Aetiology of acute gastroenteritis in children <13 years needing acute resuscitation on admission to a tertiary public children's hospital, 2014 - 2017: A retrospective cross-sectional descriptive study of 87 children

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Background. Data on the aetiology of acute gastroenteritis in children at public hospitals in South Africa (SA) are limited.
Objective. To describe the pathogens causing acute gastroenteritis in children <13 years admitted to a tertiary hospital in SA.
Methods. A retrospective cross-sectional review of admission and clinical records, as well as of a dataset of stool analyses, of 87 children presenting with severe acute gastroenteritis at the Red Cross War Memorial Children's Hospital, Cape Town, between 2014 and 2017.
Results. The median (interquartile range, IQR) age of the study sample was 7.5 (3.4 - 14.9) months. Two-thirds of the children (*n*=59; 68%) were <12 months. Girls (*n*=52) made up 60% of the sample. About a quarter (*n*=23; 27%) of the children were underweight for their age; only 10 of 37 children under 6 months (27%) were breastfed at the time of admission. Approximately half (*n*=38, 44%) of the children lived in informal housing. *Shigella* or enteroinvasive *Escherichia coli* infection was detected in 28% of the samples (*N*=61) analysed for bacterial infection; *Salmonella* was found in 26%. Adenovirus, rotavirus and norovirus were found in 14%, 13% and 10% of stool samples (*N*=87), respectively. All children presented with hypovolaemic shock or dehydration. The median (IQR) hospital stay was 5.4 (2.0 - 7.0) days. One child died from *Pseudomonas*-related septic shock.
Conclusion. *Shigella* or enteroinvasive *E. coli*, *Salmonella*, adenovirus, norovirus and rotavirus were common diarrhoeal pathogens. A shift in dominance of viral pathogens was noted.

Keywords. Diarrhoea, South Africa, children, aetiology.

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Diarrhoea is a key driver of child morbidity and mortality worldwide.[1-3] Rotavirus is documented as the leading cause of severe diarrhoea globally,[4,5] with the highest incidence of the condition occurring in sub-Saharan Africa.[6] This imposes a huge economic burden on health systems and families in developing countries, not only because of direct costs associated with hospitalisation and treatment but also because of poor nutrition and cognitive development resulting from recurrent diarrhoeal episodes.[7] In South Africa (SA), 15 - 20% of the under-5 mortality is attributed to diarrhoea.[3,8]

The three-year Global Enteric Multicentre Study (GEMS) identified infections from rotaviruses, *Cryptosporidium*, entero-invasive *Escherichia coli* and *Shigella* as the most common causes of moderate to severe diarrhoea in sub-Saharan Africa and South Asia;[9] SA was not included in the study. Public health reports that do cover SA, however, do not fully characterise the clinical, socioeconomic and other important determinants of health pertaining to diarrhoeal disease, such as breastfeeding and immunisation status of children.[10,11]

There is a paucity of data on the aetiology of acute gastroenteritis in children, since analysis of stool specimens for acute diarrhoea is not currently standard practice at public hospitals in SA. Our study aimed to determine which pathogens caused diarrhoeal disease in children under 13 years of age who required acute resuscitation at the medical emergency unit of the Red Cross War Memorial Children's Hospital in Cape Town between 2014 and 2017, and to describe the demographic profile, clinical presentation and outcomes of the study sample. The results of this study could contribute to the design of further studies that will be of benefit in the management of gastroenteritis in facilities offering healthcare to children.

Methods

This was a retrospective cross-sectional descriptive analysis of an established dataset spanning the period 2014 - 2017.

Study population

The Red Cross War Memorial Children's Hospital is the largest dedicated children's hospital in SA. It has 292 beds and serves more than 35 000 children per year. A sizeable burden of gastroenteritis cases (>6 000 admissions) were handled over the four-year period analysed in this study.

Definitions

As per World Health Organization guidelines,[10] acute diarrhoea is defined as lasting less than 14 days. Shock is defined upon two or

more of the following findings: cold hands; a capillary refill time of 3 seconds or more; and a weak and fast pulse. Severe dehydration is defined[10] as being characterised by any two of the following signs: lethargic behaviour or loss of consciousness; sunken eyes; not being able to drink or drinking poorly; or a skin pinch going back very slowly. Some dehydration is characterised by any two of the following: restless or irritable behaviour; sunken eyes; being thirsty or drinking eagerly; or a skin pinch going back slowly.

Procedures

Stool specimens were collected during the surge season (generally February - May) every year. This period is characterised by a peak in incidence, severity and intensity of diarrhoeal disease cases. Funding allowed for analysis of a convenience sample of specimens from 87 children younger than 13 presenting at the facility. All analyses were conducted by the National Health Laboratory Service, SA. The investigators were alerted when any child was identified as having acute diarrhoea accompanied by shock or dehydration.

A commercial real-time multiplex polymerase chain reaction (PCR) assay (PathoFinder, Netherlands) was used to test for rotavirus, adenovirus, norovirus and astrovirus in stool specimens. A subset of samples was also tested using an in-house PCR testing method for *Salmonella* and *Shigella* or entero-invasive *E. coli*.

Demographic characteristics recorded included: age; sex; weight; nutritional, breastfeeding and HIV status; housing conditions; access to tap water; and immunisation status. Clinical data included: duration of diarrhoea; presence of blood in the stool (dysentery); fever and vomiting; signs of clinical shock or dehydration; triage information; laboratory parameters (including blood gas); initial fluid management; length of hospital stay; use of antibiotics; respiratory support; and mortality.

Conventional descriptive statistics were used to describe the study sample. Means and standard deviations (SD) are reported for normally distributed data, and medians associated with interquartile ranges (IQR) are reported for data that are not normally distributed. Categorical variables were compared using a chi-square test for significant associations. A significance level of $p<0.05$ was used.

Results

Baseline characteristics

Baseline characteristics are shown in Table 1. The median (IQR) age of the study sample (N=87) was 7.5 (3.4 - 14.9) months; 37 children were between 0 and 6 months old. Boys (n=35) made up 40% of the sample.

Just over two-thirds of the study sample (n=59; 68%) were younger than 12 months. Of the children younger than 2 years, approximately three-quarters (n/N=57/78; 73%) were not being breastfed at the time of admission, although 79% (n=69) of all mothers reported breastfeeding their children for variable periods during infancy; 10 of the 37 children aged 0 - 6 months (27%) were being breastfed at the time of admission.

Immunisations were up to date for age in 76% (n=66) of the sample, with 92% (n=80) having received their rotavirus vaccination.

Social determinants of health

Almost half (n=38; 44%) of the study sample were reported to live in informal housing. Governmental child support grants of R560 per month (value in 2025), an important social support structure available to impoverished families, was accessed by 41 (47%) children's households.[12] The number of caregivers who were foreign nationals without permanent residency (and who therefore would not have been able to access the social grant) is unknown.

Table 1. Baseline population characteristics (N=87)

Characteristics	*n* (%)
Age (months), median (IQR)	7.5 (3.4 - 14.9)
Male	35 (40)
Weight for age, median (classified by *z*-score)	
Normal	62 (71)
Moderate to severe underweight	23 (26)
Unknown	2 (2)
HIV status	
Infected	4 (5)
Negative	51 (59)
Exposed but uninfected	29 (33)
Unknown	3 (3)
Rotavirus vaccine received	
Yes	80 (92)
No	6 (7)
Unknown	1 (1)
Received immunisations appropriate for age	
Yes	66 (76)
No	16 (18)
Unknown	5 (6)
Ever breastfed	
Yes	69 (79)
No	16 (18)
Unknown	2 (2)
Access to tap water	
Inside the house	47 (54)
Outside	39 (45)
Other	1 (1)
Housing	
Formal	49 (56)
Informal	38 (44)
Sanitation	
Toilet inside the home	47 (54)
Outside shared toilet	28 (32)
Other	12 (14)
Child support grant	
Yes	41 (47)
No	37 (43)
Unknown	9 (10)
Crowding: Number of people (adults and children) sharing the house	
2 - 4	33 (38)
5 - 7	31 (36)
8 - 10	10 (11)
Unknown	13 (15)
Maternal education level	
Primary education	5 (6)
Secondary education	55 (63)
Tertiary education	3 (3)
Unknown	24 (28)

IQR = interquartile range.

Associations between social determinants of health (infancy; breastfeeding status; weight for age; housing status; sanitation status; access to tap water in the home; access to child support grant; attending a crèche) and the presence of bacterial or viral pathogens

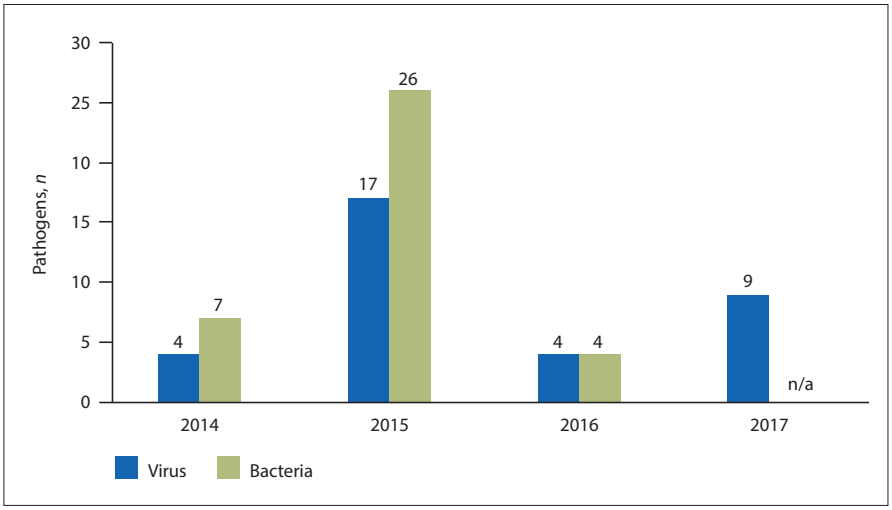

Fig. 1. Bacterial and viral pathogens identified in stool samples, organised per year (N=87)

were investigated using Pearson's chi-square test. None of these social determinants were significantly associated with the presence of a viral pathogen in the stool, except for children attending a crèche being less likely to have a viral pathogen than those cared for at home ($p<0.05$; relative risk 3.97, 95% confidence interval 1.5 - 9.3). A similar association did not hold for bacterial pathogens ($p=0.64$).

Acute gastroenteritis

All children experienced diarrhoea for <14 days. Dysentery was reported in 10 cases (12%), while the remainder presented with non-bloody diarrhoea ($n=76$). Hypovolaemic shock at presentation was reported in 42 cases (48%); the remainder ($n=45$; 52%) were all dehydrated to some degree. Other clinical symptoms reported included vomiting ($n=64$; 74%) and fever ($n=44$; 51%). Physiological measurements recorded included metabolic acidosis (venous blood pH <7.25) in 50 cases (57%) and acute kidney injury in 42 cases (48%). Close to two-thirds ($n=55$; 63%) of children were admitted to the short-stay ward, while 16 (18%) were admitted to the high-dependency care unit in the general paediatric ward and another 16 (18%) required admission to the paediatric intensive care unit.

As part of their resuscitation management, 56 (64%) children received crystalloid fluid boluses, with a median (IQR) volume of 20 (0 - 40) mL/kg and 15 (17%) required inotropic support. Initial non-invasive cardiorespiratory support was provided in 17 cases (20%) using bubble continuous positive pressure ventilation. Three children (4%) required mechanical ventilation. Reasons for mechanical ventilation included severe respiratory distress with underlying adenovirus pneumonia isolated in a tracheal aspirate in one child, while the other two had developed Gram-negative septic shock (*Pseudomonas* sp. and *Enterobacter cloacae*) and required multiple fluid boluses and inotropic support.

Most children received antibiotics ($n=68$; 78%) as an initial management strategy, which the caring clinicians subsequently reviewed and modified if necessary.

The median (IQR) length of hospital stay was 5.4 (2.0 - 7.0) days. One HIV-exposed but uninfected infant, who had presented with acute gastroenteritis complicated by hypovolaemic shock, died in the intensive care unit from overwhelming septic shock secondary to Gram-negative sepsis due to *Pseudomonas* sp. infection. All other children recovered and were discharged home.

Laboratory stool findings

Fig. 1 shows the distribution of enteropathogens across the period 2014 - 2017. No laboratory data were available for bacterial pathogens in 2017.

Bacterial enteropathogens were detected in 29 of 61 documented stool samples (48%) in the period 2014 - 2016. *Shigella* or enteroinvasive *E. coli* was the most commonly identified bacterial pathogen (28% of cases), followed by *Salmonella* in 16 cases (26%). Four specimens (7%) were infected with both *Shigella* or enteroinvasive *E. coli* and *Salmonella*.

Viral pathogens were identified in 32 of 87 (37%) stool specimens collected during the period 2014 - 2017. Adenovirus was the most common viral pathogen identified ($n=12$; 14%), followed by rotavirus ($n=11$; 13%) and norovirus ($n=10$; 12%). Multiple viruses were detected in three specimens (3%) and astrovirus in one specimen (1%).

There were no significant associations between the pathogen type and any of the categorical variables age, length of hospital stay, fever, breastfeeding status or hydration status.

Discussion

Viral or bacterial pathogens were found in 45 children's stool samples, with the most commonly occurring pathogens being *Shigella*, entero-invasive *E. coli*, *Salmonella*, adenovirus, rotavirus and norovirus. Two or more pathogens were present in 13 children's stool samples. Our findings show some similarities but also some contrasts to the GEMS study, which found rotavirus, *Cryptosporidium*, enterotoxigenic *E. coli*, *Shigella* and, in some cases, adenovirus as the common causative pathogens in moderate to severe cases of gastroenteritis in children in African and Asian countries.[9] In our study, 17 children had shigellosis-like symptoms (owing to either *Shigella* or entero-invasive *E. coli*) yet only one presented with dysentery. These findings are similar to a systemic review and meta-analysis by Tickell *et al.*,[13] which showed that absence of dysentery does not exclude *Shigella* as cause of diarrhoea. Other literature concurs, describing dysentery or acute dehydrating watery diarrhoea as two distinct clinical presentations.[14] The prevalence of cases of non-dysenteric *Shigella* in the GEMS study was 43%.[9]

Low breastfeeding rates, undernutrition and poor socioeconomic conditions may have contributed to the high prevalence of *Shigella* or entero-invasive *E. coli* and *Salmonella* infections in our study. This is similar to results from studies in Barbados[15] and Zambia.[16] Mixed bacterial and viral pathogens were found in 14 of 61 (23%) stool samples in our study. Polymicrobial infections are common in children with diarrhoea in low–middle-income countries although the significance of co-infection with regard to the development or severity of disease is unclear.[9,14] Many studies have shown high rates of enteropathogens present in stool, even in specimens taken from controls without diarrhoeal disease. These studies have also shown that co-infection from multiple enteropathogens is relatively common and associated with higher morbidity and mortality, although the exact mechanism of clinicopathogenesis is poorly understood.[14,17] Owing to the small sample size of our study and the absence of a control group, finding enteropathogens in stool specimens provides proof of carriage but is not necessarily proof of pathogenicity. Much larger and well-designed multisite

(but single-country) case-control studies would be needed for further exploration.

Adenovirus was the most common viral pathogen (14%) detected in our study, followed by rotavirus (13%) and norovirus (12%). Adenovirus has also been identified as an important pathogen in studies from other African countries, such as Tanzania (4%), Sudan (16%) and Egypt (10%),[18-20] despite rotavirus still being the more common viral pathogen. The finding may point to the effectiveness of the rotavirus vaccine rollout programme in our setting. Of note is that 92% of our study sample had received the rotavirus vaccination as per the SA childhood immunisation schedule, which provides for two doses of the Rotarix® vaccine at 6 and 10 weeks, respectively. Rotavirus was the second most common (13%) virus detected in stool samples. This rate was lower than the 18% found in an SA study from 1988, prior to the introduction of the rotavirus vaccine.[21] Rotavirus infection remains a cause of acute gastroenteritis cases in children, even in countries where rotavirus vaccination is implemented.[16,22,23] Nonetheless, a global reduction in hospitalisation and mortality due to rotavirus diarrhoea has occurred.[24]

Norovirus was the third most common viral pathogen detected in our study. Infections have been increasingly seen in countries that successfully implemented rotavirus vaccination and, in some instances, this pathogen has replaced rotavirus as the leading cause of diarrhoea in children.[25,26]

Similar to other regional and global studies, all children in our study were younger than 5, with most being under 1 year old.[15,27] Infants are the most vulnerable children in this age group. We noted a low prevalence of breastfeeding in our setting, with 18% of infants never having been breastfed and only 27% still being breastfed at presentation. Low rates of exclusive breastfeeding in SA have been noted previously.[28] In our study, 27% of children with acute gastroenteritis were either moderately or severely underweight. Being underweight is a major risk factor for diarrhoea and interventions that enhance childhood nutrition in low–middle-income countries have been shown to reduce diarrhoeal episodes.[24]

It was encouraging to note that 63% of mothers had attained secondary education. According to Unicef reports, children born to mothers without formal education have been shown to have a higher risk of mortality than those whose mothers have at least 4 years of schooling.[29,30]

Several studies have shown diarrhoeal pathogens presenting with seasonal peaks.[21,31,32] In the present study, stool specimens were collected between February and May, which represents the annual surge season in the study setting (Cape Town, SA). This period, which spans warm and relatively dry months in Cape Town, when water availability may be a challenge, is characterised by a peak in incidence, severity and intensity of diarrhoeal disease cases.

Despite some limitations, this study revealed interesting findings. Bacterial pathogens (*Salmonella* and *Shigella* or entero-invasive *E. coli*) were the most common microorganisms linked to acute diarrhoea. Viral pathogens remained common causes, but a shift in dominance was observed, with adenovirus, rotavirus and norovirus equally prominent in young children with acute gastroenteritis. Children presenting with acute diarrhoea at our facility were from socioeconomically deprived environments and a low rate of breastfeeding was noted.

Larger studies are needed to monitor the prevalence of the identified pathogens in childhood gastroenteritis, which could contribute to designing health programmes focused on poverty alleviation, housing and breastfeeding rates to address the prevalence of diarrhoeal disease among young children in SA.

Study limitations

The limitations of this study are related to the retrospective nature of the review, convenience sampling and the small sample size, as well as the lack of a control group. We did not test for parasites, which may be important contributors to the problem of diarrhoea among immunocompromised children, and particularly those with HIV.[33] However, a previous study in SA showed no difference in profile of enteropathogens between children with and without HIV infection.[34]

Incomplete bacterial analysis for 2017 is another limitation; viral analysis was conducted for the entire study period. In addition, the PCR test used in our study does not distinguish entero-invasive *E. coli* from *Shigella* species, which made it difficult to determine the aetiology of the acute gastroenteritis when these pathogens were detected. However, pathogenesis, clinical presentation and management are similar for both bacteria. As the PCR assay identified only the specific pathogens listed, we may have missed other causes of infection such as parasites. Identification of pathogen nucleic acid also does not necessarily indicate disease causation.

Conclusion

In children admitted to a tertiary SA hospital with acute gastroenteritis between 2014 and 2017, *Salmonella* and *Shigella* or entero-invasive *E. coli* were the most common bacterial pathogens detected in stool samples. Viral pathogens remained common causes, but a shift in dominance was observed, with adenovirus, rotavirus and norovirus equally prominent in young children with acute gastroenteritis.

Declaration. None.

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Author contributions. LS organised the dataset as part of an MMed dissertation, which formed the basis for his writing the manuscript. HB provided the dataset, performed the statistical analysis and contributed to preparing the manuscript. DH was responsible for analysis of the stool samples and preparing the associated data. All authors read and approved the final manuscript.

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Conflicts of interest. None.

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