

# Immunomodulation effect of *Toxoplasma gondii* on infected women with miscarriage in Mosul City

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## ABSTRACT

**Overview:** Toxoplasmosis is a relatively common disease in many Iraqi localities, such distribution is mostly undetected except in certain groups of population, like pregnant women, aborted women, congenital anomalies, and some elderlies, causing morbidity and mortality by varied methods, including immune modulation.

**Methods:** about 153 women with abortion were sub grouped to single (sporadic) and multiple (habitual) abortion, all were tested for toxoplasmosis by detection of antibodies titer, using two common methods which are 2ME latex and ELISA.

**Results:** ELISA method was more sensitive in toxoplasma antibodies detection than Latex in sporadic abortion, but was less sensitive than Latex in habitual abortion group; sporadic abortion showed 9.5% were positive comparing to habitual abortion which were 5.1% positive. On the other hand, ELISA found that 44% and 6% were positive in sporadic abortion for IgG and IgM respectively, while 43% and 2% were positive in habitual abortion for IgG and IgM respectively.

**Conclusion:** ELISA and 2ME Latex showed varied titers of antibodies in the two groups and showed that the antibodies titer was less in habitual aborted women group than the sporadic aborted women group which could be attributed to immune suppression or modulation exerted by *Toxoplasma gondii*.

**Keywords:** ELISA, immune modulation, Latex, *Toxoplasma gondii*, toxoplasmosis.

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## INTRODUCTION

*Toxoplasma gondii* is an Apicomplexa protozoa that affecting many mammals including human <sup>(1)</sup>, about half of world population are infected with this parasite, especially in developing countries, more specifically in sub-tropical and tropical countries <sup>(2,3)</sup>.

Many studies in Mosul and other localities in Iraq, showed that there is a high risk of infection with toxoplasmosis, mostly detected in pregnant women due to abortion. A study conducted in in the North of Iraq specifically in Al-Hawija and Al-Baiji Districts, and included 285 women with abortions average (1 - 3), indicated that about 40% of women were infected with toxoplasmosis <sup>(4)</sup>.

A newer study conducted in Baghdad on apparently healthy individuals who were tested for anti-toxoplasma IgM and IgG antibodies, the study included 800 persons, and found that 29 out of 135 women included in the study and reported a repeated abortion were positive for anti-toxoplasma IgM antibodies (21.5%); and totally 217 persons out of 800 (27.1%) personsshowed positive anti-toxoplasma IgG antibodies <sup>(5)</sup>.

Toxoplasmosis is considered as a problem for pre-infected pregnant women, immune compromised and AIDS patients, because such parasite affecting the host with variable pathogenic problems, like abortion and congenital anomalies in pregnant women, cerebral or ocular toxoplasmosis and their consequences which could be highly troublesome <sup>(6,7)</sup>.

Many infective microbes developed several methods to evade host defense system and maintain their survival, one of these microbes is the toxoplasma protozoa which can use many methods affecting the host cells and immune system <sup>(8)</sup>.

Many studies were conducted to compare between the ELISA and 2ME Latex methods, in order to determine which, one is more sensitive and accurate in diagnosis of toxoplasma infection. Interestingly some of these studies found that Latex showed a higher sensitivity in chronic infections rather than ELISA<sup>(9,10)</sup>.

Starting with general phenomena which is that the infected cells with *Toxoplasma gondii* showed an up-regulation of pro-inflammatory cytokines, furthermore they showed to be protected from apoptosis induction, and also such cells may show internal organelle redistribution<sup>(11)</sup>.

Cytokines delicately control the inflammatory and regulatory response to acute and chronic infection with toxoplasma parasite, many cytokines, like INF-gamma, TNF-alpha, and IL-12, are essential in protective immune reaction, but still, the over expression of such mediators have a harmful effect on the host<sup>(12)</sup>.

The intracellular parasite has the capability to inhibit the apoptotic mechanisms that induced by the immune system, to maintain its survival<sup>(13)</sup>.

The diagnostic methods are mostly depending on indirect detection of the parasite by detection of the immune response (as antibodies) which occur as a response to the infection.

**Aim of the study:** Detection of possible sensitivity variance of common serological diagnostic methods between sporadic and habitual abortion due to suspected immune modulatory effect of *Toxoplasma gondii* infection.

## MATERIALS AND METHODS

Both patients and control groups were collected Al-Batool Maternity Teaching Hospital in Mosul city over six months period starting in Nov. 2007 till Apr. 2008, as a cross-sectional study to investigate the role of *T. gondii* infection in such medical condition. The total number of included patients were 153 women suffering from abortion.

The aborted women were divided in to two groups, the first group included are the women suffering from abortion for the first time without history of any spontaneous abortion before; while the second group included are the women suffering from abortion with history previous abortion for three consecutive times or more.

All were tested for *Toxoplasma gondii* by using 2ME latex<sup>(14-25)</sup> and ELISA<sup>(26-29)</sup> techniques.

The latex kit is toxocell latex form BioKit company, Spain , while the ELISA kits are Anti-toxoplasma IgG and IgM from BioCheck company USA.

All the samples serum, and kits were brought to room temperature prior measurement, the testing were conducted according to the kits manual, and the results were recorded and statistically analyzed.

## RESULTS

The 2ME-latex test showed a significant higher result in sporadic patients in comparison to the habitual abortion patients, as shown in (Table 1).

The first group i.e. sporadic abortion group showed 9 out of 95 patients (9.5%) were positive, while the second group i.e. habitual abortion group showed 3 out of 58 patients (only 5.1%) were positive for 2ME latex test for toxoplasmosis.

**Table1: Detection of *Toxoplasma gondii* antibodies using 2ME Latex**

Groups	2Me latex No. (%)
Group (1) "sporadic abortion" (n=95)	9 (9.5)
Group (2) "habitual abortion" (n=58)	3(5.1)

On the other hand, ELISA test for *Toxoplasma gondii* showed variable results varied according to the type of immunoglobulin, as showed in (Table 2).

**Table2: Detection of *Toxoplasma gondii* antibodies using ELISA for IgG and IgM**

Groups	ELISA IgG No. (%)	ELISA IgM No. (%)
Group (1) "sporadic abortion" (n=95)	42 (44)	6 (6)
Group (2) "habitual abortion" (n=58)	25 (43)	1 (2)

Immunoglobulin type G (IgG) showed no significant variation between the group one patients (sporadic abortion), which showed 44%, and group two patients (habitual abortion), which showed 43%.

But immunoglobulin M (IgM) showed significant difference between these two groups, where the sporadic abortion patients showed higher number of positive patients in comparison to the habitual abortion group which showed very little number with positive results.

The comparison between the results obtained by using two different methods were compared in (Table3) which showed significant difference in sensitivity of detection of old or latent infection within the same group (sporadic or habitual) or in different groups.

**Table 3: Comparison of Latex, ELISA IgG and ELISA IgM results**

Groups	2Me latex No. (%)	ELISA IgG No. (%)	ELISA IgM No. (%)
Group (1) "sporadic abortion" (n=95)	9 (9.5)	42 (44)	6 (6)
Group (2) "habitual abortion" (n=58)	3(5.1)	25 (43)	1 (2)

As shown in the (Table3), the sensitivity of Latex method showed much less sensitive in detection of old or latent infection in the members of the group two, Where the Latex test showed approximately 9% positive results in sporadic abortion group, in comparison to 5% detected in habitual abortion group.

And also ELISA IgM test showed the same poor sensitivity in detection of active infection in habitual abortion group, only 2% were detected, in comparison to 6% were detected in sporadic abortion group, considering almost equal sensitivity by ELISA IgG testing results in both groups which were 44% and 43% respectively.

## DISCUSSION

Toxoplasmosis is considered as an infectious problem in many developing countries due to the effect of such parasite in causing abortion and congenital anomalies, in addition to other problems that are shared with developed countries affecting immune compromised and AIDS patients.

In this study, it was detected that the latex results were higher in sporadic group of patients in comparison to the habitual abortion group, such results were compatible with other studies which also showed similar outcome. Such results could be explained on the basis of immune modulation caused by the chronic infection with *Toxoplasma gondii*, which was manifested with frequent abortion.

Latex 2ME results is incomparable to ELISA IgG test, where IgG levels showed highly similar results in both groups, i.e. sporadic and habitual abortion were both showed 44% and 43% respectively, which may explain the variance in Latex results on the basis of life span of already excreted IgG in the early time of infection, but not newly synthesized IgG to repeated infection or activation.

ELISA IgG test showed no significant variation between the sporadic abortion, which represent the acute or short time after infection, in comparison to the habitual abortion group which represent the chronic infection with toxoplasmosis.

Such similarity also could be explained as the IgG level is the only synthesized in early stage of infection with minimum newly synthesized IgG on reactivation, which is one of the manifestations of immune suppressant or modulatory effect of *Toxoplasma gondii* parasite<sup>(12)</sup>.

On the other hand, ELISA IgM test showed a significant variation between the acute infected patients, i.e. the sporadic abortion group in comparison to the chronic infected patients, i.e. the habitual abortion group, such results may indicate some immunological changes in these patients, which is comparable to other researches which showed varied level of sensitivity of detection in acute and chronic infected patients, as indicated by Hamoo and Al-Aubaedyin 2009 and Al-Bajalan *et al.* in 2015<sup>(9,10)</sup>.

Such results could be explained by several mechanisms exerted by the parasite, starting with changing to dormant bradyzoite stage, to manipulation of produced cytokines, delay apoptosis, and even affecting gene expression of infected cells in addition to the immune cells in contact.

## CONCLUSION

ELISA and 2ME Latex showed varied titers of antibodies in the two groups and showed that the antibodies titer was less in habitual aborted women group than the sporadic aborted women group which could be attributed to immune suppression or modulation exerted by *Toxoplasma gondii*.

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