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Study the potential role of IL-17 in *Toxoplasmosis* prevalence in SLE patients

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Abstract:Toxoplasma gondii is an opportunistic pathogen that can kill congenitally infected fetuses, newborns, and immunocompromised patients by reactivating a latent infection. The aim of study knowing the extent of Toxoplasma effect of on the level of IL-17 in SLE patient. In this study, 250 blood samples from both genders female and male were collected. Using the ELISA technique, T. gondii immunoglobulins (IgG and IgM) antibodies and (IL-17) levels were assessed in all serum samples. According to the findings of this investigation, SLE patients had the greatest rate of toxoplasmosis infection. The percentage of anti-Toxoplasma IgG (50%) was higher than the percentage of anti-Toxoplasma IgM (4%), across all groups. IL-17 was highly in SLE and Toxoplasma infected patient (151.87 ± 5.99). These result is suggested that direct pro-inflammatory activity, may have a role in SLE pathogenesis. Toxoplasmosis must be diagnosed and treated in SLE patients in order to lessen the impact of the illness because most immunocompromised people are exposed to a number of possible risk factors, including Toxoplasma original infection or reactivation.

Introduction:

Toxoplasmosis is a zoonotic disease caused by Toxoplasma gondii, a protozoal parasite. Toxoplasma gondii, an obligate intracellular protozoan parasite from the phylum Apicomplexa and the order Coccidia, is the causative agent of toxoplasmosis. T. gondii's definitive hosts are felids, however encysted parasites can live in the tissues of most or all hosts for lengthy periods of time, possibly even a lifetime. Some clinical cases are caused by new T. gondii exposures, whereas others are caused by reactivation of parasites in tissue cysts. Warm-blooded animals, including humans, are frequently infected with T. gondii, which typically causes no symptoms or just mild clinical signs in immunocompetent, non-pregnant individuals. Contrarily, illnesses acquired during pregnancy can result in mild to severe congenital defects in the fetus, and immunocompromised people or animals can contract serious, life-threatening diseases. Toxoplasmosis is caused by the reactivation of a latent infection in immunocompromised persons, causing a headache, hemiparesis, reflex abnormalities, convulsions, disorientation, and drowsiness. Toxoplasmosis can also cause serious illness in people who have basic or acquired deficits in T cell activity, such as patients with Systemic Lupus Erythematosus who are on immunosuppressive medicines[1]. As a result, T. gondii infects autoimmune patients, such as those with SLE.

SLE, or systemic lupus erythematosus, is a chronic inflammatory illness that affects nearly every organ system. The disease progresses in a "predictably unexpected" manner, with episodic flares of varying severity and clinical symptoms. End-organ damage might result from uncontrolled illness. In about 15% of instances, the onset is during childhood. Although SLE is commonly associated with young adult women, it can affect children of any age and gender[2].

A long-acting cytokine called interleukin-17 (IL-17) is present in epithelia, notably the mucosa of the stomach[3]. IL-17RA, its primary receptor, is present in immunological, endothelial, and epithelial cells[4]. The immune response to bacteria and fungus depends on IL-17. IL-17 has pro-inflammatory properties due to its capacity to enhance the secretion of chemokines that attract monocytes and neutrophils, such as IL-8, monocyte chemoattractant protein-1 (MCP-1), and growth related oncogene protein[5]. Additionally, the frequency of IL-17-producing T cells in the blood is higher in SLE patients. IL-17's effects on other cell types, in addition to its direct pro-inflammatory activity, may have a role in SLE pathogenesis. Peripheral blood mononuclear cells from lupus nephritis patients produced more total IgG, anti-dsDNA IgG, and IL-6 when grown in the presence of IL-17. As a result, it is suggested that TH17 cell production is preferred in SLE

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patients. Despite this, no specific research has been conducted. IL-17 is also produced by cells other than CD4 T cells, with DN T cells being the primary producers in SLE[6]. From a theoretical standpoint, TH17 cells can grow well under the conditions of SLE. IL-2, a cytokine that promotes the formation of regulatory T cells while suppressing the growth of TH17 cells, is produced at abnormally low levels by T cells from SLE patients [7].This might be a major contributing factor in people with SLE who have circulating immune complexes containing nucleic acids and an enhanced TH17 response.

Material and method

Between October 2020 and February 2021, 250 blood samples were collected from the study groups, from both genders (128 female and 78 male), with ages ranging from 16 to 53 years (100 sample of SLE and Toxoplasma infected patient, 50 sample of SLE infected patient, 50 sample of Toxoplasma, 50 sample of healthy person as control group). Patients from Baghdad Teaching Hospital and Al-Elwiya Educational Hospital, as well as several outpatient clinics, provided samples.

An information sheet that covers various information was created and produced prior to the collection of blood samples from each study subject. Each participant in this study had five milliliters of venous blood collected from their redial vein using disposable syringes. The Gel and Clot activator tube was used to collect each blood sample. The sera were then divided among three Eppendorf tubes using micropipettes and stored at - 20 ºC after a ten-minute centrifugation at 3000 rpm.

Serology

Enzyme linked Immunosorbent Assay (ELISA) kit (Elabscience, USA) was used for detection specific anti-Toxoplasma IgG and IgM antibodies in the sera of all subjects according to the manufacturer's instructions. To determine Interleukin-17 (IL-17) [Human Enzyme Immunoassay (Elabscience) , USA was used in all subjects sera according to the manufactures instructions [8]

Statistical Analysis

To identify the impact of various factors on study parameters, the Statistical Analysis System- SAS (2012) application was employed. In this study, a significant comparison of means was made using the least significant difference (LSD) test (ANOVA). P values less than 0.01 were regarded as statistically significant.

Results

The presence of acute toxoplasmosis characterized by the presence of positive IgG antibodies in different group. This table show highly significand differences $p \leq 0.01$ between studied groups (table1).

Table 1: Comparison of IgG and IgM levels between several groups

Group	Mean ± SE of IgG	Mean ± SE of IgM
SLE+Toxo	0.560 ± 0.03	0.451 ± 0.06
Toxo	0.390 ± 0.02	0.575 ± 0.06
LSD value	0.079 **	0.204 NS
P-value	0.0001	0.217
	Means having with the different letters in same column differed significantly. ** ($P \leq 0.01$).	Non-Significant.

The presence of positive anti- *T. gondii* IgG antibodies is like a marker of lifetime exposure to toxoplasmosis. The results in this study were shown that seropositive anti-*T. Gondii* antibody IgG result was group A (41%), while the seronegative (7), group C (50%) Table 2.

Table 2: The distribution percentage of studied sample infected with toxoplasmosis anti-IgG

IgG	A	B	C	D
TOXO(+)	41	0	50	0
TOXO(-)	7	50	0	50

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The seropositive anti- *T. gondii* antibody IgM was (4%) and the seronegative was (42%). As demonstrated in table 3, statistical analysis revealed very significant differences (P0.01) between the groups under investigation.

Table 3: The distribution percentage of studied sample infected with toxoplasmosis anti-IgM

IgM	A	B	C	D
TOXO(+)	4	0	3	0
TOXO(-)	42	50	47	50

This table Show highly significand differences p≤0.01 between studied groups which were group A (151.87 ± 5.99), group B (137.63 ± 6.45), group C (99.60 ± 8.28), group D (64.43 ± 11.81) represented, as show in table (4).

Table 4: Comparison of IL-17 levels between several groups

Group	Mean ± SE of IL-17 (pg/mL)
SLE+Toxo	151.87 ± 5.99
SLE	137.63 ± 6.45
Toxo	99.60 ± 8.28
Healthy	64.43 ± 11.81
LSD value	22.532 **
P-value	0.0001
Means having with the different letters in same column differed significantly ** (P≤0.01).	

Discussions

Toxoplasmosis became more common after Iraq's occupation, with infection rates exceeding 40% compared to 2% in the 1980s[9]. In 2016, there were 335 toxoplasma patients throughout all of Iraq's governorates (Saheb, 2018). The frequency of toxoplasmosis varies across Iraq due to a number of factors, including regional climate and cultural customs[10]. A past-acquired chronic latent infection is associated with high levels of IgG and a lack of IgM antibodies [11].

Were consistent with [12]and were similar to [13]On the other hand, the findings of [14], [15]This study's findings are based on the hypothesis that samples become infected as a result of biological behavior dealing with raw meat, undercooked meat, unwashed vegetables, farming work (during daily activity, cats and other animals are in closer proximity), physiology of humans that may clarify some of them exposed to oxidative stress that causes the opportunistic parasite to infect them, and the immune system of the samples may vary in its resistance to infection due to age, gender.

The presence of positive anti- T. gondii IgM antibodies, as shown in table 3, Indicates the presence of acute toxoplasmosis. This study shown an agreement with[16], [17]on the other hand a disagreement with study results of[18].

The current study looked at the cytokine profile in SLE patients with latent toxoplasmosis infection. The observed rise in IFN- in the toxoplasmosis infected groups (A) could be related to the cytokine's participation in *Toxoplasma* infection confrontation. T cells that produce IL-17 are more common in SLE patients[19], [20],[6], SLE patients produce more IL-17 than healthy individuals. Increased IL-17 levels are probably responsible for drawing immune cells (such as neutrophils and T cells) to the target organs and activating them there, increasing the immunological response. Patients with SLE have the perfect immunological milieu for the development of IL-17-producing T cells. The resulting IL-17 is anticipated to have wide-ranging effects on the immune system, including B cell activation [7].

Therefore, it is believed that individuals with SLE tend to produce more TH17 cells than normal. This hasn't, however, received a direct response. Any study should take this into account. Additionally, key IL-17

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producers are cells other than CD4 T cells, in particular. This cytokine is produced in large quantities by SLE and DN T cells[19]

The SLE environment is ideal for the development of TH17 cells from a theoretical standpoint. T cells from SLE patients produce abnormally low levels of IL-2 (Wong *et al.*, 2000), a cytokine that inhibits the development of TH17 cells and promotes the development of regulatory T cells[6],[21], Furthermore, cells obtained from SLE patients produce more inflammatory cytokines such IL-6 and IL-21[6]. After activation with TLR7, plasmacytoid dendritic cells can drive CD4 T cells to become TH17 cells [20].

Future research will need to pinpoint the particular pathways by which IL-17 contributes to SLE pathogenesis.

Conclusion

This study suggests that SLE patients should undergo routine toxoplasma screening since T. gondii infection is more common in SLE patients with higher levels of IL-17. To prevent the likelihood of severe toxoplasmosis, clinicians should be more cautious while dealing with this patient population.

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