

## Original Article



# Human Parechovirus: an Emerging Cause of Sepsis-Like Syndrome in Infants Aged under 3 Months

Da Eun Roh , Jung Eun Kwon , Yeo Hyang Kim

Department of Pediatrics, School of Medicine, Kyungpook National University, Kyungpook National University Children's Hospital, Daegu, the Republic of Korea

## OPEN ACCESS

**Received:** Dec 4, 2019

**Revised:** May 15, 2020

**Accepted:** May 17, 2020

### Correspondence to

Yeo Hyang Kim

Department of Pediatrics, School of Medicine, Kyungpook National University, 680 Gukchaebosang-ro, Jung-gu, Daegu 41944, the Republic of Korea.  
E-mail: kimyhmd@knu.ac.kr

Copyright © 2020 The Korean Society of Pediatric Infectious Diseases

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<https://creativecommons.org/licenses/by-nc/4.0/>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

### ORCID iDs

Da Eun Roh   
<https://orcid.org/0000-0001-8932-2505>

Jung Eun Kwon   
<https://orcid.org/0000-0001-6608-3089>

Yeo Hyang Kim   
<https://orcid.org/0000-0002-1631-574X>

### Conflict of Interest

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

## ABSTRACT

**Purpose:** This study aimed to investigate the clinical characteristics of human parechovirus (HPeV) infection in sepsis-like syndrome in infants aged under 3 months.

**Methods:** Medical records of infants aged under 3 months with sepsis-like symptoms who were admitted between July 1, 2018 and August 31, 2018 were reviewed. A multiplex reverse transcription-polymerase chain reaction panel test was performed on the cerebrospinal fluid (CSF). Thirty-nine enrolled infants were categorized into three groups: 11 in group 1 (HPeV detected in the CSF), 13 in group 2 (enterovirus detected in the CSF), and 15 in group 3 (no virus detected in the CSF).

**Results:** Compared with groups 2 and 3, a higher proportion of group 1 had tachycardia, tachypnea, apnea, and hypotension ( $P<0.05$ ). A significantly lower white blood cell (WBC) count was noted in group 1 than in groups 2 and 3 ( $5,622\pm 2,355/\mu\text{L}$ ,  $9,397\pm 2,282/\mu\text{L}$ , and  $12,312\pm 7,452/\mu\text{L}$ , respectively;  $P=0.005$ ). The CSF WBC count was lower in group 1 than in groups 2 and 3 ( $0.9\pm 1.7/\mu\text{L}$ ,  $85.1\pm 163.6/\mu\text{L}$ , and  $3.7\pm 6.9/\mu\text{L}$ , respectively;  $P=0.068$ ). The proportion of patients requiring inotrope support (36.6% vs. 0% and 6.6%), mechanical ventilation (18.1% vs. 0% and 0%), and high flow nasal cannula (45.4% vs. 15.3% and 6.6%) was higher in group 1 than in groups 2 and 3. All patients recovered completely without complications.

**Conclusions:** HPeV infection shows a severe clinical course and can cause a severe sepsis-like syndrome in infants aged under 3 months. Early diagnosis and proper treatment of HPeV infection are required.

**Keywords:** Fever; Parechovirus; Infant; Sepsis; Systemic inflammatory response syndrome

## INTRODUCTION

Human parechovirus (HPeV) is a small, non-enveloped, single-stranded RNA virus that usually causes mild gastrointestinal and respiratory infections. However, it may cause severe diseases in young infants.<sup>1</sup> HPeV is common worldwide but shows variable seasonality; outbreaks occur in biennial pattern, with the peak season between summer and fall.<sup>1,2</sup> The most recent outbreak had been reported in Australia 2016.<sup>3</sup>

### Author Contributions

Conceptualization: Kim YH; Data curation: Kwon JE; Investigation: Roh DE, Kim YH; Methodology: Roh DE; Validation: Kwon JE; Writing - original draft: Roh DE, Kim YH; Writing - review & editing: Kim YH, Kwon JE.

Several studies have recognized HPeV to be a cause of sepsis-like syndrome and central nervous system (CNS) infections in infants under 3 months old. It has also been considered as a major cause of infection that requires intensive care in several cases.<sup>4)</sup> There were some reports of HPeV infection in Korea.<sup>5,6)</sup> However, the previous studies had limitation that virus study result was not taken during patient's hospitalization.

In order to investigate HPeV infection in Korean infants, the present study confirmed HPeV infection in infants under 3 months old with sepsis-like syndrome and assessed the clinical characteristics and course of disease.

## MATERIALS AND METHODS

### 1. Patients

A total of 83 infants under 3 months old were admitted with fever and sepsis like symptoms to the Department of Pediatrics at the Kyungpook National University Children's hospital between July and August 2018. Among them, 39 patients who were tested with cerebrospinal fluid (CSF) sample for HPeV detection were included in this study. For comparison of characteristics, the participating patients were categorized into 3 groups, namely, group 1 (HPeV detected), group 2 (enterovirus [EV] detected) and group 3 (no pathogen detected). Patients with known local infections (16 patients exhibiting urinary tract infection with fever and 4 patients with pneumonia), and those not undergoing CSF analysis (24 patients), were excluded.

For the purposes of the study, the presence of fever was defined either as a history of fever reported by the caregiver, or as a body temperature measurement  $\geq 38^{\circ}\text{C}$  at time of hospital presentation. Tachypnea was defined as  $\geq 60$  breaths per minute, while tachycardia was defined as  $\geq 200$  beats per minute.<sup>7)</sup> The patient was considered to have hypotension if either systolic or diastolic pressure was below the normal range for the age group.<sup>8)</sup> Apnea was defined as no respiration for  $\geq 20$  seconds, or no respiration for any duration if accompanied by bradycardia or cyanosis.<sup>9)</sup> Since the presentation of the first case diagnosed with HPeV infection, a standardized medical records form has been created for use during outbreaks or for further cases.

### 2. Laboratory tests

To confirm HPeV infection, CSF specimens obtained at admission were tested for the presence of pathogen's RNA using a reverse transcription polymerase chain reaction (RT-PCR) assay (FilmArray Meningitis/Encephalitis Panel [FA-ME], BioFire, Salt Lake City, UT, USA). This highly multiplexed assay can detect nucleic acids from seven viruses; HPeV, EV, cytomegalovirus, herpes simplex virus 1, herpes simplex virus 2, human herpes virus 6, and varicella zoster virus, five bacterial pathogens; *Streptococcus pneumoniae*, *Streptococcus agalactiae*, *Haemophilus influenzae*, *Listeria* spp, *Escherichia coli* K1, and one fungal pathogen; *Cryptococcus neoformans/gattii* responsible for community acquired meningitis or encephalitis.

Peripheral blood samples were analyzed on the day of admission for evaluation of complete blood cell counts, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), aspartate aminotransferase (AST), alanine aminotransferase (ALT), and serum sodium and potassium levels. CSF WBC count was calculated and pleocytosis was defined as  $\geq 18$  and  $\geq 9$  leukocytes per high power field for infants under 28 days old and infants between 29 and 90 days old, respectively.<sup>10)</sup>

### 3. Analysis of medical records

The characteristics and clinical course of the individual patients were analyzed from retrospective review of the medical records. The age at diagnosis, vital signs, clinical symptoms, abnormal findings on physical examination (i.e. skin mottling), blood tests, and CSF analysis (i.e. pleocytosis, glucose, protein) were compared between the patients with and without a diagnosis of HPeV infection. In addition, the overall duration of admission, need for intensive care unit (ICU) admission, use of medications (i.e. antibiotics, inotropes, or immunoglobulins), and need for respiratory support including high flow nasal cannulas (HFNCs) or invasive mechanical ventilation during the hospitalization period were also assessed in all groups.

### 4. Statistical analysis

All statistical analyses were performed using the SPSS version 25 (IBM Corp., Armonk, NY, USA) statistical software package. Data pertaining to laboratory parameters were displayed as means and standard deviations. Two-tailed Student's *t*-tests and non-parametric Mann-Whitney *U*-tests were used for comparisons between the groups. The chi-square test was used for analyzing the independent non-continuous variables. *P* values of <0.05 were considered statistically significant.

### 5. Ethics statement

Patient information was retrieved and evaluated with the approval of the Medical Records department and the Institutional Review Board of the Kyungpook National University Chilgok Hospital (IRB No. 2018-11-004).

## RESULTS

### 1. Demographic characteristics of the patients

Among the 39 patients included in this study, 11 and 13 patients had HPeV and EV infections, respectively; no virus or bacteria was detected in the CSF using the FA-ME panel in 15 patients. The patients were then classified into three groups depending on pathogen status: group 1 (HPeV detected in CSF), group 2 (EV detected in CSF) and group 3 (no virus or bacteria detected in CSF). The clinical characteristics of these three groups are outlined in **Table 1**.

Although there was no statistical difference, the mean age of group 1 was younger than group 2 and 3 (41±18 days vs. 53±24.2 days vs. 55±24 days, *P*=0.295), and the duration of fever in patients in group 1 was longer than the other groups (25.4±11.4 hours vs. 19.6±18.4 hours vs. 18.2±18.7 hours, *P*=0.326).

Compared to group 2 and group 3, clinical symptoms including skin mottling (73% vs. 38% and 27%), decreased feeding (82% vs. 38% and 60%), and irritability (64% vs. 31% and 33%) were more common in group 1. These differences were not statistically significant.

More patients in group 1 had tachycardia (64% vs. 8% and 7%, *P*<0.001), and the peak heart rate was 198.5±9.5 beats per minute, which was significantly higher than that of group 2 and 3 (180.5±15.4 beats per minute and 178.2±13.7 beats per minute, respectively, *P*=0.001). In addition, more patients in group 1 had hypotension (36% vs. 0% and 7%, respectively, *P*=0.019) which was significantly higher than that of group 2 and 3. The higher number of

**Table 1.** Comparison of clinical characteristics and medical interventions among the groups

Characteristics	Group 1 (n=11)	Group 2 (n=13)	Group 3 (n=15)	P value
Age (day)	41±18	53±24.2	55±24	0.295
Fever peak (°C)	38.9±0.4	38.8±0.4	39.0±0.5	0.261
Fever duration (hr)	25.4±11.9	19.6±18.4	18.2±18.7	0.326
Duration of admission (day)	7.1±3.6	5.1±2.4	5.6±3.1	0.211
Clinical symptoms				
Fever	11 (100.0)	13 (100.0)	15 (100.0)	1.000
Skin mottling	8 (72.7)	5 (38.5)	4 (26.7)	0.058
Irritability	7 (63.6)	4 (30.8)	5 (33.3)	0.196
Decreased feeding	9 (81.8)	5 (38.5)	9 (60.0)	0.098
Convulsions	1 (9.1)	0 (0.0)	1 (6.7)	0.568
Signs at presentation				
Tachycardia	7 (63.6)	1 (7.7)	1 (6.7)	0.001
Peak heart rate	198.5±9.5	180.5±15.4	178.2±13.7	0.001
Tachypnea	4 (36.4)	2 (15.4)	0 (0.0)	0.040
Apnea	2 (18.2)	0 (0.0)	0 (0.0)	0.068
Hypotension	4 (36.4)	0 (0.0)	1 (6.7)	0.019
ICU admissions	8 (72.7)	4 (30.8)	7 (46.7)	0.120
Interventions in hospital				
Mechanical ventilation	2 (18.2)	0 (0.0)	0 (0.0)	0.068
High flow nasal cannula	5 (45.5)	2 (15.4)	1 (6.7)	0.046
Inotropes	4 (36.4)	0 (0.0)	1 (6.7)	0.019
Antibiotics	11 (100.0)	13 (100.0)	15 (100.0)	1.000
Intravenous immunoglobulin	10 (90.9)	7 (53.8)	10 (66.7)	0.141

Values are presented as numbers (%) or mean±standard deviations unless otherwise indicated.

Abbreviations: ICU, intensive care unit; CSF, cerebrospinal fluid.

Group 1, human parechovirus detected in CSF; Group 2, enterovirus detected in CSF; Group 3, no pathogen detected in CSF.

patients in group 1 exhibited tachypnea (36% vs. 15% and 0%, respectively) and apnea (18% vs. 0% and 0%, respectively) although the differences were not statistically significant.

## 2. Laboratory findings

Laboratory test findings of the three groups are summarized in **Table 2**.

Peripheral blood tests showed that the patients in group 1 had a mean white blood cell count (WBC) of 5,622±2,355/μL, which was significantly lower compared to that of group 2 and 3 (9,397±2,282/μL and 12,312±7,452/μL, respectively,  $P=0.005$ ). No significant differences were

**Table 2.** Comparison of laboratory findings among the groups

Laboratory findings	Group 1 (n=11)	Group 2 (n=13)	Group 3 (n=15)	P value
Blood				
WBC (/μL)	5,622±2,355	9,397±2,282	12,312±7,452	0.005
CRP (mg/dL)	0.37±0.24	0.57±0.74	1.92±2.28	0.050
AST (U/L)	55.5±34.7	45.7±27.1	52.3±32.8	0.478
ALT (U/L)	35.5±30.6	38.4±36.3	57.7±70.6	0.346
Sodium (mmol/L)	131.2±5.7	135.4±1.7	135.3±2.47	0.059
Procalcitonin (ng/mL)	0.13±0.09	0.07±0.06	0.94±3.0	0.015
CSF				
WBC (/μL)	0.9±1.7	85.1±163.6	3.7±6.9	0.068
No. of patients with pleocytosis	0	4	0	0.012
Protein (mg/dL)	46.3±12.1	63.8±21.1	51.1±22.7	0.119
Glucose (mg/dL)	65.6±8.7	51.1±8.3	62.1±12.9	0.001

Values are presented as numbers (%) or mean±standard deviations unless otherwise indicated.

Abbreviations: WBC, white blood cell; CRP, C-reactive protein; AST, aspartate transaminase; ALT, alanine transaminase; CSF, cerebrospinal fluid.

Group 1, human parechovirus detected in CSF; Group 2, enterovirus detected in CSF; Group 3, no pathogen detected in CSF.

noted in the levels of hemoglobin, platelet counts, ESR, CRP, serum electrolyte level, AST, and ALT among the three groups.

CSF WBC count was lower in group 1 than in group 2 and 3 ( $P=0.068$ ). No patient in group 1 exhibited CSF pleocytosis ( $P=0.012$ ). In all groups, the total protein and glucose concentrations in the CSF were within normal ranges.

### 3. Interventions in hospital

A total of 8 patients in group 1 required intensive care; this proportion was greater than that of group 2 and 3 (73% vs. 31% and 47%, respectively) (**Table 1**). The mean duration of ICU admission in group 1 was longer than the other groups although there were no significant differences ( $4.4\pm 4.8$  days vs.  $1.5\pm 2.5$  days vs.  $1.7\pm 1.9$  days,  $P=0.199$ ).

Among the patients in group 1 who were admitted to ICU, 4 patients received treatment with inotropes for hypotension which was significantly higher than that of group 2 and 3 ( $P=0.019$ ). And 2 patients received endotracheal intubation and invasive mechanical ventilation due to apnea, and 5 patients exhibiting tachypnea required HFNC treatment. Conversely, among patients admitted to the ICU from group 2 and 3, 3 patients received HFNC treatment; no patient in these groups required endotracheal intubation or invasive mechanical ventilation (**Table 1**).

The overall duration of admission was longer in group 1 than in group 2 and 3, although the difference between the groups was not statistically significant ( $7.1\pm 3.6$  days vs.  $4.5\pm 1.2$  days vs.  $5.6\pm 3.1$  days,  $P=0.211$ ).

### 4. Prognosis

No patient required additional assessment, exhibited abnormal prognosis, or required re-admission during 3 months after discharge. All discharged patients showed normal development and growth during 3 months after discharge.

## DISCUSSION

The findings of the present study have demonstrated that HPeV may cause sepsis in infants, particularly in summer. The study also shows that although these patients may have exhibited a severe clinical course, their prognosis were essentially favorable.

In recent years, HPeV has emerged as a pathogen causing sepsis-like syndrome and CNS infections.<sup>2,11,13</sup> This small, non-enveloped, single-stranded RNA virus is a member of the Picornaviridae family and has been classified into 19 different types till date. Among them, HPeV1 and HPeV3 are the most commonly encountered in the clinical setting.<sup>1</sup> HPeV1 is the most prominent genotype, which causes mild gastrointestinal and respiratory infections. Conversely, HPeV3 can induce severe infections in infants, and is therefore clinically the most important genotype.<sup>1,2,12</sup> HPeV-specific RT-PCR provides diagnostic accuracy,<sup>13,15</sup> but CSF FA-ME is the only diagnostic tool available in Korea; the analysis outcome is available within 2 hours of sample acquisition and registration. All patients in this study had been tested for HPeV infection using samples of CSF. However, their subtypes could not be differentiated.

HPeV is evenly distributed worldwide, but there are differences in seasonality according to different HPeV genotypes. Among them, HPeV3 infection, which induces sepsis-like

syndrome or CNS infection, peaks between summer and fall, and its outbreak occurs in a biennial pattern. In the Department of Pediatrics at the Kyungpook National University Hospital, where this study was performed, the first and last patients were diagnosed in July 1, 2018 and August 15, 2018, respectively. These findings are in agreement with findings from previous studies, which suggest that the outbreak peaks in the summer and fall seasons.

The clinical course after HPeV infection varies depending on the patient's age. In children ( $\geq 3$  years old) and adults, the infection rarely causes symptomatic disease. However, it can induce severe diseases in younger infants.<sup>1,12,13</sup> Analysis of the age distribution in 106 patients diagnosed with symptomatic HPeV infections during the HPeV outbreak in England in 2016, showed that the vast majority of patients were  $< 3$  months old (98/106, 92%), and that a large proportion of patients were  $< 1$  month old (46/106, 43%).<sup>16</sup> The present study enrolled only infants aged under 3 months old, with mean age of 41 days. Analysis of the age distribution in 11 patients diagnosed with HPeV infections showed that the vast majority of patients aged 30–59 days (7/11, 64%), followed by patients younger than 30 days (2/11, 18%) and infants aged 60–90 days (2/11, 18%).

HPeV infections may cause dermatological manifestations, ranging from generalized erythema to the more characteristic erythematous or maculopapular palmar-plantar erythema. A previous study published in 2013 has mentioned that infants infected with HPeV develop skin rashes in the extremities within 3 days of the onset of fever, and the most common characteristic is a distinctive palmar-plantar erythematous rash, which disappears within 3 days of onset. All patients who developed skin rashes recovered without sequelae.<sup>6,17,18</sup> Similarly in our study, more patients in group 1 showed dermatologic manifestations such as skin mottling or palmar-plantar erythematous rash, although the differences were not statistically different.

Infants with HPeV infections often require intensive care due to severe clinical manifestations including circulatory or respiratory failure. In a report, more than half the patients exhibited sepsis-like disease characterized by circulatory shock and respiratory distress, and 17% to 23% of the patients required intensive care support.<sup>15</sup> However, considering the severity of clinical features, the duration of hospital stay in the study cohort was relatively short, and the patients recovered at the time of discharge without sequelae.<sup>16</sup> Similarly, in our study, compared to group 2 and group 3, a relatively large number of patients in group 1 (HPeV infected group) required intensive care, including respiratory support (i.e. HFNC or mechanical ventilation) and medications (i.e. inotropes) due to unstable vital signs and unfavorable clinical features (i.e. tachycardia and tachypnea, among others). All patients were also admitted for a relatively shorter duration ( $< 1$  week), were discharged without further complications, and had good follow-up outcomes. This is probably attributable to the viral characteristics; although the clinical course may have been severe during the period of viremia, it did not result in organ damage from severe inflammation. In addition, the use of antibiotics could be kept to a minimum as there were no accompanying bacterial infections confirmed on blood cultures, CSF cultures, or urine cultures.

CSF pleocytosis and blood leukocytosis are extremely rare in HPeV infection, and the total protein and glucose concentrations in the CSF were mostly normal.<sup>1,13,19,20</sup> Notably, in previous reports, patients having HPeV encephalitis with accompanying changes in the brain parenchyma (i.e. diffusion restriction) on magnetic resonance imaging did not exhibit CSF pleocytosis, and their CSF protein and glucose levels were within normal ranges.<sup>21,22</sup> The present study showed similar results to the previous studies.

The most important aspects of treating HPeV infections are early recognition and appropriate supportive care. Till date, there are no specific anti-viral drugs available for HPeV infections, and most treatments are in the form of supportive care. In the present study, 10 out of 11 patients with HPeV infection received intravenous immunoglobulin (IVIG) injections, which led to improvements in the symptoms of fever. IVIG may be administered based on its utility in treating severe EV infections and other inflammatory diseases. However, its utility in treating HPeV infections is yet to be validated.<sup>2,23,24)</sup>

This is the first study to report the clinical outcomes of HPeV infections in Korean infants under 3 months old. Unlike previous studies, our study is meaningful in that HPeV was detected on the first day of hospitalization, and their clinical manifestation and course compared with infantile EV infection and unknown infection during summer. Patients were recruited since the first case was diagnosed; data were acquired from medical records and were retrospectively analyzed. However, the present study has some limitations including a relatively small patient size and a short period of follow-up.

In conclusion, infants under 3 months old presenting with fever in summer should be assessed for the possibility of HPeV infection. Early and accurate detection is important for appropriate assessment of prognosis.

## REFERENCES

1. Olijve L, Jennings L, Walls T. Human parechovirus: an increasingly recognized cause of sepsis-like illness in young infants. *Clin Microbiol Rev* 2017;31:e00047-17.  
[PUBMED](#) | [CROSSREF](#)
2. Aizawa Y, Izumita R, Saitoh A. Human parechovirus type 3 infection: an emerging infection in neonates and young infants. *J Infect Chemother* 2017;23:419-26.  
[PUBMED](#) | [CROSSREF](#)
3. Khatami A, McMullan BJ, Webber M, Stewart P, Francis S, Timmers KJ, et al. Sepsis-like disease in infants due to human parechovirus type 3 during an outbreak in Australia. *Clin Infect Dis* 2015;60:228-36.  
[PUBMED](#) | [CROSSREF](#)
4. Cumming G, Khatami A, McMullan BJ, Musto J, Leung K, Nguyen O, et al. Parechovirus genotype 3 outbreak among infants, New South Wales, Australia, 2013–2014. *Emerg Infect Dis* 2015;21:1144-52.  
[PUBMED](#) | [CROSSREF](#)
5. Han TH, Chung JY, You SJ, Youn JL, Shim GH. Human parechovirus-3 infection in children, South Korea. *J Clin Virol* 2013;58:194-9.  
[PUBMED](#) | [CROSSREF](#)
6. Seo JH, Yeom JS, Youn HS, Han TH, Chung JY. Prevalence of human parechovirus and enterovirus in cerebrospinal fluid samples in children in Jinju, Korea. *Korean J Pediatr* 2015;58:102-7.  
[PUBMED](#) | [CROSSREF](#)
7. Fleming S, Thompson M, Stevens R, Heneghan C, Plüddemann A, Maconochie I, et al. Normal ranges of heart rate and respiratory rate in children from birth to 18 years of age: a systematic review of observational studies. *Lancet* 2011;377:1011-8.  
[PUBMED](#) | [CROSSREF](#)
8. Task Force on Blood Pressure Control in Children. Report of the second task force on blood pressure control in children--1987. *Pediatrics* 1987;79:1-25.  
[PUBMED](#)
9. Task Force on Prolonged Infantile Apnea. Prolonged infantile apnea: 1985. *Pediatrics* 1985;76:129-31.  
[PUBMED](#)
10. Byington CL, Kendrick J, Sheng X. Normative cerebrospinal fluid profiles in febrile infants. *J Pediatr* 2011;158:130-4.  
[PUBMED](#) | [CROSSREF](#)

11. Harvala H, Simmonds P. Human parechoviruses: biology, epidemiology and clinical significance. *J Clin Virol* 2009;45:1-9.  
[PUBMED](#) | [CROSSREF](#)
12. Britton PN, Jones CA, Macartney K, Cheng AC. Parechovirus: an important emerging infection in young infants. *Med J Aust* 2018;208:365-9.  
[PUBMED](#) | [CROSSREF](#)
13. Renaud C, Harrison CJ. Human parechovirus 3: the most common viral cause of meningoencephalitis in young infants. *Infect Dis Clin North Am* 2015;29:415-28.  
[PUBMED](#) | [CROSSREF](#)
14. Jeziorski E, Schuffenecker I, Bohrer S, Pain JB, Segondy M, Foulongne V. Relevance of human parechovirus detection in cerebrospinal fluid samples from young infants with sepsis-like illness. *J Clin Lab Anal* 2015;29:112-5.  
[PUBMED](#) | [CROSSREF](#)
15. Sharp J, Harrison CJ, Puckett K, Selvaraju SB, Penaranda S, Nix WA, et al. Characteristics of young infants in whom human parechovirus, enterovirus or neither were detected in cerebrospinal fluid during sepsis evaluations. *Pediatr Infect Dis J* 2013;32:213-6.  
[PUBMED](#) | [CROSSREF](#)
16. Ferreras Antolin L, Kadambari S, Braccio S, Tang JW, Xerry J, Allen DJ, et al. Increased detection of human parechovirus infection in infants in England during 2016: epidemiology and clinical characteristics. *Arch Dis Child* 2018;103:1061-6.  
[PUBMED](#) | [CROSSREF](#)
17. Loi C, Magnano M, Ravaioli GM, Neri I. An erythematous palmpoplantar rash due to human parechovirus. *Arch Dis Child* 2016;101:1070.  
[PUBMED](#) | [CROSSREF](#)
18. Shoji K, Komuro H, Miyata I, Miyairi I, Saitoh A. Dermatologic manifestations of human parechovirus type 3 infection in neonates and infants. *Pediatr Infect Dis J* 2013;32:233-6.  
[PUBMED](#) | [CROSSREF](#)
19. Schuffenecker I, Javouhey E, Gillet Y, Kugener B, Billaud G, Floret D, et al. Human parechovirus infections, Lyon, France, 2008–10: evidence for severe cases. *J Clin Virol* 2012;54:337-41.  
[PUBMED](#) | [CROSSREF](#)
20. Harvala H, Griffiths M, Solomon T, Simmonds P. Distinct systemic and central nervous system disease patterns in enterovirus and parechovirus infected children. *J Infect* 2014;69:69-74.  
[PUBMED](#) | [CROSSREF](#)
21. Verboon-Maciolek MA, Krediet TG, Gerards LJ, de Vries LS, Groenendaal F, van Loon AM. Severe neonatal parechovirus infection and similarity with enterovirus infection. *Pediatr Infect Dis J* 2008;27:241-5.  
[PUBMED](#) | [CROSSREF](#)
22. Britton PN, Dale RC, Nissen MD, Crawford N, Elliott E, Macartney K, et al. Parechovirus encephalitis and neurodevelopmental outcomes. *Pediatrics* 2016;137:e20152848.  
[PUBMED](#) | [CROSSREF](#)
23. Shakeel S, Westerhuis BM, Domanska A, Koning RI, Matadeen R, Koster AJ, et al. Multiple capsid-stabilizing interactions revealed in a high-resolution structure of an emerging picornavirus causing neonatal sepsis. *Nat Commun* 2016;7:11387.  
[PUBMED](#) | [CROSSREF](#)
24. Wildenbeest JG, Wolthers KC, Straver B, Pajkrt D. Successful IVIG treatment of human parechovirus-associated dilated cardiomyopathy in an infant. *Pediatrics* 2013;132:e243-7.  
[PUBMED](#) | [CROSSREF](#)



## 요약

**목적:** 이번 연구의 목적은 human parechovirus (HPeV)로 유발된 패혈증 의증을 보였던 3개월 미만의 영아를 대상으로 임상적 특징 및 경과를 조사하는 것이다.

**방법:** 2018년 7월 1일부터 8월 31일까지 패혈증 의증으로 입원한 3개월 미만 영아들의 의무기록을 확인하였다. 환자들은 뇌척수액을 이용하여 역전사 중합효소 연쇄반응 검사를 시행하고 결과에 따라 HPeV 감염군(1군, 11명), 장바이러스 감염군(2군, 13명), 바이러스가 검출되지 않은 군(3군, 15명)으로 구분하였다.

**결과:** 1군은 빈맥, 빈호흡, 무호흡, 저혈압, 피부 변화를 보이는 환자가 2, 3군 보다 많았다( $P < 0.05$ ). 또한 1군은 혈중 총 백혈구수가 다른 군에 비해 낮았다( $5,622 \pm 2,355/\mu\text{L}$ ,  $9,397 \pm 2,282/\mu\text{L}$  and  $12,312 \pm 7,452/\mu\text{L}$ ,  $P = 0.005$ ). 뇌척수액 백혈구 수도 1군은 2, 3군에 비하여 낮았다 ( $0.9 \pm 1.7/\mu\text{L}$ ,  $85.1 \pm 163.6/\mu\text{L}$ , and  $3.7 \pm 6.9/\mu\text{L}$ ,  $P = 0.06$ ). 치료에서도 1군은 2, 3군 보다 승압제 보조(36.6% vs. 0% and 6.6%), 기계 환기 적용(18.1% vs. 0% and 0%)과 고유량 산소 사용(45.4% vs. 15.3% and 6.6%)이 더 많았다. 모든 환자들은 합병증 없이 회복 되었다.

**결론:** HPeV 감염은 심각한 임상 경과를 보이고, 3개월 미만의 영아에서 패혈증 유사 증후군의 원인이 될 수 있다. 따라서, HPeV 감염 여부를 조기에 진단하고 적절한 치료를 시작하는 것이 필요하다.