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Retrospective analysis of clinical and laboratory findings of children with rotavirus gastroenteritis in Malatya province between 2015 and 2020

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Abstract

Aim: In the present study, our aim was to examine cases with rotavirus gastroenteritis, which is an important health problem, in detail.

Materials and Methods: Cases with acute gastroenteritis aged between 0 and 18 who referred to Inonu University Turgut Ozal Medical Centre between January 2015 and January 2020 and whose stools were examined for rotavirus antigen were included in the study. The cases who were grouped in two as "rotavirus positive and rotavirus negative gastroenteritis" were examined retrospectively in detail in terms of their states of being followed and treated as outpatient, inpatient and in intensive care.

Results: A total of 2690 children, 1340 rotavirus positive and 1350 rotavirus negative control group were included in the study. Rotavirus positive gastroenteritis was most common in winter (27.2%). 53.9% of the rotavirus positive gastroenteritis cases were followed and treated as inpatients. In rotavirus positive patients, mean age of the inpatients was 3.3±4.2 years, while mean age of the outpatients was 2.1±3.1 years and mean age of the patients in the intensive unit care was 1.6±3.2 years. The highest rates of rotavirus positive gastroenteritis cases were in 7-12 month old (19.8%), 13-24 month old (23.9%) and 25-60 month old (24.1%) age groups, while the lowest rates were in 0-2 month old (3.1%) and 3-6 month old (10.2%) age groups.

Conclusion: In our study, the lowest rate of rotavirus positive gastroenteritis cases was found in 0-2 month-old age group. It was thought that this situation might be due to the significant effect of antibodies transmitted transplacentally from the mother, especially between months 0 and 2. The increase in rotavirus positivity and hospitalization after the sixth month showed the importance of administering the rotavirus vaccine before this period once again.

Introduction

Acute gastroenteritis is the most important cause of morbidity and mortality in children after lower respiratory tract infections. Rotaviruses are the leading cause of diarrhoea in infants and children under 5 years of age, and severe gastroenteritis which causes hospitalization and infant deaths. Rotavirus gastroenteritis causes morbidity and economic loss in developing countries where treatment opportunities are insufficient and mortality in underdeveloped countries [1]. According to World Health Organization (WHO) estimates, approximately 215.000 children under the age of 5 died in 2015 due to vaccine-preventable rotavirus infection and a large majority of these children lived in countries with low income [2]. Recent studies show that 40% of diarrhoea-related hospitalizations in children under 5 years of age in the whole world are due to rotavirus infections [3]. Rotavirus is also a common cause of hospital-acquired infections in children hospitalized for other reasons [4]. The disease can be mild-asymptomatic, or it may cause death as a result of severe dehydration. Rotavirus may also cause respiratory tract infection, myocarditis, necrotising enterocolitis, pneumatosis intestinalis, meningoencephalitis and seizures [5]. Despite the improvement of personal and social hygiene and cleaning practices, there has been no decrease in morbidity and mortality due to rotavirus infection. A vaccine has been developed against rotavirus due to the frequency and severe course of the disease and the vaccine has been licensed

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in many countries [6]. Rotavirus vaccine is among the vaccines recommended by the Association of Paediatric Infectious diseases in our country. However, it is predicted that in line with the recommendations of WHO, it will be used routinely in vaccination calendar in the future [7]. In our study, we aimed to analyse the demographic, clinical and laboratory data of a large number of rotavirus positive cases and to compare these with rotavirus negative cases.

Materials and Methods

The present study is a descriptive retrospective study conducted at Inonu University Turgut Ozal Medical Centre. Patients with acute gastroenteritis between the ages of 0 and 18 who referred to the centre between January 1, 2015 and January 1, 2020 and who were examined for rotavirus antigen in the stool were included in the study. Ethics committee permission of the study was approved by Inonu University, Faculty of Medicine, Health Sciences Non-interventional Clinical Research Ethics Committee with 05.10.2021 dated and 2020/1216 numbered decision. The patients included in the study were first grouped in two as rotavirus positive and rotavirus negative patients. The patients were grouped in 7 as 0-2 months, 3-6 months, 7-12 months, 13-24 months, 25-60 months, 61-144 months and >145 months in terms of age groups. The files of 1340 patients whose rotavirus antigen were found to be positive and 1350 patients whose rotavirus antigen were found to be negative were examined retrospectively in detail in terms of their states of being followed and treated as outpatient, inpatient and intensive care patient. The patients who did not have an ID number, those who had a chronic disease or chronic diarrhoea and those who were admitted for acute gastroenteritis but whose stool samples were not taken were not included in the study. Demographic data of the patients and their haematological parameters [White blood cell (WBC) count, Haemoglobin, Haematocrit, platelet, neutrophil count, lymphocyte count], the presence of acidosis, HCO_3 - , Na+ , K+ , uric acid level, results of kidney function tests, liver function tests and C-reactive protein (CRP) were taken from electronic file records and these parameters were evaluated. Stool samples taken from patients in our hospital's laboratory were studied by using 'Rapid Adeno/Rotavirus Antigen Combo Test Card ®, China' immunochromatographic card test. This test is used all over the world; it has high sensitivity and specificity and it can give quick results. The correct method is to accept the presence of the tested antigen, even if the line in the test area is very faint [8].

Statistical analysis

Analyses were evaluated with SPSS (Statistical Package for Social Sciences; SPSS Inc., Chicago, IL) 22 package program. In the study, descriptive data were shown with n and % in categorical data, as mean±standard deviation (Mean±SD) and median (minimum-maximum) values in continuous data. Chi-square analysis (Pearson Chi-square) was used to compare categorical variables between groups. Bonferroni correction was conducted to find out from which group significance resulted. Normality distribution of continuous variables was evaluated with Kolmogorov-Smirnov test. In the comparison of paired groups, Mann Whitney U-test was used for variables which were not normally distributed. In the comparison of multiple groups, Kruskal Wallis test was used for variables which were not normally distributed. Spearman correlation test was used in the analysis of the correlation between continuous variables which were not normally distributed. In analysis, significance level was considered as $p<0.05$.

Results

A total of 2,690 children, 1,340 rotavirus antigen positive cases and 1,350 rotavirus antigen negative control group, were included in the study. Mean age of the rotavirus positive group was found as 2.6±3.6 years, while their median age was found as 1.0 years (0.0-18.0). Mean age of the rotavirus negative group was found as 3.1±4.2 while their median age was found as 1.0 years (0.0-18.0). No significant difference was found between the groups in terms of age ($p=0.229$) (Table 1).

Of the rotavirus positive cases, 42 (3.1%) were in 0-2 month-old age group, 137 (10.2%) were in 3-6 month-old age group, 265 (19.8%) were in 7-12 month-old age group, 320 (23.9%) were in 13-24 month-old age group, 323 (24.1%) were in 25-60 month-old age group, 186 (13.9%) were in 61-144 month-old age group and 67 (5.0%) were in >145 month-old age group. Of the rotavirus negative cases, 67 (5.0%) were in 0-2 month-old age group, 155 (11.5%) were in 3-6 month-old age group, 278 (20.6%) were in 7-12 month-old age group, 235 (17.4%) were in 13-24 month-old age group, 268 (19.9%) were in 25-60 month-old age group, 259 (19.1%) were in 61-144 month-old age group and 88 (6.5%) were in >145 month-old age group (Table 1).

Significant difference was found between the groups in terms of age groups ($p<0.001$). This difference was due to the difference between rotavirus positive and rotavirus negative cases in 0-2 month-old, 13-24 month-old, 25-60 month-old and 61-144 month-old age groups (Table 1).

Significant difference was found between groups in terms of follow-up ($p<0.001$). Rotavirus positive patients had significantly higher inpatient treatment rates than rotavirus negative patients. No significant difference was found between groups in terms of follow-up in the intensive care (Table 2).

In our study, mean age of the rotavirus positive patients followed as outpatient was found as 3.3±4.2 years, while the rate of those followed as inpatient was found as 2.1±3.1 and the rate of those followed in intensive care was found as 1.6±3.2 years. Significant difference was found between the groups in terms of age ($p<0.001$). Ages of the patients treated as outpatient were found to be significantly higher than those of the patients treated as inpatient and in intensive care unit (Table 3).

Rotavirus positive cases were found occur mostly in winter and least in summer (Figure 1).

pH value ($p<0.001$), HCO_3 - value ($p<0.001$), CRP value ($p<0.001$), WBC value ($p<0.001$), lymphocyte value ($p<0.001$), Na+ value ($p<0.001$) and K+ value ($p<0.001$) of the rotavirus positive group were found to be significantly lower than those of the rotavirus negative group (Table 4). On the other hand, blood urea nitrogen

Table 1. Comparison of demographic characteristics of rotavirus antigen positive and rotavirus antigen negative groups.

		Rota positive		Rota negative		
		Number	%	Number	%	p
Age, Mean±SD Median (min-max)		2.6±3.6 years 1.0 (0.0-18.0) years		3.1±4.2 years 1.0 (0.0-18.0) years		0.229*
Age group	0-2 months	42	3.1[a]	67	5.0[b]	**<0.001****
	3-6 months	137	10.2[a]	155	11.5[a]	
	7-12 months	265	19.8[a]	278	20.6[a]	
	13-24 months	320	23.9[a]	235	17.4[b]	
	25-60 months	323	24.1[a]	268	19.9[b]	
	61-144 months	186	13.9[a]	259	19.2[b]	
	>145 months	67	5.0[a]	88	6.5[a]	
Gender	Female	581	43.4	564	41.8	0.407**
	Male	759	56.6	786	58.2	

*Mann Whitney U test, **Chi-square analysis was performed. [a,b]The group with difference.

Table 2. Comparison of follow-up states of rotavirus antigen positive and rotavirus antigen negative groups.

		Rota positive		Rota negative		
		Number	%	Number	%	p*
Follow-up status	Outpatient	570	42.5[a]	689	51.0[b]	**<0.001**
	Inpatient	722	53.9[a]	595	44.1[b]	
	Intensive care	48	3.6[a]	66	4.9[a]	

*Chi-square analysis was performed. [a,b]The group with difference.

Table 3. Comparison of rotavirus antigen positive patients in terms of follow-up status.

		Age (years)		
		Mean±SD	Median (min-max)	p*
Follow-up status	Outpatient	3.3±4.2[a]	2.0 (0.0-18.0)	**<0.001**
	Inpatient	2.1±3.1[b]	1.0 (0.0-18.0)	
	Intensive care	1.6±3.2[b]	0.0 (0.0-17.0)	

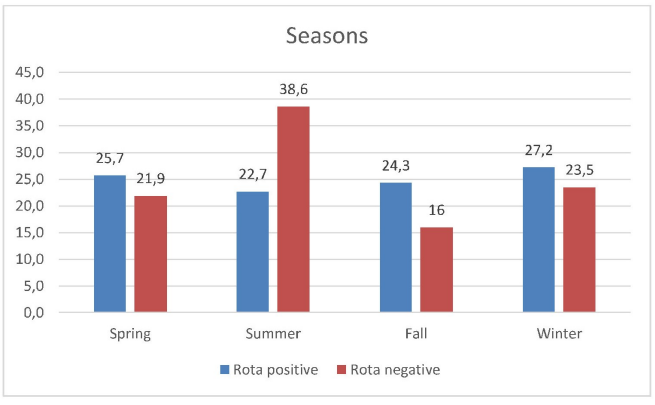

Figure 1. Distribution of rotavirus antigen positive and negative cases in terms of seasons.

(BUN) value (p<0.001), creatine (Cr) value (p<0.001), uric acid value (p<0.001), AST value (p<0.001), ALT value (p<0.001) and Hb value (p=0.006) of the rotavirus positive group were found to be significantly higher than those of the rotavirus negative group (Table 4).

Discussion

Gastroenteritis is the second most common cause of child death worldwide and its rate among the causes of death is 16% [9]. The most important cause of diarrhoea in children younger than 5 years of age is rotaviruses. Millions of children refer to outpatient clinics due to rotavirus each year in the world, approximately 2 million people are hospitalized and about 600,000 lose their lives [10]. Recent studies show that 40% of diarrhoea related hospitalizations in children younger than 5 years of age worldwide are due to rotavirus infections [3]. Rotavirus infections are more severe especially in children between 6 and 24 months of age [11]. In our study, mean age of the rotavirus positive patients followed as outpatient was found as 3.3±4.2 years, while the rate of those followed as inpatient was found as 2.1±3.1 and the rate of those followed in intensive care was found as 1.6±3.2 years. Significant difference was found between the groups in terms of age (p<0.001). The mean age of patients treated as inpatient and in intensive care unit was found to be significantly lower than those of the

Table 4. Comparison of rotavirus antigen positive patients in terms of blood values.

	Rota positive	Rota negative	p*
	Mean±SD Median (Min-Max)	Mean±SD Median (Min-Max)	
pH	7.39±0.07 7.39 (7.15-7.82)	7.41±0.08 7.41 (7.15-7.76)	**<0.001**
HCO_3 (mmol/L)	19.5±3.6 19.4 (9.7-39.1)	21.2±3.7 21.0 (10.1-42.3)	**<0.001**
CRP (mg/dL)	1.2±2.3 0.3 (0.3-35.5)	1.5±3.1 0.3 (0.3-37.9)	**<0.001**
WBC (/mm³)	10526.3±4661.2 9700.0 (11.2-35700.0)	11198.7±4595.1 10500.0 (2300.0-32000.0)	**<0.001**
Hb (g/dL)	12.0±1.9 12.0 (1.0-19.8)	11.8±1.9 11.8 (6.5-15.0)	**0.006**
Hct (%)	36.8±4.8 36.8 (10.1-62.9)	36.6±5.2 36.7 (10.3-64.3)	0.279
Neutrophil (/mm³)	5782.9±4110.6 4690.0 (220.0-29690.0)	5698.7±4090.1 4615.0 (100.0-26190.0)	0.415
Lymphocyte (/mm³)	3703.9±2861.2 2890.0 (110.0-20000.0)	4400.9±3454.1 3800.0 (190.0-19990.0)	**<0.001**
PLT (/mm³)	357324.5±139635.8 333000.0 (38000.0-1121000.0)	355707.7±143542.3 336000.0 (35000.0-975000.0)	0.806
BUN (mg/dL)	11.1±5.7 10.6 (2.0-71.1)	10.0±6.4 9.0 (2.0-147.0)	**<0.001**
Cr (mg/dL)	0.48±0.21 0.45 (0.20-5.00)	0.46±0.19 0.43 (0.20-5.90)	**<0.001**
Uric acid (mg/dL)	5.0±2.2 4.7 (0.3-15.0)	4.1±1.8 3.8 (0.0-19.0)	**<0.001**
AST (U/L)	44.0±43.2 38.0 (9.0-930.0)	39.3±26.1 33.0 (5.0-388.0)	**<0.001**
ALT (U/L)	30.0±51.7 21.0 (0.5-824.0)	24.0±28.2 17.0 (3.8-558.0)	**<0.001**
Na (mmol/L)	136.2±5.0 136.0 (124.0-161.0)	137.0±3.4 137.0 (125.0-159.0)	**<0.001**
K (mmol/L)	4.2±0.6 4.2 (2.1-7.8)	4.3±0.6 4.3 (1.9-6.4)	**<0.001**

* Mann Whitney U test was performed.

patients treated as outpatient. While rotavirus infection can be seen in all age groups, symptomatic infection rates are most common in children younger than two years of age [3]. Mortality is increased when the first rotavirus related infection is frequently seen before 2 years of age and when it courses with dehydration and malnutrition [10]. The fact that the frequency of infection is low after 24 months of age is due to the fact that natural infections reduce the incidence and severity of the next attack [12]. In our study, rotavirus infection was most frequent in children between 13-24 months of age and 25-60 months of age. Frequency was found to continue with a decrease in older age groups. The fact that the number of patients decreased with age was attributed to the fact that natural infections reduced attack incidence and severity. Although the reason why it is less severe in new-borns is not fully understood, it is thought that it may be related to antibodies that come from the mother [11,13]. In our study, infection frequency was found to be lower in early age groups between 0-2 months (3.1%) and 3-6 months (10.2%). We believe that this may be due to the protective effect of mother's milk in the first 6 months and the significant effect of the antibodies that pass transplacentally from the mother especially between 0-2 months. In a multicentre study conducted on 6679 children in Pakistan, it was found that 87% of the rotavirus positive children were younger than 2 years of age, while 61% were younger than 1 year of age [14]. In Mexico, Velazquez et al. reported that rotavirus positive gastroen-

teritis was most frequent in children 6-14 months old. Velazquez et al. also reported that the number of cases with rotavirus positive gastroenteritis decreased gradually after two years of age [15]. In Konya, Akdoğan et al. found the highest rate of rotavirus positive gastroenteritis in 6-12 month-old children [16]. In a study conducted in Malatya by Bozkurt et al., 59.1% of the rotavirus patients were found to be between 7 and 24 months of age, 15.9% were between 0 and 9 months of age and 25% were older than 24 months [17]. In our study, when age distribution was examined, it was found that the highest number of cases were in 13-24 month-old and 25-60 month-old (24.1%) age groups. When all of the cases are considered, it was found that 81.1% of the admissions consisted of children younger than 5 years of age. These results are in parallel with the results of previously conducted studies. The data of both studies we could access in national and international literature and the results of our study showed the necessity of vaccinating early age group. In addition, the significant increase in rotavirus positivity after the 6th month was attributed to less intake of mother's milk and the decrease in the immunity provided by antibodies from the mother. Therefore, the significance of rotavirus vaccination before this period was shown once again.

The recovery of rotavirus gastroenteritis-related clinical findings usually takes about a week. Sometimes, in parallel with the severity of the disease, inpatient follow-up and treatment is appropriate. Various studies have reported that rotavirus positive admissions to hospital require hospitalization more frequently. In a study conducted in Italy, 23.1% of the rotavirus-related acute gastroenteritis admissions were found to be hospitalized [18]. In a study conducted in Ankara in 2004 by Karadağ et al., 37.6% of the patients were hospitalized [19]. In a study conducted in Malatya by Bozkurt et al., 48.1% of the rotavirus positive children were hospitalized due to diarrhoea [17]. Higher rate of hospitalization in rotavirus positive gastroenteritis can be prevented with the widespread use of rotavirus vaccine. In a study conducted in China between 2009 and 2015, the prevalence of rotavirus was found to decrease to 11.2% from 40.7% with rotavirus vaccination [20]. In our study, hospitalization rate of rotavirus positive admissions was found as 53.9%. Hospitalization rate of rotavirus negative admissions was found as 44.1%. This rate was found to be higher than the hospitalization rate of rotavirus negative admissions and statistically significant difference was found ($p<0.001$). No significant difference was found between the groups in terms of intensive care hospitalization. Hospitalizations consisted largely of short-term hospitalizations in emergency service observation rooms. The aim was to prevent the patient load and transmission in services. It is thought that increasing rotavirus-related awareness in families and widespread use of vaccines will decrease hospitalizations.

Abnormal laboratory findings in rotavirus gastroenteritis are isotonic dehydration, increase in kidney function tests and metabolic acidosis. Leucocytosis is usually not seen in rotavirus gastroenteritis. However, high transaminase levels can sometimes be seen [21]. In a study conducted by Nokes et al. in Kenya, significant correlation was found between acidosis and rotavirus comorbidity [22]. In a study conducted in Thailand, metabolic acidosis was found to be 57% higher in rotavirus positive group when compared with the rotavirus negative group [23]. In Konca et al.'s study, metabolic acidosis was found in 14.2% of the patients [24]. In our study, when all admissions were evaluated, pH and HCO_3 – values were found to be lower in rotavirus positive patients. Statistically significant difference was found in terms of metabolic acidosis ($p<0.001$). Metabolic acidosis should be considered in rotavirus gastroenteritis. When our rotavirus positive acute gastroenteritis cases were grouped as hospitalized and non-hospitalized, HCO_3 - ($p=0.013$) values were found to be significantly lower in hospitalized rotavirus group. Significant difference was also found between age groups in hospitalized rotavirus positive patients in terms of HCO_3 – value ($p<0.001$). Especially in patients younger than 2 years of age, HCO_3 – values of 0-2 month-old and 3-6 month old groups were found to be significantly higher than those of 7-12 month-old and 13-24 month-old age groups ($p<0.001$).

Considering that immunity decreases and disease severity increases after 6 months, the importance of early vaccination is seen again when metabolic acidosis and life risks are also considered. The most important limitation of the study is the difficulties encountered in some situations which required the need for detailed questions and information since the study was conducted through retrospective file records.

Conclusion

As a conclusion, the present study will be a guide for other studies since it is a study conducted in Malatya at a tertiary reference hospital by using five-year long data between 2015 and 2020, 2690 admissions and a large patient population. Demographic, clinical and laboratory data of rotavirus positive and negative cases were compared and significant differences were found.

Ethical approval

Ethics committee permission of the study was approved by Inonu University, Faculty of Medicine, Health Sciences Non-interventional Clinical Research Ethics Committee with 05.10.2021 dated and 2020/1216 numbered decision.

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