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Hospital-Based Preliminary Assessment of Rotavirus Infection in Children with Gastroenteritis in Ogun State, Nigeria

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ABSTRACT

Background: Rotavirus remains the most common cause of viral gastroenteritis in developing countries, with over 450,000 deaths annually in children below five years. In developing countries such as Nigeria, routine rotavirus screening is not performed; hence the actual burden of rotavirus infection among children is not well known.

Objective: This study was designed to determine the prevalence, associated symptoms and risk factors of rotavirus gastroenteritis among children under five years in Ogun State, Nigeria.

Methods: Stool samples were collected from 186 children from 3 different hospitals in Ogun State 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.

Results: Sixty-four (34.4%) of the samples tested positive for rotavirus antigen with the highest rate (54.5%) of infection recorded in children aged 0-6 months. The male to female ratio was 1.5:1. The frequency of occurrence of clinical features among diarrheic children included fever, vomiting and dehydration (40.6%), vomiting and dehydration (25%) and fever (9.4%). Gender, age, occupation of parent and attendance of daycare/school were found to be the significant predisposing factors for rotavirus infection ($P< 0.05$).

Conclusion: This preliminary report shows that rotavirus is the major cause of gastroenteritis in children. It is therefore imperative to include rotavirus as one of the agents being routinely screen for in gastroenteritis cases and more importantly include rotavirus vaccination in Expanded Programme for Immunization (EPI) in Nigeria.

INTRODUCTION

Acute gastroenteritis (AG) is the most common gastrointestinal condition affecting people in both developed and developing countries (Andreasi *et al*., 2008). Worldwide, diarrhea remains a substantial cause of morbidity and mortality amongst children (Kotloff *et al*., 2013) and contributes up to 21% of deaths in children under 5 years of age in developing countries (Liu *et al*., 2015). Rotavirus (RV) is the most severe viral pathogen in pediatric diarrhea throughout the world (Parashar *et al*., 2003). Globally, rotavirus infection causes more than 450,000 deaths annually in children below five years, with 80 % of deaths occurring in sub-Saharan Africa and South Asia (Tate *et al*., 2012). In Nigeria, it is estimated that approximately 50,000 RV deaths occur each year (Parashar *et al*., 2009).

Rotaviruses belong to the family *Reoviridae*, which are non-enveloped viruses with an 11-segment double-stranded RNA genome (Paesi *et al.,* 2012). They are classified into 8 major groups (A-H) (Matthijnssens *et al*., 2012) and further divided into two subgroups based on the VP6 protein/gene (Patton 2012). Groups A-C is commonly known to infect humans and group A predominates in children causing severe disease. Rotavirus B and C infections have been reported to cause only sporadic cases and outbreaks (Mihavo-Kovase *et al*., 2015).

RV diarrhea is more severe than diarrhea caused by other enteric pathogens accounting for 30% to 70% hospitalizations (Imade and Eghafona, 2015), with incubation period of 1-2 days and symptoms including an average of six stools per day, severe dehydration (Bwogi *et al.*, 2016), vomiting and fever (Imade and Eghafona, 2015). It is common in children attending day care, and living in households or neighborhoods with children suffering from diarrhea is a known risk factor (Wilking *et al.,* 2012), implying that RV is mainly spread via person-to-person transmission.

Considering the seriousness of rotavirus disease burden worldwide and the fact that improved sanitation and availability of clean water have not reduced the rate of rotavirus infection (Fischer *et al*., 2007, RV vaccination is considered an important preventive and control approach globally (Grimwood *et al*., 2010). In 2009, WHO recommends that RV vaccines be included in all national immunization programs of countries with an under five mortality rate of more than 10% (WHO, 2013). Currently, there are two licensed RV vaccines, Rota Teq, a human-bovine pentavalent vaccine, and Rotarix, a G1P[8] monovalent human RV and available in many countries. Countries that have introduced the vaccines have shown a substantial decline in diarrhea-related hospital admissions and deaths (Kilgore *et al*., 2013).

According to World Health Organization (WHO), five countries including Nigeria accounted for more than half of all deaths attributable to rotavirus infection (Tate *et al*., 2012) and RV is responsible for over 32,000 deaths in under-5 Nigerian children each year (Tagbo, *et al*.,2014). The reported prevalence of rotavirus infection from global surveillance networks and hospital based studies in children ranges from 6 - 69% in different countries (Kazemi *et al*., 2006; Odimayo *et al.,* 2008; WHO, 2008; de Oliveira *et al*., 2008). Previous studies in Nigeria showed different prevalence of rotavirus infection; in a study in Katsina, North west, Nigeria, 57.2% of human rotavirus was reported among children (Joseph and Godwin 2016), while Ayolabi *et al.* 2013 and Tagbo *et al.* 2014 reported 25.8% and 56% in Lagos and Enugu States, respectively. Similarly, Imade and Eghafona 2015 ; Omatola *et al*. 2016 observed a rate of 28.3% and 18.5% among diarrheic children in Edo State and Ibadan metropolis, Nigeria respectively.

In many Nigerian hospitals, routine rotavirus screening is not performed probably due to the similarity of its clinical signs and symptoms to other agents of gastroenteritis. As a result, the actual burden of rotavirus diarrhea among children less than 5 years of age is underestimated. Definitive diagnosis of rotavirus is fundamental to the treatment and management of patients and also to the prevention of its spread. Similarly, despite the WHO recommendation, Nigeria is yet to integrate RV vaccine into its Expanded Programme for Immunization (EPI) thus the need for more information on rotavirus disease burden to aid in elimination plans which cannot be over emphasized. Consequently, this study was designed to determine the prevalence, associated symptoms and risk factors of rotavirus gastroenteritis among children less than five years in Ogun State, Nigeria.

MATERIALS AND METHODS

Ethical approval: Ethical approval for this study was obtained from the Federal Medical Centre, Abeokuta (FMCA) Ethics Committee as well as State Hospitals, Ijebu-Ode and Ota ethical review committee. Detail of the study was explained to the parents/guardians of the participants and informed consent was obtained before samples were collected.

Study area and population: The research was carried out at the Pediatric clinic of the Federal Medical Centre, Abeokuta, State Hospital, Ijebu-Ode and State Hospital, Ota. All the selected hospitals are located within Ogun State, Nigeria. Children ≤5 years of age with gastroenteritis attending these hospitals and whose parents/guardians gave consent for participation were enrolled in the study.

Study design: It was a cross-sectional hospital-based study. Eligibility criteria were hospitalized and general outpatient children from 0-59 months (<5 years) of age with gastroenteritis of ≤ 7days' duration. Children >5 years of age who presented with bloody diarrhea or whose symptoms have lasted for >7 days or acquired the gastroenteritis in the course of hospitalization for treatment of other diseases (hospital acquired gastroenteritis) and also children whose age cannot be ascertained were excluded from the study. Socio-demographic data and clinical information were collected from each participant using a standardized pro-forma.

Sample collection: About 4-5mls of stool samples were collected from each participant after examined by a Physician into a well-labeled universal container. These were transported on ice to the Department of Microbiology, University of Lagos and stored at -20ºC until analysis. A diarrhea case was defined as passage of loose, watery or blood tinged stool 3 or more times within a 24 hour period.

Rotavirus detection: Rotavirus antigens were detected using the commercially available RIDASCREEN® Rotavirus test kit (R-Biopharm AG, Germany) according to the manufacturer's instruction. The RIDASCREEN® Rotavirus test is an enzyme immunoassay for qualitative identification of rotaviruses in human stool samples and it was run as earlier described (Ayolabi *et al*., 2012).

Data analysis: Differences in proportions were determined by chi square test and the level of significance was set at p values < 0.05.

RESULTS

A total of 186 stool samples were screened for rotavirus antigen. Of these, 64 (34.4%) had detectable viral antigen. The percentage rotavirus positivity in each hospital was 46.9% for State Hospital, Ijebu-Ode, 21.9% for FMCA and 31.3% for State Hospital, Ota. Among the 186 children studied, 86 (46%) were males while 100 (54%) were females respectively. Similarly, of the 64 rotavirus-positive cases, 38 (59.4%) were males while 26 (40.6%) were females resulting in a male to female ratio of 1.5:1. There was a significant association between rotavirus infection and gender (p< 0.05) (Table 1).

Table 1: Gender distribution of rotavirus among children with gastroenteritis in Ogun State, Nigeria.

Gender	No. Tested	No. Positive (%)	χ^2 Value
Male	86	38 (44.2)	6.78
Female	100	26 (26)	
Total	186	64 (34.4)	

The distribution of children with rotavirus diarrhea by age indicates that the highest burden is among infants aged 0-6months with 54.5% prevalence and age was found to be associated with the infection (Fig. 1). Clinical features of children with rotavirus infection showed that RV gastroenteritis is more accompanied by fever, vomiting and dehydration (40.6%), followed by vomiting and dehydration (25%)

and fever (9.4%) (Table 2). Watery and mucoid stools were the types observed among those with rotavirus infection. Occupation of parents as well as attendance of daycare/school was significantly associated ($p<0.05$) with rotavirus infection. (Tables 3 and 4).

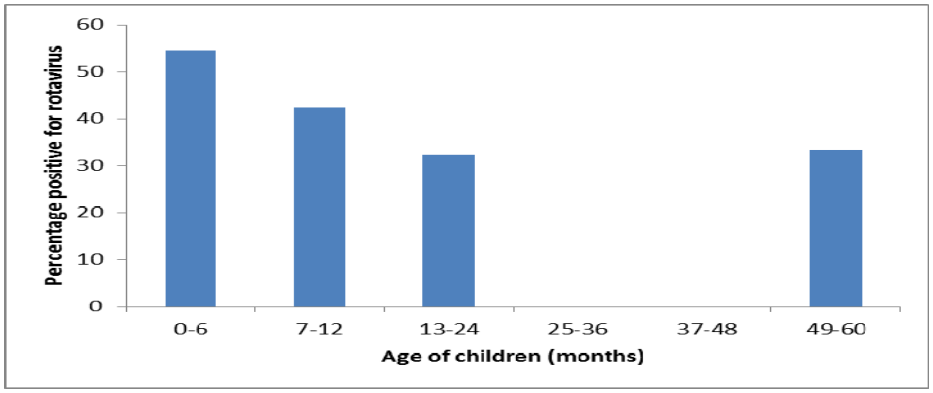

Fig. 1: Age distribution of rotavirus infection among children with gastroenteritis in Ogun state, Nigeria.

Table 2: Spectrum of signs and symptoms of rotavirus infection in children with diarrhea (n=64).

Signs and Symptoms	No. Positive	% Positive
Fever, Vomiting, Dehydration	26	40.6
Vomiting only	2	3.1
Fever only	6	9.4
Fever, Dehydration	2	3.1
Vomiting, Dehydration	16	25
Fever, Vomiting	6	9.4
Dehydration only	2	3.1
No fever, vomiting, Dehydration	4	6.3
Appearance of diarrhea:		
• Watery	40	62.5
• Mucoid	24	37.5
• Bloody	0	0

Table 3: Socio-demographic characteristics of parents/caregiver and rotavirus infection in children.

Variables (Parents/caregivers)	Rotavirus status of children		χ^2 Value
	Positive (%)	Negative (%)	
Educational background			
• Tertiary (n=92)	32 (34.8)	60 (65.2)	1.053
• Secondary (n=92)	32 (34.8)	60 (65.2)	
• Primary (n=2)	0 (0)	2 (100)	
Occupation			
• Civil servant (n=60)	18 (30)	42 (70)	8.988
• Business women/men (n=90)	26 (28.9)	64 (71.1)	
• Housewives (n=26)	14 (53.8)	12 (46.2)	
• Others (n=10)	6 (60)	4 (40)	

Table 4: Risk factors for rotavirus infection in children

No. of respondents by risk factors	Rotavirus status of children		χ^2 Value
	Positive (%)	Negative (%)	
Attendance of daycare/school			
• Yes (n=100)	24 (24)	76 (76)	10.36
• No (n=86)	40 (46.5)	46 (53.5)	
Another person in the household with diarrhea			
• Yes (n=4)	0 (0)	4 (100)	2.174
• No (n=182)	64 (35.2)	118 (64.8)	
Feeding			
• Exclusive breastfeeding (n=34)	16 (47.1)	18 (52.9)	2.95
• Breast + solid (n=152)	48 (31.6)	104 (68.4)	
Type of toilet used			
• Water system (n=162)	58 (35.8)	104 (64.2)	4.469
• Pit toilet (n=16)	6 (37.5)	10 (62.5)	
• Potty (n=8)	0 (0)	8 (100)	
Source of drinking water			
• Borehole (n=60)	26 (43.3)	34 (56.7)	4.456
• Well water (n=2)	0 (0)	2(100)	
• Sachet water (n=84)	24 (28.8)	60 (71.4)	
• Tap (n=40)	14 (35)	26 (65)	

DISCUSSION

The rate of rotavirus infection in children with gastroenteritis in this study was 34.4%. This finding is similar to a community-based study in Ile-Ife by Japhet *et al*. 2012, which reported a prevalence of 34.5% in children aged 0-5 years. This suggests that hospital-based studies are a reflection of the entire populace. This finding is higher than studies from Edo State (28.3%) (Imade and Eghafona 2015) Ibadan (18.5%) (Omotola *et al*, 2016), Ivory Coast (28.6%) (Akoua-Koffi *et al.,* 2014) and Pakistan (30.5%) (Kazi *et al*., 2014). However, it is lower when compared with studies from Enugu, Nigeria (Tagbo *et al.* 2014) and Uganda (Nakawesi *et al*., 2010), with reported prevalence of 56% and 45.4% respectively. Also, the observed prevalence is lower than the WHO global network surveillance of rotavirus diarrhea prevalence of 39-52% in the African region (Tagbo *et al.* 2014), implying that this disease burden can vary within same or different locations at a period of time. It may also be as a result of improved enlightenment on hygiene practices in the country.

There was an association between rotavirus infection and age group ($p< 0.05$). Age group of 0-6 months had the highest prevalence of 54.5% which is consistent with previous reports (Aminu *et al*. 2008; Pennap and Umoh 2010). The reason may be due to the fact that older children acquire immunity through previous exposures to the virus since almost all humans experience at least one rotavirus infection by 3years of age thereby resulting in subsequent mild or asymptomatic infections (Tagbo *et al.* 2014). This observation gave credence to the fact that RV vaccine is best administered early in infancy during 6-10 weeks of age.

In this study, higher detection rate of rotavirus gastroenteritis was recorded in male children compared with their female participants in the ratio 1.5:1 and was statistically significant ($p< 0.05$). This finding is consistent with similar studies reported in Enugu (Tagbo *et al.* 2014) and Edo State (Imade and Eghafona 2015), but in contrast with study from Jos, Nigeria with reported ratio of 1.8:1 (Junaid *et al* 2011). The reason for this preponderance observed in males is not understood. It has also been reported that boys are 2 times more likely to be hospitalized than girls (Tagbo *et al.* 2014), hence the slight male preponderance.

Rotavirus infection was found to be significantly associated with the occupation of the parents/guardians of these children. Children whose parents were housewives had the highest prevalence (53.8%), followed by those that were civil servants (30%) and then those that were business women/men (28.9%). This is in contrast to what was found in Jos, Nigeria where children whose parents were business women/men had the highest prevalence (Junaid *et al* 2011). This implies that children with low socio-economic status are more likely to be infected with rotavirus because of their low standard of living. Also in this study, children of mothers with a secondary or tertiary education level were more likely to have rotavirus diarrhea and had no statistically significant association with rotavirus infection. This finding is similar to report by (Nakawesi *et al*. 2010), but contrast to that of (Junaid *et al* 2011) in Jos, Nigeria where children of mothers with secondary or no education level were more likely to have rotavirus diarrhea. The reason for this observed difference is not clear and may be due to chance.

The major clinical features, in addition to diarrhea among rotavirus positive children included fever, vomiting and dehydration (40.6%), followed by vomiting and dehydration (25%) and fever and vomiting or fever alone (9.4%). Out of the rotavirus positive cases, only 6.3% neither presented with fever nor vomiting nor dehydration suggesting that those who had fever and/or vomiting and/or dehydration were two times more likely to have rotavirus gastroenteritis than those without.

Rotavirus infection was found to be significantly associated with children's attendance of daycare/school ($p< 0.05$) and is consistent with report (Junaid *et al*., 2011). This may be due to close contact with other children who may be asymptomatic carriers in these environments thereby increasing the risk of virus transmission. Also, toys used by children for playing in daycares can be contaminated by older asymptomatic children through their hands or finger nails and children are usually seen to put objects into their mouths or scratching their gums when they are about to start teething which can then serve as sources of infection (Omotola *et al.,* 2016).

There was no significant association between rotavirus infection and feeding, sources of water, type of toilet used and presence of another person in the household with diarrhea ($p> 0.05$). Researchers have noted that rotavirus is resilient and highly contagious and therefore, improvements in water and sanitation are unlikely to be effective preventive measures of rotavirus gastroenteritis, supporting the advocacy for mass vaccination programs (WHO, 2013).

In conclusion, the findings of this study showed that the burden of rotavirus gastroenteritis in children less than 5 years in Ogun State is high and prevalent in 0-6 months old children with males more susceptible than females. It also showed that rotavirus detection was associated with diarrhea, fever, vomiting and dehydration occurring together and the predisposing factors of rotavirus infection include gender, age, and occupation of parents and attendance of daycare/school. It is therefore imperative to include rotavirus as one of the agents to routinely screen for in gastroenteritis cases in our hospitals and more importantly include rotavirus vaccination as part of the EPI in Nigeria.

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