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Her research focuses on different aspects of acute gastroenteritis in young children in Vietnam.

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The prevalence and phylodynamics of norovirus, an agent of diarrhea, in symptomatic and asymptomatic children in Ho Chi Minh City, Vietnam

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Background

Diarrhea is a major cause of illness in low-income countries and is responsible for a significant burden of disease. Despite being projected to remain within the top ten leading causes of DALYs, diarrheal disease is often overlooked as a major global health issue and does not command the same media attention as many of the other “big infections”. The etiological agents of diarrhea include multiple viral, bacterial and parasitic pathogens. Enteric viruses, including rotavirus, norovirus, enteric adenovirus and astrovirus, play the leading role in terms of both morbidity and mortality of severe diarrhea cases in developing countries [1]. Despite widespread evidence that diarrhea has a broad range of etiologies, a relatively finite etiology is often assumed and syndromic diagnoses predominate in Vietnam.

Noroviruses (NoV) are positive-sense single-stranded RNA viruses belonging to the taxonomic family Caliciviridae and are considered to be the second most common cause of severe gastroenteritis in children under the age of five years [2]. The virus is a well-recognized cause of gastrointestinal infections in all ages, responsible for 90 % of diarrhea outbreaks worldwide [3]. However, whilst the role of NoV as an important cause of sporadic and endemic gastrointestinal infections in developed countries, the burden and the understanding of the pathogen in developing countries is less well understood [2, 3].

Vietnam, in particular, Ho Chi Minh City (HCMC) is transitioning through a period of rapid economic development. Such an economic change is bringing about a shift in the spectrum of pathogens causing infectious diseases, such as diarrhea [4]. We know very little about the burden, epidemiology, genetics or population structure of norovirus in HCMC and in other locations in Vietnam, as routine etiological diagnosis of diarrheal pathogens is seldom performed. Studies on prevalence of NoV infections in various settings suggest the presence of asymptomatic NoV carriers in the community, we are currently unsure of the prevalence of NoV carriage in healthy children in Vietnam. Such individuals represent a latent but mobile reservoir of the virus circulating in the community. This study aimed to describe the NoV prevalence, genotype and spatiotemporal dynamics of this pathogen in children in HCMC.

Results and Discussion

All NoV identified (N = 315) from symptomatic patients and healthy controls (N = 2,054) were subjected to direct sequencing and genotyping. NoV GII and GI were detected in 304 (96.5 %) and in 11 (3.5 %) of the NoV-positive stools, respectively. Among the GII strains, GII.4 was the most prevalent genotype (81.3 %; 247/304), belonging to 2 major genotypes, the GII.4-2006b (Minerva) and the novel GII.4-2010 (New Orleans) variant. The remaining genotypes included GII.2, GII.3, GII.6, GII.7, GII.9, GII.12, GII.13 and unassigned types within GII.4 lineage.

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There was a positive linear correlation between NoV infections and monthly rainfall ($R = 0.550$, $p = 0.029$), but no similar correlation with temperature ($R = 0.308$, $p = 0.330$). This association of NoV infections with the tropical rainy season may reflect differential transmission between climates as NoV infections are classically associated with the winter in temperate countries [5].

We investigated sequences of the two GII.4 variants from HCMC, comparing them with global sequences and previously published GII.4 sequences from Vietnam [6]. Using Bayesian phylogenetics, the evolutionary rate of NoV was calculated as 8.072×10^{-3} substitutions/site/year. The GII.4-2006b sequences from NoV originating in Vietnam [6] fell in the same genocluster as global GII.4-2006b viruses, clustering was independent of their time or place of isolation. This GII.4-2006b lineage could be further divided into two sub-lineages, strains from HCMC could be found in both, confirming co-circulation of divergent GII.4-2006b viruses. The GII.4-2010 strains clustered in a single lineage, separate from the GII.4-2006b genocluster lineage. The GII.4-2010 lineage could be differentiated partially by location, with Vietnamese and Belgian sub-lineages stemming from the New Orleans GII.4-2010 variant.

The Mantel test confirmed evidence of an association between isolation time and genotype within GII sequences ($p < 0.0001$) and GII.4 sequences ($p < 0.0001$). Yet, there was no similar association between geographical distance and genetic distance, or between isolation date and geographical distance. SaTScan spatiotemporal cluster detection analysis supported our original hypothesis, detected a cluster of six GII.4-1010 NoV (over other NoV GIIs (0.59 expected)) in a 3.8km radius in the northeast of the City (relative risk = 12.65, $p = 0.0003$), indicating that the initial dynamics of GII.4-2010 upon introduction were highly localized.

Conclusion

This study is the first investigating the prevalence of NoV in children with and without diarrhea in HCMC (Vietnam). NoV GII.4 variants predominate among a diversity of NoV strains co-circulating in this location and are highly endemic in HCMC. We also report the novel emergence of NoV GII.4-2010 variant in Asia, which exhibited a spatiotemporal phylogenetic signal upon strain introduction to the local population.

References

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