Risk Factors for Transaminase Elevation in Children with Epstein-Barr Virus Infectious Mononucleosis

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Research Article

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Abstract

Objective: To study the risk factors of Epstein-Barr virus (EBV) infectious mononucleosis (EBV-IM) in children with elevated transaminase.

Methods: A retrospective analysis of the clinical data of 533 children with EBV-IM who were hospitalized and diagnosed in the Affiliated Hospital of Southwest Medical University from January 1, 2018, to May 31, 2021. The alanine aminotransferase (ALT)> 40U/L or aspartate aminotransferase (AST)>40U/L was defined as elevated transaminase and divided into normal group and abnormal group based on that. Monofactor analysis and logistic regression analysis were used to explore the risk factors of EBV-IM with the elevation of transaminase, and the receiver operating characteristic (ROC) curve was drawn to evaluate the predictive ability of each indicator.

Results: Of the 533 cases, 428 cases (80.3%) were in the transaminase elevation group, there were 277 cases(52.0%) of ALT elevation and 414 cases(77.7%) of AST elevation. The multifactor Logistic regression showed that the fever, age, γ -glutamyl transferase(GGT), atypical lymphocyte(ALYM), and albumin(ALB) were associated with elevated ALT (OR=0.351, 1.140, 1.053, 1.032, 0.912, All $P<0.05$) and age, GGT, ALYM, ALB predict the area under the ROC curve(AUC) of EBV-IM with ALT elevation were 0.665, 0.890, 0.579, 0.669, and GGT, mean platelet volume to platelet count(MPV/PLT%) were correlated with increased AST(OR=1.029, 1.220, all $P<0.05$) the AUC predicted GGT and MPV/PLT(%) for EBV-IM and AST increase were 0.715 and 0.623.

Conclusion: With EBV-IM in children, Fever, age, GGT, ALYM, and ALB are risk factors for ALT elevation, and GGT, MPV/PLT(%) are risk factors for AST elevation.

Background

Epstein-Barr virus (EBV), which can infect more than 90% of the population asymptotically, is a human lymphocyte virus and belong to the human γ -1 herpes virus^[1,2]. EBV usually infects B cells in oropharyngeal lymphoid tissues, and can immortalize target lymphocytes and latent activation; it may lead to downregulation of most viral gene expressions, which can evade the host's immune response^[3-5]. EBV infectious mononucleosis (EBV-IM) is a proliferative disease of the mononuclear-macrophage system caused by EBV infection, which is one of the common infectious diseases in childhood. EBV-IM mainly manifests as a typical clinical "triad": fever, angina, and large cervical lymph nodes, which can be combined with hepatomegaly and splenomegaly, and increased heteromorphic lymphocytes^[6-8]. The crowd is generally susceptible, especially children and adolescents^[8,9]. EBV-IM can affect multiple organs and cause organ damage, of which transaminase elevation is the most common^[10-12]. Therefore, it is of great significance to investigate the risk factors for transaminase elevation in children with EBV-IM. The present study retrospectively analyzed the clinical data of 533 children with EBV-IM in the Affiliated Hospital of Southwest Medical University, and investigate the risk factors of transaminase elevation from the basic characteristics, main clinical manifestations, laboratory examinations, and other indicators, and provide evidence for early intervention.

Materials And Methods

1.1 Patients

Clinical data of 533 children hospitalized with EBV-IM from January 1, 2018, to May 31, 2021, in the Department of Pediatrics, Affiliated Hospital of Southwest Medical University were collected. There were 327 males and 206 females. The age was 5.11 ± 3.41 years, ranging from 5 months to 18 years.

1.2 Inclusion criteria

The diagnostic criteria are as follows^[13] (1) laboratory-confirmed cases: meeting any 3 of the following clinical symptoms and any 1 to 3 of the laboratory indicators. (2) clinical diagnosis cases: any 3 of the following clinical indicators and the fourth of the laboratory indicators. Clinical symptoms: a. fever; b. angina; c. large cervical lymph nodes; d. splenomegaly; e. hepatomegaly; f. eyelid swelling. Laboratory indicators: a. positivity for anti-EBV-capsid antigen (CA)-IgM and anti-EBV-CA-IgG antibodies, negativity for anti-EBV-nuclear antigen-IgG; b. negativity for anti-EBV-CA-IgM but positivity for anti-EBV-CA-IgG antibody, which is a low-affinity antibody; c. Double serum anti-EBV-VCA-IgG antibody titer increased by more than 4 times; d. Heteromorphic lymphocyte $\geq 10\%$ and (or) lymphocyte increase $\geq 5.0 \times 10^9/L$ ^[13].

1.3 Exclusion criteria

(1) Tumor infections, autoimmune diseases, hematological diseases, and children who have recently used immunosuppressive agents; (2) At the same time, acute infectious hepatitis, cytomegalovirus (CMV), herpes simplex virus (HSV), and other infections are excluded^[14]. (3) Cannot provide transaminase data

1.4 Criteria for transaminase elevation

In the present study, ALT $> 40 U/L$ or AST $> 40 U/L$ was defined as elevated transaminase, based on the results of ALT and AST detection of children with EBV-IM after admission, and they were divided into normal group and abnormal group^[15].

1.5 Methods

The basic characteristics, clinical manifestations, laboratory examination results, treatment process, and other data of the children were recorded by consulting medical records, and the children were divided into normal groups and abnormal groups.

1.6 Evaluation indexes

Evaluation indexes including basic characteristics (gender, age, season, BMI (Body Mass Index)), clinical symptom (the duration of fever, thermal spike, hepatomegaly, splenomegaly, large cervical lymph nodes, eyelid swelling, angina), laboratory examinations (white blood cell (WBC), neutrophil (NEU), lymphocyte (LYM), atypical lymphocyte (ALYM), red blood cell distribution width-variation coefficient (RDW-CV), mean platelet volume to platelet count (MPV/PLT) (%), albumin (ALB), globulin (GLO), direct bilirubin (DBIL), γ -glutamyl transferase (GGT), uric acid (UA), and so on.

1.7 Statistical analysis

The Kolmogorov-Smirnov normality test was used to determine if the data is normally distributed. Continuous data were analyzed using independent samples t-test. The Mann-Whitney U-test was used to compare differences in non-parametric variables (non-normally distributed data). Categorical variables were presented as a proportion and analyzed with the Chi-squared test. Values were expressed as n (%), the mean $\pm$ standard deviation or median (interquartile range). First, perform single-factor analysis on each indicator; secondly, perform multi-factor Logistic regression analysis on variables with statistical significance in single-factor analysis; draw receiver operating characteristic curve (ROC) curve to evaluate the predictive ability of each indicator. All statistical analyses were performed using SPSS version 25.0 (IBM Corp.). $P < 0.05$ was considered to indicate statistical significance.

Results

2.1 Incidence of transaminase elevation

Among the 533 children, 428 cases (80.3%) were complicated with elevated transaminase. Among them, there were 277 cases (52.0%) of ALT elevation, mild elevation (40-160 U/L) accounted for 63.2% (175/277), moderate elevation (160-400 U/L) 31.0% (86/277), severe increase ($> 400 U/L$) by 5.8% (16/277); AST increased in 414 cases (77.7%),

mild elevation(40-160 U/L) accounted for 84.3% (349/414), moderately increased (160 -400 U/L) 13.3% (55/414), severe increase (>400 U/L) 2.4% (10/414)

2.2 Single-factor analysis of evaluation indexes

Divided the data into ALT group and AST group, and perform univariate analysis on each evaluation index; In the ALT group, the nineteen indices, gender, age, fever, Angina, lymphadenopathy, hepatomegaly, splenomegaly, IgM, IgG, WBC, LYM, RDW-CV, MPV/PLT(%),ALYM, ALB, GLO,GGT,DBIL andUA, exhibited statistically significant differences between the normal group and abnormal group (AIP<0.05; Table 1). In the AST group, the twelve indices, gender, BMI, fever, hepatomegaly, splenomegaly, WBC, NEU, LYM, MPV/PLT(%),ALYM, albumin, GGT, exhibited statistically significant differences between the normal group and abnormal group (AIP<0.05; Table 2)

2.3 Logistic regression analysis of risk factors

The variables,which were statistically significant in the univariate analysis of the ALT group and the AST group,were subjected to multivariate logistic regression analysis. The results showed that the age, WBC, AST, and GGT are risk factors for EBV-IM combined with elevated ALT; GGT and MPV/PLT (%) are the risk factors for EBV-IM combined with elevated AST(Table 3)

2.4 Predictive value of risk factors for EBV-IM with elevated transaminase

In the ALT group, the ROC curve analysis results showed (Figure 1) that age, GGT, AYM, ALB predicted the area under the curve (AUC) of EBV-IM with elevated ALT was 0.665, 0.890, 0.579, 0.669, the best cut-off The values were 5.29y, 22.2 U/L, 11.9%, 43.5g/L (Table 4). In the AST group, the ROC curve analysis results showed (Figure 2) that the GGT, MPV/PLT (%) predicted the AUC of EBV-IM with elevated ALT was 0.715 and 0.623, and the best cut-off values are 26.05U/L,4.67% (table4);At the same time, all variables were grouped by cut-off value, and there were statistically significant differences between the normal group and abnormal group(AIP<0.05; Table 5 and Table 6).

Discussion

EBV can indefinitely proliferate target lymphocytes and the characteristics of latent activation, which proved to be the source of infectious mononucleosis (IM) in 1968^[3].EBV mainly invades pharyngeal epithelial cellsand then targets B lymphocytes. It uses the molecular mechanism of B lymphocytes to replicate the viral genome and produce memory B lymphocytes. The latter enters the circulatory system, or remains inactive until triggered to reactivate ^[4,5], and further induces T cells to transform into cytotoxic effector cells, namely atypical lymphocytes, leading to a series of immune damages^[4,5,16].

EBV-IM can cause multiple system damages, leading to some complications, such as liver damage, pneumonia, acute nephritis, meningitis, peripheral neuropathy, hepatitis, ruptured spleen, skin ulcers, hemophagocytic syndrome, etc., among which liver injury is the most common ^[10-12,17,18],which is mainly manifested as elevated transaminase. The mechanism of liver damage caused by EBV-IM is still unclear. Relevant research showed that EBV does not directly infect hepatocytes, bile duct epithelium or vascular endothelium, but causes cytotoxic CD3+ and CD8+ T lymphocyte infiltration, which leads to liver cell damage^[16]Other research showed that the level of inflammatory cytokines in the serum of EBV-IM patients is increased, and the level of interferon-gamma (IFN-γ) and its breakdown products can cause liver dysfunction^[19].Thepresent study found that the incidence of elevated transaminase in EBV-IM accounted for 80.3%, which is similar to foreign literature reports.^[20,21]

The present study conducted a monfactor analysis of possible influencing variables and further logistic regression analysis. The results found that for EBV-IM with elevated ALT, GGT, ALB, Age, and AYM were risk factors, and fever is the protective factor; for EBV-IM complicated with elevated AST, GGT and MPV/PLT% were risk factors.

The ALT in the liver is mainly found in the liver cytoplasm, and its intracellular concentration is 1000-3000 times higher than that in the serum. When the liver cells are slightly damaged, due to the degeneration and necrosis of the liver cells, the permeability of the liver cell membranes increases, etc., ALT penetrates the blood in a large amount, which makes the serum ALT content significantly increase, and the sensitivity is strong^[22]. In addition, liver enzymes also include AST and GGT. AST is mainly found in the mitochondria of the liver cytoplasm and is distributed in other parts of the human body, such as the myocardium and skeletal muscle cells. Therefore, it is less sensitive than ALT in terms of responding to liver function. ; GGT mainly exists on liver cell membranes and microsomes. Therefore, when ALT and AST increase, GGT may also increase. This study shows that when GGT>26.05U/L, there may be an increase in ALT and AST.

There was a correlation between elevated transaminases in children with EBV-IM and age^[23-26], It was considered that as age increases, the immune system gradually improves, which leads to the damage of liver cells. EBV causes a strong CD4⁺ and CD8⁺ T cell response during the pathogenic process. Mature single CD4⁺ and CD8⁺ T cells are first detected in the thymus at the 15th week, and they appear in large numbers in the periphery before birth. But it is significantly different from adult T cells in that it responds poorly to foreign antigens. As the age increases, the immune system of children is gradually improved, and the immune defense response becomes stronger^[27]. This study included 533 children with EBV-IM, a total of 277 cases (52.0%) with elevated ALT, and the incidence of liver damage in the 3 to the 6-year-old group was 35.7% (95/277), which was higher than that in other age groups. Factors and multivariate analysis suggest that age is an independent risk factor for elevated ALT, and when the age is greater than 5.26 years, it is necessary to be alert to the possibility of abnormalities. This conclusion is consistent with the results of Zhang et al.^[26], so the treatment process children pay attention and follow up. When EBV infection occurs, a series of immune reactions occur in the body, which can induce T cells to transform into cytotoxic effector cells, that is, atypical lymphocytes. The latter may cause damage to liver cells and trigger the increase of transaminase. The liver is the main source of ALB production. In the setting, when liver cell injury cannot be compensated, it can cause albumin content to decrease. This study suggested that when ALYM>11.9%, ALB<43.5g/L, EBV-IM children may have ALT abnormalities.

Fever is the most common symptom of EBV-IM, which easily attracts parents' attention. The protection mechanism is not clear at present. The possible reason is that the interval between treatment after onset is longer than that in children with fever. The interval between the non-fever group is 5(4,7) , And the fever group interval is 4(3,6). According to Mann-Whitney U test, Z=-2.632, P=0.008; Related studies suggest that MPV/PLT% may be a new diagnostic indicator of EBV-IM in children, and indirectly to predict liver injury^[28], this study shows that MPV/PLT% is a risk factor for EBV-IM with elevated AST. When MPV/PLT%>4.67, AST may be increased concurrently.

In the context of liver disease, such as alcoholic cirrhosis, RDW was higher in patients than in normal controls^[29,30]. Research suggested that RDW can be used as an index to predict liver damage in children with EBV-IM^[31,32], RDW-CV is often used instead of RDW in clinical practice. The present study showed that there is no significant difference in the distribution of RDW-CV in the non-liver damage group and the liver damage group of children with EBV-IM, and the difference is not statistically significant (P>0.05), the possible reason is that EBV-IM is mostly acute onset after occult infection, lasting for several weeks^[19], while RDW-CV is more used to respond to chronic damage.

Conclusions

In summary, after the occurrence of EBV infection, when the age is >5.29 years, GGT>22.2 U/L, ALYM>11.9%, ALB<43.5g/L, it indicates that the child has a high possibility of ALT abnormality; when GGT>26.05 U/L, MPV/PLT%>4.67% indicates that AST is more likely to be abnormal, the monitoring and follow-up of high-risk children with elevated transaminase should be strengthened. At the same time, this study has certain limitations. Because it is a single-center retrospective study, there is a bias in case selection. The result can only be used as an indirect speculation of the change of transaminase, and it needs to be confirmed by a larger sample.

Declarations

Ethics Approval and Informed Consent

The study protocol has been approved by the Medical Ethical Committee of The Affiliated Hospital of Southwest Medical University with an approval number [KY2021194] and performed according to the Declaration of Helsinki. Due to the nature of this retrospective study without any additional interventions, patients' informed consents were exempted. All personally identifiable records were kept confidential.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests The author(s) declared no potential conflicts of interest concerning the research, authorship, and/or publication of this article.

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Authors' contributions

CQ collected patient data and conducted statistical analysis, and was a major contributor in writing the manuscript. ZYM collected patient data. LWJ gave writing guidance and manuscript revision; All authors read and approved the final manuscript.

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Tables

Table 1 Comparison of estimate indexes in children with EBV-IM between the ALT normal group and ALT abnormal group

Variable	Normal n=256	Abnormal n=277	c ² /t/z	P
Characteristic				
gender			11.373 ^a	0.001
males	176(68.8)	151(54.5)		
females	80(31.3)	126(45.5)		
Season			0.389	0.943
Spring	77(30.1)	84(30.3)		
Summer	74(28.9)	85(30.7)		
Autumn	55(21.5)	59(21.3)		
Winter	50(19.5)	49(17.7)		
BMI/kg/m ²	15.42(14.31,16.91)	15.23(14.2,16.72)	-0.560	0.575
Age/years	3.5(2.21,5.21)	5.25(3.25,7.92)	-6.578 ^b	<0.001
Clinical symptom				
Fever%	240(93.8)	245(88.4)	4.565	0.033
Thermal spike%			4.507	0.212
<37.3	17(6.6)	32(11.6)		
37.3~38	21(8.2)	26(9.4)		
38.1~39	85(33.2)	90(32.5)		
>39	133(52)	129(46.6)		
Eyelid swelling%	120(46.9)	162(58.5)	7.196	0.007
Angina%	247(96.5)	256(92.4)	4.14	0.042
Large cervical lymph nodes%	242(94.5)	272(98.2)	5.195	0.023
Hepatomegaly%	65(25.4)	95(34.3)	5.023	0.025
Splenomegaly%	34(13.3)	68(24.5)	10.915	0.001
Rashes%	39(15.2)	45(16.2)	0.102	0.749
The duration of fever [d, M(P ₂₅ ,P ₇₅)]	4(3,6)	5(2,6)	-0.627	0.531
Treatment interval [d, M(P ₂₅ ,P ₇₅)]	4(3,6)	4(3,6)	-0.188	0.851
laboratory examinations				
IgM%			12.572	<0.001
negative	58(22.7)	31(11.2)		

positive	198(77.3)	246(88.8)		
IgG% ^a			7.089	0.008
negative	51(19.9)	32(11.6)		
positive	205(80.1)	245(88.4)		
WBC[*10 ⁹ /L,M(P ₂₅ ,P ₇₅)]	13.46(10.02,17.49)	15.78(11.75,20.21)	-4.072	<0.001
NEU[*10 ⁹ /L,M(P ₂₅ ,P ₇₅)]	4.04(2.84,5.81)	3.85(2.64,5.94)	-0.978	0.328
LYM[*10 ⁹ /L,M(P ₂₅ ,P ₇₅)]	7.51(5.22,10.75)	10.19(6.62,13.27)	-5.446	<0.001
RDW-CV[%M(P ₂₅ ,P ₇₅)]	13.3(12.7,13.8)	13.2(12.7,13.6)	-1.183	0.237
MPV/PLT% [M(P ₂₅ ,P ₇₅)]	4.63(3.55,6.06)	4.97(3.88,6.27)	-2.188	0.029
ALYM[M(P ₂₅ ,P ₇₅)]	11(7,15)	12(8,19)	-3.144	0.002
DBIL[μmmol/L,M(P ₂₅ ,P ₇₅)]	2.31(1.50,3.00)	2.80(2.00,4.27)	-5.820	0.001
ALB[g/L,M(P ₂₅ ,P ₇₅)]	44.6(42.55,46.55)	42.8(40.79,44.7)	-6.676	<0.001
GLO[g/L,M(P ₂₅ ,P ₇₅)]	27(24.65,29.7)	28.7(25.8,31.4)	-3.837	<0.001
GGT[U/L,M(P ₂₅ ,P ₇₅)]	13.65(11.5,18.6)	61.3(27,125.4)	-15.574	<0.001
UA[μmmol/L,`X±S]	318.78±84.88	334.93±98.52	-2.020 ^c	0.044

Notes^aNotes^a,refers to the *c*2 value^b, refers to the z value;^c, refers to the t value; ALT, alanine aminotransferase; BMI^aBody Mass Index^aSpring^aMar. to May^aSummer^aJune to Aug.^aAutumn^aSep. to Nov.; Winter^aDec. to Feb.WBC, white blood cell; NEU, neutrophil; LYM, lymphocyte; RDW-CV, Red blood cell distribution width-variation coefficient; PLT, platelet count; MPV, mean platelet volume; ALYM,atypical lymphocyte, ALB, albumin; GLO, globulin; DBIL, Direct bilirubin; GGT, γ-glutamyl transferase; UA, uric acid

Table 2 Comparison of estimate indexes in children with EBV-IM between the AST normal group and AST abnormal group

Variable	normaln=119	abnormaln=414	c ² /t/z	P
Characteristic				
gender			4.556 ^a	0.033
males	83(69.7)	244(58.9)		
females	36(30.3)	170(41.1)		
Season			6.056	0.109
Spring	31(26.1)	131(31.6)		
Summer	55(46.2)	148(35.7)		
Autumn	30(25.2)	109(26.3)		
Winter	3(2.5)	26(6.3)		
BMIkg/m ²	15(13.84,16.23)	15.44(14.26,16.89)	-2.176 ^b	0.030
Ageyears	4.173,6.25	4.21(2.58,6.75)	-0.287	0.778
Clinical symptom				
Fever%			3.202	0.362
Thermal spike%	6(5.0)	43(10.4)		
<37.3	11(9.2)	36(8.7)		
37.3~38	40(33.6)	135(32.6)		
38.1~39	62(52.1)	200(48.3)		
>39	114(95.8)	371(89.6)	4.315	0.038
Eyelid swelling%	60(50.4)	222(53.6)	0.381	0.537
Angina%	115(96.6)	388(93.7)	1.483	0.223
Large cervical lymph nodes%	113(95.0)	401(96.9)	0.498	0.480
Hepatomegaly%	27(22.7)	133(32.1)	3.918	0.048
Splenomegaly%	12(10.1)	90(21.7)	8.114	0.004
Rashes%	14(11.8)	70(16.9)	1.842	0.175
The duration of fever [d,M(P ₂₅ ,P ₇₅)]	4(3,6)	4(2,6)	-0.437	0.662
Treatment interval [d,M(P ₂₅ ,P ₇₅)]	4(3,7)	4(3,6)	-0.647	0.518
laboratory examinations				
IgM%			0.272	0.602
negative	18(15.1)	71(17.1)		
positive	101(84.9)	343(82.9)		

IgG%			0.023	0.879
negative	18(15.1)	65(15.7)		
positive	101(84.9)	349(84.3)		
WBC[*10 ⁹ /L,M(P ₂₅ ,P ₇₅)]	12.99(10.16,16.95)	15(11.12,19.17)	-2.113	0.035
NEU[*10 ⁹ /L,M(P ₂₅ ,P ₇₅)]	4.5(3.37,6.45)	3.83(2.54,5.62)	-3.28	0.001
LYM[*10 ⁹ /L,M(P ₂₅ ,P ₇₅)]	7.31(5.04,10.1)	9.31(6.1,12.87)	-4.087	<0.001
RDW-CV[% ,M(P ₂₅ ,P ₇₅)]	13.3(12.7,13.7)	13.2(12.7,13.7)	-0.412	0.681
MPV/PLT% [M(P ₂₅ ,P ₇₅)]	4.29(3.26,5.42)	5(3.88,6.29)	-4.09	<0.001
ALYM[M(P ₂₅ ,P ₇₅)]	10(7,14)	12(8,17)	-3.011	0.003
DBIL[μmmol/L,M(P ₂₅ ,P ₇₅)]	2.50(1.80,3.14)	2.60(1.70,3.70)	-1.155	0.248
ALB[g/L,M(P ₂₅ ,P ₇₅)]	44.5(42.1,46)	43.28(41.4,45.4)	-2.478	0.013
GLO[g/L,M(P ₂₅ ,P ₇₅)]	27.1(25,30)	28(25,31)	-1.291	0.197
GGT[U/L,M(P ₂₅ ,P ₇₅)]	13.6(11.6,18.8)	29.8(15.2,93.9)	-8.35	<0.001
UA[μmmol/L,`X±S]	316.59±75.44	330.22±96.70	-1.624 ^c	0.106

Notes^a, refers to the χ^2 value^b, refers to the z value^c, refers to the t value; AST, aspartate aminotransferase; BMI Body Mass Index Spring Mar. to May Summer June to Aug. Autumn Sep. to Nov.; Winter Dec. to Feb. WBC, white blood cell; NEU, neutrophil; LYM, lymphocyte; RDW-CV, Red blood cell distribution width-variation coefficient; PLT, platelet count; MPV, mean platelet volume; ALYM, atypical lymphocyte; ALB, albumin; GLO, globulin; DBIL, Direct bilirubin; GGT, γ -glutamyl transferase; UA, uric acid

Table 3 Logistic regression analysis of risk factors for EBV-IM combined with elevated transaminase

	B	S.E.	Wald	P	OR	95% C.I. for EXP(B)	
						Lower	Upper
Age	0.131/	0.056/	5.572/	0.018/	1.140/	1.022/	1.271/
Eyelid Swelling	-0.070/	0.246/	0.080/	0.777/	0.933/	0.576/	1.510/
Angina	-0.517/	0.582/	0.789/	0.374/	0.596/	0.190/	1.867/
UA	0.000/	0.001/	0.001/	0.981/	1.000/	0.997/	1.003/
IgM	0.258/	0.355/	0.529/	0.467/	1.295/	0.645/	2.598/
IgG	-0.209/	0.379/	0.305/	0.581/	0.811/	0.386/	1.704/
DBIL	0.103/	0.104/	0.983/	0.321/	1.109/	0.904/	1.360/
GLO	0.000	0.032/	1.200/	0.273/	0.965/	0.906/	1.028/
gender	0.442/0.19	0.250/0.254	3.116/0.560	0.078/0.454	1.556/1.209	0.952/0.736	2.541/1.987
fever	-1.047/-0.860	0.412/0.516	6.462/2.770	0.011/0.096	0.351/0.423	0.157/0.154	0.787/1.165
Hepato-mealy	-0.191/0.008	0.307/0.304	0.388/0.001	0.533/0.978	0.826/1.008	0.453/0.556	1.507/1.830
Splenmegaly	0.014/0.243	0.368/0.403	0.001/0.363	0.971/0.547	1.014/1.275	0.493/0.579	2.084/2.810
WBC	0.023/0.045	0.042/0.103	0.296/0.187	0.586/0.665	1.023/1.046	0.943/0.855	1.110/1.279
LYM	0.028/0.028	0.055/0.111	0.266/0.062	0.606/0.803	1.029/1.028	0.924/0.827	1.145/1.278
MPV/PL%	-0.006/0.199	0.006/0.073	0.922/7.373	0.337/0.007	0.994/1.22	0.983/1.057	1.006/1.408
ALYM	0.032/0.018	0.016/0.017	4.088/1.135	0.043/0.287	1.032/1.018	1.001/0.985	1.064/1.052
ALB	-0.092/0.011	0.043/0.040	4.450/0.080	0.035/0.777	0.912/1.011	0.838/0.935	0.994/1.094
GGT	0.052/0.029	0.007/0.006	50.892/ 20.005	0.000/0.000	1.053/1.029	1.038/1.016	1.068/1.042
BMI	/0.028	/0.054	/0.262	/0.608	/1.028	/0.925	/1.142
NEU	/-0.141	/0.125	/1.274	/0.259	/0.868	/0.680	/1.110
Constant	1.236/-1.518	2.413/1.965	0.263/0.597	0.608/0.44	3.443/0.219		

Notes: OR, odds ratio; The slash (/) in each data indicates the ALT data, the AST corresponds to data after slash; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, Body Mass Index; WBC, white blood cell; NEU, neutrophil; LYM, lymphocyte; RDW-CV, Red blood cell distribution width-variation coefficient; PLT, platelet count; MPV, mean platelet volume; ALB, albumin; GLO, globulin; DBIL, Direct bilirubin; GGT, γ -glutamyl transferase; UA, uric acid;

Table 4 AUC value for prediction of transaminase elevation in children with EBV-IM

Group	Variable	AUC	95%CI	P	sensitivity %	specificity %	Cut-of Value
ALT	GGT	0.890	0.861-0.919	<0.001	83.4	84.8	22.20
	Age	0.665	0.619-0.710	<0.001	49.8	76.2	5.29
	ALYM	0.579	0.530-0.627	0.002	57.0	57.0	11.90
	ALB	0.669	0.624-0.715	<0.001	61.7	64.5	43.50
AST	GGT	0.751	0.707-0.794	<0.001	55.3	89.1	26.05
	MPV/PLT%	0.623	0.566-0.680	<0.001	58.7	63.0	4.67

Notes: AUC, area under curve; GGT, γ -glutamyl transferase; ALYM, atypical lymphocyte; ALB, albumin; PLT, platelet count; MPV, mean platelet volume

Table 5 Comparison of cut-off value of estimate indexes in children with EBV-IM between the ALT normal group and ALT abnormal group

Variable	normal n=256	abnormal n=277	χ^2	P
GGT(U/L)			247.272	<0.001
<22.2	217(84.8)	46(16.6)		
$\geq$ 22.2	39(15.2)	231(83.4)		
Age(y)			38.415	<0.001
<5.29	195(76.2)	46(16.6)		
$\geq$ 5.29	61(23.8)	231(83.4)		
ALYM(%)			10.537	0.001
<11.9	140(57.0)	119(43.0)		
$\geq$ 11.9	110(43.0)	158(57.0)		
ALB(g/l)			36.502	<0.001
<43.5	91(35.5)	171(61.7)		
$\geq$ 43.5	165(64.5)	106(38.3)		

Notes: GGT, γ -glutamyl transferase; ALYM, atypical lymphocyte; ALB, albumin

Table 6 Comparison of cut-off value of estimate indexes in children with EBV-IM between the ALT normal group and ALT abnormal group

Variable	normaln=119	abnormaln=414	c2	P
GGT(U/L)			73.473	<0.001
<26.05	106(89.1)	185(44.7)		
≥26.05	13(10.9)	229(55.3)		
MPV/PLT%			16.613	<0.001
<4.67	74(62.2)	185(44.7)		
≥4.67	45(37.8)	229(55.3)		

Notes: GGT, γ-glutamyl transferase; PLT, platelet count; MPV, mean platelet volume

Figures

Diagonal segments are produced by ties.

Figure 1

AUC of the duration of the GGT, Age, ALYM, and ALB for EBV-IM with elevated ALT

Notes: ROC, receiver operating characteristic; GGT, γ -glutamyl transferase; ALYM, atypical lymphocyte; ALB, albumin

Diagonal segments are produced by ties.

Figure 2

AUC of the duration of the GGT,MPV/PLT% with elevated AST

Notes: ROC, receiver operating characteristic; GGT, γ -glutamyl transferase; PLT, platelet count; MPV, mean platelet volume