

# Toxoplasmosis and Female Infertility: Is there a Co-Relation?

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**Abstract** *Toxoplasma gondii* is a ubiquitous protozoan parasite that is estimated to infect one-third of the world's human population causing a wide range spectrum of diseases. Reports on the prevalence of *T. gondii* infection among infertile females are scarce. This case-control study aimed to screen the infertile females and pregnant controls for *Toxoplasma* infection investigating a possible association with infertility. A total of 319 female infertility ladies and 103 pregnant controls were examined for the presence of IgG and IgM antibodies against *T. gondii* by using enzyme-linked immunosorbent assay. Ages in infertile ladies (26.8 years  $\pm$  4.7) was comparable with that of the controls (26 years  $\pm$  5.3), ( $p > 0.05$ ). The overall seroprevalence of *T. gondii* in this study was 57.52%. Anti-*T. gondii* IgG antibodies indicating latent infection with *T. gondii* was found in 193 (61.85%) of 312 infertile ladies and 44 (44%) of 100 controls. There was a highly significant difference between the 2 groups ( $p = 0.002$ ). Our results found an association between toxoplasmosis and infertility. This finding encourage both prompting health education to prevent *Toxoplasma* infection in female population especially in childbearing age and further investigation to elucidate the causative relation between *T. gondii* infection and female infertility.

**Keywords:** *Toxoplasma gondii*, infertility, pregnant women, ELISA

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## 1. Introduction

*Toxoplasma gondii* is an obligate intracellular parasite, which affects a wide-range of mammals including human. Based on serological studies, *T. gondii* is one of the most prevalent protozoan parasites [1]. High prevalence of the infection have been reported among pregnant women and women of childbearing age from different foci in Latin America, parts of Eastern / Central Europe, the Middle East, parts of south-east Asia and Africa [2].

Human infection is acquired through ingestion of food or water contaminated with oocysts shed in the feces of cats and other felines or viable tissue cysts in undercooked or raw meat [3,4]. Most cases of toxoplasmosis are asymptomatic or mild and influenza-like, but immunocompromised patients often develop fulminating life-threatening symptoms as pneumonia and encephalitis [5,6]. Primary infection during pregnancy may cause spontaneous abortion or stillbirth. In utero infection may cause congenital toxoplasmosis with ocular and neurological manifestations.

Previous research on laboratory animals reported that infection with *T. gondii* could be a cause of infertility in experimental animals [7,8]. No previous reports about the relation between *T. gondii* infection and female infertility although about 21% of abnormal embryos and 24.2% of

miscarriages and stillbirths have been related to *T. gondii* infection [9,10]. Recently, Li *et al.* [11] recorded a relation between female infertility and toxoplasmosis in China, which raises the concern about the importance of toxoplasmosis in female fertility problems and encourage further research in this area.

The aim of this study was to investigate *Toxoplasma* seropositivity rates in infertile females and pregnant controls in Dakhalia governorate, Egypt and to record if there is a relation between infection and female infertility.

## 2. Subjects, Materials and Methods

### 2.1. Study Design and Study Populations

Through a case-control study design, we studied the association of infertility with infection with *T. gondii* in female infertility patients and control subjects in Dakhalia governorate, Egypt from May, 2012 to May, 2013. A total of 319 infertile female patients attending Gynaecology and Obstetrics department, Mansoura University, Dakhalia, Egypt were enrolled in this study. All females had been married for at least two years and were being treated for primary infertility. Chosen females experienced normal sexual life and did not have any contraceptive measures. All cases had basic investigations of infertility including hystero-salpingography, mid luteal serum

progesterone assay and semen analysis of the partner were free. 103 pregnant women attending Gynecology and Obstetrics department, Mansoura University, Mansoura, Egypt for antenatal care were included as control subjects.

This study was approved by the Ethics Committee at Faculty of medicine, Mansoura University. The purpose and procedures of the study were explained to all participants and a written informed consent was obtained from all of them.

## 2.2. Sample Collection

Three ml of venous blood was drawn aseptically from both patients and control subjects. The sera were separated by centrifugation at 3000 rpm for 5 min then stored at  $-20^{\circ}\text{C}$  till further use.

## 2.3. Serological Testing

Serum samples were screened for anti-*T. gondii* specific IgM antibodies using a commercial kit (*Toxoplasma* IgM ELISA, Calbiotech Inc., CA) to exclude acute toxoplasmosis. Negative IgM antibodies to *Toxoplasma gondii* were tested again using a commercial kit (*Toxoplasma* IgG ELISA, Calbiotech Inc., CA) for detection of for anti-*T. gondii* specific IgG antibodies. According to the manufacturer's recommendations, serum samples were diluted and used for testing; each serum

sample was tested in triplicates. Positive and negative controls were included in the kit.

## 2.4. Statistical Analysis

Data were analyzed using the SPSS 16.0 software package. A *Chi-square* test was used to analyze differences of *T. gondii* seroprevalence in the tested groups. A *P* value  $< 0.05$  was considered statistically significant.

## 3. Results

Seven samples from female infertility cases and three samples from pregnant controls were excluded due to positive anti-*T. gondii* specific IgM antibodies indicating acute infection. The age of female enrolled in the study ranged from 20 to 39 years with the mean age of  $26.8 \pm 4.7$  and  $26 \pm 5.3$  years for female infertility patients and pregnant controls respectively. The overall seropositivity rate of *T. gondii* in the present study was 57.52% (237 / 412) in both cases and control groups. Antibodies (IgG) to *T. gondii* were found in 193 (61.85%) of 312 infertile female patients cases and 44 of 100 pregnant women (44%). There was a significant difference between the 2 groups ( $P < 0.05$ ), indicating a correlation between *T. gondii* infection and female infertility (Table 1).

**Table 1. Seroprevalence of *Toxoplasma gondii* infection in female infertility patients and pregnant females controls**

Group	Number of cases	Number of seropositive cases (%)	Chi-square	<i>P</i> value	OR (CI)
Sterile	312	193 (61.85)	9.89	0.002	2.06 (1.28-3.34)
Pregnant	100	44 (44)			
Total	412	237 (57.52)			

The anti-*T. gondii* IgG antibodies detection was estimated within 4 age groups (20-24 y, 25-29 y, 30-34 y and 35-39 y). The percentage of seropositivity in the female infertility patients were 57.57%, 62.28%, 63.15%

and 73.91% respectively, while it was 34%, 46.66%, 60% and 70% respectively in the control group (Table 2). There is no significant difference ( $p > 0.05$ ) in seropositivity among these ages in both groups.

**Table 2. Age distribution of seroprevalence of toxoplasmosis in female infertility patients and pregnant women**

Age group (years)	Infertile females		Pregnant females	
	Total number of cases	No. of positive for Anti- <i>T. gondii</i> IgG (%)	Total number of cases	No. of positive for Anti- <i>T. gondii</i> IgG (%)
20-24	99	57 (57.57)	50	17 (34)
25-29	114	71 (62.28)	30	14 (46.66)
30-34	76	48 (63.15)	10	6 (60)
35-39	23	17 (73.91)	10	7 (70)
Total	312	193 (61.85)	100	44 (44)

## 4. Discussion

It is well documented that toxoplasmosis is of crucial importance due to cosmopolitan distribution and wide range of diseases it cause. It is known that toxoplasmosis has some unfavorable effects on the reproductive capacity of both men and women [5,12]. So, this case-control study was carried to estimate the seropositivity rate of *Toxoplasma* infection among infertile females. The overall detection rate of toxoplasmosis among Egyptian females in childbearing age was 57.52%, in our study in Dakhalia

governorate. This result approximates other Egyptian study of Elsheikha *et al.* [13] which reported 59.6% seroprevalence of anti-*T. gondii* IgG antibodies among blood donors in Mansoura University Hospital, Dakhalia governorate, Egypt. This high prevalence is due to lack of health education and exposure to risk factors including contact with cats, agricultural activities, eating raw unwashed vegetables, drink insufficiently boiled milk, eating insufficiently cooked meat like luncheon and shawerma [13,14].

These findings of the regional prevalence of *T. gondii* seropositivity was higher than those detected by other studies including Turkey [15], Malaysia [16], Chile [17],

India [18], Saudi Arabia [19], Mali [20] and northeast Thailand [21]. On the other hand, this result is less than the estimate of 69% and 79% among blood donors in southern Mexican state [22] and male blood donors in northeast Brazil [23] respectively. These variations in the prevalence of *Toxoplasma* among countries could be attributed to geographic and temporal factors [24].

The prevalence of anti-*T. gondii* IgG antibodies among pregnant female was 44%, which is nearly similar to that of Alexandria governorate (46.2%) [25] and of El Fayoum Governorate (45.8%) [26] but lower than the percentage recorded in another Egyptian governorate, Menoufia, which was 67.5% [14]. This may be due to difference in sample size, test used for diagnosis, population characteristics of each governorates and their exposure to relevant risk factors.

Our findings recorded a statistically significant higher prevalence ( $p < 0.01$ ) of *T. gondii* infection in infertile female patients (61.85%) in Dakhalia governorate, Egypt in comparison with the control group, which may indicate a positive correlation between toxoplasmosis and infertility. Our findings are in agreement with those of Li, *et al.* [11] who reported a high prevalence (15.9%) of anti-*T. gondii* IgG antibodies using ELISA among female infertility patients in comparison to 5.6% among pregnant-*puerperant* women. The hypothesized mechanisms for this positive correlation between infertility and chronic *Toxoplasma* infection include development of endometritis and fetal rejection due to local release of *T. gondii* from latently located cysts in endometrial tissue on stimulation during placenta formation [27], impaired folliculogenesis in ovaries, uterine atrophy and reproductive failure due to hypothalamic dysfunction as a result of chronic toxoplasmosis [28,29].

In our study, we found the prevalence of anti- *T. gondii* IgG antibodies in the older age group (30-39 years) was more than other age groups reporting 65.65% in female infertility patients and 65% in pregnant females. This result is consistent with a study carried in Menoufia governorate, Egypt among pregnant women reporting higher prevalence of anti-*T. gondii* IgG antibodies in older ages than younger ages with a percentage of 88.4 and 58.8 respectively [14]. This data on increasing *Toxoplasma* seropositivity with age correlate with the data reported by other authors [30,31]. It is logic that seropositive cases for toxoplasmosis increase with age as older ones have more chance to be exposed to parasite infection [32].

## 5. Conclusion

In conclusion, this study revealed high seropositivity of IgG antibodies for toxoplasmosis among females in child bearing age in Dakhalia governorate, Egypt. Accordingly, the implementation of health education programs aimed to primary prevention of toxoplasmosis is mandatory. Also, the infertile females had a significant higher prevalence of *T. gondii* infection than the controls especially in older ages. These data highlight the possible correlation between *Toxoplasma* infection and infertility, however further studies are required to elucidate the mechanism of this association.

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