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Research Article

Systemic Immune-Inflammation Index and Hematological Ratios as Indicators of Hepatic Dysfunction in Thalassemia-Associated Liver Disease

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Abstract

Objective: This study aimed to investigate the relationship between systemic inflammatory biomarkers and clinical and biochemical indicators of liver dysfunction in patients with thalassemia-associated liver disease. ***Methods***: A cross-sectional study was conducted involving 50 patients with thalassemia-associated liver disease. Demographic characteristics, hematological parameters, inflammatory biomarkers, and liver function tests were collected. Inflammatory indices including neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), lymphocyte-to-monocyte ratio (LMR), and systemic immune-inflammation index (SII) were calculated from routine complete blood count parameters. Pearson correlation analysis was performed to evaluate associations between inflammatory biomarkers and indicators of hepatic dysfunction, including prothrombin time (PT) and international normalized ratio (INR). Multivariate regression analysis was applied to identify independent predictors of symptom burden. ***Results***: The mean age of participants was 52.1±19.7 years, with a predominance of female patients. C-reactive protein (CRP) showed significant positive correlations with NLR ($r=0.45$, $p=0.001$), PLR ($r=0.41$, $p=0.003$), and SII ($r=0.50$, $p<0.001$) and a significant inverse correlation with LMR ($r=-0.50$, $p<0.001$). NLR exhibited a strong correlation with SII ($r=0.91$, $p<0.0001$). However, leukocyte-derived indices were not significantly associated with PT or INR. Both PT and INR correlated significantly with CRP and LMR. Multivariate analysis identified PT as the only independent predictor of symptom burden ($p< 0.0001$). ***Conclusions***: Inflammatory biomarkers reflect systemic immune activation in thalassemia-associated liver disease, whereas PT remains the most reliable indicator of disease severity. Integrating inflammatory indices with conventional liver function markers may improve clinical assessment.

Keywords: Liver disease; Neutrophil-to-lymphocyte ratio; Prothrombin time; Systemic inflammation; Systemic immune-inflammation index; Thalassemia.

مؤشر المناعة الالتهابية الجهازي ونسب الدم كمؤشرات على خلل الكبد في أمراض الكبد المرتبطة بالثلاسيميا

الخلاصة

الهدف: دراسة العلاقة بين المؤشرات الالتهابية الجهازية والمؤشرات السريرية والكيميائية الحيوية لخلل الكبد لدى مرضى أمراض الكبد المرتبطة بالثلاسيميا. **الطرائق**: أجريت دراسة مقطعية شملت 50 مريضا يعانون من أمراض الكبد المرتبطة بالثلاسيميا. تم جمع الخصائص الديموغرافية، والمعايير الدموية، والمؤشرات الحيوية الالتهابية، واختبارات وظائف الكبد. تم حساب مؤشرات الالتهاب بما في ذلك نسبة العدلات إلى الخلايا اللمفاوية (NLR)، ونسبة الصفائح الدموية إلى الخلايا اللمفاوية (PLR)، ونسبة الخلايا اللمفاوية إلى الوحيدية (LMR)، ومؤشر المناعة الالتهابية الجهازي (SII) من خلال معايير عد دم كاملة روتينية. تم إجراء تحليل الارتباط بيرسون لتقييم الروابط بين المؤشرات الحيوية الالتهابية ومؤشرات خلل وظائف الكبد، بما في ذلك زمن البروثرومبين (PT) والنسبة الدولية الطبيعية (INR). تم تطبيق تحليل الانحدار متعدد المتغيرات لتحديد المؤشرات المستقلة لحمل الأعراض. **النتائج**: كان متوسط عمر المشاركين 52.1±19.7 سنة، مع غلبة من الإناث. أظهر البروتين التفاعلي C (CRP) علاقات إيجابية ذات دلالة مع NLR ، PLR، وSII وارتباط عكسي مع LMR. أظهر NLR ارتباطا قويا مع SII. ومع ذلك، لم تكن المؤشرات المشتقة من الخلايا البيضاء مرتبطة بشكل دلالي بPT أو INR. كان كل من PT و INR مرتبطين بشكل كبير مع CRP و LMR. حدد التحليل متعدد المتغيرات PT كالمتنبئ المستقل الوحيد لحمل الأعراض ($p< 0.0001$). **الاستنتاجات**: تعكس المؤشرات الحيوية الالتهابية تنشيط المناعة الجهازية في أمراض الكبد المرتبطة بالثلاسيميا، في حين يظل PT المؤشر الأكثر موثوقية لشدة المرض. قد يحسن دمج مؤشرات الالتهاب مع مؤشرات وظائف الكبد التقليدية التقييم السريري.

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INTRODUCTION

Thalassemia is one of the most common inherited hemoglobinopathies worldwide and is characterized by defective synthesis of α- or β-globin chains, leading to chronic hemolytic anemia and ineffective erythropoiesis. The illness is a significant public health issue across the Mediterranean, Middle Eastern, and Asian communities due to its high prevalence. Patients with transfusion-dependent thalassemia (TDT) now have a far higher chance of life thanks to improvements in blood transfusion programs and iron chelation medication,

although long-term problems affecting several organs are still frequent. Liver disease is a major cause of illness and death in people with thalassemia. If left untreated, it frequently progresses to cirrhosis, fibrosis, and hepatocellular cancer [1,2]. Iron overload from frequent blood transfusions and increased intestinal iron absorption is the main cause of the multifactorial development of liver disease in thalassemia. Excess iron gradually builds up in parenchymal organs, especially the liver, because the human body lacks an efficient physiological mechanism for excreting iron. By producing reactive oxygen species through Fenton chemistry, hepatic iron deposition causes oxidative stress, which results in lipid peroxidation, mitochondrial malfunction, and hepatocellular damage. Furthermore, the primary regulator of systemic iron homeostasis, hepcidin, is suppressed by inefficient erythropoiesis, which increases intestinal iron absorption and exacerbates systemic iron excess [3,4]. Chronic inflammation has also been identified recently as a significant factor in thalassemia-related liver damage. Immune activation, iron-mediated oxidative stress, and persistent hemolysis can all set off systemic inflammatory reactions that worsen hepatic damage and fibrosis. A growing body of research indicates that inflammatory processes are crucial to the development and course of a number of chronic liver disorders, such as iron overload-related liver injury, metabolic-associated fatty liver disease, and viral hepatitis [5]. Therefore, the identification of reliable inflammatory biomarkers may help improve early detection and risk stratification of liver disease. Recently, a number of hematological inflammatory indices obtained from regular complete blood counts have drawn interest as easy-to-use and reasonably priced indicators of systemic inflammation. The neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and lymphocyte-to-monocyte ratio (LMR) are three of these markers that have been extensively studied in various inflammatory and cancerous conditions. Elevated NLR and PLR values often indicate increased inflammatory responses, whereas lower lymphocyte-related indices may indicate compromised immune regulation. These indicators represent the equilibrium between inflammatory activity and immunological regulation. These indicators have been linked to the severity of the disease, the advancement of fibrosis, and unfavorable outcomes in patients with chronic liver disorders, according to earlier research [6]. Neutrophil, lymphocyte, and platelet counts are integrated in the systemic immune-inflammation index (SII), a new biomarker that reflects the interplay between inflammatory, immunological, and thrombotic pathways. SII may offer a more thorough evaluation of systemic inflammation than specific inflammatory ratios. Elevated SII levels are linked to the degree of liver inflammation, the advancement of fibrosis, and poor clinical outcomes in individuals with chronic liver disorders, according to a number of recent studies [7,8]. Laboratory markers representing hepatic synthetic activity are still crucial for assessing the severity of liver disease, in addition to inflammatory biomarkers. Since the liver is where most coagulation factors are made, prothrombin time (PT) and the international normalized ratio (INR) are often used indicators of hepatic synthetic capacity. PT is prolonged and INR readings are raised when the liver produces fewer clotting factors, such as factors II, V, VII, and X. This could be a sign of advanced liver disease and reduced hepatic function [9-11]. Few studies have examined the connection between systemic inflammatory indices and liver illness, particularly in thalassemia patients, despite the growing interest in inflammatory biomarkers in hepatology. Examining the relationship between inflammatory biomarkers and hepatic dysfunction may offer crucial insights into the biology of the disease and possible clinical indicators of its severity, given the substantial burden of iron overload and chronic inflammation in this population. Thus, the goal of the current study was to examine the connection between clinical and laboratory markers of liver disease in thalassemia patients and systemic inflammatory biomarkers, such as NLR, PLR, LMR, and the systemic immune-inflammation index (SII).

METHODS

Study design and participants

This cross-sectional study included patients diagnosed with thalassemia who developed liver disease and were evaluated at a tertiary care center. Patients were enrolled based on a confirmed clinical and laboratory diagnosis of thalassemia. Individuals with incomplete laboratory data or other known inflammatory or infectious diseases were excluded from the study. A total of patients meeting the inclusion criteria were included in the final analysis.

Data collection

Demographic and clinical information, including age and gender, was obtained from medical records. Laboratory parameters were collected from routine hematological and biochemical investigations. The following biochemical parameters were recorded: Alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), total serum bilirubin, C-reactive protein (CRP), prothrombin time (PT), and international normalized ratio (INR). Complete blood count parameters, including white blood cells, neutrophils, lymphocytes, monocytes, and platelet counts, were also recorded.

Ethical considerations

The study protocol was approved by the Local Research Ethics Committee of the University of Sulaimani, College of Pharmacy (Certificate No: PH165-26 on April, 2026).

Statistical analysis

Statistical analysis was performed using GraphPad Prism (version 10.6.1). Continuous variables were expressed as mean ± standard deviation. Correlation analysis was performed to evaluate the relationship between inflammatory biomarkers (CRP, NLR, PLR, LMR, and SII) and liver function parameters, including ALT, AST, total bilirubin, prothrombin time, and international normalized ratio. Multiple linear regression analysis was conducted to identify independent predictors of liver dysfunction. Inflammatory indices were entered as independent variables, while liver injury markers were considered dependent variables.

RESULTS

A total of 50 patients with thalassemia-associated liver disease were included in the study. The mean age of participants was 52.1 ± 19.7 years. Biochemical analysis demonstrated elevated liver enzymes and inflammatory markers in the study population (Table 1). Correlation analysis revealed that CRP was significantly and positively associated with markers of systemic inflammation, including SII (r= 0.50, $p< 0.001$), NLR (r= 0.45, $p= 0.001$), and PLR (r= 0.41, $p= 0.003$). Notably, a strong inverse correlation was observed between CRP and LMR (r= −0.50, $p< 0.001$). Furthermore, CRP levels significantly correlated with clinical indicators of liver function, specifically prothrombin time and INR, suggesting a link between systemic inflammatory status and hepatic synthetic impairment (Table 2).

Table 1: Demographic and clinical characteristics of thalassemic patients with advanced liver disease

Variable	Result
Age (year)	52.1±19.7
Gender (Male/Female)	17/33
CRP (mg/L)	60.19±80.01
NLR	4.87±3.72
MLR	0.253±0.209
PLR	177.2±128.0
SII	1296.5±1256.3
AST (IU/L)	346.5±609.9
ALT (IU/L)	245.3±370
ALP (IU/L)	199.9±252.2
Total Bilirubin (mg/dL)	3.33±9.45
PT (seconds)	19.1±7.88
INR	1.56±0.809
HGB (g/dL)	10.4±1.49
RBC (10^{12}/L)	3.99±0.832
WBC (10^9/L)	9.74 ± 6.69
Platelets (10^9/L)	245.5±132.8

Values are presented as mean±SD.

Table 2: Pearson correlation coefficients (r) between C-Reactive Protein (CRP) and systemic immune-inflammatory indices and clinical coagulation profiles in thalassemic patients with advanced liver disease

CRP	CRP *vs.* NLR	CRP *vs.* PLR	CRP *vs.* MLR	CRP *vs.* LMR	CRP *vs.* NMR	CRP *vs.* MNR	CRP *vs.* SII	CRP *vs.* Pt	CRP *vs.* INR
R	0.447	0.406	0.1454	-0.498	0.066	-0.262	0.501	0.306	0.309
95% CI	0.192-0.645	0.144-0.615	- 0.139-0.407	-0.682 to -0.255	-0.217-0.338	-0.504-0.018	0.256-0.686	0.03-0.538	0.033-0.541
R squared	0.12	0.165	0.021	0.248	0.004	0.069	0.251	0.094	0.09543
p-value	0.0011	0.0035	0.3139	0.0002	0.651	0.066	0.0002	0.031	0.029
XY Pairs	50	50	50	50	50	50	49	50	50

Pearson correlation analysis showed that NLR was a highly significant predictor of broader systemic inflammation, exhibiting an extremely strong correlation with the Systemic Immune-Inflammation Index (SII) (r= 0.91, $p< 0.0001$) and significant positive associations with PLR, MLR, and CRP. Notably, while NLR was deeply embedded in the inflammatory profile, it showed no statistically significant correlation with Prothrombin Time (PT) or INR ($p> 0.05$). This suggests that in advanced liver disease, NLR serves as a specific marker for immune-inflammatory activity rather than a direct surrogate for hepatic synthetic dysfunction (Table 3).

Table 3: Pearson correlation coefficients (r) between the Neutrophil-to-Lymphocyte Ratio (NLR) and secondary inflammatory markers and clinical hepatic function indicators in thalassemic patients with advanced liver disease

NLR	NLR *vs.* PLR	NLR *vs.* MLR	NLR *vs.* LMR	NLR *vs.* NMR	NLR *vs.* MNR	NLR *vs.* SII	NLR *vs.* Pt	NLR vs. INR	NLR vs. CRP
r	0.491	0.402	-0.353	0.532	-0.423	0.912	-0.087	-0.102	0.447
95% CI	0.246-0.677	0.14-0.612	-0.575 to -0.083	0.298-0.706	-0.627 to -0.164	0.848-0.949	-0.357-0.196	-0.37-0.182	0.192-0.645
R squared	0.241	0.162	0.1246	0.2828	0.1786	0.831	0.008	0.01	0.197
p-value	0.0003	0.004	0.012	<0.0001	0.002	<0.0001	0.549	0.481	0.001
XY Pairs	50	50	50	50	50	49	50	50	50

Furthermore, correlation analysis demonstrated no statistically significant association between the systemic immune-inflammation index (SII) and routine liver function parameters, including ALT, AST, ALP, and TSB ($p> 0.05$ for all) (Table 4). These findings indicate that the systemic inflammatory state, as represented by the SII, reflects a distinct pathophysiological process separate from the degree of hepatocyte injury or cholestasis in patients with advanced liver disease.

Table 4: Pearson correlation coefficients (r) between the Systemic Immune-Inflammation Index (SII) and clinical liver function parameters in thalassemic patients with advanced liver disease

SII	SII *vs.* ALT	SII *vs.* AST	SII *vs.* ALP	SII *vs.* TSB
R	0.169	0.201	0.117	-0.03
95% CI	-0.118-0.43	-0.085-0.456	-0.17-0.386	-0.308-0.254
R squared	0.02853	0.04	0.014	0.0009
p-value	0.246	0.167	0.422	0.839
XY Pairs	50	50	50	50

These findings indicate that the systemic inflammatory state, as represented by the SII, reflects a distinct

pathophysiological process separate from the degree of hepatocyte injury or cholestasis in patients with advanced liver disease. Correlation analysis of prothrombin time (PT) demonstrated an expected, strong positive association with INR (r= 0.98, $p< 0.0001$) (Table 5).

Table 5: Pearson correlation coefficients (r) between Prothrombin Time (Pt) and systemic inflammatory markers and coagulation parameters in thalassemic patients with advanced liver disease

PT	Pt *vs.* NLR	Pt *vs.* PLR	Pt *vs.* MLR	Pt *vs.* LMR	Pt vs. NMR	Pt *vs.* MNR	Pt *vs.* SII	Pt *vs.* INR	Pt *vs.* CRP
r	-0.087	-0.1345	-0.169	-0.3	-0.1456	-0.259	0.118	0.983	0.306
95% CI	-0.357-0.196	-0.398-0.149	-0.427-0.115	-0.534 to -0.024	-0.407-0.138	-0.501-0.021	-0.167-0.387	0.97-0.99	0.03-0.538
R squared	0.008	0.018	0.029	0.09016	0.021	0.067	0.014	0.966	0.094
p-value	0.549	0.352	0.2412	0.0341	0.313	0.069	0.418	<0.0001	0.031
XY Pairs	50	50	50	50	50	50	50	50	50

Among the inflammatory markers, Pt showed a significant positive correlation with CRP (r= 0.31, p= 0.031) and a significant negative correlation with LMR (r= −0.30, p= 0.034). However, no statistically significant associations were observed between Pt and other systemic inflammatory indices, including NLR, PLR, and SII ($p> 0.05$), indicating that while certain inflammatory markers relate to hepatic synthetic dysfunction, the broader leukocyte-derived ratios remain independent of coagulation status in this cohort. Correlation analysis of the international normalized ratio (INR) demonstrated a near-perfect positive association with prothrombin time (r= 0.98, $p< 0.0001$), confirming data consistency. Regarding inflammatory markers, INR exhibited a significant positive correlation with CRP (r= 0.31, p= 0.029) and a significant negative correlation with LMR (r= −0.29, p= 0.043). Consistent with the prothrombin time analysis, no statistically significant associations were found between INR and the leukocyte-derived inflammatory indices such as NLR, PLR, or SII, suggesting that INR-related hepatic dysfunction is specifically linked to systemic inflammation (CRP) and immune cell composition (LMR) rather than broader inflammatory ratios in this cohort (Table **6**).

Table 6: Pearson correlation coefficients (r) between the International Normalized Ratio (INR) and systemic immune-inflammatory markers and coagulation parameters in thalassemic patients with advanced liver disease

INR	INR *vs.* NLR	INR *vs.* PLR	INR *vs.* MLR	INR *vs.* LMR	INR *vs.* NMR	INR *vs.* MNR	INR *vs.* SII	INR *vs.* Pt	INR *vs.* CRP
r	-0.102	-0.151	-0.1763	-0.2871	-0.14	-0.269	0.104	0.983	0.31
95% CI	- 0.37-0.182	-0.412-0.133	-0.433 to 0.11	-0.524 to -0.01	-0.402-0.144	-0.509-0.011	-0.183-0.374	0.97-0.99	0.033-0.541
R squared	0.01	0.023	0.031	0.082	0.02	0.072	0.011	0.966	0.1
p-value	0.481	0.23	0.221	0.043	0.334	0.059	0.477	<0.0001	0.029
XY Pairs	50	50	50	50	50	50	50	50	50

Multivariate regression analysis demonstrated that the combined clinical and biomarker profile significantly predicted symptom burden ($p< 0.0001$). However, upon examining individual predictors, only prothrombin time (PT) remained a significant independent correlation ($p< 0.0001$), whereas inflammatory biomarkers such as NLR and CRP did not contribute significantly to the model in this cohort (Table 7).

Table 7: Multivariate Analysis of Variance (ANOVA) assessing the impact of inflammatory biomarkers and coagulation parameters on symptom burden in thalassemic patients with advanced liver disease

Analysis of Variance	SS	DF	MS	F (DFn, DFd)	*p* value
Regression	2.952	9	0.328	F (9, 39) = 14.26	<0.0001
NLR	0.013	1	0.013	F (1, 39) = 0.554	0.4614
PLR	0.015	1	0.015	F (1, 39) = 0.654	0.4237
MLR	0.0007	1	0.001	F (1, 39) = 0.031	0.8619
LMR	0.0098	1	0.01	F (1, 39) = 0.424	0.5189
NMR	0.004	1	0.004	F (1, 39) = 0.161	0.6910
MNR	0.03	1	0.03	F (1, 39) = 1.314	0.2587
SII	0.004	1	0.004	F (1, 39) = 0.185	0.6691
Pt	1.915	1	1.915	F (1, 39) = 83.26	<0.0001
CRP	0.009	1	0.009	F (1, 39) = 0.401	0.5301
Residual	0.897	39	0.023		
Total	3.849	48			

DISCUSSION

The current investigation examined the relationship between clinical signs of hepatic dysfunction and systemic inflammatory biomarkers in thalassemia patients who experienced liver illness. Our results show that certain indicators of hepatic dysfunction and inflammatory status are significantly correlated with systemic inflammatory markers, specifically C-reactive protein (CRP), neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), lymphocyte-to-monocyte ratio (LMR), and the systemic immune-inflammation index (SII). These inflammatory indices are new reliable indicators of organ damage [12-14]. These results highlight the complex interaction between inflammation, immune dysregulation, and hepatic impairment in thalassemia-associated liver disease. One of the most frequent side effects of transfusion-dependent

thalassemia is liver damage, which is mainly caused by increased intestinal iron absorption as a result of inefficient erythropoiesis [2] and chronic iron overload brought on by frequent blood transfusions. Hepatocytes and Kupffer cells store excess iron, which encourages the production of reactive oxygen species and causes oxidative stress, lipid peroxidation, and hepatocellular damage. This process eventually leads to cirrhosis, fibrosis, and increasing hepatic inflammation. The pathophysiology of liver disease in thalassemia patients involves systemic inflammation and persistent immunological activation in addition to iron-mediated toxicity [3]. In this study, CRP had a strong negative correlation with LMR and strong positive correlations with NLR, PLR, and SII. These results imply that in patients with thalassemia-associated liver illness, leukocyte-derived inflammatory ratios strongly reflect systemic inflammation. Hepatocytes produce the well-known acute-phase protein CRP in reaction to inflammatory cytokines such as interleukin-6 and tumor necrosis factor-α. In a number of chronic inflammatory and hepatic illnesses, [15] elevated CRP levels have been linked to poor outcomes and the severity of the condition [16]. The observed correlations between CRP and hematological inflammatory indices in our study support the concept that these ratios may serve as surrogate markers of systemic inflammation. Given their similar reliance on neutrophil and lymphocyte numbers, NLR showed a particularly significant connection with SII among the inflammatory indicators analyzed. The neutrophil-to-lymphocyte ratio has been extensively studied in liver illnesses and has become a significant indicator of immunological dysregulation and systemic inflammation. In patients with chronic liver disease, elevated NLR levels have been linked to worse clinical outcomes, liver fibrosis, and higher disease severity [17]. The strong association between NLR and SII observed in our cohort is consistent with previous studies suggesting that these indices reflect overlapping inflammatory pathways [6]. Interestingly, NLR did not show a significant link with indicators of hepatic synthesis function like prothrombin time (PT) or the international normalized ratio (INR), despite having a substantial association with inflammatory biomarkers. This result implies that although NLR is a good measure of systemic inflammatory activity, the degree of hepatic functional impairment in advanced liver disease may not be directly reflected by it. Leukocyte-derived inflammatory indicators generally reflect systemic immunological activation rather than hepatic synthetic capacity, according to similar findings from earlier research [18]. Recently, a comprehensive inflammatory biomarker that integrates neutrophil, lymphocyte, and platelet counts has been developed: the systemic immune-inflammation index (SII). SII may have better predictive value than conventional inflammatory ratios in a number of conditions, including cancer and chronic liver problems, according to several studies [19]. However, in our study, SII was not significantly associated with conventional liver function parameters such as ALT, AST, ALP, or total bilirubin. These findings suggest that the inflammatory state represented by SII may reflect systemic immune activation rather than direct hepatocellular injury or cholestatic processes. The association between coagulation parameters that represent hepatic synthesis function and inflammatory markers was another significant finding of this investigation. Since the liver is where most coagulation components are made, prothrombin time and INR are commonly used measures of hepatic synthetic capacity. In severe liver illness, prolonged PT and elevated INR levels are frequently seen due to impaired hepatic production of clotting factors. Both PT and INR showed strong negative relationships with LMR and positive correlations with CRP in our group. These results imply that in patients with advanced liver disease, systemic inflammation may have a role in the decline of hepatic synthetic function [20]. The inverse association observed between LMR and coagulation parameters may reflect immune dysregulation associated with advanced hepatic injury. Monocytes play an important role in inflammatory signaling and fibrosis progression through their differentiation into macrophages and activation of hepatic stellate cells [21]. Reduced lymphocyte counts, reflected in decreased LMR values, may also indicate impaired immune regulation and systemic inflammatory activation, which are frequently observed in chronic liver disease. Interestingly, NLR did not show a significant link with indicators of hepatic synthesis function like prothrombin time (PT) or the international normalized ratio (INR), despite having a substantial association with inflammatory biomarkers. This result implies that although NLR is a good measure of systemic inflammatory activity, the degree of hepatic functional impairment in advanced liver disease may not be directly reflected by it. Leukocyte-derived inflammatory indicators generally reflect systemic immunological activation rather than hepatic synthetic capacity, according to similar findings from earlier research [18]. The systemic immune-inflammation index (SII) has recently emerged as a comprehensive inflammatory biomarker integrating neutrophil, lymphocyte, and platelet counts. SII may have better predictive value than conventional inflammatory ratios in a number of conditions, such as cancer and chronic liver problems, according to several studies [19]. Nevertheless, SII did not substantially correlate with traditional liver function metrics such as total bilirubin, ALT, AST, or ALP in our investigation. These results imply that systemic immune activation rather than direct hepatic damage or cholestatic mechanisms may be the cause of the inflammatory state that SII represents. The association between coagulation parameters that represent hepatic synthesis function and inflammatory markers was another significant finding of this investigation. Since the liver produces the bulk of coagulation components,

prothrombin time and INR are commonly used measures of hepatic synthetic capacity [20]. Severe liver illness often results in prolonged PT and elevated INR levels due to impaired hepatic production of clotting factors. Both PT and INR showed strong negative relationships with LMR and positive correlations with CRP in our group. These results imply that in patients with advanced liver disease, systemic inflammation may have a role in the decline of hepatic synthetic function. Immune dysregulation linked to extensive hepatic damage may be the cause of the inverse relationship between LMR and coagulation measures. Because they differentiate into macrophages and activate hepatic stellate cells, monocytes are crucial for the development of fibrosis and inflammatory signaling [21]. Decreased lymphocyte counts, which are reflected in lower LMR values, may also be a sign of systemic inflammatory activation and compromised immunological control, both of which are commonly seen in chronic liver disease. The combined clinical and biomarker profile significantly predicted symptom load in individuals with thalassemia-associated liver disease, according to multivariate regression analysis. Prothrombin time was found to be the sole independent predictor of symptom load out of all the factors examined. This result emphasizes the therapeutic significance of coagulation measures as markers of liver functional impairment and disease severity. PT prolongation has been repeatedly linked to a poor prognosis in patients with advanced liver disease and suggests decreased hepatic synthetic ability [22].

Conclusion

The current study concludes that in individuals with thalassemia-associated liver disease, systemic inflammation and hepatic dysfunction significantly interact. Our results indicate that systemic inflammatory status is strongly correlated with inflammatory biomarkers derived from routine hematological parameters, especially NLR, PLR, LMR, and the systemic immune-inflammation index (SII), as evidenced by their strong correlations with C-reactive protein (CRP).

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Conflict of interests

The authors declared no conflict of interest.

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Data sharing statement

Supplementary data can be shared with the corresponding author upon reasonable request.

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