FREQUENCY OF ROTAVIRUS INFECTION IN CHILDREN UNDER 2 YEARS OF AGE PRESENTING WITH DIARRHEA AT TERTIARY CARE HOSPITAL

Sahar Iqbal[1], Huma Gul[2], Muhammad Mujtaba[3], Farida sherazi[3], Sadia Jehanzeb[2], Irum Naz[3]

ABSTRACT

Objective: To find out the frequency of rotavirus infection in children below 2 years of age presenting with diarrhea at Northwest General Hospital, Peshawar.

Methods and material: This cross-sectional study was conducted in the Department of Pediatrics of Northwest General Hospital Peshawar from 10th August 2020 to 10th February 2021. By non-probability convenience sampling technique taking a 95% confidence interval, 5% margin of error, and population of 24% the calculated sample size was 281. The data was analyzed by SPSS V 23.0.

Results: A total of 281 cases were analyzed for this study. After analysis, the mean age was calculated as 10.960±3.93 months. The mean weight was 9.253±1.54 Kgs the mean duration of diarrhea was reported as 8.409±1.99 days. 53(18.9%) out of 281 were reported as positive for rotavirus infection. Among 281 only 20 patients which is 7.1% of the sample size got vaccinated against the Rotavirus in our study. Taking the p-value below 0.05 as significant rotavirus infection has shown significance with exclusive breastfeeding and their vaccination history.

Conclusion: Rotavirus is one of the major causes of acute gastroenteritis. The rotavirus has shown a significant relationship between vaccination against rotavirus and exclusive breastfeeding with a p-value of less than 0.05.

Keywords: Rotavirus, children, acute gastroenteritis, diarrhea, vaccination, Pakistan

INTRODUCTION

Diarrhea is one of the leading causes of death worldwide in children less than 5 years old. Rotavirus-related diarrhea resulted in the death of an estimated 200,000 children worldwide which amounts to 37% of deaths in children under 5 years in 2013.[1,2] The number of deaths rose to 228,000 in 2016.[3] In the United States of America, rotavirus infects more than 2.7 million individuals annually, resulting in 250,000 emergency department visits, and 55,000 to 70,000 hospitalizations, costing the national exchequer around 1 billion US dollars.[4]

[1] Northwest General Hospital & Research Centre, Peshawar.
[2] Hayatabad Medical Complex, Peshawar.
[3] Naseer Teaching Hospital, Peshawar.

Address for Correspondence
Dr. Huma Gul
Department of Pediatrics, Hayatabad Medical Complex, Peshawar.
drhuma96@gmail.com
+92 336 9414829

Rotavirus belongs to the Reoviridae family, and eight groups have been identified so far, defined by antigens present in their protein. Only four have been isolated from humans and animals: A, B, C, and H. Serogroups D, E, F, and G are present only in animals. In humans, the commonest causative agent of diarrhea is serogroup A.[5,6] The World Health Organization (WHO) recommended vaccination against rotavirus in 2009 and directed national immunization programs to vaccinate infants to control the diseases. Four safe and effective vaccines are available worldwide (RotaTeq, Rotarix, Rotavac, and RotaSiil).[7] Regionally, China is burdened by rotavirus-related diarrhea due to reliance on its local vaccine which has 30-50% efficacy compared to the WHO-recommended vaccines, and the coverage rate is 15 to 30% only.[8] Similarly, 78,000 children lose their lives to rotavirus diarrhea in India annually, the majority of them failing to reach their second birthday.[9] Acute diarrhea is one of the leading causes of death in children in Pakistan, largely due to poor water quality, lack of basic health facilities, and overall inadequate health literacy. Pakistan is among the four leading countries contributing to half of the global burden of rotavirus infections, with a rotavirus infant mortality rate of 67.6 per

100,000 children.[10] Basharat et al. have reported a 22% prevalence of rotavirus infection in children with acute gastroenteritis (AGE) via ELISA in 2018.[11]

The government of Pakistan introduced rotavirus vaccination in the national vaccination program in 2018. Literature about the frequency of rotavirus-related diarrhea and its risk factors, especially the association with rotavirus vaccination, in children of our province is limited. Given the burden of acute diarrhea and its consequences in young children, this study aims to determine the frequency of rotavirus infection in children below the age of 2 years with acute diarrhea at a tertiary care hospital in Peshawar, Pakistan.

METHODOLOGY

It was a cross-sectional analytical study conducted at the Department of Pediatrics, Northwest General Hospital, Peshawar, Pakistan. Ethical approval was obtained from the hospital's Institutional and Ethical Review Board. The sample size was 281, taking a 95% confidence level, 5% margin of error, and frequency of rotavirus infection as 24%.[12] Using consecutive sampling technique, 281 children below the age of 2 years with acute diarrhea (defined as one lasting for less than 14 days) were included in the study after informed consent of the parents. Children whose diarrhea started after a recent hospitalization or antibiotic use were excluded from the study.

A structured questionnaire was used to record data including age, gender, weight, duration of diarrhea, history of exclusive breastfeeding, and history of rotavirus vaccination. A stool sample from each patient was sent in a sterile container to the laboratory to screen for rotavirus infection using enzyme-linked immunosorbent assay (ELISA).

Statistical Package for Social Sciences (SPSS) version 23 was used for data analysis. Mean ± standard deviation was calculated for age, weight, and duration of diarrhea, while gender, history of exclusive breastfeeding, history of rotavirus vaccination, and presence of rotavirus infection were presented as frequencies and percentages. Stratified analysis using a chi-square test was carried out to see the effect of study variables on rotavirus infection. A p-value below 0.05 was taken as significant.

RESULTS

The study enrolled 281 patients. The mean age, mean weight and mean duration of diarrhea were 10.9 ± 3.9 months, 9.3 ± 1.5 kg, and 8.4 ± 2.0 days, respectively. Table 1 details the characteristics of the study participants.

Table 1: Characteristics of the study participants (n=281)

Variables		No. (%)
Age	Up to 12 months	183 (65.1%)
	13-24 months	98 (34.9%)
Gender	Male	200 (71.2%)
	Female	81 (28.8%)
Weight	≤ 10 Kg	181 (64.4%)
	> 10 Kg	100 (35.6%)
Duration of diarrhea	1-7 days	66 (23.5%)
	8-14 days	215 (76.5%)
Exclusive Breast Feeding	Yes	184 (65.5%)
	No	97 (34.5%)
History of rotavirus vaccination	Yes	20 (7.1%)
	No	261 (92.9%)
Rota Virus Infection	Yes	53 (18.9%)
	No	228 (81.1%)

A significantly higher proportion of patients without exclusive breastfeeding had rotavirus infection compared to the exclusively breastfed group (30.9% vs 12.5%, p<0.001). Vaccination status against rotavirus did not significantly affect the frequency of rotavirus infection (p = 0.286). (Table 2)

Table 2: Association of study variables with rotavirus infection

Variables		Rota Virus Infection		P value
		Yes (n=53)	No (n=228)	
Age	Up to 12 months	35 (19.1%)	148 (80.9%)	0.87
	13-24 months	18 (18.4%)	80 (81.6%)	
Gender	Male	39 (19.5%)	161 (80.5%)	0.662
	Female	14 (17.3%)	67 (82.7%)	
Weight	≤ 10 Kg	35 (19.3%)	146 (80.7%)	0.775
	> 10 Kg	18 (18%)	82 (82%)	
Duration of diarrhea	1-7 days	10 (15.2%)	56 (84.8%)	0.387
	8-14 days	43 (20%)	172 (80%)	
Exclusive Breast Feeding	Yes	23 (12.5%)	161 (87.5%)	<0.001
	No	30 (30.9%)	67 (69.1%)	
History of rotavirus vaccination	Yes	2 (10%)	18 (90%)	0.286
	No	51 (19.5%)	210 (80.4%)	

DISCUSSION

With acute diarrhea as one of the leading causes of death in Pakistani children fueled by overall poor hygiene, sanitation, and water quality and inadequate vaccination uptake, this study aimed to determine the frequency and risk factors of rotavirus infection in young children.

The overall frequency of rotavirus infection in this study was 18.9%. Konuksever et al. from Brazil have reported 16.4% of stool samples positive for rotavirus among children presenting with acute gastroenteritis which is consistent with our results.[13] A study conducted by Topal İ in Turkey revealed that 10.4% of stool samples were positive for rotavirus infection.[14] A study from China has reported that 10.7% of stool samples were positive for rotavirus among children with acute diarrhea.[15] This may be a result of the difference in the sample selection as they included children up to the age of 10 years. Sadeq et al. from Iraq and Laizāne et al. from Latvia have reported 52.4% and 61% positivity of stool samples for rotavirus, respectively.[16,17] 22,23 The reasons for the differences in the frequency of rotavirus infection may be the varying levels of health literacy, sanitation and hygiene, and vaccination uptake in different populations. A recent study conducted in Peshawar, Pakistan revealed a 63% frequency of the rotavirus antigen in stool specimens from children with acute diarrhea.[18] The discrepancy may be due to the difference in the inclusion criteria as they enrolled only unvaccinated children with diarrhea in that study.

Exclusive breastfeeding was associated with a lower frequency of rotavirus infection. This has been consistently observed in previous studies, including metanalysis on the topic.[19,20] Similarly, vaccination against rotavirus has been shown to reduce infections and hospitalization due to rotavirus.[21,22] Our results found no association between the history of rotavirus vaccination and rotavirus infection. The reason may be the overall lower frequency (7.1%) of vaccinated children in the study sample which may not have been enough to show the statistical association.

Age, gender, weight, and duration of diarrhea were not significantly different in those with and without rotavirus infection. These findings are consistent with previous literature on the subject.[9,14,15,18]

Though the study's strength is its relatively larger sample size, some limitations are worth mentioning. We didn't include the source of drinking water, sanitation, parents' awareness regarding rotavirus vaccination, and the seasonality in which most cases were reported.

CONCLUSION

Rotavirus infection is a common cause of acute diarrhea in children younger than two years old. Exclusive breastfeeding significantly decreased the risk of rotavirus infection in these children. Although rotavirus infection is avoidable with vaccination, the proportion of children immunized against rotavirus was quite low. Pediatricians must emphasize the importance of rotavirus vaccination to parents and encourage them to vaccinate their children to protect them against a potentially fatal infection.

Conflict of interest: None

Source of funding: None

REFERENCES

1. Tate JE, Burton AH, Boschi-Pinto C, Parashar UD. Global, Regional, and National Estimates of Rotavirus Mortality in Children <5 Years of Age, 2000-2013. *Clin Infect Dis an Off Publ Infect Dis Soc Am*. 2016;62 Suppl 2:S96-S105. doi:10.1093/cid/civ1013
2. Burnett E, Parashar UD, Tate JE. Global Impact of Rotavirus Vaccination on Diarrhea Hospitalizations and Deaths Among Children <5 Years Old: 2006-2019. *J Infect Dis*. 2020;222(10):1731-1739. doi:10.1093/infdis/jiaa081
3. Arakaki L, Tollefson D, Kharono B, Drain PK. Prevalence of rotavirus among older children and adults with diarrhea: A systematic review and meta-analysis. *Vaccine*. 2021;39(33):4577-4590. doi:10.1016/j.vaccine.2021.06.073
4. Mijatovic-Rustempasic S, Jaimes J, Perkins C, Ward ML, Esona MD, Gautam R, et al. Rotavirus Strain Trends in United States, 2009-2016: Results from the National Rotavirus Strain Surveillance System (NRSSS). *Viruses*. 2022;14(8). doi:10.3390/v14081775
5. GBD Diarrhoeal Diseases Collaborators. Estimates of global, regional, and national morbidity, mortality, and aetiologies of diarrhoeal diseases: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet Infect Dis*. 2017;17(9):909-948. doi:10.1016/S1473-3099(17)30276-1
6. Bourdett-Stanziola L, Centeno E, Cuevas-Abrego M, Durant Archibold A, Ortega-Barria E, Bucardo F. The Emergence of New Rotavirus Strains in America. *South Asian J Res Microbiol*. Published online October 27, 2021. doi:10.9734/SAJRM/2021/v11i130244
7. Cates JE, Tate JE, Parashar U. Rotavirus vaccines: progress and new developments. *Expert Opin Biol Ther*. 2022;22(3):423-432. doi:10.1080/14712598.2021.1977279
8. Yu J, Lai S, Geng Q, Ye C, Zhang Z, Zheng Y, et al. Prevalence of rotavirus and rapid changes in circulating rotavirus strains among children with acute diarrhea in China, 2009-2015. *J Infect*. 2019;78(1):66-74. doi:10.1016/j.jinf.2018.07.004
9. John J, Sarkar R, Muliyil J, Bhandari N, Bhan MK, Kang G. Rotavirus gastroenteritis in India, 2011-2013: revised estimates of disease burden and potential impact of vaccines. *Vaccine*. 2014;32 Suppl 1:A5-9. doi:10.1016/j.vaccine.2014.03.004
10. Sadiq A, Bostan N. Comparative Analysis of G1P[8] Rotaviruses Identified Prior to Vaccine Implementation in Pakistan With Rotarix™ and RotaTeq™ Vaccine Strains. *Front Immunol*. 2020;11(October):2-11. doi:10.3389/fimmu.2020.562282
11. Basharat N, Sadiq A, Dawood M, Ali S, Khan A, Ullah R, et al. Rotavirus gastroenteritis in Pakistan, 2018: updated disease burden. *BMC Infect Dis*. 2021;21(1):426. doi:10.1186/s12879-021-06123-6
12. John BM, Devgan A, Mitra B. Prevalence of rotavirus infection in children below two years presenting with diarrhea. *Med journal, Armed Forces India*. 2014;70(2):116-119. doi:10.1016/j.mjafi.2014.02.008
13. Konuksever D, Karakaya SPY. Fecal leukocyte frequency in children with acute viral gastroenteritis: a single-center experience. *Rev Assoc Med Bras*. 2024;70(4):e20230972. doi:10.1590/1806-9282.20230972
14. Samancı S, Köşker M, Çelik M, Araç E. Frequency of Rotavirus Infection In Children With Acute Gastroenteritis. *Van Med J*. 2018;25:441-444. doi:10.5505/vtd.2018.37233
15. Dong JX, Li AF, Li RQ, Chao S, Yang S, Zhao XY. Epidemiological and Clinical Features of Rotavirus and Adenovirus Related Gastroenteritis in Beijing: A Retrospective Case-control Study in Pediatric Patients. *Biomed Environ Sci*. 2020;33(3):196-200. doi:10.3967/bes2020.027
16. Sadeq T, Ali A, Hameed G. Effects of Rota Vaccine on Severity and Duration of Rotavirus Infection among Children Less Than 5 Years Old at Al Kadhimiya Pediatrics Hospital. *J Al-Rafidain Univ Coll Sci (Print ISSN 1681-6870 ,Online ISSN 2790-2293)*. Published online October 2, 2021:223-230. doi:10.55562/jrucs.v45i2.124
17. Laizane G, Kivite A, Grope I, Smane L, Miklaševics E, Ozoliņa L, et al. Clinical Characterisation of Rota Virus Infection Associated with Most Commonly Circulating Genotypes in Children Hospitalised in Children's University Hospital: A Cross-Sectional Study in

Latvia. *Proc Latv Acad Sci Sect B Nat Exact, Appl Sci*. 2019;73:312-316. doi:10.2478/prolas-2019-0049
18. Muhammad Z, Khaliq A, Shadab T, Shah SMA, Khan S, Haider Z. Frequency of Rotavirus as a Cause of Acute Diarrhea. *Med Forum Mon*. 2024;35(4):17-20. doi:10.60110/medforum.350404
19. Pratama G, Rahardjo S, Murti B. Meta-Analysis the Effects of Rotavirus Vaccine, Exclusive Breastfeeding, and Maternal Education on Diarrhea in Children Under Five. *J Epidemiol Public Heal*. 2023;8:298-311. doi:10.26911/jepublichealth.2023.08.03.02
20. Ali KB, Gadzama GB, Zailani SB, Mohammed Y, Daggash BB, Yakubu YM, et al. The Risk Factors Associated with Rotavirus Gastroenteritis among Children Under Five Years at University of Maiduguri Teaching Hospital, Borno State, Nigeria. *Niger J Med*. 2022;31(1). https://journals.lww.com/njom/fulltext/2022/31010/the_risk_factors_associated_with_rotavirus.7.aspx
21. Isanaka S, Langendorf C, McNeal MM, Meyer N, Plikaytis B, Garba S, et al. Rotavirus vaccine efficacy up to 2 years of age and against diverse circulating rotavirus strains in Niger: Extended follow-up of a randomized controlled trial. *PLOS Med*. 2021;18(7):e1003655. https://doi.org/10.1371/journal.pmed.1003655
22. Burke RM, Groom HC, Naleway AL, Katz EM, Salas B, Mattison CP, et al. Rotavirus Vaccine Is Effective Against Rotavirus Gastroenteritis Resulting in Outpatient Care: Results From the Medically Attended Acute Gastroenteritis (MAAGE) Study. *Clin Infect Dis*. 2021;72(11):2000-2005. doi:10.1093/cid/ciaa466