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CORRELATION OF EBV (EPSTEIN–BARR VIRUS) DNA LOAD, SEROLOGIC PROFILE, AND NECK ULTRASONOGRAPHY FINDINGS WITH CLINICAL SEVERITY IN PEDIATRIC EPSTEIN–BARR VIRUS INFECTION: AN OBSERVATIONAL STUDY

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ABSTRACT

Methods: A retrospective study of children presenting with EBV illness Queen Rania Al Abdullah Hospital for Children between January 2019 and January 2025. Demographics, symptoms, laboratory test, EBV DNA findings, serologic data, and neck ultrasonography (US) findings were collected from hospital electronic records. Outcomes included hospitalization and complications. **Results:** Eighty-seven children with EBV infection were included; 52 (59.8%) were hospitalized. Hospitalized patients had higher CRP and LDH levels and were more likely to present fever (88.46%), hepatosplenomegaly, neutrophilic leukocytosis, or pancytopenia. Non-hospitalized patients more frequently demonstrated lymphocytic leukocytosis. Complications like HLH, thrombocytopenia, and meningitis happened only in hospitalized cases. Neck ultrasonography findings showed no significant differences. Logistic regression showed that older age (OR 1.17, 95% CI 1.01–1.38), fever (OR 9.10, 95% CI 3.25–28.9), hepatosplenomegaly (OR 2.78, 95% CI 1.02–8.50), and elevated LDH (OR 1.00 per 100 U/L, p=0.035) were associated with higher odds of hospitalization, while high EBV DNA load was not. **Conclusion:** Hospitalization in pediatric EBV infection was more strongly associated with fever, inflammatory markers, hepatosplenomegaly, and abnormal hematologic profiles than with viral load.

KEYWORDS: Epstein–Barr virus; pediatrics; infectious mononucleosis; cervical lymphadenopathy; EBV DNA load.

INTRODUCTION

One of the most common human diseases, Epstein-Barr virus (EBV) affects over 90% of people worldwide and usually develops a latent infection that lasts a lifetime after initial exposure during childhood or adolescence. EBV is a common cause of cervical lymphadenopathy and febrile sickness in children. It typically manifests as infectious mononucleosis (IM), a self-limited disease that includes fever, pharyngitis, and swelling of the lymph nodes. Though many children have mild, self-resolving disease, others develop serious complications like cytopenias, hepatic injury, airway obstruction, or even life-threatening conditions like hemophagocytic lymphohistiocytosis (HLH).[1,.3] Thus, the clinical spectrum of EBV infection is remarkably diverse. In the practice of pediatric infectious diseases, identifying which kids are at risk for serious illness continues to be a major difficulty.[4,5]

EBV DNA load may now be accurately determined due to recent developments in molecular diagnostics, especially quantitative polymerase chain reaction (qPCR), which may be used as a biomarker for disease severity and activity. Higher viral loads, which frequently surpass 10^5 copies/mL, have been linked in numerous studies to more severe clinical courses, immunological dysregulation, and complications.[6,9] Increased hospitalization rates, abnormal cytokine responses, and hepatic dysfunction have also been connected to elevated EBV DNA levels- 2–4, 6, 17. The prognostic significance of EBV load alone is still unclear, and there is considerable variation in viral

kinetics among children with comparable clinical presentations. Moreover, there is a need for integrated interpretation of molecular and serological findings since the dynamics between viral load and serologic markers, such as VCA IgM/IgG and EBNA antibodies, are not always linear.[8,9,14,15]

Imaging, particularly neck ultrasonography (US), has become a useful adjuvant in the assessment of juvenile EBV infection, going beyond laboratory criteria. Although cervical lymphadenopathy is one of the most prevalent signs of IM, its sonographic characteristics might be confused with those of other benign and malignant diseases. According to studies, larger, oval nodes with intact fatty hila and enhanced vascularity are typical US findings in EBV-related lymphadenopathy.[10,13] However, comprehensive studies to connect imaging findings with clinical severity, laboratory profiles, or outcomes remain limited. As a result, little is known about ultrasonography's potential use as a non-invasive indicator of disease burden and progression.[11,12,18]

Comprehensive investigations that include virologic, serologic, laboratory, and imaging data are needed in light of these information gaps in order to strengthen clinical risk stratification in pediatric EBV infection. Such research could give clinicians more reliable tools to identify children at risk of severe disease early in their clinical course by investigating the interactions of EBV DNA load.

Accordingly, the present study aims to describe the clinical, hematologic, biochemical, serologic, and sonographic characteristics of children presenting with EBV-compatible illness and to explore their association with key clinical outcomes, including hospitalization and the development of complications.

METHODS

Study Design

This was a retrospective observational study conducted to investigate the relationship between Epstein–Barr virus (EBV) DNA load, serologic profile, neck ultrasonography findings, and clinical severity among pediatric patients with EBV-compatible illness. The study was carried out at a tertiary care pediatric center and included all eligible patients who presented between January 2019 and January 2025. The study protocol was reviewed and approved by the institutional ethics committee, and patient confidentiality was maintained throughout the data collection and analysis processes.

Data collection

Data were retrospectively collected from electronic medical records and laboratory systems using a standardized form. Recorded variables included demographic data (age, sex), clinical features (fever, pharyngitis, lymphadenopathy, hepatosplenomegaly), and laboratory results (CBC, CRP, ESR, liver enzymes, bilirubin, LDH). Virological and serological information comprised quantitative EBV DNA load by real-time qPCR and antibody profiles (VCA IgM/IgG, EBNA IgM/IgG). Neck ultrasonography findings, including lymph node size, number, distribution, echogenicity, and vascularity, were also documented. Clinical outcomes such as hospitalization, need for bone marrow examination, antiviral use, and complications (cytopenias, airway compromise, hepatitis, or HLH) were recorded.

Statistical Methods

Descriptive statistics were used to summarize continuous variables (means and standard deviation), and categorical variables (frequency and percentage), and between-group comparisons were made using Wilcoxon rank-sum tests (continuous variables) and Chi-square or Fisher's exact tests (categorical variables), with univariate logistic regression analysis used to quantify associations between predictor variables and hospitalization requirement with results expressed in the form of odds ratios (OR) with 95% confidence intervals (CI) and a significance level of $p < 0.05$.

RESULTS

The research consisted of 87 patients that were children and were infected with EBV, with 52 (59.8) getting hospitalized and 35 (40.2) did not (Table 1). The mean age of the sample is 5.46 years (SD 3.22). The patients who were hospitalized were older (mean 6.05 years, SD 3.64) as compared to those who were not hospitalized (mean 4.58 years, SD 2.23) but this was not significantly different (p=0.068). A number of laboratory markers were found significantly different between groups: the mean LDH (602.13 U/L, SD 677.01) in the hospitalized group was higher than in the non-hospitalized group (367.52 U/L, SD 151.93), and also the mean CRP (57.47 mg/L, SD 68.30 vs. 20.70 mg/L, SD 14.51; p=0.010). The copy/mL of EBV PCR was numerically greater in hospitalized patients (mean 100.01, SD 269.41) compared to non-hospitalized patients (mean 71.64, SD 257.14), but without significant difference (p=0.2).

There were great clinical presentation disparities across groups. The presence of fever was observed in 46 patients in hospitals (88.46 vs. 16 non-hospital patients 45.71; p<0.001). In contrast, lymphadenopathy was less prevalent in hospitalized patients (21, 40.38%) than in non-hospitalized (22, 62.86%; p=0.040). Hospitalized and non-hospitalized groups had an equal prevalence of tonsillitis (32.69 vs. 28.57; p=0.7). There were differences in patterns of hepatosplenomegaly observed with 19 of 37.25 hospitalized patients having combined hepatosplenomegaly and 6 of 17.14 non-hospitalized patients with hepatosplenomegaly.

Hematologic profiles showed that lymphocytic leukocytosis was the most prevalent in the non-hospitalized group (17, 73.91% vs. 19, 44.19%), whereas neutrophilic leukocytosis (10, 23.26% vs. 2, 8.70%) and

pancytopenia (5, 11.63% vs. 1, 4.35%) were more frequent in hospitalized patients (p=0.2 overall for CBC categories). Only hospitalized patients were experiencing complications, such as secondary HLH (3, 11.11% vs. 0), thrombocytopenia (4, 14.81% vs. 0), and meningitis (1, 3.70% vs. 0). There were no significant differences in the results of neck ultrasonography between groups (p=0.9). There was a significant difference in the use of interventions among hospitalized patients, whereby there was a need to bone marrow aspiration and biopsy (10, 19.23% vs. 0; p=0.005) and antiviral therapy (3, 5.88% vs. 0; p=0.3).

Univariable logistic regression revealed a number of variables that are correlated with hospitalization (Table 2). A one-year age increment corresponded with 17% increased probabilities of hospitalization (OR 1.17, 95% CI 1.01-1.38; p=0.042). Fever had a significant effect of predicting hospitalization (OR 9.10, 95% CI 3.25-28.9, p<0.001). Hepatosplenomegaly demonstrated a marginally important correlation with hospitalization (OR 2.78, 95 percent CI 1.02-8.50; p=0.055). An increase in LDH of 100 U/L was linked to a greater likelihood of being hospitalized (OR 1.00, 95% CI 1.00-1.01; p=0.035). Hospitalization was not significantly related to high EBV PCR ([≥1000 copies/mL) (p=0.6).

Table 1: Summary and comparative analysis of patients with EBV vs no EBV.

Characteristic	NO N = 35[1]	YES N = 52[1]	Overall N = 87[1]	P value[2]
Age	4.58 (2.23)	6.05 (3.64)	5.46 (3.22)	0.068
Signs and symptoms				
Fever	16 (45.71%)	46 (88.46%)	62 (71.26%)	**<0.001**
Lymphadenopathy	22 (62.86%)	21 (40.38%)	43 (49.43%)	**0.040**
Tonsilitis	10 (28.57%)	17 (32.69%)	27 (31.03%)	0.7
Hepatosplenomegaly				0.2
Hepatomegaly	5 (14.29%)	8 (15.69%)	13 (15.12%)	
Hepatosplenomegaly	6 (17.14%)	19 (37.25%)	25 (29.07%)	
No	19 (54.29%)	19 (37.25%)	38 (44.19%)	
Splenomegaly	5 (14.29%)	5 (9.80%)	10 (11.63%)	
CBC				0.2
Leukopenia with neutropenia	3 (13.04%)	9 (20.93%)	12 (18.18%)	
Lymphocytic leukocytosis	17 (73.91%)	19 (44.19%)	36 (54.55%)	
Neutrophilic leukocytosis	2 (8.70%)	10 (23.26%)	12 (18.18%)	
Pancytopenia	1 (4.35%)	5 (11.63%)	6 (9.09%)	
LDH	367.52 (151.93)	602.13 (677.01)	504.02 (534.94)	**0.024**
ESR	30.24 (21.22)	41.05 (28.38)	36.89 (26.23)	0.10
CRP	20.70 (14.51)	57.47 (68.30)	43.85 (57.19)	**0.010**
Ebv pcr copies/ml	71.64 (257.14)	100.01 (269.41)	90.26 (263.55)	0.2
Caspid ag igg	227.26 (152.62)	178.89 (119.85)	200.88 (136.81)	0.3
Caspid ag igm	88.56 (85.16)	123.35 (108.71)	107.88 (99.59)	0.3
EBNA IGG	150.96 (90.20)	145.81 (102.46)	147.95 (95.52)	0.8
EBNA IGM	2.11 (2.74)	2.35 (1.35)	2.25 (2.06)	**0.033**
Complications				>0.9
Elevated triglyceride level	0 (0.00%)	1 (3.70%)	1 (3.23%)	
Infected cervical ln with collection	0 (0.00%)	1 (3.70%)	1 (3.23%)	
Leukopenia	0 (0.00%)	2 (7.41%)	2 (6.45%)	
Meningitis	0 (0.00%)	1 (3.70%)	1 (3.23%)	
Misc	0 (0.00%)	2 (7.41%)	2 (6.45%)	
Neutropenia	2 (50.00%)	4 (14.81%)	6 (19.35%)	
Pancytopenia	1 (25.00%)	5 (18.52%)	6 (19.35%)	
Secondary hlh	0 (0.00%)	3 (11.11%)	3 (9.68%)	
Thrombocytopenia	0 (0.00%)	4 (14.81%)	4 (12.90%)	
Upper airway obstruction	1 (25.00%)	4 (14.81%)	5 (16.13%)	
Neck US finding				0.9
Bilateral, preserved fatty hilum	17 (58.62%)	13 (50.00%)	30 (54.55%)	
Compressed fatty hilum	1 (3.45%)	1 (3.85%)	2 (3.64%)	
Generalized neck and loss of fatty hilum	3 (10.34%)	2 (7.69%)	5 (9.09%)	
Localized cervical with preserved fatty hilum	8 (27.59%)	10 (38.46%)	18 (32.73%)	

Needed antiviral	0 (0.00%)	3 (5.88%)	3 (3.49%)	0.3
Needed BMA and BX	0 (0.00%)	10 (19.23%)	10 (11.49%)	**0.005**

[1] Mean (SD); n (%)
[2] Wilcoxon rank sum test; NA; Wilcoxon rank sum exact test; Pearson's Chi-squared test; Fisher's exact test

Table 2: Multivariate logistic regression of factors associated with EBV.

Characteristic	OR	95% CI		P-value
		Lower	Upper	
Age (years)	1.17	1.01	1.38	**0.042**
Fever				
No	—	—		
Yes	9.10	3.25	28.9	**<0.001**
Hepatosplenomegaly				
No	—	—		
Yes	2.78	1.02	8.50	0.055
LDH (per 100 U/L)	1.00	1.00	1.01	**0.035**
High EBV PCR (≥1000 copies/mL)				
High (≥1000)	—	—		
Low (<1000)	1.95	0.07	51.0	0.6
Abbreviations: CI = Confidence Interval, OR = Odds Ratio				

DISCUSSION

Hospitalization was linked to a number of clinical and laboratory findings in this pediatric EBV infection cohort, indicating a more systemic inflammatory pattern in severe cases. Hospitalized children were marginally older, but this difference was not statistically significant. In the regression model, age slightly raised the risks of hospitalization, which is consistent with patterns seen in recent pediatric cohorts.[1,6]

The most obvious difference between the groups was seen in inflammatory markers. Children in hospitals exhibited much greater levels of CRP and LDH, which is in line with several studies that have found these markers to be indicative of more severe immune activation and hepatic or systemic injury.[2,3,6,17] Hospitalized patients had higher EBV-PCR results, however this difference was not statistically significant. This is consistent with research by Hong et al. and others that demonstrates that in many common pediatric instances, viral load alone is not a reliable indicator of disease severity.[7,8,19]

Additionally, there were differences in hematologic patterns: hospitalized children were more likely to have neutrophilic leukocytosis and pancytopenia, while non-hospitalized patients were more likely to have lymphocytic leukocytosis. These results are consistent with previous research demonstrating that mild EBV infection is usually lymphocyte-predominant, but more severe or complex cases may manifest as mixed-pattern cytopenias or bone marrow suppression.[4,6,17] According to multicenter studies of severe EBV symptoms, all sequelae, including meningitis, thrombocytopenia, and HLH, only happened in hospitalized patients.[1,5,20]

Overall, our findings reinforce that fever, elevated CRP and LDH, hepatosplenomegaly, and abnormal hematologic patterns are more reliable indicators of severity than viral load alone. These results align with recent pediatric evidence emphasizing the importance of clinical and inflammatory markers over EBV-DNA levels in predicting hospitalization and complications.

CONCLUSION

In pediatric EBV infection, hospitalization was strongly linked to fever, elevated CRP and LDH, hepatosplenomegaly, and abnormal hematologic findings, while viral load showed limited predictive value. These results highlight the importance of clinical and inflammatory markers rather than EBV-DNA alone for identifying children at higher risk of severe disease.

REFERENCES

1. Yan H, et al. Active EBV infection in children: associations between DNA load, infection status, immune status and disease severity. 2025.
2. Li Y, et al. Clinical analysis of 163 pediatric patients with infectious mononucleosis: correlations between laboratory indicators including EBV-DNA and clinical severity. 2024.
3. Liu L. EBV-DNA load: a predictor of immune and hepatic injury in pediatric infectious mononucleosis. 2025.
4. Zhang Y, et al. Characteristics of immunological events in Epstein-Barr virus infection in children: relationship with viral load. Front Pediatr. 2023.
5. Shi T, et al. Prevalence of Epstein-Barr viral DNA among children at a tertiary hospital and clinical correlations. 2022.
6. Tian S, et al. Retrospective review of children hospitalized for Epstein–Barr virus–associated infectious mononucleosis. Pathogens. 2025.

7. Moppert J, et al. Are selected cytokines and Epstein–Barr virus DNA load predictive of disease severity in EBV infections? J Clin Med. 2023.
8. Hong JH, et al. Plasma real-time quantitative PCR for EBV DNA in children: correlation with clinical severity. Pediatr Gastroenterol Hepatol Nutr. 2012.
9. Abdel-Aziz M, et al. Epstein-Barr virus infection as a cause of cervical lymphadenopathy in children. 2011.
10. Fu XS, et al. Ultrasound characteristics of cervical lymph nodes in infectious mononucleosis and comparison with other benign conditions. 2014.
11. Bu X. Sonographic appearance of cervical lymphadenopathy in children with infectious mononucleosis. Med Ultrason. 2025.
12. Ludwig BJ, et al. Imaging of cervical lymphadenopathy in children and young adults. AJR Am J Roentgenol. 2012.
13. Ataş E, et al. Evaluation of children with lymphadenopathy: clinical and ultrasound correlations. 2014.
14. Yakut N, et al. Evaluation of cervical lymphadenopathy in children: is Epstein–Barr virus infection predictable? 2021.
15. Medscape. Pediatric mononucleosis and Epstein-Barr virus infection: clinical review. 2024.
16. Cederberg LE, et al. Epstein–Barr virus DNA in parental oral secretions and epidemiologic implications. Clin Infect Dis. 2019.
17. Wang C, et al. Comprehensive insights into pediatric infectious EBV: laboratory predictors and outcomes. J Infect Dev Ctries. 2025.
18. Chang SSY, et al. An approach to cervical lymphadenopathy in children. 2020.
19. Johns Hopkins Guides. The role of EBV viral load and immune response in severity of infectious mononucleosis. 2023
20. Shi T, Yan H, Tian S, et al. Multicenter cohort descriptions of EBV in children with severe manifestations including HLH and hepatic injury. 2021–2025.