Impact of latent toxoplasmosis on thyroid diseases during gestation

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Abstract

Toxoplasmosis is among the most widely diseases that distributed by the protozoan parasite *Toxoplasma gondii*. So in the case of pregnancy, latent toxoplasmosis is a risk factor which causes thyroid disease. The aim of the study was to determine the effect of latent toxoplasmosis on thyroid diseases during gestation. 214 blood samples were collected from pregnant women who admitted to different hospitals in Erbil governorate. ELISA technique was used for detecting *Toxoplasma* IgG antibody, as well as determining serum levels of thyroid hormone levels. Overall, 23.37% of tested samples were *Toxoplasma gondii* IgG seropositive. Latent toxoplasmosis has a positive correlation with thyroxin (T4) (p=0.026), however, no significant correlation was found with both thyroid stimulating hormone (TSH) and triiodothyronine (T3) (p>0.05). No significant differences were found between *Toxoplasma* IgG seropositive and seronegative groups as related to trimester, age, city, place, blood group, occupation, food habit, animal contact, disease, and vitamin D level, except the characteristic of abortion, which was significant at a p=0.042. In conclusion, latent toxoplasmosis had significant impact on the occurrence of T4 secretion during gestation. Whereas, TSH and T3 had no significant association with latent toxoplasmosis. Increasing the awareness of toxoplasmosis among pregnant women is required to avoid their deleterious effects, which has a notable impact on lowering the rate of abortion caused by this parasite.

Keywords: Toxoplasmosis; Pregnancy; ELISA; Thyroid hormones.

1. Introduction

*Toxoplasma gondii* is an obligate intracellular protozoan parasite that causes permanent infections toxoplasmosis, which is a major food pathogen (1). *T.gondii* has affected one-third of the world’s population (2). Infections spread by oocysts can be more serious than infections caused by tissue cysts. In general 80% of asymptomatic events of immunocompromised adults may be found (3). Toxoplasmosis can induce abortion and serious harm to the foetal nervous system. In the second and third trimester of pregnancy, toxoplasmosis rises, simultaneously increases inflammatory thyroid disorder (4). After *T.gondii* entering the body of pregnant women, *Toxoplasma* parasite travels, the parasite travels to various parts of the body via blood and lymph until it reaches the thyroid gland, which will consequently affect the function of thyroid gland and secreted hormones. Thyroid hormones are required for physiological systems to function regularly. As a result, understanding any factor (genetic, environmental, or intrinsic) that affects thyroid-stimulating hormone (TSH) and thyroid hormone levels is critical (5). Thyroid-stimulating hormone (TSH) induces thyroid follicular cells to produce thyroxin (T4), which account for 80% which is inactive in thyroid hormone and triiodothyronine (T3) which account for 20% which is active in thyroid hormone. By deionization action converts inactive T4 to active T3 by two enzymes called deionizes that remove iodine (6).

TSH and thyroid hormone levels range up to 65 percent among individuals due to genetic reasons, but various environmental variables can also alter thyroid function (5). According to a study done by (7–9), thyroid function is
strongly predicted by T4 and TSH, which are enhanced and changed by *Toxoplasma gondii* during pregnancy. In pregnancy, latent toxoplasmosis was linked to a slight increase in thyroid hormone production. Thyroid damage has also been documented in mice with toxoplasmosis (10). Another study performed by (11) shows that in comparison to healthy controls, individuals with toxoplasmosis had greater levels of all three hormones (T3, T4, and TSH) (12).

2. Material and methods

The present study was carried out in science and health research center at Koya university from September 1st 2021, to July 1st 2022.

2.1. Study design

Research study design is a set of procedures that divided into four groups including: blood sample collection from pregnant women, which collecting 214 blood samples from pregnant women. Serological tests using (ELISA) technique used in immunological tests to detect *Toxoplasma* IgG, and biochemical tests used to measure the level of TSH, T3 and T4 hormones.

2.2. Sample collection

A total of 6ml of venous blood was collected from 214 pregnant women (including both control and patient groups) using standard venipuncture method in the second and third trimester of pregnancy, who admitted to shahid doctor Khalid hospital in Koya and Teaching Hospital in Erbil, from July 2021 to January 2022. The serum was separated from whole blood samples by centrifuging at 3000 r/min for 10min, then transferred into sterile tubes and were divided into aliquots, and stored at -80c* until used. And stored at -80c* until used.

2.3. Diagnostic Methods of *Toxoplasma gondii*

2.3.1. Detection Anti *T. gondii* IgG antibody

The indirect ELISA technique was used with *Toxoplasma*-IgG 96 well plates coated with *Toxoplasma* antigen.

2.3.2. Biochemical tests

Sandwich enzyme-linked immunosorbent assay used for screening TSH, while competitive ELISA technique used for screening T4 and T3 hormones. These tests were used for a total of 90 samples of *T. gondii*-IgG, 50 positive and 40 negative cases.

2.4. Statistics

The concentration of each ELISA test was calculated using Graph pad program (version 8.0.2). In addition, program SPSS (version 26, Inc., Chicago, IL, USA), was used to analyze the data, and Chi–square test used to compare the nominal values of seronegative and seropositive groups. Furthermore, independent sample t-test was applied to compare the means of continuous values. For the purpose of assessing the risk factors of *T. gondii* infection in pregnant women, binary logistic regression analysis was used, and Pearson’s correlation to determine the correlation between *T. gondii* IgG and other serological parameters under study. The specificity and sensitivity of the serological tests were achieved and detected by the analysis of ROC curve.

3. Results

Out of the total 214 collected blood samples of pregnant women, 50 (23.366%) were *T. gondii* IgG seropositive and 164 (76.635%) were *T. gondii* IgG negative. %47.7 of samples were of second trimester and %52.3 of third trimester. The results showed no significant differences between *T. gondii* IgG seropositive and seronegative groups as related to the following parameters: trimester, age, city, place, blood group, occupation, food habit, animal contact, disease, and vitamins, using chi-square test. All characteristics were not significant, except the characteristic of abortion (p=0.042). The results showed that pregnant women with toxoplasmosis are more likely to have abortion than non-infected pregnant women (OR= 1, p=0.03). Despite that blood group A+ and O+ were more prevalent than others within seropositive samples; however, statistically they were non-significant. Regarding the animal contact characteristic, although that 66% of seropositive patients had no contact with animals but statistically non-significant. The mean difference of thyroid hormones levels in serum among confirmed infected pregnant women with toxoplasmosis in comparison with healthy control were determined using Independent, T test. The average mean of TSH, T3 and T4 of
patient groups+SD were 2.794±1.8050, 2.138±0.6291, 13.035±3.3568 respectively, which they were statically non-significant (Figure 1).

Figure 1 Box plots showing the distributions of serum TSH, T4 and T3 levels between patient and control groups

The correlation between toxoplasmosis and thyroid hormones were analyzed by person's correlation. In the case of positive Toxoplasma-IgG, p-values of TSH and T3 parameters at 0.607 and 0.688, were non-significant, while T4 showed significant difference at $p=0.026$.

Figure 2 The correlation between Toxoplasma IgG and thyroid hormones (TSH, T3 and T4)

The analysis of ROC curves were better explored the differences found among thyroid hormones. T4 has the highest AUC value (0.608) with 56% sensitivity and 32% specificity. Furthermore, the AUC of TSH and T3 were 0.469 and 0.510, respectively (Figure 3).
4. Discussion

Estimating *T. gondii* seropositivity in pregnant women increases the risk of fetus or newborn infection, as well as reactivation of infection in immunocompromised persons. A study by Barzinji, (13) showed that the prevalence of toxoplasmosis was 12.38% in Iraq, which is lower than the reported prevalence in other countries including Jordan 47.1%, Iran 75.7%, Yemen 45.4% and, Malaysia 13% and Brazil 24.1% (14,15). The rates of seropositivity of *T.gondii* were varied due to difference in the geographical distribution of the parasite, climatic condition, and food habits (16,17). Also, due to genetic background of the parasite and the host, and the type of immune response that stimulated by the parasite (18,19). A study by Laboudi et al., (20) was in disagreement with our data with regards to age group factor, It showed that the various age groups and seropositivity of *T.gondii* in pregnant women were statically significant ($p=0.0276$). However, as an agreement with our findings, (21) reported that there is no significant association between *T.gondii* seropositivity and age groups. The non-significant association between age and *T. gondii* infection are probably due to the low number of pregnant women in the present study. (13) was in agreement with our results, concerning to the blood groups, by which despite that the blood group (O) was more prevalence than other groups of *Toxoplasma*-IgG seropositive samples at 42.1% of total samples, however, they were statistically non-significant ($p>0.05$). As related to the factor of animal contact, 66% of total *Toxoplasma*-IgG seropositive samples were of pregnant women with non-contacts with animals, and similarly showed non-significant results. Non-significant *T.gondii* seropositivity with animal contact were also reported by (22). This is despite the fact that feces of cats play a major role in the transmission of *T.gondii*, due to carrying of a large number of oocysts. The same outcomes were confirmed by (19,23). However, some other studies by (24,25) showed that owing cat are significantly correlated with *T. gondii* seropositivity.

The results showed that 56% of *Toxoplasma*-seropositive pregnant women are consuming vegetables, but statically they were statistically non-significant. (18,19) demonstrated that raw meat and vegetables consumption was not significant with toxoplasmosis seroprevalence. In the same context, significant relationships were found between the history of abortion and the seropositivity of *Toxoplasma*-IgG. This is in agreement with (26) findings by demonstrated that frequent abortions in pregnant women have significant relationship with toxoplasmosis. However; there is in disagreement by (20) with our results, overall IgG seropositivity was higher in pregnant women with a history of abortion. As related to the characteristic of the risk factor of Vitamin D deficiency and seropositivity to *T.gondii*, our results were in agreement with the outcomes of (27) by showing no significant difference in term of vitamin D deficiency between confirmed pregnant women with *Toxoplasma* and control. Whereas (28) were in agreement with our results, their data showed non-significant relationship between Vitamin D deficiency risk factor and *T.gondii* IgG seropositivity in Saudi pregnant women. Furthermore; (29) showed that 66.66% of infected individuals under study those living in urban, and 72.7% living in rural areas were positive of *T. gondii* IgG which was statically significant due to the risk factor of contact with Oocyst at their works places.

![ROC Curve](image-url)
According to our hypothesis, dormant bradyzoites in the tissues cyst might convert to tachyzoites and reach blood circulation blood, and reach the organs including thyroid glands by cysts formation, subsequently deregulate T4 and T3 secretion. There has been little research on the relationship between \textit{T. gondii} infection and thyroid disorders. There has been little research on the relationship between \textit{T. gondii} infection and thyroid disorders. A study achieved by (9,30) included confirmed patients with thyroid disorders and Toxoplasma IgG positivity, showed that statically no significant differences were found between \textit{T. gondii} IgG positivity and thyroid diseases. Furthermore, (8,31) were agreed with our results and showed that there are significance difference between latent toxoplasmosis and thyroid dysfunction in pregnancy, \((p<0.05)\). The differences in the results might be explained by a number of variables, including the size of the samples, the type of laboratory procedures, and the location of the investigation both those who are infected with \textit{Toxoplasma} and healthy control.

5. Conclusion

Latent toxoplasmosis has significant impact on thyroxin (T4) hormone during gestation. A negative association was found between latent toxoplasmosis and the demographic characteristics of patients with exception of abortion. Most of \textit{T. gondii} infected pregnant women had more than one abortion.

Compliance with ethical standards

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Disclosure of conflict of interest

The authors declare that there is no conflict of interest.

Statement of ethical approval

The study was approved by the Ethical committee of Koya university, and the sample collection was a proved by Erbil’s general directorate of health.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

References


