RESEARCH ARTICLE

Evaluating treatment effect on interferon-alpha in female patients with systemic lupus erythematosus: a case-control study

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Abstract

Objective: To assess the effect of treatment on interferon-alpha titer in the serum of female patients with systemic lupus erythematosus.

Method: The case-control study was conducted at the Rheumatology Unit of Baghdad Teaching Hospital from January 2022 to April 2022 and comprised female systemic lupus erythematosus patients and healthy controls matched for age. The treated patients formed group A, while the untreated patients were placed in group B, and the controls were in group C. The disease severity status was confirmed using the systemic lupus erythematosus disease activity index. The serum level of interferon-alpha was determined using the enzyme-linked immunosorbent assay. Data was analysed using SPSS 21.

Results: Of the 150 subjects, 5033.3%) were in each of the 3 groups. The mean age of patients was 32.3±9 years while that of the controls was 33.0±11 years. Erythrocyte sedimentation rate, creatinine and aspartate aminotransferase were significantly higher in patient groups compared to the controls ($p<0.05$), while no-significant difference was noted between the treated and untreated groups ($p>0.05$). Interferon-alpha level was significantly high in group B compared to group A ($p=0.037$). The increase was more pronounced in those aged ≤50 years ($p<0.05$). Interferon-alpha was significantly high in group B patients with a disease duration of <1 year compared to group A ($p=0.01$). Interferon-alpha showed a significant increase in group B compared to the group A in patients with inactive systemic lupus erythematosus disease activity index and with family history ($p<0.05$).

Conclusion: Treatment had a direct impact on interferon-alpha protein level in the serum of female patients of systemic lupus erythematosus.

Key Words: Creatinine, Sedimentation, Rheumatology, Lupus Erythematosus, Interferon-alpha, Enzyme, Immunosorbent, Aspartate Aminotransferases

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Introduction

Systemic lupus erythematosus (SLE) is a multifactorial and chronic autoimmune disorder having a wide spectrum effect[1]. The main feature of the disease is the production of a wide variety of autoantibodies that attack self-antigens, such as host nuclear-antigens, immune complexes, deoxyribonucleic acid (DNA), and cellular elements[2]. The management of SLE is critically important to limit chronic complications that lead to organ damage, decrease the flare, and prevent the toxicity of immunosuppression drugs[3]. SLE patients prefer to decrease sunlight exposure, as ultraviolet (UV) rays can flare up cutaneous and other systemic symptoms[4]. Interferons (IFNs) are cytokines with antiviral activity and immunomodulatory functions[5]. IFNs are categorised into type I, type II and type III, depending on structure, genetics, function features and cell-surface receptors[6]. The type I interferon is the bigger family that consists of IFN-α, IFN-β, IFN-ω, IFN-κ and IFN-ε classes, while IFN-α has 12 proteins in humans[7]. Type I IFNs play a vital function in the immune system by mediating responses against viral invasion, and are considered a bridge that link adaptive and innate immunity[7,8]. Studies showed that the greater contributor from the type I family in SLE immune-pathogenesis is IFN-α[9,10].

The current study was planned to assess the effect of treatment on IFN-α titer in the serum of female SLE patients.

Patients and Methods

The case-control study was conducted at the Rheumatology Unit of Baghdad Teaching Hospital. Samples were collected from January 2022 to April 2022. after approval from the ethics review committee of the Iraqi Ministry of Higher Education and Scientific Research and oral informed consent was obtained from all participants. A consecutive nonprobability sampling technique was adopted. The sample comprised female

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SLE patients and healthy controls matched for age. The treated patients formed group A, while the untreated patients were placed in group B, and the controls with negative autoimmune antibodies were in group C. The SLE status was confirmed by rheumatologists in line with European Alliance of Associations for Rheumatology (EULAR) and American College of Rheumatology (ACR) diagnostic criteria[11].

Data related to age, family history, clinical history, treatment and routine laboratory parameters was obtained from the institutional medical records database. The disease severity was determined based on the guidelines of the systemic lupus erythematosus disease activity index 2000 (SLEDAI-2K)[12]. Patients who developed lupus nephritis, or had overlapping immune diseases were excluded, and so were juvenile SLE cases.

Blood samples were drawn for complete blood count (CBC) and erythrocyte sedimentation rate (ESR) testing. Serum concentrations of blood urea, creatinine, aspartate aminotransferase (AST) and alanine transferase (ALT) were measured using automated Fujifilm (FUJI DRI-CHEM SLIDE, FUJIFILM WAKO Pure Chemical Co., Osaka, Japan), while anti-nuclear antibodies (ANA) and anti-ds-DNA were estimated using enzyme-linked immunosorbent assay (ELISA) technique (Human Company, Germany).

The IFN-α titer in serum was estimated using an ELISA kit (Cell Bio Labs I, United States; Catalogue No. RDEEH3254) as per the manufacturer's instructions.

Data was analysed using SPSS 21. Data was expressed as frequencies and percentages, or mean ± standard deviation, or median with interquartile range (IQR), as appropriate. P<0.05 was considered significant at 95% confidence interval (CI).

Results

Of the 150 subjects, 50(33.3%) were in each of the 3 groups. The mean age of patients was 32.3±9 years while that of the controls was 33.0±11 years. Among the patients, adult-onset cases were 93(93%), while late-onset was noted in 7(7%) (p<0.001). The mean disease period was 4.1±1.9 years. Additionally, 59(59%) of the SLE patients were in the active state and 41(41%) were inactive (Table 1).

IFN-α level was significantly high in group B compared to group A (p=0.037). The increase was more pronounced in those aged ≤50 years (p<0.05). IFN-α was significantly high in group B patients with a disease duration of <1 year compared to group A (p=0.01). IFN-α showed a significant increase in group B compared to the group A in patients with inactive SLE and with family history (p<0.05) (Table 2).

Table-1: Baseline characteristics and laboratory investigations of the subjects..

Parameters Mean ± SD* or N (%)	Patients (N=100)	Controls (N=50)	P	Untreated (N=50)	treated (N=50))	P
Age (years)	32.3±9	33.0±11				
Age groups N (%)						
Adult-onset (≤50)	93 (93%)					
Late-onset (>50)	7 (7%)					
P	<0.001*					
Disease Duration (years)	4.1 ± 1.9					
Family History N (%)						
With	18(18%)					
Without	82(82%)					
SLEDAI-2K	6.7±3.0					
Active SLE N (%)	59(59%)					
Inactive SLE N (%)	41(41%)					
WBC (103/mL)	6.66 ± 2.63	6.38 ± 1.52	0.514	6.8 ±2.1	6.6 ±2.7	0.714
HB (g/dl)	11.0 ± 0.9	11.9 ± 1.1	0.401	11.9±1.8	10.8±1.8	0.240
ESR (mm/hr.)	42.1±36.1	11.8±9.9	<0.001*	43.2±36.6	36.7± 34.2	0.503
Creatinine (mg/dl)	0.98 ± 0.12	0.62 ± 0.11	<0.001*	0.6± 0.1	0.6±0.08	0.166
ALT (U/L)	20.91±31.42	17.24 ± 3.50	0.411	22.2± 34.4	14.7±2.9	0.371
AST (U/L)	25.37±26.50	17.23 ± 3.58	<0.001*	26 ±28	22.6± 18.2	0.637
ANA positivity N (%)	90(90%)			50(55.5%)	40(44.5%)	0.179

WBC: White blood cell, Hb: Haemoglobin, ESR: Erythrocyte sedimentation rate, ALT: Alanine transferase, AST: Aspartate aminotransferase, ANA: Antinuclear antibody. SLEDAI-2K: systemic lupus erythematosus disease activity index-2000. *Correlation was significant at p<0.05 level.

Table-2: Serum level of interferon-alpha (IFN-α) in systemic lupus erythematosus (SLE) patients and controls.

Characteristics	Mean; pg/ml					P
	SLE (N=100)	Controls(N=50)	P	Untreated (N=50)	treated (N=50))	
Age (years)	32.3±9	33.0±11				
Age groups N (%)						
Adult-onset (≤50)	93 (93%)					
Late-onset (>50)	7 (7%)					
P	<0.001*					
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NS: Non-significant. S: Significant..

Discussion

The present study suggested age as a risk factor in SLE aetiology, which was in agreement with previous studies[13,14].

The current study found a significant difference in the positivity of ANA between SLE patients and healthy controls, with positivity reaching 90% in SLE patients and there was no significant difference between the untreated and treated patients. This was reported earlier as well[15,16].

The present study showed a non-significant difference in IFN-α titer with respect to the overall sample, which was in disagreement with a majority of previous researches[17-19]. The difference could be because of different ethnicities. It could also be explained by the difference in medication and dose[20].

The present study detected significant differences in untreated SLE patients with a high mean IFN-α level compared to low IFN-α level in the treated group. This result was in contrast with data reported from Egypt[19]. Besides, a study showed no significant difference in IFN-α levels between groups taking different medications[21].

The IFN-α titer in the serum was found to be correlated significantly with age ≤50 years, which was similar to an earlier study[22].

The present study showed a negative association between IFN-α and SLEDAI, which was in agreement with on study[19], while others suggested a positive association between IFN-α and SLEDAI[23-25].

The IFN-α level in the serum of SLE patients with family history showed a significant increase compared to those without any family history, which was in agreement with earlier findings[18].

Limitation: The current study has limitations, as the sample size was not calculated which could have affected the power of the study.

Conclusion

Treatment had a direct impact on IFN-alpha protein level in the serum of female SLE patients.

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