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ORIGINAL ARTICLE – OPEN ACCESS

Seroprevalence of *Toxoplasma gondii* Infection in Pregnant Population Revisited; Changing Trends and Call for Action

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ABSTRACT

Objective: The aim of this study is to determine the seroprevalence of toxoplasmosis during pregnancy in our hospital and thus contribute to screening and management strategies.

Materials and Methods: In this retrospective cohort study, the records of 607 pregnant women were analyzed. Patients were tested for serum Toxoplasma gondii antibodies at their first antenatal visit. The seronegative cases were rescreened at 32 weeks' gestation with immunoglobulin (Ig) M and IgG for seroconversion. Demographic, clinical, and serological characteristics of patients were evaluated.

Results: During the study period, 461 (75.94%) patients were seronegative for toxoplasmosis. IgG seropositivity was detected in 110 (18.12%) patients, whereas 33 (5.43%) patients had both IgG and IgM seropositivity; low avidity was observed in 6 (0.98%) of these 33 patients. IgM seropositivity was detected in only 3 (0.49%) cases. Toxoplasma IgG and IgM tests were repeated for 93 seronegative patients at 32 weeks' gestation but seroconversion was not observed in any patient. Acute Toxoplasma infection during pregnancy was found in 9 (1.48%) patients and amniocentesis was performed in four of these. No infant was diagnosed with congenital Toxoplasma infection.

Conclusion: Congenital Toxoplasma infection is clearly a preventable and treatable disease that poses a serious public health risk. Educating people on the transmission routes and implementing routine prenatal testing both regionally and globally during gestation are key preventative measures.

Keywords: Antenatal care, pregnancy, screening, *toxoplasma gondii*, toxoplasmosis

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INTRODUCTION

Toxoplasmosis is a common zoonotic disease caused by the intracellular protozoan parasite *Toxoplasma gondii* (*T. gondii*) (1). The frequency of toxoplasmosis varies widely according to geographical region, eating habits, and socioeconomic parameters. Toxoplasmosis is more prevalent in mild climates and lower income countries (2, 3). Transmission to humans can occur by multiple routes: From food and water contaminated by oocysts in the feces of cats; eating raw and undercooked meats; drinking raw milk; eating raw eggs containing *T. gondii* cysts; and through transfusion, organ transplantation, or transplacentally during pregnancy (4).

Toxoplasmosis is usually subclinical or asymptomatic in healthy humans. Some of the non–specific symptoms are lymphadenopathy, fever, headache, and pains in muscles or joints (5). Primary infection during pregnancy or close to conception may be transmitted to the fetus transplacentally. With advancing gestation, the vertical transition rate increases and the rate of exposure of the fetus to congenital Toxoplasma infection decreases (6, 7). Undiagnosed and untreated acute Toxoplasma infection (ATI) during pregnancy can result in abortus, intrauterine growth restriction, stillbirth, and also congenital toxoplasmosis that cause severe defects in newborns, including intracranial calcification, hydrocephaly, ocular lesions, hepatosplenomegaly, hearing loss, mental retardation, and petechiae (8).

The diagnosis of ATI during pregnancy is primarily based on serological screening. After a confirmed serological diagnosis, ultrasound images and polymerase chain reaction for *T. gondii* DNA on amniocentesis are very sensitive and useful for diagnosing congenital Toxoplasma infection (9). However, a major challenge with serological testing is the failure to classify primary and chronic infection. One of the following conditions must be met for a diagnosis: No detectable serum immunoglobulin (Ig) G antibodies but detection of specific IgM/IgA/IgE antibodies; detection of low avidity serum IgG antibodies; or seroconversion from negative to positive IgG in repeated tests during pregnancy (10).

There are different applications in the world regarding routine screening for toxoplasmosis during pregnancy. Furthermore, in Turkey, the Ministry of Health has no suggestion for toxoplasmosis screening. The aim of this study is to determine the seroprevalence of toxoplasmosis during pregnancy in Bezmialem University Hospital and thus contribute to screening and management strategies.

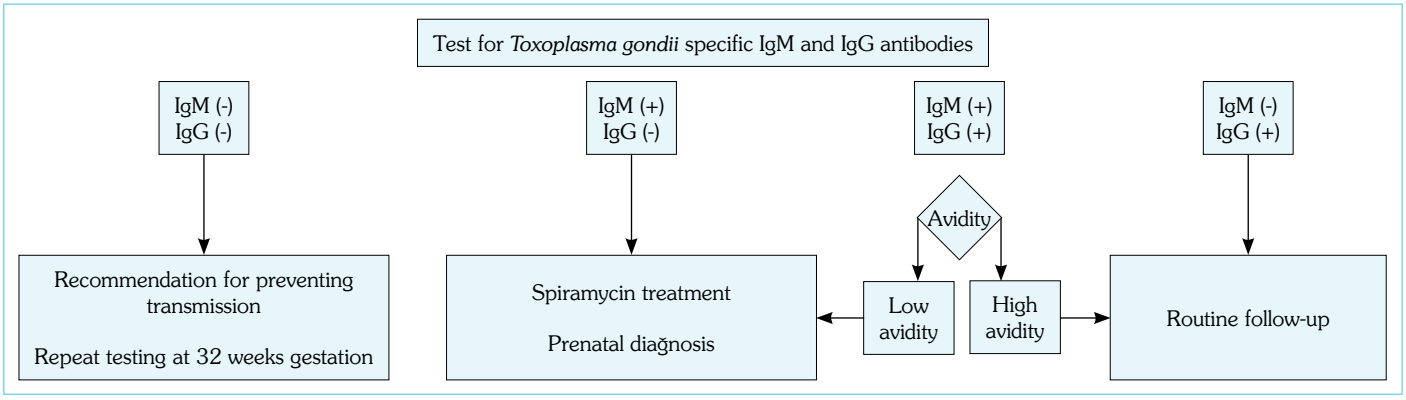

Figure 1. Algorithm for diagnosis and management of acute *Toxoplasma gondii* infection during pregnancy

MATERIALS and METHODS

This retrospective cohort study was conducted in the outpatient clinic of Bezmialem University Hospital Obstetrics and Gynecology Department between January 2019 and January 2020 and was based on patient record analysis of 607 pregnant women during their antenatal follow–up. The study protocol was approved by the local institutional ethics committee (Ethics committee of Bezmialem University, Date: July 09, 2020, No: 12/245) and was carried out in accordance with the principles set forth in the Helsinki Declaration 2008.

Patients were tested for serum Toxoplasma IgM and IgG at their first antenatal visit. During serological screening, pregnant women with IgM(-) and IgG(+) were not treated additionally. Pregnant women with IgM(-) and IgG(-) were informed about the possible routes of contacting toxoplasmosis and verbally instructed against having raw or undercooked meats, improperly washed greenery, and handling of cat litters. These cases were rescreened at 32 weeks' gestation with IgM and IgG for seroconversion. Patients with positive IgM and IgG were treated with prophylactic spiramycin (9,000,000 IU/day) while simultaneously performing an IgG avidity test, with IgM and IgG tests later reevaluated in a second reliable laboratory. Patients with IgM(+)/IgG(+)/low IgG avidity and IgM(+)/IgG(-) were diagnosed as having ATI. Spiramycin was administered and the patients referred to the high–risk pregnancy department for amniocentesis and detailed anomaly scanning (Fig. 1).

Serum samples were tested for Toxoplasma IgM, IgG, and IgG avidity, an automated test using Abbott Alinity (Abbott Laboratories, Abbott Park, IL, USA). Toxo IgM, Toxo IgG, Toxo IgG avidity levels were determined by chemiluminescent microparticle immunoassay methods according to the manufacturer's recommendations. The test results (in IU/ml) were interpreted as follows: IgM <0.5 (negative), 0.5–0.6 (gray zone), and ≥0.6 (positive); IgG <1.6 (negative), 1.6–3 (gray zone), and ≥3 (positive); IgG avidity <0.200 (low avidity), 0.200–0.300 (gray zone), and ≥0.300 (high avidity).

Statistical analysis was mainly descriptive. Demographic and outcome data were expressed as mean ± standard deviation, median [min–max], and number (percentage). Statistical analysis was performed using SPSS Version 23 software (Chicago, IL, USA).

Table 1. Demographic, clinical, and serological characteristics of patients

Characteristics	Value
Age (years)	30.8±4.94
Gravity	2 (1–7)
Parity	1 (0–3)
Gestational age at enrollment (weeks)	10.71±6.43
Seronegative patients	461 (75.94%)
IgM (–), IgG (+) patients	110 (18.12%)
IgM (+), IgG (–) patients	3 (0.49%)
IgM (+), IgG (+) patients	33 (5.43%)
Low avidity	6 (0.98%)
Seroconversion	0 (0%)
Acute infection during pregnancy	9 (1.48%)
Congenital Toxoplasma infection	0 (0%)

Values are reported as mean±SD, median (min–max) or % and number

RESULTS

In our cohort of 607 pregnant women, the average age was 30.8±4.94 years. The median gravida of the study group was 2 (range 1–7) and the median parity was 1 (range 0–3). The mean gestational age at enrollment was 10.71±6.43 weeks. During the study period, 461 (75.94%) patients were seronegative for toxoplasmosis. IgG seropositivity was detected in 110 (18.12%) patients, whereas 33 (5.43%) patients had both IgG and IgM seropositivity; low avidity was observed in 6 (0.98%) of these 33 patients. IgM seropositivity was detected in only 3 (0.49%) cases. Toxoplasma IgG and IgM tests were repeated for 93 seronegative patients at 32 weeks' gestation but seroconversion was not observed in any patient. ATI during pregnancy was found in 9 (1.48%) patients and amniocentesis was performed in four of these. No infant was diagnosed with congenital Toxoplasma infection (Table 1).

DISCUSSION

Toxoplasmosis seroprevalence can vary between countries as well as in different geographical regions or societies in the same country (11). It was stated that seroprevalence was higher in rural, temperate, and humid regions where the cat population was high

and undercooked or raw meat was eaten. According to the World Health Organization, toxoplasmosis is present in every country or region and seropositivity rates range from <10% to >90% (12). In parallel with this, studies from Turkey have reported very different prevalence rates of 17–72% (13–15). In the current study, the seroprevalence of Toxoplasma–specific IgG was 18.1% at the first trimester. This rate was lower than both population–based studies and studies among pregnant women.

Toxoplasmosis represents a significant burden of infection in pregnant women and may result in congenital Toxoplasma infection. According to a recent review, the overall prevalence of ATI in pregnant women globally was 1.1%; the prevalence was highest in the Eastern Mediterranean and African regions (2.5%) and lowest in the European countries (0.5%) (10). In our study, the rate of ATI in pregnancy was 1.4%. This result generally agreed with the previous studies conducted in Turkey with rates of 0.2–2.5% (16). Sert et al. (7) published a large retrospective analysis of 84,587 pregnant women in which the rate of ATI was 0.64% . A recent study performed in Mersin reported high ATI rates of up to 7.6% in pregnant women. This result can be explained by the region's high refugee population, climate characteristics, and eating habits (17).

There is currently no general consensus for routine toxoplasmosis screening during pregnancy. In countries where the prevalence is relatively low, such as the USA, the UK, and Canada, routine screening is not recommended (18–20). However, countries with a high frequency of toxoplasmosis (France, Austria, Germany, Belgium, Italy, Uruguay, Argentina, and Switzerland) have routine screening programs (21). In Turkey, the Ministry of Health does not have any suggestion for toxoplasmosis screening (22). The majority of the clinics in the USA perform toxoplasmosis testing if there are suspicious ultrasound findings, risk factors for toxoplasmosis, or suggestive findings of acute infection. This strategy leads to half of the congenital Toxoplasma infection cases being overlooked because approximately 50% of pregnant women with ATI are asymptomatic or may have non–specific flu–like symptoms; without antenatal screening, these cases will remain undiagnosed and untreated (23, 24). The results of a recent review support the need for universal screening of pregnant women during the gestation period to decrease vertical transmission (10). In countries where routine screening is not performed, cost–effectiveness is given as one of the reasons, however, this issue was investigated by Stillwaggon et al. (25) and they showed that routine serologic screening during pregnancy is feasible and cost–saving.

Gestational age at the time of ATI affects the risk of mother–to–child transmission. The prevalence of ATI in the first trimester (1.7%) was significantly higher than the prevalence in the second (1.0%) and third (0.1%) trimesters. Nevertheless, early studies show that severe congenital Toxoplasma infection can occur even in late gestation (10) and the risk of toxoplasmosis seroconversion among pregnant women was 2.2–fold higher than in non–pregnant women of the same age (26). Therefore, seronegative women are at great risk of developing toxoplasmosis during pregnancy. Another important point is that most infants infected in the later stages of pregnancy are asymptomatic at birth but sequelae may appear later in life (27). In light of these findings, pregnant women who were seronegative for *T. gondii* at the first trimester should undergo serological screening at the third trimester for the detection of possible seroconversion and be informed about the transmission routes of toxoplasmosis. There is very little information on seroconversion during pregnancy in the national literature. Doğan et al. (28) investigated seroconversion by scanning 153 pregnant women in the second and third trimesters, and they did not detect seroconversion later in pregnancy, as in our study. In our study group, as Doğan et al.'s routine, verbal instruction for practical measures against toxoplasmosis seems to be effective and leads to zero seroconversion rate. From the practical point, that may be the rationale behind the universal screening for toxoplasmosis. However, these data verified with further studies comparing seroconversion rate between screened and unscreened populations.

The monocentric patient selection with retrospective design was one of the limitations of the present study. Another limitation was the small sample size of patients investigated for seroconversion. In addition, case with acute infection might be overrepresented in this series due to fact that its conducted in a tertiary referral center.

CONCLUSION

Congenital Toxoplasma infection is clearly a preventable and treatable disease that poses a serious public health risk, with global incidence at 1.5 cases per 1000 live births. The aim of the present study was to contribute toward improving strategies for the screening and management of toxoplasmosis during pregnancy. We recommend spreading the awareness of transmission routes of *T. gondii* among communities and implementing routine prenatal screening both regionally and globally during gestation which are key preventative measures. However, future studies with appropriate sample size of seroconversion patients are needed for adequate results and comparison.

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Ethics Committee Approval: The Bezmialem University Non-Interventional Research Ethics Committee granted approval for this study (date: 09.07.2020, number: 12/245).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – TT, MSK; Design – TT, MSK; Supervision – MSK; Materials – HSİT, HNÖ; Data Collection and/or Processing – HSİT, HNÖ; Analysis and/or Interpretation – TT, MSK; Literature Search – TT, MSK; Writing – TT, MSK; Critical Reviews – MSK.

Conflict of Interest: The authors have no conflict of interest to declare.

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