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**Lames Husam Almansee A
Lkanaa**

College of Veterinary Medicine,
University of Kerbala, Iraq

Ali Mansoor Jasim

College of Medicine, University
of Kerbala, Iraq

Raed Hamzah Mohammed

College of Dentistry, University
of Kerbala, Iraq

Causal association of *Toxoplasma gondii* seropositivity with adverse pregnancy outcome(s) in Iraqi women, a cat-based dilemma

Lames Husam Almansee A Lkanaa, Ali Mansoor Jasim and Raed Hamzah Mohammed

Abstract

Toxoplasmosis is a common chronic parasitic disease in which cat plays a crucial role as the natural final host. The current study represents a cross sectional survey, done during September through November 2011, involved data collection from different cities in Iraq including Kerbala, Najaf, Babylon, Baghdad, Mosul, Duhok, Tikrit and Diyala. The aims of the present study were to assess seroprevalences of specific antibodies (IgG and IgM) against *Toxoplasma gondii* in serum samples from women with previous adverse pregnancy outcome measured by ELISA or agglutination tests. Furthermore, to predict if there is any significant association between this seropositivity and adverse pregnancy outcome by comparing it with a control group.

Data were collected retrospectively and randomly depending on health resources' record system from the areas included in this study. We compare *Toxoplasma* seropositivity for 2870 women with previous adverse pregnancy outcome(s) with that for 1318 women without such complications. The results showed that there was no significant association between seropositivity and adverse pregnancy outcome(s), p -value= 1.0232. It was concluded that there is no significant difference between seropositivity for *Toxoplasma* in women with adverse pregnancy outcomes compared to those with otherwise normal pregnancy. Therefore, it is recommended to seek for another reinforcing diagnostic parameter in evaluating such patients. Furthermore, population-based studies of newborns would be helpful to accurately estimate incidence of transplacentally transmitted toxoplasmosis.

Keywords: *Toxoplasma gondii*, seropositivity, pregnancy, cat

Introduction

Toxoplasmosis is a parasitic disease caused by the protozoan *Toxoplasma gondii* ^[1]. The parasite infects most genera of warm-blooded animals, including humans, but the primary host is the felid (cat) family ^[2]. Up to one third of the world's human population is estimated to carry a *Toxoplasma* infection ^[3]. Pregnancy precautions Congenital toxoplasmosis is a special form in which an unborn child is infected via the placenta. A positive antibody titer indicates previous exposure and immunity and largely ensures the unborn baby's safety. A simple blood draw at the first pre-natal doctor visit can determine whether or not the woman has had previous exposure and therefore whether or not she is at risk. If a woman receives her first exposure to toxoplasmosis while pregnant, the baby is at particular risk ^[4]. Considerable controversy and uncertainty exist concerning *Toxoplasma gondii* as a cause of multiple abortions and other adverse pregnancy outcomes. Even isolation of *T. gondii* from the endometrium shortly after abortion does not prove congenital toxoplasmosis because *T. gondii* has been found in the uteri of non-pregnant women and those with uncomplicated conceptions ^[5].

Studies showed high seroprevalence of toxoplasmosis in Iraqi women with complicated pregnancies ^[6]. These studies mostly ignoring such results in control non-pregnant women or those with normal conception outcomes. Most of these women were exposed to vigorous treatment with anti-toxoplasmosis agent depending on such serologic finding ^[7, 8] without any confirmatory investigation(s) such as amniotic fluid PCR, histopathological examination or other tests ^[5, 7]

However, in developed countries with high prevalence of toxoplasmosis, like Austria and France, it is compulsory to test all pregnant women for *T. gondii*. Women are tested for *T. gondii* antibodies on their first visit to their gynaecologist ^[9].

Correspondence

**Lames Husam Almansee
ALkanaa**

College of Veterinary Medicine,
University of Kerbala, Iraq

All seropositive women are also tested periodically every trimester for rising IgG titers; those with rising titers (who seroconvert) during pregnancy are followed clinically and their fetuses are examined for evidence of *T. gondii* infection by ultrasound, amniocentesis and fetal blood [10]. Women who have acquired *T. gondii* infection during pregnancy are treated with spiramycin if they test amniotic fluid PCR negative, and with sulfadiazine and pyrimethamine if the amniotic fluid PCR test positive, i.e. the fetus is found to be infected [11]. However, a study in Egypt recommends serological screening for high-risk pregnant women to test for *Toxoplasma* antibodies as a routine test [12].

The current study concerns the seropositivity of antitoxoplasma antibodies in Iraqi women with and without adverse pregnancy outcomes in order to predict the association between such seropositivity and adverse conception outcomes.

Material and methods

This study was performed in the period from September through November 2011. The study data included a total of 4188 married women in child-bearing age. Data regarding tests of antitoxoplasma antibodies were collected retrospectively and randomly depending on health resources' record system from the areas included in this study. The study included 2870 women that had one or more of abnormal pregnancy outcomes in their past history such as abortion and intrauterine fetal death (s) and regarded as the test group. While other 1318 women had no risk factors that represented in control group. The study aims to predict the causal association of anti-toxoplasma antibodies' seropositivity and

adverse pregnancy outcomes by comparing data in test and control groups of pregnant women.

Data from health recorder system from different areas in Iraq including Kerbala, Najaf, Babylon, Baghdad, Basrah, Mosul, Duhok, Tikrit and Diyala were recruited to mount the results of this study.

Results

Collected Data represented results of sera (N=4188; 2870 as test group and 1318 as control group) from women who were tested for anti-Toxoplasma IgG and IgM using ELISA or latex agglutination tests.

Table 1: The serologic test finding of *toxoplasma gondii* in women with adverse pregnancy outcomes

City	Total	Anti-Toxoplasma antibodies		
		negative	Positive	
			+IgM	+IgG
Kerbala	387	91	36	60
Najaf	332	94	60	83
Babylon	401	283	25	132
Basrah	181	44	16	21
Baghdad	420	160	106	154
Diyala	308	211	32	65
Mosul	376	267	34	75
Tikrit	278	203	24	51
Duhok	187	60	55	72
Total	2870			
P value 1.0232				

Table 2: The serologic test finding of *toxoplasma gondii* in the control group women

City	Total	Anti-Toxoplasma antibodies		
		negative	positive	
			+IgM	+IgG
Kerbala	187	128	23	36
Najaf	202	119	24	59
Babylon	187	103	22	62
Basrah	124	68	19	37
Baghdad	138	65	17	56
Diyala	128	73	25	30
Mosul	90	45	16	31
Tikrit	95	57	15	23
Duhok	117	71	18	28
Total	1318			
P value 1.0232				

Relatively high rates of toxoplasmosis seropositivities were reported in all included cities. Prevalence rates of toxoplasmosis among women with abnormal pregnancy outcomes (test group) were recorded to be higher compared with those without risk factors (control group) as shown in table (1).

Analysis of the current data indicates non-significant association between the two parameters in the test and control groups, p-value is more than 0.05. Analysis of anti-toxoplasma antibody seroprevalence in relation to abortion history indicates that the contribution of toxoplasmosis to adverse pregnancy outcomes in Iraq is greatly overestimated.

Discussion

Toxoplasmosis most commonly manifests as a mild, flu-like illness with low-grade fever, myalgia, malaise, and headache, but primary infection in humans may also cause spontaneous

abortion, fetal mental and psychomotor retardation, retinochoroiditis, encephalitis, and hepatitis.^[6,16, 17] *Toxoplasma gondii* is of particular concern in humans because of the potential for transmitting the disease to the unborn fetus if the mother is infected for the first time during pregnancy [12-15].

The results of this study regarding seroprevalences of antitoxoplasma antibodies in women in child-bearing age is consistent with many other corresponding works in different areas of Iraq^[7, 8] so, the seroprevalences in women with past history of adverse pregnancy outcome(s) comes with data from many previous studies. These findings indicate that the causative association of *T. gondii* in complicated pregnancies is really overestimated in Iraq. However, our current data disagree with some studies in this field which showed some causative association between the two parameters the latter finding could be attributed to bias in patients selection and

specimen collection in addition to limited sample sizes of most these studies. Furthermore, some of them had neglected the data from a control group (women with no risk factors) and thus run their evaluation depending on finding from test group only (women with complicated pregnancies).

Because *T. gondii* can be transmitted from a recently infected mother to her fetus, a rapid and accurate diagnosis of the infection is critical for establishing proper clinical care [16]. When a pregnant woman is found to be infected with *T. gondii*, the next step is to determine whether the fetus is infected. Physicians most often use polymerase chain reaction (PCR) testing of amniotic fluid to diagnose congenital toxoplasmosis [16, 17]. This vital step is almost exclusively missing leading to such overestimation of causal association of toxoplasmosis in adverse pregnancy outcomes.

Despite these risks, pregnant women are not routinely screened for toxoplasmosis in most countries (Portugal, France, Austria, Uruguay, and Italy [18-21] being the exceptions) for reasons of cost-effectiveness and the high number of false positives generated.

The connection between serological evidence and the isolation of *T. gondii* from infected tissue is essential for confirmation. Regular serological screening before pregnancy or very early in pregnancy will allow recognition of maternal infection [6].

High *T. gondii* seroprevalence has been found in many countries including Iraq (Internet 1, 2005). A study was made in 1979 and showed that 27.64% had positive reaction by indirect haemagglutination test (IHAT) and 23.14% by indirect fluorescent antibody test (IFAT), more in females than males and more with older age group [22].

Population-based studies of newborns would be helpful to accurately estimate incidence of congenital toxoplasmosis.

Conclusion

Owing to the study data, it is concluded that the serologic evidence of *Toxoplasma* diagnosis is rather misleading, and thus the causal association of toxoplasmosis with the adverse pregnancy outcomes is highly overestimated in Iraq and "cat" fingerprints in such conditions need to be reevaluated before any treatment decision for the mother or the baby.

Recommendation

It is recommended to consider more advance diagnostic test(s) such as PCR technique or histopathological evidence of the parasite in fetal, amniotic fluid or placental specimens to predict the exact role of toxoplasmosis in adverse pregnancy outcomes.

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