Clinical severity and seasonal trends of non-rotavirus diarrheagenic viruses in children under five in three sub-Saharan African countries post-rotavirus vaccine introduction: The Vaccine Impact on Diarrhea in Africa (VIDA) Study

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Background

As rotavirus vaccine (RVV) uptake increases, other viral enteropathogens will likely comprise a greater fraction of moderate-to-severe diarrhea (MSD) among children <5. The 3-year case-control Vaccine Impact on Diarrhea in Africa (VIDA) study in The Gambia, Mali, and Kenya assessed the attributable fraction (AF), clinical, and epidemiologic features of adenovirus 40/41 (AdV40/41), astrovirus, norovirus GII (NV-II), and sapovirus compared to RV following introduction of RVV.

Methods

MSD cases (children with diarrhea (≥3 loose stools/24h), plus dysentery, sunken eyes, decreased skin turgor, IV rehydration, or hospitalization) were enrolled from health centres. Randomly-selected, diarrhea-free matched controls were enrolled from home. A stool sample provided at enrolment by cases and controls was tested for enteropathogens using qPCR. Attributable fractions (AFs) for each pathogen were calculated using conditional logistic regression, adjusting for other pathogens and including interactions with age group and site; for cases, individual AFs ≥0.5 were considered etiologic. Severity was assessed using the modified Vesikari score (MVS).

Results

We enrolled 4840 cases and 6213 controls. Combining sites and age groups, the AF was 11.4% for RV; 3.5% for NV-II; 3.1% for AdV40/41; 2.9% for astrovirus; and 2.3% for sapovirus. NV-II (n=211, median=9 months) and AdV40/41 (n=130, median=11 months) peaked in infancy; RV (n=585, median=13 months), astrovirus (n=123, median=15 months) and sapovirus (n=135, median= 19 months) peaked in increasingly older children. RV peaked in the cool season in Mali and The Gambia; astrovirus and sapovirus peaked during the two cool seasons in Mali, AdV40/41 peaked in the rainy season in The Gambia. In Kenya NV-II peaked in the dry season.

Relative to RV-MSD (median MVS: 11), cases attributed to NV-II (median MVS: 10), sapovirus (median MVS: 9), and astrovirus (median MVS: 8) were milder (p < 0.01, t-test for each). Cases attributed to AdV40/41 (median MVS: 11), however, had similar severity to RV cases (p=0.0515, t-test).

Conclusions

Viral enteropathogens comprise nearly 25% of MSD. RV remains the predominant cause, equal to all other viral enteropathogens combined. Whereas AdV40/41 and RV MSD have comparable severity, other viruses cause milder disease. Seasonality varies, with RV, astrovirus, and sapovirus favouring cool temperatures.