Infectious mononucleosis in Turkish children

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SUMMARY: Cengiz AB, Çultu-Kantaroğlu Ö, Seçmeer G, Ceyhan M, Kara A, Gürgey A. Infectious mononucleosis in Turkish children. Turk J Pediatr 2010; 52: 245-254.

The aim of this study was to analyze the demographic, clinical and laboratory characteristics and prognoses of children diagnosed with infectious mononucleosis (IM). The demographic features, referral complaints, clinical and laboratory findings, follow-up, and prognoses of 44 patients diagnosed with IM between January 2000 and June 2006 at the Infectious Diseases Department of Hacettepe University İhsan Doğramacı Children's Hospital were analyzed retrospectively. The children suspected of IM based on clinical findings and whose diagnoses were proven by serological tests were enrolled in the study. In addition, the patients were divided into four groups –namely, age 0-4, age 5-8, age 9-12 and age 13-16, and the differences among groups were investigated in terms of their clinical and laboratory findings. The patients were aged between 3 months and 16 years. The median age was 4, and 56.8% of patients were below age 5. The male/female ratio was 1.6. No statistically significant variation was observed in the seasonal distribution of patients (p=0.131). The most common referral complaints were swollen cervical lymph nodes or swollen neck (68.1%), followed by fever (43.1%) and sore throat (25%). Lymphadenopathy (79.5%), tonsillopharyngitis (72.7%), splenomegaly (34%), and hepatomegaly (25%) were the most common physical examination findings. Leukocyte count was normal in 68.3% of the cases. Leukocytosis was detected in 29.5% of the patients, and leukopenia in 2.2%. Lymphocytosis was detected in 44.7% of patients. Downey cell was detected in the peripheral blood smear of 23.6% of patients, and thrombocytopenia in 11.3%. Elevated alanine aminotransferase and aspartate aminotransferase levels were detected in 61.9% and 90.4% of patients who were investigated for these parameters, respectively. The clinical, hematological and biochemical findings of patients did not vary significantly among age groups (p>0.05). Only one complication (hemophagocytic syndrome) was observed in one patient.

Key words: infectious mononucleosis, children, signs, symptoms.

Epstein-Barr virus (EBV) infections are widespread throughout the world[1-3]. The EBV disease has a spectrum ranging from asymptomatic infection to symptomatic and even fatal infection[1-3]. Infectious mononucleosis (IM) is the best-known clinical syndrome caused by EBV, and it more commonly afflicts adolescents and young adults. IM manifests itself typically as fever, tonsillopharyngitis, generalized lymphadenopathy, hepatosplenomegaly, malaise, and atypical lymphocytosis[1-4]. EBV infection develops generally during early childhood in developing countries or in the socioeconomically disadvantaged sections of developed countries, and 80 to 100% of children become seropositive by ages 3 to 6[1,2]. Primary EBV infection in infants and young children is usually asymptomatic, and only occasionally do some children manifest as classical IM as seen typically in young adult patients[1-3]. IM predominantly occurs in adolescents and young adults in the developed communities where there is delayed exposure to EBV[1-4].

Seroprevalence studies demonstrate that exposure to primary EBV infection occurs at

young ages in Turkey[5,6]. However, because the available Turkish and English literature refers to only a few studies on the clinical and laboratory findings of children diagnosed with IM in Turkey, this retrospective study was planned to evaluate the demographic features, clinical and laboratory findings and outcome in childhood IM in this country.

Material and Methods

Patients diagnosed with IM upon analysis of serum EBV antibodies between 1 January 2000 and 30 June 2006 at the Infectious Diseases Department of Hacettepe University İhsan Doğramacı Children's Hospital, a tertiary referral hospital, were enrolled in the study.

In order to identify the patients diagnosed with IM, the hospital files and medical records of patients recorded in the Pediatric Infectious Diseases Outpatient Clinic with a diagnosis of IM were reviewed retrospectively. We also reviewed retrospectively the hospital files and medical records of the patients with referral complaints of fever (>38°C), skin rash, swollen cervical lymph nodes or swollen neck, sore throat, or tonsillopharyngitis as well as of those with a preliminary diagnosis of viral exanthematous disease, cervical lymphadenitis-adenopathy, tonsillopharyngitis (excluding group A beta-hemolytic streptococcal tonsillopharyngitis), hepatosplenomegaly, splenomegaly or hepatomegaly of unknown origin, hepatitis lacking an identified etiology, EBV antibody positivity, and fever of unknown origin.

Enrollment Criteria

Among the patients aged 0-17 with suspected IM based on their symptoms and clinical findings, 44 patients with anti-viral capsid antigen (anti-VCA) IgM positive (± anti-VCA IgG positive) and anti-Epstein-Barr nuclear antigen (anti-EBNA) IgG negative with ELISA-test (quantitative microplate ELISA-Euroimmun®) were regarded to have been diagnosed with IM, and were enrolled in the study[7,8].

Parameters Reviewed for Patients Diagnosed with IM

The information obtained from the files of patients and other hospital records were entered in to a standard data form, and were encoded and transferred to a computerized setting.

The referral complaints of patients were encoded and recorded according to the presence of swollen cervical lymph nodes or swollen neck, fever, sore throat, cough, skin rash, runny or congested nose, malaise, anorexia, abdominal pain, vomiting, diarrhea, jaundice, pruritus, earache, oral mucosal lesions, and other complaints. The preliminary diagnoses of patients, whether they were recently diagnosed with an acute disease or had a chronic disease, were reviewed and recorded. The type and duration of any therapy they received from the start of symptoms through diagnosis were also added to the standard form. Physical examination findings were also recorded.

The laboratory tests of patients were reviewed and recorded, including their hemoglobin values, leukocyte and thrombocyte counts, peripheral blood smear findings, presence of Downey cells, acute phase reactants (erythrocyte sedimentation rate [ESR], C-reactive protein [CRP] levels), liver function test results (serum alanine aminotransferase [ALT], aspartate aminotransferase [AST], total bilirubin, alkaline phosphatase [ALP], gamma-glutamyl transferase [GGT], lactate dehydrogenase [LDH]), VCA IgM, VCA IgG, early antigen (EA) and EBNA IgG tests, any antibody positivity or negativity against cytomegalovirus (CMV), rubella and other viruses, throat culture results, and chest X-ray findings.

The follow-up physical examination and laboratory findings of patients who were followed after the initial examination were also recorded onto the forms. The patients were evaluated in terms of complications during follow-up, and the obtained data were recorded.

Statistical Methods

All data were transferred to a computerized setting using the Statistical Package for Social Sciences (SPSS) for Windows-version 12 (SPSS, Chicago, IL, USA). Chi-squared test, Kruskal-Wallis test, Mann-Whitney U test, and correlation analyses were performed. In statistical analyses, the p values below 0.05 were regarded as significant.

Results

Of the 44 patients diagnosed with IM, 26 (59%) were male and 18 (41%) were female, with a male/female ratio of 1.6. No variation was observed in the gender distribution of patients (p=0.228).

The patients were aged 3 months to 16 years, with a mean age of 4.8 and median age of 4. Of the patients, 56.8% were included in the age group up to 4 years (25 patients), 25% in the age group 5-8 (11 patients), 13.6% in the age group 9-12 (6 patients) and 4.6% in the age group 13-16 (2 patients). Only one patient was aged below one year (3 months). There were 5 patients aged 1 year, 7 patients aged 2 years, 7 patients aged 3 years, and 5 patients aged 4 years. Our data were not sufficient to evaluate whether or not age distribution was statistically significant.

A review of the season of diagnosis of patients according to their referral dates revealed that 6 patients (13.7%) were referred in winter, 11 patients (25%) in spring, 17 patients (38.6%) in summer, and 10 patients (22.7%) in autumn. There was no statistically significant variation in the distribution of patients diagnosed with IM according to the season of diagnosis (p=0.131).

Most of the patients had multiple referral complaints. In the entire study group, the symptom reported most commonly during diagnosis was swollen cervical lymph nodes and/or swollen neck (68.1%), followed by fever (43.1%), sore throat (25%), cough (25%), skin rash (22.7%), runny or congested nose (20.4%), and other complaints as specified in Table I.

Thirty-three of the patients (75%) referred to our hospital within seven days following the start of their complaints, and 11 patients (25%) within the second week following the start of complaints. The mean symptom period of patients before referral to the polyclinic was 7.27 days (range: 1 to 30 days).

In our study, 45.4% of the children with IM had the symptoms and findings of upper respiratory tract infections (sore throat, runny nose, congested nose). The most common finding revealed by physical examination was lymphadenopathy (79.5%), of which 94.2% were in the cervical region. This was followed by tonsillar enlargement (47.7%), splenomegaly (34%) and hepatomegaly (25%) (Table II). The presence of any of tonsillar enlargement, membranous tonsillitis or cryptic tonsillitis regarded as tonsillopharyngitis and tonsillopharyngitis was detected in 72.7% of patients.

Through history and examination findings, skin rash was detected in 22.7% of patients in the study group, and 50% of these cases had a history of antibiotic usage. The rash in 88.8% of cases was maculopapular.

There was no statistically significant variation in the clinical findings of children with IM in our study according to their ages (p>0.05). None of the patients in our study had otitis media, pneumonia, eyelid edema, or palatal petechiae.

A review of the preliminary diagnoses of patients with IM revealed that 21 (47.7%) of the patients were examined and followed with the preliminary diagnosis of lymphadenitis/lymphadenopathy with unknown etiology, 12 (27.3%) with EBV infection (IM), 6 (13.6%) with deep neck infection, 3 (6.8%) with viral exanthematous disease, 1 (2.2%) with fever of unknown origin, and 1 (2.2%) with systemic infectious disease accompanied by splenomegaly.

It was determined that one of the patients diagnosed with IM had been followed up due to IgA deficiency at our hospital. That patient had recovered without any complication.

An analysis of the hematological tests of patients revealed that 13 (29.5%) patients had leukocytosis, and 1 (2.2%) patient had leukopenia (Table III). The leukocyte count was within normal limits in 68.3% of patients. The patient with leukopenia was diagnosed with EBV secondary hemophagocytic syndrome. Through hemoglobin values and peripheral blood smear findings, it was detected that 13 (29.5%) patients were anemic. Thrombocytopenia (<150,000/mm^3) was detected in 5 (11.3%) patients (Table III). Thirty-eight (86.3%) of the patients had peripheral blood smear and differential count. In 9 (23.6%) of these smears, Downey cells were seen, and lymphocytosis (lymphocyte rate >70%)[9] was detected in 44.7% of patients (Table IV). Leukocytosis, leukopenia and anemia were evaluated

Table I. Referral Complaints (Symptoms) of Patients

Symptom	Number of cases	Percent (%)
Swollen cervical lymph nodes or swollen neck	30	68.1
Fever	19	43.1
Sore throat	11	25.0
Cough	11	25.0
Rash	10	22.7
Runny or congested nose	9	20.4
Malaise	7	15.9
Anorexia	6	13.6
Abdominal pain	3	6.8
Vomiting	2	4.5
Diarrhea	1	2.2
Jaundice	1	2.2
Pruritus	1	2.2
Earache	1	2.2
Oral mucosal lesions	1	2.2

according to the age groups[10,11]. The analysis of the hematological values of our patients did not reveal any significant variation among age groups ($p>0.05$).

It was determined that ESR and CRP had not been reviewed for each patient. Of the total patients, ESR and CRP values were available for 34 (77.2%) and 26 (59%) patients, respectively. ESR was found to be higher than 20 mm/h in 9 (26.4%) patients, and CRP had increased (>0.8 mg/dl) in 9 (34.6%) patients. There was no variation among the age groups of our patients in terms of the distribution of ESR and CRP results.

Among the liver function tests, ALT, AST, GGT, total bilirubin, and ALP results were available for less than half of the patients; LDH value was determined in only 9 patients. Normal values were acknowledged as 5-40 IU/L for ALT, 8-33 IU/L for AST, 5-40 IU/L for GGT, <1.2 mg/dl for total bilirubin, <406 U/L for ALP, and <460 U/L for LDH. Of the patients tested, increased ALT level was detected in 61.9%, increased AST level in 90.4%, increased GGT level in 38.8%, increased ALP level in 22.2%, increased total bilirubin level in 6.2%, and increased LDH level in 88.8% of patients (Table V).

Among our patients in the age group 0-4 years, the ALT values were between 20 and 837 IU/L (mean 127 IU/L), and AST values were between 37 and 637 IU/L (mean 101 IU/L). In the age group 5-16 years, ALT values were between 8 and 401 IU/L (mean 140 IU/L), and AST values were between 17 and 310 IU/L (mean 133 IU/L). The results of abnormal liver function tests did not vary significantly among age groups ($p>0.05$).

Epstein-Barr virus antibodies were tested in the serum of all 44 patients, and VCA IgM

Table II. Physical Examination Findings of Patients

Finding	Number of cases	Percent (%)
Lymphadenopathy	35	79.5
Tonsillar enlargement	21	47.7
Splenomegaly	15	34.0
Hepatomegaly	11	25.0
Hepatosplenomegaly	10	22.7
Rash	9	20.4
Membranous tonsillitis	8	18.2
Fever	5	11.3
Cryptic tonsillitis	3	6.8
Postnasal drainage	2	4.5

Table III. Hematological Parameters of Patients

Finding	Number of cases	Percent (%)
Anemia*	13	29.5
Leukocytosis**	13	29.5
Leukopenia**	1	2.2
Thrombocytopenia	5	11.3

* Hemoglobin values (lower limits by ages)[10]: 6 months-6 years: 11 g/dl 6-18 years: 11.5 g/dl

** Normal values for white blood cells[11]: 1 month-1 year: 6,900-17,200 cell/mm^3 1-12 years: 4,000-12,000 cell/mm^3 Older than 12 years: 4,000-10,000 cell/mm^3

positivity and EBNA IgG negativity were detected. In addition, VCA IgG antibody was found to be positive in 47.7% of patients, and EA antibody was found to be positive in 20.4% of patients (Table VI). The comparison of serological tests by age groups did not reveal any significant variation ($p>0.05$).

Anti-CMV IgM and IgG were tested in 24 patients. Anti-CMV IgM was found to be positive in 6 patients. CMV IgM false-positivity was detected at the rate of 25% among our patients. Anti-rubella IgM was tested in 6 patients, and was found to be positive in 3 patients.

Throat culture was taken from 18 (40.9%) patients. Group A beta-hemolytic streptococcus (GABHS) was isolated in 2 (11.1%) of these patients, and antibiotic treatment was applied.

Chest X-rays of 14 (31.8%) of 44 patients were obtained, and no finding consistent with pneumonia was detected in these radiographs.

It was learned that 20 (45.4%) of the patients had received an antibiotic treatment prior to their referral to our outpatient clinic; 4 of them had taken antibiotic parenterally and the other 16 orally. The tests of 7 (15.9%) of 44 patients diagnosed with IM had been performed at our hospital upon admission, and the preliminary diagnosis was deep neck infection in 6 of these patients and fever of unknown origin in 1 patient.

Complication was detected in one patient during the IM disease. In this patient, aged 6 years, antibody tests and other laboratory findings revealed hemophagocytic syndrome (or hemophagocytic lymphohistiocytosis) secondary to primary acute EBV infection. A four-week chemotherapy (etoposide, dexamethasone, cyclosporin A) was applied. The patient was still being followed by the pediatric hematology and immunology departments as well.

We determined that 12 of 44 patients diagnosed with IM did not present for follow-up visits, and that complications did not develop during the follow-up of patients other than the patient with hemophagocytic syndrome referred to above. It was observed that liver and spleen sizes normalized within two weeks in 81.8% of cases.

Discussion

The childhood studies on IM demonstrate that the age groups most commonly affected by the disease may differ among communities. In the study of Baehner and Shuler[12], 31.4% of 105 children (aged 16 years and younger) diagnosed in California between 1963 and 1965 were younger than 7 years. Sumaya et al.[13] reported that 47 (41.6%) of 113 children diagnosed in Texas between 1976 and 1982 were younger than 4 years. Kanegane et al.[14] reviewed 54 Japanese children with IM and found a peak incidence at 4 years of age. Chan et al.[15] found the median age as 4.1 years among 77 children diagnosed in Hong Kong

Table IV. Peripheral Blood Smear Findings of Patients

	Downey cell in peripheral blood smear	Lymphocytosis in peripheral blood smear
Number of patients with positive finding/ number of patients evaluated	9/38	17/38
Percentage of patients with positive finding (%)	23.6	44.7

Table V. Liver Function Tests of Patients

	ALT	AST	GGT	ALP	Total bilirubin	LDH
Number of patients with high test values / number of patients tested	13/21	19/21	7/18	4/18	1/16	8/9
Percentage of patients with high values (%)	61.9	90.4	38.8	22.2	6.2	88.8

ALT: Alanine aminotransferase. AST: Aspartate aminotransferase. GGT: Gamma-glutamyl transferase. ALP: Alkaline phosphatase. LDH: Lactate dehydrogenase.

between 1996 and 2001. They reported that 10.4% of patients were younger than 2 years and 57.1% were aged between 2-4 years, and that the disease was seen most commonly in the age group 2-4. Likewise, Cheng et al.[16] reported that 76.8% of 69 children diagnosed in Taiwan were younger than 7 years, with peak incidence between 2 and 5 years of age. In our study, 56.8% of patients were younger than 5 years, with a median age of 4 years.

The studies conducted in Turkey demonstrate that children have a high possibility of coming in contact with EBV at early ages[5,6]. Öztürk's study[5] detected EBV IgG positivity in 61% of 305 children living in İstanbul, aged between 3 months and 17 years, and the highest positivity was detected between 4 and 7 years of age, at the rate of 74.4%. In the study conducted by Özkan et al.[6] on 540 people, of whom 163 were aged between 0 and 19 years, VCA IgG positivity was detected as 96.3% for the age group 0-9 years, and 100% for the age group 10-19 years. Considering these seroprevalence data, our study suggests that IM may not be an extremely rare disease among young children in Turkey, due to the high incidence of primary EBV infections at early ages in our country. Although it has been reported that 10 (38.5%) of 26 patients diagnosed with IM in a Turkish university were aged between 11 and 20, and 61.5% were aged 21 and older[17], the lack of adequate publications on serologically proven IM disease among children in our country prevents us from making clearer comments.

The fact that IM is generally observed among individuals with primary contact with EBV in the second decade of life and that it is usually not seen among infants and young children is probably due to differences in the immune responses of the different age groups[3]. In addition, it has been reported that protective maternal antibodies prevent infection during infancy or persisting maternal antibodies may additionally serve to contain the infection once it occurs[18,19]. Literature suggests that the children diagnosed with IM rarely include children younger than 1 year[13,15,18]. In our study, only one patient was aged below 1 year. The seroprevalence studies in our country[5,6] demonstrate that girls have high probability of undergoing primary EBV infection before marriage and suggest that maternal passive antibodies contribute to non-development of IM during early infancy.

Our study has shown that IM does not have a variant distribution between genders, and this finding is consistent with the classical knowledge[3].

An analysis of the seasonal distribution of the diagnosis of our patients demonstrated that 63.6% were diagnosed during spring and summer, but there was no statistically significant seasonal variation, as reported in the literature[4,13,15,16].

The comprehensive studies in the literature[3,20], mostly conducted with young adult and adolescent patients, report that the symptoms include sore throat (82%), malaise (57%), headache (51%), anorexia (21%) and myalgias (20%). In our study, 25% of patients had sore throat, 15.9% had malaise, and 13.6% had anorexia, which may imply that children may be unable to sufficiently express their complaints, when considering the above-mentioned rates

Table VI. Epstein-Barr Virus Antibodies of Patients

	VCA IgM (+)	VCA IgG (+)	EA (+)	EBNA IgG (+)
Number of patients with positive test	44	21	9	0
Percentage of patients with positive test (%)	100	47.7	20.4	0

VCA: Viral capsid antigen. EA: Early antigen. EBNA: Epstein-Barr nuclear antigen.

in young adults.

When the findings of our patients were analyzed, lymphadenopathy ranked first with 79.5%, followed by tonsillopharyngitis with 72.7%. It has been reported that the most common findings among young adults with IM are lymphadenopathy (94%), pharyngitis (84%), fever (76%), and splenomegaly (52%)[3,21]. The studies conducted among children with IM reveal that the majority of children, like adult patients with IM, have fever, tonsillopharyngitis, lymphadenopathy, and hepatosplenomegaly[12,13,15,16]. The findings of our study are consistent with the literature, which states that IM findings are similar among children and adults.

More than 84% of children with IM had fever on admission[13,15,16]. In the study of Sumaya et al.[13], nearly all children have fever in their historical data reports or on the physical examination. In our study, fever was detected in 43.1% of patients as a complaint during admission and in historical data, and in 11.3% as a physical examination finding. It is known that the mean duration of fever is 7 days in IM[15]. Although the low level of fever sign (11.3%) among our patients as compared with the literature may be due to the referral of most patients after the fever period, considering that the average period of referral to our hospital was 7.27 days, the low level of fever history is also inconsistent with the literature.

The Nelson Textbook of Pediatrics states that generalized lymphadenopathy is detected in 90% of children with IM[2]. Key childhood studies also reported that lymphadenopathy is detected in more than 78.3% of children with IM[12,13,15,16]. Lymphadenopathy occurs most commonly in anterior and posterior cervical lymph nodes[1-3]. In our study as well, lymphadenopathy was detected in 79.5% of cases, and the most common localization was the cervical area (94.2%). Our findings regarding the rate and most common localization of lymphadenopathy are consistent with the literature.

The rates of tonsillopharyngitis may be as high as 78 to 88.4% among children with IM [15,16]. In our study, tonsillopharyngitis was detected in 72.7% of cases.

It has been reported that splenomegaly is detected in 46.7 to 64% of children with IM, and hepatomegaly in 10 to 77% of cases[2,12,15,16]. The splenomegaly and hepatomegaly rates detected in our study are consistent with the rates in the literature. As a rule, liver and spleen sizes have been reported to normalize in 2-4 weeks[12]. In 81.8% of our cases, liver and spleen sizes had normalized in two weeks.

In our study, upper respiratory tract infection signs (sore throat, runny nose, congested nose) were detected in 45.4% of children with IM. It was reported that upper respiratory tract infection symptoms are common (64%) among children with IM[15]. The results of our study and of that study are consistent in this respect.

Skin rash has been reported in 7.6 to 25.5% of children with IM[12,13,15,16]. Rash has been reported to be mainly maculopapular[13,15]. While one study[12] reported that there was no history of medication among the children with rash, some other studies have established a link between rash and the use of antibiotics. Sumaya et al.[13] compared a group of children who received ampicillin with another group who did not, and they concluded that rash was statistically more common in the group that received ampicillin. In the study of Chan et al.[15], 55.5% of children with IM and rash had a history of antibiotic usage. One study showed that rash was more common in children younger than 4 years[13]. In our study group, regarding the history and physical examination, 22.7% of children had rash. Half of these children had previous antibiotic usage, and there was no significant difference between the age groups.

In children with IM, the ratio of otitis media is 4.42 to 4.76% and the ratio of pneumonia is 2.85 to 5.3%[12,13]. In one study, all cases with pneumonia were younger than 4 years[13]. None of the patients in our study had pneumonia or otitis media, which may be due to the small number of our study group or to the fact that pneumonia in children with IM could be less frequent than defined in the literature.

There was no case of eyelid edema in our group. One study showed 14.2% of patients as having eyelid edema or periorbital swelling in their study group[13]. In addition, another study in the literature showed 29% of patients as having eyelid edema[15]. In the same study[15], palatal petechiae ratio in the IM group was 7%, but no case of palatal petechiae was seen

in our study.

Sumaya et al.[13] reported that some symptoms and signs in children with IM vary with age. They compared the signs and symptoms of children having IM and found that splenomegaly and hepatomegaly were more frequent in children younger than 4 years than in children between the ages of 4-16. In addition, signs and symptoms of an upper respiratory tract infection, principally a mucopurulent nasal discharge and less frequently cough, were seen in 51.1% of the younger children and 15.2% of the older children[13]. In their study group consisting of 36 children aged 0 to 14, Schmitz et al.[22] reported that the typical clinical findings of IM were found in one-eighth of the children in the age group 0-3 years. Chan et al.[15] defined that clinical findings in children with IM did not correlate with age. Similarly, our study shows that the clinical findings in children with IM did not vary significantly with age ($p>0.05$).

In the series of Fleisher et al.[23], 45 patients between 1 and 15 years of age presented with total leukocyte counts ranging from 4,400/mm^3 to 22,800/mm^3, with a mean of 12,900/mm^3. Total leukocyte counts of 33 of the cases (74%) were between 10,000/mm^3 and 15,000/mm^3. Only one child had a total leukocyte count less than 5,000/mm^3. Baehner et al.[12] reported that 4 of 99 children presented with total leukocyte counts less than 5,000/mm^3, 45 with leukocyte counts between 5,000-10,000/mm^3, 48 with leukocyte counts between 10,000 and 20,000/mm^3, and 2 with leukocyte counts of more than 20,000/mm^3. Additionally, in this study group, the peripheral blood smear of 68 children contained more than 50% lymphocytes. Baehner's[12] study showed that 63.6% of children with IM had more than 25% atypical lymphocytes in their peripheral blood smear. Chan et al.[15] reported 18% of patients with mild neutropenia and stated that lymphocytosis and atypical lymphocytes in the peripheral smear were constant findings in all age groups of children. In the study of Sumaya et al.[13], the mean peak total leukocyte count per microliter during acute IM was significantly greater in the younger age group (0-4 years) than in the older age group (4-16 years). The relative percent of lymphocytes was similar in both age groups. Atypical lymphocytes found in the peripheral blood varied significantly with age, and atypical lymphocyte percentage was higher in the older age group (4-16 years)[13]. Severe neutropenia [absolute neutrophil count (ANC) <500/mm^3] was found in 10.6% of children younger than 4, and in 6.1% of children older than 4. In addition, moderate neutropenia (ANC 500-1000/mm^3) was found in 12.8% of children younger than 4 years old, and 4.5% of children older than 4 years old[13]. Cheng et al.[16] detected that the younger age group had a higher monocyte count than the older age group. Normal leukocyte counts were seen in 68.3% of our cases, while leukocytosis and leukopenia were found in 29.5% and 2.2%, respectively. Lymphocytosis was present in 44.7% of our cases, and Downey cell was detected in 23.6% of the cases. There was no significant difference between the age groups of our cases regarding their hematological laboratory findings. Because the normal values for leukocyte counts and lymphocytosis criteria vary across studies, our findings could not be compared with these studies.

Thrombocytopenia was noted in 11.3% of our cases, but this did not vary significantly across age groups. Chan et al.[15] showed that 21% of their cases had mild thrombocytopenia without bleeding complications. In another study, 4 (4.5%) of 90 children had a thrombocyte count lower than 20,000/mm^3, and all of them had petechiae. Further, 1 of these 4 children had epistaxis and 1 had macroscopic haematuria[13]. Another study, however, showed no cases of thrombocytopenia with bleeding complications[12].

Anemia was seen in 29.5% of our cases. There were no cases with anemia in two major studies analyzing the hematological findings of children with IM[12,15]. Approximately one-third of our cases with anemia could have been due to the higher prevalence of iron deficiency anemia in our country. In a previous study conducted in our hospital, the prevalence of anemia was found to be 21.8% in the 0-17 age-grouped 2,223 children admitting to pediatric outpatient clinics, 78.4% of which was due to iron deficiency[24].

Among the cases whose acute phase reactants were investigated, 26.4% had high ESR and 34.6% had high CRP levels. Although one study conducted in patients with IM revealed

high CRP levels in 57.7% of patients[25], there is no study analyzing the relationship between ESR and CRP levels and the severity of the disease and prognosis. Our study did not include such data.

Abnormal liver function test results are seen in most IM cases. At least one of ALT, AST or LDH levels was found to be high in 90% of the patients[3]. Sumaya et al.[13] determined that 11 of 21 children younger than 4 years and 21 of 27 children older than 4 years had higher ALT and/or AST levels, and 1.8% of children had jaundice. The series of Baehner et al.[12] showed that of 45 children with IM whose liver function tests were obtained, 20 patients (44.5%) had abnormal results on one or more tests. Chan et al.[15] reported 42 (59.2%) of 71 children with IM had high ALT and AST levels; that this increase in ALT and AST was relatively lower in infants; that all children older than 10 had abnormal liver function tests; that 5.6% of cases had high bilirubin levels; and that the probability of hepatitis increased with age. The study of Cheng et al.[16] showed that hepatitis and jaundice were seen in 75.4% and 8.7% of the cases, respectively. In the same study, AST and ALT levels and hepatitis rate decreased in conjunction with lower patient ages. Among the patients tested in our study, 61.9% had high ALT, 90.4% had high AST, 38.8% had high GGT, 22.2% had high ALP, 88.8% had high LDH, and 6.2% had high total bilirubin levels, but liver function test results did not show significant differences between the different ages ($p>0.05$).

It is reported that the rate of GABHS isolation from throat swabs of IM patients was generally below 4%[26,27]. Among our patients from whom throat cultures were obtained, GABHS isolation rate was 11.1%, which is higher than the results of a study[28] conducted in kindergartens and primary schools of Ankara in groups aged 3-12 years, with a GABHS carrier rate of 3.2%. Since we were unable to differentiate whether the isolation of GABHS was due to carrier state or due to a concomitant GABHS infection, antibiotics were administered to our patients.

The majority of IM patients recover without any complications[1,2]. However, there are publications reporting 19.4 to 21.2% complication rates in children with IM[13,15]. The complication rate in our study group was as low as 2.2%, and this was due to one patient who developed hemophagocytic lymphohistiocytosis.

Among our patients in whom CMV serology tests were conducted, 25% were CMV IgM positive. It is known that CMV false-positivity may be detected in acute EBV infections because of the cross-reaction between EBV IgM and CMV IgM antibodies[22,29]. Our study demonstrated that CMV false-positivity may not be rare among children with IM. False-positive rubella IgM test results have also been reported among patients with IM[30]. In our study, six of the patients were tested for anti-rubella IgM, and the results were positive in three patients.

In conclusion, our study has revealed that the clinical findings, major hematological parameters and liver function test results do not vary among age groups. We demonstrated that IM may develop at early ages among the children living in Ankara.

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