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Study levels of PDL-1, IL-10 and TGF-β in Patients with Toxoplasmosis

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ABSTRACT

Aim of study: Determine the relationship between the parasitic infection of *T. gondii* and Programmed cell death-1 (PD-1), TGF- ß and IL-10 during abortion.
Materials/Methods: One hundred consecutive samples after abortion were collected. The placental tissue samples were put in formalin for immunohistochemistry technique**.**
Result the result of this study reveals that Residence did not have a relation with the presence or absence of Toxoplasmosis (P>0.05), age was significantly different between Toxoplasmosis groups (P<0.05), Number of abortions was not significantly different between the Toxoplasmosis group (P>0.05), PDL-1, IL-10, and TGF-β levels and their relationship during infection is significant (P<0.05).Conclusion the PDL-1, IL-10, and TGF-β levels could be a candidate as a biomarker for the pathological effect of *Toxoplasma.gondiin* during pregnancy.
***Keywords*:** Toxoplasma gondiin, PDL-1, IL-10, and TGF-β

INTRODUCTION

Toxoplasma.gondii is a protozoan eukaryotic parasite that can enter the body host as an obligate intracellular parasite and causes toxoplasmosis infection, it has the ability to cause latent infection in the host tissue such as cardiac muscle, skeletal muscles, or the central nervous system(Mendez and Koshy, 2017)The definitive host is wild felids and domestic. It has a variety of intermediate hosts mostly warm-blooded animals. Theinfections have been notified on all continents and in mundane and aquatic environments. The resistance of the oocyst wall permits the distribution of *T. gondii* within watersheds and ecosystems, and long-term constancy in several foods (Shapiro et al., 2019).

The life cycle begins when Toxoplasma enters the definitive host, mostly cats, after ingested tissue cysts, bradyzoites release into the cat's intestinal, and then divided within the schizogony process to form male and female gametes and form a zygote. The oocyte shed from the cat's intestine and ingested by a human through contaminated water or food. inside the human intestine cells, Toxoplasma undergoes asexual reproduction which called endodyogeny and results in the release of what symbolized by rapidly dividing motile tachyzoites and slowly dividing bradyzoites, the latter of which encyst in several tissues such as the brain and skeletal muscle, potentially insisting for the lifetime of the host(Milne et al., 2020)

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Toxoplasma.gondii has adverse outcomes during pregnancy especially in the first trimesters and leads to congenital toxoplasmosis it can be asymptomatic or can cause a flu-like sickness with low-grade fever, lymphadenopathy, and fatigue. Without regular prenatal screening procedures, it remains undiagnosed and untreated (Rostami et al., 2019).

The immunological strategies during infection constituents of the maternal-fetal interface through the first trimester of pregnancy wich listed by NK cells, macrophages, and T cells, whereas DCs and B cells are rare (Piccinni et al., 2015).

Tregs from mother increase during the pregnancy and prevent maternal rejection of the embryo in mice and human, Toxoplasmosis cause degrees in Tregs and lead to pregnancy miscarriage (Zhao et al., 2017).

Interferon-γ (IFN-γ) is a specific parasitic cytokine that prevents replication and improves its conversion from tachyzoite to bradyzoite stage but its inhibit trophoblast growth result in fetal death and abortion .elevation of IL-10 and TGF-β is an anti-inflammatory cytokine result in downregulation of inflammatory and reduce risk of abortion(El-Sherbini et al., 2019).

PD L1 has the ability to suppress T-cells activation during infection and reduce the severity of cytotoxic T-cells, eventually, up regulation of this protein can help in protecting the fetus and prevent abortion during infection(Schönrich and Raftery, 2019).

MATERIALS AND METHODS:

The type of the study is case control retrospective study. One hundred samples were collected from women suffering from abortion (50 diagnosed with Toxoplasmosis infection by the OnSiteToxo IgG/IgM Combo Rapid Test and confirm by IHC technique, 50 non-infected) who were attending in Women's Obstetrics & Gynecology Hospital in Karbala, Iraq. Were carried out for the period from April 2019- march 2020, The placental tissue samples were put in formalin IHC Under the supervision of Obstetrics & Gynecology specialists. Data collected from patient name, age gender, BMI, address, abortion history and if the patient have any of of autoimmune disease. The placenta is collected in three ways. First, after the curettage, the placental tissue is collected and put in formalin, second women came to the emergency room and suffering from abortion were treated with mifepristone and misoprostol or oxytocin to induce abortion, and then the is placenta collection, The third way is a ready-made block from laboratories for aborted women. All patients' ages ranged between 15 -45 years.

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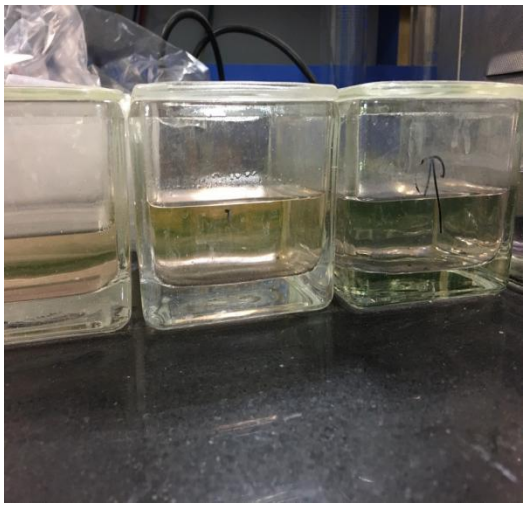

RESULTS

One hundred pregnant females were included in this study for the presence of Toxoplasmosis. Fifty cases were positive and fifty cases were negative.Demographic characteristics of the cases are presented in tables (1).

Table (1) displays the means of the patient's demographic characteristics in the patient groups. Residence did not have a relation with the presence or absence of Toxoplasmosis.Age was significantly different between the Toxoplasmosis group (higher age in Toxoplasmosis positive cases). While the number of abortions was not significantly different between the Toxoplasmosis group.The mean age of the positive cases was 29.72, age ranging (15-45). While Negative cases were 24.64, age ranging (14-40).

Table 1: Demographic characteristics of studied subjects according to Toxoplasmosis presence

		Toxoplasmosis					
		Positive		Negative		Subtotal	
		Count	%	Count	%	Count	%
Infectious disease	Yes	0	0.0%	0	0.0%	0	0.0%
	No	50	100.0%	50	100.0%	100	100.0%
Auto immune disease	Yes	0	0.0%	0	0.0%	0	0.0%
	No	50	100.0%	50	100.0%	100	100.0%
Residence	Rural	38	76.0%	37	74.0%	75	100.0%
	Urban	12	24.0%	13	26.0%	25	100.0%
Chorionic villi	Present	50	100.0%	50	100.0%	100	100.0%
	Absent	0	0.0%	0	0.0%	0	0.0%
Pregnancy	Early	50	100.0%	50	100.0%	100	100.0%
	Late	0	0.0%	0	0.0%	0	0.0%

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	Mean	SD	Range	Mean	SD	Range
Age	29.72	8.49	15-45	24.64	6.51	14-40
Number of abortions	2.04	0.90	1-4	1.76	1.10	1-7

Residence comparison done using Chi square test. Age and Number of abortions were studied using Student's t-test. $P<0.05$ was considered significant

Relation of the studied markers with the presence of Toxoplasmosis is presented in Table 2.TGF-β, PDL-1, and IL-10 marker proportions were a high significantly different between Toxoplasmosis groups $P<0.0005$.

TGF-β was found 25 (50.0%) samples positive proportion in Positive Toxoplasmosis female and 50 (100.0%) of Negative Toxoplasmosis female the staining samples was less than 1. While in 51-75% staining the sample in Positive Toxoplasmosis female was strongly positive in 4(8.0%) sample and in Negative Toxoplasmosis was less than one (0.0%).

PDL-1 was found in 27(54.0%) samples in Positive Toxoplasmosis females and 50 (100.0%) of Negative Toxoplasmosis with the staining less than 1. While in 51-75% staining the sample in Positive Toxoplasmosis was 4(8.0%) and the sample in Negative Toxoplasmosis was less than one (0.0%).

IL-10 was found in 26 (52.0%) samples in Positive Toxoplasmosis females as and 50 (100.0%) samples in Negative Toxoplasmosis the staining sample less than 1. While in 51-75% as very strong staining of the sample in Positive Toxoplasmosis was in 4(8.0%).

Table 2: The relation between TGF-β, PDL-1 and IL-10 intensity and proportions in Toxoplasmosis groups

		Toxoplasmosis					
		Positive		Negative		Total	
		Count	%	Count	%	Count	%
TGF-B	Less than one cell	25	50.0%	50	100.0%	75	75.0%
	1-10%	16	32.0%	0	0.0%	16	16.0%
	11-30%	3	6.0%	0	0.0%	3	3.0%
	31-50%	2	4.0%	0	0.0%	2	2.0%
	51-75	4	8.0%	0	0.0%	4	4.0%
PDL-1	Less than one cell	27	54.0%	50	100.0%	77	77.0%
	1-10%	12	24.0%	0	0.0%	12	12.0%

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	11-30%	4	8.0%	0	0.0%	4	4.0%
	31-50%	3	6.0%	0	0.0%	3	3.0%
	51-75	4	8.0%	0	0.0%	4	4.0%
IL-10	Less than one cell	26	52.0%	50	100.0%	76	76.0%
	1-10%	12	24.0%	0	0.0%	12	12.0%
	11-30%	7	14.0%	0	0.0%	7	7.0%
	31-50%	1	2.0%	0	0.0%	1	1.0%
	51-75	4	8.0%	0	0.0%	4	4.0%

TGF-B, PDL-1, and IL-10 marker proportions were significantly different between Toxoplasmosis groups (**P<0.0005 ***). And were studied usingChi-square test. P<0.05 was considered significant Table (3) shows the association of TGF-β and PDL-1 proportion .Was found a significant relation between TGF-β and PDL-1 proportion P<0.005.

The relation of TGF-β and PDL-1 proportion in Toxoplasmosis positive groups was found that the total number of No stain samples was 19 with almost no stain,12 samples 1-10%(weak), 1sample 11-30% (moderate), 1sample 31-50%(strong) and 3 51-75% (very strong).

Table 3: The relation of TGF-β and PDL-1 proportion in Toxoplasmosis positive samples.

TGF-B proportion		PDL-1 proportion					Total
		No stain	1-10%	11-30%	31-50%	51-75	
No stain	N	19	0	3	2	1	25
	%	76.0%	0.0%	12.0%	8.0%	4.0%	100.0%
1-10%	N	4	12	0	0	0	16
	%	25.0%	75.0%	0.0%	0.0%	0.0%	100.0%
11-30%	N	2	0	1	0	0	3
	%	66.7%	0.0%	33.3%	0.0%	0.0%	100.0%
31-50%	N	1	0	0	1	0	2
	%	50.0%	0.0%	0.0%	50.0%	0.0%	100.0%
51-75	N	1	0	0	0	3	4
	%	25.0%	0.0%	0.0%	0.0%	75.0%	100.0%
Total	N	27	12	4	3	4	50
	%	54.0%	24.0%	8.0%	6.0%	8.0%	100.0%

There is a significant relation between TGF-B and PDL-1 proportion (**P<0.005***).And were studied using Chi-square test.

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Table (4) shows the association of TGF-β and IL-10 proportion was found a significant relation between TGF-β and IL-10 proportion P<0.005.

The relation of TGF-β and IL-10 proportion in Toxoplasmosis positive groups was found that the total number of No stain samples was 19 with almost no stain,12 samples 1-10%(weak), 1sample 11-30% (moderate), 1sample 31-50%(strong) and 4 51-75% (very strong).

Table 4: The relation of TGF-β to IL-10 proportion in Toxoplasmosis positive subjects.

TGF-B proportion		IL-10 proportion					Total
		No stain	1-10%	11-30%	31-50%	51-75	
No stain	N	19	0	6	0	0	25
	%	76.0%	0.0%	24.0%	0.0%	0.0%	100.0%
1-10%	N	4	12	0	0	0	16
	%	25.0%	75.0%	0.0%	0.0%	0.0%	100.0%
11-30%	N	2	0	1	0	0	3
	%	66.7%	0.0%	33.3%	0.0%	0.0%	100.0%
31-50%	N	1	0	0	1	0	2
	%	50.0%	0.0%	0.0%	50.0%	0.0%	100.0%
51-75	N	0	0	0	0	4	4
	%	0.0%	0.0%	0.0%	0.0%	100.0%	100.0%
Total	N	26	12	7	1	4	50
	%	52.0%	24.0%	14.0%	2.0%	8.0%	100.0%

There is a significant relation between TGF-B and IL-10 proportion (**P<0.005***). Chi-square testused for the study.

Table (5) shows the association of PDL-1 and IL-10 proportion was found a significant relation between TGF-β and IL-10 proportion P<0.005.

The relation of PDL-1 and IL-10 proportion in Toxoplasmosis positive groups was found that the total number of No stain samples was 18 with almost no stain,11 samples 1-10%(weak), 1sample 11-30% (moderate), 0sample 31-50%(strong) and 3 51-75% (very strong).

Table 5: The relation between IL-10 to PDL-1 proportion in Toxoplasmosis positive samples

IL-10 proportion		PDL-1 proportion					Total
		No stain	1-10%	11-30%	31-50%	51-75	
No stain	N	18	1	3	3	1	26
	%	69.2%	3.8%	11.5%	11.5%	3.8%	100.0%
1-10%	N	1	11	0	0	0	12
	%	8.3%	91.7%	0.0%	0.0%	0.0%	100.0%
11-30%	N	6	0	1	0	0	7
	%	85.7%	0.0%	14.3%	0.0%	0.0%	100.0%

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31-50%	N	1	0	0	0	0	1
	%	100.0%	0.0%	0.0%	0.0%	0.0%	100.0%
51-75	N	1	0	0	0	3	4
	%	25.0%	0.0%	0.0%	0.0%	75.0%	100.0%
Total	N	27	12	4	3	4	50
	%	54.0%	24.0%	8.0%	6.0%	8.0%	100.0%

There is a significant relation between IL-10 and PDL-1 proportion (P<0.005). Chisquare testused for the study.

DISCUSSION

T. gondii Infection can result in adverse pregnancy consequences(Liu et al., 2018). Some researchers showed that the immune system secreted cytokines and lymphocytes maintain maternal tolerance to the stability of paternal alloantigens during normal pregnancy (Morelli et al., 2015).

Tregs additionally have a critical role in the subsistence of fetal-maternal tolerance throughout pregnancy (Huang, Chi and Qiao, 2020).Toxoplasmosis infection has significantly greater levels of abortion, bleeding of the placenta, and lower-weight fetuses (Wam et al., 2016).

In this study, the results showed that there is no clear and significant difference in the infections between pregnant women who live in rural areas and those who live in urban areas (P=0.713). The risk factors here are that women from urban areas have a higher education level and better income, which leads to high consumption of meat such as Beef, wild meat, and lamb from sources that have become multiple at the present time due to a large number of restaurants and also the spread of the raising of the cats at the present time as a representative of evolution without veterinary medical control for these animals, which makes pregnant women more exposed to infection and equal with pregnant women in rural areas, which risk factors in them In terms of the level of education and hygiene. This study finding is similar to the study done by WoyneshetGelaye and his co-workers, which indicate that the educational status and area have an insignificant association with T.gondii infection (Gelaye, Kebede and Hailu, 2015).

Study in Bobo-Dioulasso town shows being an urban citizen, high education level, and the consumption of meat compounds as potential risk factors with T. gondii infection (Bamba et al., 2017).

A recent study in Debre Tabor town, Ethiopia, explained that women who didn't educate were 5 times more prone to gain T. gondii infection than those who had the education of tertiary level (Agmas, Tesfaye and Koye, 2015).

This study also showed that there are significant differences in the risk of infection with toxoplasmosis infection according to age, as it was observed that the risk of infection for pregnant women increased with age (P=0.001).

A study conducted on pregnant women in the United States showed an increase in the incidence rate at older ages relative to the long duration of exposure time (Jones et al., 2017).

A study of risk factor suggests that women having any pet such as cats, and/or dogs were higher in the frequency of seropositive toxoplasmosis than those who don't

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have any pet. And this may explain the increase in T. gondiiseroprevalence in the younger age suggest that in some areas, the infection apparently transpired during youth due to high susceptibility to environmental conditions (Olariu et al., 2020).further study about toxoplasmosis incidence and risk factors showed that the infection can be positive in all ages but the elderly could be more susceptible because immunosuppression becomes more obvious with age(Wilking et al., 2016).

The number of miscarriages did not show any significant correlation as a risk factor for toxoplasmosis abortion. Another study of seroprevalence of toxoplasmosis shows that there was significantly more increased in women with a bad gestation and abortion history compared to those with no history. Our study shows a high prevalence rate in females with recurrent pregnancy loss (Rehman et al., 2020). In contrast to the study carried in the Kohat area of Khyber Pakhtunkhwa, which showed a seroprevalence of 14.4% with toxoplasma in pregnant women despite their previous history of recent abortion (Majid et al., 2016).

Our findings suggest the need to increase the educational level of pregnant women about the route of transmission of the infection and methods of prevention, as well as the need to increase veterinary and environmental control for household cats in addition to that, health control of restaurants and places of marketing meat.

These results may be caused by the number of samples and the long period between collecting one sample and another, and also by collecting samples from one place, due to the circumstances that occurred during the sample collection period from the demonstrations that occurred in Iraq and the subsequent spread of the Corona virus epidemic and the health measures that were followed during the crisis that led to stopping the search procedures for a while.

The present study revealed the levels of three important cytokines in immunological profile among aborted Iraqi females with toxoplasmosis. An elevation in levels of TGF-β, PDL-1, and IL-10 was observed in placental tissue that diagnosis by immunohistochemistry technique (IHC) and shown to be slightly elevated according to the negative control.

TGF-β shows a weak stain in about 32.0% of positive samples of pregnant women of middle age and has less number of abortion in the past, and it's very strong in about 8.0% associated with higher age and abortion number.

A previous study reported that the level of placental TGF-β level was decreased in mice including adverse pregnancy outcomes after Toxoplasmosis infection (Liu et al., 2014). Other study reported that TGF-β levels were raised in pregnant with acute T. gondii contagion in contrast to those of uninfected pregnant (Marchioro et al., 2018).

TGF-β1 was higher in females with anti-Toxoplasma antibody (Abdulkhaliq1, Mohammed2 and Abbas3, 2018).A higher level of TGF-β in a pregnant female with abortion, corresponded with normal pregnant women (Magdoud et al., 2013).

A study on the immune aspects during human and murine Leishmania.spp refers to that the parasites persist viable inside the parasitophorous after neutrophils endure apoptosis, these apoptotic neutrophils throughout infection are engulfed by macrophages, which induces an anti-inflammatory macrophage state and release of TGFβ (Scorza, Carvalho and Wilson, 2017).

This cytokine has a critical role during regulates the immune response through stimulating regulatory T cells to reduce inflammation, furthermore, TGF-β provokes the

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immunity responses by the development of Th17 and mucosal immunity; still, the correlation between TGF-β and immunity against T. gondii is not completely understood (Zare-Bidaki et al., 2016).

IL-10 level was increased significantly in aborted women with toxoplasmosis of the proportion of 24.0% as a weak stain also in middle age patient and very strong about 8.0% which relationship with recurrent miscarriage.

A recent study shows the rising level of IL-10 in patients with toxoplasmosis in contrast with healthy control may due to the ability of the parasite to improve TH2 cytokines including these was IL-10. Nevertheless, IL-10 is a strong antagonist to macrophages capability to kill microbes inside the cells, for example, T. gondii so, the presence of T. gondii will direct to an increase in the IL-10 (Mohamed, et al., 2018

A study of parasitic infection with malaria show low levels of IL-10 in the placenta and directly attributed to the event of low birth weight. The infection course the pathology change and reduction of the placental IL-10 (Fitri et al., 2015).

IL-10 has a role in keeping the fetus during pregnancy by suppression of Th1 cytokines production by such cells, its inhibiting INF-γ production and persistence of T. gondii in the tachyzoite stage and increase IL-4 to stimulate B-cell class switching to give IgE antibody, the antibody against the parasite. a study on IL-10 levels showed similar results in cases and control, and inadequate elevation of IL-10 levels is a normal consequence after the fetal loss because they are no longer needed for maintaining the fetus's life(Aldabagh et al., 2018).

PD L1 marker shows a significant increase in aborted women with toxoplasmosis compared with negative control, with about 24.0% as a weak, 14.0% moderate cell proportion and 8.0% as a very strong proportion which indicates to be associated with age and recurrent abortion history,

The variation in current result in positive and control may be due to a small sample number and duration of sample collection due to the hard circumstance of Iraq demonstrations and the epidemic of corona virus that synchronized with the time of collecting data and samples.

On another hand, a study on PDL1 role during pregnancy indicated that it plays a significant role in feto-maternal tolerance, deficiency of PDL1 results in the compromised outcome on pregnancy when thy examined adoptive transfer of Tregs, the main PDL-1 mediator tool, in mice in 2007 (Habicht et al., 2007) which an old study, there is a few or no study in such cytoplasm with toxoplasmosis inducing abortion in recent years.

A study found that PDL1 blockage improved fetal resorption and Tfr (t follicular) cells and it considers the fetal resorption rate and the confused immune tolerance status not only as a consequence of Tfr cell increase, but an effect of the imbalanced Th cell differentiation: in support ofTh17, Th1, and Tfh cells while against the expansion of Th2 and Treg cells (Zeng et al., 2020).

Study on infection with Lishmania.amazonensis (which is also an intracellular pathogen) shows that we observed that Lishmania.amazonensis improved PD-1 expression on both CD8+ and TCD4+ cells and PD-L1 on dendritic cells in mice (da Fonseca-Martins et al., 2019).

A recent study indicates the presence of PD-1 and PD-L1 was identified in a patient with diffuse cutaneous leishmaniasis generated by L. amazonensis, the monocytes

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expression of PD-L1 might have a role in CD4+ and CD8+ T-cell dysfunction (Barroso et al., 2018).

However, further studies should be carry out on PD L1,IL10 and TGF-β with abortion induced by *Toxoplasma.gondii* infection.

Its observed significant relation in the elevation of the TGF-β and PD L1 as seen in the IHC staining result, there was participation in 19 samples of each marker observed to be less than one proportion of staining cells (no stain), and 12 samples with a weak proportion, where the TGF-β shows positive result in 4 Various other patients, the result was 1 as moderate and strong as well as very strong in 3 samples. Also, TGF-β was moderately positive in additional 2 different patients, strong and very strong in 1 different patient, this finding point to the correlation between markers elevation during toxoplasmosis induced abortion in women.

There are no serious studies on the relationship between TGF-β and PD L1 and the effect of Toxoplasmosis infection in pregnant women immune system pregnant, a study on the effect of TGF-β on PDL1 in hepatocellular carcinoma cells shows that the TGF-β was capable of up-regulating PD-L1 expression in DCs in vitro in different manners (Song et al., 2014). As it is possible to correlate the results, assuming that DCs is present during any inflammation such as toxoplasmosis.

Study of the roles of the programmed death-1 (PD-1) receptor on lymphocytes and its ligand PD-L1 on APCs non-recovering cutaneous leishmaniasis indicate the infection inducing PD-L1 expression on dendritic cells and result in down regulating the immune response against infection when the patients treated with anti-PD-1 exposed significantly reduction in TGF-β production(da Fonseca-Martins et al., 2019).

Study of immune checkpoint during visceral leishmaniasis (VL) has further been identified that PD-1 interacts with PDL-1 lead to activation of CTLA-4(cytotoxic T-lymphocyte-associated protein 4) which is a protein aid in downregulates immune responses and elevated levels of TGFβ, as well as apoptosis of CD4+ T cells in murine VL (Kumar et al., 2017).

The result of the relation between the two markers shows a significant increase in both of them during toxoplasmosis infection ($P<0.005$*), there were weakly positive in the same 12 aborted women, even though the TGF-β were positive in other various 4 patients, also there was 1 patient showed a moderate and strong positive result in both TGF-β and IL-10 and 4 as very strong.

There were no recent study of the relationship between TGF-β and IL-10 levels with abortion in a female with toxoplasmosis infection, still, there are some studies about the roles of each during infection.

Study of feto-maternal tolerance during pregnancy indicates that the production of Treg cells and its elimination of fetal rejection is by the expression of large levels of TGF-β, interleukin IL-10(Alijotas-Reig, Llurba and Gris, 2014).

T regulatory cells provoke secretion of TGF-β and IL-10 that compromise immune response against the intracellular parasites. TGF-β induce the evolution of Th17 responses and produce

IL-17 and IL-10 cytokines demonstrate that balance among TGF-β/IL-10 inflammatory cytokines helpful for parasite dismissal with least tissue damage in cutaneous leishmaniasis(Abdoli, Maspi and Ghaffarifar, 2017).

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IL-10 and TGF-β were thought to be suppressing pro-inflammatory responses, and this was associated with high parasitemia, studies from mouse models of malaria suggest that IL-10 is needed to protect host tissue from inflammation, however, it can also improve the growth of parasites and correlated disease outcomes (Kumar, Ng and Engwerda, 2019).

More studies should be done on these markers and their role during toxoplasmosis and pregnancy tolerance, nonetheless, the genetic variation, sample numbers, and region may contribute and affect the result.

The result of the relation between the two markers shows a significant increase in both of them during toxoplasmosis infection ($P<0.005$), there were weakly positive in the same 11 aborted women and also there were 1 patient who showed a strong positive result in both markers and very strong in same 3 aborted women.

Unfortunately, there are few studies about links between PDL-1 and IL-10 as an immune check during infection and no serious studies about these link in aborted women with toxoplasmosis, most of the studies are about PDL-1 and its function during cancer and its therapy.

Blockade of the PD1/PDL-1 pathway through infections with pathogens such as Toxoplasma, Plasmodium, and leishmania returned exhausted CD8T and B cell immune responses, respectively, control the parasite reactivation, and limiting death in the chronically infected animals, in other hand IL-10-producing effector CD8and CD4 cells and Tregs, and by DCs, during the parasitic infection could defective parasite killing by macrophages at later stages of infection (Habib et al., 2018).

CD4+ T cell proliferation and, B cell clonal expansion and releasing of antibodies specific to Leishmaniasis correlate with a reduction in Surface expression of PD-1 on T cells plus PDL-1 receptor on B cells as well as macrophages. In dogs with leishmaniasis, CD4+ T cell proliferation was diminished as the disease progresses, engage with an increase in IL-10 and PD-1(Toepp and Petersen, 2020).

A study on alveolar echinococcosis immune checkpoint in mice of the role of PDL-1/PD-1 in immune control of parasite, which indicate that the There was a significant reduction of both CD4+, Foxp3+ and CD4+ IL-10+ recurrence in the spleen from primary alveolar echinococcosis in mice treated with anti-PD-L1(Wang et al., 2018).

More study should be occupied on each marker and its role in toxoplasma induced abortion and the links among it in order to understand the immune pathway, the genetic variation of each parasite, the sample size, and the resident may affect the results.

CONCLUSION

The PDL-1, IL-10, and TGF-β levels could be a candidate as a biomarker for the pathological effect of Toxoplasma gondiin during pregnancy.

Compliance with Ethical Standards

The authors declare that they have no conflict of interest.

The author declare that research involved human participants and consent was obtained.

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