BURDEN OF ROTAVIRUS DIARRHOEA IN CHILDREN IN ABUJA

ABSTRACT

Background: Diarrhoea is the second leading cause of death in children. Nigeria has the continent's highest mortality due to diarrhoeal diseases with little information on specific causes and the proportion affected by rotavirus infection. The main objectives of this study were to describe the features of young children with diarrhoea, with and without rotavirus, in Abuja the Federal Capital Territory (where there were no data).

Materials and Methods: Retrospective review of local hospital activity data related to diarrhoea was retrieved from General Hospitals in Abuja. Then a one-year prospective descriptive study of children under 5 years of age with acute diarrhoea was conducted from September 2012 to August 2013. Children with acute diarrhoea attending three government hospitals and one private hospital were recruited. Children without diarrhoea were recruited as the control group. Fecal specimens were transported in cold chain boxes from Nigeria and stored at -80 °C at the Institute of Global Health, virology section of the University of Liverpool, where all laboratory work was performed.

Results: Hospital records were poorly preserved and did not provide meaningful data for trend analyses or disease surveillance. 1331 participants were enrolled in this prospective study. Stool samples were collected from 1242 (93.3%) participants, of whom 957 (77.0%) were ambulatory, 123 (9.9%) hospitalised and 160 (12.8%) controls without diarrhoea. 881 and 450 children with diarrhoea were recruited from government and the private hospitals, respectively. The median age of the children was 8 months in the ambulatory and 9.5 months in the hospitalized group ($p<0.05$). A total of 209 (16.8%) children were vaccinated, 858 (69.1%) were unvaccinated, and 174 (14.0%) had an unclear vaccination status. Rotavirus ELISA was positive in 123 (11.4%) children with diarrhoea and 2 (1.2%) controls. Among children with diarrhoea, 92 (10.4%) of 881 children attending government hospitals had rotavirus, compared to 33 (7.3%) of 450 children attending a private hospital ($p<0.001$) where a vaccination program had been in place. The peak months for rotavirus infection were November and February. The efficacy of Rotarix® RV1 vaccine in preventing rotavirus diarrhoea was indirectly assessed to be 64.5%.

Conclusion: Rotavirus is an important pathogen in children, especially in unvaccinated children in Abuja. The introduction of a rotavirus vaccine is highly desirable in Nigeria, but this is still awaited. Local and national infrastructure are inadequate for basic surveillance of diarrhoeal disease, and this will have to be improved, together with access to virological stool testing, to monitor the planned vaccine program. The retrospective studies reported here provide indirect evidence of vaccine efficacy in Abuja but need prospective confirmation.

Keywords: Rotavirus, Acute Diarrhoea, Burden, Abuja

INTRODUCTION

Diarrhoea remains a major cause of morbidity and mortality in Nigeria (Adah et al., 1997, Aminu et al., 2008a, Cunliffe et al., 1998, Fagbami et al., 1987). In Nigeria, the number of hospitalizations, diarrhoeal consultations, and trends over time of diarrhoeal consultations have not been established. It has been estimated that diarrhoeal disease in children accounted for 8.2% - 15% of the total annual emergency and diarrhoeal treatment unit admissions in Nigeria (Tinuade et al., 2006). The age group mostly affected by rotavirus diarrhoea are children under the age of five (Junaid et al., 2011, Gollogly, 2009, Cunliffe et al., 1998, Bryce et al., 2005, Boschi-Pinto et al., 2008, Oni et al., 1991). Despite the high hospitalisation and death figures due to rotavirus diarrhoea in Nigeria, rotavirus diarrhoea is mostly not well understood by the local population of Abuja residents. Rotavirus diarrhoea is regarded as any bowel infection which is followed by passing of loose stool. Many of the residents are not aware of the vaccine availability for this type of diarrhoea and much of diarrhoeal diseases are not particularly classified in the hospitals surveyed except extreme cases of severe dehydration of hospitalised patients are tested and classified as either diarrhoeal disease or gastroenteritis. A study described Nigeria as being the third highest in the world, with hospitalizations and deaths from rotavirus diarrhoea (Aminu et al., 2008b). Nigeria has no central health surveillance system to assess and follow disease trends, and rotavirus diarrhea is poorly diagnosed in children with acute diarrhoea. The importance of this research cannot be overemphasized and cannot have come at a better time. The research has formed part of the national and international research priorities, as the Millennium Development Goal 4 aims to reduce child mortality by 2015. The aim of this study was to describe and document the age distribution, seasonality of rotavirus diarrhoea, and cases of rotavirus diarrhoea among vaccinated and unvaccinated children. The findings will be useful for planning the possible inclusion of rotavirus vaccine in the National Immunization Program, in addition to providing a baseline for monitoring the influence of the vaccine on prevalence when introduced in the immunization programme of Nigeria.

METHODOLOGY

The study was a one-year prospective survey of children with acute diarrhoea attending Zankli Medical Center (ZMC), University of Abuja Teaching Hospital (UATH) Gwagwalada, Gwagwalada Town Clinic, and Nyanya General Hospital from 1st of September 1, 2012, to August 30, 2013. The pediatric unit of ZMC (private clinic) provides the Rotavirus vaccine (Rotarix), which is administered to children less than 6 months of age as part of their routine immunization schedule.

Children aged 1 month to 5 years with complaints of acute diarrhoea were included in the study at all centers. The pediatrician identified cases of diarrhoea and referred the patients to the researcher for recruitment. After obtaining informed consent from the parents or guardians, details of the clinical history and clinical examination of stool samples were collected. A questionnaire was administered to obtain demographic details of the patient, clinical history of

the current diarrhoea episode, presence of dehydration, weight, height, other symptoms such as respiratory problems and rashes and vaccination status. Hospitalized patients were followed up to record their outcomes (death or discharge, use of intravenous solutions, and number of hospitalizations). Rotavirus vaccination status was confirmed by reviewing clinical records in ZMC. The severity of the clinical episode of diarrhoea was classified according to the Vesikari score (Ruuska and Vesikari, 1990), as modified by Nakagomi (Nakagomi et al., 2005). This is a standardised score currently accepted internationally to classify the severity of the diarrhoea episodes and is based on a series of clinical criteria. In addition to cases of diarrhoea, a control group of children without diarrhoea was included to compare the prevalence of pathogens in children with and without diarrhoea. Control children were selected from children under five years of age attending the Well Baby Clinic of UATH. Stool samples were aliquoted into a safe-lock tube and labelled with the name, date, and study number. The samples were tested for rotavirus using an ELISA kit (Rotaclone) at the University of Liverpool, United Kingdom. The vaccine effectiveness was estimated using the Hatton's method 1990.

RESULTS AND DISCUSSION

General Characteristics of the population with and without diarrhoea

A total of 1331 children were enrolled in the hospital survey from September 2012 to August 2013. The children were aged between 1 and 5 years. More males (n = 775) than females (n = 556) were enrolled in the study. Ninety-one (6.8%) patients left the hospital without providing samples, and 1240 stool samples were collected. One hundred and twenty nine (9.6%) of the 1240 were hospitalized while 1027 (77.1%) were ambulatory. One hundred and seventy five (13.1%) control children without diarrhoea were enrolled. The mean diarrhoea duration before consultation was 3 and 8 days for ambulatory and hospitalized children, respectively ($p<0.0001$). The mean number of stools per day was 2 and 5 for ambulatory and hospitalized children, respectively. Most children passed out watery stool for both hospitalized and ambulatory with an overall total of 635 (59.9%) and 380 (32.9%) had mucus. All 175 controls had solid stools.
The proportion of children experiencing vomiting was lower in ambulatory than hospitalized children (51.4% and 75.9%, respectively, $p = <0.0001$). The mean frequency of vomits experienced before consultation was between 4 and 6 times for ambulatory and hospitalised children respectively ($p<0.0001$). Less ambulatory children experienced abdominal pain (27.3%) than hospitalized children (41%) and the same trend was observed for fever ($p<0.002$ and $p<0.003$, respectively).

Oral and intravenous rehydration were recorded in 1091 (94.38%) of the 1156 children. This figure (1091) comprises 132 and 925 children in the hospitalized and ambulatory groups, respectively. Of the hundred and thirty one (80.9%) and 114 (88.3%) of the ambulatory and hospitalised children were treated with antimicrobials, respectively ($p<0.03$). The percentage of

death due to diarrhoea was 2 (1.5%) for hospitalised and 3 (0.2%) for ambulatory children. The majority of hospitalized patients improved after ORS administration.

Table 1 General Characteristics of the population with and without diarrhoea

Parameters	Ambulatory N= 1027	Hospitalised N= 129	P value
Age in months, median (IQR)	8.0 (12.0, 24.5)	9.5 (12.5, 14.0)	<0.05
Male: Female (% male)	603:424 (58.7%)	73:56 (56.5%)	0.6
Diarrhoea			
Mean (SD) duration, days	3.4 (2.6)	8.0 (16.5)	<0.0001
Mean (SD) Max frequency/24h before attending	1.8 (2.6)	4.6 (4.0)	<0.0001
Presence of vomiting (%)	528 (51.4%)	98 (75.9%)	<0.0001
Mean (SD) duration, days	0.5 (0.5)	0.7 (0.4)	<0.0001
Mean (SD) Max Frequency/24h before attending	4.1 (1.6)	5.5 (2.4)	<0.0001
Fever (%)	819 (79.7%)	117 (90.7%)	<0.003
Abdominal Pain (%)	281 (27.3%)	53 (41.0%)	<0.002
Watery (%)	549 (53.4%)	86 (66.6%)	> 0.1
Solid (%)	132 (12.8%)	5 (3.8%)	
Mucus (%)	342 (33.3 %)	38 (29.4%)	
Mucus and blood (%)	4 (0.3%)	0 (0.0%)	
Bloody (%)	0 (0.0%)	0 (0.0%)	
Normal (%)	136 (13.2%)	8 (6.2%)	> 0.01
Reduced (%)	891 (86.7%)	121 (93.8%)	
Mild (%)	721 (70.2%)	26 (20.1 %)	<0.0001
Moderate (%)	285 (27.7%)	90 (69.7%)	<0.0001
Severe (%)	21 (2.0%)	13 (10.0%)	<0.0001
Not Dehydrated	0 (100%)	0 (100%)	
None (%)	89 (8.6%)	4 (3.1%)	<0.03
ORT (%)	925 (90.0%)	124 (96.1%)	<0.02
I.V (%)	34 (3.3 %)	8 (6.2%)	>0.1

Antimicrobials used:	831 (80.9%)	114 (88.3%)	<0.03

Characteristics of the population with rotavirus diarrhoea

This table describes the characteristics of the population in the study of rotavirus diarrhoea. A total of 1242 patients provided samples in this study, of which 123 (10.06%) were rotavirus-positive and 1119 (90.09%) were rotavirus-negative. All children were aged between 1 and 5 years. The mean diarrhoea in days before the consultation was 4 days and 3 days for rotavirus positive and negative respectively (p<0.0001). The mean maximum diarrhoea in 24 hours is 3 times for both rotavirus-positive and negative (p<0.0001). The proportion of children that experienced vomiting was higher in rotavirus positive group than in the rotavirus-negative group (60.1% and 46.0%, p= <0.0001)

The mean frequency of vomiting experienced 24 h before the consultation was four and three times for positive and negative cases, respectively. Although there was no significant difference between children that experienced fever between that rotavirus positive and negative p= 0.0754, more children in the positive group had fever compared to those rotavirus negative (78.0% and 70.3%), the same trend was experienced with the mean temperature as the rotavirus positive group experiencing higher temperatures compared with those negative (37.5 and 37.4, p = <0.1622). Assessing the level of activity between the two groups, fewer children had normal activity after having rotavirus diarrhoea compared with those that are rotavirus negative (15.45% and 26.12%). More children in the rotavirus-positive cases had reduced levels of activity compared with those rotavirus negative (84.55% and 76.92%, p=0.0539). The diarrhoea severity was estimated for 1242 children. In the rotavirus-positive children, 75.61% were mild, 21.14% were moderate and 3.25% were severe. Fewer children experienced severe symptoms in the rotavirus-positive group. Oral rehydration and intravenous were recorded for 1242 of the children in this study. 95.12% of the children with rotavirus were treated with oral rehydration therapy, and 1.63% were given intravenous injection while 82.93% were treated with antibiotics. In the rotavirus-negative children, 78.35% were treated with oral rehydration solution, 3.40 were given an intravenous injection and 70.48% were treated along with antibiotics. There were more children treated with ORS in the two groups (p= <0.0001) and more children were given no treatment in the rotavirus-negative children (20.57%, p=<0.0001).

Table 2. Characteristic feature of rotavirus diarrhoea

Characteristic feature	**Rotavirus status**		
	Positive N=125	**Negative N=1117**	**pvalue**
Diarrhoea			
Mean (SD) Duration in days	4.08 (3.21)	3.39 (6.27)	**<0.0001**

Mean (SD) max no of stool/ 24h	3.9 (2.31)	3.4 (2.99)	**0.0162**
Vomiting			
Vomiting (%)	60.1%	46.0%	
Mean (SD) Duration in days	0.60 (0.49)	0.46 (0.49)	**0.0030**
Mean (SD) max no of vomits/24h	4.03 (1.60)	3.72 (2.28)	**0.0766**
Fever			
Fever (%)	78.0%	70.3%	**0.0754**
Mean (SD) Temperature	37.5 (0.68)	37.4 (0.79)	**0.1622**
Abdominal pain (%)	17.8%	26.12%	**0.0463**
Level of activity			
Normal	15.45%	23.08%	**0.0539**
Reduced	84.55%	76.92%	**0.0539**
Degree of dehydration			
Mild	75.61%	68.60%	**0.1100**
Moderate	21.14%	28.8%	**0.0696**
Severe	3.25%	2.50%	**0.6197**
Rehydration therapy			
ORS	95.12%	78.35%	**<0.0001**
IVT	1.63%	3.40%	**0.2909**
None	4.07%	20.57%	**<0.0001**
Received antibiotics	82.93%	70.48%	**0.0036**

Rotavirus detection by month

The table categorizes children with rotavirus diarrhea (both positive and negative cases) by month. The table generally showed February as the peak month of rotavirus diarrhoea 31 (23.1%) followed by November 28 (23.7%), January 23 (31.0%) and December 14 (1.75%). The months with the least cases of rotavirus diarrhoea were July 0 (0.0%) and September 2 (2.9%).

Table 3: Rotavirus detection by month

MONTHS			
	RV positive %	**RV negative %**	**Total**

September 2012	2 (1.6)	64	**66**
October 2012	6 (4.9)	56	**62**
November 2012	28 (22.8)	62	**90**
December 2012	14 (11.4)	29	**43**
January 2013	23 (18.7)	28	**51**
February 2013	31 (25.2)	76	**107**
March 2013	5 (4.1)	97	**102**
April 2013	4 (3.3)	108	**112**
May 2013	5 (4.1)	91	**96**
June 2013	1 (0.81)	99	**100**
July 2013	0 (0)	118	**118**
August 2013	4 (3.3)	125	**129**
Total	**123**	**953**	**1076**

Rotavirus-positive cases by age groups most affected

A total of 123 rotavirus-positive cases were confirmed in the study. More cases of rotavirus diarrhoea were experienced (13.0%) by children between the ages of < 6 months in the University of Abuja Teaching Hospital which is slightly followed by 6-11 months. In Zankli Medical Centre, a similar trend was observed; however, children of 6-11 months had more positive cases than children aged < 6 months (21.5% and 20.0%, $p \leq 0.0001$). In the Gwagwalada Town clinic, children aged–6-11 are the most affected (20.6%), while at Nyanya General Hospital, children with rotavirus were spread across three age groups with children of ages 18-23 (22.2%) having slightly higher positive case than children of ages 6-11 (21.2%).

Table 4: Rotavirus positive cases by age groups most affected

Age Group	**<6***	**6-11**	**12-17**	**18-23**	**24-29**	**30-59**	**Pvalue**
Study Group	**Pos/tested (% pos)**	**Pos/tested (% pos)**	**Pos/tested (% pos)**	**Pos/tested (% pos)**	**Pos/tested (% pos)**	**Pos/tested (% pos)**	
UATH	13.04	10.81	7.44	6.25	2.70	-	0.329
ZMC	20.00	21.56	4.34	2.56	0.95	6.34	<0.0001

GTC	-	20.68	-	14.28	-	-	0.009
NGH	12.85	21.23	21.00	22.22	8.10	3.57	0.092

CONCLUSION AND RECOMMENDATION

A full literature review suggests that diarrhoea, specifically rotavirus diarrhoea, has been a major 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 and 18 months, after weaning. The seasonal pattern of diarrhoea presentation and the ages affected are reported to be different in some northern states and require further investigation. 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 a marked overprescription of antibiotics, which needs to be addressed. The lack of availability of virological investigations in most clinics in Nigeria indicates that specific access is needed to support and monitor the effectiveness of vaccination campaigns. The results of this study suggest 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 year and slightly older, and indirectly supports the effectiveness of the monovalent vaccine. The findings support the planned (but delayed) introduction of the rotavirus vaccine in Nigeria but emphasize the need for adequate investment in quality-assured surveillance and virological surveillance to monitor this. The emergence of new rotavirus genotypic combinations may pose a threat to vaccine efficacy in the future.

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