Rotavirus Seasonal Distribution and Prevalence Before and After the Introduction of Rotavirus Vaccine in a Peri-Urban Community of Lima, Peru

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Abstract. We evaluated the monthly distribution of rotavirus diarrhea in a cohort of children 12–24 months of age followed as part of a diarrhea clinical trial in a peri-urban community of Lima. We observed a peak of rotavirus diarrhea in the winter months and a decrease in rotavirus prevalence after the introduction of the rotavirus vaccine in Peru.

INTRODUCTION

Severe gastroenteritis caused by rotavirus is a leading cause of childhood illness and death, particularly in developing countries.¹ Rotavirus vaccines are effective against severe rotavirus diarrhea and, if implemented appropriately, have the potential to reduce child mortality in low-income countries.² Rotavirus exhibits distinct seasonality, and has been known as “wintery diarrhea” in some parts of the world, although the effect of season on rotavirus incidence is not as extreme in the tropics as it is in temperate areas of the world.³ In Peru, although there is one review of rotavirus incidence, hospitalization, and deaths,⁴ there are no publications on rotavirus seasonality or vaccine impact after its introduction in the Peruvian National Immunization Program in 2008–2009. The aim of this study was to explore the seasonal distribution of rotavirus diarrhea in a peri-urban community of Lima, particularly after the introduction of the vaccine.

MATERIALS AND METHODS

We performed a secondary analysis on data from a community-based randomized double blind controlled trial of lactoferrin for prevention of diarrhea in Peru.⁵ Children 12–18 months of age from the District of Independencia in Lima, previously weaned, were enrolled and randomized to receive bovine lactoferrin or placebo for 6 months, with a twice daily home visit to administer the intervention and monitor diarrhea. A stool sample was collected in each diarrheal episode to determine the presence of pathogenic bacteria, viruses, and parasites.⁵ For rotavirus an immunochromatography test for rotavirus-adenovirus was used (Operon, Huerva-Zaragoza, Spain). Children with diarrhea received oral rehydration solutions and/or antimicrobials as clinically indicated and were evaluated monthly for growth measurements. Because the lactoferrin intervention did not have an impact on the overall diarrhea incidence rates and pathogen-specific diarrhea rates,⁵ for this analysis we used the longitudinal data on the lactoferrin and control groups combined together. The overall diarrhea incidences were calculated monthly, and the attributable fraction caused by rotavirus. Yearly rotavirus prevalence was compared with a χ^2 test. The main study was approved by the ethics Institutional Review

Board of Universidad Peruana Cayetano Heredia and the University of Texas Health Science Center at Houston.

RESULTS

The study was conducted from January 2008 through May 2011 in the District of Independencia, Lima. A total of 555 children were enrolled; accounting for 91,446 child/days of observation. In this community the rotavirus vaccine was introduced in early 2009. Of the enrolled children eligible for rotavirus vaccination (born after January 2009, $N = 132$), 97 children received both doses, 10 were partially vaccinated, 8 did not receive the rotavirus vaccine, and 17 had no data. In Peru the 2-dose-schedule rotavirus vaccine (Rotarix) was implemented.

During this period 1,235 diarrhea episodes were evaluated; only 52 cases of rotavirus diarrhea were detected throughout the study. The prevalence of rotavirus among diarrhea episodes was 8.2% (26 of 316) in 2008, 4.1% (15 of 362) in 2009, and 2.4% (11 of 450) in 2010. In 2011 there were no cases of rotavirus diarrhea (0 of 107); however, the study was conducted only until May 2011. There was a significant decrease in rotavirus prevalence from 2008 to 2010 in this community-based cohort ($P < 0.001$). The average age of the rotavirus episodes was 18.6 ± 2.5 months during 2008–2009 versus 19.1 ± 2.7 months during 2010–2011 ($P < 0.01$). The monthly diarrhea and rotavirus incidences were plotted and the percentage of diarrheal episodes caused by rotavirus (Figure 1). In this active surveillance study the diarrhea incidence ranged from 0.010 to 0.025 episodes/child/day. Rotavirus incidence was higher in the winter season (June through August).

DISCUSSION

In this study population we found a seasonal distribution of rotavirus diarrhea in children, with a clear peak during the winter months in Lima (June–August), and a significant decrease in diarrhea rotavirus prevalence, which seems to happen after the introduction of the rotavirus vaccine in this setting. These findings are in concordance with observations reported in other regions. In recent years the geographic differences in temporal trends in rotavirus activity have seemed less pronounced, but continue to be observed, especially after the introduction of vaccination.⁶

In this community-based cohort we found a significant decrease in rotavirus prevalence from 2008 to 2010. This could be attributable to direct protection from the vaccine and/or a secondary effect as a result of reduced transmission

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FIGURE 1. Monthly overall diarrhea incidence and rotavirus incidence in children in peri-urban Lima from March 2008 through May 2011. The dots (•) represent the monthly diarrhea incidence in episodes/child/day; the line (---) represents the average monthly diarrhea incidence; the dotted line (.....) represents the monthly rotavirus diarrhea incidence in episodes/child/day; and the black line (—) represents the percentage of rotavirus of all diarrhea cases at the beginning of each month.

of rotavirus in the community, particularly given that the children are past infancy during the follow-up period. Although the original cohort was not designed to look at this outcome, it is suggestive of a positive impact of rotavirus vaccination in community cases in peri-urban Lima. Similar results have been described in Latin America, where the introduction of rotavirus vaccine in the childhood immunization programs were highly efficacious in preventing severe rotavirus episodes and rotavirus deaths in children < 5 years of age.² In Peru, although there is no information of nationwide rotavirus-specific diarrhea rates, there has been a trend toward less overall acute gastroenteritis rates in all three regions of the country (Coast, Andes, and Jungle) from 2008 to 2011.⁷

Before the introduction of the rotavirus vaccine in the Peruvian National Immunization Program, Ehrenkranz and others⁴ estimated the rotavirus disease burden in Peruvian children based on published and unpublished reports over a 10-year period. They concluded that by 5 years of age, > 63% of Peruvian children will have experienced an episode of rotavirus diarrhea, 1 in 10 will seek care at a clinic, 1 in 20 will be hospitalized, and about 1 in 375 will die of this disease. Therefore, there was a need for a rotavirus vaccine in the country, with important potential cost savings in the outpatient and inpatient settings. Although the current study is small and the population is not representative of the Independence District, Lima or Peru, it is suggestive that now we are starting to see the impact of this important investment of the Peruvian government. One limitation of the current study is the characteristics of the study group: lack of children < 1 year of age and > 2 years of age and the short individual follow-up period. Other limitations are the lack of rotavirus genotyping analysis and no data on rotavirus mortality rates.

However, we know that despite vaccination, mild and moderate rotavirus cases will continue to occur in the community setting. Therefore, it is important to know and monitor the local seasonal distribution of this disease to allocate resources for proper diagnosis and management. Proper diagnosis or rotavirus diarrhea will reduce the usage of antibiotics

in pediatric patients, which is extremely high in peri-urban Lima.⁸ Rapid and easy diagnostic tests for rotavirus in children with acute diarrhea in primary care facilities can reduce unnecessary antibiotic prescriptions.⁹ A targeted seasonal strategy for diagnostic test recommendations should be implemented. Future studies are needed in other regions of Peru to confirm these findings.

In terms of proportions, the diarrheal episodes caused by rotavirus do decrease after vaccine introduction, but information on ages of affected children, and whether they were vaccinated or had vaccinated siblings, would be useful to understand whether this is attributable to direct protection from vaccine or a secondary effect caused by reduced transmission of rotavirus in the community, particularly given that the children are past infancy during the follow-up period.

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