Rotavirus Disease in Guinea-Bissau, West Africa: A Review of Longitudinal Community and Hospital Studies

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Rotavirus is one of the most common causes of childhood diarrheal disease and deaths in sub-Saharan Africa. This article reviews community- and hospital-based surveillance of rotavirus disease in Bissau, Guinea-Bissau, West Africa. Here, rotavirus infections exhibit a seasonal pattern, with annual epidemics occurring during the relatively dry and cooler months, from January to April, and few cases registered from May to December. Most children (74%) experience their first infection before the age of 2 years, and rotavirus has been identified as the most pathogenic of all diarrheal agents during 2 large prospective studies involving several hundred children <5 years of age. In the hospital setting, rotavirus accounts for a high case-fatality ratio (8%) and a high rate of nosocomial transmission; during the rotavirus season, 23% of all children admitted for nonrotavirus diarrheal disease acquired rotavirus infection during hospitalization (>48 h after admission).

There is currently a global effort to accelerate the introduction of new vaccines against rotavirus, one of the most severe diarrheal diseases. These attempts, which are supported by major health organizations, including the World Health Organization, the GAVI Alliance, and Program for Appropriate Technology in Health (PATH), are explained by the fact that infants and young children worldwide are heavily affected by rotavirus disease; unlike with other causes of diarrhea, the common hygienic measures appear to be ineffective in preventing rotavirus infection, and no specific treatment is available. Thus, vaccination is the cornerstone strategy to control rotavirus infection. Recent estimates suggest that diarrhea accounts for 13%–21% of all deaths in children <5 years old [1]. Globally, it is estimated that 20%–70% of all hospitalizations due to diarrhea in young children and 20% of diarrheal deaths are caused by rotavirus [2]. Although industrialized as well as developing countries are affected by rotavirus disease, the death toll is substantially higher in developing countries, and in Sub-Saharan Africa alone, ~110,000–210,000 children die each year from rotavirus infection [3, 4].

Patterns of Rotavirus Infection in the Community

Rotavirus disease constitutes one of the most important diarrheal infections in Guinea-Bissau. It is seasonal, occurring during the cooler months from January through April. In the period outside that season, very few cases are registered in the hospitals or in the community (Figure 1).

Almost all children in Guinea-Bissau experience a rotavirus infection before the age of 3 years [3]. During a prospective community follow-up of a birth cohort up to 2 years of age in Bissau from 1996 to 1998, almost...
half of the children had already had their first infection within the first year of life, and 74% had been infected by 2 years of age [5] (Figure 2). Most infections were asymptomatic within the first 3 months of life (protection provided by maternal antibodies), but only a few infections were asymptomatic in children 9–11 months of age (when maternal antibodies no longer confer protection and the majority of children contract their primary infection). The prevalence of asymptomatic infections increased in children >18 months old owing to protection conferred by previous infections. This relation was mirrored in the proportion of symptomatic infections that decreased in subsequent reinfections (44% during first infections and 20% during second and third infections) [5]. In Bissau, there is a strong tradition of breast-feeding, with an initiation rate of >99% and a median duration of 22.6 months [6]. Breast-feeding practices and maternal antibody levels are undoubtedly important in providing protection against clinical disease [7], although the level of protection attributed to breast-feeding is considered low in most studies [8]. A low pathogenicity of rotavirus disease has also been observed in children >18 months old, a pattern that might be explained by the natural immunity conferred by previous infections [9, 10].

After the first contact with the infection, some degree of natural immunity is acquired against subsequent rotavirus infections and diarrhea; the protection in Bissau is estimated to be 52% for reinfection and 70% for diarrhea [5]. The protection against reinfection and diarrhea estimated from the studies in Bissau is in accordance with estimates from other study sites [11]. Although there is a high degree of protection against subsequent rotavirus diarrhea, the protection seems to decrease over the following seasons. Whether this finding is due to waning immunity or a shift in genotypes and lack of cross-immunity from one season to another is unclear and needs to be explored. However, it is clear that the evaluation of efficacy of future rotavirus vaccines should cover ≥2 seasons.

In the analyses of pathogens identified in the fecal samples collected during weekly morbidity surveys in the project area, the pathogenicity of infectious agents was compared and expressed as an odds ratio, that is, the odds of a pathogen-positive specimen being collected from a child with diarrhea divided by the odds of a pathogen-negative specimen being collected from a child with diarrhea. Rotavirus constituted the most pathogenic of enteric infections determined in the fecal samples collected during weekly morbidity surveys in the project area (odds ratio for pathogenicity, 5.07; 95% confidence interval [CI], 3.39–7.46) [12]. The overall incidence rate of rotavirus infection in the community was 0.6 cases per child-year, whereas the incidence of rotavirus infection associated with diarrhea was 0.22 cases per child-year, and 0.3 cases per child-year for children aged 3–17 months [5].

Figure 1. Cumulative incidence of primary rotavirus infections in a birth cohort of 200 children followed until 2 years of age in Guinea-Bissau, 1996–1998 [5].
Rotavirus Disease in Guinea-Bissau

PATTERNS OF ROTAVIRUS INFECTION IN THE HOSPITAL

Many of the patterns detected in the longitudinal community surveillance could also be found in the hospital setting. During a hospital-based surveillance study conducted from April 2001 to May 2002 and from January to June 2003 at the only pediatric ward in Bissau, stool samples from all patients admitted with diarrhea or presenting with diarrhea during hospitalization were screened for rotavirus infections using enzyme-linked immunosorbent assay [13]. Among all patients admitted with diarrhea, 33% had rotavirus infection, as did 12% of children who developed diarrhea during hospitalization [14]. As observed in the community studies, children <2 years old were more commonly affected by rotavirus diarrhea than children in other age groups; 93% of the cases registered in children <2 years of age; all but 6 infants were >2 months of age [13]. Fever (risk ratio, 1.56; 95% CI, 1.64–2.10) and vomiting (risk ratio, 1.38; 95% CI, 1.11–1.73) were more commonly observed among patients with rotavirus diarrhea than among those with nonrotavirus diarrhea.

Rotavirus is a common cause of nosocomial infection [14]. Rotavirus was detected in stools of 24 (23%) of 105 children who presented with diarrhea only >48 h after admission. The overall rate of nosocomial rotavirus diarrhea was 1.6 cases per 1000 child-days (95% CI, 1.02–2.51) among 1738 patients present in the ward during the rotavirus infection season, who were followed for 11,847 child-days at risk. The probabilities of contracting nosocomial rotavirus infection were similar for boys and girls (rate ratio, 1.11; 95% CI, 0.45–2.77). The number of cases per 1000 child-days was 2.13 (95% CI, 1.06–4.25) for children <12 months of age, 3.09 (95% CI, 1.47–6.48) for children ≥1 and <2 years of age, 1.49 (95% CI, 0.48–4.65) for children ≥2 and <3 years of age, and 0.76 (95% CI, 0.11–5.43) for children ≥3 and <4 years of age [13].

MORTALITY DUE TO ROTAVIRUS INFECTION

Based on studies from Guinea-Bissau, it has been estimated that 145,000 deaths due to rotavirus infection occur in sub-Saharan Africa every year [15]. The rotavirus death rate in Guinea-Bissau is estimated to be 3.4 death per 1000 children among infants <1 year of age and 0.8 deaths per 1000 children aged 1–4 years. These figures were observed in a situation where the overall diarrheal death rate was 26.6 deaths per 1000 children in infants, and 18.2 deaths per 1000 children aged 1–4 years. A high rotavirus case-fatality ratio (8%) was observed in the hospital [13].

GENOTYPE CHARACTERIZATION OF ROTAVIRUS IN GUINEA-BISSAU

There is a variation from one year to another in the prevalence of different genotypes, as well as interseasonal variation [16, 17]. This is not surprising and seems to be explained by the fact that a great number of individuals develop immunity to
the circulating genotypes. The most frequent genotypes in the world—G1P[8], G3P[8], G4P[8], and G2P[4] [18]—are underrepresented in Bissau [16], where uncommon genotypic combinations, such as G2P[6] and G2P[8], were detected at high frequencies in 1996–2002 [16, 17, 19]. Mixed infections and animal-like genotypes, such as G8 and long G2 strains, are common. The finding of genotypes with a likely zoonotic origin is not surprising, because humans and domestic animals live side by side in the highly crowded study area. Pigs and goats commonly sleep inside people’s homes to protect the animals against theft. More recent strain characterization in 2001–2002 showed G2P[4]P[6], G2P[4], G2P[6], and G8P[6] to be the most common strains [17]. Overall, 37% of isolates had a mixed genotype, and >60% of isolates had the genotype G8, either as a single G strain or in combination with other G types.

In Guinea-Bissau, rotavirus infection is an important cause of morbidity and mortality, contributing to the high burden of diarrheal diseases. Not only are hygienic measures unlikely to control this infection, but the socioeconomic conditions in Bissau, with high levels of crowding, are also likely to exacerbate the situation [20]. The use of new effective vaccines is therefore the main preventive measure strategy to control the disease. Results from our setting would suggest that the vaccination schedule should take into account the strong breast-feeding practice, with the possibility neutralized antigens, but also the fact that most cases of rotavirus-associated diarrhea are observed among children aged 3–24 months.

Another issue that should be considered is the genotype variation from one season to another. When a rotavirus vaccine is introduced into the population, continuous rotavirus strain surveillance should be conducted for several seasons. It should also be considered whether vaccines demonstrate a similar decrease in protection against reinfection and diarrhea in the subsequent season, similar to that observed after natural infection. If so, it might be necessary to provide a booster dose before the second rotavirus season to prevent rotavirus-associated diarrhea during the second year of life. Children being admitted to the hospital could be considered another target for a booster dose because of the observed high rates of nosocomial infection in a situation where hygienic measures are unlikely to prevent infection and the fact that nosocomial infection is also present among older children. The prevention of nosocomial rotavirus infections is of practical importance not only in developing countries, because as studies from Europe and United States [21] have demonstrated similar high rates of nosocomial rotavirus infections. However, in Guinea-Bissau, implementation of a booster dose at hospitalization might be needed only as a temporary solution until full national coverage is in place and the overall national rates of infection are decreasing accordingly.

References