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Role of Some Cytokines in Pathogenicity of Toxoplasmosis in Aborted Women in Karbala,Iraq

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Abstract

210 blood samples were collected for pregnant women who aborted with toxoplasmosis and those who aborted for other reasons during the first trimester of pregnancy at the Obstetrics and Gynecology Teaching Hospital in the city of Karbala during the period 7/1/2021 until 2/22/2023. The required information was recorded according to a special questionnaire form prepared in advance. For this purpose, the results of the rapid examination, RAPID TEST, out of 210 aborted women, showed that 60 of them were infected with toxoplasmosis, a percentage of 28.5%, while 150 women aborted for other reasons, out of 210 aborted women, a percentage of 71.4%, were negative (serum) and not infected with *Toxoplasma gondii*.The results of the examination of immunological indicators showed that there was a significant increase in TNF-α cytokinetic concentrations in patients aborted with toxoplasmosis 13.18±3.49 pg/ml compared with the mean and standard error 8.45± 1.89 and 4.18±0.83 for each of the patients aborted for reasons Other women control.The results did not record any significant differences in the level of cytokinetic TGF-β for the patients who aborted with toxoplasmosis and the patients who aborted for other reasons, respectively 27.18±4.63 and 25.29±2.16 compared with the control group, as the rate was recorded at 4.66±0.78

Keywords: *Toxoplasma gondii*, Serology, TNF-α, TGF-β, Iraq

Introduction

Toxoplasmosis is one of the most common diseases in the world [1]. It has the ability to cause infections in humans and Animals [2].It is Intestinal coccidia and has been described for the first Time in the African rodent (*Ctenodactylus gundi*) 1908. It is form him that the name of species is derived gondii [3].The parasite needs hosts to complete its life cycle at though the sexual cycle and A sexual cycle occur in cats. Cats and the feline family are considered the final host. But the intermediate host is represented by all warm blood animals and birds [4].This parasite characterized by the three different stages. Each of which is the ability to cause infection in humans and animals these stages include the oocysts and tachyzoites and bradyzoites contained within the tissue cysts [5].Toxoplasmosis infects nearly 500 million people around the world and the seroprevalence varies from %5 is some countries to 90% in others. This depends on the age, geographical area, habits of populations eating fruits and vegetables that are not was well, and the infections rate rises in areas with a humid and warm climate and the infections is either

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acquired or the infections is congenital and is transmitted from the mother to the fetus through the placenta [6].Infection with the parasite may occur through the respiratory tract by in halation of the oocysts [7].After studies, there is an indication that there are other different ways of parasite transmission, including blood transfusion and organ transplantation [8].Studies have indicated that infection with parasitic diseases differs between male and females in terms of the effect of infection on mammals, including humans, and it also varies in age stages. The infection varies in females during pregnancy due to hormonal disturbances such as progesterone and estrogen, and it has an effect on the immune system during infection with parasitic [9].The parasite is transmitted from the mother to the fetus through the placenta causing fetal deformity or death. If the fetus is born, symptoms such as is hepato-splenomegaly and jaundice [10].When the mother is infected with the infection, it is transmitted to the fetus during pregnancy through the placenta, especially women who suffer from a weak immune system [11].Toxoplasmosis is a common disease between humans and animals [12].The toxoplasmosis parasite has three strains that infect the intermediate host. Namely type I, typeII and type III, these types differ according to severity of their diseases. The first type causes a fatal infection while the second and third types cause a non fatal infection [13].The second type of this strain causes ocular toxoplasmosis in human and most of the infection people have AIDS and carry the second type Strain As for the first Type strain, it causes congenital infections in humans and is rare in Animals [14].

Oocysts are produced inside the small intestinal of the final host of cats and the feline family inside these oocysts there are two sporangia sacs and each such contains four sporozoites that are long (8-2) micrometer and has a crescent shape [15] the oocyts has two layered membrane these oocyts produced by the process of sexual reproduction inside the host's intestine. They are characterized by their strong ability to resist unfavorable conditions. They remain for several months or several years in moist soil or water [16].This stage considered one of the most dangerous stages indicting both the final and intermediate hosts.They are peptides with low molecular weights ranging between 23-10 kilodaltons. Cytokinesis contributes to the regulator activation of first line defense cells including natural killer cells and phagocytic cells against foreign bodies that invade the body [17]. Cytokinesis includes lymphokinetices that are secreted from lymphocytes and monokines secreted by monounclear cells and interleukins secreted by leukocytes and chemokines produced by different types of cells such as endothelial cells and fibrillogens [18]. Interleukins are strong cytokines that appear in infections and it is a sign of immune system's response to the human body againstforeign bodies entering the body including parasitic and bacterial infections [19]. during pregnancy there are genetic modifications that encode some interleukin including that IL 1B they are anti inflammatorycytokines especially interleukin 10 it is directly related to toxoplasmosis infections [20] on the other hand normal pregnancy is characterized by an integrated or preferential immuneresponseand a regulatory T-cell response [21] with the productions of anti-inflammatory cytokines such as interleukin 10 and the conversion of growth factor beta TGFB by mother and fetal cells which represents trophoblast cell [22].It has an important role in pregnancy immunity especially with the presence of pathogens inside the cells such as *Toxoplasma gondii*.

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Materials and methods

The study was approved by the Research Committee of the Iraqi Ministry of Health, and this study was conducted from the beginning of July 2022 to the end of February 2023.210 pregnant women were taken during the first trimester of pregnancy at the Gynecology Educational Hospital in the city of Karbala, southwest of the capital, BaghdadComplete information was recorded in a special questionnaire form prepared in advance for this purpose, and after obtaining consent from the patient, venous blood was taken at a rate of 5 ml for each patient and left at room temperature for 10 to 15 minutes..Then it was placed in a centrifuge at 2500 rpm for 5 minutes to obtain the serum. The serum was stored in sterile Eppendorf tubes at 20 degrees Celsius until it was used for serum values for all patients.The initial examination was conducted using rapid chromatographic test strips by an American company, where positive cases were evaluated using antibodiesIgG and IgM .The serum was evaluated using enzyme-linked immunosorbentELISA.

Statistical analysis

The statistical analysis process was conducted for all the results of the current study using the statistical program known as the Statistical Package for the Social Sciences (SPSS) version 27. Chi-square tests and one-way analysis of variance were applied, and significant differences were determined at the probability level of 0.05 [23].

Results and discussion

The results of the current study showed that out of 210 aborted women, 60 of them were positive, at a rate of 28.57%, and were seropositive for toxoplasmosis by the rapid chromatographic test, while 150 women aborted for other reasons were recorded, at a rate of 71.43%, meaning they were seronegative and not infected with toxoplasmosis.

The current study agreed with a study conducted in the Iraqi city of Tikrit [23] where the total infection rate for positive antibodies was 38.7%. The results of the current study also agreed with[24], in the city of Sulaymaniyah, at a rate of 38.4%, and the study did not agree with[25]in the city of Tikrit, at a rate of 66%.The results of the current study also recorded a higher rate of infection with the IgG antibody than with the IgM antibody, and it also agreed with studies that converged with the results of the current study. The IgG antibody is one of the most important components involved in the humoral immune response in controlling the spread of the parasite. It begins to appear one to two weeks after infection, reaches its peak at 6 weeks, and then gradually decreases over 1-2 years. The persistence of the IgG antibody for a long period in the body gives it the ability to control parasite infection and prevent its spread[26]. Through Table No. 1, the results of the current study showed that the mean and standard error of the sera of aborted patients with toxoplasmosis in the TNFα cellular kinetics test (3.4±13.18 pg/ml) was significantly higher and the value was <=0.05 compared to the adjusted mean (1.89±8.45 pg/ml). ml) and (0.83±418 pg/ml) for both patients who aborted for other reasons and controls, respectively.The results of the current study were close to the study conducted by [27] in which the group of infected patients reached (35.17±63.10) pg/ml, and the control group reached

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(0.42±34.96) pg/ml, and it differed from the results conducted in the city of Diyala by[28] which reached the rate for patients (128.98±0.50), (pg/ml) and the control group (40.4±7.9)

Recent studies have indicated that infection with the *Toxoplasma gondii* parasite suppresses the production of INF-ɣ in order to initiate the infection and it is believed that it is responsible for producing the acute inflammatory response by activating the anti-microbial activity of infected macrophage cells by stimulating the production of INF-ɣ from killer cells. Naturally, TNF-α tolerance synergistically with INF-ɣ develop resistance against *Toxoplasma gondii* and thus play an important and crucial role in protective immunity against toxoplasmosis[29]. TNF-α is considered a cytokinetic immune response. It is produced by macrophages, lymphocytes, basophils, and monocytes. It stimulates inflammatory cytokines of the first type, IL-12. The TNF-α response is a major event in initiating immunity against *Toxoplasma gondii*[30].

The results of the current study differed from a study conducted in the city of Mosul[29]as the group of people infected with toxoplasmosis reached 98.09±7.3) (pg/ml) and the control group 90.5±1.9) pg/ml. It has been proven that cytokinetic TNF-α affects the synthesis of hormones, the formation and differentiation of the placenta, the development of the fetus, and the formation of steroids, and it has a role It is also important in the birth process and has been proven to have the ability to terminate pregnancy[31].Through Table No. 2, it was observed from the results of the current study that a significant increase in the average TGF-β for patients who aborted with toxoplasmosis compared to the rate for patients who aborted for other reasons, and through statistical analysis, at a probability level (P = 0.05), while the control group, healthy patients not infected with toxoplasmosis, decreased.The results of the current study agreed with the researcher [32]. TGF-β levels are high in people infected with toxoplasmosis, and it is considered a vital indicator of the effect of toxoplasmosis during pregnancy.Another study was conducted on immunodeficient laboratory mice infected with toxoplasmosis, and the results of the study showed that TGF-β plays an important role in the resistance represented by TCELL T cells by preventing or producing IL-12 and IFN-ɣ from natural killer cells through An increase in the secretion of TGF-β levels [33]. Despite the role of TGF-β in regulating T cells in normal pregnant patients, the results of the current study do not agree with the results reached by the researcher[34] who proved The levels of TGF-β decreased in abortion in female laboratory mice, and its action was enhanced by giving a dose of TGF-β cells, as it prevented the occurrence of spontaneous abortion in laboratory mice.This cytokinesis has a crucial role in regulating the immune response by stimulating regulatory T cells to reduce inflammation. Cytokinesis is anti-inflammatory and alters immune responses. The relationship between TGF-β and immunity against *Toxoplasma gondii* is still not fully understood[35].

Table 1. Average level of TNF-α in the serum of abortion patients and control women

Statistical differences	Lower value	Higher value	Standard error	Mean	No.	Groups TNF-α

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A	14.25	5.15	3.49	13.18	60	**Aborted women due to toxoxplasmosis**
B	11.38	3.48	1.89	8.45	150	**Aborted women due to another causes**
C	6.67	1.81	0.83	4.18	30	**Control**

Significance test using Dunkun equation

Different letters indicate a significant difference (probability ≤0.05) between the rates, while similar letters indicate no significant difference (probability >0.05) between the equations.

Table 2. represents the mean and standard error of interleukin TGF-β concentration for patients aborted with toxoplasmosis.

Statistical differences	**Lower value**	**Higher value**	**Standard error**	**Mean**	**No.**	**Groups TGF-β**
A	5.15	14.25	4.63	27.18	60	**Aborted women due to toxoxplasmosis**
A	3.48	11.38	2.16	25.29	150	**Aborted women due to another causes**
B	1.81	6.67	0.78	4.66	30	**Control**

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