DOI: 10.7860/JCDR/2022/57311.17188

Original Article

Paediatrics Section

Clinical Profile and Serotyping of Rotavirus Diarrhoea in the Postvaccination Period: A Single-centre Cross-sectional Study

GUNASEKARAN SABHARRITHA[1], KRISHNASWAMI DEVI MEENAKSHI[2], DHANDAPANI PRABU[3]

ABSTRACT

Introduction: Rotavirus is the leading cause of severe, life threatening gastroenteritis in infants and young children. As rotavirus strains vary between geographic areas, region specific genotyping information is highly vital to study rotavirus epidemiology and to monitor strain variation after vaccine introduction.

Aim: To estimate the prevalence of rotavirus diarrhoea and strains causing the infection among children younger than five years of age and to study the clinical profile of rotavirus diarrhoea to ascertain factors associated with rotavirus infection in them.

Materials and Methods: This hospital-based cross-sectional study was carried out on 150 children under five years with diarrhoea in the Department of Paediatrics, Government Medical College, Chennai, Tamil Nadu, India from November 2017 to August 2018. The clinical severity was assessed by using Vesikari score. By using PremierTM Rotaclone ELISA Kit rotavirus antigen was detected. Positive samples were tested for RNA identification by Reverese Transcriptase-Polymerase Chain Reaction (RT-PCR). The IBM Statistical Package for the Social Sciences (SPSS) version 22 was used for statistical analysis.

Results: The prevalence of rotavirus diarrhoea was 17.3% and positive samples belonged to G3 type. Prevalence of rotavirus diarrhoea among the vaccinated children was less when compared to unvaccinated children (p-value 0.034). Clinical severity score (Vesikari score) indicated that patients infected with rotavirus had severe disease as compared to rotavirus non infected patients (p-value 0.011). The duration of hospital stay was longer in rotavirus-positive children as compared to rotavirus-negative children (p-value <0.001).

Conclusion: This study highlights the serotype specific prevalence of rotavirus diarrhoea in under five children. Rotavirus has been found to have more severe and prolonged illness among unimmunised under five children; thereby, reinforcing the need for routine rotavirus vaccination.

Keywords: Acute diarrhoea, Rotavirus infection, Vesikari score

INTRODUCTION

Diarrhoea is the most important cause of morbidity and mortality in under-five children in developing countries. According to WHO, diarrhoea is the "passage of loose or watery stools atleast three times in a 24 h period", with emphasis on stool consistency rather than frequency [1]. Globally 1.7 billion children are affected by diarrhoea out of that more than half millions of children die every year [2]. UNICEF estimates that 480,000 young children die due to diarrhoea across the globe, accounting for 9% of all deaths among children under five years [3]. The National Family Health Survey shows that the prevalence of childhood diarrhoea has increased from 9-9.2% from 2016-2020 in India. Diarrhoea is the third most common cause of under five mortality [4].

Rotavirus is the leading cause of acute diarrhoea, and is responsible for about 40% of all hospital admissions due to diarrhoea among children under five years worldwide [5].

Hospitalisation rates are high (40-50%) in rotavirus infection among diarrhoea children under five years in WHO surveillance countries that have not introduced rotavirus vaccine [6]. India holds the second place among countries with the greatest number of rotavirus deaths as a proportion of All Global rotavirus Deaths in Children under five years [6]. Indian Rotavirus Strain Surveillance Network data has emphasised the need for region specific genotyping information to study rotavirus epidemiology and to monitor strain variation after vaccine introduction [7]. Variation has been observed in serotypes and genotypes of rotavirus in different geographical regions during a particular rotavirus infection season and also in different seasons. Serotypes are the classification within each group based on neutralisation assays which measures reaction of antibody against two outer capsid antigens VP7 and VP4. This assay differentiates VP7 as G types, as VP7 is a Glycoprotein and VP4 as P type, as VP4 is a protease sensitive protein. Currently there are 27G serotypes and 35P serotypes in group A rotavirus [8, 9]. Reverse transcriptase PCR is the commonly used technique for VP4 and VP7 genotyping. Globally, G1-G4 and P1A [8] and P1B [4] are the most common G and P types that cause disease in humans [10,11].

India began a phased introduction of the RotavacR vaccine in national immunisation program starting in 2016. Currently, available rotavirus vaccines are effective in reducing the disease burden, but correct understanding of local epidemiology of rotavirus infection is important for rotavirus immunisation. With the advent of rotavirus vaccination there is significant reduction in the prevalence of rotavirus diarrhoea with reduction in hospitalisation of 70 to 80% in the first year after introduction of rotavirus vaccine and reduction in childhood diarrhoea deaths of around 30-55% have been observed [12].

Considering the severity of rotavirus infection and its associated mortality and morbidity in children under five years, this study was undertaken to determine the serotype-specific prevalence of rotavirus causing diarrhoea in children under five years after the advent of rotavirus vaccination programme and to ascertain factors associated with rotavirus infection in them.

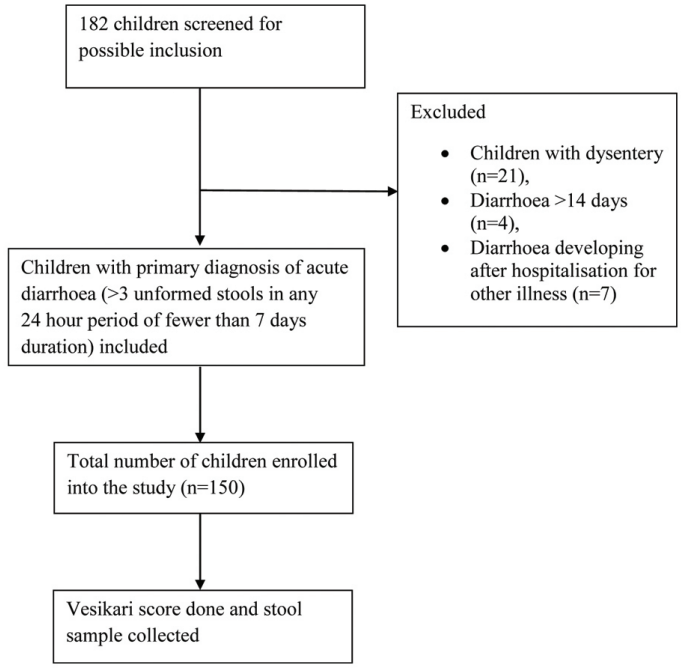
MATERIALS AND METHODS

This cross-sectional hospital-based study was conducted in Department of Paediatrics, Government Medical College, Chennai, Tamil Nadu, India from November 2017 to August 2018. The study was commenced after approval from the Institutional ethics Committee, of a tertiary care Medical College hospital (Protocol ID no 02/2017 meeting held on 14.11.2017).

Inclusion criteria: One hundred and fifty children aged less than or equal to five years with primary diagnosis of acute diarrhoea (>three unformed stools in any 24-hour period of fewer than seven days duration) were included in the study.

Exclusion criteria: Children with dysentery, prolonged diarrhoea more than 14 days, diarrhoea developing after hospitalisation due to other causes and children with a previous history of immunosuppressive therapy like steroids, chemotherapy and children with immunodeficiency syndromes were excluded from the study.

Children fulfilling the selection criteria were identified and their legal guardians were briefed about the nature of the study in local language and a written informed consent was obtained [Table/Fig-1].



[Table/Fig-1]: Flow diagram of enrollment of study participants.

Sample size calculation: Sample size was calculated using Epi Info software. With a prevalence of rotavirus infection of 39% observed in multicentre surveillance by Kang G et al., [13] and with an error margin of 8% to calculate 95% confidence interval the number of samples estimated was 142. Hence a sample size of 150 was planned.

Study Procedure

After a written informed consent, a detailed history and examination of the child was done and recorded on a predesigned proforma. Vesikari Clinical Severity Scoring System which included parameters like diarrhoea, vomiting, fever, dehydration, duration of diarrhoea and vomiting and treatment status was used to categorise according to severity [14]. The parameters were scored based on the severity of the symptoms in each category. This included the number of episodes of diarrhoea, episodes of vomiting, highest body temperature recorded, duration of diarrhoea and severity of dehydration and treatment plan. The seven parameters were subdivided into thirds according to an equally divided severity distribution (i.e., bottom third=one, middle third=two, top third=three). The scores for each of the seven parameters were added to arrive at the final score between 0-20 which was used to classify the severity [14]. An episode was considered to be mild for Vesikari scores 0-5, moderate for scores 6-10, severe for scores 11-15, and very severe for scores 16-20 [Table/Fig-2].

Stool sample was collected by placing the child on a non absorbemt sterile sheet and sample was collected using a spatula contained in the sterile leak proof stool collection container. After collecting stool sample it was sent immediately to the hospital laboratory where the sample was placed at -20°C in deep freezer. Enzyme immunoassay was performed by using Premier Rotaclone kit for the detection of rotavirus antigen in faecal samples. Samples which were positive by ELISA were sent for RT-PCR to University of Madras, Taramani. Rotavirus molecular level RNA detection was done by rotavirus-A Real-time PCR assay.

Parameters	1 point	2 points	3 points
Diarrhoea			
Maximum number of stools per day	1-3	4-5	≥6
Duration	1-4	5	≥6
Vomiting			
Maximum number of episodes per day	1	2-4	≥5
Duration (days)	1	2	≥3
Temperature	37.1-38.4° C	38.5-38.9°C	≥39°C
Dehydration	Nil	1-5%	≥6%
Treatment	-	Rehydration	Hospitalisation

[Table/Fig-2]: Vesikari clinical severity score.
Mild: 0-5; Moderate: 6-10; Severe:11-15; Very severe: 16-20

STATISTICAL ANALYSIS

The IBM SPSS version 22 was used for statistical analysis. Categorical data was expressed as rates, ratios and percentages. Continuous data was expressed as mean±standard deviation. For normally distributed parameters the mean values were compared between study groups using Independent sample t-test (2 groups). For non normally distributed parameters, Medians and Interquartile range (IQR) were compared between study groups using Mann Whitney u test (2 groups). Categorical outcomes were compared between study groups using Chi-square test. A p-value <0.05 was considered statistically significant.

RESULTS

In this study, 26 children tested positive for rotavirus, among the 150 children who were evaluated, which accounted for a prevalence of 17.3%. Majority of the rotavirus-positive children (61.53%) were in the 7-12 months age group. In this study, 55.33% of the children with diarrhoea were boys and 44.67% were girls and the boy to girl ratio was 1.2:1. Among the children with rotavirus infection, 13 (50%) were girls and 13 (50%) were boys [Table/Fig-3].

	Rotavirus infection		
Age (in months)	Positive (n=26)	Negative (n=124)	p-value
Median (IQR)	11 (7, 13.25)	12 (8, 24.75)	0.299
Up to 6 months	3 (11.53%)	26 (20.96%)	0.205
7 to 12 months	16 (61.53%)	43 (34.67%)	
13 to 24 months	4 (15.38%)	24 (19.35%)	
25 to 36 months	1 (3.846%)	18 (14.51%)	
37 to 48 months	1 (3.846%)	6 (4.838%)	
49 to 60 months	1 (3.846%)	7 (5.645%)	
Gender			
Female child	13 (50%)	54 (43.5%)	0.547
Male child	13 (50%)	70 (56.5%)	

[Table/Fig-3]: Association of rotavirus infection with age and gender in children with diarrhoea.

Majority of the children with diarrhoea had a fever (69.3%). Other common complaints were vomiting (64%), increased thirst (26%), perianal excoriation (16%), and lethargy (11.3%). In this study, 88.5% of children with rotavirus infection had fever when compared to 65.3% of the children without rotavirus infection. In this study, 23.07% of rotavirus-positive cases were not breastfed when compared to 16.93% of rotavirus-negative cases. Among the children with rotavirus infection, 6 (23.07%) children had malnutrition. Among

rotavirus-negative cases, 18 (14.51%) children had malnutrition (p=0.279).

Among the children with rotavirus infection, 3 (11.53%) children had received rotavirus vaccine while 40 (32.25%) of vaccinated children did not have rotavirus infection (p=0.034). All children had received RotavacR vaccine as per the National immunisation schedule. Among children with rotavirus infection, one child had received single dose, another child had received two doses and one child had received three doses of RotavacR vaccine [Table/Fig-4].

Clinical presentation		Rotavirus infection		Chi-square	p-value
		Positive (n=26)	Negative (n=124)		
Vomiting	Yes	20 (76.9%)	76 (61.3%)	2.280	0.131
	No	6 (23.1%)	48 (38.7%)		
Fever	Yes	23 (88.5%)	81 (65.3%)	5.412	0.020
	No	3 (11.5%)	43 (34.7%)		
Perianal excoriation	Yes	8 (30.76%)	16 (12.90%)	5.105	0.024
	No	18 (69.23%)	108 (87.09%)		
Dehydration	Severe dehydration	3 (11.53%)	5 (4.032%)	5.308	0.070
	Some dehydration	8 (30.76%)	22 (17.74%)		
	No dehydration	15 (57.69%)	97 (78.22%)		
Breast feeding	Yes	20 (76.92%)	103 (83.06%)	0.549	0.459
	No	6 (23.07%)	21 (16.93%)		
Malnutrition	Yes	6 (23.07%)	18 (14.51%)	1.172	0.279
	No	20 (76.92%)	106 (85.48%)		
Rotavirus vaccine	Yes	3 (11.53%)	40 (32.25%)	4.512	0.034
	No	23 (88.46%)	84 (67.74%)		

[Table/Fig-4]: Clinical presentation and risk factors of children with diarrhoea.

The mean Vesikari score of children with rotavirus infection was 11.81±3.93 and it was 11.81±3.93 in children without rotavirus infection (p=0.001). Among the children with rotavirus infection, 46.15% of children had severe disease and 19.23% had very severe disease; while among children without rotavirus infection only 30.64% were severe, and 4.83% were very severe disease (p=0.011).

The mean duration of diarrhoea in children with rotavirus infection was 3.69±1.26 days and 2.94±1.32 days in children without rotavirus infection (p=0.008). In the study group, 127 children were hospitalised. The duration of hospital stay was >7 days in 48% of cases with rotavirus infection and 12.74% of cases without rotavirus infection (p<0.001) [Table/Fig-5].

Vesikari score	Rotavirus infection		Chi-square	p-value
	Positive (n=26)	Negative (n=124)		
Mean (SD)	11.81 ± 3.93	9.22 ± 3.42		0.001
Mild disease	3 (11.53%)	19 (15.32%)	11.11	0.011
Moderate disease	6 (23.07%)	61 (49.19%)		
Severe disease	12 (46.15%)	38 (30.64%)		
Very severe disease	5 (19.23%)	6 (4.838%)		
Duration of hospital stay				
Mean (SD)	3.69±1.26	2.94±1.32		0.008
<4 days	7 (28%)	58 (56.86%)	16.22	<0.001
4-7 days	6 (24%)	31 (30.39%)		
>7 days	12 (48%)	13 (12.74%)		

[Table/Fig-5]: Clinical pattern of diarrhoea in children.

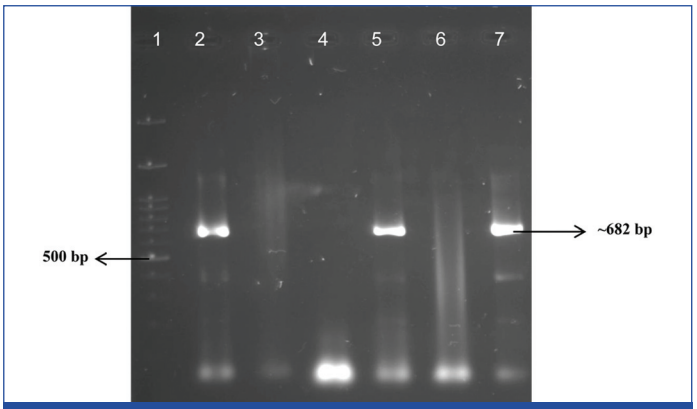
Among children who received rotavirus vaccine, the median (IQR) Vesikari score was 5 (5,7) in rotavirus-positive cases and it was 9 (6,11) in rotavirus-negative cases (p=0.115). However in the unvaccinated group, there was a significant difference in the Vesikari score between rotavirus-positive and negative cases (p<0.001) [Table/Fig-6].

Parameter	Rotavirus vaccine					
	Yes			No		
	Rotavirus infection			Rotavirus infection		
	Positive	Negative	p-value	Positive	Negative	p-value
Median Vesikari score (IQR)	5 (5,7)	9 (6,11)	0.115	13 (10,15)	9 (7,12)	<0.001

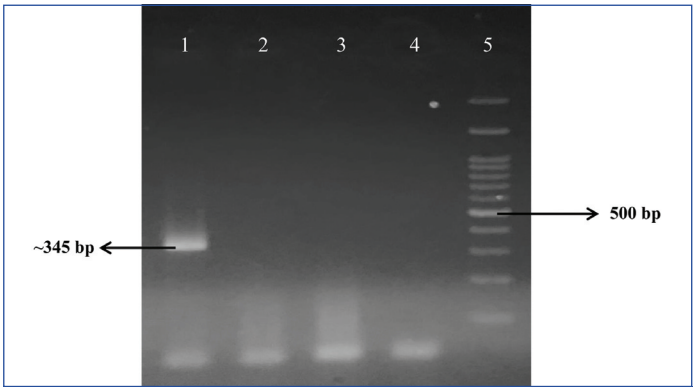
[Table/Fig-6]: Comparison of Vesikari score between vaccinated and unvaccinated children with diarrhoea.

Only 12 samples were positive by rotavirus-A Real-time PCR. Remaining samples did not amplify which may be due to degradation of RNA while transportation or low viral load at the time of specimen collection. Also inconsistency between the two tests may result from false positivity of the antigen tests and false negativity of the nucleic acid test. Causes of false positivity of the antigen test may include cross-reactivity with other microorganisms, interference and non specific reactivity. Causes of false negativity of the nucleic acid test may include RNA degradation due to the prolonged storage of specimens and variations of the RNA viruses that could not be detected by the primers that were used.

Polymerase Chain Reaction was done for 12 samples for the G (VP7) genotyping and P (VP4) genotyping detection. All 12 samples were of G3 type [Table/Fig-7]. while there was no amplification during P genotyping [Table/Fig-8].



[Table/Fig-7]: Representative gel picture for G typing for rotavirus.
Figure of rotavirus-A G (VP7) Genotyping shows the picture after Agarose gel electrophoresis to observe pattern of the bands in PCR method. Lane 1- 100 bp ladder, Lane 2, 5- Positive samples (G3 type), Lane 3,4- Negative samples, Lane 6- Negative control, Lane 7- Positive control



[Table/Fig-8]: Representative gel picture for P typing for rotavirus.
Figure of rotavirus-A P(VP4) Genotyping shows the picture after Agarose gel electrophoresis to observe pattern of the bands in PCR method.
Lane 1- Positive control, Lane 2-4- Negative samples, Lane 5- 100 bp ladder

DISCUSSION

In the present study, rotavirus diarrhoea was observed in 17.3% of children. Other studies revealed a prevalence of 22.6% and 24% and a higher proportion was seen among hospitalised patients [15,16].

Mehendale S et al., observed a rotavirus positivity rate of 39.6% as part of the Expanded Indian National rotavirus Surveillance Network study conducted between 2012 and 2014 [17]. The variation in the prevalence rates of rotavirus diarrhoea may be attributed to the methods of detection (latex slide agglutination test is less sensitive to ELISA), difference in climatic conditions and socio-demographic determinants.

In this study, prevalence of rotavirus infection was equal in both the genders, and similar results were obtained by Saravanan P et al., [15]. However, contrary findings were reported from Karnataka with a 20% higher prevalence in males [18].

In the present study, a peak infection was observed in 7-12 months old children (61.53%). It is reported that rotavirus diarrhoea occurs at an early age in developing countries with 80% below one year. [19] In contrast, in developed countries prevalence is common in second year of life [20]. The National Rotavirus Surveillance Network involving 28 hospital sites across the four geographical regions of India between 2012 and 2016 found highest rotavirus detection rates in children aged 6-23 months (41.8%), and 24.7% in children aged <6 months [21].

Clinical severity score revealed severe disease in rotavirus diarrhoea (p=0.011) and similar findings were observed by Pol SS et al., [22] However, a hospital-based cross-sectional study by Muendo C et al., found similar distribution of severe diarrhoea among all children (rotavirus-positive and negative) [23].

In the present study, 28.7% children were vaccinated and their rotavirus positivity rate was significantly lower (6.9%) as compared to unimmunised (21.49%) (p=0.034). These findings are consistent with study by Jain P et al., which showed that vaccine recipients were less likely to have rotavirus diarrhoea [24]. However, Bhatnagar S and Srivastava G, found positivity rate was comparable in rotavirus vaccinated and unvaccinated children [25]. In this study similar disease severity scores were recorded in rotavirus-positive and negative children in the vaccinated group. In the unvaccinated group, significantly higher severity score was found in the rotavirus-positive children. This was consistent with the findings by Jain P et al., [24].

Earlier reports from other countries have described rise in the circulation of strains other than the vaccine strains after the introduction of mono (G1P[8]) or pentavalent (G1, G2, G3, G4 and P[1]) vaccines [26]. In this study, all the positive samples were G3 strains.

A study conducted in Indian children below five years between 2012 and 2016 by Giri S et al., revealed G1P [8] (49.9%) and G2P [4] (9.8%) were the two most common genotypes. The common genotypes detected in the southern sites were G1P [8] (56.3%), G2P [4] (9.1%), G9P [4] (7.6%), G9P [8] (4.2%), and G12P [6] (3.7%) [27]. The National rotavirus Surveillance Network study from September 2012 to August 2016 found genotypes G1P [8] (52.9%), G9P4 (8.7%) and G2P4 (8.4%) [21].

The G3 rotavirus is one of the most common rotavirus strain reported worldwide [28]. A variant of G3 referred to as “new variant G3” was reported from Japan during 2003-2004 [29]. Ummair M et al., showed that G3P [8] (18.3%) was the most common genotype [30]. Similarly in a study by Shaheen M et al., in Egypt from May 2015 to April 2016, G3 was the most circulating rotavirus strain among the 56 characterised G types [31] In this study, positive samples showed no amplification during P typing. In a study by Cunliffe NA et al., [32] 26% of G genotype and 32% of P genotype could not be typed. It has been observed that genotypic prevalence varies from place to place and rotavirus shows rapid strain variations. Hence it is important to know the genotype information pertaining to particular region.

Limitation(s)

The limitations of the study are that it was done in a single centre with limited sample size. Also, as the study was done only a year after introduction of the rotavirus vaccine the vaccine coverage in the study population was low. Though there was a difference in infection rates among vaccinated children, the inclusion of more numbers of vaccinated children in the study population would have facilitated better understanding of the trend of rotavirus infection in the postvaccination period.

CONCLUSION(S)

Rotavirus is the leading cause of severe, life-threatening gastroenteritis in children even after implementation of vaccination. Rotavirus shows an unusual genomic diversity worldwide. During the rotavirus outbreaks, multiple strains which show combination of several G and P types are seen. This study highlights that rotavirus diarrhoea caused by G3 strain accounts for a significant proportion of diarrhoeal diseases in children less than five years. The main clinical presentation of rotavirus infected patients was diarrhoea associated with vomiting and fever. Rotavirus infected children had severe disease and longer duration of Hospitalisation when compared to rotavirus uninfected children. Immunisation is an important preventive strategy as evidenced by fewer rotavirus infections and less severe disease in immunised children.

REFERENCES

[1] WHO: The treatment of diarrhoea: A manual for physicians and other senior health workers, WHO/CDR/95.3. Geneva: World Health Organization; 1995.
[2] Ghosh K, Chakraborty AS, Mog M. Prevalence of diarrhoea among under five children in India and its contextual determinants: A geo-spatial analysis. Clinical Epidemiology and Global Health. 2021;12(4):100813. https://doi.org/10.1016/j.cegh.2021.100813.
[3] https://www.unicef.org/health/childhood-diseases.
[4] Lakshminarayanan S, Jayalakshmy R. Diarrheal diseases among children in India: Current scenario and future perspectives. J Nat Sci Biol Med. 2015;6(1):24-28. Doi: 10.4103/0976-9668.149073.
[5] Diarrhoea: Why children are still dying and what can be done. The United Nations Children’s Fund (UNICEF)/World Health Organization (WHO), 2009.
[6] https://preventRotavirus.org/Rotavirus-disease/global-burden/.
[7] Kang G, Arora R, Chitambar SD, Deshpande J, Gupte MD, Kulkarni M, et al. Multicenter, hospital-based surveillance of rotavirus disease and strains among Indian children aged <5 years. Journal of Infectious Diseases. 2009;200(Suppl1):S147-53.
[8] Fields virology vol 2, 6th edn, Estes et al., Rota viruses.
[9] Jawetz, Melnick, Adelberg. Medical Microbiology. Reoviruses, Rotaviruses, and Caliciviruses. 26th edition. 2013; NewYork: McGraw-Hill.
[10] Parashar UD, Hummelman EG, Bresee JS, Miller MA, Glass RI. Global illness and deaths caused by Rotavirus disease in children. Emerg Infect Dis. 2003;9(5):565-72.
[11] Kang G, Kelkar SD, Chitambar SD, Ray P, Naik T. Epidemiological profile of rotaviral infection in India: Challenges for the 21st century. J Infect Dis. 2005;192(Suppl 1):S120-S126.
[12] https://preventRotavirus.org/vaccine-evidence/indirect-benefits-of-Rotavirus-vaccination/.
[13] Kang G, Arora R, Chitambar SD, Deshpande J, Gupte MD, Kulkarni M. Multicenter, hospital-based surveillance of rotavirus disease and strains among indian children aged <5 years. J Infect Dis. 2009;200,(1):S147-S153. https://doi.org/10.1086/605031.
[14] Lewis K. Vesikari Clinical Severity Scoring System Manual. Path; 2011.
[15] Saravanan P, Ananthan S, Ananthasubramanian M. Rotavirus infection among infants and young children in Chennai, South India. Indian J Med Microbiol. 2004;22(4):212-21. https://doi.org/10.1016/S0255-0857(21)02765-1.
[16] John BM, Devgan A, Mitra B. Prevalence of rotavirus infection in children below two years presenting with diarrhea. Med J Armed Forces India. 2014;70(2):116-19. https://doi.org/10.1016/j.mjafi.2014.02.008. PMID: 24843198 PMCID:PMC4017201.
[17] Mehendale S, Venkatasubramanian S, Girish Kumar CP, Kang G, Gupte MD, Arora R. Expanded Indian National Rotavirus Surveillance Network in the context of rotavirus vaccine introduction. Indian Pediatr. 2016;53(7):575-81. Doi: 10.1007/s13312-016-0891-3. PMID: 27508533.
[18] Shetty AK, Kalekhan FM, Muthiravalapil SJ, Boloor R, Antony B. Detection of rotavirus and adenovirus diarrhoea in children below five years, in Dakshina Kannada District, a coastal region of Karnataka State, India. Muller J Med Sci Res. 2014;5(2):143-48. https://doi.org/10.4103/0975-9727.135749.
[19] Banerjee I, Ramani S, Primrose B, Moses P, Iturriza-Gomara M, Gray JJ, et al. Comparative study of the epidemiology of rotavirus in children from a community based birth cohort and a hospital in South India. J Clin Microbiol. 2006;44(7):2468-74.https://doi.org/10.1128/JCM.01882-05. PMID: 16825366 PMCID:PMC1489461.
[20] Paniker CK, Mathew S, Marhan M. Rotavirus and acute diarrhoeal disease in children in a Southern Indian coastal town. Bull World Health Organ. 1982;60:123-27.

[21] Girish Kumar CP, Giri S, Chawla-Sarkar M, Gopalkrishna V, Chitambar SD, Ray P, et al. Epidemiology of rotavirus diarrhea among children less than 5 years hospitalized with acute gastroenteritis prior to rotavirus vaccine introduction in India. Vaccine. 2020;38(51):8154-60. Doi: 10.1016/j.vaccine.2020.10.084.
[22] Pol SS, Dedwal AK, Ranshing SS, Chitambar SD, Pednekar SN, Bharadwaj RS. Prevalence and characterization of rotaviruses in children hospitalized for diarrheal disease in a tertiary care hospital, Pune. Indian J Med Microbiol. 2017;35(1):33-36. https://doi.org/10.4103/ijmm.IJMM_16_94. PMID:28303815.
[23] Muendo C, Laving A, Kumar R, Osano B, Egondi T, Muendo PN, et al. Prevalence of rotavirus infection among children with acute diarrhoea after rotavirus vaccine introduction in Kenya, a hospital cross-sectional study. BMC Ped. 2018;18(1):323. https://doi.org/10.1186/s12887-018-1291-8.
[24] Jain P, Varanasi G, Ghuge R, Kalrao V, Dhongade R, Bavdekar A, et al. Rotavirus infections in children vaccinated against rotavirus in Pune, Western India. Indian Pediatr. 2016;53(7):589-93. https://doi.org/10.1007/s13312-016-0893-1.
[25] Bhatnagar S, Srivastava G. Clinical profile of children (0-5 years) with rotavirus diarrhea. Int J Contemp Pediatr. 2017;4(3):947-50. https://doi.org/10.18203/2349-3291.ijcp20171704.
[26] Kirkwood CD, Boniface K, Barnes GL, Bishop RF. Distribution of rotavirus genotypes after introduction of rotavirus vaccines, Rotarix® and RotaTeq®, into the National Immunization Program of Australia. Pediatr Infect Dis J. 2011;30 (1 Suppl):S48-53. https://doi.org/10.1097/INF.0b013e3181fefd90. PMID:21183840.
[27] Giri S, Nair NP, Mathew A, Manohar B, Simon A, Singh T, et al. Rotavirus gastroenteritis in Indian children <5 years hospitalized for diarrhoea, 2012 to 2016. BMC Public Health. 2019;19(1):69. https://doi.org/10.1186/s12889-019-6406-0.
[28] Santos N, Hoshino Y. Global distribution of rotavirus serotypes/genotypes and its implication for the development and implementation of an effective rotavirus vaccine. Rev Med Virol. 2005;15(1):29-56. https://doi.org/10.1002/rmv.448 PMID:15484186.
[29] Phan TG, Trinh QD, Khamrin P, Kaneshi K, ShigekazuNakayaYU, Nishimura S, et al. Emergence of new variant rotavirus G3 among infants children with acute gastroenteritis in Japan during 2003-2004. Clinical Laboratory. 2007;53(1-2):41-48. PMID: 17323824.
[30] Umair M, Abbasi BH, Sharif S, Alam MM, Rana MS, Mujtaba G, et al. High prevalence of G3 rotavirus in hospitalized children in Rawalpindi, Pakistan during 2014. PLoS One. 2018;13(4):e0195947. https://doi.org/10.1371/journal.pone.0195947. PMID:29708975. PMCID:PMC5927433.
[31] Shaheen M, El-Daim ASE, Hosseney EN, Shoeib AR, Ali MA. Molecular characterization of rotavirus strains causing gastroenteritis in children under 5 years in Cairo, Egypt. MOJ Public Health. 2017;6(5):00187. https://doi.org/10.15406/mojph.2017.06.00187.
[32] Cunliffe NA, Ngwira BM, Dove W, Thindwa BDM, Turner AM, Broadhead RL, et al. Epidemiology of rotavirus infection in children in Blantyre, Malawi, 1997-2007. J Infect Dis. 2010;202:S168-S74. http://www.jstor.org/stable/25707019.

PARTICULARS OF CONTRIBUTORS:
1. Registrar, Department of Paediatrics, Dr. Mehta's Multispeciality Hospital, Chennai, Tamil Nadu, India.
2. Professor, Department of Paediatrics, Government Kilpauk Medical College, Chennai, Tamil Nadu, India.
3. Assistant Professor, Department of Microbiology, Dr. ALMPGIBMS, University of Madras, Chennai, Tamil Nadu, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Gunasekaran Sabharritha,
Royapettah, Chennai, Tamil Nadu, India.
E-mail: sabharrithasekar@gmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Apr 25, 2022
- Manual Googling: Jul 25, 2022
- iThenticate Software: Sep 10, 2022 (17%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Apr 24, 2022**
Date of Peer Review: **Jun 24, 2022**
Date of Acceptance: **Sep 12, 2022**
Date of Publishing: **Dec 01, 2022**