Measurement of Interleukin 17a and Transforming Growth Factor-B1 and Its Relation to Disease Activity in Systemic Lupus Erythematosus Patients

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Abstract

The study was done in January – may 2018, For measuring interleukin concentration 17-A and transforming growth factor-β1 in the serum of syst.emic lu.pus erythrmatosus (SLE) female patients(52 female) compared to the control group (36 healthy female).

An Enzyme- Link ed Immunos orbent Assay (ELISA) was used to diagnose both IL-17A and TGF β1 in SLE patients and control. In case of IL-17A High significant in.crease ($P < 0.0001$) in SLE patients (38.54 pg / mL) compare d with he althy co.ntrol (20.24 pg / mL) was observed, while in patients with SLE, the transforming growth factor-β was (70.90 pg / mL) compared to healthy control (116.66 pg / mL) ($P < 0.0001$). To all SLE patients and control, The laboratory features include full blood count ,ery.throcyte sedimentation rate ESR, ,an.d immunological tests like C3,C4,ANA and anti ds-DNA were done. ESR , WBC , ANA and Urea were significantly higher in SLE patient than con trol group (p.value 0.0001, 0.0001, 0.024, 0.0001 respectively) whereas Hemoglobin were significantly lower in SLE Patient than control group (p.value 0.0001) .C3&C4 were lower in SLE patients but with no significance value.

***Key word s** : Systemic Lupus erythrmatosus ,Interleukin -17A, Trans forming growth factor-β1, disease activity.*

Introduction

Systemic lupus erythem.atosus (SLE) is a chroz nic auto immune di sease that effect s many systems, organ s and tissues in the human bo dy such as kidney s, skin, cardiov.ascular system, lung.s, j.oints, muscles, and nervous system[(1)] . SLE has a broad variety of clinical presentations and various autoantibodies, most of which involve female of reproduactive age.[(2, 3)]. The duration of the disease differs with periods of remission and recurrence. [(4)]. Although there has been important progress in understanding its etiopathogenesis over the previous few years, the actual cause of lupus is unknown. [(4)]. Lupus pathogenesis includes many factors that are immunological, hormonal, hereditary and environmental. The incidence of disease differs among ethnic groups, among black females 1:250 and among white females 1:4300. [(5,6)] .

In SLE pathogenesis, several main players such as cytokine over manufacturing [(7,8)], oxidative stress [(9)], and apoptosis s play a significant part. [(10)]

Cytokines plays a crucial role in the proeduction, maturaetion and diffeerentiation of immune cells. The effect of cytokine s on autoimmune SLE can not be continuously anticipated. [(11)].

Interleukin 17 A is a multi-functional cyto.kine th.at influences the development of neutrophils and mediates T-helper-1 (Th1) and T-helper-2 (Th2) cytokines. [(12,13,14)].

In humans, IL-17A is mainly expressed through the T-helper-17 (Th17) subgroup of CD4 T-cells(15), but it also produces neutro phils, CD8 + and double adverse (DN) T cells, and natural killer (NK) cells [(12)].

In vivo and in vitro production of IL-17 is mainly regulated by transform ing growth fact or beta-1(TGF-β 1) and interleukin-6 (IL-6) by the activ ation of the signal trans.ducer and the activator of transcription-3 (STAT-3) in mous e and hu.man models, respectively. [(16,17)] .

Recent studies of IL-17 inhibition in achieve inanky,lsing spo.ndylitis clinical advantage will raise concerns about the potential for inhibition of IL-17 in patients with SLE or in certain symptom types. [18,19] .

There are three tightly associated members in the cytokine family of transforming growth factor β (TGF-β): TGF-β1, TGF-β 2, and TGF-β 3. β 1 is oform generated by lympho.cytes and mono.cytes with a significant immune regulatory function [20]. TGF-β 1 is the most powerful naturally occurring immune suppressant, playing a main role in regulating cell proliferation and cell manufacturing through programmed cell death. TGF-β 1 is a important negative B-cell differentiation and proliferation regulator that inhibits the development of most immunoglobulin iso-types [21]. It also co-stimulates the development of T-cells with down-regulating activities [22]. TGF-β 1 can play a dual role in inflammatory immune-mediated disease development and progression. The production of TGF-β lymphocytes in SLE is decreased, which can predispose autoreactive T-cell activation and autoantibodies production. In autoimmune diseases, infiltration of target bodies such as T-cells or immune-complex autoantibody deposition triggers early inflammatory lesions that activate local production of anti-inflammatory cytokines such as TGF-β 1 by macrophages and kidney mesangial cells to combat inflammatory mesangial cells to prevent inflammation [23]. Increased production of TGF-in 1 in tissues leads to local fibro.genesis and ultimately to severe organ damage [24]. Any SLE treatment involving manipulation of TGF- β 1 should therefore be approached with caution, considering the effects on the entire cytokine network[25].

Patients and Method

Fifty-two female SLE patients were enrolled with 23-56 years of age (32.5 ± 1.1 years). They were referred during the period January – May 2018 for diagnosis and treatment to the Consultant Clinic at the Department of Rheumatology (Alyarmook Teaching Hospital and Baghdad Teaching Hospital). A control group of thirty six subjects were also included, and they were matched patients for gender and age where the age of patients and healthy individual range between 20 - 60 years.

Clinical Examination

Patients undergoing complete history and clinical examination including activity of disease , general locoumotor system, skin, cardiogvascular, thoracic, neuroological and vascular examination.

Inves Tigations

Investigations of each sample were done by full blood count, erythrocyte sedi mentation rate, renal function tests, Com plement 3 , Comple ment 4 ,AN A, and Anti double strand.ed DNA anti body.

Est Imation of Il-17A and Tgf B1

The patients ans controls serum were tested for IL-17A and TGF β levels. Sera was analyzed according to manufacturer's protocols by sandwich enzyme-linked immu.nosorbent assay (ELISA). Quantikine® ELISA kit with. ® Catalog Number D1700 used to check IL-17A with assay range: 11.373 - 59.326 pg/ml. TGF β assay by cusabio Co., LTD, the Catalogue Number:CSB-E04725h. Assay range: 22.508-151.321 pg/ml.

Statistical Analysis

Analysis of data was carried out using SPSS-25 (Statistical Social Science Packages- version 25). The significance of differing umeans (quantitative data) has been tested using Students-t-test to differentiate between twoo independent means or Paired-t-test for paired oobservation differences (or two dependent means), Or ANOVA test for distinction between more than two independent means. Measures the association closeness by correlation coefficient between twoo quantitative continuous variables. Kruskall Wallis one-way variance analysis (KW) test was used to compare the median for > 2 independent non-related samples. The P value was considered statistically significant less than 0.05.

Results

Table 1 shows the clinical features of patients with SLE compared to healthy control, there was no significant difference in (Creatinine ,Anti-dsDNA ,C4 ,and C3) of SLE patients and healthy control. SLE patients show highly result in ESR , WBC , ANA and Urea than control ,whereas the test of Hemoglobin was lower in SLE patients than control

Table (1): C3, C4 , Anti-dsDNA, ANA, ESR, WBC, Hemoglobin, Platelets, Urea and Creatinine in the sear of pa.tients with SLE and he.althy control

	SLE patients	**Healthy control**	**P.Value**
C3 (IU/L)	0.93±0.42 (0.20-1.66)	1.08±0.33 (0.51-1.71)	0.094
C4 (IU/L)	0.37±0.17 (0.083-0.65)	0.39±0.15 (0.16-0.60)	0.746
Anti-dsDNA(IU/ml)	17.35±8.95 (6.481-36.90)	15.09±1.85 (12.1-17.80)	0.142
ANA (IU/ml)	3.25±1.92 (0.212-6.921)	1.09±0.06 (1.0-1.20)	0.0001*
ESR (mm/hour)	39.94±17.65 (15-88)	7.47±3.91 (2-17)	0.0001*
WBC (x103)	7.61±2.95 (3.8-14.30)	6.33±1.39 (4.0-9.10)	0.024*
Hemoglobin (g/dL)	11.20±1.94 (8.20-16.0)	14.16±1.58 (11.20-17.30)	0.0001*
Platelets (x103)	283.28±137.50 (89-520)	269.94±63.52 (161-364)	0.603
Urea (mg/100 ml)	41.84±14.56 (19.0-74.0)	28.33±9.01 (16.0-44.0)	0.0001*
Creatinine (umol/L)	1.03±0.34 (0.40-1.70)	1.00±0.27 (0.43-1.50)	0.641

Table (2) shows IL-1 7 A and T GF-β1 concentrations in patients with SLE and healthy con.trol. Highly siginificant diffeerence (P 0.01) was found in IL-17 A levels of patients & healthy con trol (38.54, 20.24 pg / mL) respectively , while TGF-β, the leveel in SLE patients 70.90 pg/mL and healthy control 116.66 pg/mL.

Ta ble (2): Level of IL-17 A TG F-β in the sera of SLE patients & healthy control

	SLE patients	**Healthy control**	**P.Value**
IL-1 7A (pg/ ml)	38.54±5.41 (27.054-46.621)	20.24±5.28 (11.373-28.625)	0.0001*
TGF- β (pg/ml)	70.90±13.44 (50.644-94.343)	116.66±19.71 (90.514-151.32)	0.0001*

Discussion

Systemic lupus erythematosus is a complex autoimmune disease involving various aspects of the immune system. In addition to antibody production and immune complex deposition, emerging evidence suggests that cytokines can play a major role in the pathogenesis of SLE[26] .

In our study, the comparison of TGF-β1 serum levels for both SLE patients and controls shows significant statistical difference whereas the patients with lower values than control p.value 0.001. This was consistent with the Be cker-Me rok et al'(27) outcomes, which revealed that SLE patients had reduced concentrations of TGF-β 1 (p 0.01) than controls.

Several cytokine abnormalities have been recorded in SLE and latest developments have revealed new understanding of autoimmune inflammatory reactions in cytokine regulation. The production of TGF-β1, the primary regulatory T cytokines that suppress inflammatory reaction, has been discovered to be profoundly deregulated in SLE patients in specific. They were therefore regarded as essential elements in the disease etio pathology [28]. TGF-β 1 is a extremely pleiotropical cytokine that plays a significant role in immune homeostasis maintenance [29]. TGF-β 1 includes many critical cellular procedures, including cell development, extracellular matrix formation, cell motility, hematopoiesis, apoptosis and immune function. [30]. TGF-β 1 has strong anti-inflammatory and immunosuppressive properties, controlled by all immune cells activation, proliferation, differentiation and survival [31].

Also we found the IL-17A levels were significantsly highser than controls. Other researchers showed elevated levels of IL-17A in the serum of SLE patients because these cytokines are generated by the immune-response T-helper lymphocyte, which can be deregulated in the impaired immune response. [32,33].

Increasing concentration of IL-17A in SLE patients will probably lead to the recruitment and activation of immune cells in target organs, thereby improving the immune response. In SLE patients, the immune environment is ideally suited for IL-17 A producing T-cell.

From this research we found that IL-17 A & TGF-β1 can also serve a protective function in SLE patients.

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