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Seroprevalence and risk factors of *Toxoplasma gondii* infection among Cancer and Hemodialysis Patients in southwest Iran

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ABSTRACT

Background: Due to their poor immune system, cancer patients undergoing chemotherapy and hemodialysis patients are more at risk for toxoplasmosis and its complications than the healthy people. The current study aimed to determine prevalence of toxoplasmosis in these patients and comparing it with healthy subjects in southwest Iran.

Methods: This cross-sectional study was performed on sera and buffy coat of 100 cancer patients, 47 hemodialysis patients, and 170 healthy subjects. IgG and IgM anti-*Toxoplasma gondii* antibodies in serum were measured by ELISA method. Molecular diagnosis was conducted by PCR method on buffy coat of the seropositive samples.

Results: The seroprevalence of *T. gondii* in cancer, hemodialysis patients and healthy subjects were 13%, 27.7% and 15.9% respectively. Moreover, seropositivity for IgM antibody was 2.1% in hemodialysis, 2% in cancer patients and 0.6% in healthy individuals. Our results were showed there was no significant difference between prevalence toxoplasmosis in case and control group. In molecular survey, only one case (cancer patient) was positive for Toxoplasma DNA. Contact with cats and consumption of undercooked meat were two studied risk factors which had significant associations with *T. gondii* seropositivity in the hemodialysis patients (odds ratio [OR] = 14.667; 95% confidence interval [CI] = 1.453–148.045) and control (odds ratio [OR] = 3.07; 95% confidence interval [CI] = 1.093–8.639) respectively.

Conclusion: Seroprevalence of toxoplasmosis in hemodialysis patients was higher than Healthy Individuals; however, the seroprevalence of toxoplasmosis in cancer patients was similar to the Healthy Individuals.

1. Introduction

Toxoplasma gondii is one of the Eukaryotic opportunistic pathogens with global distribution. One third of the human populations are predicted to be infected with this unicellular parasite. Toxoplasmosis is transmitted via ingesting oocyst-contaminated food or water, consuming of undercooked meat containing tissue cysts, vertical infection, organ transplantation, and blood transfusion through infected donors.[1–3]

Clinical manifestations of infection with toxoplasmosis associated with the host immune system. Toxoplasmosis in people with a complete immune system is asymptomatic, but in cancer patients undergoing chemotherapy and patients whose immune system is weakened for any reason, such as AIDS patients, transplant recipients and hemodialysis patients are more vulnerable to acute forms of toxoplasmosis such as brain damage, neurological defects, and encephalitis in the patients.[4–6]

The appropriate geographic conditions for the development of *T. gondii* oocysts, the food and health habits of a community, and the exposure to toxoplasmosis-related risk factors play an important role in the prevalence of toxoplasmosis in a community.[7,8]

The global seropositivity of *T. gondii* infection in cancer patients and control was reported 26% and 12.1%.[9] Prevalence of toxoplasmosis in Iran was reported 39.3% in the general population, 51.01% in immunocompromised patients and 43% in pregnant women.[10–12]

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Moreover, in a systematic reviews study, the prevalence of IgG antibodies against *T. gondii* was reported 58% and% 40 in hemodialysis patients and of healthy controls in Iran.[13]

Due to lack of information about the Seroprevalence and risk factors of Toxoplasma infection in patients with cancer and undergoing hemodialysis which are more vulnerable to *T. gondii*, loss of screening of toxoplasmosis in public hospitals in the region and also no vaccine is available to prevent toxoplasmosis in humans; there was a need to study of toxoplasmosis on Cancer and Hemodialysis Patients in this region. The current study, for the first time, was conducted to find out the seroprevalence, risk factors of *T. gondii* and also to detect Toxoplasma DNA in buffy coats of Cancer and Hemodialysis Patients in comparison with healthy people in Boyerahmad County, Southwest of Iran.

2. Methods

2.1. Study population and sample collection

This cross-sectional study was performed on 100 cancer patients undergoing chemotherapy who referred to the Chemotherapy Center of Shahid Rajaei Hospital in Yasuj, 47 hemodialysis patients referred to the Dialysis Center of Yasuj University of Medical Sciences, and 170 healthy subjects from October 2017 until March 2018. The subjects of both case and healthy individuals were selected from a similar region and none of the healthy individuals had a history of cancer, kidney failure, and autoimmune diseases and they have not used immunosuppressive drugs. Cancer patients included; 35 cases of adenocarcinoma, 28 cases of breast cancer, 8 cases of SCC, 5 cases of lymphoma, 7 cases of prostate cancer, 8 cases of ovarian cancer, 4 cases with multiple myeloma and 5 cases of pancreatic cancer. Of these, 55 had metastases and 45 were non-metastatic. Cancer patients entering the study had at least 3 months of chemotherapy history.

The ethics committee of the Yasuj University of Medical Sciences approved this study with ethical no. IR.YUMS.REC.1395.161. After obtaining the written consent of the participants in the study, the questionnaire containing demographic information and clinical indicators related to the prevalence of the disease was completed for all participants in the study. Subsequently, 5 ml intravenous blood sample was taken from each participant in the study. After centrifugation, the serum part was isolated to carry out serological work and its blood buffy coat was separated for molecular survey and placed at a temperature of −20 °C until the test was performed.

2.2. Serological evaluation

Sera samples were tested for IgG and IgM anti-*Toxoplasma* antibodies using a commercial ELISA kit (Euroimmune, Germany) based on the manufacturer's instructions, and using a plate reader (BioTek; Winooski, Vermont, USA).

2.3. DNA extraction and PCR amplification

DNA from buffy coat samples of seropositive individuals was extracted using the blood genomic DNA isolation kit (Favorgene, Bioteccorpmade by Taiwan). Two primers, TOXOF (CAGGGAGGAAGA CGAAAGTTG) and TOXOR CAGACACAGTGCATCTGGATT) was used to amplification a 529bp fragment of RE gene, which is repeated 200 to 300 times in the genome of *T. gondii* with highly sensitive and specific diagnosis.[14] PCR products were separated by electrophoresis on 1.5% agarose gel and stained with ethidium bromide.

2.4. Statistical analysis

Collected data were analyzed using statistical package for the social sciences (SPSS) software 19. The prevalence values relative to the features of the subjects were analyzed with a chi-square and Fisher's exact test. Also, Univariate logistic regression analysis was used to evaluate the association between the related risk factors and seropositivity of *T. gondii* infection. The level of significance was considered at 5%.

3. Results

Cancer patients underwent chemotherapy included 56 (56%) males and 44 (44%) females, hemodialysis patients included 30 (63.8%) males and 17 (36.2%) females, and control group included 98 (57.6%) males and 72 (42.4%) females. The mean age of cancer patients undergoing chemotherapy was 55 ± 14.6 years, for the hemodialysis patients, it was 57 ± 13.1, and in the control group, it was 51 ± 10.2 years. Thirteen (13%) of patients with cancer had IgG antibody and two (2%) had IgM anti-*T. gondii* antibodies. Thirteen hemodialysis patients (27.7%) had IgG antibody and one patient (2.1%) had IgM anti-T. gondii antibody, and in the control group, 27 (15.9%) had IgG antibody and one (0.6%) had IgM anti-Toxoplasma gondii antibody. Our analysis showed that the prevalence of toxoplasma was lower in the cancer patients than in the control group, but no significant relationship was observed (P value = .0.53). Also despite the seroprevalence of *T. gondii* in hemodialysis patients was more than the control group, but no significant relationship was observed (P value = .0.07) (Table 1).

Of all seropositive individuals in all three studied groups, only one of the chemotherapy-undergoing cancer patients was positive for molecular method (PCR). Also, this patient had both IgG and IgM anti-*T. gondii* antibodies.

Other studied variables in this research included residence location, occupation, education level, contact with cats, contact with soil, how to wash vegetables and how to eat meat. There was a significant relationship between positive IgG anti-*T. gondii* antibodies and contact with cats in the hemodialysis patients (odds ratio [OR] = 14.667; 95% confidence interval [CI] = 1.453–148.045), and in the Healthy subjects, there was a significant relationship between meat consumption and antibody positive cases ((odds ratio [OR] = 3.07; 95% confidence interval [CI] = 1.093–8.639) (Table 2).

4. Discussion

In cancer patients undergoing chemotherapy and hemodialysis patients which their immune system is weakened, probably recurrence of the chronic form of toxoplasmosis and the activation of the *T. gondii* tissue cysts is very high and hazardous.[14,15] The current study aimed to determine the prevalence and risk factors of toxoplasmosis in cancer patients undergoing chemotherapy, hemodialysis patients in comparison with healthy individuals in Boyer-Ahmad County, Southwest of Iran.

The current study showed that the rate of seropositivity to *T. gondii* in hemodialysis patients (27.7%) is higher than cancer patients (13%)

Table 1
The seroprevalence of anti- *T. gondii* IgG and IgM antibodies in the sera of the Cancer patients, Hemodialysis patients and Healthy subjects.

Antibodies	Cancer patients (n = 100)	Hemodialysis patients (n = 47)	Healthy subjects (n = 170)
Seroprevalence % (95% CI) Anti-*T. gondii* IgG	13 (0.731–9.331)	27.7 (3.038–11.63)	15.9 (0.419–9.01)
Seroprevalence % (95% CI) Anti-*T. gondii* IgM	2 (3.526–5.074)	2.1 (3.11–5.48)	0.6 (4.12–4.47)

Table 2
The potential risk factors assessed for seropositivity of toxoplasmosis among the Cancer patients, Hemodialysis patients and Healthy subjects.

Variable Group		Cancer Patients				Hemodialysis Patients				Healthy Individuals				
		No.	Seropositivity (%)	OR (95% CI)	p value	No.	Seropositivity (%)	OR (95% CI)	p value	No.	Seropositivity (%)	OR (95% CI)	p value
Residence	City	59	10.2	1	0.313	25	20	1	0.211	121	16.5	1.743 (0.615–4.94)	0.292
	Rural	41	17.1	1.819 (0.563–5.874)		22	36.4	2.286 (0.617–8.46)		49	10.2	1	
Occupation	Housewife	6	16.7	1	0.718	13	23.1	1.250 (0.254–6.16)	0.847	7	42.9	1	0.095
	Employee	37	13.5	1.28 (0.123–13.352)		12	33.3	0.750 (0.163–3.44)		63	12.7	5.156 (0.97–27.407)	
	Worker	8	0	3.231 (0)		0	0	0		28	21.4	2.750 (0.479–15.794)	
	Other	49	14.3	1.2 (0.121–11.865)		22	27.3	1		72	11.1	6 (1.132–31.798)	
Educational level	Illiterate	20	20	1	0.256	16	37.5	1.111 (0.142–8.68)	0.536	3	33.3	0.444 (0.038–5.206)	0.316
	Primary school	37	16.2	1.292 (0.318–5.247)		13	23.1	2.222 (0.245–20.17)		38	13.2	1.467 (0.495–4.342)	
	High school	24	12.5	1.750 (0.342–8.951)		13	15.4	3.667 (0.354–38.02)		41	7.3	2.815 (0.772–10.269)	
	Academic degree	19	0	4.039E8 (0)		5	40	1		88	18.2	1	
Contact with cats	Yes	12	25	2.6 (0.602–11.230)	0.188	5	80	14.667 (1.453–148.045)	0.017	31	6.5	0.348 (0.078–1.561)	0.151
	No	88	11.4	1		42	21.4	1		139	16.5	1	
Contact with soil	Yes	17	23.5	2.53 (0.678–9.443)	.156	9	44.4	2.578 (0.568–11.69)	0.211	28	7.1	0.398 (0.088–1.794)	0.216
	No	83	10.8	1		38	23.7	1		142	16.2	1	
Washing vegetables with disinfectants	Yes	72	11.1	1	0.368	19	42.1	3.345 (0.886–12.62)	0.71	122	13.9	1.235 (0.494–3.087)	0.651
	No	28	17.9	1.739 (0.516–5.860)		28	17.9	1		48	16.7	1	
Consuming semi-cooked meat	Yes	33	21.2	2.737 (0.838–8.936)	0.087	20	25	1.263 (0.342–4.66)	0.726	102	19.6	3.07 (1.093–8.639)	0.027
	No	67	9	1		27	29.6	1		68	7.4	1	

and healthy individuals (15.9%) living in the region, or even a study conducted by Moshfe et al. reported a seropositivity rate of 16.8% in healthy blood donors selected from Boyer-Ahmad county in the same area.[16] The difference in the rates of seroprevalence *T. gondii* in hemodialysis patients than cancer patients undergoing chemotherapy may have been associated with special care and less exposure to the parasite source in cancer patients.

Studies on prevalence of *T. gondii* in hemodialysis patients in different regions of Iran revealed a rate of 29.3% up to 80%.[13] The seroprevalence rate of 27.7% in the current study is close to the study of Saki et al. in Ahvaz province, southwest of Iran which reported a seroprevalence of 29.3% for toxoplasmosis in hemodialysis patients.[17] In comparison with other studies, the seropositivity rate of Toxoplasma in the current study was lower than studies conducted on hemodialysis patients in Mazandaran (80%), Tehran (60%), and Fars Province (59.1%); moreover seroprevalence of *T. gondii* in our study was also lower than two serological studies on hemodialysis patients in other countries including Turkey (76.5%) and Malaysia (51%).[18–22]

In a systematic review study conducted by Ahmadpour et al. (2014) to examine the overall seroprevalence rate of toxoplasmosis in cancer patients, 45.06%% was positive, moreover in a systematic review and meta-analysis in China, seroprevalence of *T. gondii* in cancer patients was found to be 20.59% compared to 6.31% in healthy individuals.[11,23] In the study performed by Hassanzadeh et al. (2017), 60.3% and 6% of individuals with immunodeficiency were positive for IgG and IgM anti-*T. gondii,* respectively.[24] In other study by Kalantari et al. (2015), 86.4% of women with breast cancer had positive anti-Toxoplasma IgG antibody and 10.3% had positive IgM antibodies.[25]

By comparing the results of these studies with the studies mentioned above, it could be conclude that the seroprevalence of *T. gondii* in Boyer-Ahmad County was not high, which could be attributed to the climatic conditions, cultural habits, geographical location, as well as the sample size. Findings of the current study revealed that contact with cats is a risk factor for being seropositive for *T. gondii* in the hemodialysis patients. Another risk factor associated with seropositivity to *T. gondii* was consumption of undercooked meat. In this finding is consistent with some of the studies from Iran and other countries which showed consumption of undercooked meat is an important factor for parasite transmission.[8,26] Method of cooking meat in the form of Kebab (undercooked meat) is quite common in the area that the current study was performed.

The limitations of this study are that only seropositive cases have been evaluated for Toxoplasma DNA, and the clinical information of some patients was not complete.

5. Conclusion

Although the seropositivity rate of toxoplasmosis in cancer patients and also of hemodialysis patients in the present study in comparison with the healthy subject was not considerable, given the specific conditions of these patients and the probable chance of reactivation of latent toxoplasmosis, and subsequent acute infections, it is necessary to carry out screening and regular tests to determine the immune status of such patients toward toxoplasmosis.

Conflicts of interest

We have no conflict of interest regarding this study.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.cegh.2019.01.007.

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