NATIONAL CENTER FOR IMMUNIZATION AND RESPIRATORY DISEASES

Prevalence of viral enteric pathogens causing infection and acute gastroenteritis during the first year of life: PREVAIL birth cohort study

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US birth cohort (PREVAIL) shows GII norovirus and sapovirus were the most prevalent viral AGE pathogens detected in infant stools in the first year of life

BACKGROUND

Birth cohort studies conducted in low- to middle-income countries have shown that noroviruses and sapoviruses are high-exposure pathogens associated with infection and acute gastroenteritis (AGE) in infants and young children.

The PREVAIL birth cohort:

- Pediatric Respiratory & Enteric Virus Acquisition and Immunogenesis Longitudinal (PREVAIL) study
- Conducted in the United States (Cincinnati, Ohio)
- Investigates the natural history and immunity to common viral pathogens associated with AGE

Here we present stool prevalence of AGE pathogens during the first year of life.

METHODS

Data collection:

- Mother-infant pairs were enrolled Mar. 2017-Jul. 2018, with 245 (93%) meeting the final eligibility criteria. Demographics are listed in **Table 1**.
- Stool specimens and symptom status questionnaires were collected at birth, weekly, and during AGE events.

Stool testing (Figure 1):

- Routine and AGE stools tested by;
- xTAG® Gastrointestinal Panel (16 viral, bacterial and protozoan pathogens)
- Realtime RT-PCR and genotyping

Definitions:

- AGE was defined as ≥ 3 loose stools in 24 hour and/or ≥ 1 vomiting episodes within 24 hours.
- Symptom status definitions listed in **Table 2**.

RESULTS

Stool testing by symptom status

- 7954 stools routine (weekly) and AGE stools were tested
- 755 stools (9%) were from symptomatic infants (**Figure 2**)

Pathogen prevalence in stools (Figure 3)

- **AGE viruses**
  - GII noroviruses were most often detected
  - Sapoviruses were the next most common virus
  - GII norovirus and sapovirus were more likely to be detected in symptomatic stools than asymptomatic stools (chi-square test, $p < 001$).
- **Bacterial AGE pathogens**
  - *C. difficile* was the most often detected bacteria
  - Other bacterial pathogens were rarely detected
  - The prevalence of *C. difficile* in symptomatic stools was slightly higher than its prevalence in asymptomatic stools (chi-square test, $p = 0.04$).
- **Co-infections (Table 3)**
  - 125 co-infections were detected among asymptomatic or symptomatic stools
  - Norovirus and *C. difficile* were present in all of the five most common co-infection pairs
- **Norovirus genotypes**
  - 13 norovirus genotypes were detected in the 405 norovirus-positive symptomatic and asymptomatic stools (**Table 4**).
  - GII.4, GII.6, GII.3, and GII.7 viruses were the most prevalent noroviruses found in both symptomatic and asymptomatic stools (**Figure 4**).
  - Additional testing (such as semi-nested PCR) is needed for stools positive for GI or GII noroviruses by realtime RT-PCR but have not yet been successfully sequenced.

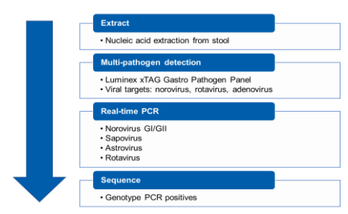
GRAPHICS

Demographics and stool testing workflow

Table 1

Maternal Demographics		N (%)
Age	18-24 years	50 (21%)
	25-34 years	155 (63%)
	35+ years	40 (16%)
Race	Black	106 (43%)
	White	127 (52%)
	Other	12 (5%)
Publicly insured		137 (56%)
<$25,000 household income		78 (32%)
Married		118 (48%)
Bachelor's degree or above		95 (39%)
Initiated breastfeeding		212 (87%)

Figure 1



Proportion of stools by symptom status and symptom status definitions

Figure 2

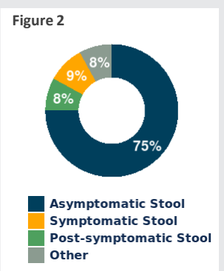
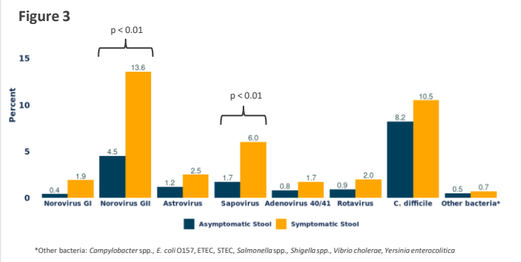


Table 2

Term	Definition
Symptomatic stool	Diarrhea stool or stool collected within 4 days before or 7 days after an AGE episode
Post-symptomatic stool	Stools collected 8-28 days after an AGE episode
Asymptomatic stool	Stool collected >28 days after or >4 days before any AGE episode
Other	Stools with incomplete reporting in the weeks leading up to and following stool collection

AGE pathogen prevalence

Figure 3



*Other bacteria: *Campylobacter* spp., *E. coli* O157, ETEC, STEC, *Salmonella* spp., *Shigella* spp., *Vibrio cholerae*, *Yersinia enterocolitica*

Co-infections

Table 3

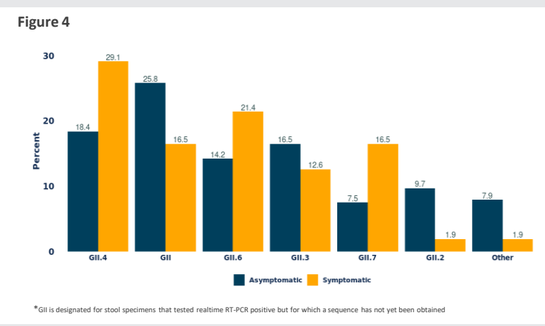
Top 5 coinfection combinations	Asymptomatic Stool	Symptomatic Stool	Total
Norovirus, *C. difficile*	28 (30.8%)	10 (29.4%)	38 (30.4%)
Norovirus, Astrovirus	13 (14.3%)	3 (8.8%)	16 (12.8%)
Sapovirus, *C. difficile*	9 (9.9%)	5 (14.7%)	14 (11.2%)
Norovirus, Sapovirus	8 (8.8%)	2 (5.9%)	10 (8%)
Norovirus, Adenovirus 40/41	2 (2.2%)	4 (11.8%)	6 (4.8%)
All coinfections	28 (30.8%)	34 (100%)	125 (100%)

Norovirus genotype distribution and GII norovirus prevalence by symptom status

Table 4

Genotype	N (%)
GII.4	79 (19.5%)
GII.6	60 (14.8%)
GII.3	57 (14.1%)
GII.7	37 (9.1%)
GII.2	28 (6.9%)
GI.6	14 (3.5%)
GI.3	11 (2.7%)
GII.12	10 (2.5%)
GII.13	6 (1.5%)
GII.1	4 (1%)
GI.5	4 (1%)
GI.2	2 (0.5%)
GII.14	1 (0.2%)
GI.6; GII.3	1 (0.2%)
GI; GII	1 (0.2%)
GI	4 (1%)
GII	86 (21.2%)
Total	405 (100%)

Figure 4



*GII is designated for stool specimens that tested realtime RT-PCR positive but for which a sequence has not yet been obtained

SCAN HERE FOR MORE INFORMATION

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