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Relation of Some Immunological Markers (IL 4, 12 and 23) with Toxoplasmosis in Aborted Women

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Abstract

Background

Toxoplasma gondii is a major cause of abortion in pregnant women. Toxoplasmosis infection in the mother during pregnancy is frequently associated with transplacental transmission of the parasite to the fetus. The purpose of this study Aims of this study determine and compared the different concentrations level of interleukin (IL) 4, 12 &23 in patients with toxoplasmosis and control groups.

Materials and Methods

From September 2020 to May 2021, a case-control study was carried out in Thi-Qar province to estimate the role of Toxoplasmosis in the occurrence of abortion among pregnant women. The current study included 120 aborted women as well as 20 healthy women as controls (Non pregnant and have no clinical history of abortion). All of these cases involved only females of reproductive age (16-44 years). Toxo-IgM and Toxo-IgG antibodies were tested first with a latex agglutination test (LAT) to detect positive samples, followed by an Enzyme Linked Immunesorbent Assay (ELISA) to detect IgG and IgM antibodies in both groups. CUSABIO method for measuring human interferon (IFN-) and 2-human cluster of differentiation 4 (CD4) (USA)

Results

IL-12 value in a patient with IgM was (48.59) which is significantly higher than the control patient value (38.69). Also, IL12 value of patients with Toxo IgG (57.48) was significantly higher than the control patient. IL-23 values of a patient with Toxo- IgG, and Toxo- IgM were (77.92&57.92) respectively which is significantly higher than the control patient value (38.38). IL-4 value in a patient with Toxo- IgG was (35.83) and Toxo- IgM was (42.67) which is significantly higher than the control patient value (25.90).

Conclusion

The concentration level of IL-4, IL-23 & IL-12 were increased in each acute and chronic infection compared with the control group).

Keywords

Toxoplasma gondii, Abortion, IL-4, IL12, IL 23.

Toxoplasma gondii is the maximum common cause of abortion in pregnant women. Toxoplasmosis contamination within the mother at some stage in pregnancy is frequently associated with transplacental transmission of the parasite to the fetus (Dubey, 2020). This parasite has three essential genotypes (kinds I, II, and III), which vary in pathogenicity and occurrence in human beings. For example, the sort II genotype is accountable for most of the people of instances of congenital toxoplasmosis in Europe and the US of America (USA) (Hussain et al., 2017). Is an Apicomplexa phylum obligate parasite (Nyonda, 2021; Ali et al., 2019). Toxoplasmosis became a serious contamination caused by it (Sparvoli & Lebrun, 2021). The asexual degree happens in any heat-blooded species (intermediate host), inclusive of birds and diverse mammals, at the same time as the sexual level takes place in tom cats (definitive host) (Aghwan, 2010). The virulence elements of the parasite, the importance of the contamination dosage, the approach of infection, the kind of infection, and the individual's immunological situation all have an impact on the development of toxoplasmosis contamination (Jeffers et al., 2018; Sibley, 2017; Zhang et al., 2019). T. Gondii contamination reasons the production of many cytokines. IL-1 and TNF are produced by using activated macrophages. Exogenous IL-1 or IL-1 combined with TNF therapy turned into stated to beautify in vivo contamination resistance. Important cytokines generated after consist of IL-12, TNF, and IFN. The proliferation of NK cells, CD4 T cells, and CD8 T cells is sparked with the aid of the discharge of IL-12 through traditional DCs, macrophages, and pDCs (Mammari et al., 2019). *Aims of this study determine and compared the different concentrations level of (IL 4, IL 12, and IL 23) in patients with toxoplasmosis and control groups and also compared variables in acute and chronic, groups.*

Materials And Methods

Study design

From September 2020 to May 2021, a case-control study was carried out in Thi-Qar province to estimate the role of Toxoplasmosis in the occurrence of abortion among pregnant women. The current study included 120 aborted women and 20 healthy women who were not pregnant and had no clinical history of abortion. All of these cases involved only females between the ages of 16 and 44 years.

Samples processing

Five milliliters of human blood were collected from each subject (patients and controls) via vein using disposable syringes and transferred to sterilized test tubes and enabled to coagulate at room temperature for 30 min, the sample was separated by centrifugation at 3000 rpm for 15 minutes to obtain serum, Measurement of IFN γ, IL 12, and IL 23 ELISA method CUSABIO (USA).

Analytical Statistics

All data in this study are presented as mean ± standard deviation. The statistical analyses were performed using SPSS (version 25). Normally distributed continuous variables were compared using analysis of variance (ANOVA) and Pearson's correlation coefficients when calculated the Correlations. $P< 0.001$ statistically significant.

Results

The two groups distinguished themselves (acute and chronic groups) significantly from each other and the control group as shown in (Table 1).

Table 1: Comparison of IL-4 level of patient's groups with a control group.

Study groups	Interleukin-4 (pg/ml)		
	Mean	SD	P .value
Aborted with TOXO IgM	112.3	± 35.83	<0.001
Aborted with TOXO IgG	113.1	± 42.67	
Control	75.21	± 25.90	

Interleukin-12

The two groups showed highly significant differences compared to each other and to the control group as illustrated in Table 2.

Table 2: Comparison of interleukin-12 of patient's groups with a control group.

Study groups	Interleukin-12 (pg/ml)		
	Mean	SD	P .value
Aborted with TOXO IgM	48.59	± 14.01	<0.001
Aborted with TOXO IgG	57.48	± 14.60	
Control	38.69	± 10.82	

Interleukin-23

The aborted with TOXO IgM group mean (57.92± 33.55) and aborted with TOXO IgG group mean (77.57± 39.73) showed highly significant differences compared to the control group as in Table 3. .

Table 3: Comparison of interleukin-23 level of patient's groups with a control group.

Study groups	Interleukin-23 (pg/ml)		
	Mean	SD	P .value
Aborted with TOXO IgM	57.92	± 33.55	<0.001
Aborted with TOXO IgG	77.57	± 39.73	
Control	38.38	± 32.28	

Discussion

IL-4 immune response against Toxoplasma gondii is said to be dependent on an early innate response that appears to involve the sequential production of IL-12 by neutrophils, dendritic cells, and macrophages, which in turn stimulates NK cell IFN- production (Nickdel et al., 2004). According to research, IFN- is the primary immune response's protective mechanism against T. gondii. In multiple studies that mostly employed neutralizing antibodies, type-2 or regulatory cytokines like IL-4 and IL-10 that decrease type-1 responses were discovered to be counter-protective. In 1995, Villard et al.

IL-4 performs an ameliorative effect and lowers mortality during the early stages of a T. gondii

infection, when the confluence of rapidly proliferating tachyzoites and the immunological response that this causes can frequently end in host death. On the other hand, the same cytokine promotes parasite growth outside of cysts, which causes the emergence of severe necrotic brain lesions. These alternating protective and exacerbating effects, which decrease short-term mortality but increase long-term morbidity, may be attributed to two things: first, the potential need for various immunological conditions to control a parasite with multiple life cycle stages in a single host; and second, IL-4's capacity to directly and indirectly inhibit pro-inflammatory cytokine production and activity through its influence on Th2 expansion (Roberts *et al.*, 1996).

The present findings seem to be consistent with other research which found a significant difference between control and patients. The mean concentrations of IL-4 in patients with T. gondii were higher compared to control (El-Shazly *et al.,* 2005).Studies utilizing *Schistosoma mansoni* (Pedras-Vasconcelos *et al.*, 2001),and *Candida albicans* (Mencacci *et al.,* 1998),demonstrate that the absence of IL-4 significantly inhibits the development of Th1 responses. Indeed, IL-4 is a potent inducer of-12 p70 production by dendritic cells. Moreover, IL-4and IFN-γ together exhibits synergistic effects in increasing IL-12 p70 production.

Recently been demonstrated that during the early phase of L. major infection, IL-4 not only enhances IL-12 production but also promotes the development of a functional DC1 phenotype. However, IL-4 only instructs the development of TH1 responses when APCs are exposed to this cytokine during primary activation by innate stimuli (Nickdel *et al.*, 2004).

A possible explanation for these results may be that IL-4 production promotes activation of innate stimuli to enable the host to define against *T. gondii.*

According to Interleukin-12 level IL12 has been identified as an important cytokine for the regulation of protective immune responses to *T. gondii.*IL-12 is an important mediator of host defense during the acute phase infection (Khan *et al.,* 1994).Production of IL-12 is restricted to a subset of hematopoietic cells including macrophages, granulocytes, B cells, and dendritic cells, and is elicited by microbial stimuli or during interaction with T cells via CD40 ligation(Schade & Fischer, 2001). The central role played by IL-12 in resistance is dramatically highlighted by the extreme susceptibility of-12 knockout (KO) mice to T. gondii infection. IFN-producing Th1 cells and early NK cell IFN-production are both induced by IL-12 production. The capacity of IFN- to trigger anti-Toxoplasma effector molecules including the immunity-related GTPase (IRG) family and guanylate-binding proteins (GBP) that destroy the parasite's phorous vacuole housing intracellular tachyzoites is what finally controls the parasite (Yamamoto et al., 2012). In-depth research using mouse models has been done on the molecular and cellular mechanisms behind the recognition of T. gondii and the subsequent release of IL-12 in response. The role of the Toll-like receptor (TLR) adaptor protein MyD88 in inducing IL-12 and fostering host tolerance to Toxoplasma was recognized early on (Scanga et al., 2002). Macrophages and dendritic cells (DCs) are the major sources of both IL-12, which act on receptors primarily expressed by T cells, NK cells, and NKT cells.IL-12 is a key factor in the induction of T cell-dependent and independent activation of macrophages and natural killer (NK) cells, and it plays a central role in Th1 development(Ismail *et al.*, 2017).

The current study found that IL12 significant difference ($P<0.001$) in comparing infection TOXO IgM, TOXO IgG and control groups .These results are consistent with those of other studies and suggest that molecular mechanisms illustrating the evolutionary adaptation of Toxoplasma to actively trigger inflammatory cytokine production to promote host survival, parasite latency, and transmission(Mercer *et al.*, 2020; Schade & Fischer, 2001).What is surprising is that-12 is produced at later as in case Toxo IgG infection more than Toxo IgM this result supported by (Mercer *et al.*, 2020).

Normal macrophages require priming by IFN-gamma or TNF to produce IL-12 Therefore, other cells that can deliver IL-12 in the absence of IFN-gamma,(e.g. dendritic cells) probably initiate production of IFN-gamma during early infection. IFN-gamma in turn renders macrophages responsive for the parasite stimulus inducing IL-12, which further enhances IFN- production(Schade& Fischer, 2001).

According to Interleukin-4 level showed highly significant differences compared to each other and to

the control group, this study agreed with(Ham *et al.*, 2020; Lieberman *et al.*, 2004). Also, our finding is consistent with (Quan *et al.*, 2013) Given the structural and functional similarities between IL-12 and-23, it seems likely that IL-23 would also play a role in resistance to infection and the development of inflammation. This hypothesis is supported by recent studies that have established that IL-23 plays a role in the development of experimental autoimmune encephalomyelitis (Cua *et al.*, 2003)

Conclusion

In this study concluded that IL-12 value in a patient with IgM was which is significantly higher than the control patient value. Also, IL12 value of patients with Toxo IgG was significantly higher than the control patient. IL-23 values of a patient with Toxo- IgG, and Toxo- IgM were which is significantly higher than the control patient value. IL-4 value in a patient with Toxo- IgG was (35.83) and Toxo- IgM was (42.67) which is significantly higher than the control patient value.

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