International Journal of Biomedicine 16(1) (2026) 26-32
http://dx.doi.org/10.21103/Article16(1)_OA2

ORIGINAL ARTICLE

Rheumatology

INTERNATIONAL JOURNAL OF BIOMEDICINE

Interplay of Serum IL-6 and Vitamin D in Overweight, Non-Anemic Women of Reproductive Age with Systemic Lupus Erythematosus

Abdulsalam A. Noorwali[1], Zahir Hussain[2*]

[1]*Department of Internal Medicine, Faculty of Medicine, Umm Al-Qura University, Makkah 21955, Saudi Arabia*
[2]*Department of Physiology, Faculty of Medicine, Umm Al-Qura University, Makkah 21955, Saudi Arabia*

Abstract

Background: Systemic lupus erythematosus (SLE) is a chronic, potentially life-threatening autoimmune disorder that damages various tissues and organs. It is more prevalent in women than in men. Real-world medical practice provides comprehensive clinical and laboratory information. A variety of factors complicate processes in patients with SLE. Two important risk factors, serum interleukin-6 (IL-6) and vitamin D, are to be investigated to determine their precise role in SLE.
Methods and Results: We analyzed variation in serum IL-6 and vitamin D, their association, and other characteristics in normal-weight SLE (NW-SLE) and overweight SLE (OW-SLE), compared with NW controls (NW-C) and OW controls (OW-C). The enzyme-linked immunosorbent assay (ELISA) kit methods were used for diagnostic purposes and to determine vitamin D and IL-6 levels. Conventional methods were used to record the other variables, including hemoglobin (Hb), hepcidin (Hp), body mass index (BMI), menstrual cycle length (MCL), and menstrual phase duration (MPD). Serum levels of IL-6 presented significant variations for NW-SLE compared to NW-C (P<0.02), and OW-SLE compared to OW-C, and OW-SLE compared to NW-SLE (P<0.01). The serum levels of vitamin D indicated a significant difference between OW-SLE compared to NW-SLE (P<0.03) and NW-SLE compared to NW-C, OW-SLE compared to OW-C, and OW-C compared to NW-C (P<0.01). Furthermore, vitamin D and IL-6 showed a significant negative correlation in OW-SLE and NW-SLE patients (P<0.01).
Conclusion: The results of this study highlight the importance of measuring serum IL-6 and vitamin D levels in conjunction with BMI assessment in patients with SLE. This study revealed an inverse relationship between vitamin D and IL-6 in patients with SLE. Since vitamin D is an important modifiable factor in SLE, and its deficiency is associated with disease activity and the risk of complications, correction of vitamin D deficiency can complement standard therapy and improve the prognosis of SLE. (**International Journal of Biomedicine. 2026;16(1):26-32.**)

Keywords: reproductive age women • overweight • non-anemic • systemic lupus erythematosus • interleukin-6 • vitamin D

For citation: Noorwali AA, Hussain Z. Interplay of Serum IL-6 and Vitamin D in Overweight, Non-Anemic Women of Reproductive Age with Systemic Lupus Erythematosus. International Journal of Biomedicine. 2026;16(1):26-32. doi:10.21103/Article16(1)_OA2

Abbreviations

25(OH)D, 25-hydroxyvitamin D; **ADA,** American Diabetes Association; **BMI,** body mass index; **BW,** body weight; **CRP,** C-reactive protein; **dsDNA,** double-stranded DNA; **ELISA,** enzyme linked immunosorbent assay; **Hb,** hemoglobin; **Hp,** hepcidin; **IL-6**, interleukin-6; **KSA,** Kingdom of Saudi Arabia; **MCL,** menstrual cycle length; **MPD,** menstrual phase duration; **NW,** normal weight; **NW-C,** normal weight control; **NW-SLE,** normal weight systemic lupus erythematosus; **OW,** overweight; **OW-SLE,** overweight systemic lupus erythematosus; **SLE,** systemic lupus erythematosus.

Introduction

Systemic lupus erythematosus (SLE) is a chronic, potentially life-threatening autoimmune disorder that can damage multiple tissues and organs.[1] It is more prevalent in women than men.[2] A medical practice specializing in rheumatology provides comprehensive clinical and laboratory information in SLE diagnostics..[3] Interleukin-6

(IL-6) functions as a proinflammatory cytokine in SLE[4,5] by binding to its membrane receptor, IL-6R, on leukocytes and hepatocytes, and contributes significantly to pathogenesis and disease activity. Some of the recent case-control and meta-analyses present elevated levels of IL-6 in patients with SLE.[6-8] Genetic polymorphism studies, however, did not establish a significant association of IL-6 with SLE.[9,10] Furthermore, the therapeutic approaches for blocking IL-6 in SLE did not present the efficacy as appears in other autoimmune diseases, and despite that, IL-6 remains an important factor, especially against certain risks associated with the pathogenesis of SLE and comorbidities.[11]

Another important factor in the pathogenesis of SLE is vitamin D. Vitamin D, a steroid hormone, regulates cell growth and modulates the immune system, and its insufficiency and deficiency complicate these processes in patients with SLE.[12] Pathogenesis of SLE and several other autoimmune diseases emphasize the potential immunomodulatory role of vitamin D.[13] Decreased levels and deficiency of vitamin D obtained in SLE patients indicate the involvement of vitamin D in the increased disease activity in SLE patients[14] though non-significant association of vitamin D has also been reported [15] possibly due to methodological/ study design, different indices employed for assessing the disease activity, little sun exposure, diverse lifestyles, cultural and ethnic background, deficient dietary intake, and geographical and seasonal variations of vitamin D levels.[15,16]The levels of Hb and Hp were investigated in patients with anemia and other hematological abnormalities in patients with SLE.[8,17,18] The influence of overweight status/ obesity on serum vitamin D and immune responses, including IL-6, was investigated in patients with SLE.[19] However, various studies show controversy about the association of BMI and vitamin D, and IL-6 and vitamin D.[16,20,21] The association of serum vitamin D and IL-6 was investigated,[22,23] and that was linked to its therapeutic potential via IL-6 and other pro-inflammatory biomarkers.[24,25]

The important roles of IL-6 and vitamin D in inflammation, immune processes, injury, and related aspects are established. Understanding their impact on SLE pathogenesis is essential. However, further research is needed to clarify the interaction between IL-6 and vitamin D in patients with SLE. We analyzed changes in serum IL-6 and vitamin D levels and their relationship, along with other characteristic features, in normal-weight and overweight patients with SLE.

Materials and Methods

A current case-control observational study was conducted at Umm Al-Qura University (UQU) and associated hospitals/clinical institutions in Makkah, Kingdom of Saudi Arabia (KSA). The study was conducted from January 1, 2023, to April 10, 2025. The number of reproductive-age women subjects in the current study (n = 409) exceeded the calculated sample size (385). Age (years) and body mass index (BMI, kg/m^2) matched subjects were consulted. Age range was 20-29 in the normal-weight controls (NW-C, n=105, BMI range: 18.5-24.9 kg/m^2), overweight controls (OW-C, n=105, BMI range: 25-29.9 kg/m^2), NW-SLE (n=100, BMI range: 18.5-24.9 kg/m^2), and OW-SLE (n=99, BMI range: 25-29.9 kg/m^2) women subjects.

The women of reproductive age included in the present work were not pregnant or breastfeeding. Obtaining subjects' consent was considered necessary. Samples/history were obtained only from ovulatory menstrual cycles. Only women with BMI levels not less than 18.5 kg/m^2 and not more than 24.9 kg/m^2 for NW-C and NW-SLE, and not less than 25 kg/m^2 and not more than 29.9 kg/m^2 for OW-C and OW-SLE, were included in the present study. Furthermore, they were not anemic, smokers, or had serious medical complications.

BMI, menstrual cycle length (MCL), menstrual phase duration (MPD), and other subject characteristics were recorded using a questionnaire.

For the identification and proper diagnosis of SLE, the key biomarker, anti-double-stranded DNA (anti-dsDNA) antibodies, was determined using an enzyme-linked immunosorbent assay (ELISA). Vitamin D was determined using ELISA kits. A hematology analyzer, Sysmex XN 100i (Sysmex Europe SE, Norderstedt, Germany), was used to measure Hb. To estimate serum IL-6 and hepcidin (Hp), ELISA kits for IL-6 and Hp, respectively, were used.

The data analysis was carried out employing the basic principles published elsewhere.[26] Statistical analysis was performed using the statistical software package SPSS version 24.0 (IBM Corp., Armonk, NY). For the descriptive analysis, results are presented as mean (M) ± standard deviation (SD). Multiple comparisons were performed with one-way ANOVA and a post-hoc Tukey HSD test. The coefficient of determination (R^2) was estimated to assess the strength of the linear relationship. A probability value of $P \leq 0.05$ was considered statistically significant.

Results

The total women subjects studied in the present study was 409. The number of subjects in the NW-C, NW-SLE, OW-C, and OW-SLE groups was 105, 105, 100, and 99 women, respectively. The data of their age (years), MCL (days), MPD (days), BMI (kg/m^2), IL-6 (pg/mL), Hp (ng/mL), HB (g/dL), and 25(OH)D (ng/mL) were collected and analyzed (Table 1).

Among groups, variation showed significant results for serum IL-6 and vitamin D ($P<0.01$). BMI varied significantly among groups ($P<0.01$) as two of our groups had NW-related BMI and two other groups had OW-related BMI. All other variables did not show significant differences among groups (Table 1).

Table 1 shows that the age values (range: 20-29 years) were 25.08±3.04, 24.87±3.14, 25.13±3.14, and 25.11±3.07 years for the NW-C, NW-SLE, OW-C, and OW-SLE groups, respectively.

The MCL presented 28.35±1.34, 28.40±1.38, 28.38±1.29, and 28.41±1.36 days, respectively, for NW-C, NW-SLE, OW-C, and OW-SLE groups. A P-value of 0.05 was obtained for group comparisons.

The MPD indicated 5.30±1.29, 5.34±1.22, 5.23±1.29, and 5.20±1.28 days, respectively, for NW-C, NW-SLE, OW-C, and OW-SLE groups.

BMI was 21.67±2.08, 21.68±2.06, 27.56±1.50, and 27.53±1.50 kg/m^2 for NW-C, NW-SLE, OW-C, and OW-SLE groups. NW-C vs. OW-C and NW-SLE vs. OW-SLE showed significant differences in BMI (P<0.01).

Serum levels of IL-6 showed 4.71±4.07, 6.13±4.32, 5.53±4.26, and 8.01±5.70 pg/mL, respectively, for NW-C, NW-SLE, OW-C, and OW-SLE women groups (Table 1). Serum levels of IL-6 presented significant variations for NW-SLE compared to NW-C (P<0.02), and OW-SLE compared to OW-C, and OW-SLE compared to NW-SLE (P<0.01) (Fig.1).

Table 1.

Characteristic variables in normal-weight and overweight reproductive-age women with SLE

Variables	Study groups				*P*-value
	NW-C	NW-SLE	OW-C	OW-SLE	
Subjects (n)	105	105	100	99	-
Age (years)	25.08±3.04	24.87±3.14	25.13±3.14	25.11±3.07	0.92
MCL (days)	28.35±1.34	28.40±1.38	28.38±1.29	28.41±1.36	0.99
MPD (days)	5.30±1.29	5.34±1.22	5.23±1.29	5.20±1.28	0.86
BMI (kg/m^2)	21.67±2.08	21.68±2.06	27.56±1.50	27.53±1.50	<0.01
IL-6 (pg/mL)	4.71±4.07	6.13±4.32	5.53±4.26	8.01±5.70	<0.01
Hp (ng/mL)	8.49±4.01	8.49±4.07	8.51±4.29	8.83±4.66	0.92
Hb (g/dL)	13.74±1.22	13.68±1.18	13.56±1.03	13.55±1.02	0.21
25(OH)D (ng/mL)	34.16±5.26	30.08±6.38	30.68±6.20	28.11±6.45	<0.01

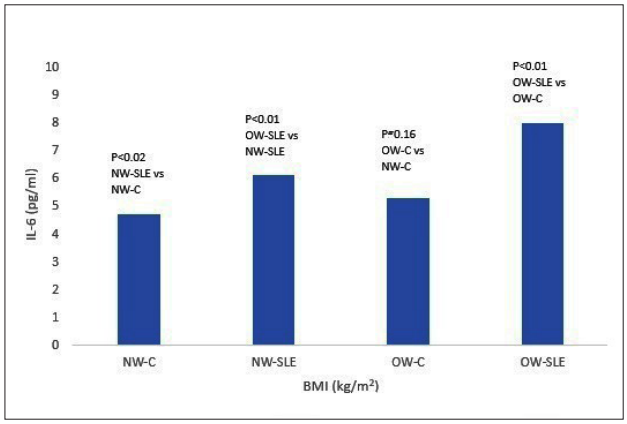

Fig.1*. Serum levels of IL-6 in the study groups*

The Hp serum levels were 8.49±4.01, 8.49±4.07, 13.56±1.03, and 8.83±4.66 ng/mL, respectively, for NW-C, NW-SLE, OW-C, and OW-SLE groups (Table 1). No significant variation of serum Hp was obtained.

The Hb values were 13.74±1.22, 13.68±1.18, 13.56±1.03, and 13.55±1.02 g/dL, respectively, for NW-C, NW-SLE, OW-C, and OW-SLE women groups (Table 1) that also showed non-significant alterations of Hb (P>0.05).

The vitamin D serum levels obtained for the NW-C, NW-SLE, OW-C, and OW-SLE women groups were 34.16±5.26, 30.08±6.38, 30.68±6.20, and 28.11±6.45 ng/mL, respectively (Table 1).

The vitamin D serum levels indicated a significant difference between OW-SLE compared to NW-SLE (P<0.03) and NW-SLE compared to NW-C, OW-SLE compared to OW-C, and OW-C compared to NW-C (P<0.01) (Fig.2).

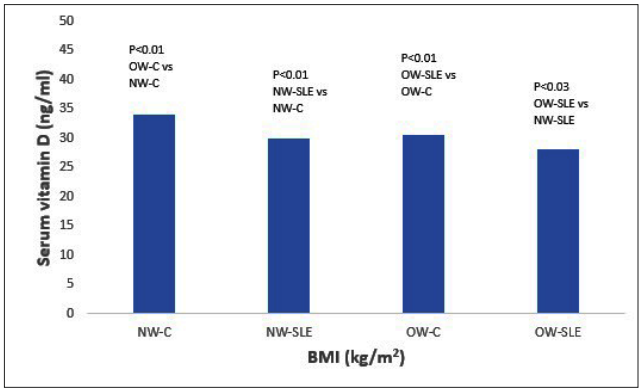

Fig.2. *Serum levels of vitamin D in the study groups.*

Table 2 shows a significant positive association between IL-6 and BMI in the OW-C (P=0.03) and OW-SLE (P<0.01) groups of women. Vitamin D correlated significantly and negatively with IL-6 in NW-SLE and OW-SLE (P<0.01).

Table 2.

Correlation of serum IL-6 with other characteristics/variables in normal-weight and overweight reproductive age women with SLE.

Variables		NW-C	NW-SLE	OW-C	OW-SLE
Age (years)	R^2	0.00	0.00	0.01	0.00
	P	0.48	0.74	0.30	0.90
MCL (days)	R^2	0.02	0.00	0.00	0.01
	P	0.16	0.50	0.61	0.31
MPD (days)	R^2	0.00	0.02	0.00	0.00
	P	0.86	0.18	0.56	0.56
BMI (kg/m^2)	R^2	0.00	0.00	0.05	0.34
	P	0.54	0.76	0.03	<0.01
Hp (ng/mL)	R^2	0.00	0.00	0.00	0.01
	P	0.89	0.80	0.82	0.46
HB (g/dL)	R^2	0.01	0.00	0.01	0.01
	P	0.23	0.66	0.48	0.31
25(OH)D (ng/mL)	R^2	0.01	0.23	0.00	0.33
	P	0.23	<0.01	0.90	<0.01

Vitamin D presented a significantly negative correlation with BMI in NW-SLE (P=0.02), and in OW-C and OW-SLE (P<0.01) (Table 3). All other characteristics/variables were not significantly associated with vitamin D.

Table 3.

Correlation of serum vitamin D with other characteristics/variables in normal-weight and overweight reproductive age women with SLE.

Variables		NW-C	NW-SLE	OW-C	OW-SLE
Age (years)	R^2	0.01	0.02	0.00	0.00
	P	0.30	0.14	0.67	0.59
MCL (days)	R^2	0.00	0.02	0.03	0.00
	P	0.71	0.17	0.06	0.61
MPD (days)	R^2	0.00	0.01	0.02	0.00
	P	0.93	0.40	0.18	0.61
BMI (kg/m^2)	R^2	0.03	0.05	0.33	0.48
	P	0.06	0.02	<0.01	<0.01
IL-6 ((pg/mL)	R^2	0.01	0.23	0.00	0.33
	P	0.23	<0.01	0.90	<0.01
Hp (ng/mL)	R^2	0.00	0.00	0.01	0.00
	P	0.79	0.95	0.32	0.62
HB (g/dL)	R^2	0.00	0.02	0.02	0.00
	P	0.93	0.17	0.14	0.64

Discussion

Various studies found elevated levels of IL-6 in patients with SLE compared with controls,[6-8,27-29] whereas other studies reported a non-significant increase in IL-6 concentration in SLE patients compared with healthy control women.[30-32] The present study finds a significant increase in IL-6 in NW-SLE women compared to NW-C, in OW-SLE women compared to OW-C, and in OW-SLE women compared to NW-SLE women.

The present investigation showed no significant association between IL-6 and age across all subject groups. Age-associated changes in IL-6 in SLE have rarely been studied. A positive association between IL-6 and age in SLE patients was reported,[11] consistent with the observation that aging is associated with enhanced production of inflammatory cytokines, including IL-6, leading to low-grade inflammation.[33] The absence of a significant association of age with any of the SLE or control groups in the present study seems due to the fact that our subjects had quite a limited age range of 20-29 years. Further studies, including a broader age range, may clarify the association between age and serum IL-6.

The elevated IL-6 levels in SLE patients across studies may be due to methodological variability, treatment effects, increased disease activity, age, sex, BMI, and other factors. It is possible that reduced or increased IL-6 levels measured at specific times reflect decreased or increased disease activity, respectively. These findings indicate that IL-6 might serve as an indicator of disease activity, inflammatory status, or post-treatment effects, rather than as a diagnostic marker. SLE patients present with various clinical manifestations driven by immunological, genetic, and environmental factors, and vitamin D is considered an immunomodulatory factor that influences patients with SLE in active disease more than in inactive disease.[1,3]

A variety of clinical features studied in SLE patients[15] reveal that the maximum incidence of SLE occurs in reproductive-age women of 20-29 years.[34] Since we collected the data for the present study in reproductive age women of 20-29 years, it can appropriately be compared with such study,[34] where vitamin D deficiency (mean 16.82±11.24 ng/mL) was suggested to occur in view of multiple interacting factors, including sun avoidance due to photosensitivity, nutritional deficiency of vitamin D, and using full length/ full body clothes that limit the skin exposure to sun.[16,35] Similar conditions were present in SLE patients in the present study.

Vitamin D plays an immunoregulatory role by decreasing autoimmune responses and disease activity in SLE. However, it is not necessary that vitamin D is a causal factor. It could possibly be a consequence of photosensitivity that inclines the patients to limit the exposure to the sun, which leads to less synthesis of vitamin D. Furthermore, certain types of medication for SLE patients may increase the catabolism of vitamin D and decrease the intestinal absorption of vitamin D, thereby enhancing the vitamin D deficiency.[34] Further studies may confirm the medication influences.

Routine and annual comprehensive screening are required to maintain serum vitamin D (25(OH)D) levels above 30 ng/mL, especially in SLE patients with active disease, glucocorticoid use, and photosensitivity. This helps manage SLE patients.[34] Control of the dietary intake of vitamin D and the effect of medication on vitamin D levels were not recorded in the present study. Furthermore, genetic polymorphisms influencing vitamin D metabolism were not studied. A larger sample size, interventional, and longitudinal investigations may confirm the precise association of vitamin D with SLE.

The levels of Hb and Hp did not vary significantly in NW and OW patients with SLE and control subjects in the present study, since the anemic patients were not included in the current study, though anemia and other hematological abnormalities are found prevalent in patients with SLE.[8,17]

The role of BMI in patients with SLE is not well understood [36] because patients with varying BMI levels have not been studied in depth. Obesity playing a pathogenetic role was investigated at a much higher level in patients with SLE than in healthy people. It was found that the overweight status/ obesity has a profound influence on serum vitamin D and inflammatory responses in patients with SLE.[19] Low serum levels of vitamin D were found to have an association with high body weight/BMI in patients with SLE,[21] though this study [21] did not provide findings by comparing the normal weight, overweight, and obese subjects. We did not study the obese subjects with SLE. However, the data from our

overweight subjects were properly compared with those from normal-weight subjects.

Obesity was found to be associated with vitamin D insufficiency in patients with SLE.[16] The lowered levels of vitamin D with increased levels of IL-6 but without the influence of BMI were found in patients with SLE.[20] This report is not in accordance with our present study. We noticed that a study by Guimarães et al.[20] did not report vitamin D and IL-6 levels across BMI levels. This could be a major reason why vitamin D concentrations did not vary among SLE patients in the quoted study.[20] To clarify this, we carried out the present study for SLE patients with NW BMI and OW BMI compared to healthy NW BMI and OW BMI controls.

Vitamin D is considered an immunomodulator that regulates adaptive and innate immune responses.[22,23] Vitamin D helps decrease pro-inflammatory adipokines, such as IL-6.[25] Decreased vitamin D levels in SLE patients are associated with elevated IL-6 and other inflammation mediators.[24,25] For example, a study by Partan et al.[12] showed the effectiveness of seluang fish oil in reducing the inflammatory response in patients with SLE by increasing serum vitamin D levels. The precise association between vitamin D and IL-6 in SLE patients requires further investigation.[25]

It would be worthwhile to conduct studies with a larger dataset of patients with SLE, both women and men, with follow-up. Since we collected data on IL-6, vitamin D, and other variables only once, this is likely insufficient to assess variation. Furthermore, changes in these variables during follow-up are necessary to assess disease activity and appropriate medication dosages. It would be necessary to evaluate age, gender, and BMI in conjunction with serum CRP levels and other cytokines, including TNF-α, as well as anti-inflammatory cytokines/biomarkers, to better understand the relationship of vitamin D with inflammatory and anti-inflammatory responses in patients with SLE.

Conclusion

The results of this study highlight the importance of measuring serum IL-6 and vitamin D levels in conjunction with BMI assessment in SLE patients. The study found an inverse relationship between vitamin D and IL-6 and demonstrated that vitamin D deficiency is the most common factor in patients with systemic lupus erythematosus. Since vitamin D is an important modifiable factor in systemic lupus erythematosus, and its deficiency is associated with disease activity and the risk of complications, correction of vitamin D deficiency can complement standard therapy and improve the prognosis of systemic lupus erythematosus.

Ethical Considerations

The study was conducted in accordance with ethical principles of the WMA Declaration of Helsinki (1964, ed. 2013) and approved by the Ethical Committee of the Faculty of Medicine, Umm Al-Qura University (UQU); Approval Number:"HAPO-02-K-012-2022-01-1069." Written informed consent was obtained from all participants.

Sources of Funding

This research received no external funding.

Competing Interests

The authors declare that they have no conflicts of interest.

Acknowledgments

The authors thank the medical consultants and laboratory experts for their invaluable support.

References

1. Amital H, Szekanecz Z, Szücs G, Dankó K, Nagy E, Csépány T, Kiss E, Rovensky J, Tuchynova A, Kozakova D, Doria A, Corocher N, Agmon-Levin N, Barak V, Orbach H, Zandman-Goddard G, Shoenfeld Y. Serum concentrations of 25-OH vitamin D in patients with systemic lupus erythematosus (SLE) are inversely related to disease activity: is it time to routinely supplement patients with SLE with vitamin D? Ann Rheum Dis. 2010 Jun;69(6):1155-7. doi: 10.1136/ard.2009.120329. Epub 2010 May 3. PMID: 20439290.
2. Izmirly PM, Parton H, Wang L, McCune WJ, Lim SS, Drenkard C, Ferucci ED, Dall'Era M, Gordon C, Helmick CG, Somers EC. Prevalence of Systemic Lupus Erythematosus in the United States: Estimates From a Meta-Analysis of the Centers for Disease Control and Prevention National Lupus Registries. Arthritis Rheumatol. 2021 Jun;73(6):991-996. doi: 10.1002/art.41632. Epub 2021 Apr 23. PMID: 33474834; PMCID: PMC8169527.
3. Borba VZ, Vieira JG, Kasamatsu T, Radominski SC, Sato EI, Lazaretti-Castro M. Vitamin D deficiency in patients with active systemic lupus erythematosus. Osteoporos Int. 2009 Mar;20(3):427-33. doi: 10.1007/s00198-008-0676-1. Epub 2008 Jul 4. PMID: 18600287.
4. Xu YD, Cheng M, Shang PP, Yang YQ. Role of IL-6 in dendritic cell functions. J Leukoc Biol. 2022 Mar;111(3):695-709. doi: 10.1002/JLB.3MR0621-616RR. Epub 2021 Aug 18. PMID: 34405445.
5. Zhang Z, Zhu S, Li Q, Wei S, Yin L, Zhu J, Yang S, Zhang W, Lai K. Investigating the role of IL-6 in the pathogenesis of systemic lupus erythematosus: Insights from bone marrow mesenchymal stem cells. Lupus. 2025 Mar;34(3):225-233. doi: 10.1177/09612033251317783. Epub 2025 Jan 30. PMID: 39882783.
6. Ding J, Su S, You T, Xia T, Lin X, Chen Z, Zhang L. Serum interleukin-6 level is correlated with the disease activity of systemic lupus erythematosus: a meta-analysis. Clinics (Sao Paulo). 2020 Oct 19;75:e1801. doi: 10.6061/clinics/2020/e1801. PMID: 33084768; PMCID: PMC7536892.
7. Pattanaik SS, Panda AK, Pati A, Padhi S, Tripathy R, Tripathy SR, Parida MK, Das BK. Role of interleukin-6 and interferon-α in systemic lupus erythematosus: A case-control

study and meta-analysis. Lupus. 2022 Aug;31(9):1094-1103. doi: 10.1177/09612033221102575. Epub 2022 May 17. PMID: 35581679.
8. Winikajtis-Burzyńska A, Brzosko M, Przepiera-Będzak H. Increased Serum Interleukin 10 Levels Are Associated with Increased Disease Activity and Increased Risk of Anti-SS-A/Ro Antibody Positivity in Patients with Systemic Lupus Erythematosus. Biomolecules. 2023 Jun 11;13(6):974. doi: 10.3390/biom13060974. PMID: 37371554; PMCID: PMC10296207.
9. Behzadi P, Sameer AS, Nissar S, Banday MZ, Gajdács M, García-Perdomo HA, Akhtar K, Pinheiro M, Magnusson P, Sarshar M, Ambrosi C. The Interleukin-1 (IL-1) Superfamily Cytokines and Their Single Nucleotide Polymorphisms (SNPs). J Immunol Res. 2022 Mar 26;2022:2054431. doi: 10.1155/2022/2054431. PMID: 35378905; PMCID: PMC8976653.
10. Metwally YF, Elsaid AM, Elsadda RR, Refaat S, Zahran RF. Impact of IL-6 and IL-1β Gene Variants on Non-small-cell Lung Cancer Risk in Egyptian Patients. Biochem Genet. 2024 Oct;62(5):3367-3388. doi: 10.1007/s10528-023-10596-2. Epub 2023 Dec 16. PMID: 38103126; PMCID: PMC11427554.
11. Mercader-Salvans J, García-González M, Gómez-Bernal F, Quevedo-Abeledo JC, de Vera-González A, González-Delgado A, López-Mejías R, Martín-González C, González-Gay MÁ, Ferraz-Amaro I. Relationship between Disease Characteristics and Circulating Interleukin 6 in a Well-Characterized Cohort of Patients with Systemic Lupus Erythematosus. Int J Mol Sci. 2023 Sep 12;24(18):14006. doi: 10.3390/ijms241814006. PMID: 37762312; PMCID: PMC10531425.
12. Partan RU, Hidayat R, Saputra N, Rahmayani F, Prapto H, Yudha TW. Seluang Fish (*Rasbora Spp*.) Oil Decreases Inflammatory Cytokines Via Increasing Vitamin D Level in Systemic Lupus Erythematosus. Open Access Maced J Med Sci. 2019 May 5;7(9):1418-1421. doi: 10.3889/oamjms.2019.308. PMID: 31198446; PMCID: PMC6542399.
13. Fragoso TS, Dantas AT, Marques CD, Rocha Junior LF, Melo JH, Costa AJ, Duarte AL. 25-Hydroxyivitamin D3 levels in patients with systemic lupus erythematosus and its association with clinical parameters and laboratory tests. Rev Bras Reumatol. 2012 Jan-Feb;52(1):60-5. English, Portuguese. PMID: 22286646.
14. Hamza RT, Awwad KS, Ali MK, Hamed AI. Reduced serum concentrations of 25-hydroxy vitamin D in Egyptian patients with systemic lupus erythematosus: relation to disease activity. Med Sci Monit. 2011 Dec;17(12):CR711-8. doi: 10.12659/msm.882131. PMID: 22129903; PMCID: PMC3628141.
15. Isenberg DA. BILAG, SLEDAI, SIS, ECLAM, WAM, SLAM .... thank you MAM. Lupus. 2007;16(11):849-51. doi: 10.1177/0961203307085124. PMID: 17971356.
16. Muñoz-Ortego J, Torrente-Segarra V, Prieto-Alhambra D, Salman-Monte TC, Carbonell-Abello J. Prevalence and predictors of vitamin D deficiency in non-supplemented women with systemic lupus erythematosus in the Mediterranean region: a cohort study. Scand J Rheumatol. 2012;41(6):472-5. doi: 10.3109/03009742.2012.697189.
17. Aldakheel FM, Alshanqiti MA, Alduraywish SA, Alshammary AF, Dabwan KH, Syed R. Clinical Assessment of Cytokine Profiles and Haematological Parameters in Patients with Systemic Lupus Erythematosus: A Cross-Sectional Study from Saudi Arabia. Front Biosci (Landmark Ed). 2023 Dec 28;28(12):358. doi: 10.31083/j.fbl2812358. PMID: 38179775.
18. Markina MV, Milovanova LY, Lysenko LV, Milovanova SY, Volkov AV, Beketov VD, Lebedeva MV, Nezhdanov KS, Moiseev SV. [Anemia of chronic diseases in the early stages of chronic kidney disease as a risk factor for cardiovascular complications in patients with glomerulonephritis]. Ter Arkh. 2024 Jul 7;96(6):606-613. Russian. doi: 10.26442/00403660.2024.06.202729. PMID: 39106502.
19. Kono M, Nagafuchi Y, Shoda H, Fujio K. The Impact of Obesity and a High-Fat Diet on Clinical and Immunological Features in Systemic Lupus Erythematosus. Nutrients. 2021 Feb 4;13(2):504. doi: 10.3390/nu13020504. PMID: 33557015; PMCID: PMC7913625.
20. Guimarães PM, Scavuzzi BM, Stadtlober NP, Franchi Santos LFDR, Lozovoy MAB, Iriyoda TMV, Costa NT, Reiche EMV, Maes M, Dichi I, Simão ANC. Cytokines in systemic lupus erythematosus: far beyond Th1/Th2 dualism lupus: cytokine profiles. Immunol Cell Biol. 2017 Oct;95(9):824-831. doi: 10.1038/icb.2017.53. Epub 2017 Jun 26. PMID: 28649995.
21. Meza-Meza MR, Vizmanos-Lamotte B, Muñoz-Valle JF, Parra-Rojas I, Garaulet M, Campos-López B, Montoya-Buelna M, Cerpa-Cruz S, Martínez-López E, Oregon-Romero E, De la Cruz-Mosso U. Relationship of Excess Weight with Clinical Activity and Dietary Intake Deficiencies in Systemic Lupus Erythematosus Patients. Nutrients. 2019 Nov 6;11(11):2683. doi: 10.3390/nu11112683. PMID: 31698711; PMCID: PMC6893805.
22. Adams JS, Hewison M. Unexpected actions of vitamin D: new perspectives on the regulation of innate and adaptive immunity. Nat Clin Pract Endocrinol Metab. 2008 Feb;4(2):80-90. doi: 10.1038/ncpendmet0716. PMID: 18212810; PMCID: PMC2678245.
23. Szymczak I, Pawliczak R. The Active Metabolite of Vitamin D3 as a Potential Immunomodulator. Scand J Immunol. 2016 Feb;83(2):83-91. doi: 10.1111/sji.12403. PMID: 26678915.
24. Gröndal G, Gunnarsson I, Rönnelid J, Rogberg S, Klareskog L, Lundberg I. Cytokine production, serum levels and disease activity in systemic lupus erythematosus. Clin Exp Rheumatol. 2000 Sep-Oct;18(5):565-70. PMID: 11072595.
25. Shevchuk S, Marynych L, Malovana T, Denyshchych L. Vitamin D level in patients with systemic lupus erythematosus: its relationship to disease course and bone mineral density. Lupus Sci Med. 2023 Aug;10(2):e000968. doi: 10.1136/lupus-2023-000968. PMID: 37558268; PMCID: PMC10414063.
26. Zahir H, Javaid A, Rehman R, Hussain Z. Statistical concepts in biology and health sciences. J Ayub Med Coll Abbottabad. 2014 Jan-Mar;26(1):95-7. PMID: 25358229.
27. Jin S, Yu C, Yu B. Changes of serum IL-6, IL-10 and TNF-α levels in patients with systemic lupus erythematosus and their clinical value. Am J Transl Res. 2021 Apr 15;13(4):2867-2874. PMID: 34017450; PMCID: PMC8129414.

28. Singh RP, Hahn BH, Bischoff DS. Interferon Genes Are Influenced by 17β-Estradiol in SLE. Front Immunol. 2021 Oct 18;12:725325. doi: 10.3389/fimmu.2021.725325. PMID: 34733276; PMCID: PMC8558410.
29. Peliçari KO, Postal M, Sinicato NA, Londe AC, Fernandes PT, Marini R, Costallat LTL, Appenzeller S. Longitudinal comparison of IL-6, IL-10, and IL-12 cytokine profiles in adult and childhood-onset systemic lupus erythematosus. J Transl Autoimmun. 2022 May 26;5:100158. doi: 10.1016/j.jtauto.2022.100158. PMID: 36683864; PMCID: PMC9846463.
30. Mak A, Tang CS, Ho RC. Serum tumour necrosis factor-alpha is associated with poor health-related quality of life and depressive symptoms in patients with systemic lupus erythematosus. Lupus. 2013 Mar;22(3):254-61. doi: 10.1177/0961203312471872. Epub 2013 Jan 18. PMID: 23334278.
31. Raymond WD, Eilertsen GØ, Nossent J. Principal component analysis reveals disconnect between regulatory cytokines and disease activity in Systemic Lupus Erythematosus. Cytokine. 2019 Feb;114:67-73. doi: 10.1016/j.cyto.2018.10.013. Epub 2018 Dec 12. PMID: 30551949.
32. Tanaka A, Ito T, Kibata K, Inagaki-Katashiba N, Amuro H, Nishizawa T, Son Y, Ozaki Y, Nomura S. Serum high-mobility group box 1 is correlated with interferon-α and may predict disease activity in patients with systemic lupus erythematosus. Lupus. 2019 Aug;28(9):1120-1127. doi: 10.1177/0961203319862865. Epub 2019 Jul 12. PMID: 31299881.
33. Giunta S, Wei Y, Xu K, Xia S. Cold-inflammaging: When a state of homeostatic-imbalance associated with aging precedes the low-grade pro-inflammatory-state (inflammaging): Meaning, evolution, inflammaging phenotypes. Clin Exp Pharmacol Physiol. 2022 Sep;49(9):925-934. doi: 10.1111/1440-1681.13686. Epub 2022 Jul 4. PMID: 35684970.
34. Oo ATZ, Oo WT, Tun KL, Myint AK, Thu Zar Aye M, Khin NE, Sone KP, Sonn P. Serum Vitamin D Level and Disease Activity in Patients With Systemic Lupus Erythematosus. Cureus. 2025 Oct 5;17(10):e93853. doi: 10.7759/cureus.93853. PMID: 41054434; PMCID: PMC12496543.
35. Kamen DL, Aranow C. The link between vitamin D deficiency and systemic lupus erythematosus. Curr Rheumatol Rep. 2008 Aug;10(4):273-80. doi: 10.1007/s11926-008-0044-3. PMID: 18662506.
36. Li H, Du X, Lv X, Hao Z, He L. Correlation between body mass index and disease activity in patients with systemic lupus erythematosus from China. Adv Rheumatol. 2025 Nov 29;66(1):3. doi: 10.1186/s42358-025-00502-2. PMID: 41318544.

***Corresponding author**: Prof. Dr. Zahir Hussain, PhD. Department of Physiology, Faculty of Medicine, Umm Al-Qura University, Makkah 21955, Saudi Arabia. E-mail: zahirhussa@gmail.com*