

# *Toxoplasma gondii* Antibodies in Type 1 Diabetes Mellitus

## Tip 1 Diyabette *Toxoplasma gondii* Antikorları

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**ABSTRACT Objective:** *Toxoplasma gondii* is a protozoan parasite, which infects up to a third of the world's population. Infections are more common and run a more protracted course in patients with Diabetes mellitus (DM). We aimed to determine the prevalence of anti-*T. gondii* antibodies in patients with type 1 DM. **Material and Methods:** The study group comprised 85 patients with type 1 DM and 85 healthy volunteers. Micro enzyme-linked immunosorbent assay and indirect fluorescent antibody technique were used. **Results:** *T. gondii* IgG sero-positivity rate in DM patients (56.62%) was significantly higher than in controls (22.4%). **Conclusion:** Parasitologic surveys should be repeated periodically in this group of patients.

**Key Words:** *Toxoplasma gondii*; diabetes mellitus

**ÖZET Amaç:** *Toxoplasma gondii* dünya nüfusunun üçte birinden fazlasını enfekte eden protozoan bir parazittir. Enfeksiyonlar diyabetli hastalarda oldukça sıktır ve enfeksiyon seyri uzar. Bu çalışmada, tip 1 Diabetes mellitus (DM)'lu hastalarda anti-*T. gondii* antikorlarının prevalansını belirlemeyi amaçladık. **Gereç ve Yöntemler:** Araştırmada 85 tip 1 DM'li hasta ve 85 gönüllü sağlıklı kişi seçildi. 'Micro enzyme-linked immunosorbent assay' ve indirekt fluoresan antikor tekniği kullanıldı. **Bulgular:** DM'li hastaların *T. gondii* IgG sero-positivitesi (%56.62) kontrollerden (%22.4) istatistiksel olarak anlamlı bir şekilde yüksek bulunmuştur. **Sonuç:** Bu hasta grubunun periyodik olarak parazitolojik takibinin yapılması gerekmektedir.

**Anahtar Kelimeler:** *Toxoplasma gondii*; diabetes mellitus

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**T***oxoplasma gondii*, which is worldwide in distribution, was found in nearly one-third of the human population.<sup>1</sup> Although serologic evidence suggests a high rate of human exposure to the organism, the disease itself is relatively rare. *T. gondii* can infect many vertebrates as well as humans, but the definitive host is the cat.<sup>2</sup>

Toxoplasmosis represents an important public health problem and is of great clinical importance in man in two major situations: as a cause of congenital infection and as an opportunistic infection of high mortality in immunosuppressed individuals.<sup>3,4</sup> Individuals with normal immunity and acute acquired *Toxoplasma* infection usually have a self-limited clinical course and rarely require specific treatment.<sup>5</sup> After the acute infection period, *T. gondii* remains viable in the form of tissue cysts, which reproduce slowly throughout the life of the host, thus characterizing the chronic in-

fection. During this phase, the tissue cysts are controlled by the humoral and cellular immune system, involving T lymphocytes and macrophages, which are continuously stimulated by parasite antigens. As a result, parasite multiplication is more active and persists for longer periods of time in less immunologically active tissues.<sup>6</sup>

Immunocompromised hosts, especially those with deficient cellular immunity, are at risk of reactivation of the chronic infection and dissemination, with the occurrence of fulminating disease. *T. gondii* is the most frequent protozoan causing opportunistic infections in the immunocompromised population.<sup>7</sup>

It is well established that infection is more common and runs a more protracted course in people with DM. There are several case reports demonstrating that diabetics have an increased susceptibility to infection.<sup>8</sup> Many specific infections are more common in diabetic patients and some are almost exclusive to that specific population. Other infections occur with increased severity and are associated with an increased risk of complications in patients with DM.<sup>9</sup>

In this study, we evaluated the sero-positivity rate of anti-*T. gondii* antibodies in patients with type 1 DM. Patients with type 1 DM are under the risk of opportunistic infections. We tried to underline the risk of severe toxoplasmosis in patients with type 1 DM with this study. This is the first comprehensive study on this subject.

## PATIENTS

Eighty-five (45 men, 40 women) patients with type 1 DM who presented to the Department of Endocrinology Erciyes University Gevher Nesibe Hospital and Kayseri Research Training Hospital and 85 healthy volunteers (48 men, 37 women) were included in the study. All patients were informed on the details of the study and a signed approval form was taken from each patients. The age range of the patient and control groups was 15-73 (mean age  $41.73 \pm 19.23$ ) and 16-73 (mean age  $41.51 \pm 19.04$ ) respectively.

## MATERIAL AND METHODS

Five millilitres of blood was drawn from the patients and serum samples were obtained by centrifugation at 1000xrpm. They were stored at -20°C until they were analyzed.

DM was diagnosed according to the current American Diabetic Association (ADA) Expert Committee recommendations (2003 ADA criteria).<sup>10</sup> The differential diagnosis between type 1 DM and type 2 DM was made by laboratory tests and clinically. Anti-islet antibodies, antibodies to insulin or glutamic acid decarboxylase (GAD) were used for the diagnosis of type 1 DM. Patients with other specific forms of DM were excluded from the study.

We used the enzyme linked immunoassay (ELISA) and indirect fluorescence antibody technique (IFAT) to screen for anti-*T. gondii* IgG and IgM antibodies. ELISA and IFAT kits were provided from EUROIMMUN commercial manufacturer.

## Statistical analysis

SPSS V.10.0 for Windows package program was used. Chi-square test was used and  $p < 0.05$  was accepted to be statistically significant.

## RESULTS

IgG antibodies to *T. gondii* were positive in 49 (57.62%) patients with type 1 DM and in 18 (21.2%) controls by both ELISA and IFAT. IgM antibodies were negative in both patients and in controls. The distributions of IgG antibodies in the two groups are shown in Table 1.

The difference in the IgG sero-positivity rate between the patient and the control group was statistically significant ( $p < 0.05$ ), (Table 1). However, IgM antibodies were not positive in any of the groups.

## DISCUSSION

Toxoplasmosis can vary from an asymptomatic, self-limiting infection to a fatal disease, as seen in patients with congenital infections or in debilitated

**TABLE 1:** IgG antibodies to *T. gondii* of patients with type 1 DM and control group.

Antibody	Patients (n= 85)		Controls (n= 85)		p value
	Number	%	Number	%	
Anti- <i>T. gondii</i> IgG (+)	49	57.6	18	21.2	0.00
Anti- <i>T. gondii</i> IgG (-)	36	42.4	67	78.8	

patients in whom underlying conditions may influence the outcome of the infection. In immunocompromised patients, the infection most often involves the nervous system, with diffuse encephalopathy, meningoencephalitis, or cerebral mass lesions.<sup>11</sup> Immunocompromised hosts, especially those with deficient cellular immunity, are at risk of reactivation of the chronic infection and dissemination, with the occurrence of fulminating disease. Patients with deficient cellular immunity such as those with neoplasms, collagen tissue diseases, transplant recipients under immunosuppressive therapy and hemodialysis patients with chronic renal failure are particularly susceptible to toxoplasma infections.<sup>12</sup> The most frequent protozoan causing opportunistic infections in immunocompromised individuals is *T. gondii*.<sup>7</sup>

The common belief is that the incidence of infection is higher in patients with DM. A number of factors greatly complicate efforts to assess the risk of infection and resulting complications in DM. The most basic is the problem of determining an appropriate estimate of the population at risk. A

number of variables, including duration of illness, severity of non-infectious complications, concurrent illnesses, level of glucose control, and even degree of medical supervision, result in a very heterogeneous group of individuals at risk even within a more narrowly defined time frame.<sup>13</sup>

Several studies demonstrated that some blood cells such as the polymorphonuclear leukocytes (PMNs) in patients with diabetes had a decreased chemotactic index resulting with inadequacy in the killing function.<sup>14,15</sup> In addition, other blood cells such as circulating monocytes were also decreased in DM patients.<sup>16</sup> However, it is clearly demonstrated that transformation of lymphocyte against the mitogen phytohemagglutinin (PHA) is destroyed in patients with DM and the lymphocytes of diabetic children had a lowered mitogenic response.<sup>13,17</sup> Studies also showed that during diabetes, the function of natural killer cells decreased.<sup>18</sup>

We assessed the sero-positivity rate of toxoplasmosis in patients with type 1 DM by ELISA and IFAT. Our results suggested a significantly higher positivity rate for *T. gondii* IgG antibodies in patients with type 1 DM compared to controls (Table 1). However, IgM antibodies were not positive in any group. These results suggest a possible increase in the susceptibility of DM patients to toxoplasmosis. In conclusion, immunosuppression is important for *Toxoplasma* infection. Type 1 DM patients should be screened periodically for *Toxoplasma* to prevent disseminated infection.

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