rotavirus vaccines in these challenging settings.

Methods We conducted a time-series analysis to examine trends in admissions to hospital for non-bloody diarrhoea in children younger than 5 years in Rwanda between Jan 1, 2009, and Dec 31, 2014, using monthly discharge data from the Health Management Information System. Additionally, we reviewed the registries in the paediatric wards at six hospitals from 2009 to 2014 and abstracted the number of total admissions and admissions for diarrhoea in children younger than 5 years by admission month and age group. We studied trends in admissions specific to rotavirus at one hospital that had undertaken active rotavirus surveillance from 2011 to 2014. We assessed changes in rotavirus epidemiology by use of data from eight active surveillance hospitals.

Findings Compared with the 2009–11 prevaccine baseline, hospital admissions for non-bloody diarrhoea captured by the Health Management Information System fell by 17–29% from a pre-vaccine median of 4051 to 2881 in 2013 and 3371 in 2014, admissions for acute gastroenteritis captured in paediatric ward registries decreased by 48–49%, and admissions specific to rotavirus captured by active surveillance fell by 61–70%. The greatest effect was recorded in children age-eligible to be vaccinated, but we noted a decrease in the proportion of children with diarrhoea testing positive for rotavirus in almost every age group.

Interpretation The number of admissions to hospital for diarrhoea and rotavirus in Rwanda fell substantially after rotavirus vaccine implementation, including among older children age-ineligible for vaccination, suggesting indirect protection through reduced transmission of rotavirus. These data highlight the benefits of routine vaccination against rotavirus in low-income settings.

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Introduction

Rotavirus accounts for more than a third of diarrhoea deaths in children younger than 5 years worldwide, with more than half of these deaths happening in sub-Saharan Africa.¹ In response to this large disease burden, two live attenuated, orally taken rotavirus vaccines (RotaTeq [RV5], Merck Vaccines, Whitehouse Station, NJ, USA, and Rotarix [RV1], GSK Biologicals, Rixensart, Belgium)² are recommended by WHO for use in all countries and especially in those with high mortality caused by diarrhoea.² By September, 2015, 79 countries had introduced one or other of these rotavirus vaccines.³ Most countries that introduced the vaccine early were high-income and middle-income countries in the Americas

and Europe, and these countries have provided much of the early evidence of the substantial effect of rotavirus vaccination. In Mexico, where rotavirus vaccine was introduced nationally in 2007, all-cause diarrhoea deaths in children younger than 5 years of age fell by 35–50% during 2008–11.^{4–6} Similar decreases of 17–39% in Brazil and 50% in Panama were documented after rotavirus vaccine introduction.^{7–9} Additionally, many other countries have noted a substantial reduction in the number of hospital admissions for all-cause diarrhoea and rotavirus after the rotavirus vaccine introduction.^{7,10–30}

Live oral vaccines, including those for rotavirus, have had poor performance in developing country settings.^{31–40} Although the reasons for this lower performance are

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Research in context

Evidence before this study

We searched PubMed for articles published since 2000 in any language using the terms “rotavirus” and “vaccine” and “sub-Saharan Africa” and “impact OR effectiveness”. Of the 42 articles identified, two articles examined the effectiveness of rotavirus vaccine in routine use in South Africa and Malawi and one study assessed the effect of rotavirus vaccine on disease burden in South Africa. We found no reports of the effect or effectiveness of rotavirus vaccine in Rwanda or of the effect or effectiveness of pentavalent rotavirus vaccine in sub-Saharan Africa.

Added value of this study

This study provides the first evidence of the effect of pentavalent rotavirus vaccine on the severe all-cause and

rotavirus diarrhoea disease burden in sub-Saharan Africa after introduction of the vaccine into the routine childhood immunisation programme. Diarrhoea and rotavirus-specific hospital admissions in Rwanda fell substantially after rotavirus vaccine implementation, including among older children age-ineligible for vaccination, suggesting indirect protection through reduced transmission of rotavirus.

Implications of all the available evidence

Our findings support the continued use of rotavirus vaccine in Rwanda and highlight the benefits of routine vaccination against rotavirus in low-income settings.

unknown and probably complex, possible explanations could be interference by maternal antibodies, concurrent oral polio vaccine administration, prevalent viral and bacterial gut infections, and malnutrition.⁴¹ Clinical trials for both the available rotavirus vaccines done in Africa and Asia showed modest efficacy (50–70%) compared with the high efficacy (85–98%) that was recorded in trials in Latin America, the USA, and Europe.^{42–46} In view of the substantial disease burden in Africa and Asia, the absolute burden of severe diarrhoea disease prevented in these settings is expected to be substantial even with moderately efficacious vaccines, but concerns remain about vaccine performance in these high burden settings.⁴⁴

In May, 2012, Rwanda became the first low-income country in Africa to introduce RV5 into its routine expanded programme on immunisation, with three doses given to infants at 6, 10, and 14 weeks of age. Rotavirus vaccine coverage in children younger than 1 year of age increased quickly to 50% in 2012, 99% in 2013, and 98% in 2014.⁴⁷ To monitor the effect of rotavirus vaccine in Rwanda, we studied trends in the number of hospital admissions for diarrhoea and rotavirus before and after the introduction of the rotavirus vaccine.

Methods

Trends in hospital admissions for diarrhoea

To assess trends in hospital admissions for diarrhoea nationally, we reviewed data from the Health Management Information System, which electronically captures monthly data for discharges from health facilities in Rwanda.⁴⁸ Data are reported to the national level using predefined discharge categories. We restricted our analysis to district hospitals that reported the number of hospital admissions for diarrhoea with or without dehydration in children younger than 5 years of age for every month from Jan 1, 2009, to Dec 31, 2014. We excluded children admitted with bloody diarrhoea and diarrhoea caused by chronic opportunistic infections as reported by the hospital.

To supplement Health Management Information System data, at four district hospitals (Kabgayi District Hospital, Muhima District Hospital, Musanze District Hospital, and Rwamagana District Hospital) and two teaching hospitals (University Teaching Hospital Kigali, University Teaching Hospital Butare), we reviewed the registries in the paediatric wards from Jan 1, 2009, to Dec 31, 2014, and abstracted the total number of admissions to hospital and the number of admissions to hospital for diarrhoea in children younger than 5 years by month of admission and age group (age <1 year vs 1–4 years).

Trends in rotavirus-specific hospital admissions and changes in rotavirus epidemiology

Active, sentinel surveillance for rotavirus diarrhoea following the standard WHO protocol⁴⁹ started in September, 2010, at one large urban referral hospital in Kigali, Rwanda, and was subsequently expanded to four additional hospitals (Kibagabaga District Hospital, Musanze District Hospital, Rwamagana District Hospital, and University Teaching Hospital Butare). In September, 2012, rotavirus surveillance was started at three more district hospitals (Kabgayi District Hospital, Kabutare District Hospital, and Muhima District Hospital), bringing the number of hospital surveillance sites to eight. Briefly, children younger than 5 years who presented to a sentinel hospital and met the case definition for diarrhoea (occurrence of three or more episodes of diarrhoea [stools of a less formed character than usual] within a 24 h period that began fewer than 7 days before the hospital visit) were enrolled and a stool specimen was collected within 48 h of admission to avoid detection of nosocomial infections. Stool specimens were refrigerated until testing for rotavirus antigen by enzyme immunoassay at the University Teaching Hospital Kigali laboratory, Kigali, Rwanda. Trends in rotavirus-specific admissions to hospital were studied at one hospital that had done surveillance continuously from Jan 1, 2011, through Dec 31, 2014, under technical supervision and support of WHO. Changes in rotavirus epidemiology

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