Ankara Eğt. Arş. Hast. Derg., 2020 ; 53(2) : 113-119

Özgün Çalışma / Original Article **DOI: 10.20492/aeahtd.597416**

PREDICTORS OF HOSPITALIZATION IN CHILDREN WITH INFECTIOUS MONONUCLEOSIS

ENFEKSİYÖZ MONONÜKLEOZLU ÇOCUKLARDA HASTANEYE YATIRMA BELİRTEÇLERİ

Yaşar TOPAL[1], Hatice TOPAL[1], Betül BATTALOĞLU İNANÇ[2]

ABSTRACT

AIM: Infectious mononucleosis (IM), characterized by fever, lymphadenopathy and pharyngitis, is a common infectious disease caused by Epstein-Barr virus (EBV). In this study, we performed a retrospective analysis of the clinical findings, laboratory data and management of children with IM due to EBV to find out the predictors of hospitalizations.

MATERIAL AND METHODS: We retrospectively reviewed the medical records of patients under the age of 18 years who were diagnosed with IM between October 31, 2017 and October 31, 2018 at Muğla Sıtkı Koçman University Medical Faculty Hospital. The study population was categorized into three groups according to the age; the 0-4 years, 5-10 years, and above 10 years. Complaints, physical examination findings, laboratory data, complications and treatment strategies of the patients were compared in these groups. Factors associated with hospitalizations and predictors of hospitalization were also investigated.

RESULTS: This study included 158 patients. The mean age of the patients was 88.9 ± 53.5 months and 93 (58.9%) were male. The most common complaint was fever (57.6%), and the most common physical examination finding was hepatomegaly (73.4%). Except for fever, rash, thrombocytopenia and AST elevation, no significant difference was found between the age groups and the clinical and laboratory findings. Antibiotic therapy was applied to 44% of the patients and 34.8% were hospitalized.
Patients who needed hospitalization were more symptomatic, had more physical examination findings and had higher acute phase reactants. Presence of fever, palatal petechiae, or exudative tonsillitis and higher levels of C-reactive protein at presentation were found to be significant predictors of hospitalization

CONCLUSIONS: More than one third of the children with IM required hospitalization. Presence of fever, palatal petechiae, or exudative tonsillitis and higher levels of C-reactive protein at presentation were associated with higher rates of hospitalizations.

Key words: *Infectious mononucleosis, children, clinical features*

ÖZET

GİRİŞ: Ateş, lenfadenopati ve farenjit ile karakterize olan enfeksiyöz mononükleoz (IM), Epstein-Barr virüsünün (EBV) neden olduğu yaygın bir bulaşıcı hastalıktır. Bu çalışmada, EBV nedenli IM'li çocukların hastaneye yatış belirteçlerini belirlemek için klinik bulgular, laboratuvar veriler ve yönetimler geriye dönük olarak incelendi.

GEREÇ VE YÖNTEMLER: Muğla Sıtkı Koçman Üniversitesi Tıp Fakültesi Hastanesi'nde 31 Ekim 2017 - 31 Ekim 2018 tarihleri arasında, İM tanısı alan 18 yaş altındaki hastaların tıbbi kayıtları geriye dönük olarak incelendi. Çalışma popülasyonu, 0-4 yaş, 5-10 yaş ve 10 yaş üstü olmak üzere 3 gruba ayrıldı. Hastaların şikayet, fizik muayene bulguları, laboratuvar verileri, komplikasyonları ve tedavi stratejileri bu gruplarda karşılaştırıldı. Hastaneye yatışla ilişkili faktörler ve hastaneye yatışın belirteçleri de incelenmiştir.

BULGULAR: Çalışmaya 158 hasta dahil edildi. Hastaların yaş ortalaması 88,9 ± 53,5 ay ve 93'ü (% 58,9) erkek idi. En sık görülen şikayet ateş (% 57,6), en sık görülen fizik muayene bulgusu hepatomegali (% 73,4) idi. Ateş, döküntü, trombositopeni ve AST artışının dışında, klinik ve laboratuvar bulguları ile yaş grupları arasında anlamlı bir fark bulunmadı. Hastaların % 44'üne antibiyotik tedavisi uygulandı ve hastaların % 34,8'i hastanede yatarak tedavi gördü.
Hastaneye yatırılan hastaların daha fazla semptom ve fizik muayene bulgularına, daha yüksek akut faz reaktanlarına sahip oldukları saptandı. Hastaneye yatış için önemli olduğu saptanan değişkenler ateş, damakta peteşi veya eksudatif tonsillit varlığı ve başvuruda yüksek C-reaktif protein seviyeleri idi.

SONUÇLAR: Enfeksiyöz mononükleozlu çocukların üçte birinden fazlası hastanede yattırılarak tedavi gördü. Ateş, palatal peteşi veya eksüdatif tonsillit varlığı ve başvuru sırasında yüksek C-reaktif protein düzeyleri daha yüksek hastaneye yatış oranları ile ilişkilendirildi.

Anahtar kelimeler: *Enfeksiyöz mononükleoz, çocuklar, klinik özellikler*

[1] Muğla Sıtkı Koçman University Faculty of Medicine, Department of Pediatrics, Muğla, Turkey
[2] Muğla Sıtkı Koçman University Faculty of Medicine, Department of Family Medicine, Muğla, Turkey

Geliş Tarihi / Submitted : Temmuz 2019 / July 2019 Kabul Tarihi / Accepted : Şubat 2020 / February 2020

Sorumlu Yazar / Corresponding Author:
Yaşar TOPAL
Muğla Sıtkı Koçman University Faculty of Medicine, Department of Pediatrics, Muğla, Turkey
Orhaniye mah, Haluk Özsoy street.48000/Muğla
Gsm: +90 533 245 37 47 **E-mail:** yasardr68@yahoo.com

Yazar Bilgileri /Author Information:
Yaşar TOPAL (ORCID: 0000-0002-7059-4823),
Hatice TOPAL (ORCID: 0000-0003-3226-0205)
Gsm: +90 533 245 3745 E-mail: haticetopaldr@gmail.com,
Betül BATTALOĞLU İNANÇ (ORCID: 0000-0001-7478-5451) Gsm: +90 505 268 55 39
E-mail: betulbattaloglu00@gmail.com

The study was approved by the local Clinical Research Ethics Committee (03.08.2017, 14/II).

INTRODUCTION

Epstein-Barr virüs (EBV) infection occurs by transmission of viruses from asymptomatic carriers to susceptible persons (1). It is primarily transmitted by oral secretions but also rarely by sexual intercourse. EBV is the most common cause of infectious mononucleosis (IM), which is characterized by fever, lymphadenopathy, and pharyngitis; in adults, however, it may remain dormant without causing any symptoms (2,3).Although EBV infections usually have a subclinical course in children and infants, there may exist signs and symptoms of otitis media, acute gastroenteritis, headache, fatigue, exanthems, signs of upper respiratory tract infection, hepatomegaly, and splenomegaly in addition to the classical signs and symptoms of IM in symptomatic cases. However, IM rarely cause life-threatening complications such as airway obstruction secondary to lymphoid hyperplasia and hypertrophy of the upper respiratory tract, meningoencephalitis, hemolytic anemia, thrombocytopenia, and splenic rupture (3-6).

Similar signs and symptoms and laboratory findings of IM may also be observed with agents like cytomegalovirus, adenovirus, rubella, human immunodeficiency virus, and toxoplasma. Therefore, serological tests are important for differential diagnosis (7). Specific serological tests for EBV are useful for diagnosis, especially for cases with a negative heterophile antibody test(2,7,8).

EBV has been detected in all populations and all areas of the world but with different geographical distribution. It has been reported that 80-86% of the adults in Turkey are EBV seropositive (8). In previous studies have revealed that the frequency of infection does not vary with seasons; but it has been reported to be more frequent in spring and autumn months in studies performed in college students low income and crowded family conditions have been found to increase the likelihood of EBV seropositivity in children from other geographical locales in Turkey (9).

Although there are some published case series from western countries and smaller case series from our country, there are an information gap about the demographic features, clinical and laboratory findings and outcomes in childhood IM in Turkey (8,9). Moreover, prevalence and risk factors for hospitalization has not been investigated in IM patients in our country. Therefore, we aimed to analyze clinical signs and symptoms, laboratory findings, and complications of EBV cases diagnosed with IM and we also aimed to identify factors predicting increased severity during IM, which was assessed by the hospitalization rates.

MATERIAL AND METHODS

The study population consisted of patients younger than 18 years who had been diagnosed with IM and whose EBV diagnosis was serologically confirmed at Mugla Sıtkı Koçman University Training and Research Hospital between 31 October 2017 and 31 October 2018. The study was approved by the local Clinical Research Ethics Committee (03.08.2017, 14/II).

Patients who were immunosuppressed or who take immunosuppressive medications were excluded.

Admission complaints, physical examination findings, laboratory data (complete blood count, serum transaminase levels, EBV serology), treatment modalities were recorded. Anemia was defined by a hemoglobin count lower than age-based normal level by two standard deviation; leucopenia by a white blood cell count lower than age-based normal level by two standard deviation; and thrombocytopenia by a thrombocyte count lower than 150000/mm3 (10,11).

Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels above 50 U/L were defined as transaminase elevation; and a C-reactive protein (CRP) level above 0.8 mg/dL defined as CRP positivity. The study population was categorized into three groups according to the age as the 0-4 years, 5-10 years, and above 10 years groups. The age groups were compared for the clinical presentation, laboratory findings, and treatment approach of IM. Hospitalized and non- hospitalized patients' demographic, clinical and laboratory findings were also compared.

Statistical Analysis

Statistical Package for Social Sciences (SPSS) for Windows-version 20.0 (SPSS, Chicago, IL, USA) software was used for statistical analyses. Kruskal-Wallis and Chi-square tests were used for statistical comparisons. The chi-square test was used in order to determine the associations between the studied variables and the occurrence of hospital admissions, whereas the Mann-Whitney test was used for the comparison between the groups of hospitalized patients and nonhospitalized patients. Univariate analysis with logistic regression was performed in order to determine the predictors of hospital admission A p value of less than 0.05 was considered statistically significant.

RESULTS

This study included 158 patients aged 8-216 months. The mean age was 88.9 ± 53.5 months and 93 (58.9%) patients were male. The highest number of cases was observed in Spring (27.8%), and the lowest number of cases occurred in Fall (21.5%) (Figure 1). The month-based analysis revealed that patient presentations most commonly occurred in March and November and least commonly in September and October.

Comparison of patient characteristics according to age groups.

The most common complaints in all age groups were fever (91 cases) followed by myalgia, neck swelling, sore throat, snoring, fatigue, nausea, headache, eyelid and periorbital swelling, abdominal pain, anorexia, redness, joint pain, and other complaints.

The prevalence of symptoms like myalgia, neck swelling, sore throat, snoring, fatigue, nausea, headache, eyelid and periorbital swelling, and abdominal pain were not significantly different across the study groups. The prevalence of fever showed a proportional increase with age, and significantly difference between the age groups in this context **(Table 1).** Loss of appetite and rash were significantly more common in the 0-4 years age group than the other age groups (p=0.04).

While the most common physical examination finding was hepatomegaly (73.4%), it was followed by respectively, lymphadenopathy (50%), exudative tonsillitis (40.5%), obstructive apnea (15.8%), periorbital edema (15.2%), maculopapular rash (13.9%), splenomegaly (12%), palatal petechiae (5.1%), and petechial and purpuric rash followed (1.3%) **(Table 1).**

Maculopapular rash was significantly more common in the 0-4 years age group than the others age groups, where as other clinical signs were not significantly different in the whole age groups Anemia was present in 17%, thrombocytopenia in 8.9%; and leukopenia in 4.4% of the patients **(Table 2).** There were no statistically significant differences in the prevalence of anemia, and leukopenia between 3 age groups but the thrombocyte count was significantly lower in the older age group. Only one of the patients with thrombocytopenia had a thrombocyte count below 50000/mm3. Relative lymphocytosis was observed in 76.6% of cases peripheral smear. Atypical cells were observed on peripheral smear in 39 (24.7%) cases.

Elevated AST levels was observed in 53.2% of the patients and elevated ALT levels was observed in 37.3% of the patients **(Table 2)**. While there was no significant difference between the age groups with respect to AST elevation; ALT elevation was significantly less common in the 0-4-year age group and significantly most common in the 5-10 years age group (p=0.016). Elevated CRP levels was observed in 55% of the patients. There was no significant difference between the age groups with respect to CRP levels.

Table 1. Symptoms and physical examination findings among age groups

	0-4 years (n=42)	5-10 years (n=77)	> 10 years (n=39)	P
Symptoms				
Fever	21 (50.0)	44 (57.1)	26 (66.7)	**0.02**
Sore throat	15 (35.7)	35 (45.5)	20 (51.3)	0.35
Headache	7 (16.7)	17 (22.0)	8 (21.0)	0.78
Ocular complaint	10 (23.8)	12 (28.6)	7 (17.9)	0.54
Snoring	15 (35.7)	29 (37.7)	13 (33.3)	0.89
Obstructive apnea	4 (9.5)	15 (19.5)	6 (15.4)	0.36
Fatigue	9 (21.4)	24 (31.2)	7 (17.9)	0.24
Myalgia	22 (52.4)	42 (54.5)	22 (56.4)	0.93
Loss of appetite	11 (26.2)	7 (9.0)	5 (12.8)	**0.04**
Nausea	9 (21.4)	24 (31.2)	7 (17.9)	0.24
Neck swelling	22 (52.4)	42 (54.5)	22 (56.4)	0.93
Abdominal pain	3 (7.1)	16 (21.0)	7 (17.9)	0.15
Joint pain	4 (9.5)	5 (6.5)	3 (7.7)	0.83
Physical examination				
Maculopapular rash	11 (26.2)	7 (9.0)	4 (10.3)	**0.03**
Palatal petechiae	3 (7.1)	2 (2.6)	3 (7.7)	0.38
Lymphadenomegaly	22 (52.4)	40 (51.9)	17 (43.6)	0.65
Petechiae, purpura	1 (2.4)	0 (0.0)	1 (2.6)	0.38
Exudative tonsillitis	15 (35.7)	33 (42.9)	16 (41.0)	0.85
Splenomegaly	6 (14.3)	10 (13.0)	3 (7.7)	0.61
Hepatomegaly	28 (66.7)	61 (79.2)	27 (69.2)	0.24
Periorbital edema	3 (7.1)	16 (21.0)	5 (12.8)	0.13

Table 2. Distribution of laboratory data by age groups

	0-4 years (n=42)	5-10 years (n=77)	> 10 years (n=39)	p
Anemia	10 (23.8)	14 (22.0)	3 (7.7)	0.14
Leucopenia*	0 (0.0)	4 (5.2)	3 (7.7)	0.21
Thrombocytopenia	0 (0.0)	7 (9.0)	7 (17.9)	**0.018**
C-reactive protein elevation	21 (50.0)	45 (58.4)	21 (53.8)	0.66
Elevated alanine aminotransferase	20 (47.6)	42 (54.5)	22 (56.4)	0.69
Elevated aspartate aminotransferase	8 (19.0)	33 (42.9)	18 (46.2)	**0.016**

* : Leucopenia by a white blood cell count lower than age-based normal level by two standard deviation

Table 3. Treatment modalities in different age groups

	0-4 years (n=42)	5-10 years (n=77)	> 10 years (n=39)	p
Hospitalization	12 (28.6)	25 (32.5)	18 (46.2)	0.21
Antibiotic use	18 (42.9)	33 (42.9)	19 (48.7)	0.81
Need for oxygen	6 (14.3)	8 (10.4)	7 (17.9)	0.51
Steroid therapy	7 (16.7)	8 (10.4)	5 (12.8)	0.61

Table 4. Characteristics of participants by hospitalization status

	Hospitalized (n=55)	Non- Hospitalized (n=103)	P
Age (months) (mean ±SD)	98.3 ± 60.7	89.8 ± 48.8	0.26
Male [n(%)]	30 (54.5)	62 (60.2)	0.41
Symptoms [n(%)]			
Fever	45 (81.8)	46 (44.7)	**<0.001**
Sore throat	32 (58.2)	38 (36.9)	**0.010**
Headache	13 (23.6)	19 (18.4)	0.439
Ocular complaint	13 (23.6)	16 (15.5)	0.210
Snoring	25 (45.5)	32 (31.1)	0.073
Obstructive apnea	15 (19.5)	6 (15.4)	0.360
Fatigue	29 (52.7)	34 (33.0)	**0.016**
Myalgia	30 (54.5)	35 (34)	**0.012**
Loss of appetite	49 (89.1)	68 (66)	**0.002**
Nausea	20 (36.4)	20 (19.4)	**0.020**
Neck swelling	21 (38.2)	65 (63.1)	**0.003**
Skin rash	9 (16.4)	14 (13.6)	0.638
Abdominal pain	14 (25.5)	12 (11.7)	**0.026**
Joint pain	7 (12.7)	5 (4.9)	0.112
Physical examination findings [n(%)]			
Maculopapular rash	10 (18.2)	12 (11.7)	**0.040**
Palatal petechia	6 (10.9)	2 (1.9)	**<0.001**
Lymphadenomegaly	31 (56.4)	48 (46.6)	0.098
Petechiae, purpura	2 (4.0)	0 (0.0)	0.086
Exudative tonsillitis	35 (63.6)	29 (28.2)	**<0.001**
Splenomegaly	7 (12.7)	12 (11.7)	0.42
Hepatomegaly	38 (69.1)	78 (75.7)	0.56
Periorbital edema	8 (14.5)	16 (15.5)	0.38
Laboratory findings (mean ±SD)			
White blood count (x10^3/mm^3)	13.7 ± 12.7	10.8 ± 4.4	0.08
Platelets (×10^3/mm^3)	255.6 ± 110.7	284.6 ± 98.4	0.09
C-reactive protein (mg/dL)	33.8 ± 40.2	11.3 ± 21.2	**< 0.001**
Alanin aminotransferase (U/l)	114.0 ± 253.0	59.0 ± 91.5	0.36
Aspartat aminotransferase (U/l)	101.0 ± 121.0	98.0 ± 87.0	0.44
Hemoglobin (mg/dl)	13.5 ± 2.1	12.6 ± 3.2	0.41

Table 5. Predictors of hospitalization all study group

	OR		
		95% Cl	p
Fever	1.231	0.765-1.354	**0.040**
Palatal petechiae	1.054	0.361-3.286	**0.001**
Exudative tonsillitis	3.232	1.326-7.474	**0.004**
C-reactive protein (mg/dL)	1.049	0.952-1.158	**0.008**

Comparison of treatment strategies
Fifty-five (34.8%) of the study population were hospitalized and seventy (44.3%) patients were using antibiotics at the time of admission **(Table 3).** The majority of the hospitalized patients (72.2%) received symptomatic treatment while those with obstructive respiratory difficulty were received prednisolone and oxygen support and those considered to have a secondary bacterial infection received antibiotic therapy. There were no significant differences in hospitalization, antibiotic use, oxygen or steroid therapy rates according to age groups.

Predictors of hospitalization
A total of 55 patients (34.8%) were hospitalized. Comparison of the patients' characteristics hospitalized for IM with those who were not was presented in **Table 4.** There was no statistically significant difference between the two groups with respect to age and gender. However, patients who needed hospitalization were more symptomatic, had more physical examination findings and had higher acute phase reactants as expected. For variables were found to be significant predictors of hospitalization according to the multivariate analysis: presence of fever, palatal petechiae, or exudative tonsillitis and higher levels of C-reactive protein at presentation **(Table 5).**

DISCUSSION

The current study investigated and compared the clinical characteristics of IM patients in different age groups. This study also identified risk factors for hospitalizations in these children. In this single-center, retrospective and observational study of 158 patients, nearly one third of the children with IM required hospitalization and multivariable analysis revealed four variables were independent predictors for hospitalization. To the best of our knowledge, this is the first study to evaluate the predictors of need for hospitalization in IM patients in our country. Hocqueloux et al.'s (12) study were shown that, 54.1% of the pediatric patients were male, most common symptoms were sore throat, ear pain, and fatigue and, most common findings were fever, cervical lymphadenopathy and pharyngitis, respectively. In the same study, C-reactive protein levels were higher than in adults.

EBV infection shows an asymptomatic course in infants and children whereas the rate of symptoms progressively increases after the adolescence (7). Although EBV may cause highly variable clinical signs and symptoms ranging from abdominal pain to upper respiratory tract infection, the most well-known clinical entity is IM which is characterized by fever, pharyngitis, and lymphadenitis (13).

Most children from the developing countries and from the lower socioeconomic classes of the developed countries contract EBV infection by the age of 4 years. In developed countries the infection more commonly occurs in the adolescence and afterwards (13,14). Jiao et al (15), in a study of 102 EBV cases, reported that 78% of cases were under the age of 7 years and 12% in the 7-14 years age group. Similarly, Kanegane H et al (16) reported a peak incidence occurring at the age of around 4 years. In a study conducted in our country reported that 56.8% of cases were under the age of 5 years (17). Our patients had a mean age of 7.3 years (88 months), with near half of patients being in the 5-10 years age group. This finding suggests that EBV cases in our province occurred in age groups similar to those reported in developed countries. The male -to- female ratio was 1.4, which is supported the existing knowledge of the absence of sex predilection for EBV infection (18).

Seasonal variability is observed in disease occurrence. More than half (54.4%) of our cases occurred in the Spring and Summer although, as indicated in the literature, there was no significant seasonal variation (17,19-21).

Although the classical triad of EBV infection consists of fever, tonsillitis, and lymphadenopathy, sign and symptoms show variability in younger children (2, 22, 23). A Danish study reported that the most common signs and symptoms were fever, cervical lymphadenopathy, tonsillitis, and fatigue; another study reported lymphadenopathy, fever, pharyngitis, and hepatomegaly as the most common signs, respectively (24, 25). There are also studies reporting higher prevalence of generalized body pain and pharyngitis but much lower prevalence of fever and/or lymphadenopathy (4, 22). Previous reports have indicated greater prevalence of complaints related to upper respiratory tract infection as well as vomiting, diarrhea, maculopapular rash, and loss of appetite in younger age groups and nonspecific symptoms in older age groups (24, 25). While our study noted that complaints like loss of appetite and rash, which are nonspecific for EBV infection, were more common in the younger age group, complaints like fever and sore throat, which are suggestive of EBV infection, had a

higher frequency in the older age group. Insufficient ability to express complaints among younger patients may have had a role in this finding. Fever was observed in more than half of the patients, and more commonly in older children. Myalgia, neck swelling, sore throat, snoring, and cervical lymphadenopathy were the other common signs and symptoms.

Hepatomegaly was revealed in nearly 2/3 of our patients while splenomegaly existed in 12% of them. Previous reports have indicated the presence of splenomegaly and hepatomegaly in about half of patients while literature data suggest a prevalence of 42-70% for splenomegaly and hepatomegaly in EBV patients (22, 23, 26). In a study conducted in our country was reported splenomegaly in 35.5% of patients and hepatomegaly in 11.1%; and hepatomegaly prevalence was more than twice in that study (27). As our hospital serves as a tertiary healthcare facility, we concluded that the referral of patients requiring advanced tests and treatments may explain such a high rate.

In our study anemia prevalence was 17%, which was lower than what was reported for pediatric age group in Turkey (17,28). Literature data indicate a thrombocytopenia prevalence of 7.3%-47%, which existed in 8.9% of our cases (24,29,30).

In a study where 156 cases with heterophil antibody positivity were studied, 2/3 of cases were found to have lymphocytosis (31). Another study analyzing leucocyte counts by age groups revealed that total leucocyte count was significantly greater in the 0-4 years age group compared to the 5-16 years age group; although atypical lymphocyte percentage was higher in the older age group, peripheral lymphocyte ratios were similar (32,33). Similar to the prior reports in the literature, relative lymphocytosis was found in more than 3/4 of our cases.

It has been reported that mildly impaired liver function tests are seen in more than 80% of cases with EBV (34,35). Wang et al (36) reported that 80% of children under the age of 16 years had elevated transaminase levels, with ALT elevation being more prominent; they also reported that this occurred more commonly in the preschool children than the adolescents. Elevated transaminase levels were observed in more than half of our cases, with a marked increase occurring especially in ALT with aging. In our study transaminase elevation was most common in the 5-10 years age group.

C reactive protein elevation is a common occurrence in patients with infectious mononucleosis. Medoviç et al (29) reported CRP elevation in 53.7% of cases with a mean CRP of 26.6 mg/L; Cengiz et al (17) reported a mean CRP of 25 mg/L. Our study revealed an elevated CRP level in 55.3% of cases.

A multicenter study demonstrated that steroids or antiviral agents exerted no effect on symptom duration or early return to school (37). However, steroid therapy was shown to provide partial relief by reducing lymphoid and mucosal edema (38). Upper respiratory tract infection was reported in less than 4% of otherwise-healthy children with EBV (39). In our study, more than twice of that percentage was admitted to hospital due to upper respiratory tract obstruction, which also formed almost half (45.5%) of the study population.

Hospitalized patients were more symptomatic and physical examination findings were higher. Especially, it was observed that palatal petechiae, or exudative tonsillitis and high levels of CRP were prominent significant in patients who were admitted in hospital. In a similar study (24), the most common symptoms and signs were fever, cervical lymphadenopathy, tonsillitis and fatigue; the most important laboratory findings were relative lymphocytosis and high levels of transaminase levels were determined. Son et al. (19) were found fever, sore throat, generalized lymphadenopathy in children who were admitted in the hospital, especially transaminase and CRP levels were more prominent in children under 3 years of age.

The rate of antibiotic use has been variably reported in the literatüre (29). Thomson et al (40) reported that 45% of IM patients who had no beta hemolytic streptococci were prescribed antibiotics during disease course. As nearly one half of our study population used antibiotics and as the CRP levels of patients taking antibiotics were significantly higher than those of non-users, CRP elevation was considered an important factor for prescription of antibiotics by physicians. Antibiotic therapy might have been initiated since EBV infection was not known during hospitalization. In addition, excessive clinical findings such as exudative tonsillitis and palatal petechia may be the reason for high antibiotic initiation before hospitalization.

In conclusion, IM caused by EBV is a benign disease common to children under the age of 10 years, which shows no important seasonal variation despite being more common in March and November. Patients who needed hospitalization were more symptomatic, had more physical examination findings and had higher acute phase reactants. Clinical signs such as fever, palatal petechiae, exudative tonsillitis, and elevated CRP are important predictors of hospitalization.

REFERENCES

1.)Odumade OA, Hogquist KA, Balfour HH Jr. Progress and problems in understanding and managing primary Epstein-Barr virus infections. Clin Microbiol Rev. 2011;24:193-209.
2.)American Academy of Pediatrics. Epstein-Barr virus infections. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. Red Book: 2018 Report of the Committee on Infectious Diseases. 31 th ed. Itasca, IL: American Academy of Pediatrics; 2018: 334-8.
3.)Dunmire SK, Hogquist KA, Balfour HH. Infectious Mononucleosis. Curr Top Microbiol Immunol. 2015;390(Pt 1): 211-40.

4.)Rea TD, Russo JE, Katon W, et al. Prospective study of the natural history of infectious mononucleosis caused by Epstein-Barr virus. J Am Board Fam Practice 2001, 14:234–242.
5.)Yoda K, Sata T, Kurata T, et al. Oropharyngotonsillitis associated with nonprimary Epstein-Barr virus infection. Arch Otolaryngol Head Neck Surg. 2000; 126:185-93.
6.)Hoagland RJ, Henson HM. Splenic rupture in infectious mononucleosis. Ann Intern Med 1957; 46: 1184–1191.
7.)Evans A, Niederman J. Epstein-Barr virus. In: Evans A (Ed). Viral infections of human epidemiology and control. New York: Plenum Publishing; 1989. p.265
8.)Fidan İ, Yüksel S, İmir T. Değişik yaş gruplarında Epstein-Barr virus antikorlarının araştırılması. İnfeksiyon Dergisi. 2005; 19: 453-456
9.)Ozkan A, Kilic SS, Kalkan A, et al. Seropositivity of Epstein-Barr virus in Eastern Anatolian Region of Turkey. Asian Pac J Allergy Immunol. 2003;21:49–53.
10.)Kalinyak KA. Anemias and other disorders of red blood cells. In: Osborn LM, DeWitt TG, First LR, Zenel JA (eds). Pediatrics. Philadelphia: Elsevier Mosby; 2005.p. 686-92.
11.)Fu P. Presentation and initial evaluation of disorders of white blood cells. In: Osborn LM, DeWitt TG, First LR, Zenel JA (eds). Pediatrics. Philadelphia: Elsevier Mosby; 2005.p. 693-7
12.)Hocqueloux L, Causse X, Valery A, et al. The high burden of hospitalization for primary EBV infection: a 6 year prospective survey in a French hospital. Clin Microbiol Infect. 2015;21:1041.
13.)Horwitz CA, Henle W, Henle G, et al. Clinical and laboratory evaluation of infants and children with Epstein-Barr virus-induced infectious mononucleosis: report of 32 patients (aged 10-48 months). Blood.1981; 57:933-8.
14.)Luzuriaga K, Sullivan JL. Infectious mononucleosis. N Engl J Med. 2010; 362:19932000.
15.)Jiao F, Yan X, Yan X, et al. Clinical analysis of 102 cases of Epstein-Barr virus infections in Chinese children. Georgian Med News. 2014;(230):35-8.
16.)Kanegane H, Kanegane C, Yachie A, et al. Infectious mononucleosis as a disease of early childhood in Japan caused by primary Epstein-Barr virus infection. Acta Paediatr Jpn. 1997; 39: 166-171.
17.)Cengiz AB, Cultu-Kantaroğlu O, Seçmeer G, et al. Infectious mononucleosis in Turkish children. Turk J Pediatr. 2010; 52:245-54.
18.)Johannsen EC, et al. Epstein-Barr virus (infectious mononucleosis, Epstein-Barr virus–associated malignant diseases, and other diseases). In: Bennett JE, et al, eds: Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases. 8th ed, Philadelphia, PA: Saunders; 2015. p.1754-71.e6
19.)Son KH, Shin MY. Clinical features of Epstein–Barr virus-associated infectious mononucleosis in hospitalized Korean children. Korean J Pediatr. 2011; 54:409-13.
20.)Cheng CC, Chang LY, Shao PL, et al. Clinical manifestations and quantitative analysis of virus load in Taiwanese children with Epstein-Barr virus-associated infectious mononucleosis. J Microbiol Immunol Infect. 2007; 40: 216-21.
21.)Chan CW, Chiang AK, Chan KH, et al. Epstein-Barr virus-associated infectious mononucleosis in Chinese children. Pediatr Infect Dis J. 2003; 22: 974-8.
22.)Balfour HH, Holman CJ, Hokanson KM, et al. A prospective clinical study of Epstein-Barr virus and host interactions during acute infectious mononucleosis. J Infec Dis. 2005, 192:1505–12.
23.)Gao LW, Xie ZD, Liu YY, et al. Epidemiologic and clinical characteristics of infectious mononucleosis associated with Epstein-Barr virus infection in children in Beijing, China. World J Pediatr. 2011, 7:45–49
24.)Topp SK, Rosenfeldt V, Vestergaard H, et al. Clinical characteristics and laboratory findings in Danish children hospitalized with primary Epstein-Barr virus infection. Infect Dis (Lond). 2015; 47:908-14.
25.)Tamir D, Benderly A, Levy J, et al. Infectious mononucleosis and Epstein-Barr virus in childhood. Pediatrics. 1974;53:330–5.
26.)Moon WY, Oh SH, Ko TS, et al. Infectious mononucleosis in children. J Korean Pediatr Soc. 1994;37:822- 31.
27.)Çağlar M, Balcı YI, Polat A, ve ark. Enfeksiyöz mononükleoz tanısı alan hastaların değerlendirilmesi. Pam Tıp Derg. 2014;7:210-3
28.)Eroğlu Y, Hiçsönmez G. Hacettepe Üniversitesi çocuk hastanesinde anemi görülme sıklığı ve nedenleri. Çocuk Sağlığı ve Hastalıkları Dergisi. 1994;37:267-71.
29.)Medović R, Igrutinović Z, Radojević-Marjanović R, et al. Clinical and laboratory differences between Epstein-Barr and cytomegalovirus infectious mononucleosis in children. Srp Arh Celok Lek. 2016;144:56-62.
30.)Saldaña NG, Colín VA, Ruiz GP, et al. Clinical and laboratory characteristics of infectious mononucleosis by Epstein-Barr virus in Mexican children. BMC Res Notes. 2012;5:361.
31.)Brigden ML, Au S, Thompson S, et al.Infectious mononucleosis in an outpatient population: diagnostic utility of 2 automated hematology analyzers and the sensitivity and specificity of Hoagland's criteria in heterophile-positive patients. Arch Pathol Lab Med. 1999; 123:875-81.
32.)Sumaya CV, Ench Y. Epstein-Barr virus infectious mononucleosis in children. Pediatrics. 1985; 75: 1003-10.
33.)Axelrod P, Finestone AJ. Infectious mononucleosis in older adults. Am Fam Physician 1990; 42:1599-606.
34.)Crum NF. Epstein Barr virus hepatitis: case series and review. South Med J. 2006;99:544-7
35.)Vine LJ, Shepherd K, Hunter JG, et al. Characteristics of Epstein-Barr virus hepatitis among patients with jaundice or acute hepatitis. Aliment Pharmacol Ther. 2012; 36:16-21
36.)Wang Y, Li J, Ren YY, Zhao H. The levels of liver enzymes and atipical lymhocytes are higher in youth patients with infectious mononucleosis than preschool children. Clin Mol Hepatol. 2013; 19:382-8.
37.)Tynell E, Aurelius E, Brandell A, et al. Acyclovir and prednisolone treatment of acute infectious mononucleosis: a multicenter, double-blind, placebo-controlled study. J Infect Dis. 1996; 174:324-31.
38.)Brandfonbrener A, Epstein A, Wu S, et al. Corticosteroid therapy in Epstein-Barr virus infection. Effect on lymphocyte class, subset, and response to early antigen. Arch Intern Med. 1986; 146:337-9.
39.)Glynn FJ, Mackle T, Kinsella, J. Upper airway obstruction in infectious mononucleosis, Eur J Emerg Med. 2007; 14: 41-2.
40.)Thompson SK, Doerr TD, Hengerer AS. Infectious mononucleosis and corticosteroids: management practices and outcomes. Arch Otolaryngol Head Neck Surg. 2005;131:900-4.

Ankara Eğt. Arş. Hast. Derg. (Med. J. Ankara Tr. Res. Hosp.), 2020 ; 53(2) : 113-119
The study was approved by the local Clinical Research Ethics Committee (03.08.2017, 14/II).