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Risk factors associated with adenovirus infection among children with Diarrhoea in Obodu local government area of Cross River State, Nigeria

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Abstract

Background: Enteric adenovirus (HAdV) is one of the most common enteroviruses associated with acute gastroenteritis (AGE) in children after rotavirus. It is considered the leading cause of death in children with diarrhoea worldwide. Objective: The purpose of this study was to determine the prevalence of adenovirus among children less than 5 years with a history of diarrhoea admitted to Obudu Medical Center and to identify the risk factors associated with infection. This study is significant as it will provide baseline data on adenovirus prevalence in children with diarrhoea in Nigeria, which is essential for designing effective public health interventions and improving hygiene practices.

Methods: From February 2019 to January 2020, fecal samples were collected from 163 children under 5 years with a history of diarrhoea admitted to Obudu Medical Center. Detection of adenovirus antigens in stool samples was done using a rapid chromatographic immunoassay. Data from each participant were collected through a questionnaire administered to parents or guardians. Chi-square and fisher exact probability tests were used to test for the observed differences between different proportions, with a P value <0.05 as an indicator of statistical significance.

Results: Of 163 fecal samples were collected between February 2019 and January 2020 and analyzed using rapid chromatographic immunoassay. The prevalence of adenovirus was found to be 12.3%, with significant associations observed between infection rates and parental occupation, toilet system, and handwashing practices. The highest infection rate (17.8%) occurred in April 2019, while no cases were detected in August 2019.

Conclusion: This study found that adenovirus infections occur in children under five years old with diarrhoea at Obudu Medical Center in Nigeria. Enhancing hygiene practices and improving sanitation infrastructure may help decrease the spread of adenovirus among children.

Keywords: Adenovirus; Diarrhoea; Risk Factors; Children

1. Introduction

Diarrhoea illness remains a significant cause of morbidity and mortality of children under age 5 years worldwide (Betew et al., 2023) with a variety of organisms including human adenoviruses (HAdVs) having been previously implicated as Culprits (Khales et al., 2024). While adenoviruses can be transmitted to people of any demographic, the virus is predominantly distributed among children, mainly those aged below five years. Adenoviruses are often spread by aerosol droplets produced during coughing or sneezing, direct inoculating of conjunctiva, fecal-oral route (mainly

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through contaminated water), surfaces or airborne particles originating from an organ (Soller et al., 2010). HAdV is a virus belonging to genus mastadenovirus, family: adenoviridae (Lu et al., 2023). Approximately 110 HAdV genotypes have so far been identified and categorized into seven species (A through G) of the genus Mastadenovirus based on certain physical as well as chemical and biological parameters (Greber, 2020). Types A, F and G cause intestinal irritation and diarrhoea (Roger, 2023). According to the Institute for Health Metrics and Evaluation in 2021, Species F (HAdV-F) is the most common cause of viral diarrhoea and the deaths of children worldwide aged under five years. HAdV-F can also be divided into two types, types 40 and 41 based on genetic differences (Rafie et al., 2021). Adenovirus is a medium-sized virus, 70-100 nm, and is non-enveloped; the nucleocapsid is filled with DNA that is linear and double-stranded, measuring 34-45 kbp in length (Lion, 2014. Supposedly, maximum adenoviral burden is that of hot climate countries with global incidence amounting to 2-6% (Jasem et al., 2020). In the Democratic Republic of Congo, a study found a prevalence of adenovirus of 6.3% (Manzemu et al., 2024); southeastern Nigeria recorded a 4.8% adenovirus frequency according to Tagbo et al. (2019). Currently, there exist no standard antiviral agents, with no treatments thus available for adenovirus infected patients. As with most adenovirus infections, patients will typically have moderate symptoms, which might be relieved with plenty of rest. To relieve symptoms, available over-the-counter analgesics and medications for lowering fever might also be used (CDC, 2023). Registered and recommended disinfectant, including hydrogen peroxide, quaternary ammonium solution, peracetic acid, and hypochlorous acid, has shown effectiveness against adenoviruses while retaining compatibility with materials and equipment upon application on inanimate surfaces (Atul, 2023). Regular handwashing with soap for about 20 seconds before eating, after defecation and while inside with distance between people, goes a long way in reducing the odds of contract with the virus and thus aids subdued virus transmission (Sudah, 2023). This study aims to determine the prevalence of adenovirus infection in children with diarrhoea and identify associated risk factors in Obudu, Nigeria.

2. Materials and methods

This was a cross-sectional study conducted from February 2019 to January 2020 at the Obudu Local Government Area Medical Center in Cross River State. The target population consisted of children, regardless of gender, aged 0 to 5 years, admitted in this medical center with a history of diarrhoea and an active bowel movement. Ethical approval was obtained from the Cross River State Ministry of Health, (CRSMOH/RP/REC/2018/100). A signed informed consent form was obtained from all participants' mother, father, or its legal guardian. All the children included in this study with assistance of their parents, completed the questionnaire covering sociodemographic, economic, and environmental risk as well as clinical factors pertinent to the project. In all, 163 fecal samples were collected aseptically and sent directly to the laboratory for analysis. Samples were analyzed every day by the method of rapid chromatographic immuno-assay screening for detection of adenovirus in fecal samples per the manufacture's recommendations, BIOZEK Laboratories, Netherlands.

Quantitative data obtained from each patient were entered into a spreadsheet created in MS Excel. Data were analyzed using the Statistical Package for the Social Sciences-SPSS (from IBM Software version 21.0). The chi-square test was used to test the statistical significance of observed differences between different proportions. A P value less than 0.05 was considered to indicate statistical significance. Descriptive summaries are presented in tabular and graphical form.

3. Results

3.1. Adenovirus infection and socio-demographic factors

Between February 2019 and January 2020, 163 children with acute diarrhoea were admitted to the Obudu Medical Center and subsequently screened for possible adenovirus infection. Of the 163 stool samples collected and analyzed in the study, 12.3% (20/163) tested positive for adenovirus. Patients were divided into 6 age groups, ranging from 1 month to 60 months, and adenovirus infection was detected in all age groups (table 1). The highest infection rates occurred in the 11 to 20-months age group, with 4 (17.4%) of the 23 patients testing positive for adenovirus (figure 1). The infection rate among girls was 13.8% (12/87) while for boys was 10.5% (8/76). Infection rates among Nigerian and non-Nigeria (p= 1) children were comparable, with 12.3% (14/114) and 12.2% (6/49) respectively. After analysis of gender (p=0.5) and age (p=0.4), there was no statistically significant difference in the detection rate of intestinal adenovirus in fecal samples and sociodemographic factors (table 1).

Table 1 Adenovirus infection and socio-demographic factors

Variable	Number tested N(%)	Number Pos N(%)	Number Neg N(%)	P value
Gender				
Male	76 (46.6)	8 (10.5)	68 (89.5)	0.5
Female	87 (53.4)	12 (13.8)	75(86.2)	
Total	163	20	143	
Nationality				
Nigerian	114 (70)	14 (12.3)	100 (87.7)	1
Non-Nigerian	49 (30)	6 (12.2)	43 (87.8)	
Total	163	20	143	
Age group (months)				
01-10	15 (9.2)	2 (13.3)	13 (86.7)	0.4
11-20	23 (14.1)	4 (17.4)	19 (82.6)	
21-30	18 (11)	3 (16.7)	15 (83.3)	
31-40	31 (19)	5 (16.1)	26 (83.9)	
41-50	25 (15.33)	4 (16)	21 (84)	
51-60	51(31.3)	2 (4)	49 (96)	
Total	163	20	143	

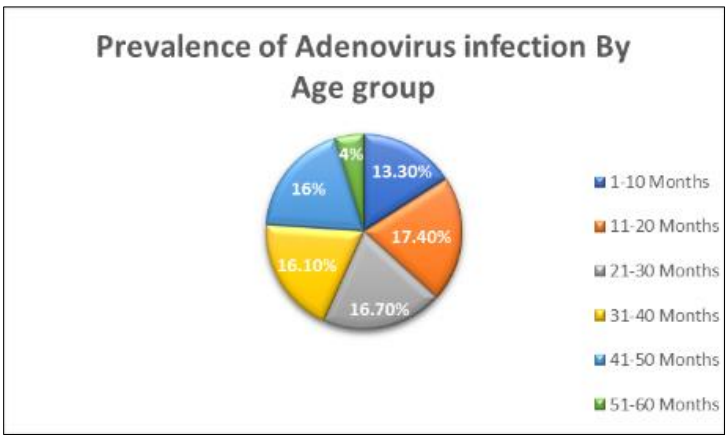

Figure 1 The incidence of adenovirus by age of participants.

3.2. Adenovirus infection and socio-economic factors

From the perspective of feeding scheme (table 2), the most infected group was breastmilk plus food formula (mixed) children, accounting for 17.2% (5/29) of the infected cases. The study also found that children of parents with a college degree were more likely to be infected, 18.2% (8/44), followed by parents with a secondary school degree, 12% (10/83). In addition, children of applying parents accounted for high percentage of 23.2% (10/43). The differences between different various professional groups were statistically significant (p=0.01).

3.3. Adenovirus infection and environmental factors

Children using borehole water as a source of hydration had the most common infection rate of 18.2% (14/77). Children using water systems and bush evacuation methods of excreta had an adenovirus infection rate of 22% (11/50) and

18.2% (2/11) respectively (figure 2). Correlation of adenovirus infection and toilet system was statistically significant (p=0.02) (table 3). The infection rates for washing hands and not washing hands were similar, 12.5% (12/96) and 11.9% (8/67) respectively. The difference in hand washing between groups was statistically significant (p=0.01).

Table 2 Adenovirus infection and socio-economic factors

Variables	Number tested N(%)	Number Pos N(%)	Number Neg N(%)	P value
Feeding status				
Breastmilk	15 (9.20	2 (13.3)	13 (86.7)	0.6
Beastmilk +food	29 (17.8)	5 (17.2)	24 (82.8)	
food	119 (73)	13 (10.9)	106 (89.1)	
Total	163	20	143	
Educational status				
No Education	17(10.4)	1 (5.8)	16 (94.2)	0.4
Primary	19 (11.6)	1 (5.2)	18 (94.8)	
Secondary	83 (51)	10 (12)	73 (88)	
Tertiary	44 (27)	8 (18.2)	36 (81.8)	
Total	163	20	143	
Parents occupation				
Traders	25 (15.3)	4 (16)	21 (84)	0.01
Farmers	85 (52.1)	4 (4.7)	81 (95.3)	
Applicants	43 (26.4)	10 (23.2)	33 (76.8)	
Civil/servant	10 (6.1)	2 (20)	8 (80)	
Total	163	20	143	

3.3.1. Adenovirus infection and clinical factors

Children with more than 7 episodes of diarrhoea per day were the smallest subgroup, accounting for only 13.5% (22/163). Children with 4-6 episodes of diarrhoea per day had a higher incidence of adenovirus infection, 17.6% (15/85) (table 4). Children with diarrhea for 1 day and 4 days had higher infection rates, 17.1% (13/76) and 16.6% (1/6) respectively. Correlation with adenovirus infection and clinical signs yielded no statistical significance.

3.3.2. Monthly distribution of adenovirus infection

Adenovirus was inexistent during the month of August 2019 (figure 3) but peak infection of 17.8 % (5/29) was observed in April 2019.

Table 3 Adenovirus infection and environmental factors

Variables	Number tested N(%)	Number Pos N(%)	Number Neg N(%)	P value
Water source				
stream water	16 (9.8)	1(6.2)	15 (93.8)	0.15
Borehole water	77 (47.2)	14 (18.2)	63 (81.8)	
Sachet water	43 (26.4)	4 (9.3)	39 (90.7)	
well water	27 (16.5)	1 (3.7)	26 (96.3)	
Total	163	20	143	

Toilet system				
Pit	102 (62.6)	7 (6.8)	95 (93.2)	0.02
Water system	50 (30.6)	11 (22)	39 (78)	
Bush	11 (6.7)	2 (18.2)	9 (81.8)	
Total	163	20	143	
Hands washing after toilet				
Yes	96 (58.9)	12 (12.5)	84 (87.5)	0.01
No	67(41.1)	8 (11.9)	59 (88.1)	
Total	163	20	143	

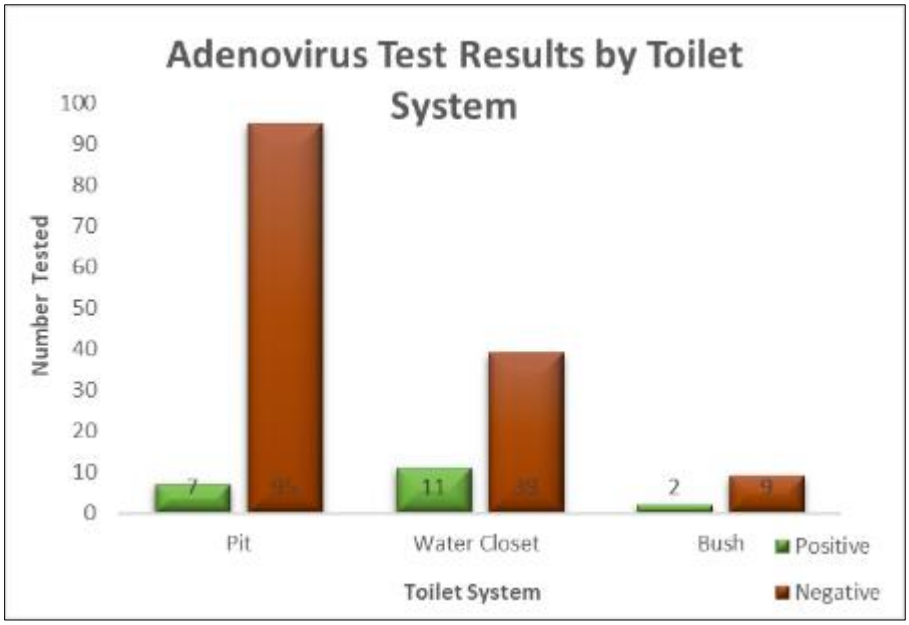

Figure 2 Bar chart showing test results by Toilet System Used

Table 4 Adenovirus infection and clinical factors

Variable	Numbert tested N(%)	Number Pos N(%)	Number Neg N(%)	P value
No liquid stool/day				
01-03	61 (37.3)	4 (6.5)	52 (93.5)	0.08
04-06	85 (52.1)	15 (17.6)	70 (82.4)	
>7	22 (13.5)	1 (4.5)	16 (95.5)	
Total	163	20	143	
No days diarrhoea				
1 day	76 (46.6)	13 ((17.1)	63 (82.9)	0.2
2 days	67 (41.1)	6 (8.9)	61 (91.1)	
3 days	14 (8.6)	0	14 (100)	
4 days	6 (3.4)	1 (16.6)	5 (83.4)	
Total	163	20	143	

According to vomit				
Yes	86 (52.8)	11 (12.8)	75 (87.2)	0.8
No	77 (47.2)	9 (11.7)	68 (88.3)	
Total	163	20	143	
Fever sign				
Yes	109 (66.9)	15 (13.7)	94 (86.3)	0.2
No	54 (33.1)	5 (9.2)	49 (91.8)	
Total	163	20	143	

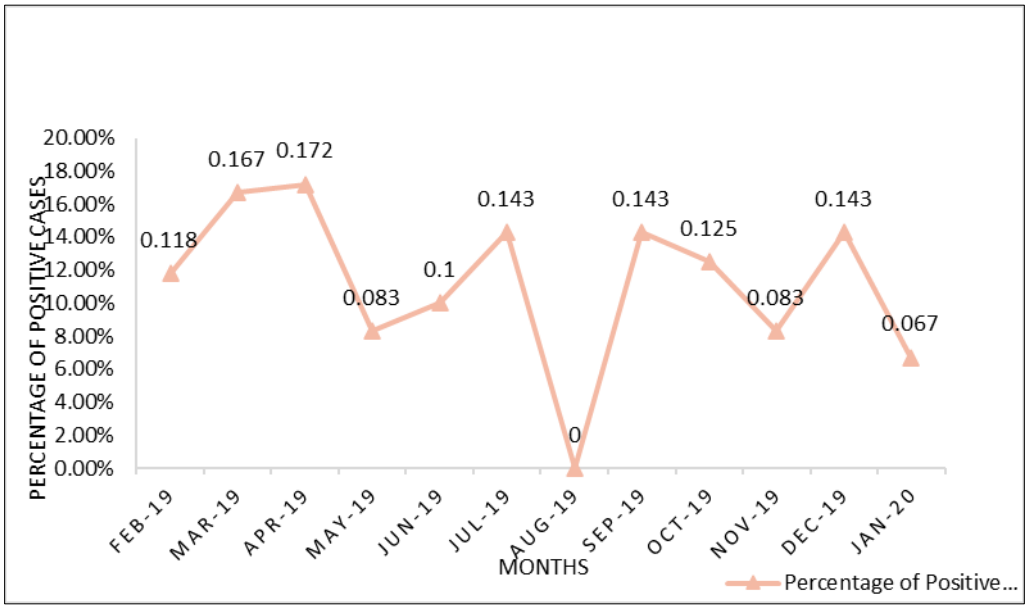

Figure 3 The trend of Positive Adenovirus Cases (Feb 2019 -Jan 2019)

4. Discussion

Human adenovirus (HAdV) is a widespread viral pathogen responsible for causing diarrhoea in children around the globe (Arpaporn et al., 2023). In this study, the adenovirus infection rate was found to be 12.3%, which is lower than the 17% reported by Owowo et al. (2019) in Akwa Ibom State, Nigeria. In other countries, lower rates of 8.3% and 9.3% were observed by Asma et al. (2024) in Tunisia and Lijuan et al. (2023) in China, respectively. Arpaporn et al. (2023) noted a higher rate of 16.5% in Thailand. The variations in detection rates between this study and others may be influenced by the economic status or geographical location of the study area. In this research, girls showed a higher infection rate than boys, with 13.8% compared to 10.5%. Gelaw et al. (2009) similarly reported a higher prevalence of adenovirus in adult women than men in Ethiopia. In contrast, Kagning et al. (2015) reported higher prevalences of 27% in males and 26.4% in females in the Ngaoundére region of Cameroon.

The infection rates among Nigerian and non- Nigerian children were relatively equal, 12.3% and 12.2% respectively. No other studies correlating this prevalence with other groups of different nationalities. The equality observed in the nationality groups may be due to both children playing together and managing their toys.

The 11-20 months age group was most affected at 17.4% . This result is consistent with the 17.2% reported by Do Nascimento et al. (2022) in a study conducted in Brazil on the age group 14–24 months. Another study by Kattareeya et al. (2019) reported that 38% of children under 2 years of age have this condition in Thailand. In general, adenovirus infections requiring clinical care are more common in younger children, who are more likely to develop serious complications.

Regarding feeding status, the results of this study showed that the incidence of enteric adenovirus was higher 17.2% in children fed with breastmilk plus food (mixed). Dilshad et al. (2016) reported lower rate of 7.82% among children with mixed diet in Iraq. The high infection rate with mixed feeding can be explained by poor maternal hygiene when preparing children food; moreover, the child's immunity decreases at <1 year of age, depending on solid food (Salam et al., 2013).

Children whose parents had higher and secondary education were more likely to be infected, 18.2% and 12% respectively. For parents with primary education, this result contradicts the publication of Msanga et al. (2020) who reported a prevalence of 65.38%, while the present study reported 5.2%.

This study documented high infection rate of adenovirus among children having applicant parents 23.2%, contrary to this study; Imade et al. (2015) documented an adenovirus infection rate of 42.2% among children having parents as traders in Benin City Nigeria. The differences between different professional groups were statistically significant. The high infection rates among applicants may be due to their lack of financial resources to care for the needs of their families, which forces them to live in crowded conditions, being one of the factors driving the spread of adenovirus infections.

Borehole water was the main source of adenovirus infection in children, accounting for 18.2% (14/77). A similar study conducted by Anup et al. (2014) reported that the proportion of children drinking borehole water was as high as 28.57% in Karnataka India. Stream water adenovirus infection rate in this study was 6.2% (1/16); In contrast to this study, Mulatya et al. (2020) reported high rate of 16.4% diarrhoeal infection rate among Kenyan children drinking stream water. However, there was no significant correlation between the type of drinking water and adenovirus infection in our study.

Depending on the toilet facilities in the study, children who used the water system after defecating were 22% and were more likely to be infected with adenovirus, but Ugochukwu et al. (2020) in Enugu Nigeria reported low rate of 8.74% diarrhoea infection among children using the water system. Among children who defecated in bushes, the observed infection rate was 18.2% , which is relatively low compared with the 22.2% reported by Onyilokwu et al. (2020) in Benue State Nigeria. There was a statistically significant correlation between the type of toilet used and adenovirus infection ($P < 0.05$). The observed statistical significance may be attributed to the lack of handwashing facilities near toilets, increasing the risk of diarrhoeal infections in children.

Our study found that 41.1% of children did not wash their hands after defecation. The statistical significance observed in this group may be due to the absence of handwashing facilities near toilets and may be positively associated with diarrhoeal diseases in children.

Vomiting was reported by 12.8%. Tsung-Pei (2012) in Taiwan reported adenovirus high infection rate of up to 16% in children with vomiting. Patient-induced vomiting was not statistically significant.

Fever occurred in 13.7% of children infected with adenovirus, Ghassan-Ghssein et al. (2018) reported low fever cases of 4.6% among Lebanese adenovirus-infected children. Another study by Jin et al. (2016) reported high prevalence of 36.4% of adenovirus cases among children having fever in Korea. Statistically, there was no significant association between fever and adenovirus prevalence.

Children with diarrhoea for 1 day were more likely to be infected with adenovirus at 17.1%, followed by children with diarrhoea for 4-5 days at 16.6%. This result is high compared to the results of Yılmaz et al. (2015) who reported adenovirus infection in 13.4% of children with more than 5 episodes of diarrhea per day. Akdag et al. (2019) also reported that in India, the prevalence of adenovirus infection in children with diarrhoea for more than 5 consecutive days was as high as 41.93%.

The highest rate of adenovirus infection was recorded in April 2019, reaching 17.7%. Other months showed fluctuations between 6.7% and 16.7%, except for August 2019, when no adenovirus was detected, aligning with the dry season in Africa. This finding contrasts with the results of Maniah et al. (2023), who reported a peak adenovirus rate of 22.2% in Saudi Arabia during the autumn month of September.

5. Conclusion

This study provides critical insights into the prevalence and risk factors of adenovirus infection in children with diarrhoea in Obudu, Nigeria. Findings highlight the need for improved sanitation, hygiene education, and surveillance

systems to mitigate the burden of adenovirus infections in vulnerable populations. Future research should explore additional viral and bacterial contributors to childhood diarrhoea.

Compliance with ethical standards

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Disclosure of conflict of interest

The authors declare that they have no conflicts of interest or funding disclosure.

Statement of ethical approval

Ethical clearance was obtained from the Cross Rivers State Ministry of Health in Calabar, Nigeria, with REC No: CRSMOH/RP/REC/2018/100.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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