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آموزش مهارت‌های کاربردی در تدوین و چاپ مقاله
Seroprevalence and Coinfections of *Toxoplasma gondii* in Childbearing Age Women in Turkey

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Abstract

**Background:** Our aim was to detect the rate of *Toxoplasma gondii* infections and the coinfections in childbearing age women in Turkey accompanying using seroprevalence data from a multicenter hospital setting.

**Methods:** Overall, 17751 childbearing age women through 16-45 years were included to the study between 2004 and 2010. The clinical samples of the patients were collected from 16 hospitals and medical centers mostly from Istanbul and three other cities from Turkey. Enzyme immunoassay tests were performed in our central laboratory in Istanbul to investigate *T. gondii* with other TORCH infections or Epstein Barr virus, Hepatitis B virus, Hepatitis C virus and Human Immunodeficiency virus as accompanying infections.

**Results:** Among the tested sera 1.34% of the women were IgM and 24.61% were IgG positive for *T. gondii*. The coinfection rate was 3.36% among the IgM positive patients. CMV, EBV, HCV and rubella were detected as coinfections. IgM seropositivities of those infection agents were accepted as acute infection. CMV and EBV were detected as 1.26% and HCV and rubella were detected as 0.42%.

**Conclusion:** Turkish female population was found infected with *T. gondii* in high rates. Some of the seropositive patients also had accompanying CMV, EBV, HCV and rubella infections. Our aim was to detect *Toxoplasma* seropositivity and the accompanying infections with their rates. While coinfections worsen the situation unless they are detected, it is important to determine exact situation of the patient for the management of the therapy.

**Keywords:** Toxoplasma prevalence, Pregnant women, TORCH, Turkey

Introduction

Toxoplasmosis is caused by the obligate intracellular protozoan *Toxoplasma gondii*. It is one of the most prevalent chronic infections affecting one third of the world’s human population (1). In many developing countries as well as our country, the exact prevalence of toxoplasmosis among pregnant women is not well recognized (2). It is very important to discover whether congenital toxoplasmosis, only the result of maternal infection, existed during pregnancy period (3). *Toxoplasma gondii* infections can cause to a more serious progression when accompanied with some other infection. For example, in pregnant women having human immunodeficiency virus (HIV), *T. gondii* infections may lead to extreme complications such as miscarriage, support the transmission of Hepatitis B virus (HBV) and HIV and birth defects (4).

*Toxoplasma gondii* seropositivity and coinfection with TORCH pathogens have been investigated in Qatar with the intention of testing the patients who are considered to be in the high risk group for TORCH pathogens, e.g. pregnant women, their fetuses, neonates, and acquired immunodeficiency syndrome (AIDS) patients to initiate the treatment. In this study, the factors associated with *T. gondii* IgG seropositivity were found as; older age, East Mediterranean or African nationality, positive Cytomegalovirus (CMV) and Herpes simplex virus (HSV)-1 serostatus and negative rubella IgG results (5).

For testing whether acute infection is obtained during gestation, most commonly toxoplasma-specific immunoglobulinG (IgG) and IgM antibodies of a pregnant woman are used (6).

In the period of first 24 wk of gestation a low IgG titer and a negative IgM test of a pregnant...
woman indicates that the infection was pregestationally acquired. If in a single serum sample a positive IgM test result points out the infection was not long ago acquired, or may be a false positive result. If false positive or true positive IgM test results are interpreted improperly the outcomes of this scenario would end in a dramatic way such as unnecessary abortions (7).

Although, the results of IgG, IgM and even avidity precisely do not indicate the exact position of the patients they are used to detect the toxoplasma infections.

In this study, our aim was to detect the prevalence of toxoplasma infections and the accompanying other TORCH infections or Epstein Barr virus (EBV), HBV, Hepatitis C virus (HCV) and HIV in women at childbearing age by testing for IgM and IgG titers.

**Material and Methods**

The sera collected from January 2004 to July 2010, of 17751 children bearing age women were studied. The samples were obtained from 16 different hospitals and medical centers from five cities in Turkey including Istanbul, Bursa, Adana, Kayseri and Kocaeli. The hospitals were mostly from Istanbul. The study was performed in Acibadem Labmed central laboratory in Istanbul.

TORCH pathogens IgM and IgG tests were run on VIDAS automated immunoanalyzer (VIDAS, Biomerieux, France), HCV tests were run on Cobas 8000 Modular Analyzer (Modular, Roche, Germany) EBV tests were run on Euroimmun Analyzer (Euroimmun Analyzer 1, Euroimmun, Germany)

**Results**

From 2004 to 2010, overall 17751 women at childbearing age were examined and evaluated for *Toxoplasma* and the accompanying infections. IgM positivity of other infections with *T. gondii* IgM positivity was accepted as coinfection. Number of *T. gondii* IgM and IgG seropositivities and coinfections are given in Table 1. The highest prevalence of positive IgM and IgG seropositivity was observed between 27-35 yr of age. *Toxoplasma* IgM and IgG positivity versus age in childbearing age women in Turkey is shown in Table 2.

*Toxoplasma gondii* IgM seropositivity was 1.34% and IgG seropositivity was 24.6%, and coinfection with the *T. gondii* infections was 3.3%. Acute CMV, EBV, HCV and Rubella infections were detected as coinfection. Their IgM seropositivities were accepted as indication of acute infection. Both CMV and EBV were detected as 1.26% and both HCV and rubella as 0.42%. No HSV type 1 or 2, or HIV infection was found to be accompanying. In addition, the other TORCH pathogens seropositivity and other studied infection agents’ seropositivity were evaluated. Accompanying infections’ seropositivity rates are given in Table 3. As it is shown in Table 2 rubella IgG was the most accompanying seropositivity with *T. gondii*. Following rubella, CMV, EBV and HSV Type 1 were detected sequentially.

**Table 1: Toxoplasma IgM and Toxoplasma IgG positivity versus age in childbearing age in women in Turkey**

| Age | T.gondii IgM pos. | T.gondii IgG pos. |
|-----|------------------|------------------|
| 16  | 1                | 3                |
| 17  | 2                | 4                |
| 18  | 2                | 6                |
| 19  | 2                | 5                |
| 20  | 1                | 16               |
| 21  | 1                | 19               |
| 22  | 5                | 36               |
| 23  | 7                | 69               |
| 24  | 7                | 91               |
| 25  | 15               | 116              |
| 26  | 19               | 166              |
| 27  | 34               | 248              |
| 28  | 31               | 300              |
| 29  | 44               | 348              |
| 30  | 17               | 327              |
| 31  | 33               | 337              |
| 32  | 25               | 342              |
| 33  | 35               | 299              |
| 34  | 14               | 229              |
| 35  | 8                | 204              |
| 36  | 5                | 185              |
| 37  | 11               | 151              |
| 38  | 4                | 116              |
| 39  | 2                | 66               |
| 40  | 5                | 60               |
| 41  | 2                | 33               |
| 42  | 0                | 20               |
| 43  | 2                | 10               |
| 44  | 0                | 4                |
| 45  | 0                | 0                |
Table 1: T. gondii IgM and IgG seropositivities and coinfections in childbearing age women in Turkey

| Years | T. gondii Ig M positive (n/%) | T. gondii Ig G positive (n/%) | Toxoplasma Ig M & G negative (n/%) | Total | Coinfection (n/%) | Coinfection (name) |
|-------|-----------------------------|-------------------------------|----------------------------------|-------|------------------|-------------------|
| 2004  | 21/ 1.40                    | 464/ 31.12                   | 1027/68.88                       | 1491  | 0                |                   |
| 2005  | 21/ 1.15                    | 798/ 43.77                   | 1024/56.17                       | 1823  | 3/ 14.28         | 1 CMV, 2 EBV      |
| 2006  | 34/ 1.66                    | 482/ 23.65                   | 1291/63.35                       | 2038  | 1/ 2.94          | 1 HCV             |
| 2007  | 36/ 1.22                    | 602/ 20.52                   | 1832/62.46                       | 2933  | 2/ 5.55          | 2 CMV             |
| 2008  | 40/ 1.27                    | 690/ 21.95                   | 1970/62.68                       | 3143  | 2/ 5.00          | 1 Rubella, 1 EBV  |
| 2009  | 55/ 1.41                    | 829/ 21.38                   | 2189/56.46                       | 3877  | 0                |                   |
| 2010  | 31/ 1.26                    | 505/ 20.64                   | 1416/57.89                       | 2446  | 0                |                   |
| Total | 238/ 1.34                   | 4370/ 24.6                   | 10749/ 60.55                     | 17751 | 8/ 3.3           |                   |

Table 2: Other infection rates accompanying T. gondii seropositivity in pregnant women in Turkey

| Years | T. gondii Ig G positive (n/%) | Rubella Ig G (n/%) | CMV Ig G (n/%) | HSV type 1 Ig G (n/%) | EBV Ig G (n/%) |
|-------|-------------------------------|-------------------|---------------|----------------------|---------------|
| 2004  | 464/ 31.12                    | 6 / 1.29          | 4 / 0.86      | 0                    | 1/ 0.21       |
| 2005  | 798/ 43.77                    | 18/ 2.25          | 9 / 1.12      | 0                    | 1/ 0.12       |
| 2006  | 482/ 23.65                    | 25/ 5.18          | 13/ 2.69      | 0                    | 1/ 0.20       |
| 2007  | 602/ 20.52                    | 15/ 2.49          | 4 / 0.66      | 0                    | 0             |
| 2008  | 690/ 21.95                    | 18 / 2.60         | 1 / 0.14      | 0                    | 0             |
| 2009  | 829/ 21.38                    | 50/ 6.03          | 10/ 1.20      | 1/ 0.12              | 0             |
| 2010  | 505/ 20.64                    | 35/ 6.93          | 11/ 2.17      | 0                    | 1/0.19        |
| Total | 4370/ 24.6                    | 167/ 3.82         | 52/ 1.18      | 1/ 0.02              | 4/ 0.09       |

Discussion
In our study evaluated seropositivity of 17751 women for Toxoplasma infection. The women between 27-35 yr of age period had the highest Toxoplasma positive IgM and IgG rates. In the population of Turkish childbearing age women we have examined the seropositivity of T. gondii as 1.34% for IgM and 24.6% for IgG, and the accompanying infection rate as 3.3%. The coinfections detected were acute CMV, EBV, HCV and rubella. Toxoplasma gondii is a worldwidespreading parasite of animals and it causes infections in humans (8). Congenital, intrauterine infections cause a wide range of amendments from congenital abnormalities to intrauterine growth deficiencies and foeatal death. There are different Toxoplasma seropositivity reports from all over the world. For example, in Maracaibo, Venezuela the overall prevalence of toxoplasmosis was 33%, while 18.2% were positive IgM (9). In Qatar among 823 women of childbearing age the T. gondii IgG and IgM was 35.1% and 5.2% respectively (5). In a study in Beirut the seroprevalence of IgG T. gondii antibodies from 2145 sera were examined in hospital and private laboratories and the seropositivity rates were found to be 55% and 67%, respectively. In addition, the IgM T. gondii antibodies from 1352 sera from hospital and 2074 sera from private laboratories were similar to each other 6.7% and 6.8%, respectively (10). In India, 300 pregnant women were screened and anti Toxoplasma IgG antibodies were detected in 15.33% cases, while 3% had positive anti Toxoplasma IgM with IgA and low avidity antibodies suggestive of acute infection during or just before pregnancy (11). In another study in Iran, 247 of the 553 pregnant women were found to be positive for IgG T. gondii
antibodies and the rate of seropositivity of latent *T. gondii* infection was 44.8 % (12).

In Turkey, although there are some studies *Toxoplasma* seropositivity rates were variable in regards with the provinces. For example: in Sanliurfa, a southeastern Anatolian city where raw meat consumption is traditionally high, 60.4% of pregnant women were found for *T. gondii* IgG, and 3% were found IgM positive (13). On the other hand, in another Anatolian city Kayseri the *T. gondii* seropositivity was 33.42% (14).

In our study, between 2004 and 2010 *T. gondii* IgM and IgG seropositivity rates were found detected as 1.34 and 24.6, respectively. These rates are relatively low when compared with the *Toxoplasma* endemic regions of Turkey where raw meat consumption is high. This may be due to the collected samples from western side of Turkey where raw meat consumption is too low.

False positive and false negative *T. gondii* IgM and IgG may mislead in interpretation of the test results. In an attempt to rectify this situation, the U.S. Food and Drug Administration has suggested confirmatory testing for positive IgM test results (15).

In Palo Alto Medical Foundation *Toxoplasma* Serology Laboratory some additional tests are studied in case of positive IgM test results. The additional tests used for confirmation of positive IgM tests enclose IgG, IgM, IgA and IgE antibodies of *Toxoplasma* (referred to as the toxoplasma serologic profile (TSP). The TSP is recorded to differentiate acquired and distant infections successfully (3). The TSP acts for a step forward and has a discriminatory power above average than the IgM tests alone (7).

Avidity testing improves the strength of effectiveness of the TSP in discovering whether a woman has been infected during gestation. Although the avidity test presents a confirmation, because of potential to improper interpretation for low-or borderline-avidity it should not be used as the only confirmatory test for pregnant women. During the first 16 wk of gestation using the TSP and the VIDAS avidity method as a confirmation test decreases the need for PCR on amniotic fluid, or unnecessary treatment of the mother with spiramycin and lessens unnecessary abortions (16).

Though *T. gondii* infections can lead to serious complications, coinfections would worsen more the patient’s situation. Coinfection with TORCH pathogens in high-risk patients in Qatar was investigated to manage the right treatment (5). In our study, we also searched for coinfections and found accompanying acute CMV, EBV, HCV and rubella with *T. gondii* infections. The aim of this investigation was to discover the disease totally in order to initiate the specific treatment.

In conclusion, the findings in the present study designated that *Toxoplasma* infections are common among Turkish female population with also accompanying infections. The advanced detection methods and evaluation of the complete toxoplasma serology and avidity tests will help to select the real acute infections. At the same time, also other tests should be studied in order to detect coinfections. As a result, all of these evaluations should aim the population to prevent from more toxoplasma infection and coinfections to have a healthy baby and a mother.

**Ethical Considerations**

Ethical issues including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc. have been completely observed by the authors.

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