Investigation of the prevalence of toxoplasmosis in patients with malignancies, southwest of Iran

Abstract

Toxoplasmosis is a parasitic disease that can affect humans, other warm-blooded animals, and cats. Cancer patients receiving chemotherapy, individuals with immunocompromised immune systems, AIDS patients, transplant recipients, and hemodialysis patients are at a greater risk of contracting toxoplasmosis.Due to the similarity of certain *toxoplasmosis* symptoms to those of cancer or chemotherapy-related problems, it is difficult to establish the existence of *toxoplasmosis* symptoms. For this reason, one of the ways to prove this infection is the ELISA test and determining the amount of antibodies in the patient. Blood was drawn from 90 cancer patients who had been admitted to the hospital and were at various stages of chemotherapy. The anti-*toxoplasma* antibody titer was then determined using the ELISA method, and the data were analyzed using SPSS version 23 software. In this study, 50 (55.6%) were women and 40 (44.4%) were men; all samples were negative for IgM antibody titers, while 50 (55.6%) were positive for IgG antibodies. In patients with positive tests, the most common clinical symptoms were lethargy and anorexia. Although anti-toxoplasma IgG antibodies were more common in men than women, no significant difference was seen between gender and infection. Additionally, compared to those with malignancies without such a history, those with a history of chemotherapy had higher anti-toxoplasma IgG antibodies. The level of anti-toxoplasma IgG in malignant patients hospitalized in this hospital was high, but statistical analysis showed a significant difference between the prevalence of toxoplasma and the type of cancer. Cancer patients are at great risk of developing severe toxoplasmosis and its consequences due to the high incidence of *T. gondii*. Therefore, oncologists should view this serious medical condition as requiring immediate attention.

Keywords: *Toxoplasmosis*, complications, *Diagnosis*, Epidemiology, prevention and control

1. Introduction

One-third of the world's population is believed to be infected by the obligate intracellular eukaryotic opportunistic pathogen *toxoplasma gondii*, which has the capacity to infiltrate and proliferate in a variety of host organs (1). *Toxoplasmosis* is a zoonosis illness that affects cats as the sole definitive host, with humans and other warm-blooded animals serving as intermediate hosts (2).

This protozoan can spread via the placenta from mother to fetus, through the use of oocyst-contaminated water and food, through the consumption of undercooked meat, through organ transplants, and through blood transfusions (3).

In most hosts with a strong immune system, innate immune responses control the growth of tachyzoites during an acute infection. During this time, tachyzoites change into bradyzoites and form cysts in the brain, eye, and muscle that stay in the host's body for the rest of its life because of an immune response or physiological stress (4,5). According to studies, cancer patients receiving chemotherapy and individuals with a compromised immune system, as well as AIDS patients, transplant recipients, and hemodialysis patients, are at a greater risk of contracting *toxoplasmosis* owing to problems such as brain damage (6–9). The risk of reactivation of latent *toxoplasma gondii* infection has been shown to be greater in several forms of cancer, including eye, brain, blood, and breast malignancies, according to research (10).

The immunological response to a *toxoplasmosis* infection is dependent on the genetic diversity and immune system of the person. It should be emphasized that the parasite may spread to all tissues, particularly the central nervous system and placenta (11).

In individuals with a compromised immune system, the illness manifests as fever, muscular discomfort, eye damage, CNS abnormalities, etc., and may cause severe damage, including encephalopathy and meningoencephalitis (2).

The frequency of *toxoplasmosis* in Iran has been estimated to be 39.3% in the general population, 51.01% in immunocompromised patients, and 44% in pregnant women (12).

The primary goal of this research was to examine *toxoplasmosis* in chemotherapy-treated cancer patients sent to Bagai 2 Hospital in Ahvaz, Iran, in 1401, and to determine whether or not this illness is associated with certain forms of cancer. The confidentiality of the participants' information and all other ethical criteria are strictly adhered to throughout this study.

2. Material and methods

2.1.Data collecting

The present study is an analytical cross-sectional investigation into the prevalence of toxoplasmosis in cancer patients referred to the oncology department of Baqaei 2 Hospital in Ahvaz for chemotherapy in 1401. According to the study conducted by Hosseini *et al*. (13), with a confidence level of 95% and an error of 9%, 90 patients with various malignancies (leukemia, lymphoma, lung cancer, breast cancer, uterine cancer, and colon cancer) were included in the study as available samples.

2.2.Blood sampling

After receiving informed permission, 3 cc of blood was drawn from each patient, and the samples were centrifuged for 5 minutes at 3000 rpm to extract the serum. The serum was then transferred to a newly labeled tube. An ELISA test was used to see if the serum had IgM and IgG antibodies against toxoplasmosis. The sera were diluted with a 1:100 dilution, as directed by the manufacturer (Pishtaz Medicine of Iran). The samples were then measured for optical absorption at 450 and 630 nm using an ELISA reader.

Interpretation of IgG results: according to the instructions of the manufacturer of the kit, people whose antibody levels are higher than 11 IU/mI are considered positive, those less than 9 IU/mI

are negative, and values of 9-11 IU/mI are considered suspicious. To report the results of the amount of IgM antibody, an index cut-off value is obtained by dividing the optical absorbance of the sample. If the obtained value is higher than 1.1, it is considered positive; a value lower than 0.9 is negative; and a value between 0.9 and 1.1 is considered suspicious. To collect information, a researcher's checklist was used, which included demographic information and possible risk factors related to *toxoplasma gondii*, such as age, gender, type of malignancy, clinical symptoms, history of chemotherapy and duration of chemotherapy.

2.3.Data analysis

The SPSS version 23 software was used throughout the process of statistical analysis. In order to determine whether or not the variables in the research followed a normal distribution, the Kolmogorov-Smirnov test was carried out. In the descriptive statistics, frequency and percentage played important roles. The number of people who tested positive for the serological test (anti-T. gondii IgG) divided by the total number of people who underwent testing for the desired type of cancer allowed researchers to determine the prevalence of toxoplasma infection in cancer patients according to the type of cancer. This allowed for the calculation of the prevalence of *toxoplasma* infection in cancer patients. The Chi-square test and the independent t-test were used to investigate whether or not there was a correlation between the qualitative and quantitative factors. The quantitative and qualitative variables were examined using an independent t-test. In order to evaluate the connection between *toxoplasmosis* and possible risk variables, a multivariable logistic regression model was used. The odds ratios were computed using ORs, and the confidence intervals were set at 95%. (CI). When the p value was greater than 0.05, statistical significance was assumed.

3.Results

In the current research of 90 patients with malignancies (50 female, 55.6%, and 40 male, 44.4%) . All samples were negative for IgM antibody titers. However, 50 samples were positive for IgG antibodies, representing 55.6% of all samples. Fifty out of ninety patients (55.6%) were positive for anti-toxoplasma antibodies. The types of cancer seen among the patients were as follows: 16 cases of lymphoma, 24 cases of leukemia, 15 cases of colon cancer, 9 cases of stomach cancer, 9 cases of breast cancer, and 17 other malignancies (including lung, ovary, sarcoma and liver). Although *toxoplasmosis* was more common in leukemia patients (70.8%), no significant difference was found between toxoplasmosis rates in patients with other types of cancer ($P = 0.576$).

Due to the similarity of certain *toxoplasmosis* symptoms to those of cancer or chemotherapy-related problems, it is difficult to establish the existence of *toxoplasmosis* symptoms. In cases of positive IgG titers, symptoms such as muscle pains, headaches, physical weakness, skin rashes, anorexia, and fever and chills were more prevalent, despite the fact that anorexia was the most common clinical symptom in the investigated subjects (36.7%), and in those with a positive test, lethargy and anorexia were the most common clinical symptoms. In terms of risk variables, no

statistically significant differences were identified between the demographic features of the analyzed populations (check the table below).

Table 1.Demographic Characteristics and Risk Factors of *toxoplasma gondii* among cancer patients

Variable		No. of samples, n (%)	No. of positives, n (%)	P.value
Sex	Women	50 (55.6)	27 (54.0)	0.832*
	Men	40 (44.4)	23 (57.5)	
Age	≤ 30	7 (7.8)	3 (42.1)	0.840*
	31 - 40	19 (21.1)	11 (57.9)	
	41 - 50	20 (20.0)	8 (44.4)	
	51 - 60	19 (21.1)	12 (63.2)	
	61 - 70	18 (20.0)	11 (61.1)	
	≥ 71	9 (10.0)	5 (55.6)	
History of chemotherapy	No	77 (85.6)	46 (59.7)	0.071*
	Yes	13 (14.4)	4 (30.8)	
Number of chemotherapy sessions	1 - 3	36 (40.0)	21 (58.3)	0.482*
	4 - 7	27 (30.0)	12 (44.4)	
	8 – 11	14 (15.6)	8 (57.1)	
	> 11	13 (14.4)	9 (69.2)	
Types of Cancer	Colon	15 (16.7)	8 (53.3)	0.576*
	Breast	9 (10.0)	5 (55.6)	
	Stomach	9 (10.0)	5 (55.6)	
	Leukemia	24 (26.7)	17 (70.8)	
	Lymphoma	16 (17.8)	6 (37.5)	
	Other	17 (18.9)	9 (52.9)	
Clinical signs	Fever	28 (31.1)	14 (28.0)	0.757**

	Chills	26 (28.9)	14 (28.0)	0.956**
	Fatigue	21 (23.3)	16 (32.0)	0.111**
	Nausea	19 (21.1)	9 (18.0)	0.625**
	Narcosis	31 (34.4)	21 (42.0)	0.312**
	Muscular pain	26 (28.9)	14 (28.0)	0.963**
	Anorexia	33 (36.7)	21 (42.0)	0.393**
	Headache	18 (20.0)	12 (24.0)	0.982**
*Chi. Square Test, **Independent samples Test				

According to the findings of a multivariate logistic regression study, there is no statistically significant difference between the prevalence of *T. gondii* in serum based on a person's gender (OR = 1.89, 95% CI: 0.61 to 5.79, p = 0.265). In spite of this, the findings of the serological tests revealed that the prevalence of anti-*Toxoplasma* IgG antibodies was much greater in men than in women.

Patients in this research ranged in age from 16 to 81 years old, making up the age group being studied. In comparison to younger age groups, it was shown that the prevalence of anti-*Toxoplasma* IgG antibodies was significantly greater in those who were between the ages of 51 and 60, as well as 61 and 70. In addition, the risk of being infected with *toxoplasma* increased in people of these ages compared to those of younger ages.

The results of the serological tests showed that people who had a history of chemotherapy were more likely to have anti-toxoplasma IgG antibodies than people who had cancer but did not have a history of chemotherapy. Our statistical analysis also revealed a significant difference between the seroprevalence of *T. gondii* in cancer patients who had a history of chemotherapy and those who did not have such a history (OR = 6.52, 95% CI: 1.31 to 32.33, p = 0.022). Patients who had more than 11 chemotherapy sessions were shown to have a greater seroprevalence of *T. gondii* antibodies in their systems. In fact, the prevalence of *T. gondii* rose when chemotherapy was administered for longer periods of time. Even though the statistical study did not demonstrate a significant relationship between the number of chemotherapy sessions and *toxoplasma* infection, the likelihood of testing positive for *T. gondii* does rise proportionally with the number of chemotherapy sessions received.

Based on the results of this study's serological analysis, there was a significant frequency of anti-toxoplasma IgG in cancer patients who were hospitalized at this facility. In spite of the fact that cancer patients had a significantly increased risk of contracting *toxoplasmosis*, statistical analysis

revealed that there was no discernible relationship between the prevalence of *toxoplasma* and the specific kind of cancer (Demographic data table above).

4. Discussion

T. gondii is thought to be an oncogenic pathogen and is thought to play a role in the induction and progression of malignant diseases. A number of theories, including preventing apoptosis and enhancing the mobility of dendritic cells and macrophages, explain this (12). Mustafa *et al*. conducted a study in Egypt in 2016 under the title of the relationship between *toxoplasmosis* and various types of human tumors. The study involved 156 patients with various cancers, and the researchers used an immunoassay method to determine the titer of IgG and IgM antibodies against *toxoplasma*. They explored the connection between *T. gondii* infection and the development of tumors, and the findings of their research indicated that *toxoplasmosis* may contribute to the development of specific kinds of cancers. The regulation of the macrophage proteome in mice that have been infected with this illness has been used in research on the function of *Toxoplasma* as an important pathogen connected to the incidence of glioma and meningioma (14).

In Our study, all samples were negative for IgM antibody titer, (50/90, or 55.6%) were female and (40/90, or 44.4%) were males; nevertheless, 50/90, or 55.6%, were positive for IgG antibodies, which is very close to the results of researchers in Turkey. (63%)(15), despite the fact that China (16.7%) (16) and Egypt (20%) had higher antibody titers (17).

In the current study, the prevalence of IgG anti-*toxoplasma* antibodies was found to be higher in men compared to women. However, there was not a significant difference found between the serum prevalence of *T. gondii* and gender (OR =1.89, 95% CI: 0.61 to 5.79. p = 0.265). This was determined by examining the multivariable logistic regression analysis. *Toxoplasmosis* was found to be more frequent in males than in females, according to a review study that was carried out in Pakistan by Shoukat et al. These researchers also found that there was a strong association between infection and gender (18).

The findings of this study indicated that the prevalence of anti-*toxoplasma* IgG antibodies was greater in the age groups of 51-60 and 61-70 than in the younger age groups. In addition, the risk of being infected with *toxoplasma* was greater in these age groups than it was in the other age groups.

The present study revealed that the frequency of *toxoplasma* antibodies in patients with cancer was very high (55.6%), although statistical analysis did not reveal a significant correlation between *toxoplasma* prevalence and cancer type. In a 2015 study conducted by Kalantari *et al.* under the title of the relationship between *toxoplasmosis* and breast cancer in Iran, the results obtained from the study of 66 women with breast cancer (29 women whose disease was newly diagnosed and 37 cases undergoing treatment and regular examinations) and also 60 healthy women without a history of cancer as a control group revealed that immunoglobulin (IgG) in breast cancer patients (86.4%) and in cancer patient controls (100%) were significantly higher (19). Mustafa *et al*. found associations between *toxoplasmosis* and many forms of cancer, including breast cancer, squamous cell carcinoma in bone, brain tumors (glioblastoma and astrocytoma), liver tumors, bladder cancer, and benign tumors. A significant relationship was seen in uterus cancer (14).

Long-term host defensive responses generated by recurrent infections may raise the prevalence of cancer by promoting inflammation and boosting cell mutations, according to the findings of a study (20). Perhaps the collapse of cell barriers and the subsequent appearance of oncogene mutations following infection with intracellular organisms are responsible for the development of cancer (21). There are indications that toxoplasmosis has the potential to cause cancer in people (22). Whereas, There is evidence that *Trypanosoma cruzi* (23), *Toxoplasma gondii* (24), *Acanthamoeba castellanii* (25), *Echinococcus granulosus* [(26)], and Trichinella spiralis (27) induce antitumor activity against various types of cancer. However, a retrospective study in Cyprus showed that Echinococcus may increase the risk of cancer in patients (28). In some studies, antigenic similarity between lung carcinoma and hydatid cyst fluid has been reported (29).

In order to minimize the mortality of malignant illnesses brought on by the complications of toxoplasmosis recurrence, it is proposed that investigations comparable to the current investigation be conducted. Although contracting some parasitic diseases are considered as opportunistic and dangerous diseases, recent studies point to the different role of these infections.

Given that positive IgG and negative IgM results might be interpreted as a latent *toxoplasmosis* infection. Therefore, the findings of this research are of significant assistance in minimizing difficulties caused by the return of toxoplasmosis in cancer patients.

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Authors contribution

R S K, M E R, A H, were the major contributors to conceptualizing and formulating the research question and designing the study.

R S K, T V were the leader of the research and project team.

M E R, A F K and MO E R, M A N, collected and analyzed the data.

R S K and A F K, wrote the first draft of the manuscript.

A H, and R S K, critically studied and appraised the first draft.

A F K and R S K, revised and developed the first draft based on a critical appraisal of their colleagues. All authors commented on the modified draft, and the final version of the manuscript was prepared. Finally, all authors approved the final manuscript.

Conflict of interest

There is no conflict of interest in this research.

Ethics

This study was approved by the ethics code IR.AJUMS.REC.1401.309, at Jundishapur University of Ahvaz.

Data availability

All the data of this research and the right to publish it are at the disposal of this journal.

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