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Clinical Characteristics of Symptomatic Rotavirus Infection in Newborn Infants and Genotype Analysis

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Objective: Clinical data on rotavirus infection in the neonatal period are still limited. In this study, we investigated the incidence and monthly distribution, clinical features, and genotypes of symptomatic rotavirus infection in newborn infants.

Methods: Medical records of newborn infants with rotavirus infection in a university hospital of Korea over a 4-year period (2011–2014) were retrospectively analyzed. These enrolled cases included hospital-acquired (HA) and community-acquired (CA) infections according to where the infection occurred. Infants included full-term and preterm infants according to the gestational age.

Results: Among 135 finally enrolled patients with symptomatic rotavirus infections, 80 (59.3%) and 55 (40.7%) cases had HA and CA infections, respectively. There were 85 (63%) and 50 (37%) full-term and preterm infants, respectively. HA infections were more common in preterm infants, whereas CA infections were more common in full-term infants (P<0.001). In the comparison between the HA group and the CA group, clinical symptoms of rotavirus infection were similar between the 2 groups. On the other hand, in comparisons between preterm and full-term groups, abdominal distension, feeding intolerance and bloody stool were more common in preterm infants, while fever was more common in full-term infants (P<0.005). The genotype of rotavirus was determined for 121 (89.6%) cases, all of which had the G4[P6] strain.

Conclusion: The type and clinical findings of rotavirus infection in preterm infants are different from those of full-term infants. G4[P6] was the only strain detected in neonatal infections regardless of where the infection occurred or the gestational age of patient.

Key Words: Clinical features, Genotype, Newborn infants, Rotavirus

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Introduction

Recently, after the introduction of vaccines, the incidence of rotavirus infection in infants and young children has decreased.[1-3] However, newborns under the age of vaccination coverage are still vulnerable to this infection.[1,2] Rotavirus is highly contagious. Its infection can occur even with a small number of virus particles, such as less than 100.[4] Rotavirus is resistant to surface-active agents commonly used for environmental disinfection in hospitals.[5] Additionally, it can survive for several weeks in an environmental medium if humidity is maintained.[6] It can spread easily to infants through contaminated hands of home caregivers or healthcare workers.[7]

Globally, seasonal characteristics of rotavirus infection in temperate regions of the world are prevalent in late autumn and winter.[8,9] However, in newborn nursery and neonatal intensive care unit (NICU) where temperature and humidity are kept constant, they may occur constantly regardless of season.[10-12] In newborns, the type of rotavirus infection is known to be more common in hospital-acquired (HA) infections than in community-acquired (CA) infections,[12-14] but it may be different after stratification according to gestational age.[15]

In most infants and young children, rotavirus causes local infection of the mucosa of the gastrointestinal tract. Therefore, their clinical manifestations by rotavirus infection are mostly watery and loose stools with typically benign clinical course and outcome.[3] Clinical symptoms of rotavirus infection in newborns are nonspecific and often asymptomatic compared to those in infants and young children.[11,16] Lactase present in the brush border of epithelial cells of intestinal villi is known to act as a receptor for viruses to invade cells.[17] Preterm infants have a lower lactase activity than full-term infants.[18] Thus, they might be less susceptible to the infection.[17] However, some preterm infants infected with rotavirus also suffer from serious gastrointestinal diseases, including bloody and mucoid stool and necrotizing enterocolitis (NEC).[14,16] On the other hand, some full-term infants infected with rotavirus rarely have seizures or cerebral white matter injury.[19]

Worldwide, common infectious strains of rotavirus in newborns differ according to regions and countries. The G genotype varies from G1-4 to G8-12, while the P genotype is mostly known as P[4], P[6], P[8] and P[11].[11,12,20] Additionally, genotypic distributions of rotavirus may differ depending on where the infection occurs and gestational age of the infected infant as well as the time of infection due to seasonal differences.[15,21,22] Thus, this study was conducted to investigate the differences in clinical characteristics and virus genotype according to where the infection occurred and gestational age in newborns with rotavirus infection.

Methods

This study was conducted to evaluate patients diagnosed with rotavirus infection in the newborn nursery and NICU in a university hospital of Korea over a 4-year period (2011-2014). Medical records and radiographic findings of subjects were retrospectively reviewed. This study was approved by the institutional review board (IRB) of Keimyung University Dongsan Hospital (IRB no. 2019-12-046). Informed consent was waived by the board.

1. Study design

The rotavirus antigen test was performed 2 to 3 times at 24- to 48-hour intervals. All out-born babies were initially tested for rotavirus antigen after hospitalization, and inborn babies were tested when they had clinical symptoms of infection, or during the outbreak of infection, exposed groups who were in the same room with the infected case were tested. Enrolled cases included HA and CA infections according to the site of rotavirus infection. Patients were divided into full-term and preterm infants according to their gestational age. Monthly distribution and seasonal characteristics of rotavirus infections were determined for study subjects. Additionally, clinical findings of rotavirus infection, including perinatal characteristics, clinical symptoms and signs, laboratory findings, complications, and viral genotypes, were investigated. Among these infants, cases with asymptomatic rotavirus infection, those who were transferred from other hospitals with rotavirus infection, and cases with a combined bacterial infection were excluded from this study.

Detection of rotavirus antigens in fecal samples was performed by immunochromatography (ICG) using a dipstick ROTA kit (Eiken, Tokyo, Japan) from 2011 to February 2012 and by enzyme immunoassay (EIA) using a VIDAS rotavirus kit (bioMérieux, Marcy-l'Étoile, France) from March 2012 to 2014.[23] Stool samples from patients with symptomatic rotavirus infection were stored at -70°C for later virus genotyping. In this study, reverse transcription-polymerase chain reaction (RT-PCR) was performed to analyze G and P genotypes of rotavirus as described by Kim et al.[24] Viral RNA extraction was performed using a Prepito Viral NA/gDNA kit (PerkinElmer, Waltham, MA, USA). PCR was performed using a PCR Pre-mix kit (Solgent, Seoul, Korea). For G genotyping, End 9 and Beg 9 primers and specific primers for G-type, including aBT1, aBT2, aBT3, and aBT4 targeting G1, G2, G3, and G4, respectively, were used. For P genotyping, Con2 and Con3 primers

and specific primers for P-type, including 1-T1, 2-T1, 3-T1, 4-T1, and 5-T1 targeting P[8], P[4], P[6], P[9], and P[10] respectively, were used.

2. Definitions of terms

The diagnostic criteria for symptomatic rotavirus infections in newborn infants were limited to satisfy both of the following 2 conditions: (1) clinical symptoms, including decreased activity, fever, diarrhea, abdominal distension, vomiting, and feeding intolerance; and (2) positive for rotavirus antigen test using fecal specimens. HA infection was diagnosed based on the timing of clinical symptoms or viral antigen tests for rotavirus: after 48 h of hospitalization in the nursery and NICU, or within 48 hours after discharge from the hospital. Additionally, if the baby was born in our hospital, hospitalized in the newborn nursery or NICU, and found to have positive viral antigen test within 48 hours after birth, and maternal infection was excluded, the case was considered as an HA infection. CA infection was defined as the case where the infection occurred at home or at the postpartum care facility. Combined bacterial infection was limited to cases in which pathogens were identified in blood samples within the first 3 days after rotavirus infection.[25] In patients with skin flora, including coagulase-negative staphylococci (CoNS), the diagnosis of bacteremia was based on both the presence of clinical signs of infection and elevated C-reactive protein, or the same bacteria were continuously detected in blood culture performed within 2 days.

Breastfeeding was limited to infants who breastfeed more than 50% of their daily intake. Feeding intolerance was defined as when the infant had clinical symptoms, including abdominal distention, vomiting, and an increase in gastric residual volume without achieving an increase in feeding volume. The ileus gas pattern was diagnosed based on simple X-ray findings, including an increase in overall air shadow in the intestine or dilatation of the small intestine. Apnea was defined as temporary cessation of breathing for a duration of >20 seconds or when accompanied by bradycardia and desaturation, even though the duration was <20 seconds.[26] Additionally, in order to exclude apnea of prematurity, the evaluation was limited to newly developed apnea after rotavirus infection. Dehydration was defined as a reduction of 10% or more compared to the weight before infection,[27] considering the physiological weight loss of the newborn. NEC was classified based on modified Bell's staging criteria.[28] Seizure was diagnosed clinically based on recurrent appearance of abnormal paroxysmal events, including symptoms of focal or multifocal clonic, focal tonic, and subtle.[29] Cerebral white matter injury was defined as diffuse, symmetric diffusion-restrictive lesions in the white matter of bilateral cerebral hemispheres, including the corpus callosum on magnetic resonance imaging.[30]

3. Statistical analysis

Data were analyzed using IBM SPSS Statistics ver. 25.0 (IBM Corp., Armonk, NY, USA). Chi-square test and Fisher's exact test were used to analyze categorical variables, while the Man-Whitney U test and t-test were used for continuous variables. *P*-values less than 0.05 were considered statistically significant.

Results

1. Study population

Of a total of 7,512 inpatients, 1,404 (18.7%) were tested for rotavirus antigen. And 155 (68.6%) of the 226 positive cases were classified as symptomatic infection. Although the rotavirus antigen test was positive, 71 (31.4%) patients with asymptomatic infection were excluded from this study. Additionally, among patients with symptomatic infections, 14 infected at other hospitals and 6 with combined bacterial infections were also excluded from this study. Among 135 finally enrolled patients, 80 (59.3%) and 55 (40.7%) cases were classified as HA and CA infection, respectively, and 85 (63.0%) and 50 (37.0%) cases were full-term and preterm infants, respectively (Fig. 1).

2. Incidence and seasonal characteristics of rotavirus infection

The monthly median value of patients with whole rotavirus infection was 10 (range, 4-22). Among them, the monthly median value of patients with HA infection was 5.5 (range, 2-15). Rotavirus infections occurred throughout the year. However, its incidence during the cold season (November-April) was higher (2.6%) than that in the warm season (May-October, 1.0%) ($P<0.05$) (Fig. 2).

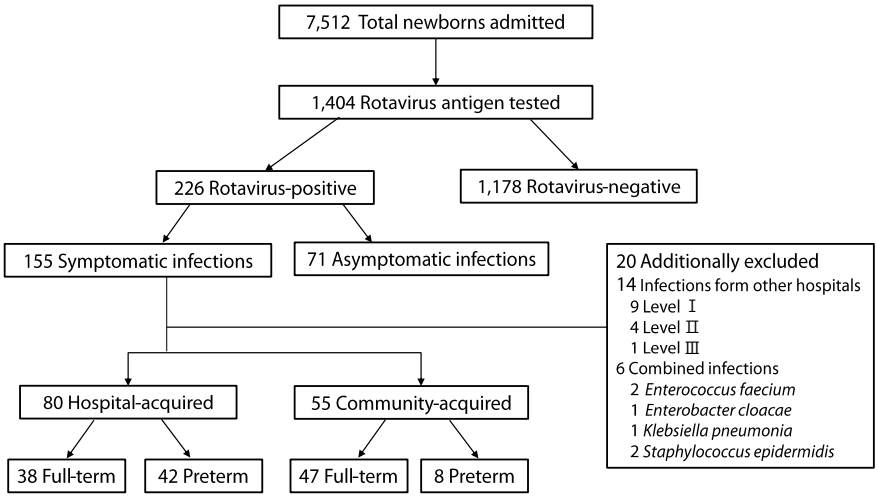

Fig. 1. Distribution of study population.

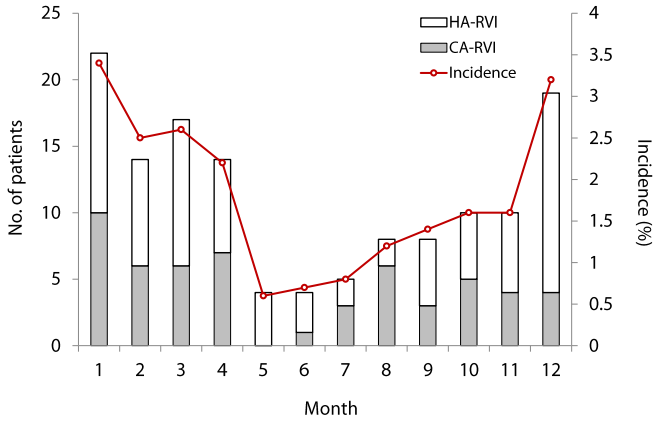

Fig. 2. Monthly distribution and incidence of patients with symptomatic rotavirus infections. HA, hospital-acquired; RVI, rotavirus infection; CA, community-acquired.

3. Types of rotavirus infection and where the infection occurred

In the HA group of 80 patients, NICU and newborn nursery were sites of infection for 52 and 28 patients, respectively. Additionally, in the CA group of 55 patients, sites of infection were postpartum care centers and homes for 45 and 10 patients, respectively (Table 1).

4. Combined bacterial infection

Causative organisms of combined bacteremia were enterococci and CoNS in 2 cases each and *Enterobacter* and *Klebsiella* in one case each (Fig. 1).

Table 1. Types of Rotavirus Infection and Where the Infection Occurred (n=135)

Type	n (%)
Hospital-acquired	80 (59.3)
Neonatal intensive care unit	52 (38.5)
Newborn nursery	28 (20.8)
Community-acquired	55 (40.7)
Postpartum care facility	45 (33.3)
Home	10 (7.4)

5. Clinical findings of rotavirus infection based on the place of the infection and viral genotype

HA infections were more common in preterm infants, whereas CA infections were more common in full-term infants (P<0.001). The rate of cesarean delivery was higher in the HA group than in the CA group (P<0.001). The proportion of outborn infants was lower in the HA group than in the CA group (15.0% vs. 70.9%) (P<0.001). The onset time of infection was later in the HA group (13.1±17.2 days) than in the CA group (6.1±2.8 days) (P<0.001). One inborn infant born to full-term showed clinical symptoms and positive antigen test within 48 hours of birth during hospitalization. The mother of this baby had no clinical symptoms and the viral antigen test was negative, so the case was classified as a HA infection. Common clinical symptoms of rotavirus infection were abdominal distension, feeding intolerance, fever, decreased activity, and watery stools. However, there was no significant difference in their frequency between the 2 groups. The proportion of bloody

stool was higher in the HA group (17.5%) than in the CA group (1.8%) (P<0.05). Most laboratory findings and complications were not significantly different between the 2 groups. The identification rate of genotype by RT-PCR was 87.5% in the HA group, similar to that in the CA group (92.7%). G4[P6] was the only strain detected in neonatal infections regardless of where the infection occurred (Table 2).

6. Clinical findings of rotavirus infection according to gestational age and viral genotype

The proportion of out-born infants was higher in the full-term group than in the preterm group (55.5% vs. 8.0%) (P<0.001). The onset time of infection was later in the preterm group (18.6±19.8 days) than in the full-term group (5.4±2.7 days) (P<0.001). Among clinical symptoms related to rotavirus infection, fever and watery stool were more common in the full-term group than in the preterm group (P<0.05). On the other hand, other symptoms including abdominal distension and feeding intolerance, decreased activity, bloody stool, paralytic ileus, and apnea were more common in preterm infants (P<0.05). Additionally, some laboratory findings such as fecal occult blood were more common in preterm infants (P<0.005). Complications were relatively rare. However, NEC was only associated preterm infants, while seizures and cerebral white matter injury were only associated with full-term infants. The identification rate of genotype by RT-PCR was 88.2% in the full-term group, similar to that in the preterm group (92.0%). G4[P6] was the only strain detected in neonatal infections regardless of the gestational age (Table 3).

Table 2. Comparison of Clinical Findings and Genotype Analysis according to Where the Infection Occurred in Patients with Symptomatic Rotavirus Infection

Variable	HA RVI (n=80)	CA RVI (n=55)	*P*-value
Gestational age (wk)	36.3±3.6	38.4±1.8	<0.001
Birth weight (g)	2,651.8±933.1	3,133.1±540.1	<0.001
GA (preterm:full-term)	42:38	8:47	<0.001
C-section	64 (80.0)	14 (25.5)	<0.001
Sex (male:female)	47:33	23:32	0.079
Birth place (inborn:outborn)	68:12	16:39	<0.001
Breast feeding	28 (35.0)	30 (54.5)	0.038
Onset of infection (day)	13.1±17.2	6.1±2.8	<0.001
Symptoms and signs			
Abdominal distension	44 (55.0)	21 (38.2)	0.081
Feeding intolerance	41 (51.3)	25 (45.5)	0.626
Fever (>37.8°C)	33 (41.3)	24 (43.6)	0.922
Decreased activity	29 (36.3)	20 (36.4)	1.000
Watery or loose stool	29 (36.3)	20 (36.4)	1.000
Bloody or mucoid stool	14 (17.5)	1 (1.8)	0.010
Ileus gas pattern	21 (26.3)	9 (16.4)	0.251
Vomiting	17 (21.3)	13 (23.6)	0.907
Tachycardia (>160/min)	15 (18.8)	9 (16.4)	0.899
Bradycardia (<100/min)	5 (6.3)	2 (3.6)	0.781
Apnea	10 (12.5)	4 (7.3)	0.489
Oliguria (<1 mL/kg/hr)	6 (7.5)	5 (9.1)	0.991
Laboratory findings			
Stool occult blood	37 (46.3)	10 (18.2)	0.001
CRP (≥0.5 mg/dL)	23 (28.8)	15 (27.3)	1.000
MA (base deficit ≥10 mEq/L)	11 (13.8)	4 (7.3)	0.369
Platelet (<150,000/mm^3)	7 (8.8)	5 (9.1)	1.000
Complications			
Dehydration	17 (21.3)	15 (27.3)	0.547
NEC (≥stage 2)	3 (3.8)	0 (0)	0.391
Seizure	0 (0)	4 (7.3)	0.053
CSF pleocytosis (≥32/mm^3)	0 (0)	1 (1.8)	0.850
White matter injury	0 (0)	2 (3.6)	0.320
Analysis of RV genotypes			
G4P[6]	70 (87.5)	51 (92.7)	0.489
PCR-negative	10 (12.5)	4 (7.3)	0.489

Values are presented as mean±standard deviation or number (%).
HA, hospital-acquired; RVI, rotavirus infection; CA, community-acquired; GA, gestational age; CRP, C-reactive protein; MA, metabolic acidosis; NEC, necrotizing enterocolitis; CSF, cerebrospinal fluid; RV, rotavirus; PCR, polymerase chain reaction.

Discussion

Rotavirus genotypes prevalent in newborn nursery or NICU patients differ by country or year in which the infection is prevalent. Regarding rotavirus genotypes of neonatal infections in individual hospitals around the world, various types such as G4P[6], G4P[8], G10P[11], G12P[11], etc. have been reported.[20] In a four-year study from 2009-2013 in a neonatal unit in Greece,[22] the distribution of rotavirus genotypes in 126 patients varied according to the year or season in which the infection occurred. Overall, G4P[8] was the most common one

Table 3. Comparison of Clinical Findings and Genotype Analysis according to Gestational Age in Patients with Symptomatic Rotavirus Infection

Variable	Full-term (n=85)	Preterm (n=50)	*P*-value
Gestational age (wk)	39.2±1.0	33.7±2.6	<0.001
Birth weight (g)	3,318.1±564.2	2,048.4±545.8	<0.001
Low birth weight (<2,500 g)	2 (2.4)	37 (74.0)	<0.001
C-section	41 (48.2)	37 (74.0)	0.006
Sex, male:female	41:44	29:21	0.359
Birth place (inborn:outborn)	38:47	46:4	<0.001
Breast feeding	40 (47.1)	18 (36.0)	0.283
Onset of infection (day)	5.4±2.7	18.6±19.8	<0.001
Symptoms and signs			
Abdominal distension	31 (36.5)	34 (68.0)	0.001
Feeding intolerance	31 (36.5)	37 (70.0)	<0.001
Fever (>37.8°C)	47 (55.3)	10 (20.0)	<0.001
Decreased activity	24 (28.2)	25 (50.0)	0.019
Watery or loose stool	38 (44.7)	11 (22.0)	0.014
Bloody or mucoid stool	1 (1.2)	14 (28.0)	<0.001
Ileus gas pattern	11 (12.9)	19 (38.0)	0.002
Vomiting	14 (16.5)	16 (32.0)	0.060
Tachycardia (>160/min)	12 (14.1)	12 (24.0)	0.224
Bradycardia (<100/min)	2 (2.4)	5 (10.0)	0.125
Apnea	4 (4.7)	10 (20.0)	0.012
Oliguria (<1 mL/kg/hr)	5 (5.9)	6 (12.0)	0.353
Laboratory findings			
Stool occult blood	21 (24.7)	26 (52.0)	0.002
CRP (≥0.5 mg/dL)	21 (24.7)	17 (34.0)	0.336
MA (base deficit ≥10 mEq/L)	6 (7.1)	9 (18.0)	0.095
Platelet (<150,000/mm^3)	5 (5.9)	7 (14.0)	0.198
Complications			
Dehydration	21 (24.7)	11 (22.0)	0.883
NEC (≥stage 2)	0 (0)	3 (6.0)	0.093
Seizure	4 (4.7)	0 (0)	0.302
CSF pleocytosis (≥32/mm^3)	1 (1.2)	0 (0)	1.000
White matter injury	2 (2.4)	0 (0)	0.722
Analysis of RV genotypes			
G4P[6]	75 (88.2)	46 (92.0)	0.689
PCR-negative	10 (11.8)	4 (8.0)	0.689

Values are presented as mean±standard deviation or number (%).
CRP, C-reactive protein; MA, metabolic acidosis; NEC, necrotizing enterocolitis; CSF, cerebrospinal fluid; RV, rotavirus; PCR, polymerase chain reaction.

at 58.7%, followed by G1P[8] and G12P[8], G3P[8], and G12P[6]. Regarding genotypic distribution of neonatal rotavirus infection in Korea, G4P[6] had a frequency of 92–100%.[11-13,31] It has been reported as an absolute strain for a long time. Additionally, in some hospitals with many out-born patients, genotypes other than G4P[6], including G1P[8], G3P[8], G9P[4], and G9P[8] have been reported to have various frequencies.[15,21] In this study, the place where the infection occurred in 55 patients with CA infection included different postpartum care facilities and individual homes. The HA group of 80 patients were continuously evaluated for 4 years, although cases were limited to those of a single hospital. However, the genotype was found to be G4P[6] in all cases regardless of place and timing of infection, seasonal changes, or gestational age of infants. This suggests that Korean herd immunity to G4P[6] strain of rotavirus has not been established.[13] Thus, the passive immunity of the infant received from the mother might be low or not contain protective antibodies against certain viral strains, making the infant vulnerable to infection by the G4P[6] strain. Additionally, some viral strains might be present in the environment of the nursery, causing persistent infections or sporadic epidemics throughout the fecal-oral route by contaminated hands of medical personnel.[10]

When evaluated based on rotavirus antigen test, the rotavirus infection rate in the NICU in Korea has been reported to be 6% to 43%.[10-12,15,21] However, this value differs greatly depending on individual hospitals. In this study, rotavirus antigen test was performed by ICG or EIA. Compared with RT-PCR, the sensitivity of ICG and EIA is reported to be 100% and 98%, respectively, and the specificity is reported to be 95% and 97%, respectively.[23] Therefore, both tests can be evaluated as relatively accurate assays. In practice, rotavirus antigen test was performed for 18.7% of all inpatients in the newborn nursery and NICU and 16.1% of them were found to be positive. The asymptomatic rate of neonatal rotavirus infection is high, accounting for 18% to ~43% of all infections.[11,12,15,16] In this study, asymptomatic infection rate was 31.4%, which was similar to those of previous reports. Additionally, similar to previous reports,[10,11] the seasonal distribution of rotavirus infections occurred throughout the year in this study, particularly during the cold season, mainly winter and spring. In this study as a whole, HA infections were more common than CA infections (59.3% vs. 40.7%). In addition, CA infections mostly occurred in postpartum care centers where babies were cared for in groups, unlike babies in homes who were cared for individually. These

results might be related to high horizontal transmission and secondary attack rates of rotavirus infection in the neonatal period when vaccination is not yet available.[12,14] In this study, most HA rotavirus infections occurred in the NICU, but occasionally occurred in the newborn nursery. During the outbreak time, infection control measures, including cohorting of patients and exposed groups, strengthening of hand hygiene, cohorting of nursing staff, and infection surveillance to identify the source of infection, were performed. However, except for stool samples from patients, no virus was detected in the hands of medical personnel or environmental factors, including the gowns of medical personnel, alcohol swabs, linens, and medical equipment.

In young infants with rotavirus infection, bacterial translocation can occur rarely from the gastrointestinal tract to the bloodstream through the intestinal mucosa, thus impairing barrier function. Causative organisms of secondary bacteremia in patients with enteritis are mainly gram-negative bacteria, including *Enterobacter* and *Klebsiella*, but *Staphylococcus* and *Candida* were also reported.[32] In this study, combined bacteremia developed in 6 patients, and enterococci and staphylococci were identified in addition to gram-negative bacteria.

In comparison according to the place of infection during this study, HA infections were more common in preterm infants, whereas CA infections were more common in full-term infants. But clinical symptoms and signs were similar between the 2 groups. However, in the comparison according to the gestational age during this study, several obvious differences in clinical findings were observed between preterm and the full-term infants. First, the onset of infection was later in the preterm group (average, 18.6 days) than in the full-term group (average, 5.4 days). This temporal difference might be related to cytopathological findings of rotavirus infection, which can selectively invade enterocytes located in the upper villi of the small intestine mucosa.[33] Lactase present in the brush border of differentiated epithelial cells of intestinal villi can functions as a receptor for the virus to enter the enterocyte.[17] Compared to full-term infants, preterm infants at 26 to 34 gestational weeks have lactase activity as low as approximately 30%.[18] Thus, extremely preterm infants are less likely to be infected with rotavirus during gestational age <32 weeks.[17] In addition, preterm infants become more susceptible to rotavirus infection as intestinal mucosal cells differentiate and enzyme activity was increased over time after birth.[17,33] Second, preterm and full-term infants showed different clinical symptoms related to rotavirus infection. Specifically, abdominal distension, feeding intolerance, decreased activity, bloody stool, and paralytic ileus were more common in preterm infants than in full-term infants. In contrast, frequencies of fever and watery stool were higher in full-term infants than in preterm infants. These differences in clinical symptoms of rotavirus infection according to the gestational age of subjects were consistent with those found in previous studies.[14,16] Notably, in the analysis of complications related to rotavirus infection, although there was no statistically significant difference between the 2 groups, NEC developed only in preterm infants, while seizures and cerebral white matter injury developed only in full-term infants. Therefore, it is necessary to investigate the molecular biological mechanisms related to these differences in complications according to gestational age in future studies.

This study had some limitations. First, the study design was retrospective. It was conducted on some total NICU patients who were hospitalized during the study period. Therefore, if the infected patient had not been tested for antigen in stool samples, the case could have been excluded from this study. Second, in this study, the diagnosis of rotavirus infection was made with a positive viral antigen test without real-time RT-PCR, so the problem of false positives or false negatives reported in 1% to 2% of antigen tests could not be solved.[23] Furthermore, this study did not investigate other viral pathogens, including norovirus, astrovirus, and adenovirus that could cause co-infection with rotavirus in young children.[34] The data for this study are from about 10 years ago. In addition, recently, our NICUs have rarely developed rotavirus infection since changes in patient care guidelines, including limiting the admission of out-born babies, and stricter measures for infection control. Thus, there is a lack of update of study data. Nevertheless, results of this study are helpful for understanding epidemiologic findings, clinical features, and genotypes of rotavirus infection in NICU patients of Korea.

In conclusion, the type and clinical findings of rotavirus infection in preterm infants, including the site of infection, the timing of onset, symptoms and signs, and complications, are different from those of full-term infants. G4[P6] was the only

strain detected in neonatal infections regardless of where the infection occurred or the gestational age of the patient.

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Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Authors' Contributions

Conceptualization & Design, Data collection, Methodology: DSK, NHR, CSK; Formal analysis: DSK, CSK; Investigation: all authors; Project administration: JCB, CSK; Writing-original draft: DSK, NHR, CSK; Writing-review & editing: all authors.

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