Public Health Bulletin
South Africa

Sentinel Syndromic Diarrhoeal Disease Surveillance, South Africa 2022

Nicola Page[1,2,3], Sandrama Nadan[1], Tersia Kruger[1], Rembuluwani Netshikweta[1], Phuti Sekwadi[1], Linda Erasmus[1]

[1]Centre for Enteric Diseases, National Institute for Communicable Diseases, a Division of the National Health Laboratory Services, Johannesburg, South Africa
[2]Department of Medical Virology, School of Medicine, Faculty of Health Sciences, University of Pretoria, Pretoria, South Africa
[3]School of Health Systems and Public Health, Faculty of Health Sciences, University of Pretoria, Pretoria, South Africa

Summary

The diarrhoeal diseases sentinel syndromic surveillance conducted in eight hospital and clinic sites in five provinces in 2022 screened 624 cases, the majority (79%; 496/624) of whom were children ≤5 years. Enteric pathogens were detected in 75% (467/624) of stools screened. The predominant enteric pathogens in children ≤5 years included adenovirus (26%; 127/496), rotavirus (23%; 115/496), *Shigella* spp. (20%; 97/495), and *Cryptosporidium* spp. (19%; 94/496). In children with vaccination cards, 78% (364/467) were fully vaccinated against rotavirus and 93% (433/467) had received at least one dose of the rotavirus vaccine. In participants >5 years, *Shigella* spp. were detected in 20% (26/128) of cases, with adenovirus in 10% (13/128) and norovirus GII in 7% (9/128). The 2022 diarrhoeal surveillance indicates that rotavirus is still a common cause of diarrhoea in children ≤5 years albeit at lower levels compared to pre-vaccine years. The detection of rotavirus in fully vaccinated children is not unexpected as the vaccine combats severe disease but does not prevent infection. High coverage (2 doses) of current vaccine and improved rotavirus vaccines are needed to address the remaining burden. In addition, the surveillance showed the importance of *Shigella* spp. in diarrhoeal disease burden in all ages.

Introduction

While the rotavirus vaccine has been hugely successful in reducing the burden of rotavirus diseases in children ≤5 years, in low- and middle-income countries (LMIC), rotavirus vaccines have shown lower immunogenicity that may explain why rotavirus is still contributing to the overall disease burden in these areas. The rotavirus vaccine (oral, attenuated human rotavirus strain 89-12; Rotarix®; manufactured by GlaxoSmithKline Biologicals; administered in two doses at 6 and 14 weeks) was introduced into the South African immunisation program in August 2009. After introduction, a decrease in both rotavirus-specific (54-58% reduction in children ≤5 years)[1] and all-cause diarrhoeal hospitalisations (45-65% reduction in children ≤12 months and 40-50% reduction in children 13-24 months)[2] was noted. Despite successful introduction of the rotavirus vaccine and improvements in access to safe water and sanitation, acute diarrhoeal diseases were still responsible for 15% of hospital admissions in children ≤5 years at a South African tertiary hospital (data from 2016).[3] The incidence of diarrhoeal diseases for 2016 (612 per 100,000) was 58% lower than the rates of the pre-vaccine introduction period of 2006–2008 (1470 per 100,000).[3] In addition, diarrhoeal mortality decreased from 3.5% to 2.9% during the same periods at this site.[3] In a Malawian study, the rotavirus vaccine was estimated to reduce overall diarrhoeal mortality by 31% in infants surviving to at least 10 weeks of age with the degree of impact strongly associated with vaccine coverage.[4]

In a community study in Soweto in 2020, diarrhoeal rates were similar between age groups. Younger children (≤5

years) were, however, more likely to present to healthcare facilities than adults (OR = 5.9 (95% CI, 1.1–31.4), p = 0.039).[5] Of all the diarrhoea cases in the community, 26.4% sought healthcare, with 4.6% hospitalized, but only 3.4% of cases had a stool specimen collected.[5] While the majority of the community diarrhoea cases were mild, 13.8% of cases felt they required healthcare but were unable to access it.[5] The results of this study highlight the limitations of conducting hospital- or laboratory-based surveillance for diarrhoeal diseases, with older children and adults less likely to present to a healthcare facility, and likely to be underrepresented in burden of disease estimations and accompanying public health interventions.

Diarrhoeal Diseases Syndromic Surveillance (DDSS) started in April 2009, mainly to monitor severe diarrhoea post-rotavirus vaccine introduction and, until 2020, it focused on children ≤5 years. However, as many pathogens contribute to the diarrhoeal syndrome, screening of stool specimens for other enteric pathogens was also conducted. Diarrhoeal diseases still contribute to morbidity and mortality in the South African population and not all patients presenting with illness have stool specimens collected for testing. Therefore, continued monitoring of rotavirus as well as other enteric pathogens in children ≤5 years, and in older children and adults, will enable monitoring of rotavirus vaccine coverage, inform development of improved rotavirus vaccine to address residual burden, and identify any other enteric pathogens driving diarrhoeal disease. The aim of the diarrhoeal diseases syndromic surveillance is to determine the magnitude of diarrhoeal disease outpatient consultations, hospitalisations and deaths in all ages at selected sentinel sites in South Africa, and to define the major aetiological agents associated with disease.

Methods

In 2022, diarrhoeal disease surveillance was conducted at sentinel sites in five provinces as part of the GERMS-SA surveillance (https://www.nicd.ac.za/internal-publications/germs-sa/), including: Red Cross Children's Hospital (Western Cape Province), Mitchell's Plain Hospital/Clinic (Western Cape Province), Pelonomi Hospital (Free State Province), Klerksdorp/Tshepong Hospital (North West Province) and Kalafong Hospital (Gauteng Province). Three clinic sites were also included: Eastridge Clinic (Western Cape Province), Jouberton Clinic (Free State Province) and Kabokweni Clinic (Mpumalanga Province).

All patients admitted to a sentinel hospital for the treatment of acute diarrhoea (as defined by the World Health Organization[6], and of ≤7 days duration) were approached for enrolment. At clinic sites, all persons presenting for the treatment of acute diarrhoea (WHO definition) were approached for enrolment. Enrolment was conducted systematically from Monday to Friday (08:00 – 17:00), after informed consent was obtained from the patient or from a parent or guardian. Demographic, clinical and outcome data were collected in a structured questionnaire by dedicated surveillance officers.

Stool specimens were collected for rotavirus (commercial EIA and standardised characterisation protocols) and enteric pathogens (commercial molecular detection kits and in-house real-time detection assays) screening at the Centre for Enteric Diseases, National Institute for Communicable Diseases.

Results

A total of 624 cases was enrolled from the eight surveillance sites, all of whom provided a stool specimen for screening. Of all cases, 79% (496/624) were children ≤5 years and 63% (391/624) were from hospital sentinel sites. Enteric pathogens were detected in 75% (467/624) of stools screened; 81% (404/496) in children ≤5 years and 49% (63/128) in patients >5 years, and in 80% (312/391) of hospital patients and 67% (155/233) of clinic cases (Table 1). Viruses and parasites were detected at higher prevalence in children ≤5 years ($p<0.001$) compared to participants >5 years and more frequently in patients presenting to hospitals compared to clinics ($p=0.001$ viruses; $p=0.006$ parasites). In addition, mixed aetiology infections were also common in younger children ($p<0.001$) compared to older cases and were detected in significantly more hospital cases compared to clinic cases ($p<0.001$). Bacteria were detected at similar levels regardless of age or facility type (Table 1).

Table 1. Pathogens detected in diarrhoea stools screened by age and health facility type, South Africa 2022. Data on HIV status (PLHIV = people living with HIV) and mortality are also included. Pathogens detected in <5% of all diarrhoea cases are not shown.

Pathogen	Number (%)	Age group (in years)		Health facility	
		≤5	>5	Hospital	Clinic
	n=624	n=496	n=128	n=391	n=233
No pathogen	157 (25%)	92 (19%)	65 (51%)	79 (20%)	78 (33%)
Viruses	336 (54%)	302 (61%)	34 (27%)	231 (59%)	105 (45%)
Parasites	121 (19%)	114 (23%)	7 (5%)	89 (23%)	32 (14%)
Mixed infections (viruses, bacteria and parasites)	466 (75%)	403 (81%)	63 (49%)	311 (80%)	155 (67%)
Adenovirus	140 (22%)	127 (26%)	13 (10%)	89 (23%)	51 (22%)
Adenovirus (Ct<28)	68 (11%)	63 (13%)	5 (4%)	47 (12%)	21 (9%)
Astrovirus	62 (10%)	56 (11%)	6 (5%)	44 (11%)	18 (8%)
Cryptosporidium spp.	100 (16%)	94 (19%)	6 (5%)	74 (19%)	26 (11%)
Norovirus GII	65 (10%)	56 (11%)	9 (7%)	48 (12%)	17 (7%)
Rotavirus	121 (19%)	115 (23%)	6 (5%)	78 (20%)	43 (18%)
Sapovirus	34 (5%)	31 (6%)	3 (2%)	23 (6%)	11 (5%)
	n=623	n=495	n=128	n=390	n=233
Bacteria	178 (29%)	142 (29%)	36 (28%)	111 (28%)	67 (29%)
Campylobacter jejuni/coli	37 (6%)	30 (6%)	7 (5%)	24 (6%)	13 (5%)
Shigella spp.	123 (20%)	97 (20%)	26 (20%)	76 (19%)	47 (20%)
Health status	**n=624**				
PLHIV	59 (9%)	10 (2%)	49 (38%)	14 (4%)	45 (19%)
Deaths		5 (1%)			

Rotavirus was detected in 19% (121/624) of stool specimens, 95% (115/121) of which were in children ≤5 years. Vaccination cards were available for 94% (467/496) of cases in children ≤5 years, with 78% (364/467) fully vaccinated (2 doses Rotarix), 15% (69/467) partially vaccinated (1 dose of Rotarix) and 7% (34/467) not vaccinated. Rotavirus was detected in 23% (83/364) of fully vaccinated children, 26% (18/69) of partially vaccinated children and 39% (7/34) of unvaccinated children ≤5 years. Most of the rotavirus cases were detected between June and September (Figure 1) with G3P[8] strains predominant (53% of rotavirus cases) and G9P[6] also circulating (24% of rotavirus cases).

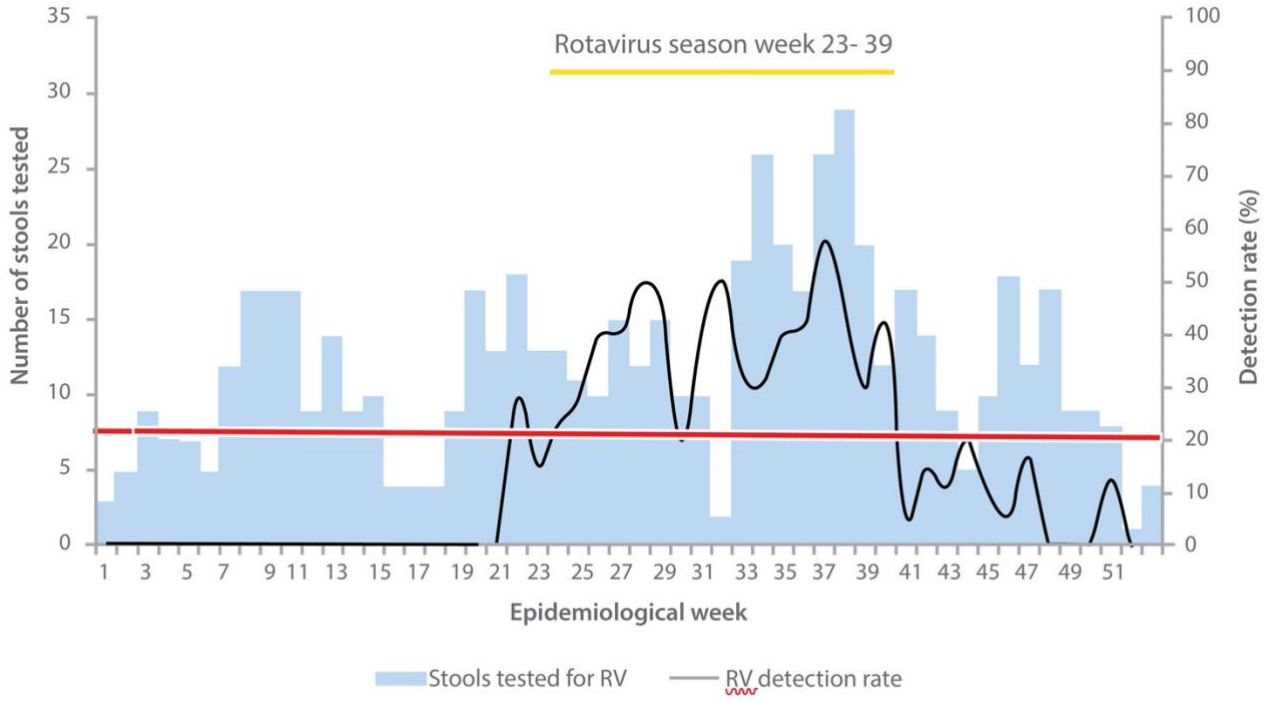

Figure 1. Number of diarrhoeal cases screened and the number of rotavirus positive cases per week in 2022, South Africa. The start of the rotavirus season is defined by rotavirus detection ≥20% for two consecutive weeks and the end of the season is defined at rotavirus detection ≤20% for two consecutive weeks.

Six hundred and twenty four specimens were also screened for other enteric viruses and parasites while one specimen was misplaced, so 623 specimens were screened for enteric bacteria. In children ≤5 years, adenovirus was detected in 26% (127/496) of cases. However, when limiting the Ct-value to ≤28, adenovirus was detected in 13% (63/496) of cases. Other enteric pathogens detected in these children included Shigella spp (20%; 97/495), Cryptosporidium spp. (19%; 94/496), norovirus GII (11%; 56/496) and astrovirus (11%; 56/496) (Table 1). In participants >5 years, Shigella spp. were detected in 20% (26/128) of cases, adenovirus in 10% (13/128) and norovirus GII in 7% (9/128; Table 1). Enteric pathogens including adenovirus, rotavirus, sapovirus, Shigella spp. and Campylobacter jejuni/coli were detected at similar levels in hospital and clinic patients (Table 1). Adenovirus at Ct- value ≤28, astrovirus, Cryptosporidium spp. and norovirus GII were detected in more hospital cases than clinic cases although only Cryptosporidium spp. (p=0.013) were statistically significant.More people living with HIV (PLHIV) were in the >5 year age group compared to children ≤5 years and presented at a clinic compared to a hospital site in the 2022 diarrhoeal surveillance. Five deaths were reported in 2022, all in children <18 months, three of whom were HIV-exposed uninfected and two HIV-unexposed uninfected. Of the five deaths, four occurred in North West Province and all four children were fully vaccinated against rotavirus. Rotavirus was detected in two children, norovirus GII in one and adenovirus in one. No pathogens included in the screening panel were detected in the fifth patient who was fully vaccinated and demised.

Discussion

Not all patients presenting at health facilities with diarrhoea will have stool samples collected for testing. In addition, routine diagnostic testing is likely to be limited to culture for bacterial pathogens only. Syndromic diarrhoeal disease surveillance enables monitoring of the aetiological agents of diarrhoea including bacteria, viruses and parasites. The lower detection rate of diarrhoeal aetiologies in cases >5 years corresponds with recent data from another South African study in older children and adults[7] and suggests that additional testing for parasites, specifically *Cystoisopora* in this population may be warranted, given the percentage of people living with HIV (PLHIV) that diarrhoeal surveillance captures (38%; 49/128). The rotavirus detection rate for 2022 (19%) was similar to 2021 (18%) and higher than the 6% in 2020 and the 11% observed in the 2019 and 2018 seasons. The season returned to a later start in June 2022 compared to the 2021 season (April 2021) and, similarly to 2021, was longer (17 weeks) than the 2018 and 2019 seasons. This was probably partially due to sub-optimal vaccination levels during the 2020 SARS-CoV-2 pandemic. While the vaccination coverage was 93% for at least one dose of Rotarix, healthcare providers are encouraged to vaccinate infants on time and in full to reduce rotavirus circulation in communities. Enteric virus prevalence trends were similar to 2021 levels for adenovirus (25% in 2021) and sapovirus (6% in 2021). However, norovirus prevalence was lower in 2022 compared to 2021 (16%), while astrovirus prevalence was higher in 2022 compared to 2021 (3%).The prevalence of bacterial pathogens and parasites was generally higher than the levels seen in 2021. This included Shigella spp. (20% in 2022; 15% in 2021) and Cryptosporidium spp. (16% in 2022; 10% in2021). Campylobacter jejuni/coli detection was lower in 2022 than the 2021 level (6% in 2022; 10% in 2021). The changes in prevalence may be partially due to concerns regarding water quality, leading to changes in water collection, storage or treatment practises as well as access to adequate sanitation in many communities, and changes in the age composition of surveillance cases or in healthcare-seeking behaviour.

Conclusions

Rotavirus prevalence remained higher than pre-SARS-CoV-2 pandemic levels. While the rotavirus vaccination coverage was 78%, continual improvement in vaccine administration will aid in decreasing rotavirus prevalence further to pre-SARS-CoV-2 levels (11%). Shigella spp. continue to be important enteric pathogens in all ages in South Africa. Additional work investigating Shigella species and serotypes should be considered to ensure data availability should a vaccine become available for potential introduction. People living with HIV are a vulnerable adult group prone to diarrhoeal complaints with surveillance indicating that these cases mainly present at clinics, necessitating continuous surveillance at these sites.

Recommendations

- Clinicians treating diarrhoea in older children and adults (> 5 years) at hospitals and clinics should consider screening for *Cystoisospora*, especially in PLHIV
- Healthcare providers are encouraged to administer two doses of rotavirus vaccine to infants before 24 weeks of age; protecting individual infants and reducing rotavirus circulation in communities
- District immunisation teams should monitor rotavirus vaccination coverage, with levels >90% aiding in decreasing rotavirus prevalence to pre-SARS-CoV-2 levels
- The NICD should expand research on Shigella species and serotypes circulating in South Africa in the next few years, including burden of disease; this will assist with data availability as vaccine development continues
- The NICD should continue diarrhoeal diseases syndromic surveillance at clinics in the short to medium term, to capture people living with HIV and presenting with diarrhoea, and to include data on adults missed at hospitals

Acknowledgements

We thank the surveillance officers at sentinel sites for data and specimen collection, field co-ordinators and GERMS-SA staff for sentinel site management, sentinel site doctors and nursing staff for aiding in recruitment of cases and obtaining clinical specimens, and intern medical scientists and student FETP trainees.

Ethical considerations

The surveillance protocol approved by University of Cape Town Human Research Ethics Committee (165/2020), University of Witwatersrand Research Ethics Committee (Human) (M190664) and University of Pretoria Research Ethics Committee (101/2017) with permissions provided by each site.

Conflicts of interest

NAP has received grants from GlaxoSmithKline and personal fees from GlaxoSmithKline and Aspen Pharmacare, outside of the submitted work. The remaining authors declare no competing interests.

References

1. Msimang VMY, Page N, Groome MJ, *et al*. Impact of rotavirus vaccine on diarrhoeal hospitalization following introduction into the South African public immunization program. *Pediatr Infect Dis J* 2013; 32:1359-1364
2. Groome MJ, Page N, Cortese MM, *et al*. Effectiveness of monovalent human rotavirus vaccine against admission to hospital for acute rotavirus diarrhoea in South African children: a case- control study. *Lancet Infect Dis* 2014; 14:1096-1104.
3. Makgatho E, Patel F, Solomon F, *et al*. The burden of acute diarrheal disease in young hospitalized urban South African children five years after rotavirus vaccine introduction: A retrospective descriptive study. *Pediatr Infect Dis J* 2019; 38:752–756
4. Bar-Zeev N, King C, Phiri T, *et al*. Impact of monovalent rotavirus vaccine on diarrhoea- associated post-neonatal infant mortality in rural communities in Malawi: a population-based birth cohort study. *Lancet Glob Health* 2018; 6:e1036-e1044.
5. Johnstone SL, Page NA, Thomas J, Madhi SA, Mutevedzi P, Myburgh N, Herrera C, Groome MJ. Diarrhoeal diseases in Soweto, South Africa, 2020: a cross-sectional community survey. *BMC Public Health* 2021 Jul 20;21(1):1431
6. World Health Organization. The Treatment of diarrhoea: a manual for physicians and other senior health workers. 4th rev. Jan 2005. Available at: https://iris.who.int/bitstream/handle/10665/43209/9241593180.pdf?sequence=1
7. Johnstone SL, Erasmus L, Thomas J, Groome MJ, du Plessis NM, Avenant T, de Villiers M, Page NA. Epidemiology and aetiology of moderate to severe diarrhoea in hospitalised patients ≥5 years old living with HIV in South Africa, 2018-2021: A case-control analysis. *PLOS Glob Public Health* 2023 Sep 8;3(9):e0001718