Prevalence of rotavirus infection among children under five years at a tertiary institution in Nigeria

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Abstract

***Background and objectives*:** Rotavirus is a significant cause of nonbacterial diarrhea, especially in infants and young children worldwide. This study evaluated the pattern of rotavirus infection in children under five years presenting with acute diarrhea in Abuja Teaching Hospital, Gwagwalada, Nigeria.

***Methodology*:** It was a cross-sectional descriptive study to describe the prevalence of rotavirus infection among children. The study enrolled children 1 to 59 months old with acute diarrhea attending General Paediatric Outpatient clinic and hospitalized in the Emergency Paediatric Unit of University of Abuja Teaching Hospital (UATH), Gwagwalada, Nigeria. Rotavirus antigen was detected in the stool by qualitative enzyme-linked immunosorbent assay (ELISA). Data were analyzed using IBM-SPSS version 25.0.

***Results*:** The study comprised of 414 diarrhoeal children aged 1–59 months, of which 226 (54.6%) were male and the mean age was 12.1 months. The overall rate of rotavirus infection was 43.0% (178/ 414). The rotavirus infection was slightly higher among females than in males (46.8% vs 39.8%; p=0.153). Children from upper and middle social classes were at 1.95 [CI=1.17–3.26] and 3.08[CI=1.77–5.34] times higher risks of rotavirus induced diarrhea than the children from the lower social class (p<0.005). Children whose mothers had post-secondary education were three times more at risk of rotavirus diarrhea [OR=3.70; CI=1.46–9.36] than those with primary or no formal education (p<0.05). Children who had never been vaccinated against rotavirus were four times more likely to suffer rotavirus infection than those who had been vaccinated [OR=3.96; 95%CI=1.13–13.89, p=0.032].

***Conclusion*:** This study found that rotavirus was an important causative agent of diarrhea in children in Gwagwalada, Abuja. Due to low rotavirus vaccination status in children, rotavirus screening tests are necessary for children with acute diarrheal disease.

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Introduction

Diarrhea is one of the leading causes of childhood morbidity and mortality globally [1]. It is responsible for nine percent of all deaths among children under five years of age worldwide [1-3]. Most of these deaths occur in developing countries of Africa and South Asia [4]. The leading cause of death in acute diarrhea is dehydration, which results from excessive loss of fluid and electrolytes in diarrhea stools [5]. The etiology of diarrhea in children can be viral, bacterial, parasitic, nutritional, or other systemic illnesses [6].

Among the enteric viruses, rotavirus is the most common cause of acute diarrhea in children between the ages of 6 and 24 months of age. The prevalence of rotavirus varies from place to place. Studies have reported the prevalence of rotavirus infection as 27% in Kenya [7], 28% in South Africa [8] and 49.4% in Ghana [9]. Preliminary results from the African Rotavirus Surveillance Network show an average prevalence of 35.6 – 49.1% [10]. Studies conducted in some towns in different regions of Nigeria showed a prevalence rate of 15.6% in Zaria [11], 19.2% in Benin [12], 22.5% in Lagos [13], and 56% in Enugu in 2014 [14], and 25.7% in 2020 [15].

Rotaviruses are in high concentrations in the stools of infected children and are transmitted primarily by the fecal-oral route. However, transmission by respiratory droplets has also been documented [16]. It is highly contagious, with an infective dose of less than 100 virus particles [17,18]. Rotaviruses are stable in the environment, surviving for an extended period on toys and ordinary surfaces found in homes, and are resistant to most soaps and disinfectants. This makes preventing a child from exposure difficult [17]. Diarrhea caused by rotavirus is more severe than that caused by other enteric pathogens, resulting in up to 50% of all hospitalizations due to diarrhea in children under five years [8]. Also, the administration of oral rehydration solution (ORS) is hampered by the accompanying vomiting, thus the propensity for severe dehydration [19,20].The Centers for Disease Control and Prevention (CDC), 2015, characterized the clinical severity of rotavirus diarrhea into sub-clinical, mild, severe, and fatal [21]. Given the infectivity and burden of rotavirus disease, the World Health Organization has recommended rotavirus vaccines in countries with an under-five mortality rate of more than 10% [22]. Rotavirus vaccines, however, do not protect against infection but do protect against severe diseases requiring hospitalization [23], which is a probable outcome for most children in African settings.

Rapid population increase and deteriorating economic situations stretch the country's available (albeit inadequate) health facilities, negatively impacting the population's health, especially children under five years. More local studies are needed to reflect the true prevalence of rotavirus and determine the clinical severity of rotavirus diarrhea in North Central Nigeria. This study is designed to provide information and insight into the prevalence of rotavirus disease in Abuja's Federal Capital Territory.

Methodology

Study area: The study was carried out at the University of Abuja Teaching Hospital (UATH), Gwagwalada, a 350-bed tertiary hospital that runs primary, secondary and tertiary health care services. Gwagwalada is a semi-urban area with an estimated population of 157,770 by the 2006 census [24] and a projected population of 360,400 in 2015 [25]. It has a municipal water supply system serving less than half of the population. Waste management in the area is inadequate as people often dump refuse by the roadside and into drainages. The hospital serves as a referral center for other hospitals in the town, the FCT, and the neighbouring states of Kogi, Kaduna, Nasarawa, and Niger. The study was conducted in the General Paediatric Out-Patient clinic (GPOPD) and the Emergency Paediatric Unit (EPU) for nine months, from October 2017 to June 2018. The study was conducted in line with the Helsinki declaration of 1964. Approval for the study was granted by the Medical Ethics Committee of the University of Abuja Teaching Hospital before the study's commencement. Signed written informed consent was also obtained from all parents or caregivers.

Study design and sample size determination: The study design was a cross-sectional, descriptive study. The sample size was calculated as 379 using the formula [26]:

$$n = \frac{z^2pq}{d^2}$$

Where;

n = The desired sample size (when the population is greater than 10,000); *z* = The standard normal deviate, usually set at 1.96, which corresponds to a 95% confidence interval; *p* = Known or estimated proportion in a target population of a particular characteristics = 55.9% from a study in Ilorin, North Central Nigeria [27].

The studied population comprised of patients seen in the General Paediatric Outpatient clinic (800/month) and those hospitalized in the Emergency Paediatric Unit (100/month) [28]. Patients seen in these two Units were approximately 5400 for six months. Thus, the adjusted sample size for the studied population, which is <10,000, was estimated as 373 using the formula;

$$nf = \frac{n}{1 + \frac{(n)}{(N)}}$$

Where;

nf = the desired sample size when the population is less than 10,000; *n* = the desired sample size when the population is more than 10,000; N = the estimate of the population.

To correct for attrition, the adjusted sample size (n_a) was calculated using the formula;

n_a = nf ÷ (1.0 – a); n_a = adjusted sample size after considering attrition, a = possible non response rate set at 10% (0.1).

Thus;

n_a = 373 ÷ 0.9 = 414

Therefore, 414 children with acute diarrheal disease were enrolled in the study.

Sampling technique: Consecutive children who satisfied the inclusion criteria were enrolled in the study.

Inclusion and exclusion criteria: Children from 1 – 59 months with acute diarrhea of ≤ 14 days and children whose parents/guardians offer signed written consent were included in the study. Children 1 – 59 months who presented with bloody diarrhea and diarrhea acquired while on admission for another disease were excluded.

Data collection: A structured, pretested questionnaire was used to collect information on socio-demographic conditions, source of water and sanitation, attendance at day care centers, and feeding habits. Information about diarrhea and vomiting was obtained. Diarrhea was defined as the passage of three or more loose or liquid stools per day (or more frequent passage than is normal for the individual) [5]. Hydration status was assessed according to WHO guidelines. Socioeconomic status was determined using Olusanya's social classification [29].

Collection of stool sample and detection of rotavirus antigen: About 5 ml of fresh stool samples were collected into clean, wide-mouth universal specimen bottles from all children enrolled after completing the questionnaire. The specimens were stored in containers in a refrigerator at a temperature of -18°C in the microbiology research laboratory at the hospital. For analysis, the labeled stool samples were transported on ice in batches every fortnightly to the Virology department of Sheda Science and Technology Complex (SHESTCO). The complex is located about 15 kilometers from the University of Abuja Teaching Hospital. The stool samples were tested for rotavirus antigen by qualitative enzyme-linked immunosorbent assay method. The test kit used was manufactured by Cortez Diagnostics, Inc. AccuDiag™ Rotavirus (Fecal) ELISA kit, product number 8306-3, USA. It had a sensitivity of 100% and specificity of 97.1%.

Data analysis

Data obtained was entered into a proforma for each patient. Data entry, validation, and analysis were done using the IBM SPSS (statistical package for the social sciences) Statistical software version 25. The socio-demographic characteristics such as age, age grouping, sex, marital status of the mother, age of mother, social class, etc., and other relevant findings were summarized and displayed in appropriate Tables. The association of socio-demographics across gender and the presence or absence of rotavirus infection was explored using the Chi-square test and $p<0.05$ were considered significant. Multivariate regression analysis was performed to assess the predictors of rotavirus infection.

Results

General characteristics of the study population: The socio-demographic characteristics of the study participants are shown in Table-1. Of the 414 children enrolled in the study, 226 (54.6%) were male and 188 (45.4%) female, with a male to female ratio of 1.2:1. The mean age of the children was 12.1 months, ranging from 1-59 months. Of the total diarrhoea cases, 93.2% (386/414) were below the age of 24 months and only 6.8% (28/414) were between the age of 25 – 60 months. More than three of every five (76.3%) children had normal nutrition, 53.6% had exclusive breastfeeding, and more than half (62.3%) of the mothers had post-secondary education. Only 18 (4.3%) children had received the rotavirus vaccine in this study. Severe diarrhoea was present in 184 (45.5%) cases.

Prevalence of rotavirus among children with acute diarrhea: Table-2 shows the prevalence of rotavirus infection across various socio-demographic characteristics of the study population. The overall rate of rotavirus infection was 43.0% (178/ 414) among the study population. The proportion of

Table-1: *Socio-demographic characteristic of the study population*

Characteristics	Frequency	Percentage
Gender		
Male	226	54.6
Female	188	45.4
Age group (months)		
1-6	106	25.6
7-12	156	37.7
13-24	124	29.9
25-59	28	6.8
Olusanya's Social classification		
Upper class	184	34.5
Middle class	124	29.9
Lower class	106	25.6
Day-care attendance		
Yes	104	25.1
No	310	74.9
Nutritional status		
Normal	316	76.3
Wasting	98	23.7
Breastfeeding pattern		
Predominant breastfeeding	192	46.4
Exclusive breastfeeding	222	53.6
Mother's Education		
Primary/None	30	7.2
Secondary	126	30.4
Post-secondary	258	62.3
Has received rotavirus vaccine		
Yes	18	4.3
No	396	95.7
Severity of diarrhoea		
Mild	92	22.2
Moderate	138	33.3
Severe	184	45.5

rotavirus infection was slightly higher among females than in males (46.8% vs. 39.8%; p=0.153) and decreased slightly with an increase in age from 49.1% among children aged 1 – 6 months to 35.7% among children between 25 – 59 months; but the decrease was not statistically significant (p=0.4). The prevalence of rotavirus infection was significantly associated with the mother's level of education, social class, vaccination against rotavirus, and breastfeeding (p<0.05), but no significant association was observed between rotavirus infection and day care attendance as well as the source of drinking water (p>0.05).

Predictors of rotavirus infection: Table-3 shows the odds of factors associated with rotavirus

Table-2: *Socio-demographic factors associated with rotavirus infection in children with acute diarrhea*

Variables	Rotavirus analysis			
	Positive n=178 n (%)	**Negative n=236 n (%)**	**Total**	**p-value**
Sex				
Male	90(39.8)	136(60.2)	226(54.6)	0.153
Female	88(46.8)	100(53.2)	188(45.4)	
Age group (months)				
1-6	52 (49.1)	54(50.9)	106(25.6)	
7-12	66(42.3)	90(57.7)	156(37.7)	0.460
13-24	50 (40.3)	74(59.7)	124(29.9)	
25-59	10(35.7)	18(64.3)	28(6.8)	
Mother's Education				
Primary/None	6(20.0)	24(80.0)	30(7.2)	0.005*
Secondary	48(38.1)	78(61.9)	126(30.4)	
Post-secondary	124(48.1)	134(51.9)	258(62.3)	
Olusanya's Social classification				
Upper	80(43.5)	104(56.5)	184(34.5)	<0.001*
Middle	68(54.8)	56(45.2)	124(29.9)	
Lower	30(28.3)	76(71.7)	106(25.6)	
Rotavirus vaccination status				
Yes	3(16.7)	15(83.3)	18(4.3)	0.027*
No	175(44.2)	221(55.8)	396(95.7)	
Exclusive Breast-feeding				
Yes	96(50.0)	96(50.0)	192(46.4)	0.007*
No	82(36.9)	140 (63.1)	222(53.6)	
Nutritional status				
Normal	154(48.7%)	162(51.3%)	316(76.3)	<0.001*
Wasting (WHZ score <-2 SD)	24(24.5%)	74(75.5%)	98(23.7)	
Source of drinking water#				
Well	14(46.7)	16(53.3)	30(7.2)	0.673
Bottle	48(40.0)	72(60.0)	120(28.9)	0.432
Sachet	86(46.7)	98(53.3)	184(44.4)	0.169
Municipal	84(47.2)	132(52.8)	216(52.2)	0.047*
Day-care attendance				
Yes	44(42.3)	60(57.7)	104(25.1)	0.870
No	134(43.2)	176(56.8)	310(74.9)	

Note: #multiple response (yes/no, only yes responses are reported); p-significant at p<0.05 by χ^2 test

infection among the study population. The analysis shows that although children below 25 months old are at higher risk of rotavirus infection than the older ones, but the risk is not significant (p>0.05). Also, female children are likely to suffer rotavirus-induced diarrhea 1.33 [CI = 0.9-1.97] times more than their male counterparts (p>0.05). Similarly, children from upper and middle social classes had 1.95 [CI = 1.17 – 3.26] and 3.08 [CI = 1.77 – 5.34] times higher risks of having rotavirus infection than the children from the lower social class (p<0.005). The risk of rotavirus infection was two times higher in children whose mothers had secondary education [OR = 2.46; CI = 0.94 – 6.46; p = 0.067] and three times higher among children whose mothers had post-secondary education [OR = 3.70; CI = 1.46 – 9.36] than the children whose mothers had either primary or no formal education (p<0.05). Children

Table-3: *Odds ratios of factors associated with rotavirus infection among children with acute diarrhoea*

Risk factors	OR (95% CI)	p value
Gender		
Female	1.33 [0.90-1.97]	0.153
Male	1	
Age group (months)		
1-6	1.73 [0.73-4.10]	0.211
7-12	1.32 [0.57-3.05]	0.515
13-24	1.22 [0.52-2.85]	0.653
25-59	1	
Olusanya's social classification		
Upper	1.95 [1.17-3.26]	0.011*
Middle	3.08 [1.77-5.34]	<0.001*
Lower	1	
Mother's education		
Primary/None	1	
Secondary	2.46 [0.94-6.46]	0.067
Post-secondary	3.70 [1.46-9.36]	0.006*
Nutritional status		
Normal	2.93 [1.76-4.88]	<0.001*
Wasting	1	
Municipal water		
Yes	1.49 [1.01 – 2.20]	0.047*
No	1	
Exclusive breastfeeding		
Yes	1.71 [1.15-2.53]	0.008*
No	1	
Rotavirus vaccination status		
Yes	1	
No	3.96 [1.13-13.89]	0.032*
Frequency of vomiting /day		
≤ 2times	1	
≥ 3times	3.37 [2.13-5.35]	<0.001*
Maximum number of loose stool/day		
≥ 7times	1.63 [1.05-2.52]	0.028*
≤ 6times	1	

**P value significant at ≤ 0.05; OR – odds ratio; CI – confidence interval.*

who had never been vaccinated against rotavirus were approximately four times more likely to suffer rotavirus infection than those vaccinated against the virus [OR = 3.96; CI = 1.13 – 13.89, p = 0.032]. The children also at risk of rotavirus infection include exclusively breastfed, have normal nutrition and drink from municipal water. Risk of increased vomiting (≥ 3 times/day) and loose stools ((≥ 7 times/day) were higher (OR: 3.37, p=0.001; OR: 1.63, P=0.03) among rotavirus infected children ($p<0.05$).

Discussion

The prevalence of rotavirus infection among diarrhea cases in this study was 43.0%. This prevalence is higher than the 25.0% previously reported in a study of 144 children across five hospitals in 2014 using the ELISA technique in Abuja [30]. The prevalence is also higher than the 32.2%, 15.6%, 13.8%, and 6.0% reported previously in Kaduna [31], Zaria [11], Jos [32], and Ilorin [33] within the same geopolitical region, respectively. It is also higher than 25.7% in a recent study in Enugu, South-East, Nigeria [15]. However, higher prevalence rates were reported in Enugu (56.0%) [14], Ilorin, Kwara State (55.9%) [27] and 59.1% in Benin, Edo State, Nigeria [34]. The variations in rotavirus prevalence may be attributed to different methodologies and the sample size of the studied population. The variation in prevalence due to differences in methods was demonstrated in a study in Benin, Nigeria [35]. They reported a prevalence of rotavirus as 13.8% when the ELISA method was used and 19.2% when the same samples were subjected to reverse transcriptase-polymerase chain reaction, RT-PCR. The variation in the rate of rotavirus infection due to differences in sample has also been recorded. In Zaria, Nigeria [36], where in a community study of 134 children with acute diarrhea over a period of three months, reported a prevalence of 9%. On the other hand, Grace and Jerald [11] in a hospital-based study in the same community involving 666 children over two years reported a prevalence of 15.6%. The prevalence rate of rotavirus in this study is higher than the WHO African Rotavirus Surveillance Network of 26% [37]. The WHO African Rotavirus Surveillance has seen a steady decline in the prevalence of rotavirus over the past decade from 40.7% [38] to 26% [37]. This decline has been attributed to the introduction of rotavirus vaccination into the national schedules by most member states.

Rotavirus was observed to be slightly but insignificantly higher in females than in males in this study. This result is similar to that of other researchers from other hospital-based studies who found no significant associations between rotavirus infection and gender [9,31,32]. In a similar study conducted in Benin, Nigeria, in 2014 [12], an insignificantly higher proportion of rotavirus-induced diarrhea among females (20%) than males (17.6%) was reported. Similarly, a slightly higher rate of rotavirus infection among female children than the males was reported in Kaduna, Nigeria, in 2017 [39]. On the contrary, Bonkoungon et al [40] observed that boys are twice more likely to be hospitalized with rotavirus diarrhea than girls. Also, Anochie et al [41] in Lagos state found that the rotavirus infection in males was three times more than that of females. The higher prevalence of rotavirus infection among females might be due to chance because, at ages below five years, there is little or no difference in lifestyles between the boy and the girl child. Besides, no study has adequately proven a higher prevalence of rotavirus infection among male or female children below five years.

The incidence of rotavirus infection slightly decreased as the children's age increased from 1-59 months, but the most affected group were children younger than two years. This group accounted for 94.4% (168/178) of all positive rotavirus cases. Several other studies have reported similar findings within and outside Nigeria [42,43,22] . The higher prevalence of rotavirus infection among children below two years may be partly due to early exposure to contaminated sources in underdeveloped settings, overcrowding, or lack of immunity in early infancy [22].. The high incidence of rotavirus among infants calls for early childhood vaccination against rotavirus.

In the present study, rate of rotavirus infection in children who drink municipal water was almost same as those who use drinking water from other sources. Bonkoungon et al [40] in a study of the epidemiology of rotavirus infection among young

children with acute diarrhea in Burkina Faso observed that municipal water intake was significantly associated with rotavirus infection. Studies have shown that rotavirus is resilient and highly contagious and, therefore, improvements in water and sanitation alone are unlikely to be effective preventive measures for rotavirus disease [23]. In addition to water sanitation, there is a need for early childhood introduction of the rotavirus vaccine, particularly in developing settings like Nigeria.

The present study found that the prevalence of rotavirus infection was significantly low among exclusively breastfed children than among those who were not. There have been conflicting results on whether breastfeeding is protective against rotavirus. Muendo et al [44] found a higher incidence of rotavirus infection in exclusively breastfed children, whereas Naficy et al [45] found a lower incidence of rotavirus diarrhea in breastfed infants. Breastfeeding reduces gastrointestinal infections because breast milk contains secretory antibodies such as IgA, immune cells, and other defence factors such as lactoferrin, oligosaccharides, and human milk glycans that protect the intestinal epithelium against pathogens [46]. Therefore, this study advocates exclusive breastfeeding for the first six months of life in agreement with the WHO and UNICEF. The two bodies advocate exclusive breastfeeding for the first six months of a child's life and handwashing with soap, community-wide sanitation, and rotavirus vaccination as a complete package against all causes of diarrhea [47].

This study found a significant correlation between the socioeconomic status of the parents and the prevalence of rotavirus infection, but no significant association was established between attendance at a day care facility and rotavirus infection. This finding is in agreement with the results of Wilking et al [48] who identified associations between socioeconomic factors and the incidence of severe rotavirus infections in an urban setting. On the contrary, Grace and Jerald [19] reported no significant association between rotavirus infection and parental socioeconomic status or attendance to a day care facility.

Conclusion

The study has shown that rotavirus is an important causative agent of childhood diarrhoea at the General Paediatric Out-patient Clinic and the Emergency Paediatric Unit of UATH Gwagwalada. The prevalence of rotavirus infection was 43.0%, and more than 90% of rotavirus infections occur in children aged 24 months and below. Due to low rotavirus vaccination status in the community, rotavirus screening tests are necessary for children with acute diarrheal disease.

Author contributions

FOS and OBB significantly carried out the literature search, writing, analysis and editing; POA, AAO and OFA gathered the data; MOD, AAO, ZG, ANY and FOS contributed to the writing; IO, AB, AL, and POA edited and proof read the work; IC and MOT contributed in lliterature search, writing and editing.

Competing interests

The authors have declared that no competing interests exist.

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