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Research Article

Rotavirus Infection Among Under Five Children Presenting with Gastroenteritis in Ibadan, Nigeria.

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Abstract

Rotavirus infection is one of the leading causes of death attributable to diarrhoea among under five children globally. It is also the most common cause of severe diarrhoeal illness in infants and young children in developing countries resulting in high mortality and morbidity**.** The epidemiology of rotavirus infection is well known in developed countries where rotavirus vaccination has been implemented. However in developing countries such as Nigeria, rotavirrus vaccination is not part of the expanded programme for immunization thus implementing the rotavirus vaccination programme has not been possible because of the cost of the vaccine. In addition, surveillance activities in developing counties are at low ebb thus information on rotavirus epidemiology in these countries is not well known. Nigeria is among the five countries accounting for over half of deaths attributable to rotavirus infection worldwide. Information on rotavirus infections and its risk factors from Nigeria is important in global rotavirus surveillance and elimination efforts. This study was designed to determine the prevalence, associated symptoms and risk factors of rotavirus infection among under five gastroenteric children in Ibadan, Nigeria. Stool samples were collected from 173 children and assayed for rotavirus antigen by Enzyme Immunoassay. A Structured questionnaire was administered to obtain socio-demographic and clinical information from each of the study participants. Thirty-two (18.5%) out of the 173 samples tested were positive for rotavirus antigen with the highest rate of infection (30.5%) among children aged 7-12 months. Rotavirus infection was highest (37.5%) among children presenting with severe gastroenteritis and lowest (12.5%) when diarrhea occurred alone (P=0.02). Presence of another diarrhoeic person in the household was the most significant risk factor for rotavirus infection (P=0.0001). Other risk factors identified included playing with toys, playing with other people /children, not washing of child's hand after visit to toilet and consumption of food that did not require cooking. Findings from this study support the inclusion of rotavirus vaccination as part of the Expanded Programme on Immunization in Nigeria. It also shows the need to test for rotavirus in diarrhoea cases especially among children that test negative for bacteria and parasitic agents.

Keyword: *Gastroentteritis, Prevalence, Rotavirus, Risk Factors, Under-Five Children*

INTRODUCTION

Rotavirus belongs to the family *Reoviridae*, which are non-enveloped viruses with an 11-segment double-stranded RNA genome (Franco *et al*., 2006; Bass *et al*., 2007). They consist of diverse serotypes classified into 7 groups (A-G) and further divided into subgroups based on antigenic differences (Clark and McKendrick, 2004). Groups A-C are known to infect humans (Anderson and Weber, 2004).

Diarrhoea attributable to rotavirus is one of the major health concerns affecting millions of children annually. It is the single leading cause of severe gastroenteritis in infants and young children worldwide (Parashar et al., 2003; Ahmed et al., 2009). Global statistics estimates that rotavirus infection account for 50% of diarrhoeal cases requiring hospitalization and 39% of all diarrhoeal deaths annually (Mast et al., 2009; Tate et al., 2012). In 2008, rotavirus infection associated diarrhoea resulted in 453 000 deaths and 5% of all deaths in children younger than 5 years globally (Tate et al., 2012). The reported number of deaths attributable to rotavirus infection is likely to be an underestimation because only hospital-based studies have been considered (Molbak et al., 2000, WHO 2004, Tate et al., 2012).

According to WHO, five countries including Democratic Republic of the Congo, Ethiopia, India, Pakistan, and Nigeria accounted for more than half of all deaths attributable to rotavirus infection (Tate *et al*., 2012). Also in 2008, Nigeria was second to India in the estimated global rotavirus-associated mortality in children under five years (Tate *et al*., 2012). High annual incidence of childhood diarrhea has been reported in Nigeria with about 20% attributable to rotavirus infection (Parashar et al., 2003). Rotavirus infection has also been shown to be an important contributor to malnutrition, a condition that is still highly prevalent among Nigerian under-five children. For children who are malnourished, rotavirus infection increases the level of malnutrition by compromising intestinal food absorption (Abiodun, 2006).

In view of the seriousness of rotavirus disease burden worldwide and the fact that improved water quality and sanitation have failed to eliminate rotavirus infection (Fischer *et al*., 2007), the use of a safe and effective rotavirus vaccine is a priority globally. The World Health Organization (WHO) in 2009 made a recommendation for global use of rotavirus vaccine as a primary public health measure for prevention of rotavirus infection with particular emphasis on countries with high diarrhoea-related mortality (Tate *et al*., 2010).

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This study was designed to determine the prevalence of rotavirus among under five children presenting with acute gastroenteritis, in three hospitals in Ibadan Metropolis. The specific objectives were to (a) determine the proportion of rotavirus-induced diarrhoea among children less than five years with gastroenteritis cases in Ibadan. (b) Identify the clinical features most likely to be associated with rotavirus gastroenteritis. (c) Determine possible risk factors associated with rotavirus gastroenteritis.

MATERIAL AND METHODS

Ethical approval: Ethical approval for this study was obtained from the University of Ibadan/University College Hospital Ethics Committee as well as Oyo State ethical review committee. The study was explained to the parents of the children and parental accent was sought and obtained before the collection of samples. Written informed consent was obtained from the parents or guardians of all children.

Study Area and Population: This study was carried out at the Pediatric Clinic and General Outpatient Departments of the University College Hospital, Oni Memorial Children Hospital and Oyo State General Hospital, Adeoyo, all in Ibadan Metropolis, Nigeria. The study population included children ≤5years of age attending these hospitals and presenting with gastroenteritis whose parent or /guardian gave assent for participation in the study.

Study Design: It was a cross-sectional study aimed at determining the prevalence of rotavirus infection among children in Ibadan Metropolis. Demographic data, medical history, clinical information and samples were collected from each participant at the time of sample collection using a structured questionnaire. A total of 173 diarrhoeic children were enrolled for the study.

Inclusion and Exclusion criteria: Only children under five years who presented within 10days of onset of gastroenteritis were included in the study. Children whose ages could not be ascertained or parental accent not obtained were excluded.

Sample Collection and Storage: About five mililitre of stool samples were collected from each child after examination by the attending Physician. A diarrhea case was defined as passage of loose, watery or blood tinged stool 3 or more times within a 24 hour period (Baqui *et al.*, 1992). Faecal samples, voided voluntarily, or induced were collected into 15ml centrifuge tube, covered and labeled accordingly before placing in transport box containing ice packs to maintain cold chain and then transported to the Department of Virology, University College Hospital, Ibadan where they were stored at -50^{0}C until tested.

Sample Processing: Each sample was processed by dispensing 9mls of phosphate buffered saline (PBS) into 15ml centrifuge tube and approximately 1-2 gm of faecal material added and homogenized. The suspensions were clarified by centrifugation and the supernatants used to test for the presence of rotavirus antigen.

Detection of Rotavirus: Rotavirus was detected in the stool specimens using the NOVATEINBIO® Rotavirus ELISA test kit, Switzerland. The NOVATEINBIO® Rotavirus test is an enzyme immunoassay for the qualitative determination of rotaviruses in stool samples. Purified Human RV antibodies are coated on the solid phase of the microwell plates to capture rotavirus antigen in stool samples. The assay was strictly carried out in accordance with the manufacturer's instruction.

Data Analysis
Differences in proportions were determined by Chi Square test and the level of significance was set at p values < 0.05.

RESULTS

Thirty-two (18.5%) of 173 diarrhoeic stool samples tested for the presence of rotavirus infection were positive for the viral antigen. The rate of infection increased with age and peaked among those in the 7-12 months (30.5%) age group and declined thereafter to a lowest rate of 6.9% among those in the 25-60 months age group (Fig 1). Out of the 173 diarrhoeic children tested, 112 were males. There was no difference in the prevalence of infection between gender (Table 1). As shown in table 2, out of the 32 rotavirus positive diarrhoeic children, 37.5% had fever and vomiting,, 25.0% had fever or vomiting alone and 40.6% had dehydration while children without fever and vomiting accounted for 9.4% and 3.1% respectively.

Table 1:
Gender distribution of rotavirus infection among children with gastroenteritis in Ibadan, Nigeria

Gender	No. Tested	No. Positive (%)	p-Value
Male	112	21 (18.8)	
Female	61	11 (18.0)	0.908
Total	173	32 (18.5)	

In comparison, clinical variables between children with or without rotavirus infection revealed that children with rotavirus infection presented more with combination of fever, vomiting and dehydration (78.1%) than children without rotavirus infection (P=0.02). Watery stools (71.9%) and mucoid stools (59.4%) were the most frequent types observed among those with rotavirus infection (Table 2). There was no significant association between rotavirus infection and socio-demographic characteristics of parents or caregivers (P> 0.05) (Table 3).

Among risk factors examined, playing with toys, playing with other people or children, presence of another person in the household with diarrhea, washing of child's hand after every visit to toilet or before meal, and consumption of food that require no cooking were significantly associated with rotavirus infection (Table 4). Rotavirus infection was not associated with attendance of a daycare, type of toilet used, source of drinking water, distance of toilet from water source and knowledge/awareness of rotavirus infection

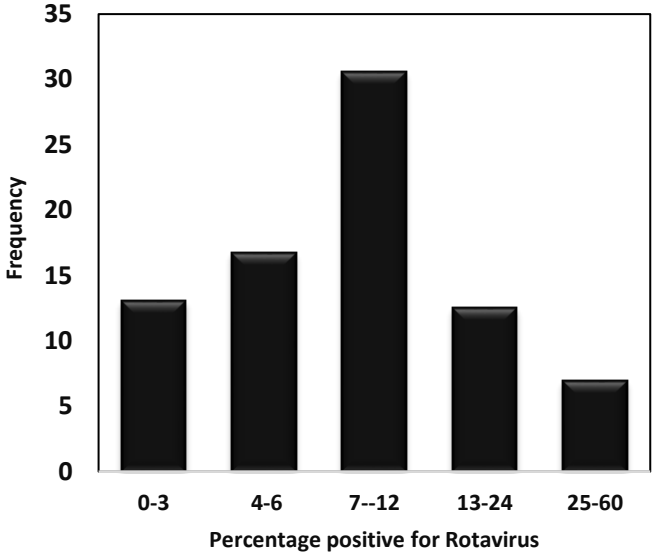

Figure 1:
Age Distribution of Rotavirus Infection Among Children with Gastroenteritis in Ibadan, Nigeria. The rate of infection increased with age and peaked among the 7-12 months (30.5%) age group and reduced drastically thereafter to a lowest rate of 6.9% among the 25-60 months age group.

TABLE 2:
Distribution of rotavirus infection by signs and symptoms (n=32)

Signs and Symptoms (Diarrhea plus)	No. Positive	% Positive
Dehydration	13	40.6
No Fever	3	9.4
No Vomiting	1	3.1
Both Fever and Vomiting	12	37.5
Vomiting only	8	25.0
Fever only	8	25.0
Appearance of diarrhea:-		
A. Watery	23	71.9
B. Mucoid	19	59.4
C. Bloody	01	3.1

TABLE 3:
Socio-demographic characteristics of parent/caregiver and rotavirus infection in children

Variables (parents/caregivers)	Rotavirus Status of Children		p-value
	Rotavirus Positive NO.(%)	Rotavirus Negative NO. (%)	
1.Educational background			
• Tertiary (n=49)	9(18.4)	40(81.6)	
• Secondary (n=52)	11(21.2)	41(78.8)	
• Primary (n=59)	9(15.3)	50(84.7)	0.841
• None (n=13)	3(23.1)	10(76.9)	
2.Religion			
• Christianity (n=118)	21(17.8)	97(82.2)	
• Islamic (n=55)	11(20.0)	44(80.0)	
• Traditional (n=0)	0(0.0)	0(0.0)	
• None (n=0)	0(0.0)	0(0.0)	0.834
3.Occupation			
• Civil servant (n=31)	8(25.8)	23(74.2)	
• Business women/men (n=97)	13(13.4)	84(86.6)	
• House wife (n=40)	10(25.0)	30(75.0)	
• Others (n=5)	1(20.0)	4(80.0)	0.273
4.Ethnic group			
• Yoruba (n=150)	29(19.3)	121(80.7)	
• Hausa (n=1)	0(0.0)	1(100.0)	
• Igbo (n=17)	2(11.8)	15(88.2)	0.846
• Others (n= 5)	1(20.0)	4(80.0)	

DISCUSSION

The rate of rotavirus infection among children who presented with diarrhea in this study was 18.5%. This finding is similar to a previous study by Adedipe in 1985 who reported a prevalence of 19% among children in Ibadan. Thus, suggesting that the burden of the disease remained unchanged over the years. Finding is also comparable with studies from Northern Nigeria (Aminu *et al*., 2008; Junaid *et al*., 2011), Dar es Salaam Tanzania (Moyo *et al*., 2007) and Israel (Grisaru-Soen *et al*., 2008) where prevalence of 13.8%, 18%, 18% and 18.4% respectively were reported. These imply that rotavirus still plays an important role in the aetiology of acute diarrhea among children.

Table 4:
Risk factors for rotavirus infection in children.

No. of respondents by risk factors	Rotavirus status of children		P-Value
	No.Positive(%)	No.Negative (%)	
1.Knowledge of rotavirus infection			
• Yes (n=8)	2(25.0)	6(75.0)	0.628
• No (n=165)	30(18.2)	135(81.8)	
2.Attendance of daycare /Nursery school			
• Yes (n=50)	9(18.0)	41(82.0)	0.914
• No (n=123)	23(18.7)	100(81.3)	
3.Playing with toys/books			
• Yes (n=133)	29(21.8)	104(78.2)	
• No (n=40)	3(7.5)	37(92.5)	**0.029**
4.Playing with other people /children			
• Yes (n=141)	30(21.3)	111(78.7)	
• No (n=32)	2(6.3)	30(93.7)	**0.034**
5.Another person in the household with diarrhea			
• Yes (n=39)	18(46.2)	21(53.8)	
• No (n=134)	14(10.4)	120(89.6)	**0.000**
6.Type of toilet used			
• Water system (n=88)	14(15.9)	74(84.1)	
• Pit toilet (n=10)	1(10.0)	9(90.0)	
• Bucket system (n=75)	17(22.7)	58(77.3)	0.420
• Bushes (n=0)	0(0.0)	0(0.0)	
• Others (n=0)	0(0.0)	0(0.0)	
7.Wash child's hand after every visit to toilet/before meal			
• Yes (n=39)	12(30.8)	27(69.2)	**0.026**
• No (n=134)	20(14.9)	114(85.1)	
8.Source of drinking water			
• Borehole (n=43)	8(18.6)	35(81.4)	
• Well water (n=50)	8(16.0)	42(84.0)	0.849
• Stream water (n=0)	0(0.0)	0(0.0)	
• Satchet water (n=80)	16(20.0)	64(80.0)	
9.Distance of toilet from water source			
• Far(n=68)	9(13.2)	59(86.8)	0.10
• Near (n=105)	23(21.9)	82(78.1)	
10.Consumption of food that do not require cooking			
• Yes (n=103)	12(11.7)	91(88.3)	
• No (n=70)	20(28.6)	50(71.4)	**0.005**

Rotavirus infection varied significantly with age of children with peak occurrence at 7-12 months. This finding is similar to previous reports from Jos, Nigeria (Junaid *et al*., 2011), Western India (Sanjay *et al*., 2013), and Thi-Qar Governorate (Hasson *et al*., 2009). The highest rate of rotavirus infection among the 7-12 months age group may be partly due to waning passive immunity. From the age of six months, the level of immunity of the child is low due to the transitional change from maternally acquired passive immunity to active immunity.

The increased susceptibility that characterizes this lag period as also suggested by Saranavan *et al*., 2004 may have contributed to the high rotavirus infection rate among this age group. In addition, Rotavirus is transmitted via faecal oral route and at this stage of the child's development they engage in activities such as crawling, toddling, and probably sucking of contaminated fingers/toys. Also, at this age the child tends to interact more with other members in a household and neighborhood and the chance of exposure to infection is likely to increase.

The rate of rotavirus infection was lowest among newborn of less than 3 months old. This could be attributed to feeding method and the stage of development. It has been suggested that during the neonatal period, most infants were protected by passively acquired maternal IgA anti-rotavirus antibodies. Also, exclusive breastfeeding decreases the chance of rotavirus infection at this age in life, as there is no complementary feeds which could increase the likelihood of gut contamination by rotavirus. Furthermore, at this age, the numbers of people infants are exposed to are limited as they are most of the time indoors with their mothers.

The rate of rotavirus infection was similar among the male than female children (P = 0.908). This is because at this age there is no difference in life style between the boy and girl child. These findings correlate with previous observations (Saranavan *et al*., 2004; Aminu *et al*., 2008; Pennap and Umoh, 2010).

The major clinical features, in addition to diarrhea among rotavirus positive children included vomiting and fever, vomiting or fever alone and dehydration. In comparison, clinical variables between children with or without rotavirus infection revealed that children with rotavirus infection presented with more fever, vomiting and dehydration than children without rotavirus infection. Similar observations had been reported elsewhere (Nguyen *et al*., 2004; Parashar *et al*., 2006; Pennap and Umoh 2010; Sanjay *et al*., 2013). Out of the rotavirus positive cases, only 12.5% neither presented with fever nor vomiting suggesting that those who had fever and/or vomiting were two times more likely to have rotavirus associated diarrhea than those without.

There was no significant association between rotavirus infection and socio-demographic characteristics of the parents / caregivers of these children. Thus, suggesting that rotavirus infects children irrespective of their socio-economic classes. Junaid *et al*., 2011 reported the similar findings among children in Jos, Nigeria. The ubiquitous nature of rotavirus and the fact that it can remain infectious for long periods on objects and ordinary surfaces found in most homes without inactivation makes it difficult to prevent children from exposure.

Rotavirus infection was found to be significantly associated with playing with toys and other people /children, presence of another person in the household with diarrhea, not washing child's hands after visiting the toilet/before meal, and consumption of food that require no cooking. Toys can be easily contaminated by older children who may be asymptomatic carriers of the virus through their finger nails, hands etc.

Children are seen to put objects into their mouths while playing or scratching their gums when they are about to start teething, such contaminated objects may serve as sources of infection (Chin 2000; Dennehy 2000). The significant association found between rotavirus infection and the presence of another person in the household with diarrhea supports the reports of de Wit *et al*., 2003 in Netherlands; Bucher and Aebi, 2006 in Switzerland and Dennehy, 2008 in US. They opined that the virus is highly infectious and as such is easily transmitted from an infected child to a healthy one. The highly infectious nature of the virus is also its Achilles' heel that makes oral vaccination highly effective in a given population.

In conclusion, this study shows that rotavirus infection is still a problem among children in Ibadan and that the rate of infection is highest in children between 7-12 months of age. Data from the study also showed that rotavirus detection was associated with diarrhoea, vomiting and fever symptoms occurring together than when these symptoms occurred singly. Some risk factors for rotavirus transmission including playing with toys and other people /children, presence of another person in the household with diarrhea, not washing hands after visiting the toilet/before meal, and consumption of food that require no cooking were identified.

The high prevalence of infection among children supports the need to introduce rotavirus vaccination as part of our Expanded Programme on Immunization in Nigeria. There is need to test for rotavirus in diarrhoea cases that test negative for bacteria and parasitic agent. A wider study considering the rural and urban distribution of the disease is recommended, as it would enable us estimate the true burden of the disease in both settings.

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