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RESEARCH ARTICLE

SEROPREVALENCE OF TOXOPLASMA GONDII AMONG CANCER PATIENTS IN AL-AMAL CENTER FOR TREATMENT OF CANCER PATIENTS IN TAIZ CITY, YEMEN

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Abstract

The current study was done in Taiz city during the period from March 2019 to march 2020, this study aimed to determine the prevalence of *Toxoplasma gondii* infection among cancer patients and to determine the association of *T. gondii* seropositivity in cancer patients with gender, age and number of chemical doses in Al-Amal Center for Treatment of Cancer Patients in Taiz governorate, Yemen, using serological test by rapid devise Toxo-kits method. A total of 368 blood samples from cancer patients were collected and examined for anti-*Toxoplasma gondii* IgG and IgM antibodies. The overall *T. gondii* seroprevalence, including both Immunoglobulin G (IgG) and Immunoglobulin M (IgM) positive individuals was 42.12% (155/368). The seroprevalence rate of IgG and IgM antibodies was 41.58% (153/368) and 14.13% (52/368), respectively. Regarding sex, no statistically significant difference was found, with 65 seropositive out of 148 (43.92%) in males and 90 out of 220 (40.91%) in females (P>0.05). The seroprevalence of *T. gondii* infection was high in all age groups, especially in younger and older cancer patients (aged from 1-10 and >80 years old), (50.00%) in each; while the lower seroprevalence (25.81%) was detected in cancer patients aged 21 to 30 years old, but the differences were not significant (P> 0.05). Moreover, the seroprevalence of toxoplasmosis was higher in individuals treated with chemotherapy (43.07%) than those not used chemotherapy (39.60%), with no significant difference (P>0.05). *T. gondii* infection remains a major threat to cancer patients, and it needs proper screening, diagnosis and treatment.

Keywords: Toxoplasmosis, Cancer patients, Chemotherapy, Yemen.

1. Introduction

Toxoplasma gondii is an obligate intracellular protozoan parasite. The first described in 1908 by Nicolle and Manceaux in tissues of North African rodent called gundi [1]. *T. gondii* is a single-cell apicomplexan parasite, infects most genera of warm-blooded animals (birds and mammals) worldwide causing toxoplasmosis [1,2,3]. The infective stages are tachyzoites, bradyzoites in tissues cysts [4-7], and sporozoites in sporulated oocyst [8].

Infection with *T. gondii* by the ingestion of sporulated oocysts with drinks or foods, these present in feces of infected cats [9]. Moreover, toxoplasmosis can be acquired upon the consumption of undercooked / raw infected bird or mammalian meat contain tissues cysts [10]. Forthermore, *T. gondii* transmitted through the gastrointestinal tract in the tachyzoites form to the body and invade various parts of the body as the heart, the muscles and the brain [11]. In addition, *T. gondii* can transmitted by organ transplantation [12, 13], there are another ways to transmission *T. gondii* such as blood transfusion [14] and transplacental transmission from the infected mother to her fetus [15].

T. gondii has two cycles which include sexual cycle in epithelial cells of cat intestine and asexual cycle in infected animals and human [16]. The tissues cysts of *T. gondii* permit the parasite to evade host immune. When the tissues cysts rupture, the released bradyzoites are killed by immune system of host. If the host immune system becomes compromised, due to AIDS or chemotherapy in cancer, these bradyzoites will develop into tachyzoites lead to active toxoplasmosis [17]. Patients receiving chemotherapy are more susceptible to *Toxoplasma* infections. Many studies have reported that the rate of reactivation of a latent *T. gondii* infection was higher in different types of cancers particularly those of the eye, brain, blood and breast [18].

T. gondii was consider the most common global parasite [7]. The prevalence of toxoplasmosis in humans worldwide was estimated to be 30–50% of the world population [19]. The prevalence is high in humid and warmer area [2, 20]. The toxoplasmosis seroprevalence appears vary from region to another region depending on exposure to infective stage. While it was recorded over 14% in United States of America [4], below 30% was observed in South East Asia and Northern Europe [21, 22], 47% in France [21], above 60% in Latin America and region tropical Africa [23, 24] and more than 80% in South America [4]. In Meddle east and North Aferica, there are no statistical accurate for toxoplasmosis prevalence [24]. Whereas, in Arab countries the overall incidence rate of toxoplasmosis is approximately 30% to 50%, making it among the global regions with the highest prevalence [25]. Furthermore, until today, there has been no widely acknowledged human vaccination against toxoplasmosis [26].

Cancer patients are at high risk of developing severe disease, from one hand being immunocompromised from the cancer itself and from the other hand reactivation of a latent *T. gondii* infection can occur due to cancer therapy [27]. Therefore, there is increasing interest in exploring the causation between *T. gondii* infection and cancer [28, 29]. Thomas his fellows demonstrated that toxoplasmosis might cause brain cancer [30]. Another study reported relationship between *T. gondii* and oral cancer [31]. Studies conducted by Yu and Zhou showed *T. gondii* to be common in cancer patients in eastern China, and that blood transfusion and chemotherapy could promote the spread of this parasite [32, 33]. Moreover, *T. gondii* is incriminated to be responsible for the progression of malignant diseases by inhibiting apoptosis, and increasing dendritic cells and macrophages motility [34, 35].

In Yemen, as a one of the least-developed countries, a few studies have been conducted on *T. gondii* infection among different population categories in different areas, mainly focusing on the epidemiology of infection among pregnant women. There is no study on the seroprevalence of *T. gondii* infection among cancer patients in Yemen. The present study aims to shed light on the prevalence of *T. gondii* infection among the vulnerable population of cancer patients and explore potential links between *T. gondii* seroprevalence and patient characteristics. This information can help improve the understanding the impact of *T. gondii* on the health and well-being of cancer patients, which is an important public health concern. The findings from this study in the Yemeni context could also contribute to the broader understanding of *T. gondii* epidemiology in cancer populations.

2. Materials and Methods

2.1. Study design, setting and population

This is a cross-sectional study conducted among cancer patients at Al–Amal Center for Treatment of Cancer Patients in Taiz city, the capital of Taiz Governorate, Yemen. It was conducted on the toxoplasmosis among cancer patients at different ages (from one to >80 years) in both sexes. Blood samples were collected from 368 cancer patients attended Al–Amal Center in Taiz city during the period from march 2019 to march 2020.

2.2. Detection of Toxoplasma gondii

A total of 368 blood samples were taken from patients with different types of cancer at Al-Amal center in Taiz city.

Three to five millilitres of venous blood samples were taken from each patient as a part of the routine investigation. The blood samples were placed in a sterile plain test tubes and allowed to clot naturally at room temperature for 30 minutes, after that, the serum was separated by centrifugation at 3000 rpm for 5 minutes. All sera were transferred to Eppendorf tubes and stored at -20 °C until being tested. The sera were examined for the presence of IgG and IgM antibodies against *T. gondii* by devise a commercially available rapid devise Toxo-kits (ENCODE, China) based on the manufacturer's instructions. The paper of kits determines the time of reading the results through twenty minutes and not read the results after twenty minutes.

2.3. Statistical analysis

By using Statistical Package for the Social Sciences (SPSS) software, version 24, the researchers calculate the frequencies of numerical data and find the association between variables by using *Chi*-square test, which considering significance when *P*-value less than 0.05.

3. Results

The results of this study showed that 155 cases (42.12%) out of the total 368 screened cancer patients were seropositive for anti-*Toxoplasma* antibodies by serological test using devise Toxo-kits, and 213 (57.88%) were negative. The overall IgG antibodies to *T. gondii* were found to be 153 (41.58%) in cancer patients and IgM antibodies were found in 52 cancer patients (14.13%). In detail, anti-*T. gondii* IgG alone was found in 103 (27.99%) of cancer patients, IgM antibodies were found in only 2 (0.54%) of cancer patients. In addition, anti-*T. gondii* IgG and IgM antibodies together were found in 50 (13.59%) of cancer patients (Table 1).

Table 1: Seroprevalence of *Toxoplasma gondii* IgG and/or IgM antibodies among 368 cancer patients.

Antibodies	Cancer patients (N=368)			
	Positive	%	Negative	%
Anti-*T. gondii* IgG	103	27.99	265	72.01
Anti-*T. gondii* IgM	2	0.54	366	99.46
Anti-*T. gondii* IgG and IgM (together)	50	13.59	318	86.41
Total	155	42.12	213	57.88

Regarding sex, the seroprevalence of *T. gondii* specific IgG antibody was higher in males (43.92%) than that in females (40.91%), but there was no statistically significant difference in the toxoplasmosis between males and females ($P > 0.05$), (Table 2).

Table 2: Seroprevalence of toxoplasmosis among cancer patients, in relation to sex.

Sex	No. of Cancer Patients	Toxoplasmosis				P value
		+Ve	%	-Ve	%	
Female	220	90	40.91	130	59.09	0.566
Male	148	65	43.92	83	56.08	
Total	**368**	**155**	**42.12**	**213**	**57.88**	

In this study, it has been found that the seroprevalence rate of toxoplasmosis observed irregular in the age groups, it was higher in the child and older cancer patients age groups (1-10 and >80 years) consisted equal rate (50.00%) in each, while the lower seroprevalence rate was found in the age group 21-30 years (25.81%). There was no statistically significant in the seropositivity of toxoplasmosis among different age groups ($P>0.05$), as shown in table (3).

Table 3: Seroprevalence of toxoplasmosis among cancer patients, in relation to age.

Age Group (Years)	No. of Cancer Patients	Toxoplasmosis				P- value
		+Ve	%	-Ve	%	
1-10	24	12	50.00	12	50.00	0.237
11-20	29	11	37.93	18	62.07	
21-30	31	8	25.81	23	74.19	
31-40	60	28	46.67	32	53.33	
41-50	67	21	31.34	46	68.66	
51-60	69	34	49.28	35	50.72	
61-70	52	25	48.08	27	51.92	
71-80	24	10	41.67	14	58.33	
>80	12	6	50.00	6	50.00	

The seroprevalence rate of infection with *T. gondii* was higher in cancer patients who exposed to chemotherapy doses (43.07%) than those not exposed to chemical doses (39.60%). Nevertheless, there was no significant difference of toxoplasmosis in the cancer patients exposed and not exposed to chemical doses ($P > 0.05$), as shown in Table (4).

Table 4: Seroprevalence of toxoplasmosis among cancer patients, in relation to chemotherapeutic doses.

Using chemotherapy	No. tested	Toxoplasmosis				P- value
		+Ve	%	-Ve	%	
No	101	40	39.60	61	60.40	0.548
Yes	267	115	43.07	152	56.93	

4. Discussion

Many previous studies conducted to investigating of toxoplasmosis infections (most of them among pregnant women) in different regions in Yemen showed the overall seroprevalence rate was ranged from 20.43% to 83.1%. To our knowledge, the current work is the first preliminary study on the seroprevalence of *T. gondii* infection among cancer patients in Yemen. Cancer patients are susceptible to infection with a diversity of pathogens, including *T. gondii* [31, 36-38]. In this study, the overall seroprevalence of toxoplasmosis in cancer patients was 42.12%. When compared to other countries, the seroprevalence reported in this study was higher than that reported from Jordan (39.5%)[39] and liked to near that reported from Iran (45%, 45.2% and 45.8)[37, 40, 41], respectively. However, the higher seroprevalence rate of toxoplasmosis reported in cancer patients in Turkey in two studies was 60.0% [42] and 63% [43], and in Iran, it was 64% [44]. Contrary to that, a lower seroprevalence of *T. gondii* infection among cancer patients was reported in other countries such as Saudi Arabia (30.6%) [45], Egypt (20%) [46] and in China, it was 21.72% [32] and 16.7% [45]. The discrepancy between the results of the current study and findings of the above-mentioned studies may be due to the geographical factors, the size of studied sample, social and economical factors, hygiene, sanitation, eating habits and weakening immunity at cancer patients.

In the present study, the seropositivity rates of anti-*Toxoplasma* IgG, IgM, and combined IgG/IgM antibodies in cancer patients were higher (41.58%, 14.13%, and 13.59%), respectively. This is typically may be due to weakened host immunity in cancer patients which may allow the reactivation of past chronic *Toxoplasma* infection or increasing the possible risk of acquiring new infection[47]. Compared to other studies conducted on cancer patients in many other countries worldwide, the closely figures of anti-*Toxoplasma* IgG were reported as 36% in Egypt [48], 39.5% in Jordan[39], 38.27% in Iraqi breast cancer women [49], and 41.51%, 45.8% and 45.2% in Iran [38, 41, 50] respectively. Whereas, the highest seropositivity of anti-*Toxoplasma* IgG was recorded in some countries such as Egypt it was 66.7%, 92%, 55.8% and 62.5% [47, 51-53] respectively, in Iraq 49.0%, 72.22% and 82.1% [54-56],

and in Iran 62.6% and 86.4% [44, 57], respectively. Also, in Nepal, IgG seroprevalence was 68.7% among patients having ocular malignancies [58].

Contrarily, the lower seropositivity rates of anti-*Toxoplasma* IgG among cancer patients were recorded in various locations of the world. In Egypt, 20% of cancer patients had anti-*T. gondii* IgG antibodies [59], while in Thi-Qar provinvce of Iraq, the positive rate of anti-*T. gondii* IgG antibodies in the cancer patients was 30% [60]. Farthermore in Iran, the seroprevalence of anti-*Toxoplasma* IgG was 36.6%, 13% and 30.6% among cancer patients [61-63], respectively. Also, different studies were conducted among cancer patients in various localities in China, anti-*T. gondii* IgG was reported in 6.02%, 35.56%, 20.59%, 16.72%, 16.0% and 6.16% [2, 3, 13, 33, 64], respectively.

Concerning of anti-*T. gondii* IgM, the seropositivity in the current study was 14.13%, which is much lower than that was recorded in Egypt (24%) among cancer patients after chemotherapy [51]. This is may be due to reactivation of a latent infection. However, our result was higher than seropositivity rates of toxoplasmosis were reported among cancer patients by other studies in different parts of the world. In Egypt, it was 9.2%, 3.8% and 4% [47, 52, 59] respectively, as well as 2.5% in Jordan [39], and 4.93% and 0.33% in Iraq [49, 54] rrespectively. Also, it was higher than that reported in other countries such as Iran (0.94%, 0.66%, 7.6% and 2%) [38, 44, 57, 62], respectively. Furthermore, the seropositivity of anti-*T. gondii* IgM in China was 6.27% [32], 1.58% [65] and 2.8% [33].

In the present study, the seroprevalence of *T. gondii* was no significantly higher in males (43.92%) than in females (40.91%). This finding is consistent with some studies were conducted in other parts of the world [32, 39, 46, 59, 61, 65, 66], with no significant differences. This may be attributed to the increased risk of exposure of males due to more outdoor activities and the habit of eating outdoor foods [67]. In contrast, some studies found a higher seroprevalence of toxoplasmosis in females than in males [10, 50, 60]. While the seroprevalence of toxoplasmosis in cancer patients equal in both males and females as study done in Basra province, Iraq [43]. The different variation between males and females seroprevalence of toxoplasmosis may be due to many factors as social activities, sex differences in immune response, difference in exposure to toxoplasmosis infection, occupational difference [68], and infection intensity [60].

In this study, the seroprevalence rate of toxoplasmosis is observed to be irregular among the age groups. This is may be attributed to the impairment of the immune system and exposure to infection dueto bad life conditions as result to the war. Some studies observed that the seroprevalence of toxoplasmosis increased with age [10, 46, 57, 69]. This was explained as reflectance to the increased possibility of exposure to toxoplasmosis during a person's lifetime.

It is known that cancer patients which exposed to chemotherapy are suffering from immune suppression that helps on activation of parasite to percent wide spread in the patient's body [31], and the immunological status of host is most important factor for infection with toxoplasmosis [37]. The present study showed that toxoplasmosis has a slightly higher seroprevalence among cancer patients receiving chemotherapy (43.07%) than those not receiving chemotherapy (39.60%), it is inagreement with study done in Thi-Qar province, Iraq [60], which reported high seroprevalence among cancer patients who area undergoing to chemotherapy (37.63%) comparing with those not exposing to chemotherapy (14.29%). This difference is because chemotherapy acts on immune inhibition in cancer patients undergoing chemotherapy. On the other hand, this study is disagreement with study conducted in Eastern China, which recorded high seroprevalence of *T. gondii* in patients no taking chemotherapy [32].

Conclusion

This study showed high seroprevalence of anti-*T. gondii* IgG and IgM antibodies among cancer patients who attended Al-Amal Center for Treatment of Cancer Patients in Taiz governorate, Yemen. At the same time, the infection showed higher in males than females and also among all age categories. Furthermore, oxoplasmosis represents a major cause of morbidity in cancer patients undergoing chemotherapy. Therefor, it is imperative that improved integrated measures should be conducted to prevent severe infection and dissemination, and also control *T. gondii* infection in cancer patients and general population.

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مقالة بحثية

الانتشار المصلي لطفيل *التوكسوبلازما جوندي* بين مرضى السرطان المترددين على مركز الأمل لمعالجة مرضى السرطان في مدينة تعز، اليمن

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المُلخّص

داء *التوكسوبلازما* واسع الانتشار على مستوى العالم، أجريت هذه الدراسة على مرضى السرطان في مركز الأمل لمعالجة مرضى السرطان في مدينة تعز اليمن بغرض تحديد نسبة الإصابة بداء *التوكسوبلازما* بين مرضى السرطان المترددين على المركز خلال الفترة من مارس 2019 إلى مارس 2020م وعلاقة الإصابة بالعمر، الجنس، والمعالجة الكيميائية لمرضى السرطان. تم التشخيص المصلي للمرضى باستخدام الكتات السريعة Toxo-kits (ENCODE, China) الخاصة *بالتوكسوبلازما جوندي*. تم جمع عينات الدم من عدد ثلاثمائة وثمان وستون (368) شخصا مصابون بالسرطان لاستكشاف مضادات *التوكسوبلازما* من النوع IgG و IgM. سجلت نسبة الاستجابة المصلية الكلية (42,12%) في 155 مريضا بالسرطان، وكانت نسبة الاستجابة المصلية للجسم المضاد IgG41,58% وللجسم المضاد IgM 14,13%. لم تسجل علاقة إحصائية ذات دلالة معنوية (P<0.05) بين نسبة الإصابة بداء *التوكسوبلازما* والجنس حيث كانت نسبة الإصابة في الذكور 43,92% وفي الإناث 40,91%. أظهرت النتائج أن معدل الانتشار المصلي لطفيل *التوكسوبلازما* مرتفعا في كل الفئات العمرية، خصوصا في صغار السن (1-10 سنوات) وكبار السن (>80 سنة) وبمعدل إنتشار 50% في كل منهما، بينما كان أقل معدل انتشار (25,81%) والذي سجل في الفئة العمرية من 21-30 سنة، مع عدم وجود فوارق إحصائية ذات دلالة معنوية في معدل الإصابة بين الفئات العمرية المختلفة (P<0.05). إضافة إلى ذلك، لا يوجد فارق إحصائي ذو دلالة معنوية بين معدل الانتشار المصلي لداء *التوكسوبلازما* في مرضى السرطان الخاضعين للمعالجة الكيميائية (43,07%) وأولئك الغير خاضعين للمعالجة الكيميائية لمرض السرطان (39,60%). (P<0.05) تظل الإصابة بداء *التوكسوبلازما* أكبر عامل مهدد للحياة لمرضى السرطان، لذا تحتاج إلى إهتمام زائد في التشخيص والمتابعة والمعالجة.

الكلمات المفتاحية: داء التوكسوبلازما، مرضى السرطان، المعالجة الكيميائية، اليمن.

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