ORIGINAL ARTICLE

Clinical Profile and Outcome of Under-five Children with Rotavirus Diarrhoea at the University of Maiduguri Teaching Hospital, Maiduguri, Nigeria

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ABSTRACT

Background: Rotavirus is the most common cause of diarrhoeal disease among children under the age of five years. It is an important cause of serious complications and death; its contribution to childhood morbidity and mortality remains very high in our setting. **Objectives:** This study was conducted to determine the clinical profile and outcome of under-five children with rotavirus diarrhoea at the University of Maiduguri Teaching Hospital (UMTH). **Methods:** The study was hospital-based descriptive in which 351 children with acute watery diarrhoea were consecutively recruited from September 2019 to March 2021. A pretested Case Record Form (CRF) was used to capture the presenting symptoms and signs of the participants. Clinical findings like axillary temperature, hydration status, features of dehydration and presence or absence of oedema were documented. The duration of hospital stay and clinical outcome of the subjects were also documented. Stool samples were collected from participants and tested for rotavirus using an immunochromatographic test. Data generated were analysed using IBM SPSS version 26. **Results**: One hundred and forty-four (41%) of the participants have rotavirus diarrhoea. Participants with rotavirus and non-rotavirus diarrhoea presented with similar clinical features. However, vomiting ($\chi 2$ =5.688, p=0.001), decline in urine volume ($\chi 2$ =7.058, p=0.006), and dehydration ($\chi 2$ =4.748, p=0.034) were found to be significantly higher in participants with rotavirus diarrhoea compared to non-rotavirus diarrhoea. Participants with rotavirus diarrhoea are likely to have a shorter duration of hospital stay compared to participants with non-rotavirus diarrhoea (U= -2.114, p=0.034). **Conclusion:** The spectrum of clinical presentations were similar among participants with rotavirus diarrhoea and non-rotavirus diarrhoea. However, vomiting was more frequently seen in participants with rotavirus diarrhoea compared to non-rotavirus diarrhoea. Rotavirus infection should be suspected in under-five children with sudden onset of acute diarrhoea and vomiting and managed accordingly in the study area.

Keywords: Rotavirus, Acute watery diarrhoea, under-five.

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Introduction

Diarrhoeal disease is a major cause of morbidity and mortality among children, especially in developing countries.[1] It is the second leading cause of death in children under five years of age after respiratory tract infection.[2] It is estimated that 1.7 billion episodes and about 525,000 deaths from diarrhoea disease occur each year in under-five children globally with about 85% of these deaths occurring in children from low-income countries.[2,3] An estimated 151,700 children die in Nigeria every year from diarrhoeal disease.[4] Rotavirus has been identified as the major cause of diarrhoea in infants and young children worldwide.[1,5] Rotavirus is a double-stranded non-enveloped RNA in the family

Reoviridae that causes mild to severe disease characterised by watery diarrhoea, nausea, vomiting, abdominal cramps and low-grade fever.[5]

The occurrence of rotavirus illness in children is similar in both developed and developing nations.[6] Mortality is however more in developing countries, due to several factors including poor access to hydration therapy and an increased number of children with nutritional disorders.[6] A hospital-based World Health Organisation (WHO) global network for surveillance of rotavirus diarrhoea reported an estimated prevalence of 39-52% in the African region.[7]

The number of deaths caused yearly by rotavirus diarrhoea has been estimated to be about 215,000 among children less than five years old worldwide.[3] Nigeria continues to be among the 10 countries in Africa with the greatest number of rotavirus disease-associated deaths per year. Up to 33,000 deaths occur annually among under-five children due to rotavirus disease in Nigeria.[3] Global estimates indicated that India, Congo (DR), Pakistan, as well as Nigeria contributed almost 49% of the global infant deaths as a result of rotavirus diarrhoea in the year 2013.[3] Various studies in Nigeria have reported rotavirus diarrhoea prevalence rate of 11-56%.[8-18] These, included only limited studies from the Northeastern part of Nigeria that only focused on the laboratory aspect of the infection and did not explore the clinical aspect of rotavirus infection.[10,11,14] There is therefore inadequate data on the clinical spectrum and outcome of rotavirus diarrhoea in children in Maiduguri. This study was conducted to determine the clinical spectrum and outcome of rotavirus diarrhoea in under-five children with acute watery diarrhoea at the University of Maiduguri Teaching Hospital (UMTH), Maiduguri, Northeastern Nigeria.

Methods

The study was hospital-based and descriptive in design, conducted at the Paediatric Outpatient Department (POPD) and Emergency Paediatric Unit (EPU) UMTH, Maiduguri, Borno State, Nigeria over 18 months from September 2019 to March 2021.

Borno State is the largest of the six (6) states in the Northeastern part of Nigeria and second in the federation in terms of land mass.[19] Public hygiene, basic sanitation and access to safe and potable water are poor.[19] Surface water is largely seasonal with rivers flowing for around three months in a year. The Alau dam holds water throughout the year; its water is treated for public supply but only extends to about 30% of the population of Maiduguri and its environs. Ground water therefore, provides the dominant (perennial) supply of water to the inhabitants of Maiduguri and its surroundings. Access to safe drinking water continues to be one of the critical issues facing residents of Maiduguri. The situation has been exacerbated by the Boko-Haram insurgency, which has almost doubled the population of the Maiduguri metropolis, with a corresponding increase in demands for water supply.[20]

Study population: Children under-five years of age presenting with acute watery diarrhoea.

Inclusion criteria: Children aged 1 month to 59 months with acute watery diarrhoea (defined as the passage of more than 3 episodes of watery stools per 24 hours for less than two weeks) whose parent/ caregiver consented.

Exclusion criteria: Children with visible blood in diarrhoeal stool, diarrhoea lasting more than 14 days and children who had received rotavirus vaccine. Children who developed diarrhoea following admission at UMTH and children referred from another health centre where they have been hospitalised for more than 24 hours for the current episode of diarrhoea, were also excluded.

Ethical considerations: Ethical approval was obtained from the UMTH Research and Ethical Committee (UMTH/REC/19/410). Informed consent (verbal and written) was obtained from parents/caregivers after a full description of the research. The study was carried out at no cost to the participants and parents or caregivers had the liberty to withdraw from the study with no consequences to their children. The study was conducted according to the best clinical and laboratory practices. Oral rehydration solution (ORS) and zinc supplement were given to each child recruited into the study at no cost. Also, health education was given to the parents/ caregivers of the children on the preparation and use of ORS, preparation and use of Salt - Sugar Solution (SSS), breastfeeding and continued feeding, personal and environmental hygiene and the need to bring children with diarrhoea or any ailment early to the hospital.

Study procedure: A case record form (CRF) was used to document the clinical characteristics; duration of hospital stays and clinical outcomes of the subjects.

Stool Sample Collection and Analysis

Three millilitres of diarrhoeic stool were collected from each child by their mothers or caregivers after educating them individually as they presented to the POPD and EPU on stool sample collection by the researchers and assistants. Mothers were asked to collect stool samples from their children in a clean dry potty for older children. For younger children, mothers were given diapers and advised to use them once for stool sample collection by putting the non-absorbent surface next to the skin and leaving the diaper uncoupled so that the moment stool is passed by the baby, the mothers can notice it and collect the stool sample. The stool from the diaper or the potty was scooped with a plastic disposable spoon and

transferred into a labelled wide-mouth universal sterile container.[21] Stool samples were collected mostly under the supervision of the researchers and research assistants in the hospital. The labelled stool specimens were analysed immediately at the EPU side lab using the Rotavirus kit® (Cortez OneStep Rotavirus Antigen RapiCard™ InstaTest).[22] The kits were validated by testing on rotavirus-positive stool samples in the Medical Microbiology Laboratory of UMTH before the commencement of the study and after testing every 30 samples. The tests were performed according to the kit manufacturer's instructions.

The specimen and stored test kits were removed from the refrigerator and brought to room temperature before testing for samples that could not be analysed immediately. The test device was then removed from the sealed foil pouch, placed on a clean flat surface and labelled accordingly. Two drops of each stool sample were dropped into the labelled specimen preparation buffer using the dropper on the buffer bottle. The solution was then mixed by vigorous shaking. Thereafter, two drops of the diluted stool mixture were dispensed into the sample well of the test device and a timer was set up for 10 minutes. The results were then read and interpreted as positive, negative or invalid.[22]

A test was considered positive when a distinct pink-coloured band appeared on the test line regions in addition to a pink line on the control line region (RV RDT +). A negative test was recorded when no line appeared in the test line region but a distinct pink line showed on the control line region (RV RDT -). An invalid test was when the control line next to the test line did not become visible within 15 minutes after the addition of the sample, such tests were repeated using a new test kit. The results of the test were then recorded.

Data analysis: Data obtained was analysed using the International Business Machine Statistical Package for Social Sciences (IBM SPSS) version 26 (SPSS, Chicago, Illinois, USA). Median (interquartile range [IQR]) was used to summarise continuous variables such as duration of symptoms. Clinical features were expressed as proportion/percentage, and chi-square was used to determine the association between clinical features with rotavirus diarrhoea. A p-value of < 0.05 was considered significant at a 95% confidence interval.

Results

Sociodemographic Characteristics of Participants

The socio-demographic characteristics of the participants are shown in Table I. One hundred and eighty-eight (53.6%) of the participants studied were in the 1-11 months age group. The median age was 11 months with (IQR=7-17) with a male-to-female (M: F) ratio of 1.1:1. Majority of the participants belongs to the low socio-economic class.

Table I: Socio-demographic characteristics of the study population

VARIABLES	FREQUENCY	PERCENTAGE (%)
Age (months)		
1-11	188	53.6
12-23	119	33.9
24-35	25	7.1
36-47	10	2.8
48-59	9	2.6
Gender		
Male	184	52.4
Female	167	47.6
Ethnic group		
Kanuri	177	50.4
Shuwa Arab	34	9.7
Fulani	26	7.4
Babur	22	6.3
Marghi	15	4.3
Others¥	77	21.9
Religion		
Islam	316	90.0
Christainity	35	10.0
Socio-economic Class		
Upper	17	4.8

Middle	83	23.6
Lower	251	71.5
Residence		
Urban	293	83.4
Rural	42	12.0
Semi-urban	16	4.6

¥ (Hausa, Igbo, Kilba, Mandara, Gamargu, Waha, Kare-kare, Guduf, Barawa, Nufe, bolewa, Chikide, Pachama, Chibok, Yoruba, Jukun, Hambaghda, Glavda, Chadian)

Clinical Manifestations of rotavirus and non-rotavirus Diarrhoea

Table II presents the comparison of clinical symptoms between participants with rotavirus diarrhoea and non-rotavirus diarrhoea. Participants with positive RV RDT had a higher proportion of vomiting (81.9%, 118/144, χ^2 =5.688, p =0.001) and a decline in urine volume (30.6%, 44/144, χ^2 =7.058, p= 0.006) compared to participants with negative RV RDT.

Table II: Comparison of clinical symptoms between participants with rotavirus and non-rotavirus diarrhoea

Variable	RV RDT+ n=144 Frequency (%)	RV RDT- n=207 Frequency (%)	Total	χ2	P value
Vomiting				5.688	0.001*
Yes	118(81.9)	129(62.3)	247		
No	26(18.1)	78(37.7)	104		
Fever				2.538	0.075
Yes	117(81.3)	181(87.4)	298		
No	27(18.7)	26(12.6)	53		
History of decline in urine volume				7.058	0.006*
Yes	44(30.6)	38(18.4)	82		
No	100(69.4)	169(81.6)	269		
Abdominal distension					
Yes	22(15.3)	31(15.0)	53	0.006	0.527
No	122(84.7)	176(85.0)	298		
Abdominal cramps/Excessive crying before stooling				1.086	0.185
Yes	21(14.6)	39(18.8)	60		
No	123(85.4)	168(81.2)	291		
Preceding flu-like symptoms ¤				0.267	0.644
Yes	95(66.0)	142(68.6)	237		
No	49(34.0)	65(31.4)	114		
Other symptoms^				0.799	0.425
Yes	27(18.8)	47(22.7)	74		
No	117(81.2)	160(77.3)	277		

μ any of (cough, nasal discharge, nasal blockage, sneezing), ^ any of (weight loss, perianal/perineal rash, body rash, oral rash, body swelling, eye discharge, ear discharge, refusal to feed, crying on micturition, generalized body weakness, difficulty in breathing). RV RDT+ (rotavirus rapid diagnostic test positive), RV RDT- (rotavirus rapid diagnostic test negative), $\chi 2$ (Chi-square), * statistically significant $p<0.05$

The median duration of diarrhoea was longer in rotavirus-negative [4 (IQR=3-7) days] than rotavirus-positive [3 (IQR=1-5) days] participants. The median duration of vomiting was however the same for both rotavirus-positive [3 (IQR=2-5) days] and rotavirus-negative [3 (IQR=2-5) days] participants. (Table III). However, both findings were not statistically significant.

Table III: Duration of diarrhoea and vomiting in participants with rotavirus and non-rotavirus diarrhoea

Variable	RV RDT+ Frequency (%)	RVRDT- Frequency (%)	Total	$\chi 2$	P value
Diarrhoea				3.865	0.146
<4days	75(52.0)	87(42.0)	162		
4-8 days	61(42.4)	102(49.3)	163		
9-14 days	8(5.6)	18(8.7)	26		
Total	144(100)	207(100)			
Vomiting				3.755	0.158
<4 days	80(67.8)	52(40.3)	132		
4-8 days	35(29.7)	72(55.8)	107		
>8 days	3(2.5)	5(3.9)	8		
Total	118(100)	129(100)			

RV RDT+ (rotavirus rapid diagnostic test positive), RV RDT- (rotavirus rapid diagnostic test negative), $\chi 2$ (Chi square)

Rotavirus-positive participants had a higher frequency of vomiting episodes than rotavirus-negative participants with a median of 4 days (IQR=3-7 days) versus 3 days (IQR=2-5 days) respectively ($\chi 2=10.321$, $p=0.005$). Diarrhoeal frequency was however similar among rotavirus-positive and rotavirus-negative participants with a median of 5 (IQR=4-7) versus 5 (IQR=4-7) respectively, ($\chi 2=5.278$, $p=0.071$). Details are shown in Table IV.

Table IV: Frequency of diarrhoea and vomiting in participants with rotavirus and non-rotavirus diarrhoea

Variable	RV RDT+ Frequency (%)	RV RDT- Frequency (%)	Total	$\chi 2$	P value
Diarrhoea				5.278	0.071
1-5/day	72(50.0)	129(62.3)	201		
5-10/day	65(45.1)	70(33.8)	135		
>10/day	7(4.9)	8(3.9)	15		

Total	144(100)	207(100)			
Vomiting				10.321	0.005*
1-5/day	78(66.1)	108(83.7)	186		
5-10/day	35(29.7)	18(14.0)	53		
>10/day	5(4.2)	3(2.3)	8		
Total	118(100)	129(100)			

RV RDT+ (rotavirus rapid diagnostic test positive), RV RDT- (rotavirus rapid diagnostic test negative), $\chi 2$ (Chi square), * statistically significant $p<0.05$.

Participants with positive RV RDT were significantly more likely to have dehydration compared to participants with negative RV RDT (27.1% vs. 17.4%, χ^2= 4.748, p =0.034). The other clinical signs were not significantly different among rotavirus-positive and rotavirus-negative participants as shown in Table V.

Table V: Comparison of clinical signs between participants with rotavirus and non-rotavirus diarrhoea

Variables	**RV RDT+ n=144 Frequency (%)**	**RV RDT- n=207 Frequency (%)**	**Total**	**$\chi 2$**	**P value**
Temperature				0.369	0.836
Subnormal	39(27.1)	51(24.6)	90		
Normal	45(31.2)	70(33.8)	115		
Pyrexia	60(41.7)	86(41.6)	146		
Dehydration				4.748	0.034*
Yes	39(27.1)	36(17.4)	75		
No	105(72.9)	171(82.6)	276		
Pedal oedema				1.066	0.356
Present	6(4.2)	14(6.8)	20		
Absent	138(95.8)	193(93.2)	331		
Nutritional Status				6.051	0.108
Overweight	6(4.2)	2(1.0)	8		
Normal	73(50.7)	92(44.4)	165		
Moderate M	17(11.8)	31(15.0)	48		
Severe M	48(33.3)	82(39.6)	130		
Other features$^{\infty}$				1.094	0.341
Yes					
No	16(11.1)	31(15.0)	47		
	128(88.9)	176(85.0)	304		

∞ any of (oral thrush, hepatomegaly, body rash, wasting, dyspnoea, tachypnoea, tachycardia, hypotonia, head lag, dermatosis, pallor, crepitations, perineal/perianal excoriation, eye discharge, ear discharge, tragal tenderness), M (malnutrition), RV RDT+ (rotavirus rapid diagnostic test positive), RV RDT- (rotavirus rapid diagnostic test negative), $\chi 2$ (Chi-square), *statistically significant $p<0.05$

Clinical Outcome of rotavirus and non-rotavirus Diarrhoea

The median duration of hospital stay was 4 days (IQR 2-5 days) for participants with positive RV RDT and 5 days (IQR 3-7 days) for participants with negative RV RDT. Participants with positive RV RDT are likely to have a shorter duration of hospital stay compared to participants with negative RV RDT (U= -2.114, p=0.034).

Table VI presents the outcome of hospitalised participants with rotavirus and non-rotavirus diarrhoea. Rotavirus infection status did not affect the outcome of hospitalised participants (χ^2 =0.460, p= 0.916).

Table VI: Outcome among hospitalised participants with rotavirus and non-rotavirus diarrhoea

Outcome	RV RDT+ n=100 Frequency (%)	RV RDT- n=144 Frequency (%)	Total	χ2	P value
				0.460**	0.916
Discharge	93(93.0)	136(94.4)	229		
LAMA	2(2.0)	2(1.4)	4		
Death	5(5.0)	6(4.2)	11		

RV RDT+ (rotavirus rapid diagnostic test positive), RV RDT- (rotavirus rapid diagnostic test negative), χ2 (Chi-square), LAMA (leave against medical advice), **Fishers Exact p-value when the expected count in cell<5

Discussion

Rotavirus is known to cause diarrhoeal disease morbidity and mortality among children under the age of five years.[1] Our study investigated rotavirus diarrhoea among under-five children with acute watery diarrhoea in UMTH and observed that rotavirus remains an important cause of diarrhoea in children.

Most of the clinical features of rotavirus diarrhoea were essentially similar to non-rotavirus diarrhoea in our study. This could be attributed to both being forms of acute diarrhoeal disease with similar pathogenesis even though the causative agents may be different. However, vomiting, history of decline in urine output, and dehydration were significantly more likely to be seen among patients with rotavirus diarrhoea compared to non-rotavirus diarrhoea. The association of vomiting with rotavirus diarrhoea is not surprising as it is known that the period of illness in rotavirus diarrhoea is acute and symptoms often start with vomiting followed by four to eight days of profuse diarrhoea.[8] This is similar to the studies done by Tagbo *et al.*,[17] Ibrahim *et al.*,[15] Potgieter *et al.*,[23] Gasparinho *et al.*[24] and Phukan *et al.*[25] who reported vomiting as the only clinical symptom significantly seen in children with rotavirus diarrhoea compared to non-rotavirus diarrhoea. Most other studies also reported vomiting as part of clinical symptoms seen with rotavirus diarrhoea.[8,16,21,26,27] The finding of a decline in urine output being significantly higher in participants with rotavirus diarrhoea compared to non-rotavirus diarrhoea is due to the significant level of dehydration found in participants with rotavirus diarrhoea compared to non-rotavirus diarrhoea in our study. Dehydration in diarrhoea usually results from loss of fluid in the diarrhoeic stools and vomitus especially when diarrhoea is profuse like what is seen with rotavirus diarrhoea.[1] The reason for the higher incidence of dehydration in participants with rotavirus diarrhoea may be due to the profuse nature of rotavirus diarrhoea which is often accompanied by

vomiting thus, it is usually classified as dehydrating diarrhoea.[7,16] In addition, high total body water in infants creates an avenue for more profound loss and resultant dehydration. Studies from Thailand,[28] India[21] and Vietnam[26] reported rotavirus diarrhoea to be more likely to present with dehydration than non-rotavirus diarrhoea. Similarly, studies done by Nokes *et al.*,[29] Nakewesi *et al.*[7] and Ojobor *et al.*[16] from Kenya, Uganda and Nigeria respectively, reported dehydration to be more common in participants with rotavirus diarrhoea compared to non-rotavirus diarrhoea.

The duration of hospital stay was shorter in participants with rotavirus diarrhoea compared to non-rotavirus diarrhoea in our study. This is likely because participants with rotavirus diarrhoea had lower co-morbidities like malnutrition, pneumonia and other forms of sepsis compared to participants with non-rotavirus diarrhoea who had a higher incidence of co-morbidities that were less readily treated and consequently stayed longer in the hospital. This is in agreement with studies done by Intusoma *et al.*,[28] and Nokes *et al.*,[29] who also found duration of hospital stay to be shorter in participants with rotavirus diarrhoea compared to non-rotavirus diarrhoea. In contrast, Aldemir-kocabas *et al.*,[30] found the duration of hospital stay to be longer in participants with rotavirus diarrhoea compared to non-rotavirus diarrhoea. This was largely because of the presence of additional complications like electrolyte imbalance, sepsis, toxic hepatitis and aseptic meningitis that were less readily treated and so stayed longer in the hospital.[30] However, Jyothirmayi *et al.*,[21] did not find any association between duration of hospital stay and rotavirus diarrhoea. Therefore, the relationship between the duration of hospital stays and rotavirus infection varies and may be influenced by several factors.

Conclusion

The spectrum of clinical presentations was similar among participants with rotavirus diarrhoea and non-rotavirus diarrhoea. However, vomiting, dehydration and declined urine volume were more frequently seen in participants with rotavirus diarrhoea compared to non-rotavirus diarrhoea. Children with rotavirus diarrhoea had a shorter duration of hospital stay compared to those with non-rotavirus diarrhoea.

Recommendations

We recommend that rotavirus diarrhoea be suspected in children presenting with acute diarrhoea, vomiting and a decline in urine output and should be managed aggressively to prevent further complications.

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