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Orjinal Araştırma / Original Article

Comparison of Community-Acquired Rotavirus Infection with Nosocomial Rotavirus Infection; Evaluation of Epidemiology, Severity and Economic Burdens

Toplumdan Kazanılmış Rotavirüs Enfeksiyonunun Nozokomiyal Rotavirüs Enfeksiyonu ile Karşılaştırılması; Epidemiyoloji, Şiddet ve Ekonomik Yükünün Değerlendirilmesi

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Abstract

Aim: The aim of this study was to evaluate the demographic data of patients with community-acquired rotavirus (CAR) gastroenteritis, the incidence of patients with nosocomial rotavirus gastroenteritis (NRG), the length of hospitalization and direct costs of these two groups, and the effect of NRG in pediatric patients.

Material and Method: The records of patients aged 0-144 months who were admitted to Halfeti State Hospital between July 2017 and July 2019 and who hospitalized for rotavirus gastroenteritis and patients who developed nosocomial rotavirus infection (NRI) while hospitalized for any reason were reviewed retrospectively. Demographic characteristics, laboratory data, direct cost analysis of patients with CAR infection and patients with NRI were examined and comparisons were made between these two groups.

Results: A total of 195 patients were included in the study, of which 29 were patients with NRI. Patients in both groups were most frequently between 25-60 months. The length of hospitalization was on average 6 days more in patients with NRG. While the average hospitalization cost of patients with positive NRI was 175.2 USD, the average hospitalization cost of patients without NRI was 120.6 USD and this difference was statistically significant (p = 0.001).

Conclusion: Rotavirus infectio; especially in children under the age of five which is common mostly in winter, can be highly nosocomial and creates a serious burden on the health system. Applications such as hand washing, the use of personal protective equipment of healthcare workers, patient isolation can reduce NRI.

Keywords: Nosocomial rotavirus, children, epidemiology, economic burden

Öz

Amaç: Bu çalışmada amaç, toplum kökenli rotavirüs (TKR) gastroenteritli hastaların demografik verilerini, nozokomiyal rotavirüs gastroenteritli (NRG) hastaların insidansını, bu iki grubun hastanede yatış sürelerini ve direkt maliyetlerini ve nozokomiyal enfeksiyonun getirdiği ek maliyeti belirleyerek pediyatrik hastalarda NRG etkisini değerlendirmektir.

Gereç ve Yöntem: Temmuz 2017-Temmuz 2019 tarihleri arasında Halfeti Devlet Hastanesi' ne başvuran 0-144 aylık hastaların rotavirüs gastroenteriti nedeniyle hastaneye yatırılan ve herhangi bir nedenle hastaneye yatırılırken nozokomiyal rotavirüs enfeksiyonu (NRE) gelişen hastaların kayıtları retrospektif olarak incelendi. TKR enfeksiyonu olan ve NRE olan hastaların demografik özellikleri, laboratuvar verileri, doğrudan maliyet analizi incelendi ve bu iki grup arasında karşılaştırmalar yapıldı.

Bulgular: Çalışmaya toplamda 195 hasta dahil edilmiş olup bunların 29' u NRE olan hastalardan oluşmaktaydı. Her iki grupta da hastalar en sık 25-60 ay arasındaydı. Hastane yatış süresi, NRG olan hastalarda ortalama 6 gün daha fazlaydı. NRE pozitif olan hastaların hastaneye yatış maliyeti ortalama 175,2 USD iken NRE olmayan hastaların ortalama yatış maliyeti 120,6 USD olup bu fark istatistiksel olarak da anlamlıydı (p = 0.001).

Sonuç: Rotavirüs enfeksiyonu; özellikle beş yaşın altındaki çocuklarda, çoğunlukla kışın yaygın olan, oldukça nozokomiyal olabilen ve sağlık sistemi üzerinde ciddi bir yük oluşturan önemli bir enfeksiyondur. El yıkama, sağlık çalışanlarının kişisel koruyucu ekipman kullanımı, hasta izolasyonu gibi uygulamalar nozokomiyal rotavirüs enfeksiyonunu azaltılabilir.

Anahtar Kelimeler: Nozokomiyal rotavirüs, çocuklar, epidemiyoloji, ekonomik yük

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INTRODUCTION

Acute gastroenteritis (AGE) is among the important causes of infectious deaths in children. Especially in developing countries, it is more likely to be seen and to cause serious illness.[1] Despite all precautions, diarrhea deaths affect 2-3 million people every year in the world. Most of these deaths occur in children under 5 years old.[2-4] Viruses are known as the most common cause of AGEs and can be counted as the most common rotavirus, human caliciviruses (norovirus and sapoviruses), adenovirus 40/41 and astrovirus AGE agents in children.[5] The reoviridae family member rotavirus, which is frequently seen as a viral factor in acute gastroenteritis, is a double-stranded 70-nm RNA virus and has an icosahedral, non-envelope, car wheel-like appearance.[6] In the mild climatic regions, rotavirus diarrhea, which is observed mostly in the winter months and frequently observed in children under 2 years of age, occurs earlier in developing countries compared to developed countries; it is clinically more severe and mortality rates are higher.[7] Rotavirus is an important risk factor for intra-hospital infections due to its high infectivity and resistance to environmental conditions. Carrier rates of healthcare workers dealing with these patients are high. [8] Rotavirus is a very common factor in patients who are hospitalized for other reasons and develop diarrhea after the third day of hospitalization. Approximately 1/3 of the patients who are hospitalized due to rotavirus infection are identified as nosocomial infections.[9] The aim of our study is to evaluate the epidemiological features, the frequency of nasocomial rotavirus development, and direct cost analysis of patients who were hospitalized for due to rotavirus gastroenteritis and patients who had a NRI while they were hospitalized for any reason.

MATERIAL AND METHOD

In our study, the records of patients aged 0-144 months who were admitted to Halfeti State Hospital between July 2017 and July 2019 who hospitalized for rotavirus gastroenteritis and patients who developed NRI while hospitalized for any reason were reviewed retrospectively. The diagnosis of AGE was accepted as >3 / day watery defecation in the last week without antibiotics and thought to be unrelated to food.[10] The presence, sensitivity and specificity of rotavirus antigen in the fresh stool samples were investigated by the qualitative immunochromatographic test kit (Rapid test diagnostics adenovirus / rotavirus AV-RV combo card test) that reported with high compatible. Patients who were admitted to the hospital with complaints of diarrhea, who started diarrhea at 72 hours after hospitalization for other reasons, or who returned to the hospital with a complaint of diarrhea within 72 hours after discharge from the hospital, with rotavirus detected in the stool sample by immunochromatographic methods were evaluated as nasocomial rotavirus enteritis. The data of the cases with macroscopic examination of the feces were watery and microscopically free of any parasites were included in the study. Stool specimens and rectal swab material that were reported to be hemorrhagic or with parasites were not included in the study. From hospital information operating system records, patient files and epicrises in the archive; age, gender, hospital admission date, hospitalization status, complaints of first application, blood tests taken during the first application and after nosocomial rotavirus detection, and rotavirus antigen tests in fresh feces were recorded. Cost analysis data; it was obtained from hospital data processing records and invoice information documents considering the components such as drugs used for patients, materials used, radiological imaging performed, laboratory examinations made, and the bed price that occurred during the stay in the service. All costs calculated in our study consist of direct medical costs. Due to the difficulty of calculation and retrospective study, indirect costs such as health personnel expenses, loss of parents' job, transportation, meal and diaper expenses are not included in the study. Turkish lira (TL) values in cost analysis of patients; for each month between the dates of the study, the average foreign exchange buying rates determined by the Turkish Republic Central Bank were calculated and converted to United States Dollar (USD). Ethics committee approval (date: 09.09.2019, session no: 10, decision no:18) was obtained from the Non-Interventional Clinical Research Ethics Committee of Harran University Faculty of Medicine.

Statistical analysis:

SPSS 25.0 package program was used for statistical analysis of the data. Categorical measurements were summarized as numbers and percentages, and continuous measurements as mean and standard deviation (median and minimum - maximum where necessary). Chi square test or Fisher test statistic was used to compare categorical variables. In comparing continuous measurements between groups, distributions were checked, Student T test was used for variables with parametric distribution, and Mann Whitney U test was used for variables without parametric distribution. Statistical significance level was taken as 0.05 in all tests.

RESULTS

The study included a total of 195 patients. The median age of the all children included in the study was 27 (min-max: 4-100) months, and 105 (53.8%) were male and 90 (46.2%) were female. While 182 (93.3%) patients were citizens of the Republic of Turkey, 13 (6.7%) patients were Syrian refugee. It was observed that 69 (35.4%) of the patients were hospitalized in the winter, 63 (32.3%) in the spring, 50 (25.6%) in the autumn, and 13 (6.7%) in the summer.

It was determined that 15.9% of the patients had fever, 32.3% had vomiting, 92.8% had diarrhea and 45.1% had fatigue.

Patients are divided into two groups; 166 (85.1%) patients who were positive for rotavirus antigen test and hospitalized with the diagnosis of community-acquired rotavirus gastroenteritis constituted the nosocomial rotavirus negative (NRN) group; 29 patients who developed rotavirus gastroenteritis while being treated in the hospital for other reasons constitute the nosocomial rotavirus positive (NRP) group. When the patients who developed NRI were examined; it was determined that

19 (65.5%) of the patients were hospitalized due to acute bronchiolitis, 4 (13.9%) of them were pneumonia, 3 (10.3%) of them were epilepsy and 3 (10.3%) of them were urinary tract infections.

After nosocomial rotavirus gastroenteritis diagnosed, when changes in treatment are examined; it was observed that probiotic treatment added to all 29 (100%) patients. All the changes in treatment are shown in **Table 1**.

Table 1. Treatment changes in patients diagnosed with nosocomial rotavirus gastroenteritis

	n	%
Probiotics added	29	100
Metronidazole added	10	34.5
Antiemetic added	17	58.6
Zinc added	18	65.5

The age of occurrence of rotavirus infection in the NRN and NRP groups was found to be most frequently between 25-60 months. Eighty-four (50.6%) of 166 patients in the NRN group and 15 (51.7%) of 29 patients in the NRP group were in this age range. When NRN and NRP groups were compared in terms of all age ranges, it was found that there was no statistically significant difference between the two groups for the development of rotavirus gastroenteritis (p = 0.708). While 84 (50.6%) of 166 patients were male and 82 (49.4%) were female in the NRN group, 21 of 29 patients (72.4%) were male and 8 (27.6%) were female in the NRP group. It was found statistically significant that NRI was higher in male children (p = 0.042). There was no statistical difference between the two groups in terms of nationality and seasonal distrubution (p = 0.415, p = 0.200 respectively). Comparison of NRN and NRP groups by age, gender, nationality and season are shown in **Table 2**.

The mean length of hospitalization in patients with nosocomial rotavirus pozitive gastroenteritis was 11 days, patients with non-nosocomial rotavirus gastroenteritis was 5 days. When the two groups were compared in terms of length of hospital stay, it was seen that the NRP group stayed in the hospital statistically significantly longer (p = 0.001). While the daily diarrhea number was 11 in the NRN group, it was 6 per day in the NRP group. When the two groups are compared; the number of daily diarrhea was statistically significantly higher in the NRN group (p = 0.001). When the mean direct cost analysis of the patients is examined; it was determined that the NRP group was 175.2 USD and the NRN group was 120.6 USD. NRP group's direct costs is statistically significantly higher than the NRN group (p = 0.001). The comparison of groups by age, length of hospitalization, diarrhea per day and direct costs analysis shown in **Table 3**. The comparison of the groups by direct cost analysis is shown in **Figure 1**.

Table 3. Comparison of groups by age, length of hospitalization, diarrhea per day and direct costs analysis

	Nosocomial Rotavirus Negative (n=166) Mean (min-max)	Nosocomial Rotavirus Pozitive (n=29) Mean (min-max)	p
Age (months)	27 (4-100)	27 (8-65)	0.881
Length of hospitalization (days)	5 (2-13)	11 (7-18)	**0.001**
Diarrhea per day	9 (4-16)	6 (4-14)	**0.001**
Costs (TL)	578 (60.7-1918.6)	835.2 (181.1-2035.8)	**0.002**
Costs (USD)	120.6 (10.5-486.6)	175.2 (31.2-557.8)	**0.001**

Table 2. Comparison of Nosocomial Rotavirus Negative and Nosocomial Rotavirus Positive groups by age, gender, nationality and season

		Total (n)	Nosocomial Rotavirus Negative		Nosocomial Rotavirus Pozitive		p
			n	%	n	%	
Age (months)	0-12	26	24	14.5	2	6.9	0.708
	13-24	57	47	28.3	10	34.5	
	25-60	99	84	50.6	15	51.7	
	>60	13	11	6.6	2	6.9	
	Total	195	166	100	29	100	
Gender	Male	105	84	50.6	21	72.4	**0.042**
	Female	90	82	49.4	8	27.6	
	Total	195	166	100	29	100	
Nationality	Citizens of the Republic of Turkey	182	156	94.0	26	89.7	0.415
	Syrian refugee	13	10	6.0	3	10.3	
	Total	195	166	100	29	100	
Seasonal distribution	Autumn	50	38	22.9	12	41.4	0.200
	Winter	69	61	36.7	8	27.6	
	Spring	63	55	33.1	8	27.6	
	Summer	13	12	7.2	1	3.4	
	Total	195	166	100	29	100	

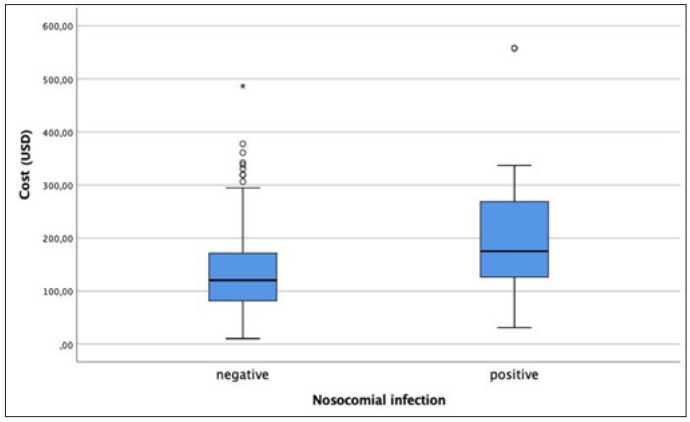

Figure 1. The comparison of the groups by direct cost analysis.

In blood gas tests; there was no statistically significant difference for pH values between the groups. The mean HCO3 values were 17.1 ± 4.0 and the mean PCO2 values were 32.5 ± 6.9 in the NRN group, while the average HCO3 values in the NRP group were 19.2 ± 4.7 and the average PCO2 values were 36.7 ± 11.4. The NRN group was found to have statistically lower HCO3 and PCO2 values than the NRP group (p = 0.001, p = 0.001 respectively). There was no statistically significant difference between the groups in terms of complete blood count and other biochemical tests.

DISCUSSION

Rotaviruses are the most common cause of severe viral AGEs under 5 years of children in the world. Rotavirus infection is one of the most important public health problems that put a high burden on health resources in developed and developing countries.[11-13] The rate of rotavirus infection prevalence in some countries of the world; it is seen that it is 17-69% in the United States, 16% in Germany, 20-28% in India and 20% in Pakistan. The incidence of the disease was reported similarly in developed and developing countries, suggesting that the level of development does not affect the frequency of rotavirus gastroenteritis.[14] In studies conducted in our country, the frequency of rotavirus can be determined at the rate of 9.8-39.8%.[15] The overall prevalence of the NRI around the world is estimated approximatelly 20% to 50%.[16] Very few studies have been performed for the prevalence of rotavirus-associated nosocomial infection in developing countries. In a study, designed in the pediatrics referral hospital of the Isfahan province, the prevalence of the NRI in Iran was 26.25%.[17] Currently available literature for pediatric population on nosocomial rotavirus burden in Central and Eastern Europe revealed that, rotaviral nosocomial infection accounts about between 22% and 55% of cases.[18] The frequency of NRI has been reported as 40% in Brazil, 27.7% in Italy, 11.1% in France and 3% in Spain. In our study, the frequency of NRI was found to be 14.8%.

NRI can progress asymptomatically in young children and the prevalence of asymptomatic infection is high in children under six months and especially newborns.[19,20] In our study, it was found that CAR and NRI were most common between the ages of 13-60 months. This can be partially explained by the fact that the infection may have been asymptomatic in young children. In previous studies, it was reported that NRI was observed in girls and boys in similar rates, although in our study; it was found that the development of nosocomial infection was more common in boys.

There are many studies showing that rotavirus gastroenteritis often peaks in winter and autumn.[21,22] In the USA and in the United Kingdom, increasing numbers of infections begin in December or January, with peaks in March or April and incidence falling to almost zero by July.[23] In our study; we found that rotavirus gastroenteritis begins in October, peaks in November and December, and incidence falling in minimum level in July.

According to our study, the average daily diarrhea per day in patients with CAR infection; it was statistically higher than NRI. HCO3 values were also statistically lower in CAR gastroenteritis, and it was found that these patients developed a more severe metabolic acidosis than patients with nosocomial rotavirus infection. More moderate metabolic acidosis in blood gas tests performed in patients who developed NRI; it may be attributed to the fact that these patients are receiving inpatient fluid treatment for other reasons, and that the tests were performed early after the onset of diarrhea.

The economic burden of NRG can be evaluated in multiple ways with direct/indirect, quantitative/qualitative, constant/variable analyses as well as cost analysis, which uses different combinations of the former categories.[24,26] In our study all costs calculated consist of direct medical costs. The mean cost for patients who had NRG was 175,2 (min-max = 31,2-557,8) USD compared to 120,6 (min-max = 10,5-486,6) USD for patients without NRG. The difference in cost was statistically significant (p = 0.001). The significant difference in cost can be attributed to prolonged length of hospital stay, additional laboratory examinations, changing and added treatments. In our study, in the treatment changes of patients after NRI; it was determined that 34.5% metronidazole treatment was initiated and probiotic support was added to all patients. We detected a significant amount of antibiotic abuse. Looking at the literature, studies evaluating the direct cost of NRG estimated that the additional cost was between 177 USD and 3,255 USD. In studies which analyzed both the direct and indirect costs, the estimated additional cost was 2,016 USD to 3,409 USD.[27-31]

CONCLUSION

Rotavirus gastroenteritis is an important infection, especially in children under the age of five which is common mostly in winter, can be highly nosocomial and creates a serious burden on the health system. In preventing NRI; in addition to applications such as hand washing, healthcare workers' use of personal protective equipment, patient isolation; we think that rotavirus vaccination, which has been included in the routine vaccination program in some countries in recent years, is also important in areas with high morbidity.

ETHICAL DECLARATIONS

Ethics Committee Approval: Ethics committee approval (date: 09.09.2019, session no: 10, decision no:18) was obtained from the Non-Interventional Clinical Research Ethics Committee of Harran University Faculty of Medicine.

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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