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INFECTIOUS MONONUCLEOSIS IN CHILDREN- CURRENT CLINICAL AND EPIDEMIOLOGICAL ASPECTS

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Abstract: *Infectious mononucleosis is caused by primary infection with Epstein-Barr virus, most commonly symptomatic in teenager and young adults. Positive diagnosis of infectious mononucleosis is based on clinical manifestations, changes of WBC counts and serum specific serological tests. We performed a retrospective study of some clinical and epidemiological aspects of infectious mononucleosis in children hospitalized in Clinical Infectious Diseases Hospital Brasov during January 2015 – June 2016. There were hospitalized more boys (72,31% cases), more from urban area (66,15% cases), each month, without an obvious seasonality. The most frequent hematological changes were monocytosis (95,38% cases) and lymphocytosis (89,23% cases). Hepatitis was frequently (75,38%), rarely associated with hepatomegaly and jaundice. A large number of children had concomitant acute infection or recent infection with CMV (37,2% cases).*

Key words: *Epstein Barr virus, infectious mononucleosis, cytomegalovirus.*

1. Introduction

Infection with Epstein-Barr virus (EBV) is widespread, causing immunization in most cases up to adulthood. In less developed countries seroconversion occurs mainly in childhood, at earlier age. Primary infection causes infectious mononucleosis in most cases, especially in teenager and young adults. The source of infection is infected people, in the course of disease or healthy virus excretory. The virus is present in oropharyngeal secretions and it is transmitted most often through saliva, easier in communities or in family. Positive diagnosis of infection is based on clinical manifestations (fever, pharyngitis, lymphadenopathy, hepatomegaly, splenomegaly, rarely jaundice), changes in serum WBC counts, frequently elevation of serum transaminase, serological tests (heterophile and specific antibody tests). Differential diagnosis is made with infectious mononucleosis due to cytomegalovirus, toxoplasmosis, acute HIV disease, viral hepatitis [1,2,3].

2. Objectives

Evaluation of some current clinical and epidemiological characteristics of

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infectious mononucleosis in children hospitalized for this condition.

3. Material and methods

It is a retrospective descriptive study, conducted on 65 patients admitted in Clinical Infectious Diseases Hospital of Brasov with confirmed infectious mononucleosis during 01.01.2015-30.06.2016. Diagnosis of acute infection with Epstein Barr virus, established by clinical and nonspecific laboratory data, was confirmed by serological (presence of heterophile antibodies and / or specific for acute phase). There were analyzed various aspects: epidemiological (age, gender, environmental origin, belonging to a school community, monthly distribution of admissions), laboratory (changes in serum WBC counts, serum transaminases and bilirubin, evaluation the immune status for cytomegalovirus), abdominal ultra-sound (hepatomegaly, splenomegaly).

4. Results

During 01.01.2015-30.06.2016 were admitted in the Clinical Infectious Diseases Hospital of Brasov 65 children with infectious mononucleosis. Patients were of both sexes; it was found a higher number of admissions in the masculine gender – 72,31% cases. In relation with environmental origin of patients they were residing both in urban and in rural; 2/3 of the patients were residing in urban areas (Table 1).

Table 1

Environmental origin and gender of patients hospitalized for infectious mononucleosis

Patients	**Gender**		**Environmental origin**	
	M(Male)	*F(Female)*	*U(Urban)*	*R(Rural)*
No	47	18	43	22
%	**72,31**	27,69	**66,15**	33,85

Children hospitalized with mononucleosis had ages ranging from 1-16 years. We found the highest frequency of admissions at 1-3 years age group (32.31%), followed by the 4-6 years old (27.69%), 11-16 years old (26.15%) and on the last place children 7-10 years old (13.84%). (Table 2). Age-gender correlations showed differences between the two genders. In the boys group the highest frequency of admissions has been found in age groups 1-3 years (38.3%) and 4-6 years (29.79%). Girls from 1-3 years age group had the lowest number of hospitalized patients (16.67%) while those from 11-16 age old had a greater proportion of hospitalizations (38.39%).

Table 2

Age and gender-age correlations of patients hospitalized for infectious mononucleosis

Age (years)	**Gender**				**Total**	
	M(47)		**F(18)**			
	No.	*%*	*No.*	*%*	*No.*	*%*
1-3	18	38,3	3	16,67	21	32,31
4-6	14	29,79	4	22,22	18	27,69
7-10	5	10,64	4	22,22	9	13,84
11-16	10	21,28	7	38,39	17	26,15

Regarding membership in a community, 50 children (76.92%) were attending nursery, kindergarten or school.

Hospitalizations for infectious mononucleosis were performed each month of the studied period, in variable number, without an obvious seasonality (Fig. 1).

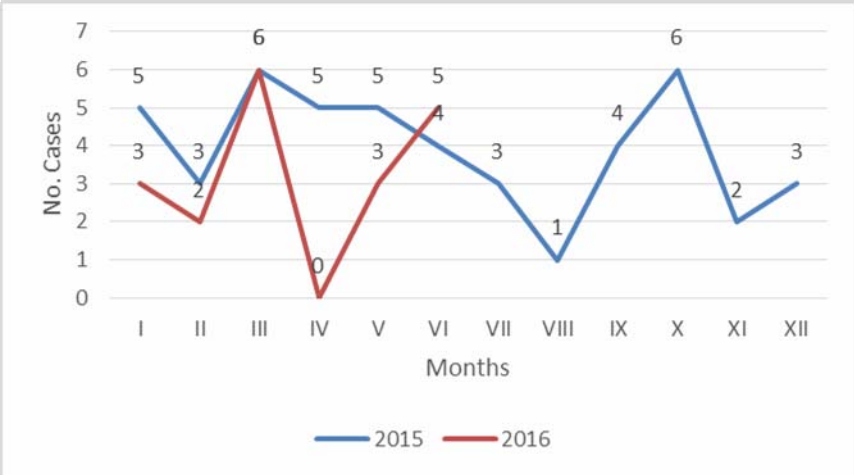

Fig. 1. *Monthly frequency of admissions for infectious mononucleosis*

Serum WBC (White Blood Cells) counts was modified, meaning leukocytosis, in 66,15% cases; in the remaining patients leukocyte count was normal. Lymphocytosis and monocytosis prevailed in leukocyte formula, in 89,23% and 95,38% patients (Table 3).

Table 3

Changes in laboratory tests in patients with infectious mononucleosis

Patients (65)	**WBC count**		**Lymphocytes count**		**Monocytes count**		**Serum transaminases (ST)**		**Serum bilirubin (29)**	
	N	**Increased level**	**N**	**Increased level**	**N**	**Increased level**	**N**	**Increased level**	**N**	**Increased level**
No.	22	43	7	58	1	62	16	49	27	2
%	33.85	66.15	10.77	89.23	4.62	95.38	24.62	75.38	93.1	6.9

Liver disease, manifested by increasing serum transaminases, has been found in 75.38% of patients**.** Increased serum bilirubin level was very rare**,** in only 2 of the 29 patients investigated (Table 3).

Abdominal ultrasounds were performed on 48 of the patients. Changes were represented by splenomegaly, very frequently found - 91,67% cases and hepatomegaly, diagnosed in a much smaller proportion of cases - 27.08% (Table 4).

Results of abdominal ultrasound in patients with infectious mononucleosis Table 4

Patients (48)	Liver		Spleen	
	Standard dimension	Hepatomegaly	Standard dimension	Splenomegaly
No.	35	13	4	44
%	72,92	27,08	8,33	91,67

The analysis of correlations between dimension of the liver toabdominal ultrasound and serum transaminase levels revealed different aspects. Hepatic cytolysis was associated with hepatomegaly in 28.83% of cases and was the only change mostly suggestive for hepatitis disease in 58.33% of patients. Isolated hepatomegaly was seen only in 6.25% of cases (Table 5).

Correlations serum transaminates (ST) – ultrasound hepatomegaly Table 5

Correlations (48 cases)	Elevated ST - Hepatomegaly	Elevated ST- Liver standard dimension	Normal ST - Hepatomegaly	Normal ST- Liver standard dimension
No. cases	10	28	3	7
% cases	20,83	58,33	6,25	14,58

Simultaneously with serological tests for the diagnosis of infectious mononucleosis were conducted tests to assess immune status for cytomegalovirus (CMV) – antibody IgM and IgG, in 43 of the patients (Table 6).

Table 6

Changes in concomitant specific serological tests for cytomegalovirus (CMV)

Patients (43 cases)	CMV IgM negative- IgG negative	CMV IgM positive- IgG negative	CMV IgM positive- IgG positive	CMV IgM negative- IgG positive
No. cases	10	8	8	17
% cases	23.25	18.60	18.60	39.53

We found the lack of immunization in 23.25% of patients, acute or very recent infection (IgM positive or IgM to IgG seroconversion) in 37,2% of cases and old immunization in 39.53% of the children.

All the aspects were found in different proportions in all age groups. Lack of immunization was more common in young children, of 1-3 years old (5/10 cases); acute or very recent infection was found in all age groups in similar proportions; old immunization was most common in children 11-16 years (Table 7).

Correlations age – CMV immunizations Table 7

CMV immunization	Age (years) – No. cases			
	1-3 (13)	4-6 (10)	7-10 (6)	11-16 (14)
IgM negative- IgG negative	5	3	1	1
IgM positive- IgG negative	2	3	-	3
IgM positive-IgG positive	2	3	1	2
IgM negative- IgG positive	4	1	4	8

5. Discussions

Data from literature mentions that in less developed countries, directly correlated with poorer socioeconomic conditions, agglomerations of people in families and homes, attending nurseries and kindergartens, with exposure to objects and toys contaminated with saliva, EBV infection occurs early in life, is mostly asymptomatic and seroconversion is seen most frequently at the age of 3-4 years. Primary infection with EBV in teenager causes infectious mononucleosis in more than half of the affected people [1,2]. In our study we found hospitalizations for mononucleosis to all age groups. More frequently were affected children aged up to 6 years (60%), situation due most likely to tight interpersonal contact in nurseries and kindergartens, with multiple possibilities of infection. A significant percentage of cases of the disease have also found in older children and adolescents (26%), most likely due through classic saliva transmission, fact mentioned in literature and other studies [1, 2], [4], [8].

There were hospitalized children of both sexes, boys more often (72,31%), situation also mentioned by Medovic et al., Son et al. and Cengiz et al.

Patients came from both urban and rural area. A greater frequency of admissions was found to children from urban, probably due to attendance in a large number and on a prolonged daily duration of nurseries and kindergartens.

Regarding the monthly admissions distribution for infectious mononucleosis we found no significant seasonal variations. The same situation is mentioned by many other authors (2,4,7).

We analyzed changes in white blood cells and the white blood cell counts. Leukocytosis was found in 66.15% of cases. Medovic et al. mention similar values (65% cases); other authors have found higher values (Son et al. – 69,1%, Soo et al. – 86,1%) or lower values (Cengiz et al. – 29,5%).

We found significant changes related to marked increase in serum monocyte (95,38% cases)m and lymphocyte (almost 90% cases). Medovic et al. mention lymphocytosis in a lower proportion of cases (74,7%), Cengiz et al. in 44,7% cases and Topp et al. to 41,7% of patients.

Mononucleosis hepatitis, diagnosed by increasing serum transaminases, has been found in a significant proportion of cases – 75,38%. Other studies showed similar or different frequencies of liver disease: Medovic et al. – 74,4%, Arama et al. – over 85%, Cengiz et al. – 61,9%, Gonzales et al. – 30,9%, Soo et al. – 83,3%.

In contrast jaundice had a very low frequency – 6,95 cases, situation mentioned also by Cengiz et al. – 6,2% cases; Gonzales found in Mexic a much higher frequency of jaundice – 42,1% cases.

Reported to the high frequency of cases of hepatitis, hepatomegaly, observed to abdominal ultrasound, was much less common, only to a quarter of the patients. Medovic et al. mention a higher frequency – 33,2% , Cengiz et al. a similar frequency to that found in our study, Gonzales et al. – 47,2% and Soo et al. – 30,6%.

Hepatomegaly was correlated with increased hepatic cytolysis only in one fifth of patients. In a significant proportion of cases (almost 59%) the liver disease was diagnosed only by increasing serum transaminases, hepatomegaly being absent. This finding suggests that in any case of infectious mononucleosis should be evaluated always serum transaminases.

Splenomegaly was common, found in almost 92% of patients. Other studies report lower frequencies – Medovic et al. – 66,7%, Gonzales et al. – 36,8%, Soo et al. – 27,8%; Balasubramanian et al. – 81% cases.

Assessing the immune status for CMV infection was performed concomitant with testing for EBV, being included in the panel of serological tests. It was found that nearly 40% of patients with infectious mononucleosis were already immunized against CMV, with specific IgG present. This situation was observed in all age groups, more common in children 11-16 years old (8/17 cases. Another finding was that other children had acute infection (IgM present) – 18,60% cases or recent infection (IgM - IgG seroconversion) – 18,60% cases. All these changes in immune status related to CMV infection suggest that up to age 16 many of the children (three quarters) pass through infection.

6. Conclusions

Admissions for infectious mononucleosis were rare and prevailed in young children attending collectivities of care and education, to masculine gender and in patients from urban areas, without an obvious seasonality.

The most frequent hematological changes were monocytosis and lymphocytosis. Mononucleosis hepatitis is common, infrequently associated with hepatomegaly or jaundice and requires laboratory tests for diagnosis; splenomegaly is a common manifestation.

A large number of children had concomitant acute infection or recent infection with CMV, situation that suggests common infection sources and transmissions pathways both for EBV and CMV; immunization against CMV is frequently until teenage.

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