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NEW DAY IN MEDICINE**

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www.bsmi.uz  
<https://newdaymedicine.com> E:  
ndmuz@mail.ru  
Тел: +99890 8061882

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## MODERN TREATMENT OF MIX INFECTION CAUSED BY EPSTEIN-BARR VIRUS AND CYTOMEGALOVIRUS

Jalilova Aziza Sadilloevna <https://orcid.org/0009-0004-6234-4631>

Bukhara State Medical Institute named after Abu Ali ibn Sina, Uzbekistan, Bukhara,  
st. A. Navoi. 1 Tel: +998 (65) 223-00-50 e-mail: [info@bsmi.uz](mailto:info@bsmi.uz)

✓ **Resume**

*Infectious mononucleosis is a widespread infectious disease worldwide, most often caused by the γ-herpetic Epstein-Barr virus (EBV), affecting 80-90% of the population. Currently, there has been an increase in the incidence rate of infectious mononucleosis among children.*

*To some extent, this is due to the insufficient improvement of diagnostics. If we analyze the official data, in 2000-2019, the statistics of EBV infection in Novokuznetsk increased by 27 times: from 0.9 per 100 thousand population in 2000 to 24.7 in 2008. This is primarily due to the high incidence rate, for example, in Uzbekistan, it occurs in the ratio of 7.5:100,000, and among children, the highest ratio is 34:100,000.*

**Key words:** Epstein-Barr virus, analyze, infectious mononucleosis, children, CMV, laboratory

## СОВРЕМЕННОЕ ЛЕЧЕНИЕ СМЕШАННОЙ ИНФЕКЦИИ, ВЫЗВАННОЙ ВИРУСОМ ЭПШТЕЙНА-БАРР И ЦИТОМЕГАЛОВИРУСОМ

Жалилова Азиза Садиллоевна <https://orcid.org/0009-0004-6234-4631>

Бухарский государственный медицинский институт имени Абу Али ибн Сины,  
Узбекистан, г. Бухара, ул. А. Навои. 1 Тел: +998 (65) 223-00-50 e-mail: [info@bsmi.uz](mailto:info@bsmi.uz)

✓ **Резюме**

*Инфекционный мононуклеоз — широко распространенное инфекционное заболевание во всем мире, чаще всего вызываемое γ-герпетическим вирусом Эпштейна-Барр (ВЭБ), поражающее 80-90% населения. В настоящее время отмечается рост заболеваемости инфекционным мононуклеозом среди детей.*

*В определенной степени это связано с недостаточным совершенствованием диагностики. Если проанализировать официальные данные, то в 2000-2019 годах статистика инфицирования ВЭБ в Новокузнецке выросла в 27 раз: с 0,9 на 100 тыс. населения в 2000 году до 24,7 в 2008 году. Это связано в первую очередь с высоким уровнем заболеваемости, например, в Узбекистане она встречается в соотношении 7,5:100 000, а среди детей наибольшее соотношение составляет 34:100 000.*

**Ключевые слова:** вирус Эпштейна-Барр, анализ, инфекционный мононуклеоз, дети, ЦМВ, лабораторное исследование

## EPSHTEYN-BARR VIRUSI VA SITOMEGALOVIRUS KELTIRIB CHIQARADIGAN MIKST INFEKSIYASINING ZAMONAVIY DAVOSI

Jalilova Aziza Sadilloevna <https://orcid.org/0009-0004-6234-4631>

Abu Ali ibn Sino nomidagi Buxoro davlat tibbiyot instituti, O'zbekiston, Buxoro sh. A. Navoiy  
kochasi 1 Tel: +998 (65) 223-00-50 e-mail: [info@bsmi.uz](mailto:info@bsmi.uz)



✓ *Rezyume*

*Yuqumli mononuklyoz butun dunyo bo'ylab keng tarqalgan yuqumli kasallik bo'lib, ko'pincha γ-gerpetik Epstein-Barr virusi (EBV) sabab bo'lib, aholining 80-90% ga ta'sir qiladi. Hozirgi vaqtida bolalar o'rtasida yuqumli mononukleoz bilan kasallanish darajasi oshgan.*

*Bu ma'lum darajada diagnostikaning yetarli darajada takomillashtirilmaganligi bilan bog'liq. Rasmiy ma'lumotlarni tahlil qiladigan bo'lsak, 2000-2019 yillarda Novokuznetskda EBV infeksiyasi statistikasi 27 baravar ko'paydi: 2000- yilda 100 ming aholiga 0,9 dan 2008- yilda 24,7 gacha. Bu, birinchi navbatda, kasallanish darajasining yuqoriligi bilan bog'liq, masalan, O'zbekistonda 7,5:100000 nisbatda va orasida uchraydi bolalar, eng yuqori nisbati 34:100 000.*

*Kalit so'zlar: Epstein-Barr virusi, tahlil, yuqumli mononukleoz, bolalar, CMV, laboratoriya*

### **Relevance**

Infectious mononucleosis (IM) is a common viral infection that typically causes fever, pharyngitis, and lymphadenopathy in young patients. The Epstein-Barr virus (EBV) is the most common cause of IM, followed by cytomegalovirus (CMV) [1-3]. Given that serological testing is associated with limitations regarding its accuracy, availability, and time to receive results, clinical differentiation based on symptoms, signs, and basic tests would be useful [4-6]. We evaluated whether clinical findings could be used to differentiate EBV-IM from CMV-IM.

Infectious mononucleosis is a widespread infectious disease worldwide, most often caused by the γ-herpetic Epstein-Barr virus (EBV), affecting 80-90% of the population [7-10].

Currently, there has been an increase in the incidence rate of infectious mononucleosis among children. To some extent, this is due to the insufficient improvement of diagnostics [11-13]. If we analyze the official data, in 2000-2019, the statistics of EBV infection in Novokuznetsk increased by 27 times: from 0.9 per 100 thousand population in 2000 to 24.7 in 2008. This is primarily due to the high incidence rate, for example, in Uzbekistan, it occurs in the ratio of 7.5:100,000, and among children, the highest ratio is 34:100,000.

The authors acknowledge that Epstein-Barr virus and one of its common forms, infectious mononucleosis, occupy a special place among herpes viruses [14]. It has been proven by researchers that Epstein-Barr virus has many mechanisms of immunosuppression, the "host" organism is less susceptible to the effects of the immune system, and at this time, disturbances in the activity of the immune system increase, leading to the formation of a chronic viral infection. The effect of this virus on the body's immune system is explained by the cessation of the production of natural interferons, the blocking of apoptosis mechanisms. Therefore, the formation of secondary immunodeficiency is indicated. It has been found to help the formation of autoimmune, tumor processes in genetically predisposed individuals.

Clinical manifestations of infectious mononucleosis in children are diverse, which causes certain difficulties in timely and correct diagnosis, as well as problems related to the differential diagnosis of infectious mononucleosis. Misdiagnosis in the prehospital stage is 40-90%, especially among children of early age. The discovery of more convenient diagnostic methods (immunoenzyme analysis, which determines the amount of viral antigens, as well as molecular biology methods - polymerase chain reaction, which is a highly sensitive and specific method for detecting different types of DNA viruses in biological samples), infectious mononucleosis caused by EBV, especially under the influence of several pathogens study of the clinic and diagnostic methods of advanced infectious mononucleosis, as well as specific aspects of their immunopathogenesis and, accordingly, the pathogenetic justification of treatment methods.

**The purpose of the study:** Study of clinical and laboratory characteristics of infectious mononucleosis caused by Epstein-Barr virus and cytomegalovirus.

### **Materials and methods**

This single-center retrospective case-control (case-case) study evaluated medical records of immunocompetent patients with serologically confirmed EBV-IM or CMV-IM from the Medical Hospital, which has 148 beds. The center's ethics committee approved the study's retrospective protocol. Patients were included if they were >14 years old and received inpatient or outpatient treatment for clinically evident and serologically confirmed EBV-IM or CMV-IM at the General Medicine and Emergency Care department between January 2018 and December 2023. Serological

confirmation of EBV-IM was based on a  $<10\times$  result for EBV nuclear antigen (EBNA) plus a  $\geq10\times$  result for viral capsid antigen IgM (VCA-IgM), which were both measured using fluorescent antibody (FA) technique. Serological confirmation of CMV-IM was based on a  $\geq0.8\times$  result for CMV-IgM, which was measured using enzyme immunoassay. All tests were performed by SRL. We regarded the initial dilution concentrations, officially provided by the manufacturer, of each examination kit as cut-off values for EBNA and VCA-IgM; this was due to the methodological difficulty involved in setting clear cut-off values for tests that use the FA technique (we discussed this issue with a staff member of SRL). The CMV-IgM cut-off value was set as 0.8 based on the value provided by the manufacturer. Although values between 0.8 and 1.2 were border-line, we selected the lowest value of the range to obtain the most sensitive results [11]. We intended to categorize patients who had diabetes mellitus, liver cirrhosis, end-stage renal diseases, or cancers or had received immunosuppressants or glucocorticoids as immunocompromised for exclusion. Pregnant women were not intentionally excluded. Doctors in charge of the patients included both resident doctors who had completed their 3rd post-graduate year at least and experienced attending physicians. All laboratory data were collected at the first visit.

### **Result and discussions**

According to the results of the study, 500 children with infectious mononucleosis were retrospectively analyzed, and 120 of them were prospectively analyzed, and all of them formed the main group of our study. 59 (49.1%) of our main group were children living in rural areas. 61 (50.9%) were children living in urban areas. 120 children under control were divided into 3 subgroups according to age to study their nature: 34 (28.3%) children aged 3 to 7 years were included in subgroup 1, 70 (58.3%) children aged 8 to 12 years were included in subgroup 2, and 16 (13%) children aged 13 to 18 years in subgroup 3.4% included children.

It is noteworthy that in all studied age groups, depending on gender, the number of boys prevailed over the total number of children.

It is very difficult to explain this pattern, the reason for this depends on the biological sex characteristics of the child's body, which are not yet clear to us. At the same time, those infected with infectious mononucleosis from 8 to 12 years of age make up more than half of those examined - 58.3%. It should be noted that it can be explained by the anatomo-physiological, pathomorphological, and local and general characteristics of the organism typical of children infected with infectious mononucleosis.

Analysis of the clinical picture of infectious mononucleosis on the 4-10th day of the disease showed that 108 (90%) children had a body temperature of 38.0-38.5°C. The fever was characterized by monotony and lasted  $7.7\pm1.3$  days regardless of taking antipyretic drugs. In 53 children ( $52.0\pm4.8\%$ ) the second wave of fever was recorded on the 9-10th day of the disease. Edema of the face and eyelids remained only in 12 (10%) children, and nasal breathing disorders were found in 70% of patients. 39 (32.5%) patients had purulent discharge in tonsils with reduced tonsillitis symptoms.

According to the results of all studies, the majority of patients were aged 1 to 7 years - 73.1% (79 patients); 21.3% of patients (23 people) are in the age group from 7 to 18 years old, 3.7% (4 people) are children under 1 year old, 1.8% (2 patients) are adults. Early hospitalization was recorded in 44.4% of the first 3 days of the disease, 41% from 4 to 7 days, and 13.9% from 8 to 24 days. In the anamnesis, an increase in body temperature from subfebrile to 40°C was noted in all but one case. Patients complained of stuffy nose, runny nose, cough, sore throat, headache, enlarged neck lymph nodes in various combinations. In the prehospital phase, 12 patients had rash, 9 patients had diarrhea, 8 patients had vomiting, 3 patients had abdominal pain, and 2 patients had meningeal syndrome. Only 5 (4.6%) patients were sent to the hospital with a diagnosis of infectious mononucleosis or suspicion of this disease. The rest often referred with the diagnosis of "acute respiratory viral infection", "tonsillitis", as well as "intestinal infection of unknown etiology" and "meningitis".

The above data allowed us to conclude that the diagnosis of infectious mononucleosis based on appearances is insufficient and requires additional research methods and primary prevention should be improved.



## Conclusion

Thus, the early days of infectious mononucleosis were characterized by symptoms of fever and intoxication, obvious damage to the oropharynx in the form of angina and difficulty breathing through the nose, enlarged liver and spleen, which made it possible to make a tentative diagnosis of the disease in the early days. Hyperthermia remained during the disease period, signs of tonsillitis decreased, hepatomegaly worsened, and clinical blood analysis showed an increase in ERT, leukocytosis, lymphocytosis, and the appearance of atypical mononuclear cells up to 52%. Complications developed in 27.4% of patients.

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