Epidemiological and molecular characteristics of HPeV infection in children <6 months hospitalized with symptoms of sepsis-like illness, Northern Italy, 2015-2018

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Background

Human parechoviruses (HPeVs) are widespread pathogens belonging to the *Picornaviridae* family and currently divided into 19 genotypes. HPeV infections are usually asymptomatic or associated with mild respiratory or gastrointestinal disease in children[1]; however, some genotypes, in particular HPeV type 3 (HPeV3), are capable of causing severe disease including sepsis-like illness especially in very young children (aged less than 3 months).

Objectives

This study aimed to evaluate the prevalence and the risk of infection from HPeV and to describe the epidemiological and molecular characteristics of HPeV infections observed in children <6 months hospitalized with symptoms of sepsis-like illness.

Methods

From January 1st, 2015, to December 31st, 2018, clinical samples (cerebrospinal fluid samples and/or blood samples) were collected for diagnosis of HPeV infection from 193 patients (median age: 21 days, range: 1 day - 6 months) hospitalized with symptoms of sepsis-like illness in two hospitals of Northern Italy. After RNA extraction, the presence of HPeV-RNA was identified by real-time RT-PCR (target 5'UTR) and a portion of HPeV VP3/VP1 junction (nt. 2159–2458) was sequenced for typing and molecular characterization[3].

Results

1 - Prevalence of HPeVs in sepsis-like illness

During the study period, 14% (27/193) of patients <6 months hospitalized with symptoms of sepsis-like illness tested HPeV-positive (Table 1). The highest prevalence of HPeV infection was identified in children <1 month and in those aged 1-2 months being 16.5% (20/121) and 10.4% (5/48), respectively (Table 1). In children aged 2-3 months and in those >3 months HPeV prevalence was 7.1% (1/14) and 10.0% (1/10), respectively (Table 1). Overall, 20/27 (74.1%) HPeV positive cases were <1 month (Fig. 1) and almost all (96.3%; 26/27) were <3 months. 59.2% (16/27) of HPeV positive cases were males (p>0.05).

2 - Risk of infection from HPeVs by age-groups

The risk of infection from HPeV in sepsis-like illness in children <1 month was nearly 5-fold higher (OR=4.7; 95%CI: 1.9-11.5) than that observed in older patients.

No difference in the risk of infection from HPeV was identified when the gender of patients was compared (OR=1.2; 95%CI: 0.8-1.4).

3 - Temporal distribution of HPeVs

As showed in figure 2, HPeV-positive cases were detected throughout the study period, mainly (12/27; 44.4%) during the summertime (from June to August).

4 – Molecular characterization of HPeV

17 out of 27 (63%) HPeV positive samples were molecularly characterized; 16 resulted HPeV-3 and 1 HPeV-5.

Age group (month)	No. of patients	No. of HPeV-pos patients	% of HPeV-pos patients
0-1	121	20	16.5%
1-2	48	5	10.4%
2-3	14	1	7.1%
3-6	10	1	10.0%
Total	**193**	**27**	**14.0%**

Table 1. Prevalence of HPeV detection in children with sepsis-like illness by age

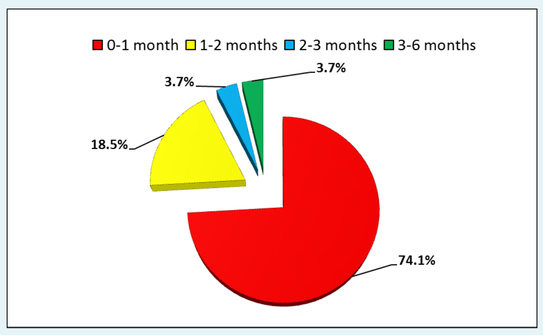

Figure 1. Distribution of HPeV-positive cases by age

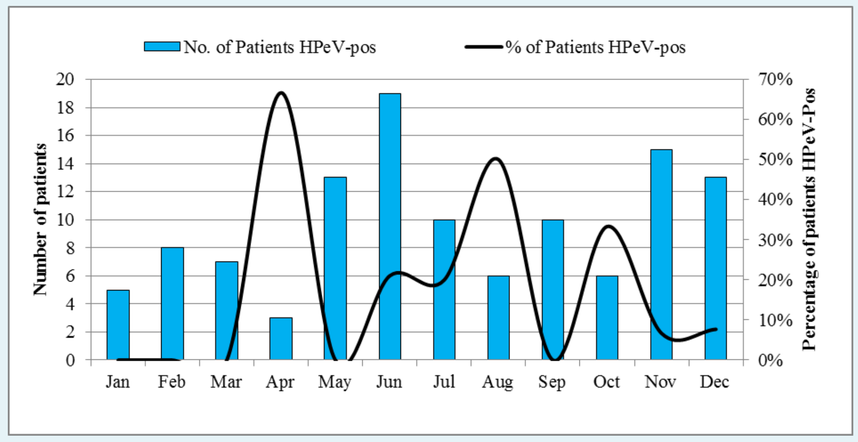

Figure 2. Temporal distribution of patients with sepsis-like illness and HPeV-positive cases

Discussion and Conclusions

This study confirmed the high prevalence of HPeV infection, particularly HPeV-3, in very young children hospitalized with symptoms of sepsis-like illness[2]. In our study, 14% of children <6 months tested HPeV-positive. Almost all were children <3 months; the risk of infection from HPeV in children <1 month was nearly 5-fold higher than that in older patients. As observed by others, HPeV was identified mainly during the summertime[2-3]. Including HPeV molecular detection in routine diagnostic tests would allow estimating the burden of HPeV infection and improving clinical management of pediatric patients. Further studies of molecular characterization and phylogenetic analyses of HPeV are needed to describe the evolution of these viruses and the association between the viral genotypes and the severity of disease or sequelae.

References

1) Watanabe, K. et al. Seropositivity and epidemiology of human parechovirus types 1, 3, and 6 in Japan. Epidemiol. Infect. 144, 3451–3460, doi: 10.1017/S0950268816001795 (2016).
2) Benschop, K. S. et al. Human parechovirus infections in Dutch children and the association between serotype and disease severity. Clin. Infect. Dis. 42, 204–210. doi: 10.1086/498905 (2006)
3) Harvala H et al. Epidemiology and clinical associations of human parechovirus respiratory infections. J Clin Microbiol. 46, 3446-3453, doi: 10.1128/JCM.01207-08 (2008).