Transactions of the Royal Society of Tropical Medicine and Hygiene 106 (2012) 445–451

Contents lists available at SciVerse ScienceDirect

Transactions of the Royal Society of Tropical Medicine and Hygiene

journal homepage: http://www.elsevier.com/locate/trstmh

Factors associated with rotavirus diarrhoea in children living in a socially diverse urban centre in Brazil

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ARTICLE INFO

Article history:
Received 23 July 2009
Received in revised form 3 February 2012
Accepted 3 February 2012
Available online 30 May 2012

Keywords:
Rotavirus
Diarrhoea
Children
Risk factors
Brazil

ABSTRACT

A case–control study, aimed at identifying factors associated with rotavirus diarrhoea cases presenting to health facilities, was conducted in children from low-income and middle-low-income families in Brazil. Cases were 390 children with diarrhoea and rotavirus in stools; controls were 1674 children without diarrhoea presenting to the same facilities. Data were collected by questionnaire and observations during home visits. Explanatory variables were grouped according to a conceptual model of causation. The ORs by non-conditional logistic regression and population-attributable fractions were calculated. Socioeconomic factors contributed a third of cases, followed by contact with diarrhoea cases and by not being breast fed. In cases aged <1 year, not being breast fed was the main determinant, followed by socioeconomic factors, and crowding and contact outside the home; in older children, socioeconomic factors followed by contact inside and outside the home were the main determinants. Environmental and sanitation variables were not associated with diarrhoea in the final model, and socioeconomic factors were only partly mediated by proximal variables. Transmission of rotavirus appears to be mostly by person-to-person contact, and shows marked social differentials not explained by the biological factors studied. The rotavirus vaccine is unlikely to protect against the full range of circulating genotypes of rotavirus, and understanding rotavirus epidemiology remains essential to the development of control policies.

1. Introduction

Rotaviruses cause approximately 138 million episodes of diarrhoea a year in under-fives worldwide, resulting in 25 million clinic visits, 2 million hospitalizations, and 440 000 deaths.[1] The incidence of rotavirus diarrhoea is similar in developing and developed nations, but mortality by the age of 5 years is 200 times higher in low-income than in high-income countries.[1] Rotaviruses were detected in Brazil for the first time in 1976,[2] not only in patients with diarrhoea[3–5] but also in sewage, rivers and creeks.[6,7] In Brazil, rotaviruses are associated with 12–42% of hospitalized acute cases of diarrhoea in children, and community–based studies indicated an average incidence of 0.25 rotavirus-related diarrhoeal episodes per child-year.[4] In the city of Salvador, where this

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doi:10.1016/j.trstmh.2012.02.001

study was conducted, 8% of children with acute diarrhoea in a community-based study,[8] and one in three children hospitalized with acute diarrhoea[9] had rotavirus in stools.

Increased severity of diarrhoea leads to increased levels of medical attention, and where cases are recruited (community, health facility, hospital) will influence which risk factors are identified in research studies. Risk factors for rotavirus diarrhoea were studied in a range of settings.[10–21] The emerging pattern, although the risks were not always statistically significant, is that contact with another case of diarrhoea (in the home or outside the home) increased the risk, and breast feeding decreased the risk, in almost all settings. Day care (and in particular the first month of day care attendance) was found to increase the risk of presenting in studies based in a health facility or a hospital, and low birth weight increased the risk in hospital studies. Proxy variables for poverty such as the education of mother and poor housing carried an increased risk of presentation to a health facility and hospitalization. Food-handling hygiene and sanitation were investigated, with inconsistent results, only in a few studies (Supplementary Table 1).

This study aims to further our understanding of the factors associated with rotavirus diarrhoea presenting to a health facility in a socially variable urban setting in a middle-income country.

2. Methods

2.1. Study design, study population and data collection

The study was carried out between 2002 and 2004 in Salvador, Brazil which has a population of 2.5 million and marked socioeconomic inequalities. This analysis is part of a wider case–control study, investigating determinants of diarrhoea presenting to a health facility, by specific aetiologic agents, in children aged 0–10 years.[22] Cases were children presenting with diarrhoea as a main complaint in five health facilities of Salvador, which are owned by, or sell their services to, the public health system, and controls were selected from children attending the same health facilities, at well-baby consultations or because of other health problems not related to diarrhoea, such as orthopaedic procedures or evaluation before a surgical operation. There was imbalance between health centres in numbers of controls recruited; this reflected the proportion of children attending for diarrhoea compared with other causes suitable for inclusion as controls in each of the units. Rotavirus vaccine was not an issue, because the study was conducted before it was licensed In Brazil (in July 2005) and later introduced in routine vaccinations in 2006. Controls were frequency matched to cases by age and health insurance, as a proxy of socioeconomic status. Potential cases and controls who reported any episode of diarrhoea during the preceding 3 weeks were excluded. The person responsible for the child answered a questionnaire on socioeconomic conditions, characteristics of the dwelling and the domestic and peridomestic environment, child's health and occurrence of exposures to risk factors, defined as transient,[23] in the 10 days preceding the beginning of the diarrhoea episode, or the interview for controls. One week after the interview, a home visit was made, and complementary information about the house and the peridomestic environment was collected by direct observation, together with information, for cases, about the episode itself. Cases gave a stool sample, and were only included in the study when the sample was obtained. One out of approximately five control children, frequency matched by age, was asked for a stool sample; if the child was unable to provide one, the following child in the list would be asked until the sample was obtained. Seventy-three percent of the stool samples were collected at the first contact, and the remainder at the home visit. In this investigation, cases are the children with diarrhoea who tested positive for rotavirus, and controls are all the children without diarrhoea. None of the 384 controls who provided stools had rotavirus infection at the laboratory examination.

2.2. Laboratory examinations

Approximately 10% (wt/vol) suspensions in Tris-HCl Ca+2 0.01 M (pH 7.2) were prepared from the faecal specimens. Group A rotaviruses were detected by a combined enzyme immunoassay for rotavirus A and adenovirus (EIARA),[24] following the instructions of the manufacturer (Bio-Manguinhos, Oswaldo Cruz Foundation, Ministry of Health, Brasilia, Brazil). Concomitantly, stool suspensions were used for dsRNA extraction by the glass powder method,[25] followed by polyacrylamide gel electrophoresis (PAGE).

2.3. Data analysis

There were 390 cases and 1674 controls. At a significance level of 5%, this study had an 80% power to detect ORs of at least 1.45 for factors with an exposure frequency between 20% and 70% among the controls. The analyses were carried out following a pre-defined conceptual causal model (Figure 1), similar to the framework suggested by Victora et al.,[26] which maps the proposed relationships between social and biological determinants of rotavirus diarrhoea, separating direct biological causes from the social determinants that must act through a biological cause. In our model, socioeconomic factors occupy the most distal level. Three blocks at the intermediate level include the routes of pathogen transmission in diarrhoea (environmental contamination, food handling/preparation and person-to-person contact). The third and most proximal level includes only breast feeding.

Non-conditional logistic regression models were used to estimate the association between diarrhoea and potential determinants; all the models included age, as a continuous (months) variable, and gender as confounding factors, and the health centre of enrolment as a random effect factor. The random effect was used to model the heterogeneity of diarrhoea risk across the health centres that is not explained by the variables in the model (the so-called fixed effects). The Wald test was used to assess the significance of the associations. The covariates that, in these initial models, presented a p-value $\leq$0.20 were admitted to the next step, of intrablock backward selection, and only the covariates with p-values $\leq$0.05 at this second step