Cryptosporidium and Rotavirus Diarrhoea in Children under the Age of Five Years in FCT Abuja, Nigeria

B. Balarabe-Musa[1*] and N. T. Dabo[2]

[1]*Department of Biological Sciences, University of Abuja, Nigeria.*
[2]*Department of Biological Sciences, Bayero University, Kano, Nigeria.*

Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

| *Original Research Article* |

ABSTRACT

Introduction: Diarrhoea is the second leading cause of death among children, and Nigeria has the continent's highest mortality with little information on the specific cause, proportion affected by *Cryptosporidium* and Rotavirus, and the prevalent genotypes for Rotavirus.
Aim: To identify children with diarrhoea, in Abuja in the Federal Capital Territory; to estimate the proportion of children with *Cryptosporidium* and rotavirus diarrhoea.
Study Design: One-year cross-sectional study of children under five years with acute diarrhea.
Duration: The study was conducted in Abuja from June 2018 to May 2019.
Methodology: *Cryptosporidium* and Rotavirus ELISA were done with commercially available kits.
Results: Stool samples were collected from 1450 participants, of whom 1185 (81.7%) were ambulatory, 109 (7.5%) were hospitalized, and 156 (10.7%) were controls without diarrhoea. *Cryptosporidium*-ELISA was positive among 274 (21.1%) children with diarrhoea and 23 (1.7%) of children without diarrhoea, with August and September as peak months for infection. Rotavirus-ELISA was positive among 231 (17.8%) children with diarrhoea and 29 (2.2%) controls, with November, December, and January as peak months. Children of 12 to 17 months were most affected for both and Rotavirus (39.8%) and *Cryptosporidium* (37.2%).

Corresponding author: Email: bintabalarabe@gmail.com;

Conclusion: *Cryptosporidium* and Rotavirus are essential pathogens in children, especially among Rotavirus unvaccinated children in Abuja. Local and national infrastructure is inadequate for essential surveillance of diarrhoeal disease, and this will have to be improved, together with access to virological and parasitic stool testing, to monitor the planned vaccine program, especially for Rotavirus.

Keywords: Cryptosporidium; rotavirus; diarrhea; children; Abuja.

1. INTRODUCTION

Diarrhoea is a health condition caused by many illnesses and bowel disturbances resulting in the passing of excessive, watery, loose feces more frequently than average. The bowel disturbance results from an imbalance in absorption and secretion properties of the intestinal tract [1]. The diarrohea-causing pathogens are classified into bacteria, viruses, and parasites, where Enteropathogens, such as rotaviruses, entero-adherent pathogenic *Escherichia coli* (EAEC), and enterotoxigenic *Escherichia coli* (ETEC) were identified as essential pathogens of diarrhoeal episodes [2].

Cryptosporidium and Rotavirus are pathogens of pediatric importance due to the high burden of death and morbidity in children below the age of five in both developed and developing countries [2]. Rotavirus is the most common cause of severe diarrhoea in children, and nearly every child on the planet has been infected with it at some point [3]. The virus enters the body via the fecal-oral pathway, infecting and damaging the cell lining of the small intestine, causing gastroenteritis in infants aged zero to fifty-nine months [3,4]. Cryptosporidiosis is a parasitic disease caused by *Cryptosporidium parvum*, a protozoan parasite belonging to the Apicomplexa phylum [5]. Cryptosporidiosis is a common cause of diarrhoeal sickness in humans, and it affects various populations of people. In immune-compromised individuals, such as patients with acquired immunodeficiency syndrome or severely malnourished children, *Cryptosporidium spp.* diarrhoea can be severe and chronic (Orlandi *et al.*, 2001).

Most African countries experience the burden of diarrhoea. It was estimated that 10.6 million deaths due to diarrhoeal diseases of all ages occur annually worldwide, of which 45% occur in Africa [6]. A report in 2009 from UNICEF/WHO showed that Nigeria had the second-highest number of cases of hospitalizations, deaths, and outpatient visits after India [7]. Recently, it has been shown that diarrhea mortality and morbidity have been on the decline [8,9]. This incidence was attributed to the introduction of the rotavirus vaccines [10] and the spread and use of oral rehydration therapy (ORT) [11]. However, diarrhea remains a significant cause of death among children under five in both outpatients and inpatients in Sub-Saharan Africa [8]. The mortality burden in Sub-Saharan Africa reveals the constant magnitude of this preventable disease in the region. Therefore, it is suggested that careful planning and evaluation of interventions to control the causes and reduce mortality due to diarrhoea is essential [12].

This research, therefore, focuses on assessing some of the clinical indicators, causes, and deaths due to acute diarrhea among children under the age of five in a hospital setting for one year in Abuja, Nigeria. As a result, this study aims to evaluate some of the clinical signs, causes, and mortality associated with acute diarrhea in children under the age of five in a hospital environment in Abuja, Nigeria, for a year. The findings of this study will aid in the planning of the rotavirus vaccine's possible inclusion in the National Immunization Program and establish a baseline for assessing the vaccine's influence on prevalence if it is implemented in Nigeria's immunization program.

2. MATERIALS AND METHODS

2.1 Study Area

The study was carried out in Abuja, the Federal Capital Territory of Nigeria. Nigeria has a total population of 150 million people according to the 2006 population census, of which about 5 million people live in Abuja[13]. Abuja experiences two variations of weather typical to sub-Saharan Africa, the dry season (summer) and rainy season in between the two seasons; there is a brief interlude of harmattan occasioned by the northeast trade wind, which is accompanied by dust haze with intensified cold and dry air (Odjugo, 2010). The rainy season begins in February and ends in October, daytime

temperatures reach 28 °C (82.4°F) to 30°C (86.0 °F) and night time is as low as 22 °C (71.6 °F) to 23 °C (73.4 °F). In the dry season, daytime temperatures can soar as high as 40 °C (104.0 °F), and nighttime temperatures are as low as 12 °C (53.6 °F). Even the chilliest nights can be followed by daytime temperatures well above 30 °C (86.0 °F). The high altitudes and undulating terrain of the FCT act as a moderating influence on the territory's weather[14].

2.2 Study Site

Asokoro (District) General Hospital is a government-owned hospital that provides services in the medical areas such as Paediatrics and child health, Ante-natal, Post-natal, and Obstetrics, Accident and Emergency, Medical laboratory, Radiology, Opthalmology and so on. The hospital has a patient attendance of over 15,000 monthly, of which 7000 are pediatric inclined. The pediatric ward has 30 beds for the hospitalized children.

2.3 Study Design

The study was a one-year cross-sectional study of children with acute diarrhoea, conducted between June 01, 2018, to May 31, 2019. A cross-sectional, hospital-based study design was used to determine the burden of diarrhoea in hospitalized and ambulatory children, year incidence of Cryptosporidium and rotavirus diarrhoea, respectively.

2.4 Enrolment

All children aged between one month and five years of age attending Asokoro District Hospital with a clinical diagnosis of acute diarrhoea were identified and invited to participate. Invitation to participate was independent of the severity of the episode. Acute diarrhoea was defined as three or more watery stools <14 days duration, following the WHO definition used in other studies [7].

2.5 Inclusion Criteria

All children aged between one month and five years hospitalized or attending the outpatient clinics with a complaint of acute diarrhoea, independent of disease severity. Children were included if the parents provided informed consent and collected stool samples before leaving the study setting.

2.6 Exclusion Criteria

Parents who leave the premises without their child giving a stool sample were excluded from the final analysis as they were unaccompanied minors. However, a tally was kept to allow the interpretation of data from the children enrolled.

2.7 Sample Collection, Labelling, and Storage

A questionnaire was administered to obtain demographic data from patients. This questionnaire included patient name, age, gender, date of visit to the outpatient pediatrics department. Anthropometric data were also obtained by measuring height using a measuring tape; the child's weight was measured with an electronic weighing scale. The temperature was taken using a clinical digital thermometer. During the interview, clinical data were also obtained from patients, such as episodes of diarrhoea, vomiting, and treatment. The parents of children were then issued with sterile universal bottles to collect samples from the nappy of their children. The date of stool submission and consistency were recorded. A study number was assigned to each subject's questionnaire, and the same study number was written on the universal sample bottle. The stool samples were aliquot into three safe lock Eppendorf tubes, labeled and stored at -20°C. The samples were then transported on ice to the Zankli Research lab, Abuja, stored and frozen. The labeled tubes were arranged in labeled storage boxes, recorded and entered in Excel, then stored at -80°C.

2.8 Sample Analysis

To identify *Cryptosporidium* spp and Rotavirus, stool specimens were tested using an ELISA kit following the manufacturer's instructions.

2.9 Database and Statistical Analysis

A database was created in Epi info version 7 (CDC Atlanta, USA). Completed questionnaires were coded and entered in the software. At the end of the study and different occasions, two independent persons among the research assistants were employed to confirm the data entered in the software to the information on the questionnaires. Analysis was done using the Epi info version 7 software. Chi-square and statistical significance ($p .05$) were ascertained to compare proportions and variables that are continuous, and the Mann-Whitney test was used.

3. RESULTS

3.1 General Characteristics of Children with Diarrhoea in Asokoro District Hospital

One thousand one hundred eighty-five children with diarrhoea were enrolled from June 01, 2018 to May 31, 2019 (12 months), aged one month to 5 years. 109 (7.5%) were managed as inpatients, and 679 (46.8%) were male. The median age of hospitalized patients was 13.0 months, slightly higher than a median of 20 months in ambulatory patients.

The mean diarrhoea duration before the consultation was 2.5 days and 2.3 days for ambulatory and hospitalized children, respectively (p<0.0001). The mean numbers of stools per day were 3 and 5 for ambulatory and hospitalized children, respectively. The diarrhea severity was estimated for 1185 (46.8%) children. In total 154 (12.9%) were mild, 1006 (84.8%) moderate and 134 (11.3%) severe episodes. Severe episodes were observed more frequently in hospitalized children (64.2%) than ambulatory cases (5.4%) (p<0.0001). Most children passed watery stools (both hospitalized and ambulatory cases), 881 (74.3%), while 250 (21.0%) had mucus and blood. All 156 controls had solid stools.

3.2 Enrolment by Month (Seasonality) for all Children in the Study

Table 2 showed more diarrhoea cases in October 130 (10.9%), August, and January 114 (9.6%). April and June also showed slightly high diarrhea consultations with 106 (8.9%) respectively. May, February, and September had the lowest number of enrolments in the study, with 100 (8.4%), 99 (8.3%), respectively. Overall, there is a significant difference in enrolment by months (p=0.0167).

Table 1. General characteristics of children with Diarrhoea in Asokoro district hospital

Parameters	Ambulatory	Hospitalised	P-value
	N= 1185	N= 109	
Age in months, median (IQR)	20.5 (11.0, 36.0)	13.0 (9.5, 30.0)	<0.05
Male: Female (% male)	679:506 (57.3)	66:43 (60.5)	0.6
Diarrhoea			
Mean (SD) duration, days	2.5 (0.9)	2.3 (1.1)	<0.0001
Mean (SD) Max frequency/24h before attending	4.9 (1.1)	5.6 (1.2)	<0.0001
Presence of vomiting (%)	793 (66.9)	93 (85.3)	<0.0001
Mean (SD) duration, days	3.1(0.9)	3.3(1.1)	<0.0001
Mean (SD) Max Frequency/24h before attending	3.1(1.5)	3.3(1.1)	<0.0001
Fever (%)	791(66.7)	94 (86.2)	<0.003
Abdominal Pain (%)	1026 (86.5)	109 (100)	<0.002
Stool appearance			
Watery (%)	788 (66.6)	93 (85.3)	> 0.01
Solid (%)	159 (13.4)	-	
Mucus (%)	01 (0.08)	-	
Mucus and blood (%)	234 (19.7)	16 (14.6)	
Bloody (%)	01 (0.08)	-	
Level of activity			
Normal (%)	158 (13.3)	-	> 0.01
Reduced (%)	1027 (86.6)	109 (100)	
Level of dehydration			
Mild (%)	154 (13.0)	-	<0.0001
Moderate (%)	967 (81.6)	39 (35.7)	<0.0001
Severe (%)	64 (5.4)	70 (64.2)	<0.0001
Rehydration			
None (%)	159 (13.4)	-	<0.03
ORT (%)	976 (82.3)	44 (40.3)	<0.02
I.V (%)	50 (4.2)	65 (59.6)	>0.01
Antimicrobials used	1024 (86.4)	109 (100)	<0.03

Table 2. Enrolment by month for all children in the study (N=1294) p > 0.05

Month	Enrolment	Percentage
June-18	106	8.1
July-18	110	8.5
August-18	114	8.8
September-18	99	7.6
October-18	130	10.0
November-18	110	8.5
December-18	104	8.0
January-19	114	8.8
February-19	99	7.6
March-19	102	7.8
April-19	106	8.1
May-19	100	7.7
Total	1294	100

3.3 Characteristics of the Population with Rotavirus Diarrhoea

Table 3 describes the characteristics of the population in the study with rotavirus diarrhea. All children were between the ages of 1 month to 5 years. The mean duration of diarrhoea in days before the consultation was four days and 2.7 days for Rotavirus positive and negative, respectively (p<0.0001). The proportion of children that experienced vomiting was higher in the Rotavirus positive group than the rotavirus negative group (87.0% and 64.4%, p<0.0001). The mean frequency of vomits experienced 24 hours before the consultation was similar in Rotavirus positive and negative cases and, although more children in the positive rotavirus group had fever compared to those who were Rotavirus negative (87.0% and 64.3%), this was significant (p<0.0001). Assessing the activity level between the two groups, fewer children had regular exercise after having rotavirus diarrhea than rotavirus negative (17.5% and 20.2%), but this does not achieve significance. The diarrhea severity was estimated for 1294 children. In the rotavirus-positive children, 19.4% were mild, 16.5% were moderate, and 26.1% were severe. Oral rehydration and intravenous therapy were recorded for 1294 of the children. 16.4% of the children with Rotavirus were treated with oral rehydration therapy, and 28.7% were given intravenous fluids, while 17.7% were treated with antibiotics. In the rotavirus-negative children, 83.5% were treated with oral rehydration solution, 71.3% were given intravenous fluids, and 82.2% were treated with antibiotics. There were more children treated with ORS in the rotavirus positive group (p= <0.0001), and more children were given no treatment in the negative rotavirus group (81.1%, p=<0.0001).

3.4 Rotavirus Detection by Gender

Table 4 shows the rotavirus-positive cases by gender. Overall more males, 745 (57.5%), were recruited in the study compared to females 551 (42.5%), but a greater proportion of males were Rotavirus positive 154 (11.9%) compared to females 77 (7.6%). (p<0.01).

3.5 Rotavirus Positive Cases by Age Groups Most Affected

A total of 231 rotavirus-positive cases were confirmed in the study. A more significant proportion of diarrhea cases were Rotavirus positive (17.8%). A more substantial proportion of diarrhoea cases were Rotavirus positive (39.8%) in children between 12-17 months of the study. A similar trend is experienced. However, children of 6-11 months with more positive cases compared with children < 6 months (26.4% and 14.2%, p<0.0001). Fewer cases of rotavirus diarrhoea were experienced with children between the ages of 30-60 (3.8%).

3.6 Rotavirus Detection by Month

A total of 1294 children with diarrhoea (cases) were able to provide the samples. Two hundred thirty-one children were confirmed to have Rotavirus, and 1063 children were negative for Rotavirus. Table 8 describes children with rotavirus diarrhea (positive and negative cases), distributed into months. The table generally showed November as the peak month of rotavirus diarrhoea 42 (18.1%), followed by December and January 29 (12.5%). The months with the minor cases of rotavirus diarrhoea were June and July 10 (4.3%).

Table 3. Clinical Signs and symptoms of Children with Rotavirus Diarrhoea According (N=1294)

Characteristic feature	Rotavirus status		
	Positive N=231	Negative N=1063	P-value
Diarrhoea			
Mean (SD) Duration in days	4.0 (3.21)	2.7 (0.8)	<0.0001
Mean (SD) max no of stool/ 24h	3.9 (2.31)	3.4 (2.99)	0.0162
Vomiting			
Vomiting (%)	201 (87.0)	685 (64.4)	
Mean (SD) Duration in days	0.6 (0.49)	0.4 (0.49)	0.003
Mean (SD) max no of vomits/24h	4.0 (1.60)	3.4 (0.8)	0.0766
Fever			
Fever (%)	201 (87.0)	684 (64.3)	<0.0001
Mean (SD) Temperature	37.5 (0.68)	37.4 (0.79)	<0.0001
Abdominal pain (%)	17.70	82.20	<0.0001
Level of activity			
Normal	20.20	79.70	<0.0001
Reduced	17.50	82.40	0.0539
Degree of dehydration			
Mild	19.40	80.50	0.11
Moderate	16.50	83.50	0.0696
Severe	26.10	73.80	0.6197
Rehydration therapy			
ORS	16.40	83.50	<0.0001
IVT	28.70	71.30	0.2909
None	18.80	81.10	<0.0001
Received antibiotics	17.70	82.20	0.0036

Table 4. Rotavirus Detection in Diarrhoea cases by Gender (N=1294)

Gender	Rotavirus Positive %	Rotavirus Negative %
Male	154 (11.9)	591 (45.6)
Female	77 (5.9)	474 (36.6)
Total	231 (17.8)	1063 (82.1)

Table 5. Rotavirus positive cases by age groups

Age groups	Positive	Negative	% positive
<6	33	48	14.2
6-11	61	208	26.4
12-17	92	168	39.8
18-23	12	40	5.1
24-29	24	145	10.3
30-60	9	459	3.8

3.7 Severity Score (Nakagomi) By Vaccination Status

The rotavirus vaccination status of children between the ages of 5 is summarized in Table 7 of those who knew their vaccination status. However, a high percentage of children were vaccinated and unvaccinated with severe diarrhoea (40.4%, 34.5%) respectively compared to those that had mild diarrhoea in both groups. The advantages of the vaccine are emphasized

during the announcements, this may be due to the inconsistency in the parents' response and the inability to display the vaccine cards during the interviews.

3.7.1 A cohort of vaccinated children in the study with reported cases of diarrhoea

This is a descriptive study of children vaccinated with the rotavirus vaccine (Rotarix®□) in the private hospital surveyed one year previous to

the current research. The immunization unit records showed that from June 01 2016 to May 31, 2017, 564 children had received the rotavirus vaccine in this center. Records also showed that 49 of these children (8.7%) had rotavirus diarrhea after being vaccinated. Rates of rotavirus diarrhoea in the unvaccinated group of these children could not be ascertained as the unit does not keep such records. During the study, staff of the immunization unit was interviewed about methods of documenting children that returned to the clinic with diarrhea. It was discovered that, although the records of vaccinated children in the immunization unit are independent of the primary children's hospital records, the hospital folder numbers were written in the immunization record book. Therefore, hospital records could be linked to ascertain those children that returned with rotavirus diarrhoea to the clinic after immunization.

3.7.2 Characteristics of the children with diarrhoea according to *Cryptosporidium* status

Table 7 describes the characteristics of the population in the study with *Cryptosporidium* diarrhoea. All children were between the ages of 1 month to 5 years. The mean duration of diarrhoea in days before the consultation was 2.3 days and 2.5 days for *Cryptosporidium* positive and negative, respectively (p<0.0001). The proportion of children that experienced vomiting

was less in the Cryptosporidium positive group than the *Cryptosporidium* negative group (6.5% and 85.1%, p<0.0001). The mean frequency of vomits experienced 24 hours before the consultation was not similar in *Cryptosporidium* positive and negative cases and, although fewer children in the *Cryptosporidium* positive group had fever compared to those that were *Cryptosporidium* negative (6.2% and 85.1%), this was significant (p<0.0001). Assessing the activity level between the two groups, fewer children had regular exercise after having *Cryptosporidium* diarrhoea than those with *Cryptosporidium* negative (8.0% and 13.3%), but this does not achieve significance. The diarrhoea severity was estimated for 1294 children. In the *Cryptosporidium*-positive children, 8.0% were mild, 76.6% were moderate, and 15.3% were severe. Oral rehydration and intravenous therapy were recorded for 1294 of the children. 76.2% of the children with *Cryptosporidium* were treated with oral rehydration therapy, and 15.6% were given intravenous fluids, while 91.7% were treated with antibiotics. In the *Cryptosporidium* negative children, 12.9% were treated with oral rehydration solution, 78.0% were given intravenous fluids, and 86.3% were treated with antibiotics. There were more children treated with ORS in the *Cryptosporidium* positive group (p= <0.0001), and fewer children were given no treatment in the *Cryptosporidium* negative group (1.4%, p=<0.0001).

Table 6. Rotavirus (RV) Detection in Diarrhoea Cases By Month (N=1294)

Month	Rotavirus Positive cases	% Positive
June-18	10	4.3
July-18	10	4.3
August-18	13	5.6
September-18	15	6.4
October-18	20	8.6
November-18	42	18.1
December-18	29	12.5
January-19	29	12.5
February-19	23	9.9
March-19	15	6.4
April-19	14	6.0
May-19	11	4.7
Total	231	100

Table 7. Rotavirus vaccination status of children

Hospital	Vaccinated		Unvaccinated		Unknown	
	<11	≥ 11	<11	≥ 11	<11	≥ 11
	224(17.3%)	524(40.4%)	68(5.2%)	447(34.5%)	01(0.07%)	30(2.3%)

Table 8. 2x2 table of rotavirus positivity (RV+ or RV-) among vaccinated and unvaccinated children in the study to estimate vaccine effectiveness in the study

CCS	Outcome			Total
Exposure		RV+	RV-	
	Vaccinated	32	716	748
	Unvaccinated	179	336	515
Total		211	1052	

Using data from this study, PPV = 748/1052= 0.711; PCV = 32/231 = 0.138; VE = 74.3%

Table 9. Cohort of vaccinated children in the study from June 01 2017 to May 31, 2018

Period	Number of vaccinated children	Number of vaccinated children with rotavirus diarrhoea
12 months	564	49

Table 10. Clinical signs and symptoms of children with *Cryptosporidium* Diarrhoea (N=1249)

Characteristic feature	Cryptosporidium		
	Positive N=274	Negative N=1020	P-value
Diarrhoea			
Mean (SD) Duration in days	2.3 (0.7)	2.5(0.9)	<0.0001
Mean (SD) max no of stool/ 24h	5.5(0.9)	4.8(1.1)	<0.0001
Vomiting			
Vomiting (%)	18 (6.57)	868 (85.1)	0.0003
Mean (SD) Duration in days	2.3 (0.7)	3.1 (0.9)	0.003
Mean (SD) max no of vomits/24h	3.1 (1.4)	2.3 (0.7)	0.0003
Fever			
Fever (%)	17 (6.2)	868 (85.1)	<0.0001
Mean (SD) Temperature	37.3 (0.2)	37.0 (0.14)	<0.0001
Abdominal pain (%)	252 (22.2)	883 (77.80)	0.0166
Level of activity			
Normal	22 (8.0)	136 (13.3)	0.0012
Reduced	252 (91.9)	884 (86.6)	0.0173
Degree of dehydration			
Mild	22 (8.0)	132 (12.9)	0.0005
Moderate	210 (76.6)	796 (78.0)	0.0005
Severe	42 (15.3)	92 (9.0)	0.0005
Rehydration therapy			
ORS	209 (76.2)	811 (79.5)	<0.0001
IVT	43 (15.69)	72 (7.0)	0.0883
None	22 (8.0)	137 (1.4)	<0.0001
Received antibiotics	252 (91.97)	881 (86.37)	0.0127

The entire participants in the study showed that there were 21.1% positive cases compared with 78.8% negative cases.

Of the *Cryptosporidium* positive cases, the age group with the mildest cases are 12-17 months, followed by 6-11 months. The lowest was recorded in children between the age of 30-60 and 18-23 months.

The peak infection for *Cryptosporidium* was August 2018, followed by September 2018; the lowest was recorded for November and December 2018.

4. DISCUSSION

The incidence of rotavirus diarrhoea was 17.85% out of the 1063 and 21.17% for Cryptosporidium in children surveyed. This research is consistent with the global rotavirus detection rate, as stated by Hart and Cunliffe 2002. This prevalence may likely reduce in the nearest future the introduction of the rotavirus vaccine in some African

countries, especially some countries in West Africa such as Niger, Ghana, and Cameroun, which are border countries to Nigeria and another part of the world. The introduction of the rotavirus vaccine to border countries with Nigeria could benefit Nigeria by giving it regional herd immunity as the government is yet to introduce the rotavirus vaccine into the national immunization schedule. Again, there has been a steady decline in morbidity and mortality due to diarrhoea all over the world in recent years [12]. This could be due to many factors which vary from region to region and country to country.

Some older studies on Rotavirus and Cryptosporidium in Nigeria have reported similar results. For example, a study in Oyo state reported 7.7% of diarrhoea cases to be Rotavirus

positive [15], and in Edo state, 17.2% were Rotavirus positive [16]. A study in Osun state recorded 13.8% [17], while in Niger state, 5.3% prevalence of Rotavirus was reported in children with diarrhoea [18]. Other more recent studies showed similar findings, for example, a study from a state bordering Abuja in which were 18% of cases was Rotavirus positive [19]. Another survey from Plateau state recorded 13.8% [20], and the most recent study from Edo state also reported 13.8% rotavirus positivity in diarrhoea cases [21], as did an older study in Osun State, again 13.8% in 1986 [22]. Variations in the percentage of rotavirus cases in the studies cited above could be due to several factors such as the number of participants in the study, age of participants, the sensitivity of diagnostic kits or methods of ascertaining positive cases, and the season the study was undertaken.
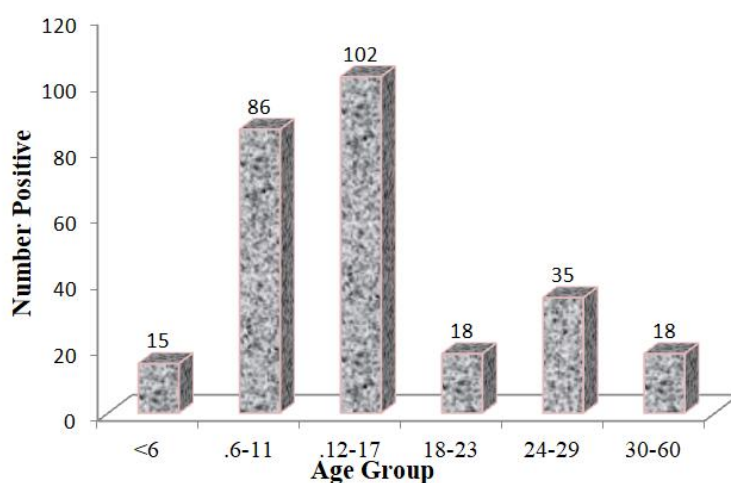
Fig. 1. *Cryptosporidium* ELISA test (positive) by age group
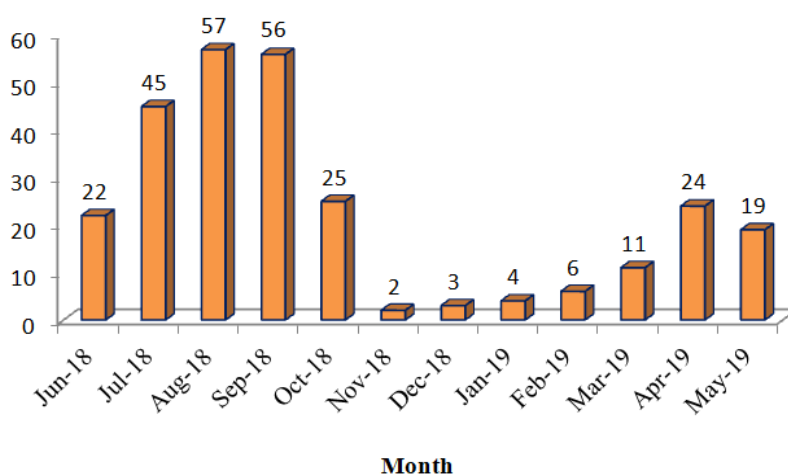
Fig. 2. *Cryptosporidium* ELISA outcome by month

In the study, children under the age of two years were most affected with rotavirus diarrhoea. The age group of children mostly affected with rotavirus diarrhoea were children between the ages of 12-17; the age group of children affected by Cryptosporidium-associated diarrhoea is children between the period of 12-17 months then 6-11 months. This result is similar to a study from Nigeria, where children between the ages of 12-17 months were reported to have been most affected by rotavirus diarrhoea [23]. Contrary to these findings, a report from Kano said that children between the ages of 41 months to 50 months were most affected by rotavirus infection. This is a massive shift from the usual period of children reported with rotavirus infection and suggests that more rotavirus studies should be carried out in the northern part of Nigeria to understand the differences [24].

Although rotavirus diarrhoea is generally not affected by good hygiene, some studies in Nigeria suggested that rotavirus diarrhoea is associated with poor hygiene practices, environmental and socio-economic levels [23].

Abuja is also a well-planned city with improved waste and sewage systems, modern housing, and a sound emergency system in most hospitals. This may be the reason for the low incidence of diarrhea reported. However, prevalence rates of Rotavirus reported in some studies on diarrhoea in Nigeria ranged from 7.7% to 33.3% [15,25]. Some of the states bordering Abuja reported 18% in Kaduna and 17.3% in Plateau State [26]. Two recent studies also reported rotavirus prevalence from Nigerian children of a similar range [27, 21]. Nigeria was set to introduce the rotavirus vaccine into the national immunization schedule in 2014 but could not meet the year target and hoped it could be introduced sooner.

Children with diarrhoea were classified according to the model of care (inpatient and outpatient), case, and control. The total number of children with diarrhoea (cases-1138) and without diarrhoea (controls-156) was 1294, and samples were obtained from all participants. The success in obtaining samples from participants is similar to a Malawian study where recruitment was done between 2012 and 2014 [28]. Samples were successfully obtained from 99% of study participants. Results from the present study had shown that there were more outpatients compared to inpatients. This could be that most children enrolled with diarrhoea had mild to moderate symptoms and did not require hospitalization. Children without diarrhoea were sampled, as studies from other West African countries also revealed cases of asymptomatic rotavirus infections (29, 30].

The age group of participants in this study is children with acute diarrhoea between 1 month to five years. It was observed that the age group primarily enrolled are children between the ages of 7 to eleven months 373 (29.8%). Previous studies of children registered for diarrhoea or similar studies enrolled more children between these ages. The DHS data of 2014 from Nigeria showed that children between the ages of 12 to 24 months had the peak of diarrhoea consultations. However, the results were not directed to Rotavirus and cryptosporidium-associated diarrhea. From other studies, reasons given by most researchers about the most affected age groups are the effect of weaning children where food is not handled correctly, the impact of mothers weaning their babies at this age from breastfeeding, the mobility and high activities of children at these ages and also the effect of mother's antibodies on the breastfed younger child [31]. Statistically, there is a significant difference between the age groups by enrolment p<0.0001.

The seasonality of all-cause diarrhoea in the study showed exciting findings. The enrolment pattern of children with diarrhoea varied between age groups. In children less than six months old, the peak enrolment period was November followed by October, and the least was in August for both Cryptosporidium and Rotavirus. October and November mark the encroachment of the harmattan period, which is entirely in place in December. These findings are similar to Chao et al. [32], who assessed the seasonality of diarrhoeal pathogens in three years. December is one of the coldest months of the year, which extends to January and February. The month of March sometimes marks the beginning of the rainy season in Abuja. Children between the ages of 7-11 were primarily enrolled in March, followed by November, then February. Children between the ages of 12 and 17 were mainly enrolled between February and August, with peaks around February and March. Children between the ages of 18-23 were recruited primarily in November, and children from 24-29 months had a peak period of enrolment in July. Children between the ages of 30-59 months had peak enrolment in August. The reason for these variations is not known. Still, assumptions around

these variations suggest that infections that lead to diarrhoea among children less than two years old mainly occur between October to February, and these months are known to be the peak period of rotavirus infection among children less than two years old from previous publications (33,34,35). For example, older publications suggested that the dry season of October to April was the peak of rotavirus infection and that children in the first six months of life are most affected [36]. Children above two years old revealed that peak periods are around July and August, suggesting other causes. Overall, the seasonality pattern showed that peak months for all diarrhoea cases are in November 2018 and February 2019.

It is important to note that Abuja is a city from which most of the population travels during religious and national public holidays. The seasonality of diarrhoea in Abuja for this study may have been affected by the Christmas and New Year holidays as most residents travel home or to neighboring states at festive periods to celebrate such holidays with their families. It is also known in Abuja that most working classes take their annual holidays around this time of the year. Therefore, it is probable that most families would have been back to Abuja in February and settled to continue work for the rest of the year. This could have been the reason for the low enrolment in December for all age groups. Although the results could be compared to other similar studies with similar findings, the seasonality of rotavirus infection in Abuja may not change in some years to come due to the pattern of activities in the city. From most studies conducted in other regions of Africa, rotavirus infection was expected to peak in the dry cooler months of the year, and in Nigeria, the cooler months have been known to occur in December, January, and some part of February. Contrary to all findings in the past and current study, a study conducted in Kano state (North-western Nigeria) in 2010 reported that the peak seasonality for rotavirus infection was found to be in April with a seasonal peak of about 77% among the participants, and at lowest in July [37].

Children in this study were mainly treated with oral rehydration salt 976 (82.3%) and antimicrobials 1024 (86.4%) among inpatients. Less ambulatory children were treated with intravenous injection 65 (59.6%). A similar trend was observed in hospitalized children, of whom 44 (40.3) were treated with ORS and 109 (100%) with antimicrobials. These findings are similar to Unger et al. (2014), who reported treating

diarrhoeal disease in children under five. Furthermore, this could also suggest that although most children in the study had reduced activities during the consultation, they only had mild to moderate symptoms of acute diarrhoea.

Nigeria, Africa's most populous country, has yet to introduce the rotavirus vaccine into its national immunization program. This was set for 2014 but was postponed, and a new date has not been announced. Other West African countries such as Niger, Togo, Mali, Senegal, and Sierra Leone introduced the vaccine in 2014; Burkina Faso and The Gambia introduced the vaccine in 2013; while Ghana had introduced the vaccine since 2012 into its national immunization program. All countries in West Africa that introduced the vaccine were GAVI eligible [38]. Out of these countries, only three introduced the Rotateq (pentavalent vaccine). These are The Gambia, Burkina Faso, and Mali. All others introduced the Rotarix (monovalent RV1) vaccine.

Nigeria was estimated to have a population of 183,000,000 people in 2015 (NPC, 2015). There is no estimate of the number of children under five since the 2006 national population census. In Nigeria, rotavirus diarrhoea is more endemic in the extreme northern states such as Sokoto, Zamfara, Katsina, Jigawa, Kano, Yobe, and Borno states where the current Boko Haram terrorist activities had worsened since 2011 and till late 2015. Nigeria has no central health surveillance system, and viral diarrhoea is one of the most poorly diagnosed diseases in the country, with very poor or absent hospital recordings. This observation was confirmed still to be valid during the current study.

This is the first study on rotavirus diarrhoea conducted in Abuja, Nigeria. In this study, data collection was limited to Abuja, while most residents live in satellite towns around Abuja. In addition, the data collection was limited to patients that consulted doctors in selected hospitals. The study was also modified to children under five years, excluding those aged less than one month. The study describes the burden of all-cause diarrhoea and rotavirus diarrhoea in hospitalized and ambulatory patients of children between 1 month to five years. There are no published data on rotavirus diarrhoea in Abuja. Therefore, the yearly incidence of Rotavirus can only be compared with other states in Nigeria where such research has been conducted in the past and other countries in Africa, especially those bordering Nigeria.

The study plan did not initially include estimation of vaccine efficacy. Still, the opportunity arose to look at this at Zankli Medical Centre, where records were available for a cohort of children vaccinated the previous year with the Rotarix RV1 vaccine. As described earlier, at least 8.6% of 564 vaccinated groups are known to have been seen at that center over the following year with rotavirus diarrhoea. However, it is recognized that some parents only use the Zankli Medical Clinic to obtain the rotavirus vaccine. They do not otherwise maintain a Clinic record card nor start other consultations in the clinic for their child. Therefore, follow-up of this group of vaccinated children to detect any occurrence or recurrence of rotavirus diarrhoea may be incomplete and may underestimate the actual number affected. Children might also have attended other centers (records were not linked) or not presented to any clinic. There were no records of frequency of rotavirus diarrhoea episodes in unvaccinated children for comparison.

A prospective controlled study of vaccinated versus unvaccinated children would be the best way to estimate vaccine efficacy. For example, in a recent publication from Malawi, the incidence of rotavirus diarrhoea in children given a monovalent rotavirus vaccine showed protection compared to controls. In addition, the incidence of diarrhoea decreased in vaccinated children year on year [28]. This and other prospective studies show protection of around 55-65%, depending on whether it is against hospitalization with diarrhoea or against clinic visits with less severe diseases [39].

Finally, all nineteen participants that died in this study were females aged less than two years. All children from this group had severe diarrhoea and had not been vaccinated, of which 60% of the children were ambulatory patients. Therefore, it was assumed that cause of death includes other pathogens or illnesses associated with diarrhea which was suggested from the findings of Chao et al., [32].

5. CONCLUSION AND RECOMMENDATION

A complete literature review suggests that all-cause diarrhoea, specifically rotavirus diarrhoea, followed by *Cryptosporidium* diarrhoea, has been a significant cause of disease in children in different States in Nigeria (as in the rest of Africa) for more than 30 years. In most studies, the peak age affected is between 6 to 18 months after weaning. However, the seasonal pattern of diarrhoea presentation and affected periods are different in some northern states and require further investigation.

In this prospective study, the average age of recruits (57.5% boys) was 7-11 months, and the most frequently affected age groups were 12-17 months 152(12.1%) then 6-11 months 373(29.8%). In most centers, the highest numbers of attendances were in the colder months November-January for Rotavirus. Children with *Cryptosporidium* diarrhoea were estimated to be 274 (21%) in the study, with age group 12-17 months most affected. There was a clear seasonal peak occurring in August and September for children with *Cryptosporidium* diarrhoea. Only a few parents were aware that rotavirus vaccinations were available, and only a quarter could remember if/how often their child might have been vaccinated. Vaccination cards were often not available for verification for the study.

A more significant proportion of children with diarrhoea with less severe disease (judged by activity scores) had been vaccinated than the children with worse activity scores.

The surveillance of diarrhoeal disease in Nigeria, the largest country in Africa, is inadequate for meaningful analysis of disease trends. Oral rehydration is managed according to WHO recommendations, but there is marked overprescribing of antibiotics, and this needs to be addressed.

The lack of availability of virological investigations in most clinics in Nigeria means that specific access would be needed to support and monitor the effectiveness of vaccination campaigns. Nevertheless, this work suggests that Abuja resembles most other states in Nigeria and nearby countries in the incidence and prevalence of rotavirus diarrhoea in children under the age of 1 and slightly older and indirectly supports the effectiveness of the monovalent vaccines.

The findings support the planned (but delayed) introduction of the rotavirus vaccine in the whole of Nigeria but emphasize the need for adequate investment in quality assured surveillance and virological surveillance to monitor this.

CONSENT

All authors declare that 'written informed consent was obtained from the patient to publish this

case report and accompanying images. A copy of the written consent is available if requested.

ETHICAL APPROVAL

Ethical approval was obtained from the Asokoro District hospital research ethics committee. In addition, a consent form was administered to the parent/guardian of children before enrolment into the study.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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