

# An outbreak of rotavirus infection in a neonatal intensive care unit: A case–control study

 Benhur Şirvan Çetin,<sup>1</sup>  Ayşen Orman<sup>2</sup>

<sup>1</sup>Department of Pediatric Infectious Diseases, Erciyes University, Faculty of Medicine, Kayseri, Türkiye

<sup>2</sup>Department of Neonatology, Mersin University, Faculty of Medicine, Mersin, Türkiye

## ABSTRACT

**Objective:** This study aimed to retrospectively evaluate a rotavirus (RV) outbreak in a neonatal intensive care unit (NICU) with clinical signs and symptoms and complications in the cases.

**Material and Methods:** A case–control study was conducted with RV infected and non-infected neonates in our 97-bed NICU between August 24, 2017, and November 08, 2017. Demographic, clinical, and laboratory features were evaluated.

**Results:** The outbreak started on August 24, 2017, and the last case was detected on November 8, 2017. In the study period, 33 patients had a hospital-acquired RV infection during hospitalization. The number of screened neonates was 280, and the prevalence was 11.7% (33/280). For the control group, 47 neonates with no RV infection were randomly selected. Male was 57.6%, and the median postnatal age was 4.5 days. Premature was 32.1%, and low birth weight was 37.2%. There was no difference between case and control groups regarding gender, postnatal age, birth weight, gestational age, and mortality. Bloody stool was detected in 13 neonates who were RV infected (39.4%). Twelve neonates presented necrotizing enterocolitis (NEC), and 11 of them were infected with RV. No neonate with RV infection presented complications from the central nervous system or intussusception. Bacterial co-infection was seen in 28.2% of all neonates, and there were no differences between case and control groups. However, the sepsis (clinical or proven) rate was higher in the case group than in the control group. C-reactive protein value was higher and metabolic acidosis was more frequent in the case group. The only variable related to the mortality was NEC.

**Conclusion:** Although RV infection has a mild course in the neonatal period, patients should be followed up for complications like NEC. In hospitalized neonates, RV is transmitted in a high percentage. When an infection is detected in a NICU patient, all patients should be screened, and infection control measures should be strictly enforced.

**Keywords:** Healthcare-associated infection; hospital-acquired; neonates; outbreak; rotavirus; intensive care unit.

**Cite this article as:** Çetin BŞ, Orman A. An outbreak of rotavirus infection in a neonatal intensive care unit: A case–control study. Jour Umraniye Peditr 2022;2(2):63–69.

**Received (Başvuru):** 31.08.2022 **Revised (Revizyon):** 31.08.2022 **Accepted (Kabul):** 04.09.2022 **Online (Online yayınlanma):** 13.10.2022

**Correspondence (İletişim):** Dr. Benhur Şirvan Çetin. Erciyes Üniversitesi, Tıp Fakültesi, Çocuk Enfeksiyon Hastalıkları Bilim Dalı, Kayseri, Türkiye.  
**Phone (Tel):** +90 505 701 18 78 **e-mail (e-posta):** benhurçetin@gmail.com

© Copyright 2022 by Istanbul Provincial Directorate of Health - Available online at www.umraniyepediatri.com

# Yenidoğan yoğun bakım ünitesinde rotavirüs enfeksiyonu salgını: Bir olgu kontrol çalışması

## ÖZET

**Amaç:** Bu çalışmada, yenidoğan yoğun bakım ünitesinde ortaya çıkan bir rotavirüs salgınının, olguların demografik, klinik ve laboratuvar özellikleri ve komplikasyonlarıyla birlikte değerlendirilmesi amaçlandı.

**Gereç ve Yöntemler:** Doksan yedi yataklı yenidoğan yoğun bakım ünitesinde 24 Ağustos 2017-08 Kasım 2017 tarihleri arasında rotavirüs ile enfekte olan ve olmayan yenidoğanlarla bir olgu kontrol çalışması yürütüldü. Olguların demografik, klinik ve laboratuvar özellikleri değerlendirildi.

**Bulgular:** Salgın 24 Ağustos 2017 tarihinde başladı ve son olgu 08 Kasım 2017 tarihinde tespit edildi. Çalışma sürecinde 33 yenidoğan, hastane kaynaklı rotavirüs enfeksiyonu geçirdi. Taranan yenidoğan sayısı 280, rotavirüs enfeksiyonu prevalansı %11,7 (33/280) idi. Kontrol grubu için rotavirüs enfeksiyonu olmayan ve aynı dönemde yatan 47 yenidoğan rastgele seçildi. Erkek oranı %57,6 ve ortalama yaş 4,5 gündü. Prematüre doğum %32,1 ve düşük doğum ağırlığı oranı %37,2 idi. Olgu ve kontrol grupları arasında cinsiyet, postnatal yaş, doğum ağırlığı, gebelik yaşı ve mortalite açısından fark yoktu. On üç yenidoğanda kanlı dışkı tespit edildi ve bu olguların tümü rotavirüs ile enfekteydi (%39,4). On iki yenidoğanda nekrotizan enterokolit gelişti ve bu olguların 11'i rotavirüs ile enfekteydi. Rotavirüs enfeksiyonu olan hiçbir yenidoğan, santral sinir sistemi veya invajinasyondan kaynaklanan komplikasyonlar göstermedi. Bakteriyel koenfeksiyon tüm yenidoğanlarda %28,2 oranında görüldü, olgu ve kontrol grupları arasında fark yoktu. Ancak olgu grubunda sepsis (klinik veya kanıtlanmış) oranı kontrole göre daha yüksekti. Olgu grubunda C-reaktif protein değeri daha yüksek ve metabolik asidoz daha sıklıkla görüldü. Mortalite ile ilgili tek değişken nekrotizan enterokolit gelişimi idi.

**Tartışma:** Yenidoğan döneminde rotavirüs enfeksiyonu hafif seyretse de hastalar nekrotizan enterokolit gibi komplikasyonlar açısından izlenmelidir. Hastanede yatan yenidoğanlarda rotavirüs yüksek oranda bulaşır ve bir yenidoğan yoğun bakım ünitesi hastasında enfeksiyon tespit edildiğinde tüm hastalar taranmalı ve enfeksiyon kontrol önlemleri sıkı şekilde uygulanmalıdır.

**Anahtar Kelimeler:** Sağlık bakımıyla ilişkili enfeksiyon; hastane kaynaklı enfeksiyon; rotavirüs; yenidoğan; salgın; yoğun bakım ünitesi.

## ORCID ID

B.Ş.Ç.: 0000-0002-8470-4907; A.O.: 0000-0003-1783-0185

<sup>1</sup>Erciyes Üniversitesi, Tıp Fakültesi, Çocuk Enfeksiyon Hastalıkları Bilim Dalı, Kayseri, Türkiye

<sup>2</sup>Mersin Üniversitesi, Tıp Fakültesi, Neonatoloji Bilim Dalı, Mersin, Türkiye

## INTRODUCTION

Rotavirus (RV) is one of the most important diarrheal agents in young children and infants, including nosocomial infections in neonates both in developed countries as well as in developing countries. Approximately 2 million people worldwide receive inpatient treatment due to RV infection, and an average of 600,000 deaths occur each year due to RV diarrhea (1). RV infection is easy to spread in institutional care or hospital settings. However, there is very little literature information about the characteristics and course of outbreaks in neonatal intensive care units (NICUs) (2). Studies show that diarrhea due to RV is less common in the neonatal period than in infancy and can be completely asymptomatic in some newborn babies (3, 4). On the other hand, RV infection, especially in premature babies, may have complications such as necrotizing enterocolitis (NEC) and secondary bacteremia (5-8). This study aimed to retrospectively evaluate an RV outbreak we experienced in our NICU, clinical signs and symptoms, and complications in the cases.

## MATERIALS AND METHODS

### Study Population

Gaziantep Cengiz Gökçek Maternity and Children's Hospital serves a wide area in the southeast Anatolia region. In addition to serving a large urban population in Türkiye, this center also serves as a referral center for Jarablus and Al-Bab, which are border regions of Syria with Türkiye. NICU in this hospital had a 97-bed (56-bed 3<sup>rd</sup> level, 17-bed 2<sup>nd</sup> level, and 10-bed 1<sup>st</sup> level) capacity, and approximately 20% of patients admitted to NICU in the study period had been transferred from or born in Syria. The number of patients discharged from our NICU in the year of the study was approximately 110 per month. During the outbreak, the number of screened neonates was 280.

Our study included a subgroup of patients hospitalized in NICU between August 24, 2017 and November 08, 2017. After detecting the index case, patients diagnosed with hospital-acquired (HA) RV infection formed the case group in the following 2 months. HA infection was defined as the presence of RV in stool samples of neonates at least 72 h after admission

to the hospital, provided that previously no symptoms of gastroenteritis were presented. In addition to the case group, a control group was formed by randomly selecting cases hospitalized in the NICU, and no RV was detected in the same period.

Hospital records of the patients were analyzed retrospectively. In each neonate, epidemiological and clinical data were recorded, including gender, place of birth, birth weight, gestational and postnatal age at admission, underlying medical conditions, symptoms, clinical findings, and complications (diarrhea, bloody stool, NEC, bacterial co-infection, proven, or clinical sepsis), time of the RV acquired, length of the RV positivity, length of stay (LOS) in hospital, and mortality. Consistency of stool was categorized into formed, seedy, watery or loose, and bloody mucoid. Diarrhea was defined as a twofold or greater increase in the frequency of watery or looser than normal stool within 24 h.

### Laboratory Tests

The case and control groups' basic laboratory and stool examination results were evaluated retrospectively. Stool samples were kept at 4°C and tested within 24 h for RV antigen with a rapid qualitative immunochromatographic method (RIDA®QUICK RV/Adenovirus combi, R-Biopharm, Germany) in accordance with the working procedure of the manufacturer. According to the product sheet, the sensitivity and specificity were 100.0% and 94.4%, respectively. Stool samples were tested for RV daily for the 1st week and twice a week routinely during the outbreak so that a cohort of positive cases could be made. Neonates who developed a new gastrointestinal symptom tested for RV immediately. Blood tests included white blood cell (WBC), platelet count, C-reactive protein (CRP), and blood gas analysis. Metabolic acidosis was diagnosed by an HCO<sub>3</sub> concentration of <18 mmol/L.

### Statistical Analysis

The statistical data analysis was performed using IBM SPSS for Windows (IBM statistics for Windows version 25, IBM Corporation, Armonk, New York, United States). In descriptive statistics of the data, mean±standard deviation for normally distributed variables and median (interquartile range) values for non-normally distributed variables were used. The qualitative data were analyzed by Chi-square test, while the quantitative data by Student's t-test or Mann–Whitney test, as appropriate.  $p < 0.05$  was accepted as a cutoff value for statistical significance.

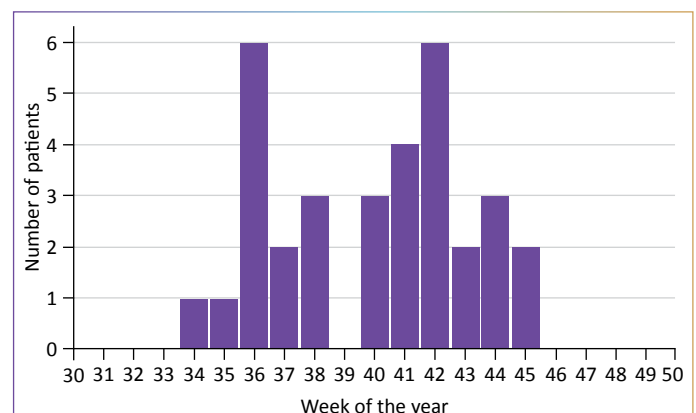
### Ethics Committee Approval

This study was reviewed and approved by the Erciyes University Clinical Research Ethics Committee (Date: June 29, 2022, Number: 2022/486). The study was carried out according to the Declaration of Helsinki Principles. The data were analyzed anonymously.

## RESULTS

The index case was a 10-day-old boy admitted to the NICU with gastroenteritis and jaundice. The patient could not be tested rapidly for RV because admission coincided with a national holiday. The first RV test was performed on the 6th day and resulted positive. After the first case was detected, all patients were screened for RV as described above. The outbreak started on August 24, 2017, and the last case with a HA RV infection was detected on November 08, 2017. In the study period, 33 patients had a HA RV infection during hospitalization. The prevalence was 11.7% (33/280). The distribution of the patients by week is shown in Figure 1. For the control group, 45 patients without a RV infection were selected randomly.

In our study group, males were 57.6% (45/78), and the median postnatal age was 4.5 days (Interquartile range: 9 days). Premature (gestational age <37 weeks) was 32.1% (25 neonates) and low birth weight was 37.2% (29 neonates). There was no difference between case and control groups regarding gender, postnatal age, birth weight, and gestational age (Table 1). While the rate of children born in Syria was 17.9% among all neonates, it was higher in the case group than in the control group (30.3% and 8.9%, respectively,  $p=0.017$ ). Neonatal infection (33.3%), jaundice (25.6), and respiratory distress (24.3%) were the most commonly seen underlying medical condition at the time of admission. There were no differences between case and control groups regarding underlying medical conditions (Table 1). Diarrhea was detected at similar rates in the case and control groups (72.7% and 60.0%, respectively,  $p=0.17$ ). Bloody stool was detected in 13 neonates; all were RV infected (39.4%). In the study period, 12 neonates presented NEC, and 11 were infected with RV. No neonate with RV infection presented complications from the central nervous system or intussusception. Bacterial co-infection was seen 28.2% of all neonates, and there were no differences between the case and control groups (27.3% vs. 28.9%, respectively). However, on the other hand, the sepsis (clinical or proven) rate was higher in the case group than control (45.5% vs. 22.2%,  $p=0.02$ ). Demographic and clinical features of case and control groups are presented in Table 1.



**Figure 1.** Distribution of the number of patients newly diagnosed with hospital-acquired RV infection.

**Table 1. Demographic and clinical features of hospital-acquired (HA) Rotavirus positive cases and control group**

| Variables                                                | Total (n=78) | Case Group (n=33) | Control Group (n=45) | p                |
|----------------------------------------------------------|--------------|-------------------|----------------------|------------------|
| Demographics                                             |              |                   |                      |                  |
| Gender                                                   |              |                   |                      |                  |
| Male, (%)                                                | 45 (57.6)    | 20 (60.6)         | 25 (55.6)            | 0.41             |
| Age at the admission, median day (IQR)                   | 4.5 (9)      | 5 (13)            | 3 (7)                | 0.91             |
| Birth weight, median gram (IQR)                          | 2770 (816)   | 2600 (1020)       | 2780 (710)           | 0.22             |
| Low birth weight ≤2500 g, n (%)                          | 29 (37.2)    | 16 (48.5)         | 13 (28.9)            | 0.09             |
| Normal birth weight >2500 g, n (%)                       | 49 (62.8)    | 17 (51.5)         | 32 (71.1)            |                  |
| Gestational age, median week (IQR)                       | 38 (2)       | 38 (2)            | 38 (2)               | 0.88             |
| Full-term ≥37 weeks, n (%)                               | 53 (67.9)    | 22 (66.7)         | 31 (68.9)            | 0.51             |
| Preterm <37 week, n (%)                                  | 25 (32.1)    | 11 (33.3)         | 14 (31.1)            |                  |
| Place of birth                                           |              |                   |                      | <b>0.017</b>     |
| Syria, n (%)                                             | 14 (17.9)    | 10 (30.3)         | 4 (8.9)              |                  |
| Türkiye, n (%)                                           | 64 (82.1)    | 23 (69.7)         | 41 (91.1)            |                  |
| Underlying medical condition                             |              |                   |                      | 0.36             |
| Respiratory distress, n (%)                              | 19 (24.3)    | 12 (36.4)         | 7 (15.5)             |                  |
| Neonatal infection, n (%)                                | 26 (33.3)    | 11 (33.3)         | 15 (33.3)            |                  |
| Jaundice, n (%)                                          | 20 (25.6)    | 5 (15.1)          | 15 (33.3)            |                  |
| Congenital anatomic defects and surgical problems, n (%) | 4 (5.1)      | 3 (9.0)           | 1 (2.2)              |                  |
| Metabolic diseases, n (%)                                | 1 (1.28)     | 1 (3.0)           | 0 (0)                |                  |
| Symptoms and clinical findings                           |              |                   |                      |                  |
| Diarrhea, n (%)                                          | 51 (65.4)    | 24 (72.7)         | 27 (60.0)            | 0.17             |
| Bloody stool, n (%)                                      | 13 (16.7)    | 13 (39.4)         | 0 (0)                | <b>&lt;0.001</b> |
| Necrotizan enterocolitis, n (%)                          | 12 (15.4)    | 11 (33.3)         | 1 (2.2)              | <b>&lt;0.001</b> |
| Bacterial co-infection, n (%)                            | 18 (23.1)    | 9 (27.3)          | 9 (20.0)             | 0.58             |
| Sepsis (clinical or proven), n (%)                       | 25 (32.1)    | 15 (45.5)         | 10 (22.2)            | <b>0.02</b>      |
| IQR: Inter quantile range.                               |              |                   |                      |                  |

In laboratory values, WBC and platelet counts were not different between groups. While CRP median value was higher and metabolic acidosis was more common in the case group than in the control (Table 2). The median day of admission when patients were infected with RV, and the median duration of RV antigen positivity in the stool was 7 days (Table 2 and Fig. 2). The median day of LOS in RV-infected neonates was more than in non-infected ones (25.5 vs. 10 days,  $p<0.001$ ). The general mortality rate in the study population was 7.7%. While mortality in the case group is more than control (12.1% vs. 4.4%, in Table 2), the difference was not statistically significant ( $p=0.20$ ). We also evaluated the factors affecting mortality in the whole study group. Variables that differ between surviving and de-

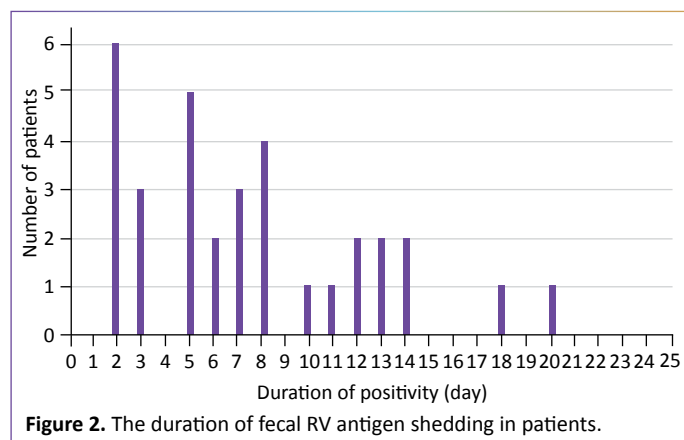
ceased infants were birth weight, gestational age, NEC, sepsis, and LOS (Table 3). When we performed logistic regression analysis with these variables, we found that only NEC was associated with mortality ( $p=0.013$ ).

During the outbreak, all healthcare workers have trained again in infection control policies and practices according to relative guidelines of the Hospital Infection Committee. Attention was paid to maximum compliance with hand hygiene and contact isolation measures. The frequency of cleaning the environment and common areas (such as nurse and doctor desks, keyboards, drug preparation areas, and baby weighing scales) had increased. Neonates with positive RV were tried to be brought together in a separate section in NICU. However, it was often

**Table 2. Laboratory features and outcomes of the patients**

|                                                                         | Total (n=78) | Case group (n=33) | Control group (n=45) | p                |
|-------------------------------------------------------------------------|--------------|-------------------|----------------------|------------------|
| <b>Laboratory values</b>                                                |              |                   |                      |                  |
| WBCs×10 <sup>3</sup> cells/μL, median (IQR)                             | 9.5 (6.7)    | 10.6 (8.2)        | 9.3 (5.8)            | 0.71             |
| PLTs×10 <sup>3</sup> cells/μL, median (IQR)                             | 281 (152)    | 274 (179)         | 293 (141)            | 0.49             |
| CRP mg/dL, median (IQR)                                                 | 3 (30)       | 12 (37)           | 1 (14)               | <b>0.03</b>      |
| Metabolic acidosis, n (%)                                               | 9 (11.5)     | 7 (22.6)          | 2 (4.4)              | <b>0.02</b>      |
| <b>Outcomes</b>                                                         |              |                   |                      |                  |
| Day of hospitalization at the time of Rotavirus infection, median (IQR) |              | 7 (10)            | N/A                  |                  |
| Length of rota positivity, median day (IQR)                             |              | 7 (9)             | N/A                  |                  |
| Length of hospital stay, median day (IQR)                               | 10 (21)      | 25.5 (27)         | 10 (5)               | <b>&lt;0.001</b> |
| Mortality, n (%)                                                        | 6 (7.7)      | 4 (12.1)          | 2 (4.4)              | 0.20             |

CRP: C-reactive protein; IQR: Inter quantile range; PLT: Platelet; WBC: White blood cell.

**Figure 2.** The duration of fecal RV antigen shedding in patients.

not possible to relocate neonates who were in severe condition and needed level 3 intensive care, and contact isolation measures were taken in their place. Daily antigen screening in stool was performed in the 1<sup>st</sup> week of the epidemic. In the following weeks, all inpatients were screened routinely at admission and twice a week to try to catch asymptomatic babies.

## DISCUSSION

It is generally believed that RV infection is less common in newborns and is mainly asymptomatic (9, 10). Although asymptomatic RV infection exists, it is rarely described in the scientific literature, resulting in underestimating its prevalence. In Greece, Koukou et al. (10) found asymptomatic RV infection in NICU at 19%. In a study by Yeom et al. (11) from South Korea, RV antigen was routinely tested in the stool of 228 newborns

**Table 3. Association of variables with mortality in all patients**

| Variables                                 | Discharged from the hospital (n=72) | Exitus (n=6) | p                |
|-------------------------------------------|-------------------------------------|--------------|------------------|
| Gender, male n (%)                        | 43 (59.7)                           | 2 (33.3)     | 0.39             |
| Birth weight, median gram (IQR)           | 2790 (720)                          | 1760 (1220)  | <b>0.001</b>     |
| Gestational age, median week (IQR)        | 38 (2)                              | 33 (9)       | <b>0.009</b>     |
| Place of birth, Syria n (%)               | 12 (16.7)                           | 2 (33.3)     | 0.29             |
| HA Rotavirus infection, n (%)             | 29 (40.3)                           | 4 (66.7)     | 0.39             |
| NEC, n (%)                                | 7 (9.7)                             | 5 (83.3)     | <b>&lt;0.001</b> |
| Bacterial co-infection, n (%)             | 15 (20.8)                           | 3 (50)       | 0.13             |
| Sepsis (clinical or proven), n (%)        | 19 (26.4)                           | 6 (100)      | <b>&lt;0.001</b> |
| Length of hospital stay, median day (IQR) | 10 (17)                             | 37.5 (34)    | <b>0.01</b>      |

HA: Hospital acquired; NEC: Necrotizing enterocolitis.

who were >34 weeks and were admitted to the NICU. In 34.2% of those patients, RV antigen was found positive in the stool. Shim et al. (12) found RV positivity at a rate of 25.2% in their study, which screened 702 newborns hospitalized in the NICU. Sharma et al. (13) also found the prevalence of RVI in the NICU as 18.4%. In different studies from different countries, RV infection is estimated to be between 11% and 35% (10). In literature, most cases of RV infections in neonates are HA. Tai et al. (14) recognized 72.4% of RV gastroenteritis cases as HA, while Shim et al. (12) reported a rate of 93% for HA in preterm neonates.

Our study is one of the largest series of RV outbreaks in a NICU. The outbreak lasted nearly 3 months, 33 cases had HA RV infection, and we found RV positivity rate of approximately 11%. The rate we found in our study cannot be generalized, but it is noteworthy that it is a rate similar to the one in the literature. Since the neonates remained in the incubator and did not have direct contact, we thought there was cross-contamination between the cases. In general, it is challenging to identify transmission risk factors for RV. It seems that the high contagiousness of fomites, the poor sanitation of surfaces and hands using standard hygiene procedures, and the subclinical transmission to hospital staff play a substantial role in the spread of the virus and the incidence of nosocomial outbreaks (10).

One of the differences we found in comparisons with the control group was the place of birth of the cases. With the available data, we could not explain the fact that more people with the infection were born in Syria. Some of these cases may be started shedding RV in the stool before hospitalization, and we may not have been able to detect community-acquired RV infection because of the false-negative results of the sample we took during hospitalization. However, for this hypothesis to be correct, we need to show a higher prevalence of RV infection among Syrian-born people. We could not find any study in the literature to support this.

Clinical manifestation of RV infection in neonates has been associated with diarrhea (64–77%), (15) presenting with watery stool in term neonates, and bloody mucoid stool in preterm neonates (13). In our study, diarrhea was observed in 72.7% of infected cases, and bloody stool was observed in 39.4%. Diarrhea is often defined as a result of a subjective evaluation, and it can be seen that diarrhea develops very frequently in hospitalized newborns due to existing diseases or drugs used. Diarrhea was observed at a high rate in the control group also. In the study of Koukou et al. (10) between 2009 and 2013, 126 RV-infected neonates were evaluated, and the most common findings were diarrhea (81%), weight loss (54%), feeding intolerance (39.7%), fever (34.9%), dehydration (28.6), and vomiting (26.2%). In the same study, 19% of the cases were asymptomatic. In other studies, the most common manifestations of the infection among premature neonates were feeding difficulty, abdominal distension, and lethargy. However, the symptoms commonly seen in full-term neonates were fever, diarrhea, and vomiting (12). These results revealed that RV infections in preterm infants generated more systemic symptoms and differed from infections in full-term or older infants, who primarily

manifested as fever or gastrointestinal symptoms (12).

It has been reported that RV infection affects the central nervous system in the newborn period and may cause complications such as convulsions, aseptic meningitis, encephalitis, cerebellitis, and secondary bacterial infection (4, 6, 16). In a study comparing community-acquired and HA neonatal RV infection findings, feeding intolerance, respiratory symptoms, jaundice, seizure, and weight loss were more common in HA RV infections (10). It was also reported that the incidence of convulsions in patients with positive RV antigen was significantly higher than in the negative group (11).

Severe clinical symptoms like bloody diarrhea associated with abdominal distention resulting in NEC and even bowel perforation have been reported, especially in preterm and low birth weight neonates (5, 15). In a study by Tai et al., (14) 100 patients, including newborns and infants, were evaluated. It has been reported that bloody and mucous stools are more common than watery diarrhea in HA RV infections in this age group, and the frequency of NEC is increased in HA infections. Yavanoğlu et al. (4) evaluated ten nosocomial RV-infected newborns, and NEC did not develop in their cases. In our study, we found that the probability of bloody stool and NEC development is higher in RV-infected cases. It would be appropriate to look for RV antigen in newborns, especially in the presence of bloody stools. It has been reported that maturational changes in the intestine of premature neonates lead to an increased incidence of NEC after RV infection (10). This may explain why preterm neonates show various symptoms than full-term neonates or older infants; instead of fever and watery stool, preterm infants with RV infection present blood/mucous in stool and NEC (10, 13, 14).

Gözmen et al. (17) reported that the rate of secondary bacteremia after RV infection in children was seen in only 5 out of 376 children. We found a rate of 27.3% for bacterial co-infection, but the most common among them was urinary tract infections. Although the exact mechanism has not been demonstrated, it is thought that secondary bacteremia is associated with damaged intestinal epithelium after RV infection.

There is not enough study in the literature about the duration of RV stool excretion in newborns. Although it is generally accepted that the excretion lasts for 10–15 days, sometimes there is no viral excretion for a long time, and then the shedding may start again (13). Typically, a longer hospital stay, which coincides with smaller and sicker newborns, raises the risk of nosocomial RV transmission (9).

We did not see an increased death rate due to RV gastroenteritis. However, when we looked at the possible relationship of all the variables we examined with mortality, we saw that only the development of NEC was an independent variable on mortality. Since our sample group is small and we could not look at many variables, it would not be correct to infer mortality risk factors with this study alone.

Although fecal-oral transmission is responsible for RV infection, the intra-hospital spread mechanism is unclear. Due to the nature of the RV, it is very difficult to eradicate the virus from the hospital environment, and the disease can occur even with a

very low viral load. Proper hand washing with alcohol-based hand sanitizers and chlorhexidine is essential for virus removal (18). Sharma et al. (13) showed that breast milk protects against the development of RV infection.

### Limitations of the Study

The small number of the study group (33 RV infected patients), the absence of an objective assessment of the presence of diarrhea and the lack of genotyping of RVs were the main limitations of our study. Since the clinical profile of RV infections was mentioned in our study, the inability to conduct molecular studies would not make a difference in this respect. Additional parameters could also be evaluated in our study. The effects of breast milk or antibiotic use on prognosis and more comprehensive laboratory parameters could be examined. Since these neonates have many comorbid features, it may not always be possible to establish a direct relationship between laboratory parameters and the course of RV infection. The workers were not screened for RV. This would have been considered for possible source identification. Consequently, our results cannot represent the whole population of neonates. Nevertheless, this study is one of the largest HA RV case series in the literature that describes the clinical picture and outcomes in the NICU.

### CONCLUSION

RV outbreak in NICU is a rare condition. Although RV infection has a mild course in the neonatal period, patients should be followed up regarding complications, especially for NEC. RV infection in hospitalized neonates is nosocomially transmitted in a high percentage and when infection is detected in a NICU patient, all patients should be screened and infection control measures should be strictly enforced.

**Ethics Committee Approval:** Erciyes University Clinical Research Ethics Committee granted approval for this study (Date: June 29, 2022, Number: 2022/486).

**Conflict of Interest:** No conflict of interest was declared by the authors.

**Financial Disclosure:** The authors declared that this study has received no financial support.

**Authorship Contributions:** Concept – BŞÇ, AO; Design – BŞÇ; Supervision – BŞÇ, AO; Materials – AO; Data collection and/or processing – AO; Analysis and/or interpretation – BŞÇ, AO; Literature review – BŞÇ; Writing – BŞÇ, AO; Critical review – AO.

**Etik Kurul Onayı:** Erciyes Üniversitesi Klinik Araştırmalar Etik Kurulu'ndan bu çalışma için onay alınmıştır (Tarih: 29 Haziran 2022, Sayı: 2022/486).

**Çıkar Çatışması:** Yazarlar çıkar çatışması bildirmemişlerdir.

**Mali Destek:** Yazarlar bu çalışma için mali destek almadıklarını beyan etmişlerdir.

**Yazarlık Katkıları:** Fikir – BŞÇ, AO; Tasarım – BŞÇ; Denetleme – BŞÇ, AO; Malzemeler – AO Veri Toplanması ve/veya İşlenmesi – AO; Analiz ve/veya Yorum – BŞÇ, AO; Literatür Taraması – BŞÇ; Yazıyı Yazan – BŞÇ, AO; Eleştirel İnceleme – AO.

### REFERENCES

1. Parashar UD, Gibson CJ, Bresee JS, Glass RI. Rotavirus and severe childhood diarrhea. *Emerg Infect Dis* 2006;12:304–6.
2. Posfay-Barbe KM, Zerr DM, Pittet D. Infection control in paediatrics. *Lancet Infect Dis* 2008;8:19–31.
3. Chang LY. Rotavirus in the neonatal intensive care unit: Different clinical characteristics in premature neonates. *Pediatr Neonatol* 2012;53:1.
4. Yavanoğlu Atay F, Güran Ö, Bilgin L. Epidemic of rotavirus infection in neonatal intensive care unit. *Forbes J Med* 2021;2:154–7.
5. Rotbart HA, Levin MJ, Yolken RH, Manchester DK, Jantzen J. An outbreak of rotavirus-associated neonatal necrotizing enterocolitis. *J Pediatr* 1983;103:454–9.
6. Johansen K, Hedlund KO, Zweyberg-Wirgart B, Bennet R. Complications attributable to rotavirus-induced diarrhoea in a Swedish paediatric population: Report from an 11-year surveillance. *Scand J Infect Dis* 2008;40:958–64.
7. Lowenthal A, Livni G, Amir J, Samra Z, Ashkenazi S. Secondary bacteremia after rotavirus gastroenteritis in infancy. *Pediatrics* 2006;117:224–6.
8. Tan BF, Chen YC, Lee CN, Chang LY, Hsieh WS, Tsao PN, et al. Pseudo-outbreak of rotavirus infection in a neonatal intensive care unit. *J Microbiol Immunol Infect* 2016;49:947–54.
9. Bhan MK, Lew JF, Sazawal S, Das BK, Gentsch JR, Glass RI. Protection conferred by neonatal rotavirus infection against subsequent rotavirus diarrhea. *J Infect Dis* 1993;168:282–7.
10. Koukou D, Chatzichristou P, Trimis G, Siahaniidou T, Skiathitou AV, Koutouzis EI, et al. Rotavirus gastroenteritis in a neonatal unit of a greek tertiary hospital: Clinical characteristics and genotypes. *PLoS One* 2015;10:e0133891.
11. Yeom JS, Park JS, Kim YS, Kim RB, Choi DS, Chung JY, et al. Neonatal seizures and white matter injury: Role of rotavirus infection and probiotics. *Brain Dev* 2019;41:19–28.
12. Shim JO, Son DW, Shim SY, Ryoo E, Kim W, Jung YC. Clinical characteristics and genotypes of rotaviruses in a neonatal intensive care unit. *Pediatr Neonatol* 2012;53:18–23.
13. Sharma R, Hudak ML, Premachandra BR, Stevens G, Monteiro CB, Bradshaw JA, et al. Clinical manifestations of rotavirus infection in the neonatal intensive care unit. *Pediatr Infect Dis J* 2002;21:1099–105.
14. Tai IC, Huang YC, Lien RI, Huang CG, Tsao KC, Lin TY. Clinical manifestations of a cluster of rotavirus infection in young infants hospitalized in neonatal care units. *J Microbiol Immunol Infect* 2012;45:15–21.
15. Ramani S, Sowmyanarayanan TV, Gladstone BP, Bhowmick K, Asirvatham JR, Jana AK, et al. Rotavirus infection in the neonatal nurseries of a tertiary care hospital in India. *Pediatr Infect Dis J* 2008;27:719–23.
16. Abe T, Kobayashi M, Araki K, Kodama H, Fujita Y, Shinozaki T, et al. Infantile convulsions with mild gastroenteritis. *Brain Dev* 2000;22:301–6.
17. Gözmen S, Sükran Gözmen K, Apa H, Aktürk H, Sorguç Y, Bayram N, et al. Secondary bacteremia in rotavirus gastroenteritis. *Pediatr Infect Dis J* 2014;33:775–7.
18. Chandran A, Heinzen RR, Santosham M, Siberry GK. Nosocomial rotavirus infections: A systematic review. *J Pediatr* 2006;149:441–7.