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Comparison Of Human Metapneumo Virus Single Infection And Coinfection In Pediatric Patients In A Tertiary Hospital

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ÖZET

Amaç: Çocuklarda toplumdan kazanılmış akut sonulom yolu enfeksiyonuna neden olan Human Metapneumovirüs (HMPV) ilk kez 2001 yılında izole edilmiştir. Hafif üst solunum yolu enfeksiyonundan bronşolit ve pnömoniye kadar farklı spektrumda hastalık oluşturabilmektedir. İmmün sistemi baskılanmış hastalarda ciddi klinik tabloların oluşmasına ve bu hastaların hastaneye yatışına sebep olabilmektedir. Çalışmamızda tekli ve ko-enfeksiyon şeklinde tespit edilen HMPV bir yıllık sonuçları geriye yönelik tarandı ve enfeksiyonun epidemiyolojik özelliklerinin ortaya konması amaçlandı.

Yöntem: Çalışmaya Ocak 2018-Aralık 2018 tarihleri arasında, çocuk hastalıkları kliniklerinden moleküler laboratuvarına gönderilen 1506 nazofarengal sürüntü örneğine ait test sonuçları dahil edildi. Nükleik asit izolasyonu EZ-1 virüs kit v.2.0 (Qiagen, ABD) ile yapıldı. Multipleks real time PZR (Fast Track Diagnostics, Junglister Luxembourg) kullanılarak etken tespit edildi. Veri analizinde 22.0 IBM SPSS versiyonu kullanıldı. İstatistiksel önemlilik eşik düzeyi $p < 0.05$ alındı. Tek etken ve ko-enfeksiyon şeklinde iki grup oluşturuldu. İki grubun cinsiyet, yaş ve örnek gönderilen bölüm yönünden karşılaştırması ki-kara analizi ile yapıldı.

Bulgular: Örneklerin 52'sinde HMPV tek etken şeklinde tespit edilirken, 63'ünde ko-enfeksiyon şeklinde saptanmıştır. Tek etken HMPV saptanan hastaların 23'ü (%44.2) kız, 29'u (%55.8) erkektir. Yaş dağılımı olarak 17'si (%32.7) 1 yaş altında, 22'si (%42.3) 1-5 yaş arası, 13'ü (%25) 5 yaş üzerinde olup; hastaların 35'i (%67.3) poliklinik, 17'si (%32.7) servis hastasıydı. Ko-enfeksiyon saptanan hastaların 25'i (%39.7) kız, 38'i (%60,3) erkek; 26'sı (%41.3) 1 yaş altında, 27'si (%42.9) 1-5 yaş arası, 10'u (%15.9) 5 yaş üzerinde; 48'i (%76.2) poliklinik, 15'i (%23.8) servis hastasıydı. İki grubun cinsiyet ($p=0.6$), yaş ($p=0.4$) ve bölüm ($p=0.2$) yönünden karşılaştırmasında istatistiksel fark saptanmadı (Tablo 1).

Sonuç: HMPV çocukluk döneminde bronşolit etkenleri arasında RSV'den sonra en sık görülen etkenler arasında yer almaktadır. Çalışmamızda da etken ekim-nisan arası bronşolit sezonu olarak adlandırılan dönemde tespit edilmiştir. Ocak, şubat ve mart ayları vaka sayılarının en fazla olduğu aylar olmuştur. Tekli etken ve ko-enfeksiyon arasında epidemiyolojik özellikleri açısından istatistiksel fark saptanmamıştır.

Anahtar Kelimeler: Human Metapneumovirüs, multipleks PZR, çocuk, bronşolit

ABSTRACT

Aim: Human Metapneumovirus (HMPV) was first isolated in 2001. It may cause different spectrum of illnesses, ranging from mild upper respiratory tract infection to bronchiolitis and pneumonia. . It sometimes induces severe manifestations in infants and immunosuppressed persons . The aim of this study was to investigate the prevalence of HMPV in children with acute respiratory infection and to determine the epidemiological characteristics of HMPV infection, which was detected as single and co-infection.

Metod: In this study, the results of nasopharyngeal swab specimens aged between 0-18 years patients admitted to the Molecular Unit of the Medical Microbiology Laboratory of Meram

Medical Faculty Hospital of Necmettin Erbakan University between January 2018 and December 2018 were analyzed retrospectively. EZ1 Virus Mini Kit V 2.0 (QIAGEN, Germany) was used for nucleic acid extraction Multiplex real-time [FTD 21, Junglinster, Luxemburg] polymerase chain reaction were used during the study period.

Findings: HMPV (9.1%) was detected in 115 patients (52 single and 63 co-infections). The majority of the cases were outpatients; 67.3% in single infection group and 76.2% in coinfection group. Infection was more common in male patients; 55.8% in single infection group and 60.3% in coinfection group. Cases 1 to 5 years of age were the majority in both groups: 42.3% for single infection and 42.9% for coinfection. There was no significant difference between the two groups in terms of age, gender and department. Cases most often recorded in February and March . The most common coinfection was detected by RSV.

Conclusion: HMPV is one of the most common causes of bronchiolitis in childhood that RSV is not detected cases. In this study HMPV was detected in the period called as broncholite season between October and April. No statistically significant difference was found between the single infection and co-infection group in terms of epidemiological characteristics.

KeyWords: *Human Metapneumovirüs, multiplex PCR, child, broncholite*

Introduction

Acute respiratory infections are among the most important causes of morbidity and mortality in children, especially in developing countries. Viruses are the etiologic agent pathogen in approximately 80 % of acute respiratory infections (1). Identifying the prevalence of the viruses that causing acute respiratory infection is essential to avoid antibiotics overuse (2)

In recent years, studies on respiratory viruses have gained importance and new viral agents such as HMPV (Human Metapneumovirus) have started to be identified, apart from the classical agents such as influenza and respiratory syncytial virus (RSV). HMPV was first identified in 2001. It is a member of the *Metapneumovirus* genus within the *Pneumo-viridae* subfamily of *Paramyxoviridae* family. It may cause different spectrum of illnesses, ranging from mild upper respiratory tract infection to bronchiolitis and pneumonia. It sometimes induces severe manifestations in infants and immunosuppressed persons (3).

However, the available information regarding its epidemiology is limited due to a deficient suspicion and its clinical manifestations resemble with other respiratory viruses such as the influenza virus and the respiratory syncytial virus (2). The aim of this study was to investigate the prevalence of HMPV in children with acute respiratory infection and to determine the epidemiological characteristics of HMPV infection, which was detected as single and co-infection.

Patients and Methods

In this study, the results of 1506 nasopharyngeal swab specimens of patients admitted to the Molecular Unit of the Medical Microbiology Laboratory of Meram Medical Faculty Hospital of Necmettin Erbakan University between January 2018 and December 2018 were analyzed retrospectively. 249 results of adult patients were excluded from the study. Results of 1257 patients aged between 0-18 years were investigated. The children were either seen at outpatient departments or admitted to pediatric wards of the same hospital. EZ1 Virus Mini Kit V 2.0 (QIAGEN, Germany) was used for nucleic acid extraction .Multiplex real-time [FTD 21, Junglinster, Luxemburg] polymerase chain reaction were used during the study period.

22.0 IBM SPSS version was used for data analysis. Statistical significance threshold was taken as $p < 0.05$. Two groups were formed as single agent and co-infection. The comparison of the two groups in terms of gender, age and sample section was performed by Chi-square analysis.

Results

HMPV (9.1%) was detected in 115 patients (52 single and 63 co-infections). The majority of the cases were outpatients; 67.3% in single infection group and 76.2% in coinfection group. Infection was more common in male patients; 55.8% in single infection group and 60.3% in coinfection group. Cases 1 to 5 years of age were the majority in both groups: 42.3% for single infection and 42.9% for coinfection. There was no significant difference between the two groups in terms of age, gender and department (Table 1). Cases most often recorded in February and March (Figure 1). The most common coinfection was detected by RSV (Figure 2).

Table 1: Distribution of demographic data in single infection and co-infection

	HMPV single infection (n=52)	HMPV coinfection (n=63)	P
Sex			0.6
female	23(%44.2)	25 (%39.7)	
male	29(%55.8)	38(%60.3)	
Age			0.4
<1 age	17(%32.7)	26(%41.3)	
1-5 age	22(%42.3)	27(%42.9)	
>5 age	13(%25)	10(%15.9)	
department			0.2
outpatient	35(%67.3)	48(%76.2)	
inpatient	17(%32.7)	15(%23.8)	

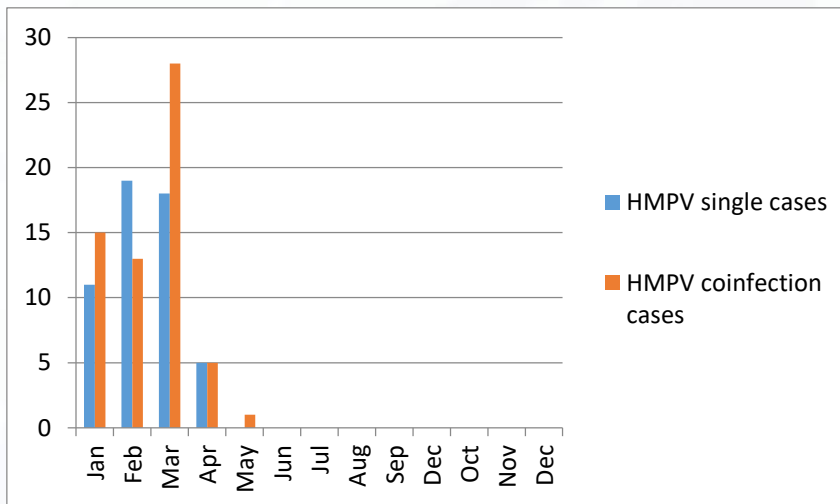


Figure 1: Monthly distribution of cases

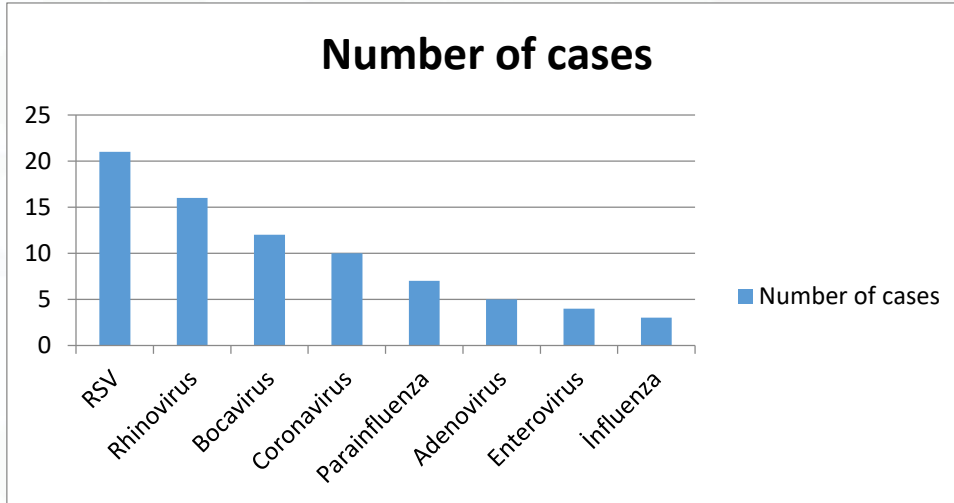


Figure 2: Distribution of viral agents in coinfection cases

Discussion

HMPV is one of the viral agent that should be considered when RSV is not detected in children younger than 2 years with acute bronchiolitis. There are studies reporting that the prevalence of agents varies between 6% and 16% in the world. In our country, rates ranging from 10.8% to 13% have been reported (4). One year data were evaluated in this study and the rate was 9.1%.

It has been described in Western countries that the prevalence of HMPV increases during the late winter months and the beginning of the spring. However, cities such as Hong Kong reported the virus during late spring and summer months (5). In countries with a moderate climate HMPV has a seasonal occurrence overlapping with RSV circulation (6). Similarly in this study, the majority of cases were detected during the RSV season.

Recently, HMPV co-infections with other respiratory viruses such as RSV, parainfluenza, influenza virus and adenovirus have been reported. Differences in clinical signs between individuals co and mono-infected with HMPV have been reported, but the relation is obscure (7). Several studies have found a coinfection rate of < 10%. However, Greesill et al. reported that 70% of RSV –infected children who required intensive care were coinfecting with HMPV (8). In present study coinfection rate has been detected 5% (63 cases).

It was reported that majority of dual infections occur with RSV and dual infection (HMPV-RSV) increased clinical severity (9). Semple et al reported that dual infection with HMPV and RSV confers a 10-fold increase in relative risk of admission to a pediatric intensive-care unit for mechanical ventilation (10). In another study, compared clinical features of HMPV single infection and HMPV coinfection, only the duration of the hospitalization was different, being longer in the coinfections group. In this study Rhinovirus and Adenovirus were most commonly detected in coinfections (11). In this study, RSV was the most common in coinfections. However, since the outpatient patients were also included in our patient group, the clinical course could not be monitored.

Seroprevalence studies show that HMPV infection is more common especially in children aged 6 months to 2 years. It has been suggested that HMPV infection affects particularly older children compared to RSV infections (6). Garcı́a-Garcı́a et al reported that the mean age of HMPV single infection as 14.37 months and in the co-infection group as 12.9 months; no difference was found between the two groups in terms of mean age (11). In our study, children between the ages of 1 and 5 were the majority of cases in both single infection and co-infection groups. In this study also no significant difference was found between the two groups in terms of age.

It has been suggested that HMPV infections affect male more (12). In present study, 55.8% in the single infection group and 60.3% in the co-infection group were male patients. In a study held in Croatia showed not only HMPV infections affected more often male than female, but also males were generally more often hospitalized due to acute respiratory infections (6).

Incidence of hMPV infection can substantially vary from year to year. In a study a high incidence of hMPV infection (25.3%) was observed during the 2005–2006 winter-spring season, whereas a much lower rate of infection (4.7%) during the following season was found (13). Another study indicates that HMPV infections show biennial outbreak pattern characterized by alternation of winter and spring (6). In this study virus was monitored throughout the year. However, in order to establish the prevalence correctly, the virus should be monitored in successive years.

Consistent with previous epidemiological data, HMPV was detected during winter and early spring, which was described as RSV season, and it was found that males were more affected than females. In comparison to other studies, a relatively lower rate was found. Its clinical manifestations, seasonal characteristics and affected age group resemble RSV. Nowadays, in cases that RSV is not detected, HMPV should be considered as a viral factor.

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