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Thrombocytopenia in Systemic Lupus Erythematosus Related to Prognostic Factors and Rehabilitative Interventions for Adults

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Abstract: Systemic lupus erythematosus (SLE) is an autoimmune disease of chronic nature, having a wide range of hematological manifestations. Thrombocytopenia is a frequent and medically important adverse effect which affects morbidity and the quality of life. This experiment sought to describe the commonness and the severity of thrombocytopenia. It also aimed at determining the prognostic factors that could be linked with severe thrombocytopenia, as well as the patterns through which the various treatments and quality-of-life results could be used within a period of 12 months**.** A cross-sectional study was carried out on 107 participants who were having SLE. The cohort data on the clinical appearance at presentation and SLE disease activity (SLEDAI) in Thi-Qar-Iraq hospitals in March 2024 - March 2025 was analyzed as the baseline data. Odds ratios were used to determine prognostic factors of severe thrombocytopenia. Rehabilitative interventions and modalities of treatment were recorded. At 6 and 12 months, clinical outcomes such as platelet count, disease activity, bleeding incidents, and hospitalization were measured. Thirty-eight point three percent of the participants had high disease activity (SLEDAI ≥ 20). The predictive value of lupus nephritis (OR 3.12), a SLEDAI score of 20 (OR 2.89), the presence of anti-phospholipid antibodies (OR 2.45), and having a positive direct Coombs test (OR 2.31) were also important prognostic factors of severe thrombocytopenia. The most common treatments were corticosteroids (89.7) and hydroxychloroquine (78.5). The high adherence rates were found in rehabilitative interventions with low-impact aerobic exercise (62.6%) and patient education (55.1%). Mean platelet count (68.3→112.4 x 109/L), bleeding events, SLEDAI scores, and all functional and quality of life parameters, including the SF-36 physical component (+14.4) and pain VAS (−23.6 mm), showed significant improvements at 12 months**.** SLE patients exhibit thrombocytopenia, which is severe yet prevalent, and correlates well with renal involvement, high disease activity, and anti-specific antigens autoantibodies. The combination of the therapy with pharmacologic therapy and programmed rehabilitation interventions, with a major relief in the hematologic parameters, disease control, and patient-reported functional outcomes and quality of life at 12 months, also became correlated with the multidisciplinary approach to treatment.

Keywords: Thrombocytopenia; adult patients; risk factors; and systemic lupus erythematosus.

INTRODUCTION

Thrombocytopenia or a reduction in platelet count that is less than 150,000 platelets per microliter of blood is a significant hematological aberration that is commonly linked with Systemic Lupus Erythematosus (SLE) [Fayyaz, A. *et al*., 2015], an autoimmune illness capable of afflicting a variety of organ systems. Thrombocytopenia in SLE is a multifactorial pathophysiology process that involves both immune-mediated processes and secondary effects of the disease itself [Ahn, S. M. *et al*., 2022; Jallouli, M. *et al*., 2012].

The immune system, in the case of SLE patients, malfunctions by attacking the body parts, including platelets. It may develop an autoimmune reaction that creates anti-platelet antibodies, which are used to destroy the platelets, especially in the spleen [Manger, K. *et al*., 2002]. Besides, the immune complexes may lead to the activation of the complement system, which may further worsen the platelet destruction. Besides autoimmune destruction, SLE may also lead to the swelling of the spleen or splenomegaly [Zhao, H. *et al*., 2010], which has the potential to trap platelets and reduce their circulation, adding to the thrombocyopaemia [Ward, M. M. *et al*., 2006].

Thrombocytopenia in SLE has a wide clinical manifestation. Some patients also end up developing bleeding complications such as petechiae, purpura, and, in some severe cases [Hepburn, A. L. *et al*., 2010], life-threatening hemorrhages. Thrombocytopenia especially occurs more in times of disease flare, which is usually accompanied by disease flare and thrombosis or severe bleeding, one of the complications that can occur with the risk of thrombocytopenia [Linge, P. *et al*., 2018].

Thrombocytopenia in SLE is a condition that requires the investigation of the history, physical examination of the patient, and laboratory [Song,

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Y. *et al*., 2022]. Differentiation of immune-mediated thrombocytopenia with other possible etiologies, including hypersplenism or drug-induced thrombocytopenia, is of absolute necessity. The management of thrombocytopenia in SLE is specific to the clinical situation of the patient and could be through the administration of corticosteroids to suppress the autoimmune response or other immunosuppressive drugs in extreme cases [Chen, H. *et al*., 2011]. The epidemiological studies of thrombocytopenia in SLE show that thrombocytopenia can be seen in between 20-30 percent of SLE patients, and it is an important aspect of the overall clinical treatment of SLE [Arnal, C. *et al*., 2002].

PATIENTS AND METHODS

This longitudinal cross-sectional research was carried out to examine prognostic factors that occur in thrombocytopenia in systemic lupus erythematosus (SLE) and determine the effects of a rehabilitative intervention on clinical outcomes and functional outcomes. One hundred and seventy-one adult patients who met the criteria of the American College of Rheumatology (ACR) of SLE were recruited. Thrombocytopenia, or a platelet count less than 150 x 109 /L, was seen in all subjects. The research under consideration took place in Thi-Qar, Iraq, hospitals in between March 2024 and March 2025.

At the baseline, demographic and clinical variables, which included age, gender, body mass index (BMI), length of disease, and comorbidity, were taken in a systematic manner. The SLE Disease Activity Index (SLEDAI) was used to measure disease activity, in which the patients were categorized under the inactive/mild, moderate, high, and very high disease activity. All participants were subjected to a complete laboratory test, including complete blood counts to define the severity of thrombocytopenia (mild, moderate, and severe), immunological (anti-dsDNA, anti-Smith, and antiphospholipid antibodies), and complement (C3, C4), and a direct Coombs test. The presentations included clinical signs of mucocutaneous bleeding, fatigue, and arthritis.

A multivariate logistic regression analysis was conducted to find out factors associated with severe thrombocytopenia (below 50 x109/L). The variables to be used in the model were the following: lupus nephritis, a high disease activity (SLEDAI > 20), the presence of antiphospholipid antibodies, the existence of an anti-dsDNA test, the absence of C3 complement, age, years of disease, and a positive direct Coombs test. The strength of these associations was determined by the calculation of odds ratios (OR) and the 95% confidence intervals (CI). After initial medical treatment, patients were given a multidisciplinary rehabilitative program in terms of organization, as well as on top of regular pharmacotherapy. This program involved aerobic exercise of low intensity, patient education, physical therapy, and psychological assistance. The compliance to such interventions was tracked during the research. Re-evaluation of clinical outcomes (6-12 months) took into account a change in platelet count, SLEDAI scores, and bleeding occurrences.

SPSS, version 26.0, was used to conduct statistical analysis. Continuous variables are stated in the form of mean +- standard deviation (SD), whereas the frequency and percentages are provided in the form of a table in categorical variables. Paired t-tests were used in continuous analysis of comparison between baseline and follow-up results, and the McNemar test was applied in testing of categorical comparison. The p-value was taken into consideration to be statistically significant at less than 0.05.

RESULTS

Table 1. Distribution of the demographic parameters of 107 patients in our cross–sectional study.

Variable	Patients Outcomes
Age (years), mean ± SD	36.4 ± 11.2
Female sex	98 (91.6%)
Male sex	9 (8.4%)
BMI (kg/m²), mean ± SD	25.1 ± 4.3
Comorbidity	
Hypertension	41 (38.3%)
Depression/Anxiety disorders	36 (33.6%)
Antiphospholipid syndrome	29 (27.1%)
Chronic kidney disease	24 (22.4%)

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Osteoporosis/Osteopenia	21 (19.6%)
Thyroid disorders	18 (16.8%)
Diabetes mellitus	15 (14.0%)
Cardiovascular disease	12 (11.2%)
Fibromyalgia	14 (13.1%)
Sjögren syndrome (secondary)	11 (10.3%)
Avascular necrosis	5 (4.7%)
Disease duration (years), mean ± SD	6.8 ± 4.9
Smoking status	12 (11.2%)
Married/Partnered	58 (54.2%)
Education ≥ College	61 (57.0%)

Table 2. Classification the clinical features in the patients.

Clinical feature	Patients outcomes
Platelet count (×10⁹/L), mean ± SD	68.3 ± 32.1
Severe thrombocytopenia (<50 ×10⁹/L)	46 (43.0%)
Moderate thrombocytopenia (50–99 ×10⁹/L)	37 (34.6%)
Mild thrombocytopenia (100–150 ×10⁹/L)	24 (22.4%)
Mucocutaneous bleeding	61 (57.0%)
Petechiae/Purpura	48 (44.9%)
Epistaxis	29 (27.1%)
Gingival bleeding	22 (20.6%)
Menorrhagia (females only, n=98)	31 (31.6%)
Fatigue (self-reported)	89 (83.2%)
Arthralgia/Arthritis	72 (67.3%)
Skin rash (malar/discoid)	54 (50.5%)

Table 3. Classification of the activity of systemic lupus erythematosus through the SLEDAI-2K scoring system.

Classifications	Scores	Patients	Percentage	MEAN (SD)
Inactive/Mild	0–5	11	10.3%	3.8 ± 1.2
Moderate	6–10	19	17.8%	8.1 ± 1.4
High	11–19	36	33.6%	14.9 ± 2.5
Very High	≥ 20	41	38.3%	24.2 ± 3.8
Overall	—	107	100%	14.7 ± 6.8

Table 4. Characterization of laboratory features in the patients.

Parameters	Patients	Reference range
Anti-dsDNA positive	77 (72.0%)	—
Anti-Smith antibody positive	34 (31.8%)	—
Anti-phospholipid antibodies positive	39 (36.4%)	—
Low C3 (<90 mg/dL)	70 (65.4%)	90–180 mg/dL
Low C4 (<10 mg/dL)	63 (58.9%)	10–40 mg/dL
Hemoglobin (g/dL), mean ± SD	10.8 ± 1.9	12.0–16.0
WBC (×10⁹/L), mean ± SD	4.2 ± 1.8	4.5–11.0
ESR (mm/hr), mean ± SD	42.6 ± 18.3	0–20
CRP (mg/L), mean ± SD	8.4 ± 6.2	0–5
Creatinine (mg/dL), mean ± SD	1.1 ± 0.5	0.6–1.2
Proteinuria (>0.5 g/day)	38 (35.5%)	<0.15 g/day
Direct Coombs test is positive	29 (27.1%)	—

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Table 5. Prevalence of the clinical features rate according to thrombocytopenia severity in patients.

Severity	Platelet Range (×10⁹/L)	N (%)	Mean platelet ± SD	Bleeding events
Mild	100–150	24 (22.4%)	121.3 ± 14.2	5 (20.8%)
Moderate	50–99	37 (34.6%)	72.8 ± 13.6	19 (51.4%)
Severe	<50	46 (43.0%)	28.4 ± 12.9	37 (80.4%)
Total	—	107 (100%)	68.3 ± 32.1	61 (57.0%)

Table 6. Categorization of treatments used into patients.

Treatments	*Patients (%)*	*Duration Outcomes*
Corticosteroids (any)	96 (89.7%)	8.4 ± 3.2
High-dose pulse (≥1 mg/kg)	52 (48.6%)	2.1 ± 0.8
Low-dose maintenance	44 (41.1%)	10.2 ± 2.6
Hydroxychloroquine	84 (78.5%)	11.4 ± 1.8
Azathioprine	45 (42.1%)	7.8 ± 3.4
Mycophenolate mofetil	28 (26.2%)	8.1 ± 2.9
Intravenous immunoglobulin (IVIG)	23 (21.5%)	1.2 ± 0.5
Rituximab	17 (15.9%)	—
Cyclophosphamide	8 (7.5%)	3.4 ± 1.1
Thrombopoietin receptor agonists	6 (5.6%)	4.8 ± 2.3
Splenectomy	3 (2.8%)	—

Table 7. Characterizing rehabilitative interventions presented to participants.

Intervention	N (%)	Adherence rate (%)
Low-impact aerobic exercise	67 (62.6%)	74.2%
Patient education programs	59 (55.1%)	82.1%
Physical therapy	52 (48.6%)	68.5%
Psychological support/CBT	40 (37.4%)	71.3%
Occupational therapy	32 (29.9%)	65.8%
Aquatic therapy	24 (22.4%)	78.9%
Yoga/Tai Chi	19 (17.8%)	81.4%
Nutritional counseling	35 (32.7%)	76.3%

Table 8. Enrolling clinical features of patients in post – interventions at 6 and 12 Months.

Measurements	Baseline	6 Months	12 Months	P-value
Platelet count (×10⁹/L), mean ± SD	68.3 ± 32.1	94.7 ± 38.4	112.4 ± 41.7	<0.001
Platelet recovery (≥100 ×10⁹/L), n (%)	—	63 (58.9%)	76 (71.0%)	0.003
Complete response (≥150 ×10⁹/L), n (%)	—	34 (31.8%)	49 (45.8%)	<0.001
SLEDAI score, mean ± SD	14.7 ± 6.8	9.2 ± 5.1	6.8 ± 4.3	<0.001
Bleeding events, n (%)	61 (57.0%)	18 (16.8%)	9 (8.4%)	<0.001
Relapse (after initial response), n (%)	—	12 (11.2%)	25 (23.4%)	—
Hospitalization, n (%)	42 (39.3%)	14 (13.1%)	8 (7.5%)	<0.001
Mortality, n (%)	—	2 (1.9%)	3 (2.8%)	—

Table 9. Assessment of functional outcomes and measurements of health in patients.

Measure	*Baseline*	*12-Month*	*Mean change*	*P-value*
SF-36 Physical Component	38.2 ± 9.1	52.6 ± 8.4	+14.4	<0.001
SF-36 Mental Component	41.5 ± 10.3	53.8 ± 9.2	+12.3	<0.001
Fatigue Severity Scale (1–7)	5.8 ± 1.3	3.9 ± 1.5	−1.9	<0.001
6-Minute Walk Test (meters)	342 ± 78	418 ± 65	+76	<0.001
HAQ-DI (0–3)	1.4 ± 0.6	0.8 ± 0.5	−0.6	<0.001
Beck Depression Inventory	18.2 ± 7.4	11.6 ± 6.1	−6.6	<0.001
Pain VAS (0–100 mm)	58.3 ± 22.1	34.7 ± 18.9	−23.6	<0.001
Grip Strength (kg)	18.4 ± 6.2	23.1 ± 5.8	+4.7	<0.001

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Table 10. Univariate analysis was performed for risk factors related to patients with thrombocytopenia.

Risk factors	OR	95% CI	P-value
Lupus nephritis	3.12	1.47–6.62	0.003
SLEDAI ≥ 20	2.89	1.38–6.05	0.005
Anti-phospholipid antibodies	2.45	1.12–5.36	0.011
Anti-dsDNA positive	2.18	0.98–4.85	0.056
Low C3 complement	1.94	0.89–4.23	0.094
Age < 30 years	1.76	0.84–3.69	0.134
Disease duration > 5 years	1.52	0.73–3.17	0.264
Direct Coombs positive	2.31	1.02–5.23	0.044

DISCUSSION

Thrombocytopenia was universal in nature, and the mean platelet count in our cohort was 68.3 +- 32.1 x 10 9/L. The prevalence of the severity (43% severe, 34.6% moderate, 22.4% mild) and the high correlation between severity and bleeding (20.8 to 80.4). This is in line with a few reports [Tsokos, G. C. 2020; Tsokos, G.C. 2010; Lewis, M. J., & Jawad, A. S2017] that point out thrombocytopenia as a significant risk factor of hemorrhagic manifestations of SLE. Symptoms of bleeding are the most common (mucocutaneous bleeding in 57.0% and menorrhagia in 31.6%), which is similar to those often reported in clinical practice. Of importance is that it is significantly related to lupus nephritis (OR 3.12, p=0.003). Thrombocytopenia was shown to be an independent predictor of extreme organ damage, especially renal, and general death in SLE as demonstrated in a Canadian study [Yen, E. Y., & Singh, R. R. 2018].

The high disease activity (SLEDAI > 20, OR 2.89, p=0.005) is not surprising, and it validates the idea that thrombocytopenia is an indicator of active SLE. It may cause thrombocytopenia by attacking the platelets by immunity and ironically predisposing to thrombosis, a paradox called the antiphospholipid syndrome. Such a high risk relating to a positive direct Coombs test (OR 2.31, p=0.044) indicates the presence of a broader autoimmune diathesis, which is frequently manifested by the co-existence of autoimmune hemolytic anemia and thrombocytopenia (Evans syndrome) in SLE patients [Tsokos, G. C. *et al*., 2016]. The marginal correlation between anti-dsDNA antibodies (p=0.056) also supports the association between the global serological activity and the association [Fanouriakis, A. *et al*., 2020].

The modalities of treatment used denote the contemporary guideline-based treatment. Corticosteroids (89.7) and hydroxychloroquine (78.5) were mainly used, which is the norm. The application of steroid-sparing immunosuppressants, such as azathioprine (42.1%), and mycophenolate mofetil (26.2) also follows the approaches to the treatment of the refracting cytopenias and comorbid organ tests. The use of the second-line agents, including the IVIG (21.5%), and rituximab (15.9) in a limited number of patients is in agreement with the literature that reports the effectiveness of these agents in refractory immune thrombocytopenia. It's decreasing place as the preferred method as biologic and targeted therapies account for the low rate of splenectomy (2.8%) [Velo-García, A. *et al*., 2016; Costa Pires, T. *et al*., 2020; Roussotte, M. *et al*., 2022]

The levels of high adherence to interventions (65.8%-82.1) to low-impact aerobic exercise, patient education, and psychological support indicate that the methods are well-accepted and practical. The high increase in SF-36 Physical and Mental Component Summaries, fatigue, 6-Minute Walk Test, HAQ-DI, and pain VAS at 12 months. The British studies determined that psychosocial and educational interventions could enhance health-related quality of life, fatigue, and depression in patients with SLE. Likewise, physical enhancement is in line with the research indicating the safety and efficacy of exercise in SLE, which tends to overrule deconditioning and exhaustion by chronic illnesses [Ziakas, P. D. *et al*., 2005]. The extensive rehabilitation program seems to cover the symptom burden (fatigue, 83.2%) as well as arthralgia (67.3% comorbidity) and depression/anxiety (33.6% comorbidity), claimed to be persistent even with immunosuppressive therapy. It is shown that there is a significant improvement in the clinical outcomes at 6 and 12 months [Pamuk, O. N. *et al*., 2023; Jung, J. H. *et al*., 2016; Bertsias, G. K. *et al*., 2013]. The success of the combined medical/rehabilitative method can be confirmed by the improvement in the number of platelets (MEAN) of 68.3 to 112.4 x109/L (p<0.001) and

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the decrease in the percentage of bleeding incidences (57.0 percent to 8.4 percent) ($p<0.001$). The similar substantial reduction in the SLEDAI scores and the reduction in hospitalizations vividly highlight the idea that multidisciplinary care has the capacity to alter the evolution of the disease and patient-centered outcomes.

CONCLUSION

Our observation indicates that thrombocytopenia is closely related to both an elevated disease activity (mean SLEDAI 14.7) and a high morbidity. 43 percent of patients had severe thrombocytopenia (43 < 50 x 109/L), which showed significant associations with lupus nephritis (OR 3.12), very high disease activity (SLEDAI 43 SLEDAI 20: OR 2.89), and any positive outcome of anti-phospholipid antibodies (OR 2.45). Although there was a significant clinical improvement of the patient with the increase in platelet count (68.3 to 112.4 x 109/L) and a 57.0 to 8.4% reduction in the incidence of bleeding with immunosuppressive therapy, the incorporation of rehabilitative activities (such as aerobic exercise, physical therapy, and CBT) was essential. The interventions were linked to high adherence rates (up to 82.1 percent) and corresponded with the large improvements in the functional capacity (6-minute walk test +76 meters), the quality of life (SF-36 scores), and pain/fatigue improvements ($p < 0.001$ in all cases).

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