

The health benefits of rotavirus immunization for children in Palestine

Results of a vaccine impact analysis



Rotavirus vaccination in Palestine has significantly reduced the burden of diarrhea among children, and the benefits were sustained through a vaccine product switch.

Rotavirus represented a significant public health burden in both Gaza and the West Bank prior to the introduction of rotavirus vaccination. In 2016, the Palestinian Ministry of Health (MOH) added the rotavirus vaccine ROTARIX® to its routine immunization program. Working with the Rostropovich-Vishnevskaya Foundation (RVF), a global development and research organization that promotes the well-being of children, the Palestinian MOH demonstrated the significant health impact of the rotavirus vaccination program in children by analyzing surveillance data prior to and for two years following the introduction of ROTARIX.¹

In 2018, the MOH decided to switch to ROTAVAC®, a more affordable rotavirus vaccine made in India and prequalified by the World Health Organization (WHO). Through an economic analysis in partnership with RVF and the MOH, PATH confirmed that, while either vaccine was cost-effective, the switch to ROTAVAC was cost-saving to the MOH.² Building on the previous surveillance work, PATH also worked with RVF and the MOH to continue studying health indicators for an additional two years following the switch to ROTAVAC in order to confirm the continued health benefits of the rotavirus immunization program.

The results of this impact analysis confirm the significant benefit that the rotavirus immunization program has had on reducing the disease burden caused by rotavirus in Palestine. The findings also indicate that these benefits have been sustained through the transition from ROTARIX to ROTAVAC, providing reassurance of similar performance and safety across the two products. (Manuscript is in development for submission to a peer-reviewed journal.)

BACKGROUND

Rotavirus causes about one-third of child deaths due to diarrhea globally. In 2019, rotavirus caused an estimated 151,514 deaths in children younger than five years of age.³ Additionally, millions more children require home treatment and/or hospitalization each year, a considerable burden to families and communities. Young children with severe rotavirus diarrhea urgently need oral rehydration or intravenous fluids or risk dying from dehydration. In many low- and middle-income countries, this type of urgent care can be difficult to access, making rotavirus vaccination critical to saving children's lives worldwide.

WHO recommends that all national immunization programs include rotavirus vaccine.⁴ To date, more than 100 countries worldwide have introduced rotavirus vaccines.⁵ Many of these countries have observed swift and significant declines in diarrhea-related hospitalizations and deaths.⁶

Monitoring the trends in diarrheal and rotavirus-specific disease surveillance has been instrumental in documenting the impact of rotavirus vaccination in many countries. In the Eastern Mediterranean region, rotavirus accounted for up to 45 percent of diarrhea-related hospitalizations between 2010⁷ and 2015.⁸ In response, approximately two-thirds of countries in this region have adopted rotavirus vaccine into their national immunization programs.⁹

Before rotavirus vaccine introduction, 23 percent of diarrhea cases among children in Gaza and the West Bank occurred among children younger than six months of age—the highest proportion of all age groups.¹⁰ In the first year after the introduction of ROTARIX in 2016, the rotavirus vaccination program achieved a coverage rate of 97 percent of age-eligible infants. Two years later, RVF conducted a study of the impact of the vaccination program in children younger than five years of age. Results indicated a 27 percent drop in outpatient diarrhea cases in Gaza. In the West Bank, surveillance at a large children’s hospital showed a 65 percent decrease in rotavirus prevalence among pediatric outpatient and inpatient acute gastroenteritis cases.²

Additionally, rotavirus vaccination has been associated with a small increased risk of intestinal intussusception in certain locations, primarily in high- and middle-income countries. This was not previously evaluated in Palestine. While no association between ROTAVAC and intussusception has been found during vaccine development¹¹ or post-marketing surveillance in India,¹² it remains an important safety issue to monitor as use of the vaccine expands globally.

METHODS

PATH, RVF, and the Palestinian MOH conducted a public health impact analysis of the rotavirus vaccine product transition to ROTAVAC by building on existing surveillance activities in Gaza and the West Bank.

In Gaza, outpatient care of children is provided through a network of 22 clinics run by the United Nations Relief and Works Agency for Palestinian Refugees in the Middle East (UNRWA) and 28 clinics run by the Palestinian MOH. Both systems collect surveillance data on diarrhea cases due to any cause. This assessment utilized both UNRWA and MOH data.

In the West Bank, Caritas Baby Hospital performs laboratory testing for enteric pathogens, including rotavirus, for all children with acute gastroenteritis. Approximately two-thirds of the stool samples tested are from hospitalized children and the rest are from children seen at their outpatient clinic. For this assessment, data were collected on the prevalence of rotavirus-positive infections among all inpatient and outpatient diarrhea cases in children younger than five years of age.

To assess for the potential risk of intussusception associated with rotavirus vaccination in Palestine, the collaborators monitored for cases at two hospitals in 2019

and 2020. The Caritas Baby Hospital in Bethlehem is the main children’s hospital for the Southern parts of the West Bank, while the Al Shifa Hospital in Gaza City is the only hospital providing pediatric surgical services to the children living in Gaza. This analysis includes a review of these data.

These all-cause and rotavirus-specific diarrhea surveillance data were used to assess the impact of vaccine introduction on disease occurrence and proportion of rotavirus-positive diarrhea, respectively. Models for surveillance data collected compared three periods—pre-introduction (before May 2016), ROTARIX (May 2016 to September 2018), and ROTAVAC (October 2018 to March 2020)—to assess the effects of each vaccine separately. The models also compared just pre-introduction (before May 2016) and post-introduction (May 2016 to March 2020) to measure the overall impact of the two vaccines. Finally, the team also ran the models including data from April through September 2020 to assess possible disruptions due to the onset of the COVID-19 pandemic.

RESULTS

This analysis assessed the impact of the introduction of ROTARIX and subsequent switch to ROTAVAC in the Palestinian immunization program. Overall, both vaccines were associated with significant reductions in rotavirus prevalence and all causes of diarrhea with no safety concerns.

In Gaza, outpatient diarrhea cases decreased substantially following ROTARIX introduction and remained suppressed following the transition to ROTAVAC, indicating no disruption in health benefits. In the West Bank, the proportion of rotavirus-positive diarrhea also declined dramatically following ROTARIX introduction, with continued suppression after the transition to ROTAVAC.

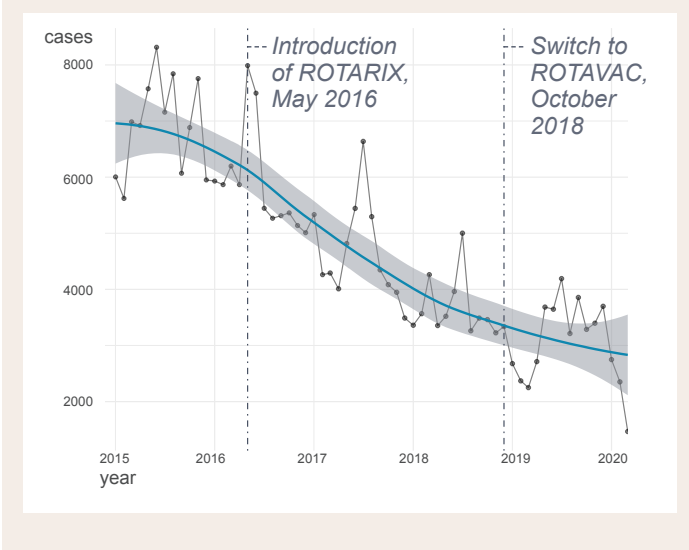
Surveillance in Gaza

During the pre-introduction period, outpatient clinics in both the UNRWA and MOH networks in Gaza combined recorded an average of 6,760 cases of diarrhea per month. After rotavirus vaccine was introduced in May 2016, Gaza saw an annual decline in cases of 19 percent over the ROTARIX period, with an additional 4 percent annual decline in the ROTAVAC period. Both decreases are superimposed on a distinct seasonal pattern with peaks in the summer months, as shown in Figure 1.

When combining the ROTARIX and ROTAVAC periods, there was a 55 percent total decrease in diarrhea cases due to any cause compared to the pre-introduction period.

While the full analysis only included data through March 2020, a follow-on analysis incorporated data from April to September 2020. These data showed a continued decline in diarrheal cases while using ROTAVAC. However, work is ongoing to fully understand the impact of disruptions due to the COVID-19 pandemic on health care utilization in Gaza.

Figure 1. All-cause diarrhea cases by month and year in Gaza, January 2015 to March 2020.



Surveillance in the West Bank

Data from Caritas Baby Hospital in West Bank showed reductions in the average monthly number of both rotavirus-positive and overall diarrhea cases after introduction. The data also showed a decline in the proportion of diarrhea cases testing positive for rotavirus. Figure 2 illustrates the decrease in rotavirus-positive and -negative diarrhea by month after both rotavirus vaccine introductions.

Rotavirus positivity rates decreased from an average of 30 percent of all cases of diarrhea (200 rotavirus cases per month) in the pre-introduction era to 12 percent of all cases of diarrhea (115 rotavirus cases per month) following ROTARIX introduction. This reflects a 64 percent reduction in rotavirus positivity rates after ROTARIX introduction.

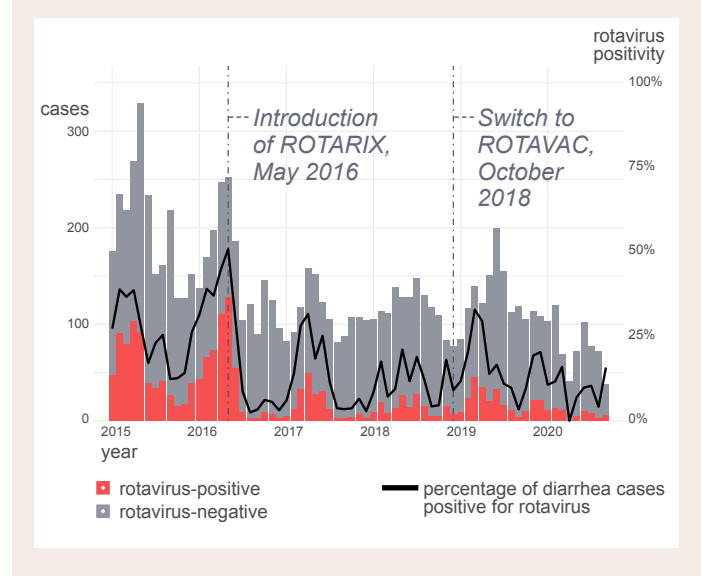
When combining the ROTARIX and ROTAVAC periods, there was a 69 percent overall reduction in rotavirus positivity compared to the pre-introduction period.

When data from April through September 2020 are added, these rates show a continued decline. As with the assessment in Gaza, work is ongoing to fully understand the impact of disruptions due to the COVID-19 pandemic on health care utilization in the West Bank.

The West Bank also observed seasonality of rotavirus infections but with peaks in the winter months instead of the summer months, as was seen for diarrhea cases due to all causes in Gaza.

Consistent with the variation in rotavirus disease burden seen across age groups, significant differences in vaccine impact by age were also observed. Reductions in rotavirus cases following vaccine introduction were seen in all children younger than five years of age, but the greatest reduction was seen in the 6- to 11-month age group—those at highest risk of rotavirus who had been targeted for vaccination—in 2017. This reduction was sustained in subsequent years and supplemented by a greater impact in the 12- to 23-month age group in 2018, reflecting protection among children who had been immunized two years prior. A smaller but still significant reduction in rotavirus cases in children older than 24 months, who had been ineligible for vaccination during the first years of the program, may reflect some indirect or “herd” protection due to decreased virus circulation within the community.

Figure 2. Rotavirus-positive and rotavirus-negative outpatient and inpatient diarrhea cases by month and year at Caritas Baby Hospital, West Bank, January 2015 to September 2020.



Intussusception

Surveillance for intussusception revealed a small number of cases. In Gaza, 42 intussusception cases in infants younger than 12 months of age were confirmed between November 2018 and June 2020. In the West Bank, 53 suspected intussusception cases in infants were reported at Caritas Baby Hospital from 2015 to 2019. None of the cases occurred during the potential high-risk period of 21 days following the first dose of rotavirus vaccine, providing reassurance that intussusception remains unrelated to rotavirus vaccination.

CONCLUSIONS AND IMPLICATIONS FOR OTHER COUNTRIES

Between 2016 and 2020, rotavirus vaccination resulted in a 55 percent decrease in all causes of diarrhea in Gaza and a 69 percent decrease in rotavirus positivity rates in the West Bank. These benefits have been sustained through a rotavirus vaccine product switch.

This impact analysis encompassed two different surveillance activities, one tracking clinical diarrhea cases of any cause, and the other tracking rotavirus-specific diarrheal disease. These activities cover two separate,

References

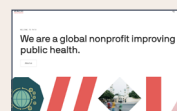
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non-overlapping populations in Gaza and the West Bank, with minimal travel between the territories. Despite these differences, these two sets of data provide complementary indications of rotavirus vaccine impact in Palestine, one providing scale and the other providing specificity.

The UNRWA and MOH surveillance of all-cause diarrhea in Gaza offers a robust proxy indication of the impact of the vaccination program on the burden of rotavirus in children. Surveillance in the West Bank provides more focused information on pathogen-specific disease and benefits from having been operational for several years. Both assessments present strong evidence that the rotavirus immunization program has had a substantial impact on reducing the burden of rotavirus disease among children in Palestine. Additionally, the transition from ROTARIX to ROTAVAC continued to build on the significant health benefits of the rotavirus immunization program, with no adverse effects on protection during or after the transition.

Any WHO-prequalified rotavirus vaccine can successfully reduce the burden of rotavirus diarrhea in young children. Assessing a variety of characteristics, including cost, cold chain requirements, and doses required, will help decision-makers choose the best vaccine for their country.

ADDITIONAL RESOURCES



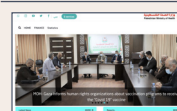
PATH website
www.path.org



PATH's Defeat Diarrheal Disease (DefeatDD) Initiative
www.DefeatDD.org



Rostropovich-Vishnevskaya Foundation
www.rostropovich.org



Palestinian Ministry of Health
www.moh.gov.ps/portal/en/



Rotavirus Organization of Technical Allies (ROTA): Vaccine Evidence
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