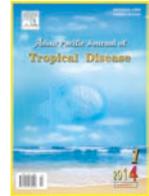


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Toxoplasma gondii in women with bad obstetric history and infertility: a five-year study

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PEER REVIEW

ABSTRACT

Peer reviewer

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Comments

The paper studied the seroprevalence of *T. gondii* in women with bad obstetric history and infertility in which they report 28% and 37.5% prevalence of *Toxoplasma* in patients with BOH and infertility, respectively. It is a well written paper and highlights the role of *Toxoplasma* in the two conditions.

Details on Page S238

Objective: To evaluate the role of *Toxoplasma gondii* in women with bad obstetric (BOH) history and in women with primary and secondary infertility.

Methods: This study was conducted in the Department of Microbiology, Jawaharlal Nehru Medical College and Hospital for a period of 5 years from January 2004 to December 2009. Quantitative determination of IgM antibodies to *Toxoplasma gondii* infection was done by IgM capture ELISA in patients with history of BOH or infertility.

Results: Out of a total of 441 subjects included in the study, 417 (94.6%) had a BOH and 24 (5.4%) subjects had infertility. *Toxoplasma* was found to be more common in females with two or more abortions 52 (76.5%). Similarly in patients with infertility due to *Toxoplasma*, secondary infertility (66.7%) was more common than primary infertility. About 40.3% patients with BOH and 20% patients with infertility had healthy live issues after treatment with spiramycin.

Conclusions: Toxoplasmosis is thus, an easily treatable cause of abortions and infertility. All antenatal females and females with infertility should be screened for toxoplasmosis.

KEYWORDS

Bad obstetric history, Infertility, *Toxoplasma gondii*

1. Introduction

Reproductive failure either due to infertility or repeated abortions is one of the most distressing problems for married couples. An infectious etiology for infertility or repeated abortions suggests an easily treatable solution for an otherwise lengthy and expensive treatment for the same.

Toxoplasma gondii (*T. gondii*) is an important cause of bad obstetric history (BOH) leading to habitual abortions and now its role as a cause of infertility has also been

established[1,2]. Approximately one-third of the population are exposed to this parasite[3]. Toxoplasmosis is the most dangerous for the foetus when the mother acquires infection during pregnancy[4].

The clinical implications of infection due to *Toxoplasma* in pregnant patients are manifold. Such patients may have spontaneous abortions, stillbirth, intrauterine growth retardation, preterm deliveries or foetal anomalies. In addition to the risk of gestational complications and congenital infections, it has been suggested

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that toxoplasmosis has some unfavourable effects on reproductive capacity in both men and women[2].

The role of toxoplasmosis in habitual abortions is well established, however, only a few studies had been done for its association with infertility. This baseline study is probably the first study from North India to evaluate the role of *T. gondii* in infertility. We assessed the role of *T. gondii* in two distinct groups: (i) in women with BOH; and (ii) in women with primary and secondary infertility.

2. Materials and methods

This study was conducted in the Department of Microbiology, Jawaharlal Nehru Medical College and Hospital for a period of 5 years from January 2004 to December 2009.

A total of 441 patients attending the antenatal clinic were included in the study. A detailed clinical history, along with the history of risk factors was obtained from all the cases. The subjects were divided into two distinct groups:

Group 1: A total of 417 cases with BOH defined as previous history of ≥ 1 pregnancy wastages, intrauterine deaths, preterm deliveries, intrauterine growth retardation, unexplained early neonatal deaths or with congenitally malformed children were included in this group.

Group 2: Twenty four females with history of infertility, either primary or secondary, were recruited in the second group. Infertility was defined as inability to conceive for more than a year despite regular unprotected intercourse. Primary infertility was defined as those cases in which conception had never occurred whereas the term secondary infertility was difficulty conceiving after already having conceived either carried the pregnancy to term, or had a miscarriage.

2.1. Microbiological evaluation for toxoplasmosis

Quantitative determination of IgM antibodies to *T. gondii* infection was done by IgM capture ELISA (test kit, Adaltis laboratories, Italy). The test was performed according to the manufacturer's instructions. The interpretation was based on cut off calculated as per the instruction provided in the manual. If the index was <0.1 , the test was considered negative, 1.0 to 1.2 equivocal and an index of >1.2 was considered positive. The assay has a detection limit of 2.21 IU/mL.

2.2. Statistical analysis

Statistical analysis was done using student's *t*-test and

Chi-square test.

3. Results

Out of a total of 441 subjects included in the study, 417 (94.6%) had a BOH and 24 (5.4%) subjects had infertility. The mean age of presentation as a case of BOH was (26.0 ± 3.2) years, with majority of the patients in the 20–30 year age bracket, while the mean age of presentation of infertility cases was (28 ± 5) years. Anti *Toxoplasma* IgM antibodies were found in 120 (28%) females of Group 1 and 9 (37.5%) Group 2 females. Patients in both of the groups with toxoplasmosis [98 (81.7%) Group 1 with BOH, 7 (77.8%) Group 2 infertility] were predominantly from rural background. None of the patients in either group gave history of contact with cats or any other pet animals which was considered as a significant risk factor for toxoplasmosis.

Amongst the females with BOH, 120 (28%) found positive for anti *Toxoplasma* IgM antibodies, more than half of 68 (57%) presented with history of previous abortion. *Toxoplasma* was found to be more common in females with two or more abortions 52 (76.5%) as compared to the females who had a single abortion 16 (23.5%) ($P < 0.05$). Twenty six (21.7%) females gave history of foetal loss, 10 (7.5%) due to intrauterine deaths and 16 (13.3%) were early neonatal deaths. Sixteen (13.3%) subjects gave birth to live babies, with 10 (7.5%) neonates having congenital anomalies and 6 (5%) had intrauterine growth retardation (Figure 1). Sixty two (53.3%) subjects of Group 1, with IgM antibodies against *Toxoplasma* were treated successfully with spiramycin and a good number 25 (40.3%) of them went on to have healthy live issues.

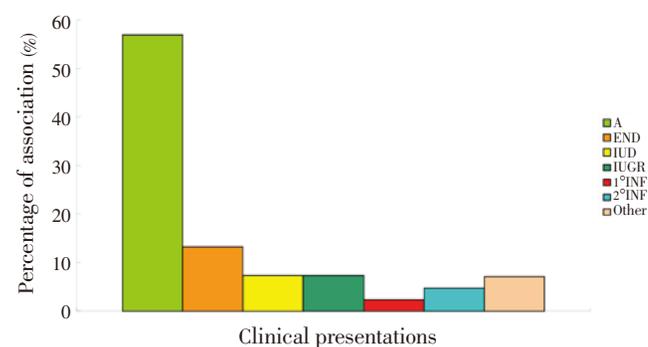


Figure 1. Association of toxoplasmosis with different clinical presentations.

A=Abortion, END=Early neonatal death, IUD=Intrauterine death, IUGR=Intrauterine growth retardation, 1°INF=Primary infertility, 2°INF= Secondary infertility.

Another important association of *T. gondii* was seen with infertility. Out of the 9 cases of infertility attributable

to *Toxoplasma*, 6 (66.7%) had secondary infertility and 3 (33.3%) had primary infertility. Two out of 10 cases which were followed after treatment with spiramycin, gave birth to healthy live babies.

4. Discussion

In the present study, it is evident that *T. gondii* plays a vital role in pregnancy wastage and its occurrence in patients with BOH is a considerable risk factor. Persistence of encysted forms of *Toxoplasma* in chronically infected uteri, and their subsequent rupture during placentation lead to infection of the baby in the first trimester and often to recurrent miscarriages[5]. *T. gondii*, which is a known etiological agent in recurrent pregnancy loss, was found as a cause of BOH in 28% of pregnant women in the present study. This is similar to what has been reported earlier[6].

Women in all age groups were susceptible to the *Toxoplasma* infection, although the younger age group was more commonly infected. Majority of patients (81.7%) with BOH in our study had a rural background. Rural background had been noted as a risk factor for toxoplasmosis in other studies as well[7]. This could be due to rural women, particularly of younger age groups, are more actively involved in outdoor activities and thus are at greater danger of being exposed to infection. No history of contact with cats was elicited in this study. Consumption of pork products was investigated in two studies, and both found a strong association with infection[8,9]. But in our study, none of the females gave the history of consumption of raw or undercooked pork or lamb[10]. Exposure to other animals or consumption of unwashed fruits and vegetables may have been the source of infection. Contact with soil or vegetables or fruit contaminated with soil was identified as a risk factor for *Toxoplasma* infection in pregnancy in two studies[8–10].

In our study, *T. gondii* was strongly associated with multiple abortions. Recurrent abortions were noted in 76.5% cases of *Toxoplasma* related BOH, while 16 (23.5%) females with toxoplasmosis had a single abortion. Sarkar *et al.* have also reported the highest prevalence of *T. gondii* in females with two followed by three abortions[11]. However, some authors had reported toxoplasmosis as a cause of recurrent abortions in 12%–27% females only[6,12]. *T. gondii* also emerged as an important risk factor for intrauterine deaths (7.5%), congenital anomalies (5%), intrauterine growth retardation (5%) and early neonatal deaths (13.3%). Sarkar *et al.* reported that after abortions, the commonest form of pregnancy wastage due to toxoplasmosis are stillbirths, followed by premature deliveries, congenital anomalies, and early unexplained

neonatal deaths[11]. Sixteen (40.3%) patients with BOH, being treated with spiramycin went on to have a healthy live issue.

In our study, an unexpectedly high association of *T. gondii* with infertility (37.5%) was also observed. It was associated more with secondary (66.7%) than primary infertility (33.3%). A good number of them (77.8%) were from rural background. None of them were exposed to any of the animals accountable for being a risk factor for *T. gondii*. Once treated, 20% of them conceived normally. Few studies have addressed the issue of infertility related to *T. gondii*[1]. More studies on association of *T. gondii* with infertility should be conducted.

We advise that every female with not only BOH but also infertility must be thoroughly screened for toxoplasmosis. In Austria and France, it is compulsory by law to test all pregnant women for *T. gondii* on the first visit to their gynaecologist[13,14]. Early diagnosis of toxoplasmosis is essential to start appropriate treatment on time to reduce the transplacental transmission. Treatment of a pregnant woman who acquires infection at any time during pregnancy reduces the chances of congenital transmission by about 60%[15].

In our study, we used IgM ELISA for the detection of toxoplasmosis. It is easy to perform test with reproducible results. Serological tests form the backbone of diagnosis. These may include the titration of serum IgG, IgM and IgA immunoglobulins. IgA is useful in the diagnosis of recent foetal and newborn infections. IgG is very useful for screening purposes and follow up of active infection, but IgM are the specific immunoglobulins which detect recent infection in mother[16,17].

We suggest that history of a single abortion is also helpful to investigate *T. gondii*. Serum samples from rural areas can be collected and sent to higher centres for testing and the patient need not come to a city for the test to be done. The doctors at the primary health care can easily treat this infection with spiramycin or leucovorin so that the patients can achieve a successful delivery cost effectively.

Conflict of interest statement

We declare that we have no conflict of interest.

Comments

Background

Reproductive failure either due to infertility or repeated

abortions is one of the most distressing problems for married couples. An infectious etiology for infertility or repeated abortions suggests an easily treatable solution for an otherwise lengthy and expensive treatment for the same. *T. gondii* is an important cause of BOH leading to habitual abortions and now its role as a cause of infertility has also been established.

Research frontiers

The role of toxoplasmosis in habitual abortions is well established, however, only a few studies had been done for its association with infertility. This baseline study is probably the first study from North India to evaluate the role of *T. gondii* in infertility.

Related reports

Sarkar *et al.* have reported the highest prevalence of *T. gondii* in females with two followed by three abortions.

Innovations & breakthroughs

In this study, an unexpectedly high association of *T. gondii* with infertility (37.5%) was observed. It was associated more with secondary (66.7%) than primary infertility (33.3%). A good number of them (77.8%) were from rural background. Once treated, 20% of them conceived normally.

Applications

Every female with not only BOH but also with infertility must be thoroughly screened for toxoplasmosis. Early diagnosis of toxoplasmosis is essential to start appropriate treatment on time to reduce the transplacental transmission. Treatment of a pregnant woman who acquires infection at any time during pregnancy reduces the chances of congenital transmission by about 60%.

Peer review

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