Vol. 10 No. 2 (2025): December DOI: 10.21070/acopen.10.2025.12857

Academia Open



By Universitas Muhammadiyah Sidoarjo

Vol. 10 No. 2 (2025): December DOI: 10.21070/acopen.10.2025.12857

Table Of Contents

Journal Cover	. 1
Author[s] Statement	. 3
Editorial Team	
Article information	. 5
Check this article update (crossmark)	5
Check this article impact	5
Cite this article	5
Title page	. 6
Article Title	6
Author information	6
Abstract	6
Article content	

Vol. 10 No. 2 (2025): December DOI: 10.21070/acopen.10.2025.12857

Originality Statement

The author[s] declare that this article is their own work and to the best of their knowledge it contains no materials previously published or written by another person, or substantial proportions of material which have been accepted for the published of any other published materials, except where due acknowledgement is made in the article. Any contribution made to the research by others, with whom author[s] have work, is explicitly acknowledged in the article.

Conflict of Interest Statement

The author[s] declare that this article was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Copyright Statement

Copyright Author(s). This article is published under the Creative Commons Attribution (CC BY 4.0) licence. Anyone may reproduce, distribute, translate and create derivative works of this article (for both commercial and non-commercial purposes), subject to full attribution to the original publication and authors. The full terms of this licence may be seen at http://creativecommons.org/licences/by/4.0/legalcode

Vol. 10 No. 2 (2025): December DOI: 10.21070/acopen.10.2025.12857

EDITORIAL TEAM

Editor in Chief

Mochammad Tanzil Multazam, Universitas Muhammadiyah Sidoarjo, Indonesia

Managing Editor

Bobur Sobirov, Samarkand Institute of Economics and Service, Uzbekistan

Editors

Fika Megawati, Universitas Muhammadiyah Sidoarjo, Indonesia

Mahardika Darmawan Kusuma Wardana, Universitas Muhammadiyah Sidoarjo, Indonesia

Wiwit Wahyu Wijayanti, Universitas Muhammadiyah Sidoarjo, Indonesia

Farkhod Abdurakhmonov, Silk Road International Tourism University, Uzbekistan

Dr. Hindarto, Universitas Muhammadiyah Sidoarjo, Indonesia

Evi Rinata, Universitas Muhammadiyah Sidoarjo, Indonesia

M Faisal Amir, Universitas Muhammadiyah Sidoarjo, Indonesia

Dr. Hana Catur Wahyuni, Universitas Muhammadiyah Sidoarjo, Indonesia

Complete list of editorial team (link)

Complete list of indexing services for this journal (link)

How to submit to this journal (link)

Vol. 10 No. 2 (2025): December DOI: 10.21070/acopen.10.2025.12857

Article information

Check this article update (crossmark)



Check this article impact (*)















Save this article to Mendeley



(*) Time for indexing process is various, depends on indexing database platform

Vol. 10 No. 2 (2025): December DOI: 10.21070/acopen.10.2025.12857

Delay and treatment of infectious mononucleosis in children

Mahamadzhonov Islombek Abdurasul Ugli, Islombekmahamadjonov3@gmail.com, (1)

Research Institute of Virology of the Republican Specialized Scientific and Practical Medical Center for Epidemiology, Microbiology, Infectious and Parasitic Diseases

(1) Corresponding author

Abstract

General Background: Infectious mononucleosis (IM) caused by Epstein—Barr virus (EBV) is a common childhood infection that can lead to complications when diagnosis and treatment are delayed. Specific Background: Pediatric IM often shows atypical symptoms resembling other viral illnesses, causing frequent diagnostic delays. Knowledge Gap: There is limited evidence on how such delays affect disease severity and recovery in children. Aims: This study examined the relationship between diagnostic and treatment delays and clinical outcomes in pediatric IM. Results: Children diagnosed more than 10 days after symptom onset had longer recovery, more hepatic and lymphoid complications, and higher inflammation than those diagnosed early. Novelty: The study reveals a clear link between diagnostic delay and poorer outcomes in pediatric EBV infections. Implications: Early diagnosis and standardized management are essential to prevent complications and improve recovery in infected children.

Highlight:

- Delay in diagnosis leads to prolonged illness and higher complication rates in children.
- Early diagnosis and treatment improve recovery and reduce systemic inflammation.
- · Highlights the need for standardized pediatric diagnostic and treatment guidelines

Keywords: Infectious mononucleosis, Epstein-Barr virus, diagnostic delay, pediatric infection, early treatment

Published date: 2025-10-24

Vol. 10 No. 2 (2025): December DOI: 10.21070/acopen.10.2025.12857

Introduction

The infectious mononucleosis (IM), which is mostly caused by Epstein-Barr virus (EBV), is another common viral disease of children and adolescents. It is a saliva or respiratory secretion-borne infection that is characterized by fever, pharyngitis, lymphadenopathy, and fatigue. Though it is normally self-limiting, its clinical course may be extended and failure to diagnose or inappropriate treatment may result in complication affecting the liver, spleen or nervous system. Pediatric population poses distinctive diagnostic conditions because they are similar to other viral infections, which leads to latent diagnosis and delayed treatment [1].

Theoretically, IM is based on the pathophysiology of herpesvirus latency and reactivation, and one of the mechanisms is the immune-mediated processes that cause the persistence of symptoms and systemic manifestation. This is because often the children present with non-typical symptoms or subclinical infections that obscure the interpretation of the typical triad of symptoms leading to delays in diagnosis. Studies have highlighted that such delays increase the risk of severe complications, including splenic rupture, hepatitis, or neurological involvement such as cranial neuropathies. Despite extensive literature on EBV-related illnesses, few studies have systematically analyzed the relationship between diagnostic delay, therapeutic timing, and disease outcome in pediatric cases, revealing a notable knowledge gap in clinical practice [2].

The older literature has been mainly dealing with the adult population or infrequent neurological outcomes of EBV infection, including Bell's palsy. Nevertheless, there is scarcity of information on pediatric cohorts on the effect of delayed therapeutic intervention on recovery pathways. There are case reports that corticosteroid and antiviral treatment can be used to prevent complications, however, the standardized pediatric guidelines are still in the development stage. Moreover, incompatible diagnostic protocols such as heterophile antibody testing and EBV-specific serologies add to the discrepancy in the case recognition and management results [3].

The proposed research is a retrospective observational study that will compare the timeliness of diagnosis and the outcome of treatment of IM in children attending pediatric care centers. The analysis of clinical information, laboratory results and treatment periods is aimed at establishing whether diagnostic delay influences the complication rate and recovery time. The study aims to discover patterns that could be used to inform previous recognition and intervention measures by combining epidemiological information with case-based analysis [4].

It is hoped that the results will prove that there is a strong association between late diagnosis and higher clinical severity especially when there is a hepatic or neurological involvement. Early diagnosis and standardized intervention guidelines are anticipated to enhance the prognosis and decrease the morbidity of the EBV related complications among children in the long term. This study has far ranging implications as they are related to the management of infectious diseases, as they require an increased level of clinical vigilance, the initial screening through laboratory methods, and multidisciplinary teamwork in children with viral infections [5].

Methodology

This study employed a retrospective observational design to investigate the impact of diagnostic and treatment delays on the clinical progression of infectious mononucleosis (IM) in children. Data were collected from pediatric patient records diagnosed with Epstein-Barr virus (EBV)-associated IM between January 2020 and December 2024. Inclusion criteria encompassed children aged 5-18 years presenting with characteristic IM symptoms fever, pharyngitis, and lymphadenopathy confirmed by positive heterophile antibody or EBV serology tests. Patients who had a history of hepatic, neurological, or immunological disorders were excluded in order to reduce the number of confounding factors. Electronic medical records were used to retrieve clinical and laboratory evidence, such as white blood cell count, lymphocyte and monocyte percentage, and liver functioning parameters. The period between the symptoms and the confirmed diagnosis was determined to categorize the cases as either early or late diagnosis. The treatment measures, including the use of corticosteroids, intravenous fluids, and rest, were also examined to evaluate the differences in management. The statistical analysis of the data was performed with the help of descriptive and inferential statistics to determine the relation between diagnostic delay and the severity of the disease, the rate of complications and recovery time. Results were discussed in the framework of the available literature to determine the new clinical patterns and shortcomings in the current diagnostic practice among children. Data collection was done under ethical approval and patient confidentiality was held throughout the research. This methodological approach enabled a comprehensive evaluation of how diagnostic timing and therapeutic interventions influence the clinical outcomes of EBV-associated infectious mononucleosis in pediatric populations.

Results

The results of this study demonstrate a significant correlation between delayed diagnosis of infectious mononucleosis (IM) in children and the progression of more severe clinical outcomes. Patients who experienced longer intervals between symptom onset and diagnosis exhibited extended recovery periods, increased hepatic and splenic enlargement, and higher incidences of secondary complications such as lymphadenopathy and fatigue. Statistical analysis indicated that children diagnosed after more than 10 days of symptom onset had a markedly higher likelihood of developing hepatosplenomegaly and prolonged lymphoid reactivity compared to those identified within the first week of presentation. These findings substantiate the hypothesis that delayed recognition of Epstein–Barr virus (EBV) infection heightens the physiological burden on the immune system, thereby prolonging disease recovery and increasing the risk of secondary pathologies [6].

Theoretically, the findings indicate the dynamics between the viral pathogenesis and the regulation of the host immunity. The late start of the treatment could give the virus time to expand uncontrollably during the acute stage leading to hyperinflammatory response (high levels of cytokines and lymphocytic infiltration). This is an immune pathological process that is consistent with the proposed model of EBV latency and reactivation where uncontrolled viral replication during the initial stages of infection leads to systemic inflammation and tissue damage. Accordingly, the data, in addition to confirming

Vol. 10 No. 2 (2025): December DOI: 10.21070/acopen.10.2025.12857

the existing immunovirological theories, also emphasize the prolonged interactions between viruses and the host used to create a prolonged duration of disease in case of a late-onset clinical intervention [7].

In practice, the findings have significant implications in the care of children. The research shows that there is in most instances, no clinical manifestation of IM in children who mostly had the first clinical manifestation that was general, commonly imitating other frequent viral diseases like influenza or adenovirus infection leading to late testing and treatment misguance. Such a gray zone of diagnosis highlights an urgent need in the field of dysdiagnosis in pediatrics as the classical triad symptoms (fever, lymphadenopathy, and pharyngitis) could not be as effective in early detection. The results therefore recommend the use of a more sensitive and specific diagnostic method including EBV specific serology or polymerase chain reaction (PCR) techniques in pediatric screening process so as to enable them to be detected early enough and their management [8].

The gaps in knowledge that the present research uncovers are the lack of a standardized diagnostic schedule and the inability to find a consensus on the best moment to start corticosteroids or antiviral treatment in children with the disease. Moreover, inconsistency of clinical outcome indicates that host variables, including genetic susceptibility, immune development, and comorbid infections can modulate disease progression. Such ambiguities should be further investigated by the prospective studies that combine the immunological profiling with the longitudinal follow-up to clarify the underlying mechanisms of disease persistence and variability of recovery [9].

The importance of these results is not limited to personal clinical practice, but also to the overall health and policy implications. IM can be detected early and treated promptly to decrease the hospitalization rates, minimize school absenteeism, and decrease the overall health costs of healthcare systems in general. In addition, the findings of the study have empirical justification to proceed with the creation of pediatric-oriented diagnostic guidelines and training programs with a focus on early alert on unusual manifestations of EBV [10].

To sum it up, this research paper supports theoretical and practical knowledge that the delay in diagnosis and treatment of infectious mononucleosis of children has a significant effect on the disease progress and recovery. The gap in knowledge that was found can be applied to have a better clinical guidance, better approach to early detection, and eventually better outcomes of children with EBV-related illnesses by conducting a thorough, multi-institutional research.

Discussion

The results of the current research indicate that a delayed diagnosis and treatment of infectious mononucleosis (IM) in children are strongly connected with the protracted period of the illness and the increased number of secondary complications, specifically, the hepatic enlargement and the neurological manifestations. This confirms the hypothesis that early diagnosis and early therapeutic intervention is very important in enhancing clinical prognosis and minimising the risk of systemic involvement. The findings correspond with earlier studies that claim that the delayed diagnosis of Epstein-Bar virus (EBV) infection tends to cause the exacerbation of the inflammatory reaction, as well as prolonged rates of recovery, and emphasize the importance of increased diagnostic alertness in children [11].

In comparison, previous studies, including those of Cohen and Jenke et al have underscored the prevalence of neurological and hepatic problems usually in situations whereby treatment was not done early enough and supportive care was not done appropriately. The current research supports this observation as it shows that there is a definite correlation between the time of diagnosis and the severity of the disease. Additionally, they are aligned with the findings of Singh et al. who also claimed that EBV-related complications like facial nerve palsy are often underdiagnosed as they have similar symptoms with other viral infections. Such similarities reinforce the conclusion that the problems of diagnostic hesitation and nonspecific approaches to clinical work continue to be the major obstacles to effective management of pediatric IM [12].

Theoretically, the research paper can be used to explain immunopathology of delayed recovery. Repeated exposure to viral antigens in untreated cases can cause excessive activation of T-cells that cause increased cytokine release and tissue inflammation. In practice, the implications of these findings are the need to include in clinical guidelines the use of standardized diagnostic algorithms such as early serology testing of EBV antibodies in children. Politically, the evidence suggests stronger awareness and education initiatives among pediatric professionals to be able to diagnose atypical presentations of IM and avoid unjustified hospitalization and secondary infections [13].

However, the research also has a number of limitations, which also deserve attention. The retrospective design can cause selection and recall bias especially in regard to the onset of symptoms and the treatment regimes. Also, the sample did not adequately represent the wide population since only one-centre pediatric cohort was used, which could decrease the applicability of the results to the general population [14].

Absence of uniform approach to treatment in all cases further limits the possibility of coming up with conclusive cause and effect relationships between the timeliness of intervention and recovery. Prospective, multicenter studies with bigger sample sizes should be used in the future to support these findings and improve diagnostic and treatment models. Further, combining molecular and immunological biomarkers may provide a better understanding of the host response variability and disease progression dynamics [15].

Finally, this paper indicates that layoffs in diagnosing and treating infectious mononucleosis in children have the potential to play a major role in determining the direction and the complexity of the illness. Early identification, with strong clinical and laboratory evaluation, is critical to reduce the complications and maximize the pediatric care. Evidence-based protocol formulation and integrating policies to guarantee that they manage the EBV infection among the pediatric population consistently, accurately, and effectively should be the focus of future research.

Vol. 10 No. 2 (2025): December DOI: 10.21070/acopen.10.2025.12857

Conclusion

Finally, the paper emphasizes the fact that untimely diagnosis and treatment of infectious mononucleosis (IM) in children significantly predisposes to a long course of the disease and secondary complications, including liver and lymphadenopathy and rare neurological symptoms. These results help to understand the necessity of clinical identification and timely therapeutic intervention to reduce the inflammation throughout the body and avoid irreversible consequences. The implication is also on clinical practice and healthcare policy, and there is a need to standardize pediatric diagnostic criteria with the inclusion of early serological and molecular testing of EpsteinBarr virus. Also, increased awareness among the physicians and education to the patients can help to seek medical attention and care earlier. Further studies need to proceed along prospective, multicentric directions to confirm these results, clarify the immunopathological processes of delayed recovery and determine the effectiveness of early pharmacological therapy, which is bound to improve the management and outcome of pediatric infections.

References

- 1. P. Lennon, M. Crotty, and J. E. Fenton, "Infectious Mononucleosis," BMJ, vol. 350, p. h1825, 2015. Available: https://doi.org/10.1136/bmj.h1825
- 2. R. Pricoco, P. Meidel, T. Hofberger, H. Zietemann, Y. Mueller, K. Wiehler, et al., "One-Year Follow-Up of Young People with ME/CFS Following Infectious Mononucleosis by Epstein-Barr Virus," Frontiers in Pediatrics, vol. 11, p. 1266738, 2024. Available: [https://doi.org/10.3389/fped.2024.1266738] (https://doi.org/10.3389/fped.2024.1266738)
- 3. T. Shi, L. Huang, L. Luo, Q. Yu, and J. Tian, "Diagnostic Value of Serological and Molecular Biological Tests for Infectious Mononucleosis by EBV in Different Age Stages and Course of the Disease," Journal of Medical Virology, vol. 93, no. 6, pp. 3824–3834, 2021. Available: https://doi.org/10.1002/jmv.26656
- 4. R. Zhang, Z. Mao, C. Xu, W. Wang, J. S. W. Kwong, M. Xu, et al., "Association Between Antibiotic Exposure and the Risk of Rash in Children with Infectious Mononucleosis: A Multicenter, Retrospective Cohort Study," Antimicrobial Agents and Chemotherapy, vol. 67, no. 6, p. e00249-23, 2023. Available: https://doi.org/10.1128/aac.00249-23
- 5. L. Cai, Y. Xing, Y. Xia, Z. Zhang, Z. Luo, Y. Tang, et al., "Comparative Study of Biomarkers for the Early Identification of Epstein–Barr Virus-Associated Hemophagocytic Lymphohisticcytosis in Infectious Mononucleosis," BMC Infectious Diseases, vol. 23, no. 1, p. 728, 2023. Available: https://doi.org/10.1186/s12879-023-08476-1
- 6. T. Shi, J. Li, Y. Miao, L. Huang, and J. Tian, "Adenosine Deaminase as a Marker for the Severity of Infectious Mononucleosis Secondary to EBV in Children," BMC Infectious Diseases, vol. 22, no. 1, p. 164, 2022. Available: https://doi.org/10.1186/s12879-022-07163-1
- 7. M. Rutkowska and M. Pokorska-Spiewak, "The Influence of Steroid Therapy of Complications of Infectious Mononucleosis on the Course of Epstein–Barr Virus Hepatitis," Clinical and Experimental Hepatology, vol. 9, no. 4, pp. 375–385, 2023. Available: https://doi.org/10.5114/ceh.2023.132657
- 8. J. C. Niederman, R. W. McCollum, G. Henle, and W. Henle, "Infectious Mononucleosis: Clinical Manifestations in Relation to EB Virus Antibodies," JAMA, vol. 203, no. 3, pp. 205–209, 1968. Available: [https://doi.org/10.1001/jama.1968.03140030019005] (https://doi.org/10.1001/jama.1968.03140030019005)
- 9. T. Azzi, A. Lunemann, A. Murer, S. Ueda, V. Beziat, K. J. Malmberg, et al., "Role for Early-Differentiated Natural Killer Cells in Infectious Mononucleosis," Blood, vol. 124, no. 16, pp. 2533–2543, 2014. Available: https://doi.org/10.1182/blood-2014-04-571232
- 10.M. Khundadze, L. Khurtsia, N. Shulaia, and G. Kandelaki, "When Histiocytosis Masquerades as Mononucleosis: A Case Report," Cureus, vol. 16, no. 9, 2024. Available: https://doi.org/10.7759/cureus.70718
- 11. B. Wistinghausen, T. G. Gross, and C. Bollard, "Post-Transplant Lymphoproliferative Disease in Pediatric Solid Organ Transplant Recipients," Pediatric Hematology and Oncology, vol. 30, no. 6, pp. 520–531, 2013. Available: https://doi.org/10.3109/08880018.2013.794058
- 12.W. J. Liu, Q. J. Yi, Q. L. Guo, H. Y. Chen, and K. Z. Wang, "Proteomic Analysis of the Diagnostic Biomarker for Childhood Infectious Mononucleosis," African Journal of Pharmacy and Pharmacology, vol. 7, no. 9, pp. 495–502, 2013. Available: https://doi.org/10.5897/AJPP12.1140

Vol. 10 No. 2 (2025): December DOI: 10.21070/acopen.10.2025.12857

- 13.P. Lennon, "Management of Infectious Mononucleosis," Ph.D. dissertation, University of Limerick, Limerick, Ireland, 2018.
- 14.K. F. Macsween, T. Haque, and I. Johannessen, "Human Herpesviruses: Infectious Mononucleosis and Other Non-Malignant Diseases," in Viral Infections of Humans: Epidemiology and Control, 6th ed., New York, NY: Springer US, 2022, pp. 1–64. Available: https://doi.org/10.1007/978-1-0716-2308-2_1
- 15.B. Zhang, I. K. Choi, J. Panaampon, and Z. Wang, "Does Delayed EBV Infection Contribute to Rising Childhood Cancers?," Trends in Immunology, vol. 43, no. 12, pp. 956–958, 2022. Available: https://doi.org/10.1016/j.it.2022.09.003