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Anti-*Toxoplasma gondii* Antibodies in Haemodialysis Patients

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Abstract: Problem statement: In situations of immunodeficiency, *Toxoplasma gondii* emerges as a life-threatening infection. *Toxoplasma gondii* is transmitted parenterally, flourish in immunocompromised subjects and, most toxoplasma infections are asymptomatic. Studies have shown that there is a immunodeficiency in renal failure patient such as hemodialysis patients and these patients have a high risk for many infections. There is no evidence about toxoplasmosis in hemodialysis patients in Iran. **Approach:** In the present study, we aimed to investigate the prevalence of anti-*T. gondii* antibodies in hemodialysis patients with chronic renal failure. This case-control study was carried out on 44 hemodialysis patients and 44 healthy controls for the prevalence of anti-*T. gondii* antibodies by ELISA. Anti-IgG, IgM and IgA *T. gondii* antibodies positivity were found to be 26 (59.10%), 3 (6.80%) and 3 (6.80%) of the 44 hemodialysis patients, respectively and 16 (36.40%) of the 44 control subjects were Anti-IgG *T. gondii* antibodies positivity and all of control subjects were negative for Anti-IgM and IgA *T. gondii* antibodies. The difference between them was statistically significant ($p = 0.032$). 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 ($p<0.001$). **Results:** These findings confirm a high prevalence of toxoplasma infection in hemodialysis patients and these patients are a risk group for toxoplasma infection. Results showed that 3 hemodialysis patients had an acute and active infection. **Conclusion:** Moreover, it is recommended that hemodialysis patients who are susceptible to toxoplasma infections should be identified by *T. gondii* IgG and IgM and/or IgA 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.

Key words: Haemodialysis, anti- toxoplasma antibodies, ELISA, IgG, IgA, IgM

INTRODUCTION

Toxoplasmosis is a cosmopolitan zoonotic disease caused by the parasitic protozoan *Toxoplasma gondii* (Chen and Tan, 2009). This parasite is an obligate intracellular organism and is found in two forms in humans. The actively proliferating tachyzoites are usually seen in the early, more acute phases of the infection. The resting forms or tissue cysts are primarily found in muscle and the brain, probably as a result of the host immune response (Garcia and Bruckner, 1997). This infection can be acquired through the eating of raw or undercooked meat containing tissue cysts or by exposure to soil, food, or water contaminated with oocysts excreted in the feces of cats or other felines infected with the parasite. The infection can also be transmitted vertically from an infected woman to a fetus during pregnancy (Tenter *et al*., 2000; Montoya and Liesenfeld, 2004; Remington *et al*., 2006).

Approximately one-third of the world's population is infected by *Toxoplasma gondii* (Sensini, 2006). Serological studies show a considerable variation in the prevalence of Toxoplasma infection from 0-95% in different parts of the world and indeed between different population groups within the same country (Asthana *et al*., 2006; Ghorbani *et al*., 1978; Abu-Zeid, 2002; Fan *et al*., 2002; Montoya and Remington, 2000). About 20% of the population of the USA is seropositive for IgG for *T. gondii*, making this one of the most prevalent infections (Dubey, 2009). In France, the rate of seropositivity has been reported to reach 80% (Feldman, 1982). In Brazil, toxoplasmosis is an important public health problem in many areas, with serological prevalence ranging from 50-84% for *T. gondii* infection in adults (Bahia-Oliveira *et al*., 2003; Spalding *et al*., 2005). Shin *et al*. (2009) reported that the recent seroprevalence of *T. gondii* ranges from

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0.79-12.9% in the Korean population. In Turkey, it was reported to be 36% in Kayseri (Zamani *et al*., 2007) reported that *T. gondii* infection has shown considerable prevalence in Iran and seropositivity ranges from 5.7-87%. Assmar *et al*. (1997) reported 51.8% prevalence in general population of Iran. Ghorbani *et al*. (1978) showed 55.7% prevalence in a rural area in northern Iran. In Khuzestan province, South-west Iran, Ghorbani *et al*. (1981) reported 17.7% prevalence in 1977. According to Salahi-Moghaddam and Hafizi (2009) study the prevalence of Toxoplasma infection was 68.4% in general population in south of Tehran.

The prevalence of infection is related to several factors, including nutritional habits, contact with soil, age, rural or urban settings (Remington *et al*., 2006; Cook *et al*., 2000) and frequency of contact with domestic animals and climatic conditions such as humidity (Kamani *et al*., 2009). Acute toxoplasmosis is asymptomatic and limited in 80% of immunocompetent individuals (Derouni *et al*., 1987; Blanc-Jouvan *et al*., 1996). However, in about 20% of Toxoplasma cases, acute infection is accompanied by febrile lymphadenopathy, asthenia and lymphomonocytosis, with the course of infection being self-limited (Feldman, 1968). Immunocompromised hosts, especially those with impaired cellular immunity, are at risk of recrudescence of chronic infection and dissemination, with the occurrence of fulminating disease. Patients with neoplasia, collagen tissue disease, transplant recipients under immunosuppressive therapy or haemodialysis patients with chronic renal failure have deficient cellular immunity and this makes them susceptible to the infection (Yazar *et al*., 2003). In immunocompromised patients, the infection most often involves the nervous system, with diffuse encephalopathy, meningoencephalitis or cerebral mass lesions (Garcia and Bruckner, 1997).

Toxoplasma gondii is the most frequent protozoan causing opportunistic infections in immunocompromised individuals (Ferreira and Borges, 2002). Several researches have been carried out on the immune response in patients with CRF and proved there was impairment of cell-mediated immunity (Langhoff and Ladefoyed, 1988) also these patients have a significant lower immune response to vaccines such as tetanus vaccine than healthy subjects (Sotoodeh Jahromi *et al*., 2009). CRF patients are under risk from a variety of infections (Assarehzadegan *et al*., 2009), however a high precentage of positivity for *T. gondii* antibodies have been detected in these patients (Yazar *et al*., 2003; Abbas *et al*., 1996; Ocak *et al*., 2005), either due to their depressed immune status (Nelson *et al*., 1985).

Toxoplasmosis in patients who are immunocompromised because of underlying chronic renal failure has received relatively little attention. In this study, the seropositivity rate of anti-*T. gondii* antibodies in patients with chronic renal failure was evaluated.

As there is not any document about this infection in hemodialysis patients in IRAN, this study aimed to assess the risk of severe toxoplasmosis in patients with chronic renal failure undergoing haemodialysis by monitoring IgG, IgM and IgA antibodies to *T. gondii*. This is the first study of Toxoplasmosis in Irania hemodialysis patients.

MATERIALS AND METHODS

Patients and sera: This case-control study was carried out on all patients (44), undergoing regular haemodialysis, in the haemdialysis unit of Motahari hospital of Jahrom university of Medical Sciences, between June 2008 and September 2008. And the length of time on haemodialysis treatment was recorded for them. In addition, we selected 44 healthy volunteers with normal ceratinine and BUN and without any underlying renal disease, as a control group. Data including sex, age and the length of time on haemodialysis treatment were obtained from all of the hemodialysis patients and their medical records. The sera taken from the case and the control groups were stored at -20°C until required.

Serologic technique: For determination of anti-*T. gondii* antibodies, all sera were tested by Enzyme-Linked Immunosorbent Assay (ELISA) kits. We used ELISA kits purchased from the comercial manufacturer DIA.PRO (Diagnostic Bioprobes Srl. [20128]-Italy), for determination of anti-*T. gondii* IgG and IgM antibodies and IBL (International GmbH RE58241-Germany), for determination of anti-*T. gondii* IgA antibody, which were performed following the manufacturer´s instructions. On the basis of the ELISA, subjects were diagnosed as either positive/negative for specific IgG, IgM and IgA antibodies to *T. gondii*.

Ethics: The study was approved by the ethics committee of Jahrom University of Medical Sciences.

Statistical analyses: The general information and ELISA results were analyzed by SPSS V.15 for windows. Analytical tests including the chi-square test and t-test were used and P values less than 0.05 were considered as significant.

RESULTS

From 44 patients were 30 males and 14 females and aged between 25 and 88 (mean: 59.11±14.33). And the length of time on haemodialysis treatment was from 1-120 months (mean: 25.89±26.84). In control group, from 44 healthy volunteers were 28 males and 16 females, who were aged between 25 and 88 (mean: 58.98±14.32).

In the present study, 26 of 44 (59.1%) cases in the patient group and 16 of 44 (36.4%) healthy volunteers (control group) were found to be positive for IgG antibodies. The percentage of people who were anti-*T. gondii* IgG positive in the CRF patient group was found to be significantly greater than in healthy volunteers (P<0.05). Anti- IgM and IgA *T. gondii* antibodies positivity were found to be 3 (6.8%) and 3 (6.8%) of the 44 haemodialysis patients, respectively and all of control subjects were negative for Anti-IgM and IgA *T. gondii* antibodies (0%) and the difference between them was statistically significant (p<0.05). The sero-prevalence distributions of the two groups are shown in Table 1.

We also investigated the relationship between duration of hemodialysis treatment and anti-*T. gondii* antibodies seropositivity. We observed that the seropositivity rate increased with the increasing length of time on hemodialysis treatment, indicating a statistically significant difference between these two parameters (p<0.05).

DISCUSSION

Toxoplasmosis is an opportunistic protozoan parasite infection, widespread in humans and animals and emerges as a life-threatening risk in immunocompromised individuals (Navia *et al*., 1986).

Uremic patients are affected with suppressed cellular and humoral immune responses (Vanholder *et al*., 1993; Stuart, 1976). It has been suggested that because of reduced circulating T-cells and increased suppressor cells, then haemodialysis can not return the impairment of the immune status in CRF (Glorieux *et al*., 2009). These factors probably contribute to the acquired immune suppression in uremia and the high incidence of infection among dialysis patient, in that infection is very common and the major cause of death, of end-stage renal diseases (Schollmayer and Bozkurt, 1988).

The epidemiology of End-Stage Renal Disease (ESRD) and renal replacement therapy have increasing rates. With the improvement of renal replacement therapy, the known prevalence of ESRD continues to increase in most countries; it is currently higher than 2000 per million population (pmp) in Japan, about 1500 (pmp) in the United States and about 800 pmp in the European Union (Barsoum, 2006). There was an increasing trend in the incidence of ESRD in Iran from 38.5 pmp in 1998-49.9 pmp in 2000. The prevalence and incidence of ESRD has been increasing in Iran from 238 and 49.9 pmp in 2000-357 pmp and 63.8 pmp in 2006, respectively (Mahdavi-Mazdeh *et al*., 2008). There are now more than 24 000 people with ESRD in Iran and their number has drastically increased over the recent years (Nafar *et al*., 2008).

The present study revealed a higher percentage of anti-Toxoplasma IgG antibodies positivity in CRF patients undergoing haemodialsis (59.1%) than in the controls (36.4%) with a statistical significance (p<0.05). In addition, anti-*T. gondii* IgM and IgA antibodies were detected in 6.8% of patients, but all of control subjects were negative for them (Table 1) and the difference between them was statistically significant (p<0.05).

The statistically significant differences between case and control groups was similar to other studies (Yazar *et al*., 2003; Abbas *et al*., 1996; Ocak *et al*., 2005). Although the prevalence of anti-Toxoplasma IgG antibodies in the present study was more than the results of Abbas *et al*. (1996) studies and less than the results of Ocak *et al*. (2005) study. These differences may be due to prevalence of Toxoplasma infection in different population (Zamani *et al*., 2007; Azab *et al*., 1992).

Also, in this study, three hemodialysis patients were positive for Anti-IgM and IgA *T. gondii* antibodies and had an acute infection.

There was positive significant correlation between duration of hemodialysis treatment and seropositivity rate of Toxoplasma. Such correlation was shown by Ocak *et al*. (2005) in Turkey Abbas *et al*. (1996) in Egypt.

Table 1: The results of serological tests for antibodies to *T. gondii* in CRF pateints undergoing haemodialysis and in the control group

Subjects	Haemodialysis patients (n = 44)		Healthy controls (n = 44)		
Anti-toxoplasma antibody	No.	(%)	No.	(%)	p-value
IgG	26	59.1	16	36.4	0.032
IgM	3	6.8	0	0.0	0.039
IgA	3	6.8	0	0.0	0.039

CONCLUSION

In conclusion, haemodialysis patients should be tested for *Toxoplasma gondii* regularly. Clinicians should be more alert with these patients and parasitological surveys of them should be periodically carried out to prevent the risk of severe toxoplasmosis.

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