

Rotavirus Genotype Trends and Gastrointestinal (GI) Pathogen Detection in the United States, 2013-16: Laboratory Results from the New Vaccine Surveillance Network (NVSN)

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Background

The availability of vaccines has resulted in an escalation of post vaccine introduction strain surveillance efforts globally. The New Vaccine Surveillance Network (NVSN) has conducted active AGE surveillance in the USA since 2006 and currently operates at pediatric hospitals and emergency departments at 7 geographically diverse sites. Stool samples from AGE cases are forwarded to the Centers for Disease Control and Prevention (CDC), Atlanta for RVA genotyping and multiple GI pathogen testing. Here we report genotyping and multipathogen testing results for RVA AGE cases detected through the NVSN during the 2013-2016 RVA seasons.

Methods

From 2013 to 2016, 1160 RVA antigen-positive stool samples from the 7 sites were collected from AGE cases \leq 18 years of age. RVA RNA was extracted and then amplified using multiplexed one-step RT-PCR or qRT-PCR genotyping assays targeting the most common human RVA G and P genotypes, as well as Rotarix and RotaTeq vaccine strains. For genotype confirmation and advanced molecular characterization of vaccine strains, rare strains, and lineage variants, a subset of samples were subjected to Sanger and/or next generation sequencing. To test RVA cases for co-infection with other GI pathogens, total nucleic acid extracts from stool were assayed with the Luminex xTAG Gastrointestinal Pathogen Panel (GPP), which detects and differentiates 15 GI pathogens.

Results

Of the RVA antigen-positive samples submitted to CDC, 848 (73.1%) contained amplifiable RVA RNA by one-step RT-PCR or qRT-PCR assays. Out of these, 805 (94.9%) were fully genotyped, while 43 (5.1%) were non-typeable. Of typeable, 622 (77.3%) were collected from children \leq 5 years of age, while 183 (22.7%) were from children $>$ 5 years of age. Genotype analysis of samples from both age groups revealed that G12P[8] was the dominant genotype in all 3 seasons, identified in 72.2% of strains nationally. G12P[8] has been the predominant RVA genotype detected by the NVSN since 2012. Genotype G2P[4] was the second most common strain (8%), followed by G1P[8] and G9P[8] (7% and 4%, respectively). Vaccine strains (RotaTeq and Rotarix) were detected in 0.2-3.3% of genotyped samples each season. Uncommon/unusual strains (e.g., G12P[4], G3P[4], G2P[8], G12P[6], G6P[8], G2P[6], G3P[6] and G9P[4]) were detected sporadically. Mixed genotypes such as G9G12P[8] were also identified in $<$ 1% of strains genotyped. GPP testing results showed that RVA was the only pathogen detected in 619 of the AGE cases (73%), while RVA plus one or more GI pathogens were detected in 169 (20%) of the samples. Rotavirus was not detected in 60 (7%) of the AGE cases. The most common RVA co-infections

were with Shigella (22.7%), Norovirus (18%), Clostridium difficile (16.3%), Adenovirus 40/41 (8.7%) and Salmonella (8.1%).

Conclusion

This study shows the continued predominance of genotype G12P[8] as the major cause of RVA AGE through the 2014-2016 seasons and in 20% of RVA AGE cases, one or more additional GI pathogens was detected. Continuous surveillance is required to monitor the long-term effects of vaccine use on the epidemiology and evolutionary dynamics of circulating RVA strains as well as non-rotavirus etiologies of AGE.