Effect of mixed infection of toxoplasmosis and Cytomegalovirus on Interleukin 17 levels in pregnant women in Wasit Governorate

Amenah hussein chichan AL-Asadi, Abdul Kareem Aakool Rabeea AL-Tamemy and Alaa Ali Matrood Al-khafaji

Department of Biology, College of Science, Wasit University.

Abstract

Objective: ***Toxoplasma gondii, cytomegalovirus*** **(CMV)** are the most frequent causative factors of congenital infections globally. While these agents cause asymptomatic or mild infections in pregnant women, primary infections occurring due to the agents crossing the placenta barrier in early pregnancy may cause congenital malformations, intrauterine growth retardation, spontaneous abortions, premature birth and fetal death.

Methods : The study was conducted in Wasit province, and samples were collected from different regions of Wasit Governorate, from Al-Zahra Teaching Hospital, AL- Kut Hospital for Gynecology obstetric and pediatrics, Al haj jalal Hospital, Martyr Dr. Fayrouz General Hospital and some of the private clinics, during the period from October 2021 to February 2022. There is 440 specimens of venous blood were collected from pregnant women suspected infection with toxoplasmosis , cytomegalovirus and both. Blood samples were collected from pregnant women were tested by Enzyme Linked Immune Sorbent Assay (ELISA).

Result: from 440 samples 415 positive the results refer to highest levels of IgM 15 (3.6%) appear in Al-Kut center in cases of both infection (toxoplasmosis and CMV) and lowest 0% in Badrha and Al-Hay city, whereas the highest levels of IgG recorded 108 (26%) also in Al-Kut center cases of both infection (toxoplasmosis and CMV) but the lowest levels recorded in Al-Hay city. The total number 415 women infected with different pathogens (*Toxoplasma gondii , cytomegalovirus* and both) there are 117 had history of abortion . The study found that the highest concentration of interleukin- 17 in women with acute toxoplasmosis (anti-Toxo IgM 78.42 ng\L), another hand the lowest concentration of interleukin-17 was in chronic Cytomegalovirus infection (CMV-IgG 40.62 ng\L) than control group (38.18 ng\L).

Conclusions

The pregnant women infected with toxoplasmosis are more at risk of miscarriage than other infected pregnant. Most cases of Recurrent Spontaneous Abortion occur in women who have a combined infection for both Toxoplasma and CMV. The highest level of interleukin-17 occurs in pregnant with acute toxoplasmosis, while it decreases in pregnant women with chronic infection with CMV

Key words ***Toxoplasmosis*** **,** ***Cytomegalovirus*****, combined infection, IL-17, wasit province**

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Introduction

Toxoplasma gondii: One of the most prevalent parasite illnesses affecting humans and warm-blooded species. It is spread globally, and 30% of individuals are affected globally. .The prevalence of T. gondii infection can be affected by some factors, such as hot and humid climates, dietary and cultural habits, health conditions, and socioeconomic status. **(Sadeghi Dehkordi *et al*., 2022).** It is intracellular parasite can it crosses the placenta, affects the health of the fetus, and is thought to cause convulsions, mental retardation, hydrocephaly retinochoroiditis, and even death to the fetus in pregnant women (**Weiss & Kim., 2011**).

According to **Peyron *et al*. (2011)**, the age of gestation has a significant impact on the likelihood and severity of symptoms as well as congenital infection. Early toxoplasmosis diagnosis and treatment of prenatal and maternal toxoplasmosis were extremely helpful in preventing complications; according to reports, the majority of afflicted newborns were mostly asymptomatic at birth, and after a few years, vision impairment was also noted.

Cytomegalovirus: A double-stranded DNA virus it can cause a variety of illnesses in people **(Griffiths, *et al*., 2015; Collins-McMillen, D., *et al*., 2018)**. It is circulates worldwide and is endemic in the human population without seasonal variation **(Goodrum, 2016; Kim and Lee., 2018).** The herpesvirus family, often known as the herpesviridae or human herpesvirus-5 (HHV-5), includes the human cytomegalovirus (HCMV), which gets its name from the infected cells' distinctive intranuclear inclusions that have a

cytomegalic appearance **(Kotton *et al*., 2018; Fakhreddine *et al*., 2019**). In healthy persons, HCMV infection may not cause any symptoms, but in immunocompromised patients, it can be fatal **(Pass and Arav-Boger, 2018; Martí-Carreras and Maes, 2019).** It is a widely disseminated virus, and in immunocompromised individuals with congenital cytomegalovirus (cCMV) illness, symptoms can range from mild to severe end-organ failure **(Ngai *et al*., 2018; Mozaffar *et al*., 2018).** It is the most common etiological agent for viral intrauterine, and congenital infections recently in the world (**Van Zuylen *et al.,* 2014).**

Materials and Methods

The study was conducted in Wasit province, and samples were collected from different regions of Wasit Governorate, from Al-Zahra Teaching Hospital, , AL- Kut Hospital for Gynecology obstetric and pediatrics, Al haj jalal Hospital, Martyr Dr. Fayrouz General Hospital and some of the private clinics, during the period from October 2021 to February 2022. There is 440 specimens of the blood was taken from pregnant women's veins. Suspected infection with toxoplasmosis and cytomegalovirus and both. The women's venous blood (5 ml) was aseptically drawn from their veins, transferred to (a gel tube), allowed to coagulate, then retract and centrifuged at 5000 R\M for five minutes. The acquired serum was divided and refrozen until utilised to determine Toxoplasmosis, cytomegalovirus; Serum assays were carried out using ELISA, and IL-17 level was measured by ELISA kit (Human IL-17/ Shanghai YL Biont, China) in all recruited pregnant women according to the manufacturer's instruction.

Statistical Analysis

The values of the parameters are given in terms of mean and standard error and differences between means have been assessed by one-way analysis of variance (ANOVA) least significant difference

(LSD) using the computer program Statistical Program for Social Science 26 (SPSS 26) discovery version 2015. The difference was considered significant at probability value was equal for less than ($p \leq 0.05$).

Results and Discussion

Out of a total of 440 samples collected, 25 were negative and 415 were positive from different regions

2.4. Interleukin 17 levels in women infected with toxoplasmosis

In this investigation, patients with serological evidence of acute *T.gondii* infection had IL-17 concentration levels that were statistically substantially greater than those of healthy pregnant women. The mean blood level of IL-17 in all *T.gondii*-infected pregnant women was 64.99 ng/L, and it was 78.42 ng/L and 60.51 ng/L in the acute and chronic phases of the infection in those pregnant women who had positive *T.gondii* IgM and IgG tests, respectively. The mean blood concentration of IL-17 in healthy women (control group) was (38.18 ng/L) ($P < 0.005$) substantially higher than the mean in the group with positive *T.gondii* IgM antibodies. The early rise in IL-17 serum levels in the current study are consistent with the findings of other researchers, including **Gazzinelli, *et al*. (1993)**, who discovered that IL-17 levels have been observed to rise early in the course of toxoplasmosis. Another researcher discovered that IL-17 was associated with neutrophil growth and early recruitment, both of which are necessary for the early phases of infection to remove the parasites (**Kelly *et al*., 2005).**

Evangelista, *et al*., (2021) findings indicate that the

activation of an inflammatory response to infection by *T. gondii* and suggest that increased production of IL-17 may be a protective factor against infection of the fetus. **Hussein, Talib. W. *et al*., 2022** in Baghdad reported the level of IL-17 increased significantly in patients groups in comparison with healthy control ,infected women (3.26±1.69 pg/ml Mean ±SD) , Healthy Control (1.61±0. 69 pg/ml Mean ± SD). The significant increasing level of IL-17 secreted from Th17 cells. However, a variety of immune cells including CD8+ and NK cells. Also secrete IL17 provides innate immunity from the recruitment of neutrophils which make the host resistant against *T. gondii* infection.

The results of IL-17A levels that reported by **Baqer, Noor N., *et al*., (2021)** in Bagdad, demonstrate statistically significant differences in recurrent abortion (6.45 ± 0.960 pg\ ml p= 0.0015), and recurrent abortion with toxoplasmosis (6.584 ± 0.8538 pg/ ml p= 0.0005) comparing with healthy (4.284 ± 0.7275 pg/ml) and pregnant women (5.029 ± 1.235 0.1843 pg/ ml) with probability ($p < 0.05$).

Evangelista, *et al*., (2021) in Brazil recorded, significantly high levels of IL-17A in the group with acute toxoplasmosis (202.0 ± 24.80 pg/ mL) compared to the group in the chronic phases(12.96 ± 6.039 pg/mL), and to the uninfected group (5.541 ± 2.002 pg/mL) ($p<0.05$). Additionally , the levels of IL-17A in pregnant women with chronic disease were higher than in uninfected pregnant women , although not significant .

2.6. Interleukin 17 levels in women infected with both pathogen toxoplasmosis and *CMV*

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All pregnant women who had both infections had an average blood level of IL-17 of 45.84 ng/L. However, in healthy women the mean was (38.18 ng/L), concentrations were slightly higher. Whereas the mean of IL-17 in acute and chronic phase with both infection with positive both IgM, IgG antibodies was (47.92, 44.11 ng/L) respectively.

Arnaud, S. *et al*., (2015) discuss some factors that effect on severity and development of Uveitis (potentially blinding inflammatory disease) they suggested Interleukin 1β (IL-1β) levels were markedly increased in viral uveitis, as were IL-10 levels, whereas IL-17A levels were augmented in toxoplasmic uveitis. Interleukin 17 (IL-17)-producing Th17 cells and T regulatory cells; Th17 cells represent a subset separate from Th1 and Th2 cells, with distinct effector functions. Numerous studies have confirmed the central role of Th17-type cytokines in autoimmune pathology **(Weaver CT *et al*., 2006; Amadi-Obi A. *et al*., 2007).** A pathogenic role for local IL-17A in ocular toxoplasmosis was demonstrated in a recent study by **Sauer, A*. et al*., (2012).**

In immunocompetent individuals, toxoplasmosis is the most frequent cause of posterior uveitis. The requirement of limiting both parasite multiplication and tissue destruction suggests that the balance between T-helper (Th) 17 and T-regulatory cells is an important factor in toxoplasmosis-induced retinal and other tissues damage **(Sauer, A*. et al*., 2012).**

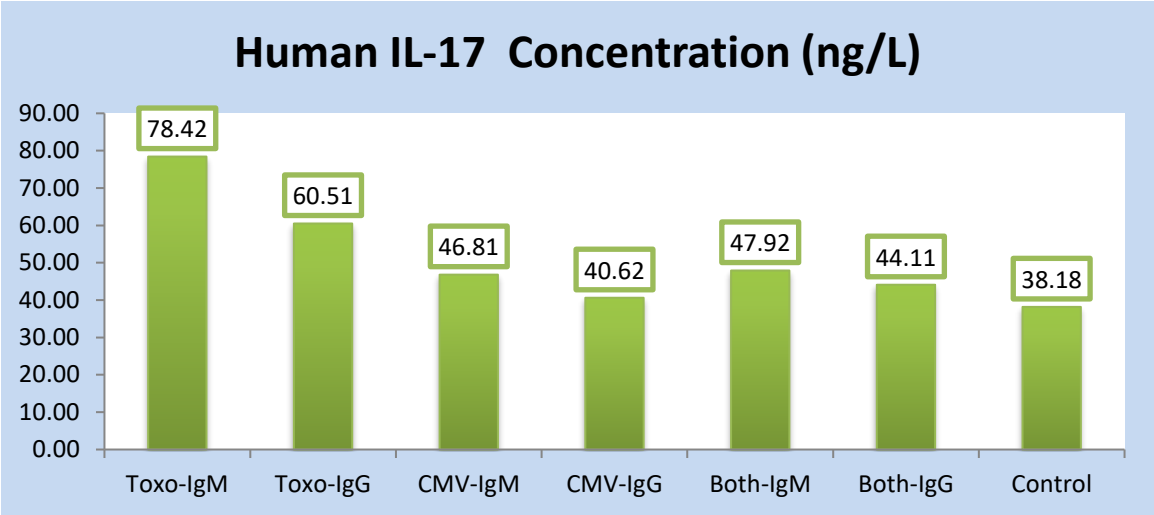

Figure (3.6) Mean Concentration (ng/L) of IL17 in all causes.

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