Gastroenterology and Hepatology From Bed to Bench. *2011; 4(1): 34-37*

ORIGINAL ARTICLE

The evaluation of interleukin-8 chemokine in chronic and acute *Toxoplasma gondii* infection

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ABSTRACT

Aim: We investigated whether the level of IL8 was different in patients with chronic and acute *Toxoplasma gondii* infection during the pregnancy compared with control group.

Background: It is well established that *T.gondii* infection induces a strong cell-mediated immune response.

Patients and methods: ELISA was used to determine the level of IL8 in sera of 568 pregnant women. Patients were divided into three groups according to a *T.gondii* serology. The first group included 202 women with positive IgG titres, the second group was 66 women with IgM and negative IgG *T.gondii* serology; and the third group comprised the sera of 300 healthy pregnant women with negative *T.gondii* serology and served as controls.

Results: The level of IL8 in group I was within normal range similar to control group. However, the level of IL8 was increased in those pregnant patients with positive IgM *T.gondii* serology.

Conclusion: The serum levels of pro-inflammatory cytokines such as IL8 seem to be increased in patients with serological evidence of acute *T.gondii* infection.

Keywords: *Toxoplasma gondii*, IL8, Pregnancy.

(Gastroenterology and Hepatology From Bed to Bench 2011; 4(1): 34-37).

Introduction

Toxoplasmosis, a zoonosis caused by a protozoan, *Toxoplasma gondii*, is probably the most widespread human parasitosis. *T.gondii* belongs to genus *Toxoplasma*, whose primary host is kittens or cats. *T.gondii* life cycle has two main stages, the sexual and the asexual phase. Asexual phase occur in warm blooded animals, and human acquire the parasite in this phase (1).

Received: 19 August 2010 *Accepted*: 18 November 2010
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Most pregnant women with acute acquired infection do not experience obvious symptoms or signs (2). Acute and latent *T.gondii* infections during pregnancy are most commonly diagnosed by detecting the immunoglobulin IgG and IgM antibodies in the serum samples of the patients using enzyme-linked immunosorbent assay (ELISA) (Fig. 1) (3).

Chemokines are a group of chemotactic polypeptides that are key mediators of leukocyte activation and chemotaxis (1, 4). They are divided into groups of related families based on the arrangement of cysteine residues in their

amino-terminal domain (5). The C-X-C or b-chemokines, of which IL-8 is a prototype, are primarily involved in the recruitment and activation of neutrophils, although they may attract other leukocyte populations (4).

Interleukin-8 (IL-8) is produced by macrophages and other cell types such as epithelial cells and endothelial cells. Primary function of IL-8 is the induction of chemotaxis in its target cells like neutrophil and granulocytes (3). IL8 has an important role in the innate immune response. Interleukin-8 is often associated with inflammation. It has been cited as a pro-inflammatory mediator in Toxoplasmosis (1). It is well recognized that T cell-mediated immunity plays a central role in the host response to intracellular pathogens (2). T cell- mediated immunity and activated macrophages have been shown to play important roles in resistance to T cell-mediated immunity *T. gondii* infection (6-8).

In the current study we evaluated the serum levels of IL8 in three groups of pregnant women serums; Group I women with IgG positive, *T. gondii* serology, group II IgM positive *T. gondii* serology and group III, a control group, with negative *T. gondii* serology.

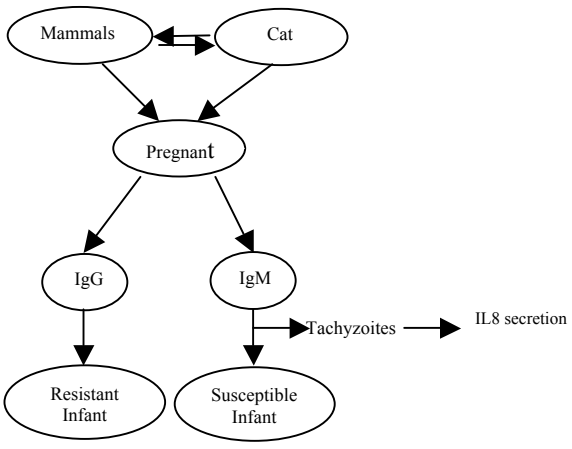

Figure 1- The circulation of *Toxoplasma gondii* transmission form animals to pregnant women.

Materials and Methods

The pregnant women who participate in this study were attending rural and urban health care centers.

During the period of January 2007 to July 2009, 538 pregnant women were recruited for this study. Two hundred and thirty five (43.9%) and 333 (56.1%) samples were collected from rural and urban areas respectively. After obtaining consent, demographic data, clinical data (including obstetric history, gestational age) and behavioral data (including animal contacts, exposure to cat faeces) was obtained from all women recruited.

Sera from the 568 pregnant women was collected and analysed for anti-*T. gondii* IgM and IgG antibodies as described previously (9). IL8 level was measured by commercial Enzyme Linked Immunosorbant Assay kit (Human IL8/NAP-1 ELISA, Bender MedSystems, Austria) in all recruited pregnant women according to the manufacturer's instruction.

For data analysis and statistics, the PC-based software SPSS version 13.0 was applied. Percentages were compared by rates and proportion; 95% confidence intervals are reported and the differences were considered to be statistically significant when the p value obtained was less than 0.05.

Results

The IgG antibodies were found in 121 of 333 (36.3%) urban and 81 of 235 (34.5%) rural pregnant women, whereas IgM antibodies to *T.gondii* were found in 40 of 333 (12%) urban pregnant and 26 of 235 (11%) rural pregnant women (Table 1). The mean serum concentration of IL8 was not statistically significant different when urban and rural subjects were compared (Table 2).

The mean serum concentration of IL-8 in chronic and acute phase of *T.gondii* infection in pregnant women with positive *T.gondii* IgG serology was 116.1 pg/ml and 134.8 pg/ml in pregnant women with positive *T.gondii* IgM serology. However, in healthy subjects, the mean IL-8 serum concentration was (mean 68.9 pg/ml) ($P < 0.001$) significantly lower than the mean IL-8 serum concentration in pregnant women with positive *T.gondii* IgM serology.

Table 1- Seroprevalence of toxoplasmosis in different groups of pregnant women according to different variables

	control	IgG positive	IgM positive
Miscarriage			
Yes	46 (54.1)*	25 (29.4)	14 (16.5)
No	254 (52)	177(40.4)	52(10.8)
Cat traffic			
Traffic			
Yes	46 (52.9)	36 (41.4)	5 (5.7)
No	254 (52.8)	166 (34.5)	61 (12.7)
Keeping			
Yes	52 (55.3)	29 (30.9)	13 (13.8)
No	248 (52.3)	173 (36.5)	53 (11.2)
Residence			
Urban	172 (51.7)	121 (36.3)	40 (12)
Rural	128 (54.5)	81 (34.5)	26 (11)
Education			
Under diploma	122 (48.4)	89 (35.3)	41 (16.3)
Educated	178 (56.3)	113 (35.8)	25 (7.9)

* Figures in the parentheses represent percent.

The mean IL-8 serum concentration in pregnant women with limited educational achievements was statistically higher than the mean IL-8 serum concentration educated women ($P< 0.006$).

Eighty seven of 568 patients had been contact with cats. Of these 87 subjects, 54% of them had negative *T.gondii* serology and belonged to control group. There was no significant difference in the mean IL-8 serum concentration between the groups (Table 2).

Table 2- Comparison of mean level of IL8 in different groups of pregnant women.

		Mean level of IL8
Study groups		
I	IgG +	116.1
II	IgM+	134.9
III	control	68.9
Education		
Educated		
	IgG +	102.3
	IgM+	114.2
	control	62.6
Under diploma		
	IgG +	133.6
	IgM+	147.4
	control	78
Residence		
Rural		
	IgG +	133
	IgM+	158.5
	control	53.5
Urban		
	IgG +	104.8
	IgM+	119.5
	control	58
Miscarriage		
No		
	IgG +	121.4
	IgM+	145.8
	control	69.45
Yes		
	IgG +	65.7
	IgM+	94.2
	control	87.9

Discussion

Acute toxoplasmosis causes host cell lysis and an inflammatory infiltrate consisting of lymphocytes, macrophages, and neutrophils. One signal for the observed cellular infiltrate after *T. gondii* infection is the release of pro-inflammatory chemokines from infected cells. Infection of primary fibroblasts, as well as transformed epithelial cell lines, with *T.gondii* stimulates secretion of the pro-inflammatory chemokines like IL-8. The chemokine response is dependent on invasion by live tachyzoites and subsequent host cell lysis. Furthermore, supernatants or lysates from *T.gondii* infected fibroblasts could elicit significant IL-8 secretion (10).

Increased level of IL-8 correlates with early acute inflammation or with a reactive form of toxoplasmosis. IL-8 is responsible for activation and recirculation of neutrophils and neutrophils can phagocytose and kill or inhibit tachyzoites of *Toxoplasma* and showed that human intestinal epithelial cells infected with *T.gondii* elicit rapid secretion of IL-8 (7), so it has an important role in innate immunity in response to *toxoplasma*.

In our study, the concentration of IL-8 level in patients with serological evidence of acute infection with *T.gondii* was statistically significantly higher than in healthy subjects. There was no significant difference in the mean IL-8 serum concentration when urban and rural subjects were compared. Furthermore a history of previous miscarriage or exposure to cats was not associated with a significant difference in the mean IL-8 serum concentration.

In this report, we demonstrate that mean level of IL-8 in pregnant women with serological evidence of *T.gondii* infection was higher than other groups. The significance of this finding for the outcome of the pregnancy remains uncertain.

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