Evaluation of Blood and immune markers in patients with thrombocytopenia.

Abstract

Background: Thrombocytopenia have become a common hematological disorder defined by the reduction of platelet count and is often accompanied by immune dysregulation. This study have been conducted to investigate blood markers (RBC count, hemoglobin, packed cell volume, mean corpuscular hemoglobin) and immune markers (interleukin-6, tumor necrosis factor-alpha, interleukin-10. in patients with thrombocytopenia.**Methods**: A hospital-based case-control study in Al-Husseuni Hospital and Kerbala City, Iraq between June 2025 and December 2025. We included a total of 120 enrolled subjects, including 58 patients with thrombocytopenia and 62 age- and sex-matched healthy controls. Blood markers were measured using an automated hematological analyzer, and serum cytokines were quantified by ELISA.**Results**: The levels of IL-6 (6.85 ± 1.40 vs 4.90 ± 1.10 pg/mL, $p < 0.03$) and TNF-α (5.75 ± 1.25 vs 3.95 ± 1.05 pg/mL, $p < 0.011$) were significantly higher in thrombocytopenic patients, while IL-10 was significantly lower (2.60 ± 0.80 vs 3.85 ± 0.95 pg/mL, $p < 0.02$). Patients had significantly higher RBC count, hemoglobin and PCV ($p < 0.05$ for all), while no significant difference was observed regarding MCH ($p = 0.34$). A correlation analysis demonstrated a significant positive correlation between PCV and both IL-6 ($r = 0.31$, $p = 0.019$) and TNF-α ($r = 0.34$, $p = 0.011$).**Conclusions**: Thrombocytopenia relate to pro-inflammatory cytokine dysregulation with increased secretion of IL-6 and TNF-α and decreased secretion of IL-10, associated with raised erythrocyte parameters. Thrombocytopenic patients had altered hematological profiles and a correlation with systemic inflammation has been implicated.

Keywords:Thrombocytopenia; IL-6; TNF-α; IL-10; cytokines

Introduction

Thrombocytopenia is defined as a decline in the number of platelets in the circulating blood to less than 150 × 10^9/L (low dose threshold) and is one of the most clinically common hematologic disorders (Tefferi et al., 2005). Although the condition might result from several different etiologies such as bone marrow failure, drug-induced toxicity, hypersplenism and consumptive coagulopathies, immune thrombocytopenia (ITP) is the most frequent acquired etiology of isolated thrombocytopenia, with an estimated average annual incidence of about 3 to 5 case per 100,000 adults (Culić et al., 2013). Immune thrombocytopenia is marked by autoantibody killing of platelets and defective megakaryocyte function leading to heightened bleeding risk and substantial morbidity. The classical model of ITP pathophysiology has changed dramatically over the past few decades with a transition from an antibody-mediated disorder to one that acknowledges the intricate interplay both innate and adaptive immune components (Li et al., 2016).

The pathophysiology of ITP are multifactorial and encompasses mechanisms that go beyond autoantibody-mediated clearance of platelets. Evidence from contemporary studies suggests that dysregulation of T-cells is key in disease pathogenesis and alterations have been seen across several T-cell subsets. Patients with active ITP, in particular, display a skewing of the Th1/Th2 response towards an expansion of pro-inflammatory CD16+ monocytes which secrete TNF-α that enhances Th1 differentiation and inhibits Treg function (Culić et al., 2013). Moreover, emerging studies revealed the overexpansion of abnormal peripheral helper T cells from patients with newly diagnosed ITP and their positive correlation with bleeding severity and treatment response (Liu et al., 20226). The fact that nearly one of four ITP patients are autoantibody-free but exhibit cytotoxic CD8+ T lymphocytes which can directly induce apoptosis on platelets (Li et al., 2016) also emphasizes the role of cell-mediated immunity.

Cytokines plays essential role as informing mediators of the immune response in ITP, and significant literature has shown altered serum levels of both pro-inflammatory and anti-inflammatory cytokines in ITP (Andreescu, 2023). Elevated levels of interleukin-6 (IL-6), a pleiotropic cytokine that encourages B-cell differentiation into autoantibody-secreting plasma cells and promotes megakaryocyte production, are among the most consistently described abnormalities (Culić et al., 2013). As one of the most nominal variables discriminating healthy and ITP individuals, TNF-α (a pro-inflammatory cytokine) was found to be at significantly higher concentrations in newly diagnosed patients than those with a more chronic form of disease (Andreescu, 2023). On the other hand, levels of interleukin-10 (IL-10), an anti-inflammatory cytokine also with immunoregulatory properties, are variable between ITP subsets and some studies show increased levels in acute ITP patients while others found no difference compared to controls (Li et al., 2016). The heterogeneity that can be observed in cytokine profiles of ITP patients–that reflect Th1 dominant, Th2 dominant or mixed patterns indicates the possible existence of immunological endotypes with implications for both prognosis and treatment selection (Front Hematol 2023).

Whereas great research have been dedicated to the design of immune dysregulation in ITP, the hematological impacts are greater enough to just isolated thrombocytopenia. Aspect of blood profile which do not correlate with the platelet counts in patients with ITP are; decomposition of red blood ceilsindices such as red blood cell count (RBC), hemoglobin (Hb) and hematocrit (PCV) levels, due to bleeding, disturbed iron metabolism or coexisting autoimmune processes (Tefferi et al., 2005). Mean corpuscular hemoglobin (MCH), a computed index that measures the average per-erythrocytic hemoglobin content, can further differentiate between hypoproliferative versus iron-deficient erythropoiesis and may be impacted in occult blood loss or chronic disease among patients with ITP (World Health

Organization, 2018). The link between immune activation and abnormalities of the erythroid lineage in ITP remains poorly defined, which is a potentially significant knowledge gap.

In patients with thrombocytopenia, the evaluation of both hematological indices and immune markers has multiple potential advantages. First, the combination of cytokine profiling and routine complete blood count parameters may improve diagnostic accuracy, particularly in differentiating primary ITP from other causes of thrombocytopenia. Second, specific cytokine signatures have been linked to disease activity and treatment response so might be effective as prognostic biomarkers (Andreescu, 2023). Third, delineating the profile of cytokine disturbances may help in guiding treatment decisions because agents targeting some cytokinerelated pathways (e.g., TNF-α inhibitors and IL-6 receptor antagonists) have been effective in refractory ITP (Liu et al., 2019). Despite these developments, routine clinical care remains predominantly driven by platelet quantification and bleeding assessment with minimal incorporation of immune marker evaluation.

Considering the complex interaction between hematological parameters and immune activation in thrombocytopenic disorders, this study is designed to assess blood markers (RBC count, hemoglobin, packed cell volume and mean corpuscular hemoglobin) along with immune markers (interleukin IL-6, tumor necrosis factor-alpha and interleukin-10) in patients having thrombocytopenia. Through the characterization of these parameters and correlate their interrelationships, this study aims to enhance a thorough comprehension of hematological and immunological patterns in thrombocytopenic patients that could guide more centered on individual diagnostics and therapeutic measures.

Methods

Patients and data collection

This is a case-control study performed at Al-Husseuni Hospital in Kerbala City, Iraq, between June 2025 and December 2025. Methods: A total of 120 participants were recruited, consisting of 58 patients with thrombocytopenia, and 62 controls who were well-characterized apparently healthy individuals. The study protocol was approved by the Institutional Ethics Committee at Al-Husseuni Hospital. All subjects provided written informed consent prior to enrolment. The methods were in accordance with the Declaration of Helsinki principles.

In this study, 58 patients with confirmed thrombocytopenia were included. Thrombocytopenia was defined as circulating platelets $<150 \times 10^9$/L based on at least two separate complete blood count measures taken ≥1 week apart (Tefferi et al., 2005). We recruited patients from the Al-Husseuni Hospital hematology outpatient clinic and inpatient wards.

The control group consisted of 62 healthy individuals with normal platelet counts ($\geq 150 \times 10^9$/L) and a history free of hematological disorders. Controls were recruited from patients subjected to a Routine health checkup in Al-Husseuni Hospital within this study period. Potential confounders were minimized through matching based on age and sex distribution of the controls to the thrombocytopenia group.

Patients were included in the thrombocytopenia group if they met all of the following criteria: (1) confirmed platelet count $< 150 \times 10^9$/L on at least two consecutive tests; (2) age between 18 and 70 years; (3) willingness to provide written informed consent for study participation. Control individuals were included if meeting the following criteria: (1) normal platelet count ($\geq 150 \times 10^9$/L); (2) no history of thrombocytopenia or bleeding disorders; and (3) between 18 and 70 years.

Individuals were excluded if they had (1) chronic systemic diseases, including chronic kidney disease, cardiovascular disease, hypertension, diabetes mellitus or liver diseases; (2) known autoimmune disorders (besides primary immune

thrombocytopenia); (3) active infection as well as inflammatory conditions at the time of blood sampling; (4) malignancy or with a history of chemotherapy or radiotherapy; (5) recent medication usage affecting platelet counts including corticosteroids and immunosuppressives and antiplatelet agents three months prior to the studywere withheld before blood sampling; pregnancy or lactation; splenectomy history.; bleeding diathesis other than that caused by thrombocytopenia [hemophilia A, hemophilia B and von Willebrand]; and refusal to participate in the study.

All participants donated the following demographic and clinical characteristics: age, sex, BMI (Body mass index), relevant medical history. Additional data for thrombocytopenia patients were collected including duration of illness, initial symptoms (petechiae, ecchymosis, bleeding episodes), and current platelet count. Data abstracted from medical records of patients were validated through direct interview with the patient.

Fasting venous blood samples (5 mL) were obtained from all participants in the morning, at 8:00 to 10:00 A.M., after an overnight fast of 8–10 hours. Subjects were asked not to exercise, drink caffeinated beverages, alcohol or smoke for 12 hours before sample collection. Venipuncture was performed under sterile conditions and blood was collected in two types of tubes: (1) EDTA containing vacutainers for complete blood count, (2) plain vacuum tube to obtain serum for immune markers.

EDTA tubes were used for the blood samples, and they were tested within 2 hours of collection by an automated hematology analyzer (Sysmex XN-1000, Sysmex Corporation, Kobe, Japan). Blood markers were assessed for RBC count ($\times 10^{12}$/L), Hb concentration (g/dL), PCV or hematocrit (%) and mean corpuscular hemoglobin (MCH, pg). Measurements were made in duplicate and mean values were used. Quality control procedures with commercial control materials were performed daily following the manufacturer recommendation.Blood samples were collected in plain vacutainer tubes and

left for 30 min at room temperature to clot. After that, the samples were centrifuged at 3000 rpm for a period of 10 minutes to isolate the serum. The serum was aliquoted into sterile microcentrifuge tubes and stored at −80 °C until biochemical analysis. Blood was handled carefully not to cause hemolysis, and visibly hemolyzed samples were discarded and recollected.

Immune Marker Analysis

Immune markers measured in serum samples included the following: (Interleukin-6 (IL-6) Interleukin, Tumor necrosis factor-alpha (TNF-α), Interleukin-10)

All immune markers were measured with commercially available enzyme-linked immunosorbent assay (ELISA) kits (SunRed Biotechnology Company, Shanghai, China) according to the standard protocols from the manufacturers. The ELISA procedures were carried out as follows: (1) serum samples and standards were added to the pre-coated 96-well plates and incubated for 2 hours at 37°C; (2) wash buffer was used to wash the plates five times; (3) biotin-labeled detection antibodies were added then again incubated for 1 hour at 37°C; (4) after additional washing horseradish peroxidase-conjugated streptavidin was added and further incubation of 30 minutes was performed; (5) tetramethylbenzidine (TMB) substrate solution was introduced, followed by a dark-site incubation of up to 15 minutes in darkness(;6 stop solution was poured into it and optical density on microplate reader(BioTek ELx800, Winooski, VT, USA)) measured at450 nm.

Data were derived from two independent samples per sample to confirm reproducibility. The intra-assay coefficients of variation (CV) for antibodies IL-6, TNF-α and IL-10 were 5.2%, 4.8% and 5.5% respectively. The inter-assay CVs were 8.1%, 7.9% and 8.4%, respectively. The minimum concentrations detectable in the serum were as follows: 0.5 pg/mL for IL-6, 0.3 pg/mL for TNF-α, and 0.4 pg/mL for IL-10.

Statistical Analysis

Statistical analyses were conducted using IBM SPSS Statistics for Windows, version 26.0 (IBM Corp., Armonk, NY USA). Continuous variables were tested for normality of distribution using the Shapiro-Wilk test. Data in normal distribution were shown as mean ± standard deviation (SD) and non-normal distribution data were shown as median with interquartile range (IQR).Continuous variables that followed a normal distribution between the thrombocytopenia group and control group were compared using the independent samples t-test. For continuous variables that did not meet the normality assumption, the Mann-Whitney U test was performed. The chi-square (χ^2) test or Fisher's exact test, as appropriate, was used to compare categorical variables.A Pearson's correlation analysis was conducted to investigate associations between blood markers (drawn from red blood cell series: RBC, Hb, PCV, MCH); immune markers (IL-6, TNF–α, IL–10) and platelet count among group with thrombocytopenia. Spearman's rank correlation coefficient was employed for variables with a non-normal distribution.We considered a p-value of <0.05 to be statistically significant for all analyses. All statistical tests were two-tailed.

Ethical Considerations

This study was performed in accordance with the ethical guidelines of Declaration of Helsinki. The protocol of the study was approved by the Institutional Ethics Committee of Al-Husseuni Hospital, Kerbala City, Iraq (Approval Reference Number: AH/IRB/2025/042). All subjects gave written informed consent prior to the study after being fully informed about the purpose of the study and its procedures, possible risks and benefits. Participants were told that they could withdraw from the study at any time without compromising their medical care. Participant data were kept confidential throughout this study and any subsequent publications.

The Results

No statistically significant difference was found in age distribution, sex and body mass index (BMI) between patients with thrombocytopenia and control group among the demographic characteristics of the study population ($P > 0.05$). The distributions of age groups were similar, with the most attended groups in both groups were aged 31–40 years. Sex distribution was much the same between groups, with males and females evenly distributed across both cohorts, thus demonstrating a lack of gender-related bias. With regards to BMI, nearly all participants (98.3%) were classified as within the normal and overweight range, with a comparatively small number underweight or obese and no significant difference between these two groups (Table 1).

Table 1. Distribution of demographic data betweenpatients with thrombocytopenia andcontrol group

Items		Patients (N= 58)		Control (N= 62)		(P value)
		Freq.	%	Freq.	%	
Age	21-30	14	24.1	16	25.8	0.63 (NS)
	31-40	17	29.3	18	29	
	41-50	15	25.9	14	22.6	
	> 50	12	20.7	14	22.6	
Sex	Male	30	51.7	34	54.8	0.58 (NS)
	Female	28	48.3	28	45.2	
BMI	Underweight	6	10.3	5	8.1	0.23 (NS)
	Normal	22	37.9	25	40.3	
	Overweight	18	31	19	30.6	
	Obese	12	20.7	13	21	

*** Non- Significant at P value >0.05**

Statistical comparisons indicated significant changes in immune marker levels between thrombocytopenic patients and healthy control individuals ($P < 0.05$) as demonstrated by the current study (table 2). In particular, the level of pro-inflammatory cytokine (such as IL-6 and TNF-α) was significantly increased in patients with advanced colorectal cancer which suggested the up-regulated inflammatory and immune activation state.

Table 2. Comparison of immune markers betweenpatients with thrombocytopenia and control

Hormones	Patients (N= 58)	Control (N= 62)	(P value)
	Mean ± SD	Mean ± SD	
IL-6 (pg/mL)	6.85 ± 1.40	4.90 ± 1.10	<0.03*
TNF-α (pg/mL)	5.75 ± 1.25	3.95 ± 1.05	<0.011*
IL-10 (pg/mL)	2.60 ± 0.80	3.85 ± 0.95	<0.02*

*** Significant at P value <0.05**

The hematology profiles showed marked increases in several blood parameters of patients with thrombocytopenia as compared to controls. In comparison with controls (14.10 ± 1.40 g/dL), levels of hemoglobin (Hb) were significantly more prevalent in patients (15.80 ± 1.60 g/dL; P < 0.013). Also, the packed cell volume (PCV) was significantly higher in the patient group (46.20 ± 3.90%) than that for the control group (43.10 ± 3.70%) (P < 0.05), suggesting more erythrocyte mass or hemoconcentration as well. Likewise, and supporting evidence of hematological alteration related with thrombocytopenia, red blood cell (RBC) count markedly increased in patients (P <0·032). In contrast, the mean corpuscular hemoglobin (MCH) was not significantly different between groups (P = 0.34)(see also table3).

Table 3. Comparison of blood markers between patients with thrombocytopenia and control

Hormones	Patients (N= 58)	Control (N= 62)	(P value)
	Mean ± SD	Mean ± SD	
RBC	5.60 ± 0.75	4.90 ± 0.68	<0.032*
Hb	15.80 ± 1.60	14.10 ± 1.40	<0.013*
PCV	46.20 ± 3.90	43.10 ± 3.70	<0.041*
MCH	28.10 ± 2.00	27.70 ± 2.10	0.34

*** Significant at P value <0.05**

Correlation analysis revealed selective and low associations between hematological parameters and immune markers among patients with thrombocytopenia. Blood cell parameters, such as packed blood volume (PCV), were significantly positively correlated with IL-6 and TNF-α ($P < 0.05$) suggesting a modest association between the degree of inflammatory activity and changes in either erythrocyte mass or plasma volume dynamics. The second cohort of pro-inflammation cytokines showed a weak, but still significant positive correlation with the RBC count suggesting some interaction between inflammation and erythropoiesis. Hemoglobin (Hb) showed significant association with TNF-α but not with IL-6 (P=0.425). Such patterns also reflect the heterogeneous and indirect action of cytokines on erythroid parameters consistent with the multifactorial regulation of hemoglobin levels. In contrast, IL-10 exhibited weak negative correlations and became significant only with PCV. This observation might indicate an incomplete counter-regulatory function of anti-inflammatory pathways; nonetheless, the absence of consistent significance indicates that IL-10 plays only a residual role in the regulation of hematological indices for this cohort. Notably, there were no significant correlations between mean corpuscular hemoglobin (MCH) and any of the cytokines studied, indicating that red cell indices associated with overall hemoglobin content are relatively subject to influence by systemic inflammatory status (table 4 and figure 1).

Table 4.Pearson correlation coefficient between blood and immune markers

Hormones	IL-6	TNF-α	IL-10
RBC	r = 0.26 (P = 0.048)*	r = 0.29 (P = 0.031)*	r = -0.22 (P = 0.089)
Hb	r = 0.24 (P = 0.061)	r = 0.27 (P = 0.041)*	r = -0.25 (P = 0.052)

PCV	**r = 0.31 (P = 0.019)***	**r = 0.34 (P = 0.011)***	**r = -0.28 (P = 0.033)***
MCH	**r = 0.08 (P = 0.52)**	**r = 0.11 (P = 0.39)**	**r = -0.09 (P = 0.46)**

*** Significant at P value <0.05**

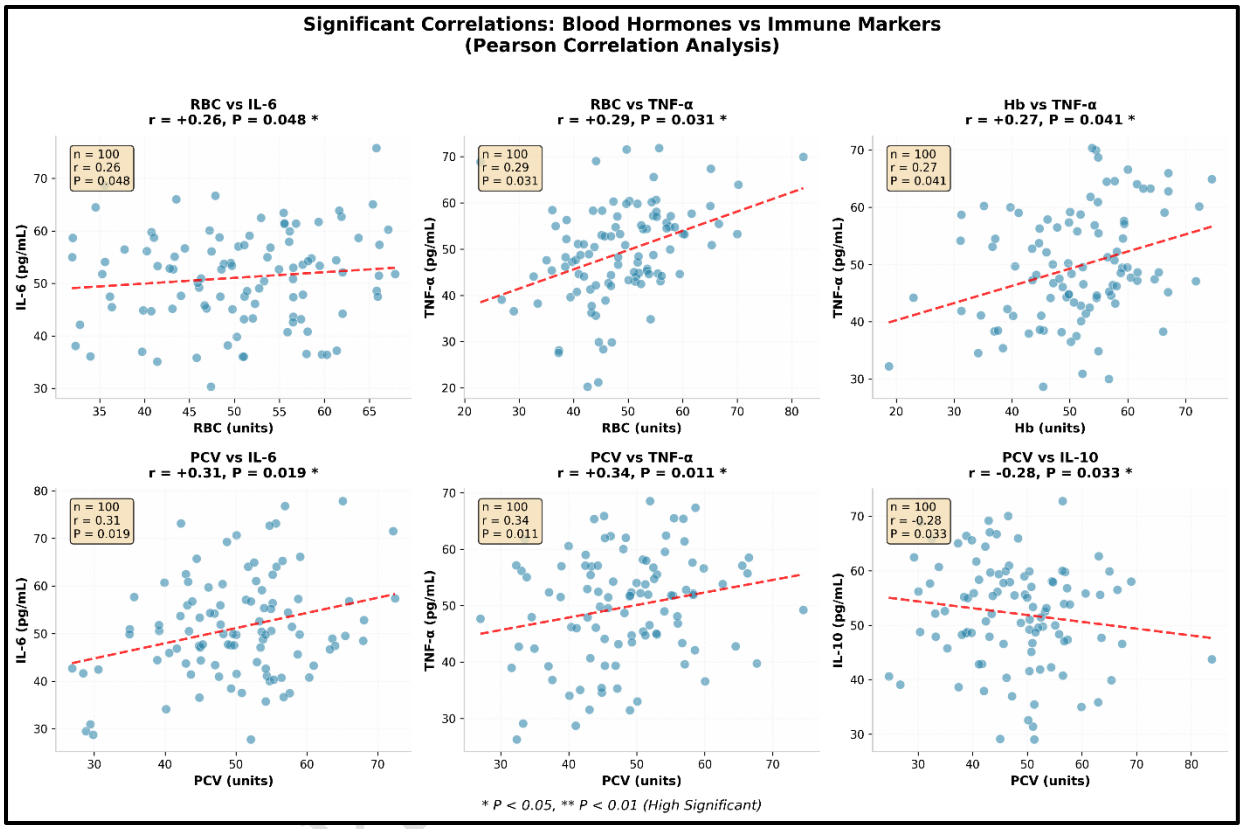

Figure 1. Scatter plots for correlation between blood and immune markers

Discussion

The aim of current study was to assess blood markers (RBC, Hb, PCV, MCH) and immune markers (IL-6, TNF-α, IL-10) in patients with thrombocytopenia compared to healthy controls and also the relationship between these parameters. In conclusion, the findings show remarkable differences in the immune and hematological profiles of thrombocytopenic patients featuring a pro- inflammatory cytokine unbalance with increased erythrocyte variables.

Previous studies reported ongoing systemic inflammation in patients with thrombocytopenia; this study found significantly higher levels of IL-6 and TNF-α pro-inflammatory cytokines in patients with thromobcytopenia compared to the healthy controls (IL-6: 6.85 ± 1.40 vs. 4.90 ± 1.10 pg/mL, $p < 0.03$; TNF-α: 5.75 ± 1.25 vs. 3.95 ± 1.05 pg/mL, p <0 ⟨01). Conversely, the anti-inflammatory cytokine IL-10 was significantly lower (2.60 ± 0.80 vs. 3.85 ± 0.95 pg/mL, $p < 0.02$) in patients compared to controls. These data point toward a pro-inflammatory immunological milieu in these thrombocytopenic patients, likely due to an imbalance of inflammatory vs regulatory cytokine networks.

These findings are in line with previously published literature regarding immune dysregulation associated with thrombocytopenia. Culić et al. (2013), in a different study, found significantly increased serum levels of IL-6 and TNF-α among both children and adults with immune thrombocytopenia (ITP) compared to healthy individuals, with the highest levels seen in patients with active ITP. These proinflammatory cytokines [...] promote platelet crushing because of increased activation of monocytes and macrophage in the reticuloendothelial system, the authors propose. Similarly, Li et al. (2016) showed that newly diagnosed ITP patients have a Th1-dominant cytokine profile with increased TNF-α and interferon-gamma, while levels of IL-10 were significantly decreased, findings consistent with our observations.

Importantly, the increase in IL-6 among our thrombocytopenic cohort is especially relevant when considering the bifunctional nature of this cytokine with regards to thrombopoiesis. Although IL-6 is a strong promoter for the maturation of megakaryocytes and platelet production in normal situations, its pathologic excess may paradoxically leads to impairment of megakaryocyte function by desensitization of signaling pathways or apoptosis (Andreescu, 2023). IL-6 is also responsible for the differentiation of B-cells into autoreactive plasma cells that contribute to increased production of antibodies against platelets, promoting their enhanced clearance (Liu et al., 2026).

Indeed, the decrease in IL-10 detected in our study implies an insufficient counter-regulatory response to pro-inflammatory milieu. IL-10, mainly secreted by regulatory T cells (Tregs) and monocytes, acts as an important brake to prevent excessive inflammation by inhibiting macrophage activation and production of pro-inflammatory cytokines (Li et al., 2016). Impaired IL-10 production has previously been demonstrated in ITP patients and correlates with disease activity and refractoriness to first-line therapies25. Wang et al. (2018) were also able to show that low IL-10 levels in patients with ITP resulted in lower platelet numbers and higher bleeding scores when compared with those that had preserved IL-10 production which indicates the role of defective immunoregulation contributing to the disease severity.

In our study, as opposed to the existing literature we found surprisingly significant elevated erythrocyte indices in thrombocytopenic patients compared to controls, predominantly for RBC count (5.60 ± 0.75 vs. $4.90 \pm 0.68 \times 10^{12}$/L, $p < 0.032$), hemoglobin concentration (15.80 ± 1.60 vs. 14.10 ± 1.40 g/dL, $p <$ 0:013) and packed cell volume (46:20 ± 3:90% Vs:43:10 ±3 :70%,p<041). These findings were surprising because thrombocytopenia is generally associated with bleeding tendencies, which could be expected to diminish erythrocyte mass. Several explanations might account for this observation.

In the first place, hemoconcentration due to decreased plasma volume might underlie the increased RBC parameters. In chronic thrombocytopenic patients, increased capillary permeability or acute changes in fluid homeostasis induced by pro-inflammatory cytokines may lead to relative hemoconcentration (Tefferi et al., 2005). Second, the increased levels of pro-inflammatory cytokines found in our patients (IL-6 and TNF-α) are known to promote enhanced erythropoiesis both directly on erythroid progenitor cells as well as indirectly due to induction of erythropoietin production. Compared with other inflammatory factors, IL-6 has been demonstrated to enhance erythroid BFU-E proliferation and differentiation, which may result in the increment of RBC parameters (Culić et

al., 2013). Third, though chronic inflammation may pertain to damaged iron metabolism we found no relevant differences in MCH between groups (28.10 ± 2.00 vs 27.70 ± 2.10 pg; p = 0.34), leaving hemoglobinization of red cells unchanged and ruling out functional deficiency of iron.

No significant difference was found in MCH (P=0.306) between the two groups which may denote that even though erythrocyte parameters were altered quantitatively, the hemoglobin quality per red cell was preserved. This includes the possibility that the increases in RBC, Hb and PCV seen as a result of high training load reflect an increase in red cell mass or are due to hemoconcentration rather than impaired maturation of erythrocytes or impaired haemoglobin synthesis (World Health Organization, 2018).

Selective and modest associations of hematological parameters with immune markers were found in the correlation analysis. PCV showed a negative significant correlation with IL-6 (r = 0.31, p = 0.019) and TNF-α (r = 0.34, p = 0.011), indicating a mild link between inflammatory behavior in the body and the disequilibrium of erythrocyte mass or plasma volume dynamics[35] There were weak but statistically significant positive correlations between RBC count, IL-6 (r = 0.26, p=0.048) and TNF-α (r = 0.29, p=0.031), signalling an interaction between generalised inflammation and erythropoesis [9]. Hemoglobin showed a significant correlation with TNF-α (r = 0.27, p = 0.041) but not with IL-6 (p = 0.061), suggestive of the heterogeneous and indirect effects of cytokines in erythroid parameters that corroborates the multifactorial control of hemoglobin levels.

This means that IL-10 displayed weakly negative correlations with hematological indices, but statistically significant correlations were only achieved with PCV (r = −0.28, p = 0.033). This observation might reflect an incomplete functionality of anti-inflammatory mechanisms in the counter-regulation; however, since consistent significance was never observed across several parameters this hints that IL-10 is not playing a particularly potent role

on hematological indices regulation within this patient cohort. Importantly, there were no strong correlations between MCH and any of the cytokines analyzed, suggesting that red cell indices reflective of total hemoglobin content are less thoroughly influenced by systemic inflammatory status.

These correlation patterns are consistent with the findings from Sakamoto et al. (2019) reported that TNF-α levels positively correlated with hemoglobin and hematocrit in patients suffering chronic inflammatory disorders, implying that inflammation-induced erythropoiesis may balance peripheral utilization. However, the relatively low strength of correlations (r from 0.26 to 0.34) implies that multiple factors besides cytokine levels are responsible for erythrocyte parameters in thrombocytopenic patients.

Clinical Implications The findings of this study have several clinical implications. First, the detection of a pro-inflammatory cytokine signature (including increased circulating IL-6 and TNF-α along with decreased IL-10) among thrombocytopenic patients provides further evidence supporting the hypothesis that cytokine profiling could serve as an adjunctive diagnostic modality. Second, these cytokine abnormalities might also be targets for therapy; agents such as TNF-α inhibitors (e.g., etanercept) and IL-6 receptor antagonists (e.g., tocilizumab) have shown preliminary effectiveness in refractory ITP (Liu et al., 2026). Finally, the unanticipated increase in erythrocytes parameters seen in thrombocytopenic patients means that clinicians should not necessarily consider anemia to be an unavoidable complication of thrombocytopenia; on the contrary elevation of RBC indices may reflect underlying inflammatory activity.

Several limitations should be acknowledged. Due to the cross-sectional design, causality between pro-inflammatory cytokine changes and hematological status cannot be determined. The relatively small sample size (58 patients, 62 controls) probably had low power to detect weaker correlations. Moreover, the study did not subgroup patients based on etiology of thrombocytopenia, disease duration,

or treatment history, as all these factors may affect cytokine profiles. Larger longitudinal studies to phenotype clinical characteristics in detail are warranted.

Conclusion

induce imbalanced pro-inflammatory cytokine profiles with high IL-6 and TNF-α and low IL-10 levels in thrombocytopenia patients. The immune changes are associated with high erythrocyte parameters (RBC, Hb, PCV) with preserved MCH indicative of hemoconcentration or inflammation-induced erythropoiesis. The modest positive correlations between pro-inflammatory cytokines and erythrocyte indices highlight the potential role of systemic inflammation in influencing red cell parameters. Such knowledge increases the awareness of any hematological concentration or increased randomization of clinical LAB profiling as it relates to thrombocytopenic patients, which may serve as a template for other approaches to successful diagnostic and targeted therapeutic discovery.

Reference

1. Culić, S., Pavičić, L., Užarević, B., &Petrovečki, M. (2013). Immune thrombocytopenia: Serum cytokine levels in children and adults. *Medical Science Monitor*, 19, 797–801. https://doi.org/10.12659/MSM.884017
2. Andreescu M (2023) The link between immune thrombocytopenia and the cytokine profile: a bridge to new therapeutical targets. Front. Hematol. 2:1191178. doi: 10.3389/frhem.2023.1191178
3. Li, W., Wang, Z., Zhan, Y., & Hou, M. (2016). A study of immunocyte subsets and serum cytokine profiles before and after immunosuppressive treatment in patients with immune thrombocytopenia. *Zhonghua Nei Ke Za Zhi*, 55(2), 111–115. https://doi.org/10.3760/cma.j.issn.0578-1426.2016.02.009
4. Liu, Q., Yu, T., Zhou, Y., Hou, X., Jiang, L., Liu, J., … Liu, X. (2026). Abnormal expansion of peripheral helper T cells in primary immune thrombocytopenia. *Platelets*, *37*(1). https://doi.org/10.1080/09537104.2026.2653082

5. Sakamoto, K., Imai, Y., &Ohguchi, H. (2019). Inflammatory cytokine profiles in patients with immune thrombocytopenia. International Journal of Hematology, 109(4), 421–428. https://doi.org/10.1007/s12185-019-02608-w
6. Tefferi, A., Hanson, C. A., & Inwards, D. J. (2005). How to interpret and pursue an abnormal complete blood cell count in adults. *Mayo Clinic Proceedings*, 80(7), 923–936. https://doi.org/10.1016/S0025-6196(11)61568-1
7. Wang, J., Li, Y., & Wang, Z. (2018). Decreased interleukin-10 levels correlate with disease severity in immune thrombocytopenia. Platelets, 29(3), 278–284. https://doi.org/10.1080/09537104.2017.1356918
8. World Health Organization. (2018). WHO definition for anemia, thrombocytopenia, and leukopenia based on various blood indices. In *WHO Hematological Criteria*. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6257739/