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Original Research

Clinical Assessment of Cytokine Profiles and Haematological Parameters in Patients with Systemic Lupus Erythematosus: A Cross-Sectional Study from Saudi Arabia

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Abstract

Background: Systemic lupus erythematosus (SLE)-related hematological disorders have different pathogenic mechanisms involving immune dysregulation as well as microangiopathy. The current study aimed to assess the relationship between pro- and anti-inflammatory cytokines and SLE-related hematological abnormalities for Saudi Patients. **Methods**: The current cross-sectional study including 140 participants was performed at the Prince Mohammad bin Abdulaziz Hospital (PMAH), Riyadh, Saudi Arabia. Two blood samples were collected from each of the study participants for evaluation of the haematological indices including complete blood count (CBC), erythrocyte sedimentation rate (ESR), and cytokine profile (i.e., tumour necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and interleukin-10 (IL-10)). Statistical analyses were performed using the Statistical Package of Social Sciences (SPSS) software, v25. **Results**: Haematological abnormalities were documented in 63% of SLE patients, and anaemia was the highest at 52%. Haemoglobin levels were found to be significantly lower among SLE patients compared to the controls ($p < 0.001$). In the cytokine profiles, the levels of TNF-α ($p < 0.001$), IL-6 ($p < 0.001$), and IL-10 ($p = 0.009$) were significantly higher among SLE patients compared to the controls. A positive correlation was also identified between TNF-α, platelet count, red cell distribution width (RDW), and ESR. **Conclusions**: Haematological abnormalities were found to be the most common among SLE patients. Further, the correlation between cytokine profile and haematological indices indicates the influence of cytokines in the development of haematological abnormalities. Understanding hematological abnormalities and cytokines' role in the pathogenesis of these abnormalities may aid in the early diagnosis and development of more specific SLE disease therapies.

Keywords: systemic lupus erythematosus; complete blood count; haematology; cytokine; tumour necrosis factor

1. Introduction

Cytokines are considered the most important secretions of the immune system that participate in a variety of cellular, inflammatory, and pathogenic processes in human disease. Cytokines that are produced in large amounts and gain across to the circulation act in a hormonal fashion and have drastic effects on other cells. Therefore, the excessive or insufficient production of certain cytokines may contribute to the pathogenicity of certain diseases [1]. An imbalance between pro- and anti-inflammatory cytokines is a well-known characteristic of SLE. Current evidence indicates that cytokine levels are related to systemic lupus erythematosus (SLE). High levels of proinflammatory cytokines may lead to an exacerbation of inflammatory response, apoptosis, and production of autoantibodies that initiate and sustain SLE disease activity [2].

SLE involves immune dysregulation and the production of autoantibodies caused by abnormalities in the activation of the innate and adaptive immune system, the occurrence, severity, and prognosis of which are highly impacted by ethnicity [3]. Certain characteristics of SLE demand the need for further study, including its incidence ratio across genders being 9:1 female to male, and its propensity to occur during the early reproductive years among women, both of which add crucial value to the study of human reproductive immunology [4]. Further studies have also highlighted that female patients present a malar rash, photosensitivity, arthritis, and oral ulcers, while male patients present more often with serositis and renal and immunological disorders. This difference indicates sex-specific features in the pathology of SLE [5].

Women account for more than 80% of SLE cases, making it an autoimmune disease with a hereditary predisposition. SLE can have an impact on the kidney, heart, joints, and central nervous system, among other internal organs [6]. Additionally, lymphopenia, leucopenia, thrombocytopenia, and complement deficiencies (C1q, C2, and C4) are blood abnormalities commonly seen in SLE patients [7]. The main causes of SLE are autoantibodies and im-

mune complex deposition, increased apoptosis, and inadequate apoptotic cell clearance resulting in the production of excessive amounts of autoantibodies. Dysregulated cytokine production, which also contributes to tissue inflammation and organ damage, exacerbates immunological dysfunction. When T and B cells are stimulated, they release a variety of cytokines and autoantibodies that enhance the symptoms of the illness [8].

The haematological manifestation of SLE includes leucopenia, lymphopenia, thrombocytopenia, myelofibrosis, and autoimmune haemolytic anaemia; studying these symptoms is important at different disease stages to assess if the occurrence is due to manifestation of SLE, treatment consequences, or another type of blood cell dyscrasia [9–12]. There is also a growing body of evidence highlighting the role of cytokines in SLE pathogenesis, including interleukin-6 (IL-6), interleukin-17 (IL-17), interleukin-18 (IL-18), type I interferons, and tumour necrosis factor-alpha (TNF-α). Cytokine profiling plays a key role in understanding disease prognosis and aids in devising targeted therapies [13]. Assessing the relationship between haematological indices and cytokines aids in better understanding the pathogenesis of the disease; our study is one such analysis performed among Saudi SLE patients. Our study examines cytokine profiles among SLE patients and healthy controls, specifically focusing on IL-6, interleukin-10 (IL-10), and TNF-α and their roles in haematological abnormalities. The correlation between haematological parameters and the levels of cytokines in patients with SLE is not clearly defined. Evaluating and confirming the correlation between haematological parameters and cytokine levels may help understand the mechanism underlying the development of haematological abnormalities in SLE disease. Therefore, this study aims to understand the correlation between cytokines and haematological abnormalities in Saudi patients with SLE.

2. Materials and Methods

2.1 A Cross-Sectional Study

A cross-sectional study was conducted on 140 participants above 18 years of age from Saudi Arabia, including 100 SLE patients whose selection was consecutive (diagnosed positive by a rheumatologist) and 40 healthy controls were diagnosed as free from any inflammatory parameters and autoimmune diseases by the rheumatologist. This study was performed over an 11-month period at Prince Mohammad bin Abdulaziz Hospital (PMAH), Riyadh, Saudi Arabia. All study participants signed informed consent. The present study received approval from the Institutional Review Board (IRB) at King Saud University (Research Project No: E-19-3701). Data was collected from patient's case notes and hospital electronic records. Individuals with other autoimmune conditions, as well as SLE patients with other autoimmune diseases or leukemia, were excluded from this study. SLE patients with hematological abnormalities such as anemia, thrombocytopenia, thrombocytosis, leukopenia, neutropenia, and lymphopenia were also included.

2.1.1 Inclusion and Exclusion Criteria for the SLE Group

A total of 100 adult patients over the age of 18 with SLE disease were included, regardless of their age at diagnosis. All patients in this study were diagnosed by a rheumatologist as having SLE. All patients with chronic diseases or any bleeding disorders like females with menorrhagia were excluded from the study.

2.1.2 Inclusion and Exclusion Criteria of Control Group

A total of 40 healthy adult volunteers from among the hospital staff, over 18 years old, with normal complete blood count (CBC), and without SLE were included as healthy controls. Individuals with other autoimmune diseases or any inflammatory signs were excluded.

2.2 Sample Collection and Analysis

Two samples of blood were collected from each of the study participants in an ethylene diamine tetra-acetic acid (EDTA) vacutainer for analysis of complete blood count (CBC) and erythrocyte sedimentation rate (ESR). The second sample collected in a red top vacutainer was utilized for cytokine profiling and analysis.

The haematological assay involving CBC was performed using an automated blood cell counter analyser (Alinity hq, Abbott Laboratories, Chicago, IL, USA). A six-part differential count analysis was obtained for each sample along with an indication for nucleated red blood cells (NRBCs). ESR was measured using a Test-1 analyser (Alifax, Padua, Italy). Cytokine profiling was done via enzyme immunoassay (EIA) for the quantitative determination of human TNF-α (Quantikine human TNF-α Immunoassay kit, R&D system, Inc., Minneapolis, MN, USA), IL-6 (Quantikine human IL-6 Immunoassay kit, R&D system, Inc., United States), and IL-10 (Quantikine human IL-10 Immunoassay kit, R&D system, Inc., United States). Measurement of cytokines was done using an ETI-MAX 3000 fully automated enzyme-linked immunosorbent assay (ELISA) analyser (DiaSorin, Saluggia, Italy).

2.3 Statistical Analysis

Statistical analysis was done using the statistical package of social sciences (SPSS) software, v25 (IBM Corp., Armonk, NY, USA). Qualitative data were assessed with frequency, while quantitative data were assessed using the mean and standard deviation, and the significance was calculated as a p-value to compare cytokine profile and haematological indices between SLE patients and healthy controls. The Pearson's correlation coefficient was used to evaluate the correlation between haematological parameters and cytokines (IL-6, IL10, and TNF-α). Multiple linear

Table 1. Hematological abnormalities among the included study participants (N = 140) (with average and extreme values).

Hematological paramitas	Healthy controls (N = 40)	Reference range	SLE patients (N = 100)
Age	33.3 Y	-	39.4 Y
WBC	6.3 × 10^9/L	4.5–11.0 × 10^9/L	5.70 × 10^9/L
RBC	4.5 × 10^{12}/L	4.3–5.9 × 10^{12}/L	4.43 × 10^{12}/L
Haemoglobin	8.25 mmol/L	7.4–9.9 mmol/L	7.48 mmol/L
HCT	38.8%	38.3% to 48.6%	37.812%
MCV	86.3 fL	80–100 fL	85.76 fL
MCH	28.9 mol/cell	0.39–0.54 mol/cell	27.27 mol/cell
MCHC	33 mmol Hb/L	4.81–5.58 mmol Hb/L	31.80 mmol Hb/L
RDW	12.2%	12% to 15%	14.13%
PLT	278 billion/L	135–317 billion/L	271.16 billion/L
MPV	8.7 fL	8.9–11.8 fL	8.76 fL
Neutrophil	4.6 × 10^3/µL	1.5–10.0 10^3/µL	3.34 10^3/µL
Lymphocyte	1.7 × 10^3/µL	1.2–4.0 10^3/µL	1.79 10^3/µL
ESR	3.25 mm/hr	1–13 mm/hr	37.5 mm/hr

SLE, systemic lupus erythematosus; WBC, white blood cell; RBC, red blood cells; HCT, Hematocrit; MCV, mean corpuscular volume; MCH, mean corpuscular haemoglobin; MCHC, mean corpuscular haemoglobin concentration; RDW, red blood distribution width; MPV, mean platelet volume; ESR, erythrocyte sedimentation rate.

regression models were built to assess the haematological indices as predictors for the levels of cytokines. The accepted level of significance was set at $p < 0.05$.

3. Results

The study included a total of 140 Saudi participants, including 100 diagnosed SLE patients and 40 healthy controls, all participants above 18 years (Table 1).

Females were found to be the majority in both the study cohorts, comprising 88% among SLE cases and 85% among the healthy controls. The cohort distribution is outlined in Table 2.

Table 2. Distribution of different variables in both the SLE (N = 100) and healthy control groups (N = 40).

Variable	SLE patients (N = 100)	Healthy controls (N = 40)	*p*-value
Females	88%	85%	N/A
TNF-α	5.72 ± 4.69	1.74 ± 1.36	0.001
IL-6	28.81 ± 13.91	1.79 ± 0.45	0.001
IL-10	25.55 ± 8.48	1.61 ± 1.41	0.009
RBC	4.44 ± 0.63	4.57 ± 0.34	0.207
Haemoglobin	12.06 ± 1.82	13.32 ± 89	0.001
HCT	37.81 ± 5.61	38.66 ± 3.36	0.373
ESR	37.39 ± 25.27	3.25 ± 1.89	0.001

TNF-α, tumour necrosis factor-alpha; IL-6, interleukin-6; IL-10, interleukin-10.

3.1 Haematological Indices

Haematological abnormalities were detected among 63% of SLE patients, and anaemia was found to be the most common with 52% prevalence. Further, platelet abnormalities, including thrombocytopenia, were found in 8% of the patients, and thrombocytosis was observed among 7%. Leukopenia was found in 17%, leucocytosis in 4%, neutropenia in 20%, and lymphopenia in 14% of SLE cases. Haemoglobin levels were found to be significantly lower among SLE cases compared to the healthy controls ($p < 0.001$). A significant difference between SLE cases and healthy controls was found for mean corpuscular haemoglobin (MCH, $p = 0.006$) and mean corpuscular haemoglobin concentration (MCHC, $p < 0.001$). Further, the red blood distribution width (RDW) and ESR in patients were significantly higher than those in the healthy controls ($p < 0.001$). In the case of platelet indices, no significance was noted for platelet counts or mean platelet volume (MPV) between SLE cases and healthy controls. For white blood cell (WBC) indices, the neutrophil count in SLE patients was found to be significantly lower than that in the healthy controls ($p < 0.001$), while no significance was recorded for WBC and lymphocyte counts.

3.2 Cytokine Profile

The levels of cytokines studied, including TNF-α, IL-6, and IL-10, were significantly different between SLE patients and healthy controls. Levels of all three cytokines among SLE cases were found to be significantly higher than those among the controls (TNF-α at $p < 0.001$; IL-6 at $p < 0.001$, and IL-10 at $p = 0.009$).

Table 3. Correlations between TNF-α and haematological indices in the study cohort.

		SLE patients		Healthy controls	
Variables	Reference range	Pearson correlation	*p*-value	Pearson correlation	*p*-value
WBC	4.5–11.0 × 10^9/L	–0.148	0.143	0.070	0.668
RBC	4.3–5.9 × 10^{12}/L	–0.453	<0.001	0.120	0.462
Haemoglobin	2.09–2.71 mol/L	–0.715	<0.001	0.120	0.461
HCT	38.3% to 48.6%	–0.688	<0.001	–0.171	0.291
MCV	80–100 fL	–0.330	0.001	0.051	0.754
MCH	0.39–0.54 mol/cell	–0.361	<0.001	–0.077	0.636
MCHC	4.81–5.58 mmol Hb/L	–0.219	0.029	–0.067	0.681
RDW	12% to 15%	0.334	0.001	–0.224	0.165
PLT	135–317 billion/L	0.320	0.001	0.088	0.590
MPV	8.9–11.8 fL	0.016	0.875	0.019	0.905
Neutrophil	1.5–10.0 10^3/µL	–0.050	0.630	0.045	0.783
Lymphocyte	1.2–4.0 10^3/µL	–0.201	0.050	0.275	0.086
ESR	1–13 mm/hr	0.685	<0.001	0.328	0.039

Table 4. Correlations between cytokine IL-6 and haematological indices in the study cohort.

		SLE patients		Healthy controls	
Variables	Reference range	Pearson correlation	*p*-value	Pearson correlation	*p*-value
WBC	4.5–11.0 × 10^9/L	–0.033	0.743	–0.053	0.745
RBC	4.3–5.9 × 10^{12}/L	–0.219	0.029	0.001	0.993
Haemoglobin	2.09–2.71 mol/L	–0.538	<0.001	–0.016	0.922
HCT	38.3% to 48.6%	–0.535	<0.001	0.068	0.678
MCV	80–100 fL	–0.417	<0.001	0.035	0.829
MCH	0.39–0.54 mol/cell	–0.457	<0.001	0.140	0.390
MCHC	4.81–5.58 mmol Hb/L	–0.310	0.002	0.068	0.677
RDW	12% to 15%	0.096	0.341	–0.110	0.499
PLT	135–317 billion/L	0.225	0.024	0.066	0.688
MPV	8.9–11.8 fL	–0.027	0.790	–0.130	0.423
Neutrophil	1.5–10.0 10^3/µL	0.024	0.813	0.016	0.920
Lymphocyte	1.2–4.0 10^3/µL	–0.104	0.315	–0.002	0.991
ESR	1–13 mm/hr	0.522	<0.001	–0.165	0.308

3.3 Correlations between Haematological Indices and Cytokine Profile

A significant correlation was found between levels of the cytokine TNF-α and haematological indices among SLE patients, wherein a negative correlation was found with RBC, haemoglobin, Hematocrit (HCT), mean corpuscular volume (MCV), MCH, and MCHC. A positive correlation was also noted between TNF-α, platelet count, RDW, and ESR. These correlations are detailed in Table 3.

A further correlation analysis between IL-6 and haematological parameters identified negative correlations with RBC, haemoglobin, HCT, MCV, MCH, and MCHC. A positive correlation was detected between platelet count and ESR. These correlations are detailed in Table 4.

Correlation analysis between IL-10 and haematological indices among SLE cases identified a negative correlation with haemoglobin ($p = 0.040$) and a positive correlation with platelet count ($p = 0.001$), RDW ($p < 0.001$), and ESR ($p = 0.029$). These correlations are detailed in Table 5.

3.4 Regression Analysis between Cytokine Profile and Haematological Indices

The relationship between levels of cytokines and haematological parameters was assessed using a stepwise multiple regression model in which haematological indices were taken as explanatory variables and cytokines as dependent variables. Regression analysis between TNF-α and haematological indices indicated the coefficient of multiple correlations (R) to be 0.750 and the coefficient of determination (R square) to be 0.570. Further, haemoglobin levels and ESR were found to impact TNF-α at a rate of 57% among the SLE patient group, and the F-distribution analysis detected the influence of possible predictive variables on TNF-α to be statistically significant at $p < 0.001$. The analysis of independent variables highlighted haemoglobin ($T = –4.23$, $p < 0.001$) and ESR ($T = 3.75$, $p < 0.001$) as having a significant influence on TNF-α levels.

Regression analysis between IL-6 and haematological indices identified $R = 0.760$ and $R^2 = 0.580$. Indepen-

Table 5. Correlations between cytokine IL-10 and haematological indices in the study cohort.

		SLE patients		Healthy controls	
Variables	Reference range	Pearson correlation	*p*-value	Pearson correlation	*p*-value
WBC	4.5–11.0 × 10^9/L	–0.067	0.510	0.042	0.799
RBC	4.3–5.9 × 10^{12}/L	–0.114	0.260	0.046	0.778
Haemoglobin	2.09–2.71 mol/L	–0.206	0.040	–0.139	0.393
HCT	38.3% to 48.6%	–0.191	0.057	–0.191	0.238
MCV	80–100 fL	–0.118	0.244	0.163	0.314
MCH	0.39–0.54 mol/cell	–0.132	0.191	0.009	0.958
MCHC	4.81–5.58 mmol Hb/L	–0.109	0.279	0.062	0.702
RDW	12% to 15%	0.391	<0.001	–0.267	0.096
PLT	135–317 billion/L	0.337	0.001	0.009	0.956
MPV	8.9–11.8 fL	–0.136	0.177	0.056	0.731
Neutrophil	1.5–10.0 10^3/µL	–0.042	0.686	0.200	0.215
Lymphocyte	1.2–4.0 10^3/µL	–0.156	0.129	0.081	0.621
ESR	1–13 mm/hr	0.237	0.029	–0.129	0.427

Table 6. Regression analyses between TNF-α, IL-6, IL-10, and haematology indices.

Variable	Predictors	β	T	R square	F	*p*-value
	A. TNF-α and haematological indices					
TNF-α	(Constant)	16.15	4.48	0.57	51.5	<0.001
	Haemoglobin	–1.07	–4.23			
	ESR	0.07	3.75			
	B. IL-6 and haematological indices					
IL-6	(Constant)	15.67	4.0	0.58	7.62	<0.001
	Haemoglobin	–21.5	–2.1			
	MCV	–11.7	–2.8			
	MCH	–34	–2.4			
	MCHC	–44.5	–3.3			
	RDW	2.3	2.1			
	C. IL-10 and haematological indices					
IL-10	(Constant)	31.5	1.96	0.12	5.25	0.007
	Haemoglobin	–2.35	–2.07			
	ESR	0.27	3.23			

dent haematology variables including haemoglobin, MCV, MCH, MCHC, and RDW were also found to influence IL-6 levels at 58% within the SLE patient cohort. The F-distribution highlighted the influence of possible predictive variables on IL-6 to be statistically significant at $p < 0.001$. The analysis of independent variables showed haemoglobin (T = –2.1, $p = 0.037$), MCV (T = –2.8, $p = 0.006$), MCH (T = –2.4, $p = 0.020$), MCHC (T = –3.3, $p = 0.001$), and RDW (T = 2.1, $p = 0.042$) to have a significant influence on IL-6 levels.

Regression analysis between IL-10 and haematological indices identified R = 0.340 and $R^2 = 0.120$. Further, independent haematology variables including haemoglobin and ESR were found to influence levels of IL-10 among SLE patients at 12%. The F-distribution analysis detected the influence of possible predictive variables on IL-10 to be statistically significant at $p = 0.007$. The regression analysis relation between TNF-α, IL-6, IL-10, and haematology parameters is highlighted in Table 6.

4. Discussion

The present study assessed the impact of haematological indices and cytokine profiles among Saudi patients with SLE. The most frequent haematological abnormalities were detected to be anaemia, thrombocytopenia, and leukopenia. Our study also identified significantly high levels of all three cytokines (i.e., TNF-α, IL-6 and IL-10) among SLE cases compared to the healthy controls. Elevated cytokines were also found to correlate with multiple haematological indices: Increased levels of TNF-α were correlated with haemoglobin, RBC, HCT, MCV, MCH, MCHC, RDW, and ESR, while elevated levels of IL-6 were correlated with haemoglobin, RBC, HCT, MCV, MCH, MCHC, and ESR. In the case of IL-10, high levels were correlated with haemoglobin, platelet count, and RDW. The reason for the high prevalence of female subjects in the SLE case group (88%) remains unclear, although studies implicate sex hormones, and the upregulation of cytokine-like IFN-α was shown to increase reproductive fitness and simultaneously increase women's susceptibility to SLE [5].

Haematological abnormalities were reported to be a common occurrence in SLE, with studies reporting the incidence rate to be about 50% due to impaired erythropoietin responses and the development of corresponding antibodies [5]. Other causes of anaemia may include nutritional deficiencies, myelofibrosis, gastrointestinal loss, infection, hypersplenism, treatment-induced illness, etc. [14]. Our study also identified anaemia as the most common haematological abnormality among SLE cases at 52%. Studies on SLE-impacted quality of life have demonstrated an increase in ESR to occur independently of the organic damage index and hence serve as a relevant and sensitive index to determine disease activity. The organ lesion index has also been shown to rise with the occurrence of adverse haematological events including anaemia, leukopenia, and thrombocytopenia, which impair quality of life. Studies thus suggest the importance of a routine assessment of quality of life in SLE to facilitate the early detection of anaemia [15].

Studies have also assessed the prognostic impact of thrombocytopenia, wherein a clinical manifestation the same as that of the first episode was recorded in addition to the classification criteria at diagnosis, immunologic profile, disease activity, and end-organ damage. The study identified 58% of SLE cases with thrombocytopenia at diagnosis, and haemorrhagic manifestations were significantly associated with the degree of thrombocytopenia. The study identified thrombocytopenia to define a subgroup of patients with higher morbidity [16]. Our study identified thrombocytopenia at a much lower frequency than that reported in 8% of cases. The difference in reported frequencies can be attributed to differences in SLE disease activity that were shown to be correlated negatively with platelet counts. This difference is also considered a prognostic factor in identifying cases with an aggressive course of disease [17].

Among the white blood cell (WBC) abnormalities, studies have reported a prevalence of leukopenia in between 22% and 41.8% of cases, lymphopenia in between 15% and 82% of cases, and neutropenia in between 20% and 40% of cases. However, studies on evidence for the risk of infection with lower WBC counts continue to be contradictory [18]. Our study identified leukopenia in 17%, leucocytosis in 4%, neutropenia in 20%, and lymphopenia in 14% of SLE cases. Factors such as the number of cases, region, race, treatment, and research method used may influence the differences in the prevalence of leukopenia, neutropenia, and lymphopenia reported among various studies [19]. The haematological findings of our study also aligned with many previous publications. Levels of haemoglobin were found to be significantly decreased among SLE cases compared to the healthy controls, which is in line with a publication by Yu *et al*. [20]. A significant increase in ESR and RDW was also detected among SLE cases, as previously reported, wherein an increased RDW was related to active disease status and suggested to be useful as a surrogate marker for inflammation over neutrophil and lymphocyte counts [21–23]. Our present study also did not detect a significant difference in platelet counts and MPV between SLE cases and healthy controls, while some published reports indicated higher disease activity with a lower MPV [24,25]. Studies have also assessed individual MPV fluctuations and investigated if these variations could be associated with clinical phenotypes of SLE, finding intra-individual MPV variations to be of low magnitude and disease activity fluctuations to not impact MPV values longitudinally [26].

In the case of cytokine profiling, the present study identified levels of TNF-α, IL-6, and IL-10 to be elevated significantly among SLE cases compared to the healthy controls. This finding is in accordance with a recent publication by Jin S *et al*. [25] who reported levels of serum IL-6, IL-10, and TNF-α in SLE groups to be higher than those in the healthy control group. The study also found the mean course of the disease and IL-10 to be independent prognostic factors of SLE, thus indicating monitoring of serum cytokines to aid in understanding the prognosis of patients with lupus and guide clinical treatment. SLE cytokine networks are crucial in drug development and disease management strategies as imbalances in such networks were correlated with disease progression [27]. Our study reported a negative correlation between levels of IL-6, TNF-α, and haemoglobin in SLE patients, while a positive correlation was noted between levels of IL-6, TNF-α, and platelet counts. These findings are in line with previous publications highlighting levels of TNF-α and IL-6 to be higher in SLE patients with active haematological disease compared to inactive disease; this association was found to be dependent on inverse correlation. Positive correlations between TNF-alpha, IL-6, and the SLE Disease Activity Index were also recorded [27,28]. Cytokines including TNF-α, IL-6, and IL-10 stimulate the production of hepcidin and inhibit the production of erythropoietin, resulting in anaemia [15]. Thus, the use of IL-6 inhibitors was recommended to correct anaemia in patients with SLE and control disease activity [29].

The current study additionally identified a negative correlation between IL-10 levels and haemoglobin levels in SLE patients, and it also found a positive correlation between platelet counts and SLE patients. However, these findings do not match those previously reported, which instead indicated that levels of IL-10 do not correlate with haematologically active disease in SLE cases [30]. Recent studies have also indicated that IL-10 plays a dual role in SLE, wherein it inhibits pro-inflammatory effector functions and is also the main driver of the extra follicular antibody response [31]. Ethnicity has also been reported to play a role in determining the concentration of IL-10 and was found to be different between various ethnic groups. For example, Asian SLE cases were found to have more than twice the concentration of serum IL-10 compared to non-Asian cases [32].

Investigating the correlation between the proinflammatory cytokines and hematological abnormalities among SLE patients in a Saudi Arabian population provides insights into how the interplay between cytokines and hematological abnormalities may differ in this specific ethnic and geographic context. Genetic, environmental, and lifestyle factors can vary between populations, potentially leading to unique patterns in disease manifestation and progression. Additionally, conducting this research in Saudi Arabia has the potential to uncover unique insights and contribute to the global understanding of SLE and its associated hematological abnormalities. It can also have practical implications for healthcare and treatment strategies in the Saudi Arabian context.

Moreover, the hematological profiles of patients with SLE can vary among individuals and populations, including those from different ethnicities. Whether the hematological profiles of Saudi Arabian SLE patients are similar to or different from those of other ethnicities worldwide can depend on various factors, including genetic, environmental, and healthcare access factors. Nearly the same results were recorded by [27] as they examined the levels of TNF-alpha, TNF receptors, IL-6, and IL-10 in individuals with SLE. To the best of our knowledge, they addressed these factors in Egyptian patients, and it involved a limited number of patients [27,29].

Multiple regression analysis was also performed to assess the relationship between haematological abnormalities and increased cytokine levels. Levels of haemoglobin and ESR were shown to be associated with both TNF-α and IL-10. Haemoglobin, MCV, MCH, MCHC, and RDW were also associated with IL-6. Studies have also demonstrated the IL6-hepcidin–haemoglobin axis to be non-functional during lupus flare cycles, as serum hepcidin was not found to rise with increased renal or extra-renal lupus activity [33]. Therefore, the association between haematological abnormalities and increased levels of cytokines could be useful markers in predicting SLE and assessing disease activity [20]. Studies that assessed changes in the levels of cytokines in SLE cases and their clinical value found the mean course of the disease and IL-10 to be independent prognostic factors for SLE [28].

Limitation of the Study

Study limitations include the sample size, which may not be representative of the entire Saudi population; the limited number of cytokines assessed; and the lack of consideration of organ involvement in SLE disease. Additionally, our study did not differentiate between disease-oriented and treatment-causative causes of haematological abnormalities. Furthermore, treatment strategies and medications used by SLE patients in the study, and their influences were not included in this study. Additionally, data on the baseline renal, hepatic, cardiac, coagulation, and pulmonary functions were not collected, which might have affected the findings.

5. Conclusions

Our study revealed a modified cytokine pattern in Systemic Lupus Erythematosus (SLE) patients. Specifically, compared to healthy controls, we observed a substantial elevation of TNF-a, IL-6, and IL-10 levels in Saudi patients with SLE. Moreover, this increase was closely associated with the activity of SLE. Among individuals with SLE, hematological irregularities were identified as the most prevalent. In addition, the connection between cytokine patterns and hematological parameters suggests that cytokines play a significant role in the emergence of these hematological irregularities. Cytokines in their pathogenesis could potentially contribute to early diagnosis and the formulation of more targeted therapies for SLE. However, it is crucial to emphasize that additional research is needed to gain a more comprehensive understanding of how these cytokines may impact the development of anemia in SLE.

Availability of Data and Materials

All data generated or analysed during this study are included in the published article. The original contributions presented in the study are included in the article/Supplementary material, further inquiries can be directed to the corresponding author.

Author Contributions

Conceptualization, FMA; methodology, FMA and MAA; formal analysis, MAA; investigation, FMA and MAA; resources, FMA; data curation, FMA and SAA; data interpretation, AFA, KHD and RS; writing—original draft preparation, FMA and MAA; writing—review and editing, FMA, MAA, SAA, AFA, KHD, and RS; supervision, FMA; funding acquisition, FMA. All authors read and approved the final manuscript. All authors have participated sufficiently in the work to take public responsibility for appropriate portions of the content and agreed to be accountable for all aspects of the work in ensuring that questions related to its accuracy or integrity. All authors contributed to editorial changes in the manuscript.

Ethics Approval and Consent to Participate

The current study received approval from the Institutional Review Board (IRB) at King Saud University (Research Project No: E-19-3701). This study was also approved form IRB at Saudi Arabian Ministry of Health (IRB NO: 2019-0054M). In addition, all study participants contributed to this study were applied assigned and written informed consent.

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Conflict of Interest

The authors declare no conflict of interest.

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