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Circulating Levels of Interferon Regulatory Factor-5 Correlates with Disease Activity in Systemic Lupus Erythematosus Iraqi Patients

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Abstract

Objectives: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease characterized by a diversity of the phenotypes among the patients. SLE is still one of the great challenges due to the lacking of specific biomarkers for diagnosis, assessing disease activity, and prediction of response to therapy. This study aimed to investigate the role of circulating levels of IRF5 protein in sample of SLE Iraqi patients and its correlation with disease activity, to identify a potential immunological biomarker to mirror disease activity.

Methods: Blood samples were taken from 59 participants diagnosed with SLE cases classified according to the American College of Rheumatology (ACR) criteria. They were scored through the SLE disease activity index 2000 (SLEDAI-2K) to estimate the disease activity, and according to it they were subdivided into "SLE-1 group" (SLEDAI-2k ≤5), and "SLE-2 group" (SLEDAI-2k >5), as well as age and gender matched healthy control group. Circulating levels of IRF5 protein were measured in sera samples by ELISA method.

Results: Our result revealed that the circulating levels of IRF5 protein were significantly higher in the SLE-2 group rather than control group ($P < 0.01$), while there was a non-significant difference between SLE-1 group and control group ($P > 0.05$), as well as between both SLE patient groups. Moreover, the circulating IRF5 protein levels were found to be correlated positively and significantly with disease activity index in both SLE patient groups. The correlation between the circulating levels of IRF5 protein with other parameters revealed that a significant positive correlation was found in SLE-1 group with ESR and globulins, and negative correlation with Hb and (albumin/globulin) ratio, while in SLE-2 group were positively correlated with urea, creatinine, and uric acid. The analysis of receiver operator curves (ROC) for circulating levels of IRF5 protein in SLE-1 and SLE-2 groups showed a good accuracy to distinguish SLE patients from healthy individuals (AUC = 0.758, sensitivity = 65.5%, and specificity = 69%,), and (AUC = 0.788, sensitivity = 77.3%, and specificity = 72.0%,), respectively.

Conclusion: The circulating levels of IRF5 protein correlate with disease activity in SLE patients reflects the possibility of using it as a potential immunological biomarker for diagnosis, and monitoring the disease activity.

Keywords: IRF5 protein, lupus erythematosus, systemic, Iraqi patients

Introduction

Systemic lupus erythematosus (SLE) is a chronic multi-system autoimmune disease. It is characterized by the production of excessive auto-antibodies due to break of immune system tolerance to self-antigen.[1-3] This subsequently leads to formation of circulating immune complexes, and immunologically mediated tissues injury.[4-6] SLE is a heterogenous disease with a wide range of clinical manifestations and immunological disorders. Although the etiology and pathogenesis of SLE are still obscure, several lines of evidence documented that immune disorders may be caused by genetic susceptibility and/or environmental factors.[7-9] The incidence of SLE primarily afflicts women in the reproductive years rather than men, with female to male ratio of approximately 9:1.[10,11] The diversity in the clinical manifestations among the patients is a great obstacle and might reflect the differences in underlying pathogenesis. SLE is still one of the great challenging for physicians and investigators. For more accurate diagnosis it is necessary to find a new reliable and specific biomarker for SLE.[12-14] Interferon regulatory factor-5 (IRF5) is a member of the IRF family of the transcription factors. It encodes a 60-63-KDa polypeptides, acts as a regulator of the production of numerous pro-inflammatory cytokines, including type I interferon IFNs (alpha and beta), IL-12, IL-6, IL-23, and tumor necrosis factor alpha (TNF-α).[15,16] It has been shown that the immune response against viral, fungal, and bacterial infections is regulated by IRF5.[17] Several recent studies revealed important roles of IRF5 in innate and adaptive immunity, cell growth regulation, apoptosis, and macrophage polarization.[18] Many genome-wide association studies document that there is a robust correlation between IRF5 SNPs and SLE, and that IRF5 high-risk variants play an important role in SLE pathogenesis.[19] Numerous studies reported that IRF5 risk variants generally correlated with elevated IRF5 expression levels in SLE blood cells, and with interferon-alpha activity in SLE patients.[20] To date, there are few studies about endogenous and extracellular IRF5 protein. Wang and his colleagues (2018), they determined the level of IRF5 protein in WBCs of community-acquired pneumonia (CAP) patients and healthy donors using flowcytometry techniques.[21] Idborg et al. (2019), who confirm the presence of extracellular IRF5 protein in circulation. They measured the concentration of it in plasma of SLE patients and age matched healthy controls. The techniques that used are immunoprecipitation followed by Mass spectrometry (IP-MS) and ELISA method.[22] This study aimed to determine the concentration of circulating IRF5 protein in sera of sample of Iraqi SLE patients, and examine its correlation with disease activity to identify its predictive value using ROC analysis for SLE diagnosis as a potential immunological biomarker reflects disease severity.

Materials and Methods

Subjects

A total of 59 patients diagnosed with SLE disease (56 females and 3 males) were recruited from the rheumatology unit of Baghdad Teaching Hospital between November 2020 and February 2021. The SLE patients had met the 1997 American

College Rheumatology (ACR) revised criteria for the classification of SLE.[23] Patients with other autoimmune disease, malignant disease, kidney disease, liver disease, alcohol intake, cigarette smoking, and other acute infections were excluded. Full history was taking, clinical examination and all the required routine laboratory tests were performed for all patients in order to assessment the disease activity score using SLE disease activity index 2000 (SLEDAI-2K) score,[24] and according to it they were subdivided into "SLE-1 group" (SLEDAI-2k ≤5) and "SLE-2 group" (SLEDAI-2k >5). A total of 29 age matched healthy controls were also recruited with no evidence of any chronic medical illness.

Samples Collections

Venous blood specimens of 5 ml were drawn after overnight fasting from each participant, then the blood was immediately divided into two portions. The first one (2 ml) was transferred into tube containing K3EDTA, and they were stirred gently for a few seconds to avoid blood clotting and they were used for hematological parameters determination. The reminder blood was transferred into a glass tube with a gel separator. The blood samples were allowed to clot for 10 minutes at 37°C in a water bath, then they were centrifuged at 3000 × g for 10 minutes. The obtained clear serum was dispensed in several aliquots, and stored frozen at –20°C until being used to estimate the different parameters included in the study. Hemolyzed sera were excluded.

Determination of Circulating Levels of IRF5 Protein

IRF5 protein levels were estimated in sera samples using Human IFR5 (interferon regulatory factor5) ELISA kit was supplied by (My BioSource Company, USA) according to manufacturer's protocol.

Laboratory Testing

Complete blood count (CBC) was done by Abbott Hematology auto-analyzer (Cell-DYN-Ruby, USA). Erythrocyte sedimentation rate (ESR) was determined by the Westergren method. General urine examination (GUE) was determined by routine techniques. Protein urea was quantified by 24-h urine collections. Anti-nuclear antibodies (ANA) and ds-DNA antibodies (ds-DNA) were determined using ELISA method by Naissa Immuno auto-analyzer (Neomedica, Europe). While C3 and C4 concentrations were determined using turbidimetry method by Hipro Immuno auto-analyzer (Hipro, China). Other biochemical tests were performed by colorimetric methods according to the manufacturer's instructions using commercial kits.

Statistical Analysis

The results were presented as mean ± standard deviation (mean ± SD). The differences among the studied groups were calculated by applying analysis of variance one-way (ANOVA), and followed by post hoc Tukey analysis to test the differences between every two groups within ANOVA. The degree of correlation between parameters was calculated by Pearson's correlation test. The percentage of significance was obtained by r and P values. The P-value is considered significant if it is < 0.05, and highly significant if it ≤0.01. Receiver Operator Characteristics curve (ROC) analysis was constructed for circulating levels of IRF5 protein to estimate its diagnostic yield for SLE disease, the area under the curve were considered exceptional (1–0.9), excellent (0.9–0.81), good (0.8–0.71), fair (0.7–0.61), and poor (0.6–0.5). The statistical analyses were performed using software statistical package for social science (SPSS) version 26.0 (IM SPSS, Chicago, IL, USA) and GraphPad Prism, version. 9.3.1 (San Diego, California, USA).

Results

The demographic data, clinical and Immunological characteristics of the 88 participants, 59 patients diagnosed as SLE according to the American College Rheumatology (ACR) criteria, and 29 healthy controls are described in Table 1. The treatment with medication that used at time of enrollment were also mentioned.

It is clear from the results in Table 1 that among the 59 SLE patients, 95% (M:F = 3:56) are females. As for organ involvement, 45 patients (76.2%) had immunological disorders, and 31 patients (52.5%) had hematological disorders. The next common manifestations were arthritis in 25 patients (42.3%) and oral ulcers in 22 patients (37%), followed by renal disorders in 16 patients (27.1%). As for medications, most of the SLE patients under therapy, 48 patients (81.3%) with Prednisolone treatment, 43 patients (72.8%) with Hydroxychloroquine treatment, and 15 patients (25.4%) with Azathioprine treatment. There were no statistical differences in age, gender, and BMI among the three studied groups (SLE-1, SLE-2, and control), as well as in disease duration between the SLE patient groups ($P > 0.05$). However, there is a significant difference in SLEDAI–2K score between the SLE patient groups ($P < 0.05$). The number of SLE patients with family history in SLE-1 group and SLE-2 group are 4 (14%) and 8 (27%), respectively. On the other hand, all controls with no family history. To investigate the role of circulating levels of IRF5 protein in SLE pathogenesis, sera samples of SLE patients and controls were analyzed. The results showed that circulating levels of IRF5 protein were significantly increased in SLE-2 group with a mean of 1.75 ± 0.65 ng/ml as compared with control group with a mean of 1.24 ± 0.19 ng/ml ($P < 0.01$). Upon comparison between SLE-1 group and control group the results show a slight increase of circulating levels of IRF5 protein in SLE-1 group with a mean of 1.48 ± 0.65 ng/ml than control group. But this increase was statistically non-significant, as well as non-significant difference was observed between SLE patient groups as shown in Figure 1.

Moreover, the circulating levels of IRF5 protein in SLE-1 and SLE-2 groups were significantly and positively correlated with disease activity index (SLEDAI-2K), ($r = 0.441$, $P = 0.017$) and ($r = 0.502$, $P = 0.005$), respectively as shown in (Figure 2A and 2B).

Additionally, we found a significant positive correlation between circulating levels of IRF5 protein and relative expression of IRF5 mRNA levels in both SLE-1 and SLE-2 groups, ($r = 0.887$, $P < 0.0001$) and ($r = 0.847$, $P < 0.0001$), respectively. Data not shown as it is another part of our project and it is under publication elsewhere.[25] The correlation of circulating levels of IRF5 protein with other parameters in both SLE patient groups were summarized in Table 2. Circulating levels of IRF5 protein in SLE-1 group were positively and significantly correlated with ESR ($r = 0.452$, $P = 0.014$) and globulins ($r = 0.463$, $P = 0.011$), and negative correlation with Hb ($r = –0.459$, $P = 0.012$) and (albumin/globulin) ratio ($r = –0.484$,

Table 1. **Baseline characteristics of SLE patients and healthy controls**

Characteristic		Total SLE patients	SLE-1 group	SLE-2 group	Control group	*P*-value
Demographic data						
Samples number		59	29	30	29	-
Age (year), mean ± SD (range)		34.59 ± 10.96 (14–55)	34.53 ± 10.8 (18–55)	34.66 ± 11.2 (14–53)	33.03 ± 9.6 (18–52)	0.81
BMI (Kg/m^2), mean ± SD		27.17 ± 6.1	26.06 ± 6.3	28.32 ± 5.5	26.35 ± 5.6	0.285
Gender Female, *n* (%) Male, *n* (%)		56 (95%) 3 (5%)	27 (93%) 2 (7%)	29 (97%) 1 (3%)	26 (90%) 3 (10%)	0.574
Disease duration (year), mean (range)		4.85 (0.1–33)	4.64 (0.3–23)	5.04 (0.1–33)	-	0.956
Family history with SLE Yes, *n* (%) No, *n* (%)		12 (20%) 47 (80%)	4 (14%) 25 (86%)	8 (27%) 22 (73%)	-	-
Clinical and immunological manifestations						
Vasculitis, *n* (%)		2 (3.3%)	0 (0%)	2 (6.6%)	-	-
Arthritis, *n* (%)		25 (42.3%)	10 (34.5%)	15 (50%)	-	-
Myositis, *n* (%)		0 (0%)	0 (0%)	0 (0%)	-	-
Pleurisy, *n* (%)		3 (5%)	0 (0%)	3 (10%)	-	-
Proteinuria, *n* (%)		12 (20.3%)	0 (0%)	12 (40%)	-	-
Hematuria, *n* (%)		2 (3.3%)	0 (0%)	2 (6.6%)	-	-
Urinary casts, *n* (%)		2 (3.3%)	0 (0%)	2 (6.6%)	-	-
Oral ulcers *n* (%)		22 (37.2%)	10 (0%)	12 (43.3%)	-	-
Alopecia, *n* (%)		11 (18.6%)	4 (13.8%)	7 (33.3%)	-	-
Fever, *n* (%)		10 (16.9%)	3 (10.3%)	7 (33.3%)	-	-
New rash, *n* (%)		11 (18.6%)	5 (17.2%)	6 (36.6%)	-	-
Thrombocytopenia, *n* (%)		12 (20.3%)	3 (10.3%)	9 (30%)	-	-
Leucopenia, *n* (%)		4 (6.7%)	3 (10.3%)	1 (3.3%)	-	-
Anemia, *n* (%)		29 (49.1%)	11 (37.9%)	18 (60%)		-
Low complement *n* (%)		18 (30.5%)	3 (10.3%)	15 (50%)	-	-
(+) ANA, *n* (%)		40 (67.7%)	15	25		-
(+) ds-DNA antibodies, *n* (%)		36 (61%)	15 (51.7%)	21 (70%)	-	-
SLEDAI-2K, mean ± SD (range)		7.37 ± 3.94 (2–18)	4.1 ± 0.72 (2–5)	10.53 ± 3.08 (6–18)	-	<0.01
Medications						
Prednisolone Treatment	Yes, *n* (%) No, *n* (%)	48 (81%) 11 (19%)	22 (76%) 7 (24%)	26 (87%) 4 (13%)	-	-
Hydroxychloroquine Treatment	Yes, *n* (%) No, *n* (%)	43 (73%) 16 (27%)	19 (66%) 19 (34%)	24 (80%) 6 (20%)	-	-
Azathioprine Treatment	Yes, *n* (%) No, *n* (%)	15 (25%) 44 (75%)	8 (28%) 21 (72%)	7 (23%) 23 (77%)	-	-
Methotrexate Treatment	Yes, *n* (%) No, *n* (%)	3 (5%) 56 (95%)	1 (3%) 28 (97%)	2 (7%) 28 (93%)	-	-

The collected data was analyzed by mean ± SD (mean ± standard deviation), range (minimum-maximum), or number (percentage). *P*-value was used for the comparison among the three studied groups (SLE-1, SLE-2, and control). $P > 0.05$ = non-significant differences, $P < 0.05$ = significant differences, $P \leq 0.01$ = high significant differences. BMI, body mass index; ANA, anti-nuclear antibodies; ds-DNA antibodies, double strand deoxy nucleic acid antibodies; SLEDAI-2K, Systemic lupus erythematosus disease activity index 2000.

$P = 0.008$). While circulating levels of IRF5 protein in SLE-2 group were positively correlated with urea ($r = 0.632$, $P < 0.0001$), creatinine ($r = 0.751$, $P < 0.0001$), and uric acid ($r = 0.595$, $P = 0.001$).

In order to estimate the ability of circulating levels of IRF5 protein to distinguish the active SLE patient from healthy subjects as a diagnostic biomarker. We analyzed it using ROC curve analysis. The result showed that the circulating levels of IRF5 protein in SLE-1 and SLE-2 groups had a good ability to discriminate SLE patients from healthy persons. By which the AUC, sensitivity and specificity were (0.758, 65.5%, 69.0%), and (0.778, 72.4%, 70.0%) respectively, at the cut off value of 1.35 (ng/ml), and 1.365 (ng/ml) respectively, which was the good value of SLE correct prediction, as shown in (Fig 3A and 3B).

Discussion

This study has been prepared to evaluate the circulating levels of IRF5 protein in a sample of SLE Iraqi patients, and to examine the association with disease activity index and other parameters. Moreover, applying the ROC curve analysis in

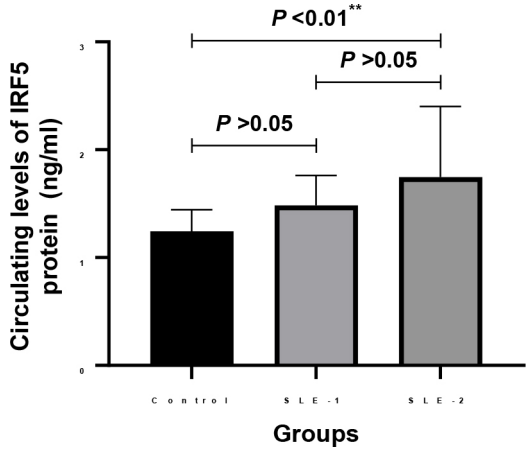


Fig. 1 **Circulating levels of IRF5 protein among the studied groups. The results were expressed as mean ± SD (mean ± standard deviation), $P > 0.05$ = statistically non-significant differences, * Statistically significant differences at $P < 0.05$, ** Statistically significant differences at $P \leq 0.01$.**

Table 2. **The correlation between circulating levels of IRF5 protein (ng/ml) with other biochemical parameters**

Parameter	Circulating levels of IRF5 protein (ng/ml)			
	SLE-1 group $n = 29$		SLE-2 group $n = 30$	
	r	*P*-value	*r*	*P*-value
Demographic data				
Age (year)	0.353	0.06	0.124	0.515
Gender (F/M)	–0.259	0.175	–0.76	0.689
BMI (Kg/m^2)	0.218	0.255	0.084	0.659
Disease duration (year)	0.098	0.612	-0.001	0.997
Family history with SLE	–0.222	0.309	0.409	0.058
Hematological parameters				
WBC X 10^3/UL	–0.297	0.118	0.353	0.060
RBC X 10^6/UL	–0.245	0.201	–0.212	0.261
Hb (gm/dl)	–0.459	0.012*	–0.269	0.151
PLT X 10^3/UL	0.153	0.429	0.366	0.051
ESR (mm/1 hr)	0.452	0.014*	0.106	0.546
Biochemical parameters				
Urea (mg/dl)	0.145	0.452	0.632	<0.0001**
Creatinine (mg/dl)	0.04	0.838	0.751	<0.0001**
Uric acid (mg/dl)	0.353	0.060	0.595	<0.001**
GOT (U/L)	-0.069	0.723	0.352	0.057
GPT (U/L)	0.224	0.242	0.184	0.0331
ALP (U/L)	0.366	0.051	-0.51	0.79
Total serum protein (g/l)	0.207	0.281	-0.172	0.364
Serum albumin (g/l)	-0.394	0.063	-0.180	0.340
Globulins (g/l)	0.463	0.011*	0.011	0.954
Albumin /globulins	-0.484	0.008**	-0.098	0.608
Total cholesterol (mg/dl)	-0.052	0.787	0.328	0.077
Tri glyceride (mg/dl)	0.065	0.737	0.272	0.145
VLDL (mg/dl)	0.063	0.747	0.272	0.145
HDL (mg/dl)	-0.214	0.264	0.098	0.607
LDL (mg/dl)	-0.029	0.879	0.302	0.105

r, Pearson coefficient. $P > 0.05$ = statistically non-significant correlation, *Statistically significant correlation at $P < 0.05$, **Statistically significant correlation at $P \leq 0.01$. BMI, body mass index; WBC, white blood cells; RBC, red blood cells; Hb, hemoglobin; PLT, platelets; ESR, erythrocyte sedimentation rate; GOT, glutamate oxaloacetate transaminase; GPT, Glutamate Pyruvate Transaminase; ALP, alkaline phosphatase; vLDL, very low-density lipoprotein; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

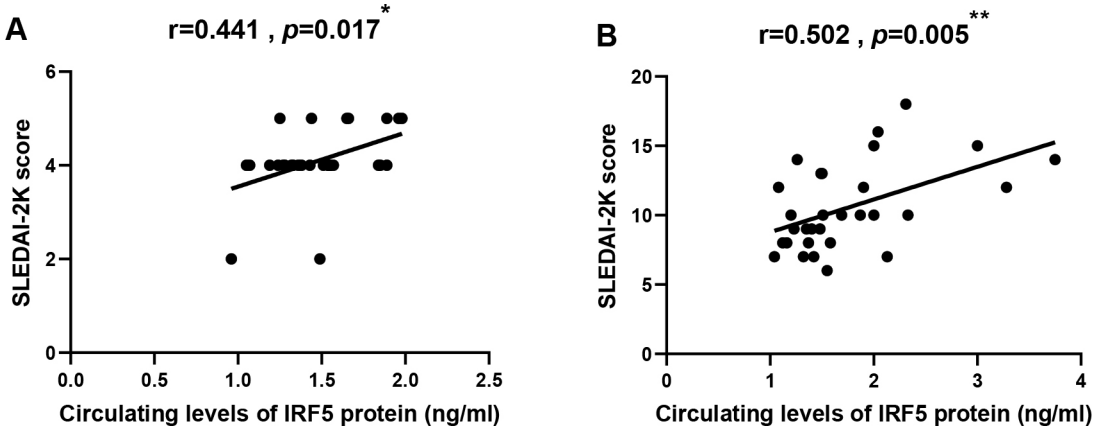
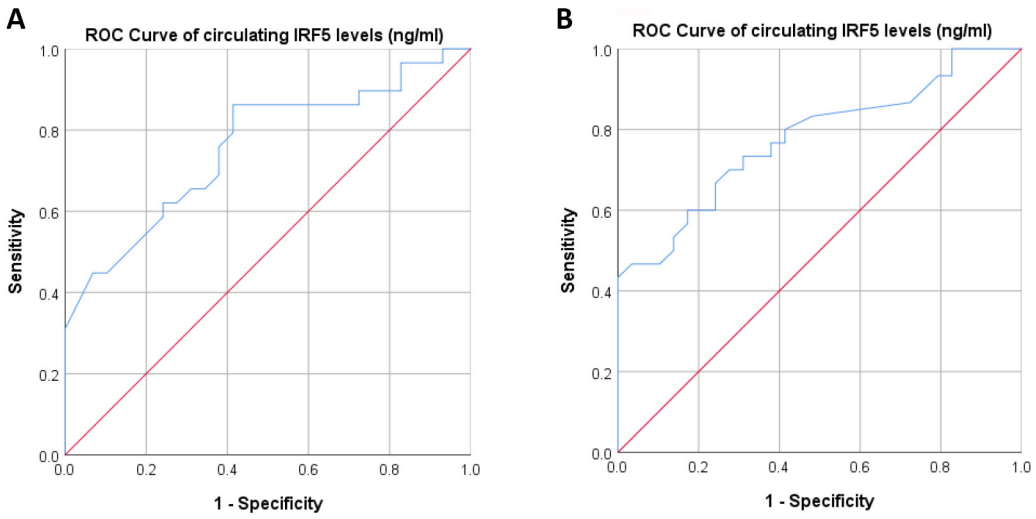


Fig. 2 **(A and B), the correlation between Circulating levels of IRF5 protein (ng/ml) and SLEDAI-2K score in SLE-1 group and SLE-2 group, respectively. *r*, Pearson coefficient. $P > 0.05$ = statistically non-significant correlation, *Statistically significant correlation at $P < 0.05$, ** Statistically significant correlation at $P \leq 0.01$.**

order to predict the ability of it for diagnosis of SLE patients as an immunological biomarker. Our result revealed that circulating levels of IRF5 protein were found to be increased in both SLE-1 and SLE-2 groups as compared with healthy controls, and correlated positively and significantly with disease activity index.

IRF5 is a transcription factor plays an important role in inflammatory response. it is likely a key regulator of the toll like receptors (TLRs). In the case of the unstimulated cell, IRF5 is generally localized in the cytoplasm as a monomer. Activation of the above receptors leads to cascading signals. IRF5 undergoes posttranslational modification, which eventually leads to homodimerization, a critical event prior to nuclear translocation.[17] The extracellular protein of IRF5 still has an unknown function in the circulation and away from complete transcription factors and other nuclear molecules. It can have an unknown function or may regardless of the function.[22] The functions of extracellular and intracellular protein might be different and unusual secretion is also probable.[26] Our finding is in agreement with Idbord et al., who found that circulating levels of IRF5 protein were significantly higher in SLE patients compared with control individuals. They reported that the high level of IRF5 protein in plasma samples of SLE patients may be reflected the increase of cell death during apoptosis clearance in SLE patients.[22] In other hands, we cannot only be clarified by this reason because the reports of transcription factor in circulation are limited.[27,28] There is no information about the function of extracellular of IRF5 protein. However, the fact that IRF5 may be present in microparticles, known to mediate cell-cell signaling thus further studies are needed about circulating IRF5 protein.[22] The expression of IRF5 gene is significantly raised in peripheral mononuclear cells (PBMC) from SLE patients as compared to age-matched healthy individuals, and this can stimulate the expression of type I interferon.[29] The elevated serum levels of IFN- alpha have been shown to be associated with the activity and severity of SLE disease. These findings support to explain our results about the positive correlation between circulating levels of IRF5 protein and disease activity.[30] Numerous studies in different countries population have showed that the hematological abnormalities are present in most of SLE patients. The common hematological syndrome in SLE patients is anemia, which is most often owing to the anemia of chronic disease. ESR levels were significantly increase in SLE patients during SLE flare and infections as compared to healthy controls.[31-33] Many studies indicated that ESR considered an important factor in assessing SLE disease activity, as ESR elevates when disease activity increase. It is believed that the reason for the high rate of erythrocyte sedimentation is the decrease in the concentration of proteins in the blood plasma, as well as the change in the shape of the surface of the erythrocytes and their adhesion to each other.[34] These findings may be explaining our results about the negative correlation between Hb and circulating IRF5 protein, as well as the positive correlation between it and ESR level. SLE is characterized by raised levels of autoreactive antibodies and gamma globulin. The production of autoantibodies requires the synthesis of gamma globulin and this led to increase the globulin levels in blood SLE patients.[35,36]

Our results about positive proteinuria in SLE patients as shown in Table 1 are in agreement with previous studies that documented the presence of protein in urine in SLE patients.[37,38] Serum albumin was determined in SLE patients as a part of routine biochemical tests. The decrease of serum albumin levels in SLE patients may be caused by elevating albumin catabolism as a result of chronic inflammation and/or because of poor diet from proteins content and calories. Moreover, the common manifestation in SLE patients is nephritis which characterized by attack the kidney membranes due to the presence of auto-antibodies against these membranes. Consequently, membranes are disrupted and impaired its



Group	AUC	SE	*P*-value	95% IC	Cut-off value	Sensitivity	Specificity	PPV	NPV	Accuracy
SLE-1	0.758	0.064	0.001	0.633-0.883	1.350	65.5%	69.0%	67.9%	66.7%	67%
SLE-2	0.778	0.06	<0.001	0.659-0.896	1.365	72.4%	70.0%	72.4%	70.0%	71.1%

Fig. 3 **(A&B) Receiver operator curve (ROC) analysis for the predictive value of circulating levels of IRF5 protein in SLE-1 (*n* = 29) and SLE-2 (*n* = 30) versus healthy controls (*n* = 29), respectively. AUC = area under the curve, SE = standard error, CI = confidence interval, PPV = positive predictive value, NPV = negative predictive value.**

filtration ability. In normal condition the filtering membranes do not allow albumin and another blood proteins to be missing in the urine. However, in lupus nephritis the protein loss in urine which in turn lowers serum albumin concentrations,[39,40] and this lead to decrease the ratio of albumin/globulin. Kwon et al. (2018) found that the (albumin/globulin) ratio in SLE with nephritis was lower than in SLE without nephritis.[36] All above findings supported our results about the positive correlation between circulating level of IRF5 protein and globulins, as well as a negative correlation with the ratio of (albumin/globulin). Our results of the positive correlation with urea, creatinine, and uric acid could be explained by the existence of some patients with lupus nephritis as shown in Table 1. Consequently, the existence of any criterion correlated with kidney disorder for example proteinuria and hematuria lead to raise the score of disease activity. Therefore, patients with lupus nephritis graded the high score of disease activity among the patients, subsequently increasing their levels of circulating IRF5 protein. ROC curve analysis, it showed that circulating levels of IRF5 protein in SLE-1 and SLE-2 groups could represent a good predictor for SLE diagnosis.

Conclusion

Our study results suggests that the IRF5 may play an important role in SLE pathogenesis, and IRF5 may be useful in diagnosis of SLE. The circulating levels of IRF5 protein associated with disease flare in SLE patients reflect the possibility of using it as a potential biomarkers for diagnosis, monitoring the disease course and response to therapy. Moreover, the ELISA method is more rapid and inexpensive rather than real time PCR for determination of IRF5 gene expression.

Conflict of Interest

None.

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