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Original Article

Comprehensive insights into pediatric infectious mononucleosis: a retrospective study

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Abstract

Introduction: The objectives of this study were to identify clinical and laboratory markers of infectious mononucleosis (IM) in children, investigate the risk factors for liver damage and prolonged hospitalization, and enhance Epstein-Barr virus (EBV) diagnostic precision.
Methodology: This retrospective study analyzed 288 pediatric IM cases hospitalized from January 2023 to December 2024. Clinical features, laboratory parameters, and EBV-DNA loads were evaluated using statistical analyses to identify predictors of disease severity and outcomes.
Results: Among the 288 children (median age: 5 years; 48.3% male), fever, cervical lymphadenopathy, creatine kinase (CK), IgM, and CD4/CD8 ratios were significantly associated with high EBV-DNA load. Liver damage (35.1% of cases) correlated with age, splenomegaly, alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma-glutamyltransferase (GGT), lactate dehydrogenase (LDH), ferritin, and immune markers ($p < 0.05$). Prolonged hospitalization was associated with hepatomegaly, ALT, AST, GGT, LDH, and ferritin levels ($p < 0.05$). Multivariate analysis identified fever as a predictor of high EBV-DNA load; while age, LDH, and ferritin were independent risk factors for liver damage. Hepatomegaly was a key predictor of extended hospitalization ($p < 0.05$).
Conclusions: IM predominantly affected children aged 3–7 years in Hangzhou. Fever predicted high EBV-DNA load, while elevated LDH, ferritin, and hepatomegaly signaled increased risks of liver damage and prolonged hospitalization, informing more precise management strategies.

Key words: children; infectious mononucleosis; Epstein Barr virus; liver damage; clinical features; retrospective.

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Introduction

Infectious mononucleosis (IM), primarily caused by the Epstein-Barr virus (EBV), is a common self-limiting condition in children. It is characterized by fever, pharyngitis, cervical lymphadenopathy, and hepatosplenomegaly. While more than 90% of the global population becomes infected with EBV at some point in their lives, the incidence of IM is particularly high among children and adolescents [1]. Although IM is usually benign, it can rarely lead to severe complications, such as EBV-associated hemophagocytic lymphohistiocytosis (HLH) or chronic active EBV infection [2,3]. This highlights the importance of early recognition and management of the condition.

Epidemiological patterns of IM vary by region. In developed countries, IM typically peaks during adolescence, while in developing regions, such as China, it is more common among children aged 4 to 6 [4–6]. Improvements in socioeconomic and healthcare conditions in China have been linked to a gradual shift in the age at which primary EBV infection occurs, underscoring the need for updated research on the age distribution and clinical characteristics of IM. Recent studies indicate that EBV-DNA load correlates with disease severity and immune status, with higher viral loads associated with liver damage and potential progression to autoimmune hepatitis [7–10]. Nevertheless, the specific relationships among EBV-DNA load, clinical manifestations, and laboratory

findings in pediatric IM have yet to be thoroughly investigated.

Existing studies are limited by small sample sizes, geographic restrictions, and insufficient analysis of factors influencing hospitalization duration. This study addresses these gaps by analyzing the clinical and laboratory data of 288 pediatric IM patients, examining the associations between EBV-DNA load, liver damage, and hospital stay. The findings aim to enhance the diagnostic precision and treatment strategies, ultimately improving outcomes and quality of life for the affected children.

Methodology

Study population

A total of 288 pediatric patients diagnosed with IM were retrospectively enrolled between January 2023 and December 2024 at the First People's Hospital of Hangzhou. The inclusion criteria were: age ≤ 18 years, and diagnosis of IM based on expert consensus on the diagnosis and treatment principles of EB virus infection-related diseases in children [11]. The exclusion criteria were: presence of malignant tumors, congenital malformations, severe organ dysfunction, or immunodeficiency; and incomplete clinical or laboratory data.

Data collection

Demographic and clinical data were collected upon admission; including gender, age, season of onset, clinical symptoms, and laboratory findings. The laboratory parameters included hematology (complete blood count including hemoglobin, platelet count, and neutrophil count), liver function (alanine aminotransferase (ALT), aspartate aminotransferase (AST), and gamma-glutamyltransferase (GGT)), other biomarkers (creatine kinase (CK), creatine kinase-MB (CK-MB), lactate dehydrogenase (LDH), prealbumin, ferritin, and EBV-DNA load), immune parameters (immunoglobulins (IgG, IgA, IgM), complement (C3, C4), TBNK lymphocyte subsets (the distinct populations of lymphocytes, which include T cells, B cells, and NK (natural killer) cells), and cytokines (IL-6, IL-10)), and EBV DNA. The quantification of EBV DNA was performed utilizing a standardized diagnostic platform comprising the EBV nucleic acid amplification kit (Guangzhou Da'an Gene Co., Ltd., Guangzhou, China) in conjunction with the RTQ-960 real-time fluorescence quantitative polymerase chain reaction (PCR) system (Aikang Biotechnology (Hangzhou) Co., Ltd., Hangzhou, China). This state-of-the-art platform, based on real-time fluorescent quantitative PCR (qPCR) technology, enables precise detection and quantification of EBV DNA viral load with optimized sensitivity and specificity parameters. This standardized methodology ensured consistent and reproducible results across the patient cohort in this study.

Definitions

Liver damage was defined as ALT, AST, or GGT levels exceeding twice the upper limit of normal (ALT: 0–40 U/L, AST: 0–40 U/L for males and 0–35 U/L for females, GGT: 0–45 U/L). Hematological damage was defined as absolute neutrophil count (ANC) < 1.5 × 10^9/L, platelet count < 100 × 10^9/L, or hemoglobin levels below the age-specific reference range. Myocardial damage was defined as CK or CK-MB levels exceeding normal reference values.

Study design

The clinical manifestations, laboratory findings, and hospitalization duration in the selected 288 pediatric patients were analyzed. The patients were stratified into groups based on median EBV-DNA load (< 3710 copies/mL vs. ≥ 3710 copies/mL), median hospitalization duration (> 7 days vs. ≤ 7 days), and presence or absence of liver damage. Comparative analyses were performed between these groups to identify significant differences and potential risk factors.

Statistical analysis

Statistical analyses were performed using SPSS software version 25.0 (IBM Corp, Armonk, NY, USA). Categorical variables were expressed as counts with corresponding percentages, and analyzed using Chi-square tests or Fisher's exact tests where appropriate. Continuous variables were presented as mean ± standard deviation for normally distributed data, or median (P25, P75) for non-normally distributed data; with analyses conducted using Student's t-tests or non-parametric methods respectively.

Variables demonstrating statistical significance in univariate analyses were subsequently incorporated into multivariate logistic regression models to identify independent predictors of EBV DNA load, hospitalization duration, and hepatic dysfunction. Statistical significance was established at $p < 0.05$, and 95% confidence intervals (CI) were calculated for all relevant parameters.

Ethical approval

This study was approved by the Ethics Committee

of the First People's Hospital of Hangzhou (Approval No.: ZN-2024478-01). The requirement of informed consent was waived because of its retrospective design.

Results

Patient demographics

This study assessed the demographic and baseline clinical characteristics of 288 children diagnosed with IM (Table 1). Since this was a retrospective analysis, standardized reference intervals established by the Chinese Health Industry Standards (WS/T 779–2021) were utilized, which are explicitly documented in the table. All laboratory assessments were conducted in accordance with rigorous institutional standard operating procedures (SOPs), employing standardized analytical platforms and validated reagents to ensure measurement consistency and reliability. This standardization protocol was maintained throughout the data collection phase to optimize analytical precision and accuracy.

Clinical presentation and epidemiology

The IM patients included 139 males and 149 females, with a median age of 5 years (range: 3 to 7 years). The median hospital stay was 7 days (range: 7 to 9 days). Regarding the season of onset, there were 91 cases in spring, 73 in summer, 70 in autumn, and 54 in winter. The primary clinical manifestations included

Table 1. Baseline characteristics of infectious mononucleosis.

Characteristic (normal range)	Value (mean ± standard deviation or median (P25, P75))
Gender (male/female), %	139/149 (48.26%/51.74%)
Age (years)	5 (3, 7)
Fever (yes/no), %	263/25 (91.32%/8.68%)
Tonsil enlargement (yes/no), %	283/5 (98.26%/1.74%)
Cervical lymphadenopathy (yes/no), %	263/25 (91.32%/8.68%)
Hepatomegaly (yes/no), %	141/147 (48.96%/51.04%)
Splenomegaly (yes/no), %	109/179 (37.85%/62.15%)
Eyelid edema (yes/no), %	169/119 (58.68%/41.32%)
Rash (yes/no), %	19/269 (6.60%/93.40%)
WBC ((4.1–11.9) × 10^9/L)	13.25 (9.70, 16.60)
Lymphocyte (17–71%)	65.00 (58.00, 73.00)
Neutrophil (13–77%)	25.70 (18.80, 32.00)
ALC ((1.2–8.7) × 10^9/L)	8.40 (5.90, 11.40)
ANC ((0.8–8.3) × 10^9/L)	3.20 (2.10, 4.60)
NLR	0.40 (0.24, 0.54)
RBC ((4.0–5.7) × 10^{12}/L)	4.60 (4.36, 4.85)
Hemoglobin (112–156 g/L)	127.41 ± 10.34
Platelets ((100–300) × 10^9/L)	209.00 (172.25, 254.00)
CK (24–170 U/L)	54.5 (43, 73)
CKMB (≤ 25 U/L)	19 (16, 22)
ALT (7–50 U/L)	44 (24, 94)
AST (13–35 U/L)	54 (42, 86)
GGT (7–45 U/L)	19 (13, 41)
Liver damage (yes/no), %	101/186 (35.19%/64.81%)
Blood system damage (yes/no), %	37/251 (12.85%/87.15%)
Myocardial damage (yes/no), %	13/273 (4.55%/95.45%)
IgG (4.950–12.740 g/L)	11.75 (9.87, 13.40)
IgA (0.330–1.890 g/L)	1.71 (1.17, 2.41)
IgM (0.650–2.010 g/L)	1.70 (1.30, 2.28)
C3 (0.7–1.4 g/L)	0.96 ± 0.19
C4 (0.100–0.400 g/L)	0.27 (0.22, 0.34)
Total lymphocyte count ((2.5–7.2) × 10^9/L)	7.41 (5.33, 9.63)
CD3+ Absolute count ((0.96–3.64) ×10^9/L)	6.14 (4.57, 8.15)
CD8+ Absolute count ((0.26–1.38) × 10^9/L)	4.32 (3.15, 6.33)
CD4+ Absolute count ((0.55–2.19) × 10^9/L)	1.09 (0.82, 1.44)
CD16/56 ((0.08–0.68) × 10^9/L)	0.61 (0.41, 0.96)
CD19+ Absolute count ((0.27–1.22) × 10^9/L)	0.30 (0.19, 0.48)
CD4/CD8 (0.72–2.88)	0.24 (0.17, 0.33)
LDH ((97–350) U/L)	462.50 (396.00, 543.75)
IL-6 (0–20.0) pg/mL)	11.34 (5.40, 19.68)
IL-10 (0–5.9) pg/mL)	16.21 (8.72, 26.96)
Prealbumin (200–400) mg/L)	111 (93, 132)
Ferritin (M: 21.81–274.66 F: 4.63–204.00) (ug/L)	117.89 (80.76, 178.31)
Plasma EBV-DNA load (< 500 copies/mL)	3710 (3100, 4230)
Hospital days	7 (7, 9)
Onset season (spring/summer/autumn/winter)	91/73/70/54 (31.60%/25.35%/24.31%/18.75%)

WBC: white blood cells; ALC: absolute lymphocyte count; ANC: absolute neutrophil count; NLR: neutrophil lymphocyte ratio; RBC: red blood cell; CK: creatine kinase; CK-MB: creatine kinase isoenzyme; ALT: alanine aminotransferase; AST: aspartate aminotransferase; GGT: gamma-glutamyltransferase; LDH: lactate dehydrogenase; IL: interleukin.

fever (91.32%), pharyngitis (98.26%), and cervical lymphadenopathy (91.32%). Additionally, some children presented with hepatomegaly (48.96%), splenomegaly (37.85%), periorbital edema (58.68%), and a small number exhibited a rash (6.60%).

Routine blood tests and biochemical tests

The routine blood tests assessed various parameters, including white blood cell count, neutrophil percentage, lymphocyte percentage, total lymphocyte count, total neutrophil count, red blood cell count, platelet count, hemoglobin, and the neutrophil-to-lymphocyte ratio (NLR). The white blood cell count was 13.25 (9.70, 16.60) × 10^9/L, with a predominance of lymphocytes at 65.00 (58.00, 73.00) %, consistent with previous studies on blood parameters in viral infections. The platelet count was 209.00 (172.25, 254.00) × 10^9/L, and the hemoglobin level was 127.41 ± 10.34 g/L. The neutrophil count was 3.20 (2.10, 4.60) × 10^9/L. All values were within normal ranges, although 12.85% of the children showed signs of hematologic damage.

Table 2. Univariate analysis of plasma Epstein-Barr virus (EBV) DNA load in infectious mononucleosis.

Variable	**< 3710 (copies/mL)**	**≥ 3710 (copies/mL)**	**OR (95% CI)**	**χ^2**	***p* value**
Gender (male/female)	51/49 (51.00%)	45/53 (45.92%)	1.23 (0.70, 2.14)	0.51	0.47
Fever (yes/no)	89/11 (89.00%)	95/3 (96.94%)	3.91 (1.06, 14.49)	4.75	**0.03**
Tonsil enlargement (yes/no)	99/1 (99.00%)	95/3 (96.94%)	0.32 (0.03, 3.13)	0.28	0.60
Cervical lymphadenopathy (yes/no)	96/4 (96.00%)	85/13 (86.73%)	0.27 (0.09, 0.87)	5.41	**0.02**
Hepatomegaly (yes/no)	45/55 (45.00%)	54/44 (55.10%)	1.50 (0.86, 2.63)	2.02	0.16
Splenomegaly (yes/no)	39/61 (39.00%)	38/60 (38.78%)	0.99 (0.56, 1.75)	0.00	0.97
Eyelid edema (yes/no)	54/46 (54.00%)	63/35 (64.29%)	1.53 (0.87, 2.71)	2.17	0.14
Rash (yes/no)	6/94 (6.00%)	4/94 (4.08%)	0.67 (0.18, 2.44)	0.09	0.77
Blood system damage (yes/no)	14/86 (14.00%)	10/88 (10.20%)	0.70 (0.29, 1.66)	0.67	0.41
Liver damage (yes/no)	37/63 (37.00%)	39/59 (39.80%)	1.13 (0.64, 2.00)	0.16	0.69
Myocardial damage (yes/no)	4/96 (4.00%)	4/94 (4.08%)	1.02 (0.25, 4.20)	0.00	1.00
Variable	**< 3710 (copies/mL) (mean ± standard deviation)**	**≥ 3710 (copies/mL) (mean ± standard deviation)**	**Mean difference (95% CI)**	***t* value**	***p* value**
Hemoglobin (g/L)	127.23 ± 9.94	127.10 ± 10.76	0.13 (– 2.78, 3.03)	0.09	0.93
C3 (g/L)	0.95 ± 0.17	0.97 ± 0.20	– 0.02 (– 0.07, 0.04)	– 0.59	0.55
Variable	**< 3710 (copies/mL) (median (P25, P75))**	**≥ 3710 (copies/mL) (median (P25, P75))**	**Median difference (95%CI)**	***Z* value**	***p* value**
Age (years)	5 (3, 7)	5 (3, 7)	0 (–1, 1)	– 0.17	0.87
WBC (× 10^9/L)	12.85 (9.78, 16.98)	14.05 (10.5, 16.25)	–0.8 (–2.1, 0.60)	– 1.03	0.30
Lymphocyte %	66.9 (58.25, 74.08)	65.05 (58.78, 73.78)	0.4 (–2.3, 3.3)	– 0.28	0.78
Neutrophil %	23.95 (18.8, 31.55)	26.75 (18.78, 32.25)	–1.5 (–4.1, 1.4)	– 0.92	0.36
ALC (× 10^9/L)	8.1 (5.9, 11.58)	9.15 (6.23, 11.93)	–0.5 (–1.6, 0.6)	– 0.93	0.35
ANC (× 10^9/L)	3.15 (2.1, 4.08)	3.25 (2.38, 4.8)	–0.3 (–0.7, 0.1)	– 1.41	0.16
NLR	0.37 (0.24, 0.54)	0.41 (0.24, 0.54)	–0.02 (–0.08, 0.03)	– 0.78	0.44
RBC (× 10^{12}/L)	4.63 (4.40, 4.83)	4.56 (4.35, 4.85)	0.03 (–0.07, 0.13)	– 0.58	0.56
Platelets (× 10^9/L)	205 (165.5, 242)	209 (163.75, 252)	–4 (–21, 13)	– 0.46	0.65
CK (U/L)	54.5 (45, 73.75)	50 (40, 67)	6 (0, 11)	– 2.07	**0.04**
CKMB (U/L)	19 (16, 22)	19 (16, 21)	0 (–1, 2)	– 0.44	0.66
ALT (U/L)	46.5 (26.25, 93.75)	47 (26.75, 113.5)	–1 (–11, 8)	– 0.18	0.86
AST (U/L)	59.5 (44.25, 86.75)	56.5 (41, 95.25)	0 (–8, 7)	– 0.04	0.97
GGT (U/L)	21 (14, 40.5)	20 (14, 44)	0 (–3, 4)	– 0.31	0.76
IgG (g/L)	11.8 (10.05, 13.73)	12 (10.6, 13.95)	–0.2 (–1.02, 0.6)	– 0.62	0.53
IgA (g/L)	1.67 (1.2, 2.39)	1.82 (1.28, 2.55)	–0.16 (–0.4, 0.09)	– 1.33	0.18
IgM (g/L)	1.58 (1.30, 2.20)	1.88 (1.52, 2.49)	–0.26 (–0.44, 0.06)	– 2.50	**0.01**
C4 (g/L)	0.27 (0.22, 0.34)	0.28 (0.23, 0.33)	–0.01 (–0.03, 0.02)	– 0.48	0.63
Total lymphocyte count (× 10^9/L)	6.80 (5.08, 9.00)	8.06 (5.29, 10.81)	–0.68 (–1.65, 0.27)	– 1.36	0.17
CD3+ absolute count (× 10^9/L)	5.84 (4.44, 7.68)	6.70 (4.63, 9.45)	–0.55 (–1.43, 0.24)	– 1.37	0.17
CD8+ absolute count (× 10^9/L)	4.25 (2.99, 5.60)	4.96 (3.39, 7.08)	–0.60 (–1.30, 0.11)	– 1.65	0.10
CD4+ absolute count (× 10^9/L)	1.04 (0.75, 1.39)	1.01 (0.76, 1.35)	0.01 (–0.11, 0.13)	– 0.18	0.86
CD16/56 (× 10^9/L)	0.53 (0.38, 0.88)	0.65 (0.45, 1.01)	–0.09 (–0.20, 0.02)	– 1.69	0.09
CD19+ absolute count (× 10^6/L)	0.26 (0.18, 0.44)	0.29(0.18, 0.45)	0.01 (–0.05, 0.05)	– 0.23	0.82
CD4/CD8	0.23 (0.17, 0.32)	0.21 (0.15, 0.27)	0.03 (0, 0.05)	– 1.97	**0.05**
LDH (U/L)	476.5 (428.75, 559.75)	462 (385.5, 562.00)	3 (–28, 34)	– 0.20	0.84
IL-6 (pg/mL)	13.27 (5.46, 19.40)	12.95 (6.36, 24.26)	–0.8 (–3.25, 1.82)	– 0.58	0.56
IL-10 (pg/mL)	16.81 (9.53, 26.96)	18.88 (11.92, 32.71)	–2.57 (–6.51, 0.9)	– 1.44	0.15
Prealbumin (mg/L)	111 (97.75, 129.25)	106 (91.00, 128)	4 (–5, 12)	– 0.92	0.36
Ferritin (ug/L)	107.97 (80.02, 178.70)	119.71 (92.69, 191.50)	–10.77 (–29.34, 7.79)	– 1.22	0.22
Hospital days	7 (7, 9)	8 (7, 9)	0 (–1, 0)	– 1.44	0.15
Onset season (spring/summer/autumn/winter)	25/26/31/18	38/25/24/11	NA	5.26	0.15

CI: confidence interval; OR: odds ratio; WBC: white blood cells; ALC: absolute lymphocyte count; ANC: absolute neutrophil count; RBC: red blood cells; NLR: neutrophil lymphocyte ratio; CK: creatine kinase; CK-MB: creatine kinase isoenzyme; ALT: alanine aminotransferase; AST: aspartate aminotransferase; GGT: gamma-glutamyltransferase; LDH: lactate dehydrogenase; IL: interleukin. Values in bold font indicate statistical significance ($p < 0.05$).

The biochemical tests focused on liver and myocardial function. With regard to liver function, ALT was elevated at 44 (24, 94) U/L, and AST was elevated at 54 (42, 86) U/L, while GGT was within the normal range at 19 (13, 41) U/L. Liver damage was noted in 35.19% of the children, aligning with clinical symptoms of hepatomegaly and suggesting that infections such as EBV can impact liver function. Regarding myocardial function, CK level was 54.5 (43, 73) U/L and CK-MB was 19 (16, 22) U/L; both within normal limits; however, 4.55% of the children exhibited signs of myocardial damage. Furthermore, the LDH level was 462.5 (396, 543.75) U/L, indicating potential organ damage in patients with infectious mononucleosis.

Immune function parameters

The immune function parameters that were assessed included immunoglobulins, complement levels, TBNK lymphocyte subpopulations, and ILs. Immunoglobulin and complement levels remained within normal ranges. The total TBNK lymphocyte count was 7408.78 (5326.75, 9630.51) × 10^6/L, CD3 was 6140.80 (4568.07, 8149.67) × 10^6/L, and CD8 was 4324.04 (3152.97, 6329.59) × 10^6/L. IL-10 levels were elevated at 16.21 (8.72, 26.96) pg/mL, while the CD4/CD8 ratio was significantly decreased at 0.24 (0.17, 0.33). These findings highlighted the immunological changes associated with IM, suggesting that EBV infection elicited a robust cellular immune response characterized by altered T-cell dynamics and increased IL-10 production.

Inflammatory and immune markers

The ferritin levels were within normal ranges in 98.89% of patients, while prealbumin was reduced to 111 (93, 132) mg/L, indicating liver damage and inflammation. These findings, combined with the baseline characteristics and clinical manifestations observed, provide critical insights into the impact of EBV-induced IM in pediatric patients.

The key trends in the analyses, such as the high incidence of fever and organ enlargement, underscore the importance of these markers in the diagnosis and management of EBV infections. Additionally, the detailed analysis of hematological and immunological parameters offers a comprehensive overview of the clinical features of IM, serving as a basis for the development of targeted therapeutic approaches.

Blood EBV-DNA load and clinical implications

The patients were stratified into two groups based on the median blood EBV DNA load (> 3,710 vs. ≤ 3,710 copies/mL), reflecting the skewed distribution of the data. Significant differences were observed between these groups in key clinical parameters, including fever and cervical lymphadenopathy (p = 0.02). Children presenting with fever exhibited higher EBV-DNA loads (p = 0.03), suggesting heightened immune responses in cases with elevated viral loads.

The CK levels also differed significantly between the groups (p = 0.04), although all values remained within normal limits. The immune markers showed notable differences, with elevated IgM (p = 0.01) and altered CD4/CD8 ratios (p = 0.049) in the high-load group, indicating intensified immune responses and significant shifts in T-cell dynamics.

The findings, summarized in Table 2, emphasize the potential of blood EBV-DNA load as a biomarker for assessing infection severity and guiding clinical management. Higher EBV-DNA loads were associated with more severe clinical manifestations and pronounced immune abnormalities, highlighting their utility in predicting patient prognosis and tailoring therapeutic interventions. These results underscore the influence of viral load on disease presentation and provide valuable insights for the personalized management of EBV-induced IM.

Univariate analysis of length of hospital stay

The children were categorized into long-stay (> 7 days) and short-stay (≤ 7 days) groups based on the median length of hospital stay, accounting for the skewed distribution of the data (Table 3).

Significant differences in hospital stay were observed across age groups (p < 0.01), with older children experiencing longer stays. Hepatomegaly and splenomegaly were more prevalent in the long-stay group (p < 0.01 and p = 0.01, respectively), suggesting a stronger association of liver and spleen involvement with extended hospitalizations.

Elevated levels of ALT, AST, and GGT were noted in the long-stay group (p < 0.01), reflecting prolonged disease activity or liver dysfunction. Immune markers, including IgG, IgA, IgM, total TBNK lymphocytes, CD3, CD8, and LDH, were significantly higher in the long-stay group, whereas C3 and CD4/CD8 ratios were reduced (p < 0.05). These findings indicate increased cellular turnover and suggest more extensive tissue damage and heightened inflammatory responses.

Ferritin levels were markedly elevated in the long-stay group (p < 0.01), emphasizing the role of acute-phase reactants in signaling intense inflammation or ongoing infection.

Table 3 highlights the significant clinical and laboratory differences between short- and long-stay patients, underscoring the utility of these parameters in assessing disease severity. This information can equip pediatricians with critical tools to identify children at risk of severe outcomes; and help with implementing timely interventions, improving prognosis, and optimizing care strategies.

Univariate analysis of liver damage

The children were divided into two groups based on the presence or absence of liver damage. There was a significant increase in the incidence of splenomegaly in children with liver damage ($p < 0.01$), suggesting that liver and spleen involvement often occurred simultaneously. The percentage and total count of lymphocytes were higher in the liver damage group; while NLR, neutrophil percentage, and total neutrophil count were lower (lymphocyte percentage, NLR, neutrophil percentage, and total neutrophil count $p < 0.01$; total lymphocyte count $p = 0.02$), which aligns with the lymphocytic increase observed in IM,

Table 3. Univariate analysis of hospitalization days in infectious mononucleosis.

Variable	**≤ 7 days**	**> 7 days**	**OR (95%CI)**	χ^2	***p* value**
Gender (male/female)	81/81 (50.00%)	58/68 (46.03%)	1.17 (0.74, 1.87)	0.45	0.5
Fever (yes/no)	151/11 (93.21%)	112/14 (88.89%)	0.58 (0.26, 1.33)	1.67	0.2
Tonsil enlargement (yes/no)	159/3 (98.15%)	124/2 (98.41%)	1.17 (0.19, 7.11)	0	1
Cervical lymphadenopathy (yes/no)	147/15 (90.74%)	116/10 (92.06%)	1.18 (0.51, 2.73)	0.16	0.69
Hepatomegaly (yes/no)	63/99 (38.89%)	78/48 (61.90%)	2.55 (1.58, 4.12)	15.02	**< 0.01**
Splenomegaly (yes/no)	50/112 (30.86%)	59/67 (46.83%)	1.97 (1.22, 3.20)	7.68	**0.01**
Eyelid edema (yes/no)	91/71 (56.17%)	78/48 (61.90%)	1.27 (0.79, 2.04)	0.96	0.33
Rash (yes/no)	12/150 (7.41%)	7/119 (5.56%)	0.74 (0.28, 1.93)	0.39	0.53
Blood system damage (yes/no)	24/138 (14.81%)	13/113 (10.42%)	0.66 (0.32, 1.36)	1.28	0.26
Liver damage (yes/no)	33/128 (20.50%)	68/58 (53.97%)	4.55 (2.71, 7.64)	34.72	**< 0.01**
Myocardial damage (yes/no)	6/154	7/119	1.51 (0.49, 4.61)	0.53	0.47
Variable	**≤ 7 days (mean ± standard deviation)**	**> 7 days (mean ± standard deviation)**	**Mean difference (95% CI)**	***t* value**	***p* value**
Hemoglobin (g/L)	126.53 ± 10.35	128.55 ± 10.26	– 2.02 (– 4.43, 0.39)	– 1.65	0.1
C3 (g/L)	0.99 ± 0.19	0.93 ± 0.19	0.06 (0.01, 0.10)	2.3	**0.02**
Variable	**≤ 7 days (median (P25, P75))**	**> 7 days (median (P25, P75))**	**Median difference (95%CI)**	***Z* value**	***p* value**
Age (years)	5 (3, 6.25)	6 (4, 8)	– 1 (– 2, 0)	– 3.18	**< 0.01**
WBC (× 10^9/L)	12.95 (9.6, 16.6)	13.4 (9.7, 17.1)	– 0.5 (– 1.7, 0.7)	– 0.81	0.42
Lymphocyte %	64 (57.78, 72)	66.9 (59, 75)	– 2.4 (– 5, 0)	– 1.96	0.05
Neutrophil %	26 (20, 33.1)	24 (17.38, 32)	2.15 (0, 4.7)	– 1.81	0.07
ALC (× 10^9/L)	8.1 (5.9, 11.15)	8.95 (5.88, 11.6)	– 0.5 (– 1.5, 0.4)	– 1.07	0.28
ANC (× 10^9/L)	3.4 (2.25, 4.6)	2.95 (2.08, 4.70)	0.2 (– 0.2, 0.6)	– 1.12	0.26
NLR	0.4 (0.27, 0.54)	0.36 (0.23, 0.53)	0.04 (– 0.01, 0.09)	– 1.54	0.13
RBC (× 10^{12}/L)	4.58 (4.35, 4.84)	4.64 (4.36, 4.86)	– 0.04 (– 0.12, 0.05)	– 0.92	0.36
Platelets (× 10^9/L)	210.5 (174.75, 261.25)	206.50 (166.50, 248.50)	7 (– 7, 22)	– 0.99	0.32
CK (U/L)	55 (44, 73.75)	53 (43, 73)	1 (– 4, 6)	– 0.31	0.76
CKMB (U/L)	18 (16, 21)	19 (15.75, 23)	– 1 (– 2, 1)	– 0.86	0.39
ALT (U/L)	32 (21.5, 61)	76.5 (31, 138.5)	– 28 (– 45, – 16)	– 5.97	**< 0.01**
AST (U/L)	49 (41, 62)	69.5 (48.75, 119.25)	– 21 (– 30, – 14)	– 6.12	**< 0.01**
GGT (U/L)	17 (13, 26)	28.5 (15.5, 62)	– 8 (– 13, – 4)	– 4.74	**< 0.01**
Plasma EBV-DNA load (copies/mL)	3410 (2825, 4220)	3960 (3135, 4255)	– 270 (– 740, 0)	– 1.78	0.08
IgG (g/L)	11.45 (9.14, 12.73)	12.15 (10.6, 14.2)	– 1.17 (– 1.90, – 0.40)	– 3.14	**< 0.01**
IgA (g/L)	1.54 (1.08, 2.29)	1.87 (1.34, 2.52)	– 0.31 (– 0.53, – 0.09)	– 2.72	**0.01**
IgM (g/L)	1.61 (1.23, 2.07)	1.79 (1.43, 2.49)	– 0.26 (– 0.44, – 0.09)	– 2.89	**< 0.01**
C4 (g/L)	0.28 (0.22, 0.34)	0.26 (0.22, 0.32)	0.02 (0, 0.04)	– 1.83	0.07
Total lymphocyte count (× 10^9/L)	6.68 (5.23, 9.03)	8.07 (5.85, 10.73)	– 1.03 (– 1.80, – 0.20)	– 2.48	**0.01**
CD3+ absolute count (× 10^9/L)	5.63 (4.40, 7.49)	6.94 (5.23, 9.52)	– 1.15 (– 1.82, – 0.46)	– 3.3	**< 0.01**
CD8+ absolute count (× 10^9/L)	3.92 (2.82, 5.34)	4.97 (3.57, 7.42)	– 1.10 (– 1.70, – 0.57)	– 3.96	**< 0.01**
CD4+ absolute count (× 10^9/L)	1.19 (0.86, 1.51)	1.01 (0.77, 1.40)	0.10 (– 0.01, 0.21)	– 1.75	0.08
CD16/ 56 (× 10^9/L)	0.60 (0.39, 0.95)	0.61 (0.44, 1.01)	– 0.04 (– 0.12, 0.05)	– 0.81	0.42
CD19 (× 10^9/L)	0.30 (0.20, 0.53)	0.28 (0.17, 0.41)	0.05 (0.001, 0.09)	– 2	0.05
CD4/CD8	0.29 (0.19, 0.40)	0.21 (0.15, 0.26)	0.07 (0.05, 0.1)	– 5.28	**< 0.01**
LDH (U/L)	446 (379.25, 509.5)	494.5 (425, 584.5)	– 51 (– 78, – 24)	– 3.75	**< 0.01**
IL-6 (pg/mL)	12.33 (5.38, 20.30)	10.25 (5.59, 19.40)	– 0.11 (– 2.04, 2.02)	– 0.11	0.91
IL-10 (pg/mL)	16.12 (7.83, 25.68)	16.31 (9.84, 29.53)	– 1.98 (– 4.94, 0.76)	– 1.41	0.16
Prealbumin (mg/L)	113 (92, 132)	109 (94.5, 134)	0 (– 8.00, 7.00)	– 0.05	0.96
Ferritin (ug/L)	106.43 (74.19, 157.45)	132.00 (91.09, 207.26)	– 27.45 (– 44.34, – 10.67)	– 3.29	**< 0.01**
Onset season (spring / summer / autumn / winter)	49/38/41/34	42/35/29/20	NA	1.88	0.6

CI: confidence interval; OR: odds ratio; WBC: white blood cells; ALC: absolute lymphocyte count; ANC: absolute neutrophil count; RBC: red blood cells; NLR: neutrophil lymphocyte ratio; CK: creatine kinase; CK-MB: creatine kinase isoenzyme; ALT: alanine aminotransferase; AST: aspartate aminotransferase; GGT: Gamma-glutamyltransferase; LDH: lactate dehydrogenase; IL: interleukin. Values in bold font indicate statistical significance ($p < 0.05$).

suggesting a viral infection. The liver damage group exhibited higher levels of IgG, IgA, IgM, total TBNK lymphocytes, CD3, CD8, CD16/CD56, and LDH; while C3, CD19, and the CD4/CD8 ratio were significantly decreased ($p < 0.05$); suggesting that liver damage in IM patients may lead to immune dysfunction. This could be related to the liver's role in maintaining immune homeostasis and immune tolerance. Ferritin levels were significantly elevated in the liver damage group ($p < 0.01$), indicating that ferritin may serve as an indicator of liver damage.

Comparison of the clinical and laboratory markers of children with and without liver damage, suggested that the high LDH levels in older preschool children with splenomegaly were more likely to experience liver damage (Table 4).

Logistic regression analysis of IM patients

Logistic regression analysis was performed on significant variables based on the results of univariate analysis, and revealed that fever was a risk factor for increased blood EBV load in IM patients ($p = 0.03$) (Table 5). Age, neutrophil count, LDH, and ferritin were identified as risk factors for liver damage in IM

Table 4. Univariate analysis of liver damage in infectious mononucleosis.

Variable	No	Yes	OR (95% CI)	χ^2	*p* value
Gender (male/female)	91/95 (48.92%)	47/54 (46.53%)	1.10 (0.68, 1.79)	0.15	0.70
Fever (yes/no)	172/14 (92.47%)	90/11 (89.11%)	0.67 (0.29, 1.53)	0.93	0.33
Tonsil enlargement (yes/no)	182/4 (97.85%)	100/1 (99.01%)	2.20 (0.24, 19.93)	0.06	0.81
Cervical lymphadenopathy (yes/no)	170/16 (91.40%)	92/9 (91.09%)	0.96 (0.41, 2.26)	0.01	0.93
Hepatomegaly (yes/no)	85/101 (45.70%)	56/45 (55.45%)	1.48 (0.91, 2.41)	2.49	0.12
Splenomegaly (yes/no)	59/127 (31.72%)	50/51 (49.50%)	2.11 (1.28, 3.47)	8.79	**< 0.01**
Eyelid edema (yes/no)	107/79 (57.53%)	61/40 (60.40%)	1.13 (0.69, 1.84)	0.22	0.64
Rash (yes/no)	15/171 (8.06%)	4/97 (3.96%)	0.47 (0.15, 1.46)	1.78	0.18
Blood system damage (yes/no)	24/162 (12.90%)	13/88 (12.87%)	1.00 (0.48, 2.06)	0	0.99
Myocardial damage (yes/no)	7/178 (3.78%)	6/95 (5.94%)	1.61 (0.53, 4.92)	0.29	0.59
Variable	**No (mean ± standard deviation)**	**Yes (mean ± standard deviation)**	**Mean difference (95% CI)**	***t* value**	***p* value**
Hemoglobin (g/L)	126.98 ± 10.55	128.02 ± 9.84	– 1.03 (– 3.54, 1.47)	– 0.81	0.42
C3 (g/L)	0.99 ± 0.19	0.92 ± 0.19	0.08 (0.03, 0.12)	3.04	**< 0.01**
Variable	**No (median (P25, P75))**	**Yes (median (P25, P75))**	**Median difference (95% CI)**	***Z* value**	***p* value**
Age (years)	4 (3.00, 6.00)	6 (4.00, 8.00)	– 1 (– 2, – 1)	– 3.96	**< 0.01**
WBC (× 10^9/L)	13.05 (9.6, 16.28)	13.4 (9.7, 17.90)	– 0.5 (– 1.8, 0.7)	– 0.84	0.4
Lymphocyte %	63 (57.30, 70.03)	70 (60.50, 77.05)	– 6.1 (– 8.9, – 3.7)	– 4.56	**< 0.01**
Neutrophil %	27.3 (21.80, 34.05)	20.7 (14.35, 29.90)	5.8 (3.3, 8)	– 4.48	**< 0.01**
ALC (× 10^9/L)	8.1 (5.8, 10.83)	9.2 (6.2, 13.15)	– 1.2 (– 2.3, – 0.2)	– 2.39	**0.02**
ANC (× 10^9/L)	3.6 (2.3, 4.85)	2.7 (2.00, 3.8)	0.70 (0.30, 1.10)	– 3.52	**< 0.01**
NLR	0.41 (0.29, 0.57)	0.31 (0.23, 0.47)	0.12 (0.07, 0.17)	– 4.63	**< 0.01**
RBC (× 10^{12}/L)	4.59 (4.36, 4.84)	4.62 (4.36, 4.85)	– 0.01 (– 0.09, 0.08)	– 0.16	0.87
Platelets (× 10^9/L)	214.5 (178.50, 262.00)	197 (163, 239.5)	16.00 (1.00, 31.00)	– 2.11	**0.04**
CK (U/L)	57 (45, 74.5)	51 (41.00, 70)	5.00 (0.00, 10.00)	– 1.88	0.06
CKMB (U/L)	19 (16.00, 22)	19 (16.00, 22)	0.00 (– 1.00, 1.00)	– 0.19	0.85
ALT (U/L)	28 (21, 42.250)	124 (90.5, 216)	– 95.00 (– 108.00, – 85.00)	– 13.69	**< 0.01**
AST (U/L)	45 (39.00, 55.25)	99 (81, 154.50)	– 56.00 (– 66.00, – 49.00)	– 12.99	**< 0.01**
GGT (U/L)	14.5 (13.00, 21)	61 (32, 103.50)	– 42.00 (– 53.00, – 31.00)	– 11.47	**< 0.01**
Plasma EBV-DNA Load (copies/mL)	3710 (3065, 4247.5)	3910 (3102.50, 4230.00)	– 20.00 (– 490.00, 250.00)	– 0.56	0.58
IgG (g/L)	11.5 (9.19, 13.00)	12.00 (10.9, 14.5)	– 1.3 (– 2, – 0.5)	– 3.26	**< 0.01**
IgA (g/L)	1.56 (1.08, 2.41)	1.84 (1.34, 2.47)	– 0.28 (– 0.5, – 0.04)	– 2.34	**0.02**
IgM (g/L)	1.62 (1.22, 2.17)	1.79 (1.51, 2.54)	– 0.31 (– 0.48, – 0.13)	– 3.32	**< 0.01**
C4 (g/L)	0.28 (0.22, 0.35)	0.27 (0.22, 0.32)	0.02 (0, 0.04)	– 1.5	0.13
Total lymphocyte count (× 10^9/L)	6.80 (5.23, 8.77)	8.28 (5.79, 11.18)	– 1.47 (– 2.35, –0.60)	– 3.26	**< 0.01**
CD3+ absolute count (× 10^9/L)	5.64 (4.37, 7.51)	7.21 (5.24, 9.88)	– 1.58 (– 2.31, – 0.83)	– 4.09	**< 0.01**
CD8+ absolute count (× 10^9/L)	3.93 (2.89, 5.38)	5.38 (3.86, 8.15)	– 1.47 (–2.12, – 0.90)	– 4.83	**< 0.01**
CD4+ absolute count (× 10^9L)	1.09 (0.83, 1.44)	1.10 (0.79, 1.44)	0.02 (– 0.09, 0.14)	– 0.42	0.67
CD16/ 56 (× 10^9/L)	0.58 (0.37, 0.87)	0.68 (0.45, 1.13)	– 0.12 (– 0.22, – 0.03)	– 2.54	**0.01**
CD19+ absolute count (× 10^9/L)	0.31(0.20, 0.50)	0.27 (0.15, 0.43)	0.05 (0.003, 0.10)	– 2.09	**0.04**
CD4/CD8	0.26 (0.20, 0.39)	0.2 (0.14, 0.26)	0.07 (0.04, 0.1)	– 4.97	**< 0.01**
LDH (U/L)	446 (383.50, 510.50)	544.5 (450.25, 636.25)	– 96.00 (– 125.00, – 68.00)	– 6.31	**< 0.01**
IL-6 (pg/mL)	12.33 (5.46, 22.34)	9.14 (5.36, 17.99)	1.2 (– 0.81, 3.65)	– 1.11	0.27
IL-10 (pg/mL)	15.6 (8.40, 25.66)	17 (10.99, 30.03)	– 2.90 (– 5.97, 0.11)	– 1.9	0.06
Prealbumin (mg/L)	108 (91.00, 127.00)	105.5 (91.00, 124.25)	4.00 (–4.00, 12.00)	– 0.88	0.38
Ferritin (ug/L)	102.77 (71.69, 145.98)	171.85 (112.29, 261.31)	– 59.63 (– 79.64, – 41.70)	– 6.55	**< 0.01**
Onset season (spring / summer / autumn / winter)	60/41/47/38	30/32/23/16	NA	3.43	0.33

CI: confidence interval; OR: odds ratio; WBC: white blood cells; ALC: absolute lymphocyte count; ANC: absolute neutrophil count; RBC: red blood cells; NLR: neutrophil lymphocyte ratio; CK: creatine kinase; CK-MB: creatine kinase isoenzyme; ALT: alanine aminotransferase; AST: aspartate aminotransferase; GGT: gamma-glutamyltransferase; LDH: lactate dehydrogenase; IL: interleukin. Values in bold font indicate statistical significance ($p < 0.05$).

patients ($p < 0.05$) (Table 6), while hepatomegaly was a risk factor for prolonged hospital stay in IM patients ($p = 0.02$) (Table 7).

Discussion

Classification of IM patients based on key indicators

The classification of IM patients according to blood EBV-DNA load, duration of hospitalization, and liver damage revealed distinct clinical and laboratory differences. Stratification by EBV-DNA load showed significant variations in fever, cervical lymphadenopathy, CK levels, IgM, and CD4/CD8 ratios; indicating a correlation between EBV-DNA load and these clinical markers. Similarly, classification

Table 5. Logistic regression analysis of plasma EBV-DNA load in infectious mononucleosis.

Variable	*β*	SE	Wald χ^2	OR (95% CI)	*p* value
Fever	1.53	0.7	4.8	4.63 (1.18, 18.27)	**0.03**
Cervical lymphadenopathy	– 1.55	0.8	3.77	0.21 (0.04, 1.02)	0.05
CK	– 0.001	0.002	0.57	1.00 (1.00, 1.00)	0.45
IgM	0.41	0.22	3.47	1.51 (0.98, 2.33)	0.06
CD4/CD8	– 1.2	0.87	1.87	0.30 (0.06, 1.68)	0.17

SE: standard error; CI: confidence interval; OR: odds ratio; CK: creatine kinase. Values in bold font indicate statistical significance ($p < 0.05$).

Table 6. Logistic regression analysis of infectious mononucleosis hospitalization days.

Variable	*β*	SE	Wald χ^2	OR (95% CI)	*p* value
Age	0.08	0.07	1.53	1.09 (0.95, 1.24)	0.22
Hepatomegaly	0.81	0.36	5.12	2.24 (1.11, 4.51)	**0.02**
Splenomegaly	– 0.08	0.36	0.05	0.92 (0.45, 1.88)	0.83
ALT	0.01	0.01	1.69	1.01 (1.00, 1.02)	0.19
AST	0.01	0.01	0.43	1.01 (0.99, 1.02)	0.51
GGT	– 0.01	0.01	2.92	0.99 (0.98, 1.00)	0.09
IgG	0.04	0.04	1.16	1.04 (0.97, 1.12)	0.28
IgA	0.09	0.21	0.16	1.09 (0.72, 1.65)	0.69
IgM	– 0.01	0.23	0	0.99 (0.63, 1.56)	0.96
C3	– 1.02	0.95	1.14	0.36 (0.06, 2.33)	0.29
Total lymphocyte count	0	0	0.28	1.00 (1.00, 1.00)	0.60
CD3+ absolute count	0	0	0.11	1.00 (1.00, 1.00)	0.75
CD8+ absolute count	0	0	0.09	1.00 (1.00, 1.00)	0.76
CD4/CD8	– 0.69	0.86	0.64	0.50 (0.09, 2.73)	0.43
LDH	0	0	0.21	1.00 (1.00, 1.00)	0.64
Ferritin	0	0	0	1.00 (1.00, 1.00)	0.96
Liver damage	0.62	0.5	1.55	1.85 (0.70, 4.91)	0.21

SE: standard error; CI: confidence interval; OR: odds ratio; WBC: white blood cells; ALC: absolute lymphocyte count; ANC: absolute neutrophil count; RBC: red blood cells; NLR: neutrophil lymphocyte ratio; ALT: alanine aminotransferase; AST: aspartate aminotransferase; GGT: gamma-glutamyltransferase; LDH: lactate dehydrogenase. Values in bold font indicate statistical significance ($p < 0.05$).

Table 7. Logistic regression analysis of infectious mononucleosis liver injury.

Variable	*β*	SE	Wald χ^2	OR (95% CI)	*p* value
Age	0.22	0.08	7.9	1.25 (1.07, 1.46)	**0.01**
Splenomegaly	0.41	0.39	1.11	1.51 (0.70, 3.23)	0.29
Lymphocyte (%)	0	0.04	0	1.00 (0.93, 1.07)	1
Neutrophil (%)	0.06	0.05	1.2	1.06 (0.96, 1.17)	0.27
ALC	0.03	0.04	0.49	1.03 (0.95, 1.12)	0.48
ANC	– 0.52	0.2	6.58	0.59 (0.40, 0.88)	**0.01**
NLR	0.28	0.58	0.24	1.33 (0.43, 4.10)	0.62
Platelets	0	0	0.52	1.00 (1.00, 1.01)	0.47
IgG	0.01	0.02	0.06	1.01 (0.96, 1.05)	0.81
IgA	– 0.03	0.09	0.14	0.97 (0.81, 1.16)	0.71
IgM	0.31	0.26	1.41	1.37 (0.82, 2.29)	0.24
C3	– 0.38	1.16	0.11	0.68 (0.07, 6.68)	0.74
Total lymphocyte count	0	0	0.21	1.00 (1.00, 1.00)	0.65
CD3+ absolute count	0	0	0.87	1.00 (1.00, 1.00)	0.35
CD8+ absolute count	0	0	0.35	1.00 (1.00, 1.00)	0.56
CD16/56	0	0	1.93	1.00 (1.00, 1.00)	0.17
CD19+ absolute count	0	0	1.01	1.00 (1.00, 1.00)	0.32
CD4/CD8	– 0.84	1.16	0.53	0.43 (0.04, 4.18)	0.47
LDH	0.01	0	5.12	1.01 (1.00, 1.01)	**0.02**
Ferritin	0.01	0	8.05	1.01 (1.00, 1.01)	**0.01**
Hospital days	0.27	0.09	8.9	1.30 (1.10, 1.55)	**< 0.01**

SE: standard error; CI: confidence interval; OR: odds ratio; ALC: absolute lymphocyte count; ANC: absolute neutrophil count; NLR: neutrophil lymphocyte ratio; LDH: lactate dehydrogenase. Values in bold font indicate statistical significance ($p < 0.05$).

based on liver damage demonstrated differences in age, splenomegaly, hematological and immunological markers, and ferritin levels; suggesting an association between liver damage and clinical-laboratory parameters. Additionally, classification by duration of hospitalization revealed notable differences in age, hepatomegaly, splenomegaly, immune markers, and ferritin; underscoring a potential link between hospitalization duration and clinical variables.

Correlation between EBV DNA load and clinical manifestations

Children with higher EBV DNA loads also exhibited increased IgM levels, suggesting a link between elevated EBV DNA load and more severe clinical manifestations, consistent with previous research [3]. In contrast, a lower CD4/CD8 ratio indicates that a higher EBV DNA load may result in significant tissue damage or a heightened immune response. Fever, a common symptom of EBV infections, was more prevalent in the group with high EBV DNA loads, suggesting that monitoring blood EBV DNA levels could be a useful marker for fever in pediatric cases. Notably, cervical lymphadenopathy was less common in the high load group, which may indicate milder clinical symptoms in cases with a prolonged disease course. Variations in CK levels across the different EBV DNA load groups may be due to sampling biases and require further investigation in larger cohorts.

Association of clinical and laboratory markers with hospitalization duration

A range of clinical and laboratory markers, including age, hepatomegaly, splenomegaly, liver function parameters, immune markers, LDH, liver damage markers, and ferritin, were associated with the duration of hospitalization. Multivariate analysis revealed that hepatomegaly was an independent risk factor for extended hospitalization, indicating its potential as a predictor for hospitalization length. These markers, which are readily available in primary healthcare settings, hold significant clinical relevance, highlighting the importance of actively monitoring liver function in hospitalized children. Although a certain correlation was observed between these factors and the length of hospital stay, changes in length of hospital stay may not only be caused by the condition itself, but may also be influenced by doctors' decisions. Therefore, this outcome needs to be implemented with caution.

Association between liver damage and laboratory markers

Age, neutrophil count, LDH, and ferritin were found to be associated with liver damage. Older children and those with splenomegaly were more prone to liver damage, likely due to the inherently weaker immune responses in younger children [12]. The neutrophil count and ratio decrease, and lymphocyte count and ratio increase, in cases of liver damage; leading to a decreased neutrophil-lymphocyte ratio (NLR). The pathophysiology involves the virus entering hepatocytes, inducing damage, and triggering immune responses, where lymphocytes target infected cells [13]. LDH, an important marker of cellular injury, was significantly elevated in the presence of liver damage, reinforcing its role as a biomarker for hepatic injury [14]. Elevated LDH levels reflect cellular necrosis and immune activation [15], which are associated with prolonged hospitalization.

Role of ferritin as a diagnostic marker

Ferritin, an acute-phase reactant, was elevated in children with liver damage, supporting its use as a diagnostic marker, particularly for HLH, with sensitivity levels approaching 84%. The dynamic monitoring of ferritin levels is critical in understanding disease progression and potential complications [16].

Treatment considerations

The investigation's scope was specifically delineated to analyze clinical and laboratory parameters of pediatric IM; and treatment modalities were intentionally excluded from the analytical framework. The established clinical approach to pediatric IM predominantly involves supportive care interventions. Corticosteroid therapy may be indicated in cases presenting with severe complications, including significant airway obstruction or hepatic involvement. Contemporary clinical practice does not routinely advocate antiviral therapy for typical IM cases, as the condition generally demonstrates spontaneous resolution with symptomatic management. Comprehensive treatment algorithms are documented in clinical practice guidelines, with therapeutic approaches tailored to disease severity and specific complications [11].

Limitations and future directions

This retrospective study offers valuable insights into the clinical and laboratory characteristics of patients with IM, particularly regarding risk factors for liver damage and prolonged hospitalization. The

findings enhance our epidemiological understanding of IM in economically developed coastal regions of China. However, the study's limitations stem from its retrospective design and reliance on data from a single center, which may introduce selection bias and restrict the generalizability of the results.

Future research should incorporate more extensive subgroup analyses to assess the impact of factors such as age, gender, and disease severity on the clinical progression of EBV infections. A prospective cohort design with broader multi-center participation would help alleviate the biases associated with retrospective studies and improve the generalizability and applicability of the findings. Additionally, future studies should account for additional confounders and increase sample sizes to enhance the precision and robustness of the conclusions.

Conclusions

In developing countries, such as China, the onset of IM is primarily observed in preschool-aged children. Children with IM should be closely monitored for fever. It is essential to assess ANC, LDH, and ferritin levels in the case of children who are suspected of having IM, with particular attention given to potential liver damage in preschool-aged children. Liver damage and hepatomegaly in hospitalized children with IM may prolong the duration of hospitalization and increase the economic burden on families. Early diagnosis and timely treatment are crucial for improving social outcomes.

Data availability

All data included this study are available upon request from the corresponding author.

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Authors' contributions

CW, literature review, data collection, statistical analysis, manuscript writing and revision; SS, manuscript writing; YZ, data collection; GL, research design and technical support; CJ, research design, quality control, guidance, review, and responsible for the overall article.

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Conflict of interests

No conflict of interests is declared.

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