Anti-Toxoplasma gondii antibodies in hemodialysis patients receiving long-term hemodialysis therapy in Turkey

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ABSTRACT

Objectives: Toxoplasma is a globally distributed pathogen for humans and animals. In situations of immunodeficiency, *Toxoplasma gondii* (*T. gondii*) emerges as a life-threatening infection. *Toxoplasma gondii* is transmitted parenterally, flourish in state immunosuppression and, most toxoplasma infections are asymptomatic. In the present study, we aimed to investigate the prevalence of anti-*T. gondii* antibodies in hemodialysis patients with chronic renal failure. We undertook a prospective study of our maintenance hemodialysis patients to determine whether these sources posed a risk for transmission of *T. gondii*.

Methods: This study was carried out on patients undergoing regular hemodialysis in the dialysis units (Hemodialysis Center of Antakya State Hospital, Emir Hemodialysis Center and Antakya Hemodialysis Center, Hatay, Turkey) between January 2004 and June 2004. Two hundred and fifty-five hemodialysis patients and 50 healthy controls were studied for the prevalence of anti-*T. gondii* antibodies by enzyme-linked immunosorbent assay.

Results: Anti-immunoglobulin G (IgG) and immunoglobulin M (IgM) *T. gondii* antibodies positivity were found to be 195 (76.5%) of the 255 hemodialysis patients and 24 (48%) of the 50 control subjects. The difference between them was statistically significant ($p<0.05$). In addition, an increase of the seropositivity rate was detected with increasing length of time on hemodialysis treatment, indicating a statistically significant difference between these 2 parameters ($p<0.05$).

Conclusion: These findings confirm a high prevalence of toxoplasma infection in hemodialysis patients. These patients are a risk group for toxoplasma infection. Moreover, it is recommended that hemodialysis patients who are susceptible to toxoplasma infections should be identified by *T. gondii* IgG and IgM specific serological tests. Therefore, patients undergoing hemodialysis should be screened for toxoplasma before dialysis to prevent the dissemination of this infection through the hemodialysis procedure.

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Toxoplasma gondii (T. gondii) is an obligate, intracellular protozoan parasite in the order Coccidia.[1] Toxoplasmosis is caused by the protozoan parasite, *T. gondii*, where humans and other warm-blooded animals are its hosts. The infection has a worldwide distribution, and the incidence of toxoplasmosis varies around the world. The highest rate in our country reaches up to 55%.[2-8] Approximately one-third of all humanity has been exposed to this parasite.[1]

Humans become infected through ingestion of food contaminated with tissue cysts or oocysts.[1] In immunocompetent hosts, infection is usually benign

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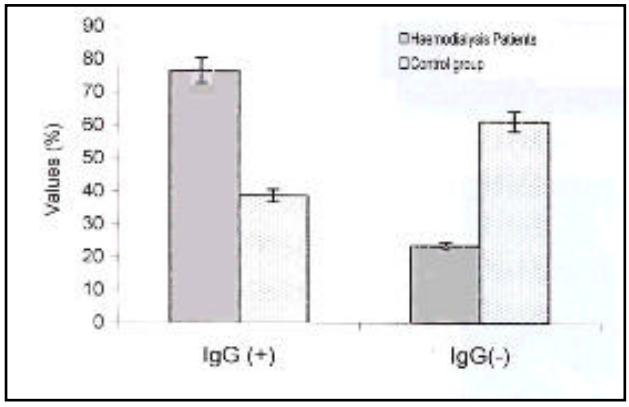

Figure 1 - The ratio of Toxoplasma IgG antibodies in hemodialysis patients and healthy control group.

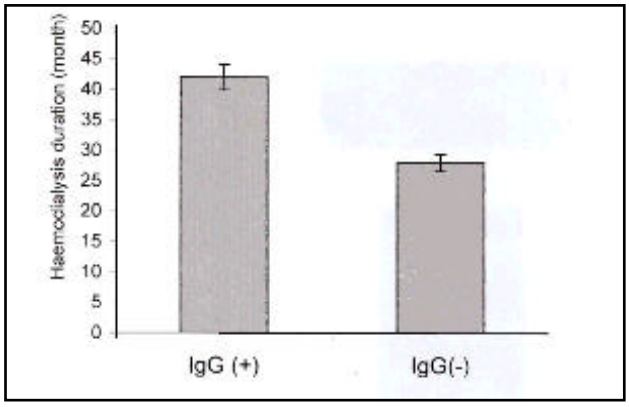

Figure 2 - The length of hemodialysis duration and seropositivity of Toxoplasma IgG antibody.

owing to a rapid, effective cellular immune response. However, persons with defective cellular immunity are at risk for severe sequelae including death. For human immunodeficiency virus-infected persons, cerebral toxoplasmic encephalitis is an important cause of morbidity and mortality.[9-11] *Toxoplasma gondii* is one of the major opportunistic infectious agents in immunocompromised individuals such as hemodialysis patients. The protozoan *T. gondii* can cause serious disease when transmitted to the fetus or the immunodeficient patient. Although it is usually asymptomatic in immunocompetent adults, it can cause severe disease manifestations and even death in immunocompromised patients. Disease in these patients can be due to recently acquired infection or more commonly due to reactivation of a latent infection.[9,12]

There are many studies regarding the immune response in patients with chronic renal failure and it is related with impairment of cell-mediated immunity. Hemodialysis patients are under many different infection risks due to their depressed immune status, or through hemodialysis.[9-12] In this study, we undertook a prospective study of our maintenance hemodialysis patients to determine whether these sources posed a risk for transmission of *T. gondii.* Our objective was to determine the seroprevalence of *T. gondii* IgG and IgM antibodies in hemodialysis patients and to ascertain whether they have an increased risk through occupational exposure.

Methods. This study was carried out on patients undergoing regular hemodialysis in the dialysis units (Hemodialysis Center of Antakya State Hospital, Emir Hemodialysis Center and Antakya Hemodialysis Center, Hatay, Turkey) between January 2004 and June 2004. In the present study, 255 patients with chronic renal failure, undergoing hemodialysis, aged between 14 and 91 were selected from 3 hemodialysis units in Hatay. History of blood transfusion of hemodialysis patients, and time on dialysis (time span since initiation of hemodialysis therapy) were recorded. In addition, 50 healthy volunteers were selected as a control group, who were aged between 15 and 71. In order to determine the seroprevalence of *T. gondii* infections in hemodialysis patients, blood samples for antibody study were collected from 255 patients and that of control group comprising 50 healthy persons of similar age and gender were taken in the study. Blood samples were taken from the patients and the 50 healthy volunteers and centrifuged at 1500 rpm for 5 min to obtain serum samples and preserved at -20°C in deep freeze until tested. The existence of *T. gondii* IgG and IgM antibodies in the serum samples were tested using a second-generation commercial enzyme-linked immunosorbent assay (ELISA). We used the ELISA technique to determine *T. gondii* employing anti-*T. gondii* IgG and IgM antibodies, ELISA kits were purchased from the commercial manufacturer Abbott (Abbott Laboratories, USA).

Statistics. Statistical analyses were performed using a chi-square test, where *p* values less than 0.05 was considered statistically significant. Using Statistical Package for Social Sciences (SPSS, version 10) software, the statistical analyses was carried out.

Results. In this study, the mean age of the patients was 53.94 ± 17.27 years, 175 of whom were males (68.6%) and 80 of them were females (31.4%). The mean age of the healthy control group was 51.44 ± 12.27 years, 25 of them were male and 25 females. The hemodialysis patients and the control group demonstrated similar gender and age distributions. Toxoplasma IgG antibody positivity was determined in 195 (76.5%) of the 255 patients

and 21 (42%) of the 50 individuals in the healthy control group. The difference was found significant ($p<0.05$). In addition, toxoplasma IgM antibody positivity was determined only in 2 (0.8%) of the 255 patients, while all of the subjects in the control group were determined as seronegative by the ELISA. Although the percentage of hemodialysis patients positive for the anti-*T. gondii* IgM antibodies (0.8%) was found to be greater than in the healthy volunteers (0%), the difference between the groups was not statistically significant ($p>0.05$). Though positive toxoplasma IgG antibody was found to be 71.4% (125/175) of the male patients, this ratio was 87.5% (70/80) of the female patients included in this study. Seropositivity of toxoplasma IgG was detected 32% (8/25) in male and 52% (13/21) in the female of the healthy control group. The seropositivity of toxoplasma IgG was significantly different between in both hemodialysis patients and healthy control groups male and female (**Figure 1**). *Toxoplasma gondii* IgM antibodies indicating acute infection was detected in one man and one woman amongst the hemodialysis patients. The IgM antibody was not detected in the healthy control group.

The relativity between the hemodialysis duration and seropositivity of *T. gondii* antibody was also searched in this study. Hemodialysis duration was found to be 42 ± 32.9 months in the patients with toxoplasma IgG seropositive and 28.1 ± 32.5 months in toxoplasma IgG seronegative patients. Significant correlation was also found between the length of period on hemodialysis and the existence of toxoplasma IgG ($p<0.05$) (**Figure 2**).

Discussion. *Toxoplasma gondii* is a coccidian parasite of felines, humans and other warm-blooded animals as alternative hosts. Toxoplasmosis can be frequently found in the general population. Epidemiological studies have shown that the infection has a worldwide distribution and it is most common in tropical areas. In immunocompromised individuals (especially congenitally infected infants, organ transplant recipients, hemodialysis patients and individuals with AIDS), toxoplasmosis may cause life-threatening complications. Laboratory diagnosis relies on detection and quantitation over time of specific toxoplasma IgG and IgM antibodies.[9,12,13]

Toxoplasmosis demonstrates various clinical manifestations. In immunocompetent individuals, toxoplasmosis is generally asymptomatic, however, it sometimes manifests with fever, malaise, headache, myalgia, asymptomatic lymph node enlargement, and chorioretinitis when it locates in the eye. In immunocompromised patients, *T. gondii* could cause life-threatening infections like encephalitis, pneumonia and chorioretinitis. The use of serological tests for the demonstration of specific antibody to *T. gondii* is the primary method of diagnosis.[14-16] The course of toxoplasmosis in almost all immunocompetent individuals is relatively benign, but it is a serious and often life-threatening disease in immunodeficient patients.[16] Determination of toxoplasmosis incidence in various risk groups in the society and establishment of these risk groups play a significant role in taking the necessary precautions against this disease.

In this study, we investigated the incidence of *T. gondii* infection in hemodialysis patients. While the prevalence of *T. gondii* IgG antibodies was 76.4% (195/255), the prevalence of anti-*T. gondii* IgM was 0.8% (2/255). In healthy control group, *T. gondii* IgG antibodies were detected as 42% (21/50). Anti-*T. gondii* IgM antibodies were detected in 2 of hemodialysis patients (0.8%), but none of the controls in this study. A statistically significant difference was determined for the *T. gondii* IgG antibodies between hemodialysis patients and the healthy control group ($p<0.05$). These findings may be due to the hemodialysis patients having immunocompromised, and susceptible to infections. It has been suggested that changes in immune response to infectious agents in patients on hemodialysis might be due to impaired monocyte function, uremia and overproduce proinflammatory cytokines, such as interleukin-1 beta, tumor necrosis factor-alpha and interleukin-6.[17]

Studies on the prevalence of *T. gondii* infection among hemodialysis patients are limited in our country. Yazar et al[7] investigated the distributions of anti-*T. gondii* IgG and IgM antibodies in sera obtained from 173 hemodialysis patients. While 8 (20%) of 40 healthy controls were seropositive for *T. gondii* IgG, 97 (56%) of 173 hemodialysis patients were seropositive for *T. gondii* IgG. In addition, anti-*T. gondii* IgM antibodies were detected in 1.73% of hemodialysis patients, but none of the control patients in their study.[7] Ustun et al[6] reported 68.5% toxoplasma IgG and IgM antibody positivity in the 108 cirrhotic patients and 48% in 50 subjects in the control group. The difference was found to be significant ($p<0.05$). The rate of toxoplasma IgG seropositivity was determined as 75% by Aydemir et al,[2] 62.5% by Bahar et al[3] in hemodialysis patients.[2,3] In our study, toxoplasma IgG antibody prevalence was found 76.5% in hemodialysis patients. This result approaches the seroprevalence of *Toxoplasma* reported by Aydemir et al.[2] However, it is higher than that reported by Bahar et al.[3]

A study conducted in Eastern Anatolia, in Elazig, in 1997, seropositivity of the *Toxoplasma* antibodies was found to be as 55% in general population.[4] Altintas et al[5] investigated the seroprevalence of anti-*Toxoplasma* antibodies in sera obtained from 9410 patients in Western Anatolia. They found anti-*Toxoplasma* IgG antibodies were positive in

4651 (49.4%) of those patients.[5] The seroposivity rate in Turkey generally reaches up to 55%. These values are similar to the rates that we have detected in our control group (42%), but lower than those in hemodialysis patients (76.5%).[4,5]

With regard to studies from other countries on the seroprevalence of *T. gondii* antibody in hemodialysis patients, Abbas et al[10] detected that *Toxoplasma* IgG antibodies were 38.3% in patients with chronic renal failure and 15% in the normal controls with a statistical significant difference.[10] Gutierrez et al[18] investigated the presence of IgG anti-*Toxoplasma* antibodies in serum samples of several population groups in Spain. They determined that the rate of infection by *T. gondii* was prevalent, especially among intravenous drug users (47.6%). *Toxoplasma* IgG antibody prevalence was found to be 49.6% in immunocompetent adults with suspected active toxoplasmosis. In infants, IgG antibodies were detected as 12.2%, and in pregnant women there was 30% IgG anti-*Toxoplasma* antibody seropositivity.[18]

Wang et al[19] investigated that *Toxoplasma* antibodies in immunodeficient patients. *Toxoplasma gondii* specific IgG antibodies in serum samples from 371 immunodeficient patients were detected by ELISA. The positive rates of patients with solid malignancies received chemotherapy were detected as 19%, chronic liver diseases as 33.3%, systemic lupus erythematosus as 16.5% and leukemia as 45.4%, being significantly higher than that of the control group ($p<0.05$).[19] In their study, Galvan et al[20] investigated *Toxoplasma* antibodies in 100 patients with AIDS. Anti-toxoplasma IgG was found to be 50% and IgM antibodies was 1%.[20]

Patients on regular hemodialysis treatment are immunodeficient.[21] Patients on chronic hemodialysis suffer from general immune incompetence, resulting in a high incidence of infectious complications, impaired response to vaccinations and a high incidence of malignancy. Although various abnormalities in T cell function of hemodialysis patients have been described, it remains unclear whether this is due to an intrinsic T cell defect.[22] Bacterial, parasitical and viral infections represent the most frequent complications in patients with chronic renal failure due to the changes in the immunological status of such patients.[23]

In conclusion, these results confirm a high prevalence of *Toxoplasma* infection in hemodialysis patients. Hemodialysis patients are a risk group for *Toxoplasma* infection. In addition, it is recommended that hemodialysis patients who are susceptible to *Toxoplasma* infections should be identified by *T. gondii* IgG and IgM specific serological tests. Therefore, patients undergoing hemodialysis should be screened for *Toxoplasma* before hemodialysis to prevent the dissemination of this infection through hemodialysis procedure.

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