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Infectious Mononucleosis in Adults: Some Clinical and Epidemiological Features of Infectious Mononucleosis

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Abstract: the article highlights the clinical and epidemiological features of infectious mononucleosis in adults based on an analysis of 222 patients who underwent treatment at the infectious diseases department of St. Michael's Clinical Hospital in Kyiv from 2017 to 2023. Infectious mononucleosis is primarily caused by the Epstein-Barr virus, although other etiological agents include cytomegalovirus and human herpesvirus type 6. The aim of the study was to assess the incidence and epidemiological characteristics of infectious mononucleosis in adults over a six-year observation period. The research included a retrospective analysis of medical records, clinical manifestations, and laboratory-confirmed diagnoses. The study demonstrated that the incidence of infectious mononucleosis remained stable from 2017 to 2019, followed by a complete absence of cases in 2020–2021, likely due to the impact of pandemic restrictions related to coronavirus disease 2019. In 2022–2023, a resurgence of cases was observed, indicating the return of viral circulation. The average annual incidence rate was calculated at 34 cases per year, which aligns with epidemiological data reported in the literature. Among the analyzed patients, 57.3% were men and 42.7% were women, with the highest prevalence observed in the age group of 18 to 29 years, accounting for 70.3% of cases. The study found that Epstein-Barr virus was detected in 57.1% of male and 42.9% of female patients, whereas cytomegalovirus was more frequently identified in women (10.8%) than in men (4.5%). A significant proportion of patients (77.02%) were hospitalized with alternative preliminary diagnoses, primarily lacunar tonsillitis (36.5%), as well as follicular tonsillitis (2.5%), hepatitis (1.5%), meningitis (1.75%), and fever of unknown origin (0.5%). These findings indicate that infectious mononucleosis in adults often presents with a polymorphic clinical picture, which may complicate early diagnosis. Statistical analysis was performed using Student's *t*-test, Wilcoxon *W*-test, the Chi-square method, and Spearman's correlation coefficient, with a significance threshold of *p*=0.05. The results emphasize the need for improved differential diagnosis strategies, drawing clinicians' attention to other manifestations of infectious mononucleosis, such as fever, generalized lymphadenopathy, and hepatosplenomegaly. The study highlights the role of infectious mononucleosis as a significant clinical disease in adults and substantiates the need for continuous epidemiological monitoring.

Keywords: [Infectious Mononucleosis](#); [Etiology](#); [Epidemiology](#); [Prevalence](#); [EBV](#); CMV; clinical manifestations.

Introduction

This infectious disease is usually caused by the Epstein-Barr virus (EBV), also known as human herpesvirus 4, which is a widely prevalent double-stranded DNA herpesvirus. [1,2] Other causes of the disease include cytomegalovirus (CMV), [3] as well as human herpesvirus type 6. [4] Human immunodeficiency virus and adenovirus can induce a mononucleosis-like syndrome. [5] The disease is characterized by a classic triad of symptoms: fever, pharyngitis, and generalized lymphadenopathy. [6] Most cases of symptomatic IM occur in adolescents or young adults. [7] In our study, we analyzed the course of IM caused by EBV and CMV.

It is usually a benign, self-limiting disease that requires only symptomatic treatment, although in some cases, it may follow a complicated or prolonged course, leading to a reduced quality of life. [8]

The Epstein-Barr virus remains one of the most widespread viruses worldwide. After infection, an individual remains a carrier of the virus for life, periodically shedding it in saliva, which facilitates the spread of the infection within the population. [9]

Over the past five years, the COVID-19 pandemic has significantly affected the collection and analysis of up-to-date statistical data on various infectious diseases, including infectious mononucleosis. The forced reorientation of the healthcare system towards combating the pandemic and the introduction of anti-epidemic restrictive measures contributed to a decrease in the activity of other viral infections, in particular due to the so-called "natural displacement" of competing pathogens.

According to the Public Health Center of Ukraine, in 2019, 5,467 cases of infectious mononucleosis were registered in Ukraine, of which 4,597 (84.6%) occurred in children under the age of 17. [10] According to the literature, approximately 90% of the global population has antibodies to the pathogen. In developed countries, the seropositivity rate is lower, and primary infection occurs later. [7]

Epstein-Barr virus is primarily transmitted via airborne droplets through close contact with oropharyngeal secretions. Other possible

transmission routes include sexual contact, blood transfusion, and organ transplantation. During the initial infection, Epstein-Barr virus specifically targets B-lymphocytes in the oropharyngeal epithelium, forming virocytes, predominantly CD8+ T-cells, in the bloodstream. After the acute phase, the virus can persist in oropharyngeal secretions for up to 32 weeks [7, 12] and remain in the body for decades. In healthy Epstein-Barr virus-seropositive adults, the virus can be detected in oropharyngeal secretions in 10–20% of cases. [11]

Aim

The aim of the study was to analyze the incidence of infectious mononucleosis in adults and the characteristics of the epidemic process from 2017 to 2023 among individuals of different age groups residing in Kyiv.

Materials and Methods

Medical records of inpatients diagnosed with infectious mononucleosis who were hospitalized in the infectious diseases department of St. Michael's Clinical Hospital in Kyiv from 2017 to 2023 were analyzed. The diagnosis was established based on serological detection of IgM and IgG antibodies to the infectious mononucleosis pathogen.

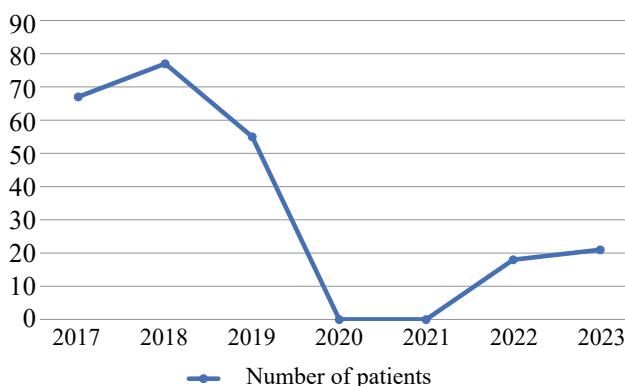
Results and Discussion

All hospitalized patients underwent a comprehensive clinical and laboratory examination.

Statistical analysis methods for comparing two independent samples included Student's t-test for normally distributed data and the Wilcoxon W-test for non-normally distributed data. The Chi-square method was used to compare qualitative differences. Correlation analysis was performed using Spearman's rank correlation coefficient to assess relationships between variables. The critical significance level (p) was set at 0.05.

During the period from 2017 to 2023, a total of 222 patients were hospitalized in the infectious diseases department of St. Michael's Clinical Hospital in Kyiv, with a subsequently laboratory-confirmed diagnosis of infectious mononucleosis. The dynamics of infectious mononucleosis cases are presented in Figure 1.

From Figure 1, it can be observed that the number of patients from 2017 to 2019 ranged

**Figure 1.** Dynamics of IM cases by year

from 55 to 77, indicating stable virus circulation. In 2020–2021, no cases were reported, which may be attributed to the peak of the COVID-19 pandemic. Another possible reason for the absence of reported cases is the temporary reorganization of our hospital to admit only patients with coronavirus infection, which could have led to the redirection of infectious mononucleosis cases to other medical facilities. The number of cases began to recover in 2022 and 2023, suggesting a return to the typical level of virus circulation.

The average annual number of infectious mononucleosis cases recorded at our institution from 2017 to 2023 was 34 cases ($34 \pm 8.6\%$). Although this is an absolute count and not directly comparable to population-based incidence rates, the observed number of cases is within the range of values reported in the literature, which vary from 11 to 48 cases per 1,000 individuals annually [7].

Among patients with infectious mononucleosis, there were 122 men ($57.3 \pm 2.57\%$) and 100 women ($42.7 \pm 2.57\%$). The age of the patients ranged from 18 to 65 years. The proportion of men with infectious

mononucleosis exceeded that of women, accounting for $59.1 \pm 2.57\%$ compared to $40.9 \pm 2.57\%$, respectively. The data are presented in Table 1.

Among the examined patients with infectious mononucleosis, the proportion of individuals aged 18 to 30 years was 156 ($70.3 \pm 0.6\%$), those aged 31 to 64 years accounted for 63 ($28.3 \pm 2.28\%$), and those older than 65 years comprised 3 ($1.35 \pm 0.35\%$).

According to the etiological factor, it was determined that among men, Epstein-Barr virus was the causative agent in $47.3 \pm 5.59\%$ of cases, while cytomegalovirus was identified in $4.5 \pm 2.47\%$ of cases. Meanwhile, among women, Epstein-Barr virus infection was observed in $35.6 \pm 5.59\%$ of cases, and cytomegalovirus in $10.8 \pm 2.47\%$ of cases. Thus, the prevalence of Epstein-Barr virus among men exceeded that among women by 11%, whereas the proportion of women with cytomegalovirus infection was 6.3% higher than that of men. The overall distribution of infectious mononucleosis cases by pathogen and gender is presented in Table 2.

Table 2. Etiology of IM by pathogen and gender

Patients	EBV		CMV	
	n	%	n	%
men	105	57.1 ± 4.24	10	29.4 ± 7.65
women	79	42.9 ± 4.24	24	70.6 ± 7.65
total		184		34

The preliminary diagnosis of infectious mononucleosis was established in 216 patients ($97.3 \pm 0.89\%$) upon admission to the infectious diseases hospital. Among them, only 171 pa-

Table 1. Age characteristics of IM patients

Patients	18-29 years		30-64 years		>65 years	
	n	%	n	%	n	%
men	94	60.3 ± 26.8	28	$52.8 \pm 6.12^*$	1	33.3 ± 4.68
women	62	39.7 ± 26.8	25	47.2 ± 6.12	2	66.6 ± 4.68
total	156	$1.5 \pm 0.6^{**}$	53	$29.5 \pm 2.28^{**}$	3	$46 \pm 2.49^{**}$

Note: * – the differences are significant between the age groups 30-64 years and >65 years, $p=0.05$

** – the identified differences between these groups are statistically significant, $p=0.05$

tients ($77.02 \pm 2.58\%$) were hospitalized with a suspected diagnosis of infectious mononucleosis. Patients were admitted with the following preliminary diagnoses: lacunar tonsillitis in 146 cases ($36.5 \pm 2.5\%$), follicular tonsillitis in 10 cases ($2.5 \pm 0.8\%$), meningitis in 7 cases ($1.75 \pm 2.5\%$), hepatitis in 6 cases ($1.5 \pm 0.6\%$), and fever of unknown origin in 2 cases ($0.5 \pm 0.35\%$). The data are presented in Table 3.

Table 3. Preliminary diagnoses of patients referred to the infectious diseases hospital

№	Preliminary diagnosis	n	%
1.	Lacunar tonsillitis	146	36.5 ± 2.5
2.	Follicular tonsillitis	10	2.5 ± 0.8
3.	Meningitis	7	1.75 ± 0.7
4.	Hepatitis	6	1.5 ± 0.6
5.	Fever of unknown origin	2	0.5 ± 0.35

From the data in Table 3, it can be concluded that patients with lacunar tonsillitis (146 cases, $36.5 \pm 2.5\%$) were more frequently admitted to the infectious diseases department, as a manifestation of Epstein-Barr virus infection. This indicates insufficient clinical attention to other manifestations of infectious mononucleosis, such as fever, generalized lymphadenopathy, and hepatosplenomegaly.

Conclusions

1. Our study demonstrated that until 2019, the incidence of infectious mononucleosis remained relatively stable, ranging from 55 to 77 cases per year. In 2020–2021, no cases were recorded, likely due to the COVID-19 pandemic and the implementation of quarantine measures. Since 2022, the incidence has gradually increased,

suggesting a return of viral circulation to pre-pandemic levels.

2. The average annual number of infectious mononucleosis cases was 34. Although this is an absolute figure, it falls within the range of values reported in the literature. Males were more frequently affected than females (57.3% vs. 42.7%), and the highest incidence was observed in the 18–29 age group (70.3%).

3. The primary etiological agent was the Epstein-Barr virus, detected in 57.1% of male and 42.9% of female patients. Cytomegalovirus was more frequently identified in women (10.8%) than in men (4.5%).

4. In the modern clinical setting, infectious mononucleosis exhibits a polymorphic presentation, complicating timely diagnosis. A significant proportion of patients (77.02%) were hospitalized with alternative preliminary diagnoses, including lacunar tonsillitis (36.5%), follicular tonsillitis (2.5%), hepatitis (1.5%), meningitis (1.75%), and fever of unknown origin (0.5%).

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Conflict of interests

The authors declare no conflicts of interest.

Consent to publication

All authors have read the manuscript and agreed to its publication.

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A – Research concept and design, B – Collection and/or assembly of data, C – Data analysis and interpretation, D – Writing the article, E – Critical revision of the article, F – Final approval of article.

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Інфекційний мононуклеоз у дорослих: дяякі клініко-епідеміологічні особливості інфекційного мононуклеозу

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Анотація: у статті висвітлено клініко-епідеміологічні особливості інфекційного мононуклеозу у дорослих на основі аналізу 222 пацієнтів, які проходили лікування в інфекційному відділенні Свято-Михайлівської клінічної лікарні в Києві у період з 2017 по 2023 рік. Інфекційний мононуклеоз переважно спричиняється вірусом Епштейна-Барр, проте серед його збудників також відзначають цитомегаловірус та герпесвірус людини 6-го типу. Метою дослідження було оцінити частоту та епідеміологічні характеристики інфекційного мононуклеозу у дорослих за шестирічний період спостереження. Дослідження включало ретроспективний аналіз медичної документації, клінічних проявів та лабораторно підтверджених діагнозів. Було встановлено, що захворюваність на інфекційний мононуклеоз залишалася стабільною у 2017–2019 роках, після чого у 2020–2021 роках не було зареєстровано жодного випадку, ймовірно, через вплив пандемічних обмежень, пов’язаних із коронавірусною хворобою 2019 року. У 2022–2023 роках зафіксовано відновлення випадків захворювання, що свідчить про відновлення циркуляції вірусу. Середньорічний рівень захворюваності розраховано на рівні 34 випадків на рік, що відповідає епідеміологічним даним, наведеним у літературі. Серед проаналізованих пацієнтів 57,3% становили чоловіки, а 42,7% – жінки, причому найвищий рівень поширеності відзначено у віковій групі від 18 до 29 років (70,3%). У ході дослідження встановлено, що вірус Епштейна-Барр був виявлений у 57,1% чоловіків і 42,9% жінок, тоді як цитомегаловірус частіше діагностували у жінок (10,8%), ніж у чоловіків (4,5%). Значна частина пацієнтів (77,02%) була госпіталізована з альтернативними попередніми діагнозами,

зокрема лакунарною ангіною (36,5%), а також фолікулярною ангіною (2,5%), гепатитом (1,5%), менінгітом (1,75%) та лихоманкою неясного генезу (0,5%). Отримані результати свідчать про те, що інфекційний мононуклеоз у дорослих часто має поліморфну клінічну картину, що може ускладнювати ранню діагностику. Статистичний аналіз проведено із застосуванням *t*-критерію Стьюдента, *W*-критерію Вілкоксона, методу хі-квадрат та коефіцієнта кореляції Спірмена, при рівні значущості $p=0,05$. Результати підкреслюють необхідність удосконалення стратегій диференційної діагностики, акцентуючи увагу клініцистів на інших проявах інфекційного мононуклеозу, зокрема гарячці, генералізованій лімфаденопатії та гепатосplenомегалії. Дослідження підкреслює значущість інфекційного мононуклеозу як клінічно важливого захворювання у дорослих та обґрунтovanу необхідність постійного епідеміологічного моніторингу.

Ключові слова: інфекційний мононуклеоз, етіологія, епідеміологія, поширеність, ЕБВ, ЦМВ, клінічні прояви.



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