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Role of some Immunological and non-Immunological Parameters in Prognosis and diagnosis of Systemic lupus erythematosus in Iraqi women patients

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ABSTRACT

Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by autoantibody's presence in the circulation and involvement of many systems. The current study aims to study the role of some immunological and non-immunological parameters in SLE development and to illustrate the correlations between these parameters. The current study included 50 blood samples collected from SLE patients and apparently healthy control. The methods of work included Complete Blood Count (CBC) analysis to assess blood components, you mean to analyse Hb, WBC, ESR, ELISA technique to measure serum levels of TLR-7, IL-17, and TNF-γ, antinuclear antibody test (ANA) and double-strand DNA antibody (anti ds DNA). The study results showed a significant increase in serum levels of each WBC ($p< 0.005$), ESR ($p< 0.001$), IL17($p< 0.004$), TLR7($p< 0.005$), IFN-γ ($p< 0.001$), ANA ($p< 0.001$), and anti dsDNA ($p< 0.001$) in SLE patients compared to apparently healthy control but the Hb is decreasing level was low in the SLE patients compared with control. In conclusion, the low hemoglobin, WBC, and ESR are non-specific parameters associated with SLE pathogenesis. ANA, Anti-ds-DNA as excellent biomarkers for the diagnosis of SLE and serum level of TLR-7, TNF-γ, and IL-17 were evaluated in SLE patients compared to healthy people and they may be suggested as a prognostic tool in SLE patients.

Keywords: ANA, anti-dsDNA, autoimmune disease, IFN-γ, IL17, Systemic lupus erythematosus, TLR7.

الخلاصة

الذئبة الحمامية الجهازية هي أحد أمراض المناعة الذاتية تتميز بوجود الأجسام المضادة الذاتية في الدورة الدموية ومشاركة العديد من الأنظمة. تهدف الدراسة الحالية إلى دراسة دور بعض المتغيرات المناعية وغير المناعية في تطور مرض الذئبة الحمراء وتوضيح الارتباط بين المتغيرات. تضمنت الدراسة الحالية ٥٠ عينة دم تم جمعها من مرضى الذئبة الحمامية و الأشخاص الأصحاء. تضمنت طرق العمل تحليل CBC لتقييم مكونات الدم، Hb، WBC، و ESR، وتقنية ELISA لقياس مستويات المصل من TLR-7، و IL-17، و TNF-، واختبار الأجسام المضادة للنواة (ANA) والجسم المضاد DNA مزدوج الشريطة (anti ds DNA). أظهرت نتائج الدراسة زيادة معنوية في مستويات المصل لكل WBC ($p <0.005$)، ESR ($p <0.001$)، IL17 ($p <0.004$)، TLR7 ($p <0.005$)، IFN-γ ($p <0.001$)، <0.001, ANA ds dna($p< 0.001$) في مرضى الذئبة الحمراء مقارنةً بالاصحاء ولكن وجد ان الهيموغلوبين يتناقص في مرضى الذئبة الحمراء مقارنة بالأشخاص الأصحاء في الختام، تم تقدير فقر الدم، WBC، و ESR هي معلمات غير محددة مرتبطة ببدء مرض الذئبة الحمراء. تم تقييم ANA و Anti-ds-DNA كمؤشرات حيوية ممتازة لتشخيص مرض الذئبة الحمراء ومستوى المصل من TLR-7 و TNF-γ و IL-17 تم تقيمه في مرضى SLE مقارنة بالأشخاص الأصحاء وتم اقتراحهم كأداة تنبؤ في مرضى الذئبة الحمراء.

INTRODUCTION

Systemic lupus erythematosus (SLE) is an autoimmune characterized by the involvement of many systems in the body by inflammation due to auto-antibodies. The pathway of immunopathology involved in SLE development is not understood despite many theories are suggested by the researchers. For

this reason, SLE diagnosis is difficult to do even after the advanced methodology involved in the diagnosis of this autoimmune disease [1]. The current study was designed to evaluate some immune markers (Toll-like receptor-7(TLR-7), Interleukin-17(IL-17), and Interferon-γ (TNF-γ)) and their Correlation to SLE disease Innate and adaptive immunity are both involved in the pathogenesis of the disease. Toll-like receptor (TLR) is one of the mechanisms of innate immunity of SLE. TLR is activated by nucleic acids (RNA and DNA) released from dead cells, especially TLRs that are found on the cell's membrane. The TLR activation by the nucleic acids leads to the activation of pro-inflammatory cytokines activating transcriptional factor (like nuclear factor kappa beta, NF-Kb) leading to cytokine production and release. The activation of endosomal TLRs (TLR-7 and TLR-9) are due to binding the TLRs with de-methylated DNA and RNA leading to DNA and RNA-specific autoantibodies in SLE patients [2][3]. Cytokines are soluble factors which are mostly generated by immune cells and in turn play crucial roles in the differentiation, maturation, and activation of various immune cells. These cytokines may exert either proinflammatory or anti-inflammatory effects. The abnormal release or functions of diverse cytokines may reflect the imbalance among different immune cell subsets, such as Th1/Th2 and Th17/Treg, thus contributing greatly to SLE pathogenesis [4].

Interleukin-17 is another cytokine that has a role in the pathogenesis of SLE as this type of cytokine works to protect the host as a pro-inflammatory cytokine. However, this interleukin is associated with undesired consequences as it has a role in the progression of autoimmune diseases and cancer [5]. The targeting of IL-17 can be a treatment strategy to treat SLE in clinical trials [6]. The inflammatory cytokines release is due to the stimulation of some TLRs (TLR7) for a long time which leads to the production of IL-17 from T cells [7]. The role of some immunological and non-immunological parameters like Hb, ERS, WBC, TLR7, IL17, IFN-gamma, ANA, and dsDNA in SLE development and diagnosis is the aim of this study.

MATERIALS AND METHODS

Subject and Blood Samples Collection

This study included 50 SLE female patients and 50 healthy females, their ages ranged between 16 to 50 years, which collected from Medical City (Consultant of Arthritis, Consultant of Dermatology, Lobby of Hematology and Arthritis)/ Baghdad Teaching Hospital. The blood samples were collected during the period from August 26 to October 20, 2022. The SLE patients were diagnosed by the consultant and the immunology unit in the above-mentioned hospital according to the protocols followed by them. The data related to age, duration of illness treatment, and history of other diseases were recorded in addition to the fact that the diagnosis was made by clinical examination (the consultant physicians). The study was performed according to the Helsinki Declaration of ethical principles for medical research involving human subjects.

Hematological and Serological Analysis

The collected blood samples of patients and controls were distributed into two portions, 2 ml in an ethylene diamine tetra-acetic acid (EDTA) tube which was used to measure total Hb, erythrocyte sedimentation rate (ESR) using the Westergren method, and cell blood count (CBC) using Automated CBC analyzer. Three milliners of the collected blood samples were placed in a gel tube and the serum was separated using a centrifuge (3000 rpm for 10 min), and then the serum was distributed into 0.5 ml Eppendorf tubes that were immediately frozen at -20º C until the evaluation of other understudying parameters which included antinuclear antibody test (ANA) and double-strand DNA antibody (dsDNA). The diagnostic criteria involved the assessment of total erythrocyte sedimentation rate (ESR), WBC count, antinuclear antibody test (ANA), and dsDNA. As well as, the primary diagnosis was made by the specialist doctor in the hospital through the patient's initial symptoms and signs in addition to the above-mentioned laboratory analyses.

Serum Cytokines Determination

The cytokines were measured using Enzyme-linked Immunosorbent Assay kits. Interferon-gamma (Sandwich Human IFN-γ ELISA Kit),

IL-17A (PicoKine™ ELISA), and TLR7 the three cytokines kites were adapted from MyBioSource, Inc California, San Diego (USA). ELISA was performed according to the manufacturer's instructions.

Statistical analysis

Statistical Package for Social Science (SPSS) was used to elucidate the differences in parameters using IBM SPSS Statistics 26.0. (Armonk, NY: IBM Corp). Normality test was used to estimate the normal and non-normal distribution of data, Analysis of Variance (ANOVA) (parametric test for normally distributed data), Mann-Whitney (non-parametric test for abnormally distributed data), and chi-square test was used to compare between studied groups. To evaluate the discrimination value of the study parameters for SLE and normal subjects, we evaluated the area under the curve (AUC) using the receiver operating curve (ROC). Data analyses were performed by using SPSS 17.0.

RESULTS AND DISCUSSION

Some haematological parameters in SLE patients and controls were measured like haemoglobin and white blood cell account (Table 1). Haemoglobin was significantly higher in the control group's serum (13.65 ± 0.12 gm/dl) than in the SLE patients' serum (11.8 ± 0.29 gm/dl, p< 0.001). White blood cell account was significantly higher in the SLE patients (7.8 ± 0.61 $X10^3$/µl) than in the control group (5.93 ± 0.22 $X10^3$/µl, p=0.005). Erythrocytes sedimentation rate (ESR) was also measured in both groups (Table 2). ESR is significantly high in SLE patients (29.42 ± 2.5 mm/hr) than in the control group (14.48 ± 0.79 mm/hr, p<0.001).

Table 1. Some Hematological Parameters in SLE patients and Controls.

Hematological Parameters	SLE Patients (No. = 50)	Control (No. = 50)	*P*-value
Hb Mean ± S.E. (gm/dl)	11.8 ± 0.29	13.65 ± 0.12	< 0.001
WBC Mean ± S.E.($X10^3$/µl)	7.8 ± 0.61	5.93 ± 0.22	0.005

Mann-Whitney test was used to compare between non parametric data (Non-immunogenic Parameters) of studied groups

Table 2. Erythrocytes sedimentation rate in SLE patients and control group.

ESR	Patients (No. = 50)	Control (No. = 50)
Mean ± S.E. (mm/h	29.42 ± 2.5	14.48 ± 0.79
P-value	< 0.001	

Mann-Whitney test was used to compare between non parametric data of studied groups.

The receiver operating characteristic (ROC) curve is used to evaluate the prediction accuracy of a classifier model. The WBC (with AUC 0.667, cut-off value ≥7.835 10^3/µL, had 44% sensitivity and 90% specificity) and ESR (with AUC 0.799, cut-off value ≥ 24 mm/hr, had 60% sensitivity and 98% specificity) of SLE patients are more discriminative than Hb (with AUC 0.204, cut off value ≥16.60 g/dL, had 0.2% sensitivity and 100% specificity) in distinguishing between SLE patients and control group as shown in Figure 1 and Table 5.

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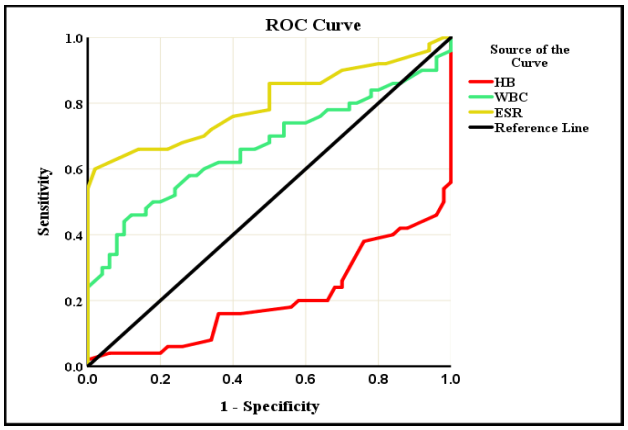

Figure 1. Receiver operating characteristic (ROC) of three parameters of SLE patients.

The three parameters are hemoglobin (Hb), white blood cells (WBC), and erythrocytes sedimentation rate (ESR). SLE: systemic lupus erythematosus. Hb (with AUC 0.204, cut-off value ≥16.60 g/dL, had 0.2% sensitivity and 100% specificity) was less discriminative power than the reference line. WBC (with AUC 0.667, cut-off value ≥7.835 10^3/µL, had 44% sensitivity and 90% specificity) and ESR (with AUC 0.799, cut-off value ≥ 24 mm/hr, had 60%

sensitivity and 98% specificity) are more associated with SLE development.

Some immunological parameters, IFN-γ, IL-17, and TLR-7 were measured, and study the association of these parameters with SLE (table 3). The IFN-γ serum level was significantly high (271.11 ± 5.1 pg/ml) in SLE patients' serum than in controls serum (147.67 ± 9.9 pg/ml. p< 0.001). IL-17 serum level was also significantly high in the SLE patients' serum (406.17 ± 16.01 pg/ml) than in the serum of controls (249.77 ± 29.1 pg/ml, p=0.004). TLR-7 serum level was significantly higher in the SLE patients' serum (28.46 ± 0.71 ng/ml) than in the serum of controls (21.24 ± 1.6 ng/ml, p=0.005).

Table 3. Some immunological parameters in the SLE patients' serum and control group serum.

Immunological Parameters	Patients (No. = 50)	Control (No. = 50)	*P*-value
IFN-γ Mean ± S.E. (pg/ml)	271.11 ± 5.1	147.67 ± 9.9	< 0.001
IL-17 Mean ± S.E. (pg/ml)	406.17 ± 16.01	249.77 ± 29.1	0.004
TLR-7 Mean ± S.E. (ng/ml)	28.46 ± 0.71	21.24 ± 1.6	0.005

Mann-Whitney test was used to compare between non parametric data of studied groups. S.E: Standard Error

All three immunological parameters (IFNγ, IL-17, and TLR-7) are associated with SLE development. The level of serum IL-17 of SLE patients (with AUC 0.951, cut-off value ≥ 282.642 pg/ml, had 100% sensitivity and 92% specificity) was more sensitive and specific parameter associated with SLE development followed by serum IFNγ (with AUC 0.909, cut off value ≥ 216.257 pg/ml, had 98% sensitivity and 85% specificity) and TLR-7 (with AUC 0.882, cut off value ≥23.778 ng/ml, had 92% sensitivity and 82% specificity) respectively as shown in Figure 2 and Table 5 when measured by ROC.

The interferon-gamma (IFNγ), interleukin-17 (IL-17), and Tool like receptor 7 (TLR-7) are associated with systemic lupus erythematosus (SLE) development. IL-17 (with AUC 0.951, cut-off value ≥ 282.642 pg/ml, had 100% sensitivity and 92% specificity) was a more sensitive and specific parameter associated with SLE development followed by IFNγ (with AUC 0.909, cut-off value ≥ 216.257 pg/ml, had 98% sensitivity and 85% specificity) and TLR-7(with AUC 0.882, cut off value ≥23.778 ng/ml, had 92% sensitivity and 82% specificity) respectively.

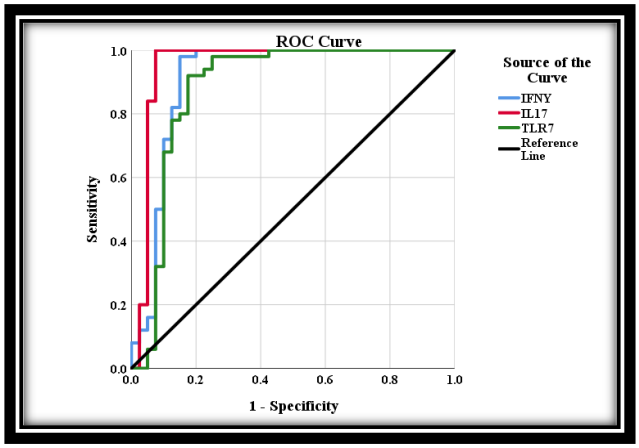

Figure 2. Receiver operating characteristic (ROC) of immunological parameters of SLE patients.

Antinuclear antibody test (ANA) and Double strand DNA antibody (dsDNA) in SLE patients and control were estimated (Table 4).

Table 4. Antinuclear antibody test and Double strand DNA antibody in SLE patients and control

Parameters	Patients (No. = 50)	Control (No. = 40)	*P*-value
ANA Mean ± S.E. (U/ml)	3.86 ± 0.26	0.988 ± 0.029	< 0.001
dsDNA Mean ± S.E. (U/ml)	3.54 ± 0.21	0.962 ± 0.039	< 0.001

Mann-Whitney test was used to compare between non parametric data of studied groups.

The serum ANA of SLE patients was highly significantly increased (3.86 ± 0.26 U/ml) as compared with serum ANA in the control group (0.988 ± 0.029 U/ml, < 0.001). The serum dsDNA of SLE patients was also highly significantly increased (3.54 ± 0.21 U/ml) as compared with serum dsDNA in the control group (0.962 ± 0.039 U/ml, < 0.001). The increased antinuclear antibodies (with AUC 1.00, cut-off value ≥1.782 U/ml, had 100% sensitivity and 100% specificity) and double-strand DNA antibodies (with AUC ≥ 1.706 U/ml, cut-off value 1.00, had 100% sensitivity and 100% specificity) are the highest discriminative parameters associated with systemic lupus erythematosus development

(Figure 3 and Table 5). Pearson Correlation of the Blood parameters showed that the Hb of the SLE patients was negatively correlated with ESR (p=0.0016), IFN-γ (p=0.0083), IL-17(p=0.002), ANA (p=0.002), and dsDNA (p=0.0058) but not with WBC and TLR-7 in the SLE patients' blood.

The WBC of the SLE patients was positively correlated with IFN-γ (p=0.004), but no relation between WBC and other parameters (ESR, IL-17, TLR-7, ANA, dsDNA). However, the ESR was positively correlated with IFN-γ (p=0.0052), IL-17 (p=0.008), TLR-7 (p=0.006), ANA (p=0.0017), and dsDNA (p=0.0072) in the SLE patients' blood Table 6 shows these results

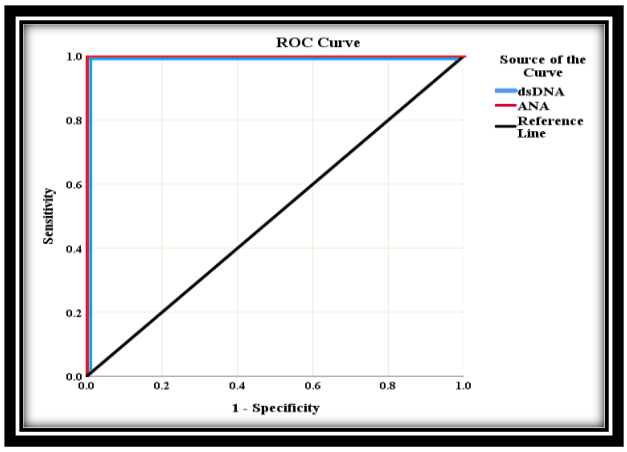

Figure 3. Receiver operating characteristic (ROC) of antinuclear antibodies and double-strand DNA antibodies in serum of systemic lupus erythematosus patients.

Table 5. Pearson Correlation of the Blood parameters.

Test Result Variable(s)	AUC	Sensitivity	Specificity	Cut off Value	*P* value
Weight	0.687	66 %	70 %	≥ 64.50 Kg	0.001
HB	0.204	0.2 %	100 %	≥ 16.60 g/dL	< 0.001
WBC	0.667	44 %	90 %	≥ 7.835 10^{-3}/uL	0.004
ESR	0.799	60 %	98 %	≥ 24.00 ml/hr.	< 0.001
IFN-γ	0.909	98 %	85 %	≥ 216.257 pg/ml	< 0.001
IL-17	0.951	100 %	92 %	≥ 282.642 pg/ml	< 0.001
TLR-7	0.882	92 %	82 %	≥ 23.778 ng/ml	< 0.001

Table 6. Pearson Correlation of the Blood parameters.

Parameters	r- value	*P*-value
HB vs. WBC	0.031	0.77 NS
HB vs. ESR	- 0.438	0.0016**
HB vs.	- 0.403	0.0083**
HB vs. IL-17	- 0.321	0.002**
HB vs. TLR-7	- 0.204	0.054 NS
HB vs. ANA	- 0.476	0.002**
HB vs. dsDNA	- 0.411	0.0058**
WBC vs. ESR	- 0.097	0.36 NS
WBC vs. IFN-γ	0.298	0.004
WBC vs. IL-17	0.065	0.54 NS
WBC vs. TLR-7	0.192	0.07 NS
WBC vs. ANA	0.089	0.4 NS
WBC vs. dsDNA	0.122	0.25 NS
ESR vs. IFN-γ	0.413	0.0052**
ESR vs. IL-17	0.279	0.008**
ESR vs. TLR-7	0.286	0.006**
ESR vs. ANA	0.386	0.0017**
ESR vs. dsDNA	0.406	0.0072**

chi-square test was used to compare between studied groups, Ns: no significant

Pearson Correlation of the interleukins parameters and toll-like receptor showed that IFN-γ of SLE patients was positively correlated with IL-17 (p=< 0.001), TLR-7 (p=< 0.001), ANA (p=< 0.001), and dsDNA (p=< 0.001). The IL-17 of SLE patients was positively correlated with TLR-7 (p=0.007), ANA (p=0.0014), and dsDNA (p=0.001). While TLR-7 of SLE patients was also positively correlated with ANA (p=0,003) and dsDNA (p=0,002). Finally, dsDNA was positively correlated with ANA(p=0.001) in SLE patients' serum (Table 7)

Table 7. Pearson Correlation of the Interleukins parameters.

Parameters	r- value	*P*-value
IFN-γ vs. IL-17	0.631	< 0.001**
IFN-γ vs. TLR-7	0.567	< 0.001**
IFN-γ vs. ANA	0.618	< 0.001**
IFN-γ vs. dsDNA	0.634	< 0.001**
IL-17 vs. TLR-7	0.284	0.007**
IL-17 vs. ANA	0.391	0.0014**
IL-17 vs. dsDNA	0.351	0.001**
TLR-7 vs. ANA	0.315	0.003

TLR-7 vs. dsDNA	0.321	0.002
dsDNA vs. ANA	0.814	0.001**

chi-square test was used to compare between studied groups

Discussion

SLE is characterized by many hematological disorders. Some important blood issue found in this study in SLE patients which was low hemoglobin as compared with the control group. Anemia is a common blood disorder in SLE patients, it may be found in 50% of the patients with SLE which means that the count of red blood cells is few due to autoimmune antibodies. The WBC was also found to be low in SLE patients (leukopenia) but it is more common than anemia as it calculates to be about 95% of SLE patients. leukopenia is developing due to the action of auto-antibodies that destroy WBC [8]. Another hematological parameter is ESR which is a non-specific test used to investigate inflammation. Because the ESR is non-specific, it can be lowered by the administration of some anti-inflammatory drugs like cortisones and can cause misdiagnosis in SLE patients. ESR was significantly high in SLE patients in this study who are primarily diagnosed by physicians.

More specific parameters were also used in this study for discrimination between SLE patients and apparently healthy control. Cytokines like IFN-γ and IL-17 as well as TLR-7 appear to be associated significantly with SLE development. Studies have shown that the level of IFN-γ in the serum of patients with SLE is higher than that in healthy individuals [9], and there is a high level of IFN-γ in SLE patients earlier than detection of auto-antibodies. Another study that corresponded to this result showed that the level of TNF-γ was significantly elevated in newly diagnosed SLE patients' comparison to healthy controls groups [10]. The B lymphocyte stimulator/B cell-activating factor/TNF ligand superfamily-13B is activated by high serum levels of IFN- γ in SLE patients, which is associated with nephritis and arthritis [11]. IFN-γ secreted by Th1 promotes the immune-pathogenesis of SLE in turn IFN-γ has an important role in Th1 maturation. Moreover, IFN-γ inhibits CD4+ T-cell transformation to Th2[12]. Another important cytokine other than IFN-γ measured in this study is IL-17 which was found to be increased in SLE patients [13].

IL-17 has reportedly been linked to the emergence of inflammation and is crucial for the development of autoimmune disorders [14].IL-17 produced from Th17 is involved in the immune-histopathological changes of SLE [15, 16]. Th2 shift to Th1 and Th17 in SLE patients as a consequence of IFN-γ production and this shifting is an important event that mediates SLE pathogenesis [9]. Studies have found that positive correlation between serum IL-17 levels was observed in SLE patients, and suggest that they have key roles in modulating the course of this disease [14, 17]. The result of the current study is in agreement with previous studies of Wong *et al.,* (2008) and Zhao *et al.,* (2010) who have reported elevation in IL-17 serum concentrations, as well as increased number of Th-17 cells in adult-onset SLE patients [18,19]. Toll-like receptor 7 appears to play a key role in SLE pathogenesis [20]. This study discovered that TLR7 expression was higher in SLE patients than in healthy controls because TLR7 generates type I interferon and encourages the activation of B lymphocytes that are capable of producing autoantibodies [21]. This result was agreeing with the previous study that showed TLR7 serum levels were greater in patients than in the control group [22]. Both DNA and RNA bind endogenously with TLR7 in the cell surface receptors of B cells and auto-antibodies production [20].

Despite the high level of serum, ANA was observed in SLE patients in another study, it's also found to be high in some conditions like inflammation and metabolic disorders [23] so it cannot be used this test alone for SLE diagnosis despite this study confirm that these antibodies were raised in serum of SLE patients significantly. It must take into consideration the clinical picture and symptoms of the disease and anti-dsDNA antibodies. On the bases of these facts, the ANA should be companied by anti-dsDNA antibodies in SLE-suspected individuals [24]. Both ANA and dsDNA were raised in this study of SLE patients and both are significantly associated with SLE and had 100% sensitivity and 100% specificity. Antinuclear antibody counts are higher in women and increase with

age [25]. Sex hormones, particularly estrogens have a marked influence in the pathogenesis of autoimmune disorders and predispose the female sex to the recurrence of these diseases [26]. While anti-dsDNA antibody, one canonical parameter to diagnose and classify SLE, is dependent as a marker for monitoring the disease prognosis, and its value increased in the presence of ANA positivity in the patients [27]. The tested parameters in this study are correlated with each other. The Hb of SLE patients is decreased accompanied by an increase in IFN-γ, ESR, IL-17, ANA, and sdDNA. While WBC is significantly raised in association with increased serum IFN-γ of SLE patients but there is no association between WBC and other parameters (ESR, IL-17, TLR-7, ANA and dsDNA). The increased ESR in patients' serum is accompanied by IFN-γ, IL-17, TLR-7, ANA and dsDNA. Most importantly TLR-7 is associated with ANA and dsDNA and ANA is associated with and dsDNA in SLE patients' serum. The overall results of the tested parameters can confirm the clinical symptoms in the diagnosis of the SLE autoimmune disease.

CONCLUSIONS

In conclusion, some SLE parameters are non-specific for SLE despite, they raised in the SLE patients like Hb, ESR, and WBC. Other parameters are relatively specific for SLE like IFN-γ, IL-17, and TLR-7 and are also raised in SLE patients. The third group of the SLE parameters is highly specific for SLE which are ANA and dsDNA. However, the overall clinical and these parameters are required for accurate diagnosis of SLE.

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Ethical Approaval

Ethical approval Ref.: BCSML/0822/0003B.

Informed Consent

All patients gave their written informed consents before inclusion.

Disclosure and Conflict of Interest: The authors declare that they have no conflicts of interest.

REFERNCES

[1] S. Molina Rios, R. Rojas Martinez GM Estévez Ramirez, YF Medina. Systemic Lupus Erythematosus and Antiphospholipid Syndrome After COVID-19 Vaccination. A Case Report. Mod Rheumatol Case Rep. 2022 Mar 04

[2] MG. Tayem, L. Shahin, J. Shook, MM Kesselman. A Review of Cardiac Manifestations in Patients With Systemic Lupus Erythematosus and Antiphospholipid Syndrome With a Focus on Endocarditis. Cureus. 2022 Jan;14(1):e21698.

[3] M. Scheen, A. Adedjouma, E. Esteve, D. Buob, N. Abisror, V. Planche, O. Fain, JJ Boffa S. De Seigneux, A. Mekinian, F. Haidar. Kidney disease in antiphospholipid antibody syndrome: Risk factors, pathophysiology and management. Autoimmun Rev. 2022 May;21(5):103072.

[4] D. L. Su, Z. M. Lu, M.N. Shen, X. Li, & L.Y. Sun, Roles of pro- and anti-inflammatory cytokines in the pathogenesis of SLE. *Journal of biomedicine & biotechnology*, *2012*, 347141. https://doi.org/10.1155/2012/347141.

[5] N. Amatya, AV. Garg, SL. Gaffen . IL-17 Signaling: The Yin and the Yang. Trends Immunol.May;38(5):310-322. 2017 doi: 10.1016/j.it.2017.01.006.

[6] T. Koga, K. Ichinose, A. Kawakami, GC Tsokos. Current Insights and Future Prospects for Targeting IL-17 to Treat Patients with Systemic Lupus Erythematosus. Front Immunol.Feb1;11:624971. 2021 doi: 10.3389/fimmu.2020.624971.

[7] J.C. Martin,. D. L. Baeten,. R. Josien,. Emerging role of IL-17 and Th17 cells in systemic lupus erythematosus, Clinical Immunology,Volume 154, Issue 1,2014,Pages 1-12, 2014

[8] JC. Santacruz, MJ. Mantilla,I. Rueda ,S Pulido,G. Rodriguez-Salas, J. Londono. A Practical Perspective of the Hematologic Manifestations of Systemic Lupus Erythematosus. Cureus. 2022 Mar 7;14(3):e22938. doi: 10.7759/cureus.22938

[9] A. Paradowska-Gorycka, A. Wajda, B Stypinska, E. Walczuk, E. Rzeszotarska, M Walczyk, et al. Variety of endosomal TLRs and interferons (IFN-a, IFN-b, IFNg) expression profiles in patients with SLE, SSc and MCTD. Clin Exp Immunol 2021 204:49–63. doi: 10.1111/cei.13566

[10] S. Mohammadi, S. Sedighi, A. Memarian, &Y. Yazdani. Overexpression of interferon-γ and

indoleamine 2, 3-dioxygenase in systemic lupus erythematosus: relationship with the disease activity. *LaboratoriumsMedizin*,41(1), 41-47. 2017

[11] V. Oke, I. Gunnarsson, J. Dorschner et al. High levels of circulating interferons type I, type II and type III associate with distinct clinical features of active systemic lupus erythematosus. Arthritis Res Ther 2019;21:107

[12] W. Liu, , S. Zhang, &J. Wang,. IFN-γ, should not be ignored in SLE. *Frontiers in Immunology*, *13*, 954706. 2022

[13] J. Yang,Y. Chu, X. Yang, D. Gao, L. Zhu X. Yang, et al. Th17 and natural treg cell population dynamics in systemic lupus erythematosus. Arthritis Rheum 60:1472–83. 2009 doi: 10.1002/art.24499

[14] D**.** Zhao, M. Guo, B. Liu et al . Frontline science. Tim-3-mediated dysfunctional engulfment of apoptotic cells in SLE. J Leukoc Biol, 102: 1313–22 23 . 2017

[15] T. Schmidt, H-J. Paust, CF. Krebs, J-E. Turner, A. Kaffke, SB. Bennstein, et al. Function of the Th17/interleukin-17A immune response in murine lupus nephritis. Arthritis Rheumatol, 67:475–87. 2015 doi: 10.1002/art.38955.

[16] T. Koga ,K. Otomo, M. Mizui, N. Yoshida M. Umeda, K. Ichinose, et al. Calcium/Calmodulin-dependent kinase IV facilitates the recruitment of interleukin-17-Producing cells to target organs through the CCR6/CCL20 axis in Th17 cell-driven inflammatory diseases. Arthritis Rheumatol , 68:1981–8. 2016. doi: 10.1002/art.39665

[18] CK. Wong, LC. Lit, LS. Tam, EK. Li, PT. Wong, CW. Lam. Hyperproduction of IL-23 and IL-17 in patients with systemic lupus erythematosus: implications for Th17-mediated inflammation in auto-immunity. Clin Immunol; 127: 385–393.2008.

[19] XF. Zhao, HF. Pan, H. Yuan, et al. Increased serum interleukin 17 in patients with systemic lupus erythematosus. Mol Biol Rep; 37: 81–85 2010

[20] T. Wang, J. Marken, J. Chen, V. B.Tran, Q. Z. Li, ,M. Li, & N. V Giltiay. High TLR7 expression drives the expansion of CD19+ CD24hiCD38hi transitional B cells and autoantibody production in SLE patients. *Frontiers in immunology*, *10*, 1243, 2019.

[21] M. Santiago-Raber,.I. Dunand-Sauthier, T Wu,. Q Li,. S. Uematsu, S. Akira, W. Reith, C Mohan, B.L. Kotzin, S. Izui,. Critical role of TLR7 in the acceleration of systemic lupus erythematosus in TLR9-deficient mice, Journal of Autoimmunity; 34 (4): 339-348.2010.

[22] B. D. Lyn-Cook, C. Xie, J Oates., E. Treadwell, B. Word, G Hammons, & K. Wiley, Increased expression of Toll-like receptors (TLRs) 7 and 9 and other cytokines in systemic lupus erythematosus (SLE) patients: ethnic differences and potential new targets for therapeutic drugs. *Molecular immunology*, *61*(1), 38–43. 2014

[23] Q. Ge,. X. Gu,. W. Yu,. G. Zhang, W. Liang,.M. Li, G. Zhai, M. Yan. Antinuclear antibodies in healthy population: Positive association with abnormal tissue metabolism, inflammation and immune dysfunction. International Immunopharmacology, Volume 113, Part A,2022,109292 ,https://doi.org/10.1016/j.intimp.2022.109292.)

[24] D. A. González, Varela, A. R Varela, I. M Rodríguez , A.G. Vera, M.D. Sánchez,. A.A. Esquivel, C.C. Rodríguez, A. C. de León, Anti-dsDNA antibodies in systemic lupus erythematosus: A combination of two quantitative methods and the ANA pattern is the most efficient strategy of detection, Journal of Immunological Methods,Volume 427,2015,Pages 30-35, https://doi.org/10.1016/j.jim.2015.09.003.

[25] AS. Wiik, N. Bizzaro. Missing links in high quality diagnostics of inflammatory systemic rheumatic diseases. It is all about the patient! *Autoimmun Highlights.;* 3:35–49. 2010

[26] J. Gołąb, M. Jakóbisiak,W. Lasek, et al. *Immunologia.* Warszawa: PWN; 2014.

[27] B. Grygiel-Górniak, N. Rogacka, & M Puszczewicz, Antinuclear antibodies in healthy people and non-rheumatic diseases - diagnostic and clinical implications. *Reumatologia*, *56*(4), 243–248.2018. https://doi.org/10.5114/reum.2018.77976

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