Correlation of latent toxoplasmosis in cancer patients in Iraq and its neighboring countries (2010 – 2019) (review)

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Abstract

Background: *Toxoplasma gondii* is an obligatory intracellular protozoan parasite. The infection with toxoplasmosis is a major opportunistic pathogen in patients who are immunocompromised like patients having cancer disease. Electronic databases were reviewed for *T. gondii* infection in cancer patients. The estimation collected prevalence of toxoxplasmosis infection in different types of cancer patients ($p < 0.001$), This review was designed to evaluate the seroprevalence rate of toxoplasmosis infection among cancer patients in Iraq and its neighboring countries from 2010 to 2019. The searching process was included of 15 studies. The results of current review showed that toxoplasmosis infection in patients with malignancy had a higher prevalence in Iraqi patients compared with its neighboring countries ($P < 0.001$). This review hypothesized to focus on the *T. gondii* and its serious outcomes, and its crucial role in pathogenesis with different kinds of cancer, also to carry out further studies and research to prevent and control toxoplasmosis among populations infect with different kinds of cancer worldwide.

Keywords: Toxoplasmosis, malignancy, cancer patients

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Introduction

Toxoplasma gondii is a worldwide zoonotic parasite that infects both humans and animals [1]. The infective stage are oocysts in cat feces contaminating undercooked meat, drinking water, organ transplants from infected donors, and from infected women to her fetus via placenta [2]. *T. gondii* infection in immunocompetent individuals is rarely symptomatic, but occurred in immunocompromised patients may result in a severe illness or even lethal damage [3]. The individuals with impaired immunity (e.g., cancer patients, patients with HIV, and transplant recipients) have incompetent immune responses, led to the activation of the quiescent form bradyzoite to the active form which is called tachyzoite, resulting to acute infection [4]. The identification of the parasite antibodies (i.e., IgG and IgM specific Abs) in the serum samples considered the most routine diagnosis techniques of toxoplasmosis. The most common serological techniques known as immunofluorescence antibody assay (IFA)

and enzyme-linked immunosorbent assay (ELISA) [4].

Cancer is a disease that caused by abnormal cells division, and affecting both developing and developed countries, a status report on the global burden of cancer worldwide using the GLOBOCAN 2018 estimates of cancer incidence and mortality produced by the International Agency for Research on Cancer, with a focus on geographic variability across 20 world regions according to the evidence, there were estimated 18.1 million new cancer cases and 9.6 million cancer deaths [1, 2]. The rate of death is growing up due to cancer disease worldwide. It has been expected that about 11 million mortality case will occur in 2030 [3].

Meanwhile, the diagnosis and treatment at an early stage can decrease nearly one third of the cancer cases [4]. Mortality can caused by the clinical manifestation of Toxoplasmosis in humans, especially in patients with impair immunity. The reactivation of latent *T. gondii* can resulted from chemotherapy , radiation to patients with cancer, corticosteroids immune suppressive therapy, and splenectomy these risk factors can result to impairing both cellular and humoral immune system [5].

Early clinicians information regarding the seroprevalence rate of toxoplasmosis can help for appropriate diagnosis, treatment, and control of infections caused by *T. gondii*, in different populations. This review was done in order to evaluate the seroprevalence of toxoplasmosis among cancer patient in Iraq and its neighboring countries from 2010 to 2019.

Patients and Methods

We searched databases, including PubMed, Science Direct, Scopus, Google Scholar; and Iraq Academic Scientific Journals. We systematically searched the scientific literatures for studies that reported *T. gondii* infection in patients with different types of cancer, from 2010 to 2019. The databases were searched using the keywords "*Toxoplasma gondii*" and "toxoplasmosis", "cancer" "malignancy" "carcinoma". The clinical signs of toxoplasmosis in immunocompromised patients are similar to those occurring in immunocompetent persons but in more fulminating and disseminated pattern.

Statistical analysis

In this study The Statistical Analysis System- SAS (2012) program was used to detect the effect of difference factors in study parameters. Least significant difference – LSD test was used to significant compare between means. This study was performed to determine the association between the seroprevalence of T. gondii and cancer in Iraq and its neighboring countries population [6].

Results

Prevalence of T. gondii Abs (IgG, IgM) in cancer patients

This review was included 15 records studies. The analysis contained, 2,741 individuals, which included 1,401 IgG seropositive cases. According to the recording electronic database of all journals,

and scientific website, this review did not recover a publication from similar it.

Table (1): Prevalence of toxoplasmosis in cancer patients in Iraq and its neighboring countries from 2010 to 2019

	No.	First author	Years	Province	Type of cancer	No. of case	IgG(+)	(%)	IgM(+)	(%)	Serological test	Ref.
Iraq	1.	Molan, A.-L. and F Rasheed	2016	Baghdad	Breast	106	60	37.5	1	0.9	Elisa	[7]
					Thyroid glan	94	42	44.6	0	0		
					Rectum	50	27	54	0	0		
					Leukemia	50	18	36	0	0		
	2.	Albayati, N.	2017	Baghdad	Brain	78	52	66.6	0	0	Elisa	[8]
					Lymph nod	22	10	45.4	1	4.4		
					colon	19	10	52.6	1	5.2		
					Urinary bladd	18	10	55.5	0	0		
	3.	Al-Aboody, B	2017	Thi-Qar	Malignancy	100	36	36	0	0	Elisa	[9]
	4.	Hamid., D.M.	2017	Baghdad	Liver	20	11	55	3	15	Elisa	[10]
					Lung	25	17	68	3	12		
					Uterus	23	13	56.5	5	21.7		
					Colon	21	13	61.9	6	28.5		
					Breast	89	39	43.8	11	12.3		
					Kidney	178	93	52.2	28	15.3		
	5.	Ahmed, D.F. & E Saheb	2017	Baghdad	Breast	80	62	77.5	0	0	Elisa	[11]
					Colorectal	31	24	77.4	0	0		
					Ovary	11	6	54.5	1	9		
	6.	Assim, M.M.a.E.	2018	Baghdad	Breast	90	65	72.2	0	0	Elisa	[12]
	7.	Al-Tameemi, I., et	2019	Basrah	Malignancy	56	46	82.1	13	23.2	Elisa	[13]
Iran	8.	Fallahi, S., et al	2014	Tehran	Leukemia	535	208	38.8	51	9.5	Elisa	[14]
	9.	Kalantari, N., et a	2015	Babol	Breast	66	57	86.3	5	7.5	Elisa	[15]
	10.	Gharavi, M.J., M Roozbehani, and Mandeh	2017	Tehran	Leukemia	170	96	56.4	10	5.9	Elisa	[16]
	11.	Saki, J., S. Tavako and M. Pedram	2017	Khuzestan	Malignancy	372	155	41.6	24	6.4	Elisa	[17]
	12.	Kalantari, N., et a	2018	Babol	Leukemia	101	37	36.6	0	0	Elisa	[18]

Saudi Arabi	13.	Imam, A., et al.	2017	Qassim region	Malignancy	137	71	51.8	1	0.7	Elisa	[19]
Turkey	14.	Alim, M., S. Ozce and N. Ozpinar	2018	sivas	Malignancy	100	60	60	1	1	Elisa	[5]
Jordan	15	Khabaz, M.N., L. Elkhateeb, and J. Al-Alami	2010	Amman	Malignancy	99	63	63.6	0	0	Elisa	[20]

Prevalence of toxoplasmosis in cancer patients (Iraq)

This is the first review of toxoplasmosis in cancer patient from Iraq. In Iraq toxoplasmosis was raised after Iraq occupation with a frequency of infection more than (40% compared to 2%) in the eighties[21]. Among the 1,161 CA. patients in Iraq, the highest sero-positive rate of toxoplasmosis was observed in patients who had in colorectal cancer patients (77.42 ± 0.05 %), followed by Lung cancer patients (68.00 ± 1.25%), breast cancer patients (62.53 ± 7.65) Table (2). Results suggested that high percentage infection with cancer in Iraqi people who are infected with toxoplasmosis because of many points such as smoking, about 85% of lung cancer cases was associated mainly with history tobacco smoking, whereas about 10% to 15% have no history of tobacco smoking [22]. Exposure to coal-burning smoke consider other source for lung cancer [23].

Recently research stated that the dangers of brain cancer in human rises in patients with toxoplasmaosis, most cases were having brain cancer 78 out of 137 and the highest rate of toxoplasmosis was among them (66.66%) [24]. Concentration of IgG was increased in cancer seropositivity with toxoplasmosis [24].

Table (2): Percentage of IgG and IgM according to the type of cancer in Iraq

Type of cancer	Mean ± SE	
	IgG (%)	IgM (%)
Breast	62.53 ± 7.65	3.31 ± 3.02
Thyroid gland	44.60 ± 1.00	0.00 ± 0.00
Rectum	54.00 ± 1.00	0.00 ± 0.00
Leukemia	36.00 ± 0.05	0.00 ± 0.00
Brain	66.60 ± 0.05	0.00 ± 0.00
Lymph node	45.40 ± 0.25	4.50 ± 0.00
Colon	57.90 ± 0.05	17.57 ± 0.05
Urinary bladder	55.50 ± 1.00	0.00 ± 0.00
Malignancy	36.00 ± 0.05	0.00 ± 0.00
Liver	55.00 ± 0.00	15.00 ± 0.05
Lung	68.00 ± 1.25	12.00 ± 0.05
Uterus	56.52 ± 1.00	21.73 ± 0.75
Kidney	52.24 ± 0.05	15.37 ± 0.05
Colorectal	77.42 ± 0.05	0.00 ± 0.05
Ovary	54.55 ± 1.00	9.09 ± 0.25
LSD (P-value)	11.059 * (0.0316)	5.772 * (0.0328)
* (P≤0.05).		

About seven sites in the body and probably others may affected with cancer as a result of drinking alcohol. According to the recent studies about cancer deaths attributable to alcohol consumption increased to approximately 480,000 (5.8% of the total number of cancer deaths) in both sexes combined—360,000 (7.8%) men and 120,000 (3.3%) women[25]. The infection with toxoplasmosis can result from many reasons such as the geographical variation, customs, habits, difference in genetic susceptibility and the possible risk factors, these factors increase the susceptibility to the infection with toxoplasmosis in immunecompromised patients [26] .

Table (3): Comparison the percentage of IgG and IgM among 3 provinces in Iraq

Countries	Mean ± SE	
	IgG (%)	IgM (%)
Baghdad	57.25 ± 2.72	6.93 ± 2.07
Thi-Qar	36.00 ± 1.00	0.00 ± 0.00
Basrah	82.1±1.66	23.2 ±0.24
LSD (P-value)	8.026 * (0.0419)	2.963 * (0.050)
* (P≤0.05).		

According to seropositive to (anti-T. gondii IgG and IgM Abs) among three provinces (Baghdad, Thi-Qar and Basrah) the findings shows higher rate of toxoplasmosis was in Basrah compared to Thi-Qar and Baghdad. These results have direct negative effect on the public health. According to the records done by several studies Basra , Thi-Qar and

Muthana provinces showed the maximum increase in cancer infections [27]. Iraq community especially in Basra province the finding shows large percentage of the neoplastic disease such as leukemia , lymphoma and other type of cancer, these results may explain of high levels of contamination in the air, soil and water, which is spread widely. Therefore, the maximum rate of cancer diseases was shown in industrialized communities with increased environmental risk factors which lead to initiate cancers [28]. In Baghdad, increased the percentage between cancer and toxoplasmosis are require depth studies establish to realistic links between the identified environmental risk factors and the prevalence of cancers[29].

Prevalence of toxoplasmosis in cancer patients (Iran)

In Iran (553) out of (1,244) cancer patients was IgG seropositive to toxoplasmosis. In Iran the most common cancer type is leukaemia, and according to resent studies about 661 / million children under 14 years old are diagnosed with leukaemia, this can explain that the mortality rates associated with the sero-positive of toxoplasmosis [30]. In southwest of Iran most investigation according to several studies concluded that the children with malignance cancer diagnosed with high prevalence of acute and chronic toxoplasmosis and they requires special attention [17]. While another study in Iran established that the positive rate for toxplasmosis antibodies was (86.4%) in woman with the control women (78.3%) [31]. Accuracy and early diagnosis of infection with toxoplasmosis especially in people who are immunocoprmised can help in the prevention and control of the disease, [14].

Prevalence of toxoplasmosis in cancer patients (Turkey)

According to the results of ELISA method which was done by (Mehtap Alim) study , the result shows that CA. patients were suffering from different kinds of cancer such as (stomach, breast, lung, colon and ovarian) cancer are sero-positive for Toxoplasma IgG. Accordingly, IgG seropositivity was in 60 (60.0%) out of 100 cancer patients, IgM positivity was in one individual in all 100 individuals enrolled in (Mehtap) study, and the difference between the groups was found to be insignificant ($p>0.05$) [5]. Many studies cannot clarified the mechanisms of how T. gondii initiates tumorigenesis. Inducement of the immune system for long time as a result of inflammation responses of T. gondii may increase the host induces mutations and may affect the cancer growth. Accordingly, the oncogenic products (resulted from long induced of immune system by intracellular pathogens) gradually accumulating inside the host cells after rupturing the cellular barriers [32]. More recent reports show that the development of cancer result from infection with T. gondii parasite can occur by exportation of (miRNAs) into host cell, which can affect the regulation of the hosts gene expression [33]. Medically , it will be appropriate for immunocompromised

patients to be periodically evaluated their infection with Toxoplasma [34].

Prevalence of toxoplasmosis in cancer patients (Saudi Arabia)

In Saudi Arabia only one study shows that 41 (29.9%) out of total 137 cancer patients were seropositive for anti-Toxoplasma IgG, while one case (0.7%) was seropositive for anti-Toxoplasma IgM. Cancer patients are more disposed to infections and the risk of the reactivation of toxoplasmosis experienced before is higher in these patients [34].

Prevalence of toxoplasmosis in cancer patients (Jordan)

In Jordan only one study shows that 63 patients out of total (99) cancer patients were seropositive for anti-Toxoplasma IgG, while no cases were seropositive for anti-Toxoplasma IgM. These findings suggest the possibility that treatment with immunosuppressive agents predisposed cancer patients to reactivation of T. gondii infection[35].

Table (4): Comparison between Iraq and its neighboring countries in the percentage of IgG and IgM Abs

Countries	Mean ± SE	
	IgG (%)	IgM (%)
Iraq	56.13 ± 2.81	6.56 ± 1.99
Iran	51.98 ± 9.26	5.89 ± 1.60
Saudi Arabia	51.82 ± 1.00	0.72 ± 0.05
Turkey	60.00 ± 1.00	1.00 ± 0.05
Jordan	63.60 ± 1.00	0.00 ± 0.00
LSD (P-value)	7.615 * (0.0392)	3.569 * (0.0452)
* (P≤0.05).		

According to findings in table 4 Jordan has highest rate of seropositive cases for anti-Toxoplasma IgG Ab among other countries that neighbored Iraq. In Jordan the mortality rate can reach to 14% caused by malignant cancer [36]. According to previous studies in Jordan and Syria the data collected from applications for cancer treatments for refugees people in the period between (2010 and 2012, and between 2009 and 2011) respectively, the finding show the cancer in refugees people causes a substantial burden on the health systems of the host countries. Improvement of health systems one of the recommendations to improve prevention and treatment and that's done by operating procedures and innovative financing schemes, securement of sustainable funding sources, and development of electronic cancer registries [37]. However, most previous studies reported high rate of cancers in industrialized countries. With current trends it is estimated that by the year 2020)70%(of the new cases of cancer will be diagnosed in developing countries it may result from changes in lifestyle, and increases in life expectancy [36].

In Turkey cancer is ranks as the second cause of mortality and has a serious impacts on the productivity of the labour force, in

addition to high treatment costs so it is an important health issue. According to several studies show a significant results between the distribution of cancer cases and geo-environmental factors [38].

In Iraq according to the table 4 findings the incidental rates of anti-T. gondii IgG and IgM among the patient group was (56.13 ± 2.81, 6.56 ± 1.99) respectively . The cancer patients suffering from impaired immune function and this is the major cause to increase the antibodies production against Toxoplasma [39]. Other scientist proposed that the continuous infections may enhance cancer because long-term patients defensive responses stimulate inflammation, which rises the rates mutation[40]. Because of high radiation waves emitted from the Internet bridges that raised the percentage infection with cancer as a consequence. These results have direct negative effect on the public health, particularly in developing countries. In Iraq there are different pollination sources the most danger one is the pollination with depleted uranium (DU) because it impair the public health through poisoning. The increase in the rate of different type of cancers results from exposure to (DU) because it diagnosed as carcinogenic agent. Iraq was exposure to ammunition for long period extended from Gulf Wars of 1991 to 2003 result in contamination more than 350 locations in Iraq. In the last decades, each year Iraq recorded about 7000 to 8000 cancer. The prevalence rate per 100,000 individuals has risen in Baghdad and Basra. The pollution sources may have serious effects on the public health and led to increase the infection with different kinds of cancer such as: breast, lung, and Leukemia and Lymphoma cancer. In Iraq soil contaminated with uranium have a long-radiation hazard to human health through exposure via the food chain (plant uptake into edible food crops) [27].

Conclusions

This review provides a comprehensive view of the seroepidemiology of toxoplasmosis infection in Iraqi cancer patients and its neighboring countries. This review recommends the researchers to pay more attention to seroprevalence of toxoplasmosis in cancer patients. Hence, this topic need more exceptional efforts focused on Toxoplasma seroprevalence and its risk factors must be collected to improve prevention strategies for control of the disease in immunocompromised individuals.

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