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Review Article

Toxoplasma gondii Infection in Immunocompromised Patients in Iran (2013-2022): A Systematic Review and Meta-Analysis

Aref Teimouri [1], Fatemeh Goudarzi [2], Kimia Goudarzi [1], Rasoul Alimi [3], Keivan Sahebi [4], Hassan Foroozand [4], *Hossein Keshavarz [2,5]

1. *Department of Parasitology and Mycology, School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran*
2. *Department of Medical Parasitology and Mycology, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran*
3. *Department of Epidemiology and Biostatistics, School of Health, Torbat Heydariyeh University of Medical Sciences, Torbat Heydariyeh, Iran*
4. *Student Research Committee, Shiraz University of Medical Sciences, Shiraz, Iran*
5. *Center for Research of Endemic Parasites of Iran (CREPI), Tehran University of Medical Sciences, Tehran, Iran*

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***Correspondence**
Email:
hkeshavarz@tums.ac.ir

Abstract

Background: *Toxoplasma gondii* infection (toxoplasmosis) has the potential to cause a serious disease in immunocompromised patients and can be fatal in this population. We conducted a systematic review and meta-analysis to assess comprehensively the pooled seroprevalence of toxoplasmosis among immunocompromised patients including HIV/AIDS patients, cancer patients, and transplant recipients in Iran.

Methods: PubMed, Web of Science, Scopus, Embase, and Google Scholar databases (international) and Scientific Information Database (SID), Magiran, IranMedex, and IranDoc databases (national) were systematically searched for all reports that possibly contained data for *T. gondii* prevalence in different immunocompromised populations in Iran between 2013 and 2022.

Results: Overall, IgG seroprevalence rate of toxoplasmosis in Iranian immunocompromised patients was 45.1% (95% confidence interval (CI), 37.4–52.9). IgG seroprevalence rate of toxoplasmosis in 12 studies that included 2279 cancer patients, 19 studies that included 2565 HIV/AIDS patients and in 3 studies that included 200 transplant recipients was 43.6% (95% CI, 30.2–57.0), 45.9% (95% CI, 34.8–57.1) and 45.8% (95% CI, 32.5–59.0), respectively. Moreover, IgM seroprevalence rate in the 26 studies was 2.6% (95% CI, 1.4–3.7).

Conclusion: Our findings represent a high seroprevalence rate of *Toxoplasma* IgG among immunocompromised patients. Health improvement and education toward prevention of toxoplasmosis is of great importance for these susceptible populations.

Introduction

Toxoplasmosis, one of the most common parasitic infections worldwide, is caused by an opportunistic protozoan parasite *Toxoplasma gondii* (1). Humans acquire the infection through consumption of tissue cysts in raw or uncooked meat or via ingestion of contaminated water, food or soil with oocysts from environment or infected cats' faeces (2,3). Other routes of transmission include vertical transmission, blood transfusion and transplantation (4–6).

Although the infection with *T. gondii* in healthy individuals appears to be asymptomatic or presents as a self-limited febrile disease, it can cause a serious condition and even be life threating in immunocompromised patients including HIV positive patients, organ transplant recipients, cancer patients and any candidates of immunosuppressive therapies (7–9).

The prevalence of the infection in humans varies greatly in different parts of the world, ranging from 16-40% in United States and United Kingdom to 40-80% in Central and South Europa, tropical areas of Africa and Latin America (8, 10). In Iran, the seroprevalence rate of *T. gondii* was estimated to be 39% in general population and 50% in immunocompromised patients which is considerably significant (11,12).

Toxoplasmosis has the potential to cause a serious disease in immunocompromised patients and can be fatal in this population (13). More commonly, the infection in immunocompromised patients occurs because of reactivation of the latent infection rather than an acutely acquired one. The most common manifestation of the infection with *T. gondii* in immunocompromised patients is toxoplasmic encephalitis (TE), which causes fever, headache, ataxia, seizures and decreased level of consciousness as well as loss of memory (14,15). Transplanting an organ from a seronegative donor to a seropositive recipient can lead to reactivation of the latent infection in recipient due to immunosuppressive therapies. Moreover, transplantation of an infected organ from a seropositive donor to a seronegative recipient receiving immunosuppressive drugs can initiate the infection. The latter appears to be more dangerous and fatal (16).

Given the increase in the prevalence of immunocompromised patients, it is critical to gather information regarding the prevalence of *T. gondii* in this population in order to properly diagnose and manage the infection. Therefore, we conducted a systematic review and meta-analysis to investigate the prevalence of *T. gondii* in immunocompromised patients in Iran between 2013 and 2022.

Methods

Search strategy and selection criteria

The present study is in accordance with the preferred reporting items for systematic reviews and meta-analysis (PRISMA) statement (17). Five international databases of PubMed, Web of Science, Scopus, Embase and Google Scholar and four national databases including Scientific Information Database (SID), Magiran, IranMedex, and IranDoc, were respectively searched for English and Persian publications between January 1, 2013 and July 5, 2022, for all reports that possibly contained data for *T. gondii* prevalence in different immunocompromised populations. The databases were searched using the keywords "toxoplasmosis", "*Toxoplasma gondii*", "*T. gondii*", "cancer", "malignancies", "transplant", "HIV", "AIDS", "acquired immune deficiency syndrome", "immunocompromised", "immunodeficiency", "immune deficiency", "Iran", "Islamic Republic of Iran", and "seroprevalence" (alone or combined). Papers written in Persian

and English were included. Studies were excluded if they were reviews, repeated studies, or animal studies. All identified titles and abstracts were carefully screened by two independent experienced systematic reviewers (AT and FG) to find relevant articles. The full text of articles considered as potentially relevant based on title and abstract were independently examined by the same two reviewers. Any disagreements with the selected studies were resolved by discussion and involvement of another two authors (RA and KS).

Data extraction and quality assessment

The information that was extracted from the relevant articles included year of publication, province, region, patient group, design of the study, sample size, seroprevalence of IgG and IgM positive cases (Table 1, 2). Two reviewers (FG and AT) independently extracted the data and reached a consensus after discussing controversial literatures. The quality of the included publications was assessed based on the criteria (18, 19). These criteria were created based on the Grading of Recommendations Assessment, Development and Evaluation method (20), and including the diagnostic approach of *T. gondii* infection and matching of case and control subjects. Quality assessment of the included studies was carried out using the Joanna Briggs Institute (JBI) critical appraisal instrument for studies reporting prevalence data (21).

Statistical analysis

Preliminary analyses including summations, subtractions, divisions, multiplications and estimation of percentages were conducted using Microsoft Excel. Statistical and meta-analyses were carried out using STATA statistical software v.14 (Stata Corp, College Station, TX, USA). Overall pooled prevalence of *T. gondii* infection in immunocompromised patients (95% confidence interval, CI) was calculated, using random-effects model, and presented as a forest plot (22). Statistical heterogeneity of results was appraised using a x^2 -based Q-test and I^2 statistic. I^2 values of 0, 25, 50, and 75% were considered as 'no', 'low', 'moderate', and 'high' heterogeneities respectively (23). The fixed effects model was used when literature heterogeneity not existed; otherwise, the random-effects model was employed.

Publication bias, sensitivity and meta-regression analyses

Publication bias was assessed using Egger's regression asymmetry test and visual inspection of the funnel plot (24). A sensitivity analysis was carried out using random-effect model through systematic omitting of a single study to evaluate robustness of the pooled prevalence estimate (25).

Results

Literature Search

As shown in Fig. 1, the literature search yielded 1926 relevant studies, which included 1499 duplicates. After a careful examination of each article's title and abstract, 34 studies were found eligible for the final analysis (Fig. 1).

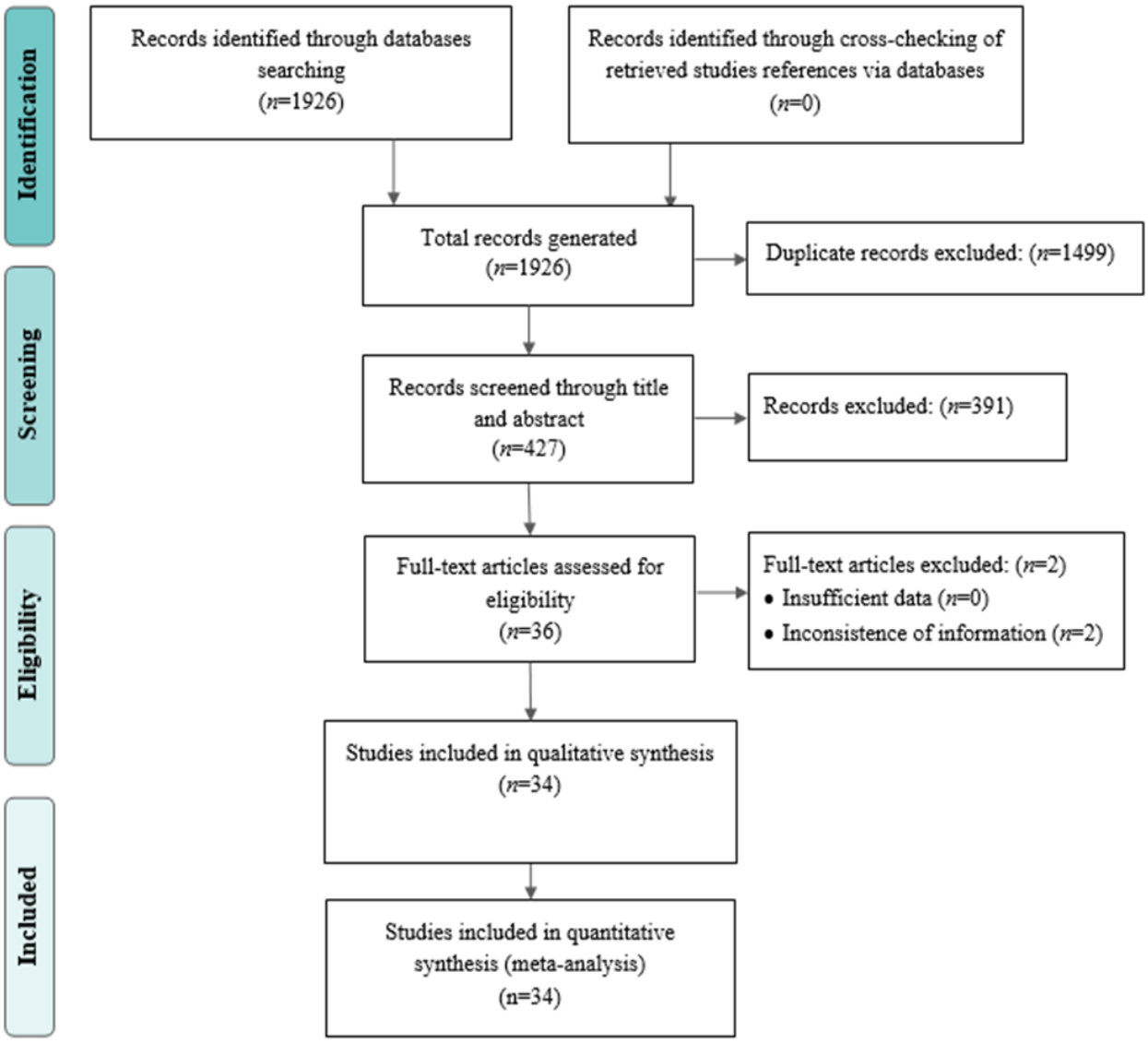

Fig. 1. Flow diagram describing the study design process

Characteristics of the eligible studies

Table 1 presents the characteristics of the 34 eligible studies meta-analyzed. In brief, 19 publications described *T. gondii* infection in HIV/AIDS patients, 12 articles investigated *T. gondii* infection in cancer/malignancy patients, whereas 3 studies reported *T. gondii* infection in transplant recipients. The identified studies were conducted in Iran. In terms of epidemiological design, 26 of the included publications were cross-sectional studies, 6 were case-control studies, 1 comparative and 1 retrospective study (Table 1). Regarding the risks of bias assessments, 29 studies (85%) had low risks of bias, 3 studies (9%) included medium risks of bias, and two study (6%) included high risks of bias.

Table 1: Baseline characteristics of included studies (based on IgG assessment)

Year	Province	Patient group	Number of cases	IgG-positive cases	Seroprevalence (%)	Age range	Serological test	Design	Ref
2013	Tehran	HIV	100	65	65	>15	ELISA	Case-control	(26)
2013	Khouzestan	HIV	42	31	73.81	18-54	ELISA	Case-control	(27)
2013	Tehran	Transplant	50	27	54	Different	ELISA	Cross-sectional	(28)
2013	Khouzestan	Renal Transplant	100	34	34	16-80	ELISA	Case-control	(29)
2014	Tehran	Cancer	535	208	38.88	Children	ELISA	Comparative study	(30)
2014	Kordistan	HIV	94	18	19.15	>18	ELISA	Cross-sectional	(31)
2015	Mazandaran	Cancer	66	57	86.36	20-50	ELISA	Cross-sectional	(32)
2015	Mazandaran	HIV/AIDS	82	79	96.34	Different	ELISA	Cross-sectional	(33)
2016	Bushehr	Malignancy	86	21	24.42	Different	ELISA	Cross-sectional	(34)
2016	Qom/Isfahan	Transplant	50	26	52	Different	ELISA	Case-control	(35)
2017	Markazi	HIV/AIDS	49	10	20.41	NA	ELISA	Cross-sectional	(36)
2017	Tehran/Alborz	Leukemia	170	96	56.47	10-60	ELISA	Cross-sectional	(37)
2017	Isfahan	HIV	20	10	50	Different	ELISA	Cross-sectional	(38)
2017	Qom/Isfahan	Cancer	112	70	62.5	Different	ELISA	Cross-sectional	(38)
2017	Fars/Yazd	HIV	90	19	21.11	20-58	ELISA	Cross-sectional	(39)
2017	Khouzestan	Cancer	372	155	41.66	Children	ELISA	Cross-sectional	(40)
2018	Fars	HIV	251	39	15.54	14-83	ELISA	Cross-sectional	(41)
2018	Mazandaran	Blood cancer	101	37	36.63	<18	ELISA	Case-control	(42)
2018	Kermanshah	HIV	358	157	43.85	3-68	ELISA	Cross-sectional	(43)
2018	Fars	HIV	246	51	20.73	Different	ELISA	Retrospective study	(44)
2018	Khouzestan	AIDS	379	131	34.56	NA	ELISA	Cross-sectional	(45)
2019	Tehran	Cancer	106	44	41.51	NA	ELISA	Cross-sectional	(46)
2019	East Azerbaijan	HIV	124	47	37.90	Different	Chemiluminescence	Cross-sectional	(47)
2019	Kohgiluye & Boyer-Ahmad	Cancer	100	13	13	Different	ELISA	Cross-sectional	(48)
2019	Tehran	HIV	149	69	46.31	18-74	ELISA	Cross-sectional	(49)
2019	Yazd	HIV	84	44	52.38	Different	ELISA	Cross-sectional	(50)
2019	Alborz	HIV	102	44	43.14	20-60	ELFA	Cross-sectional	(51)
2020	Tehran	HIV/AIDS	108	95	87.96	5-60	ELISA	Cross-sectional	(52)
2020	Mazandaran	HIV	102	70	68.63	Different	ELISA	Cross-sectional	(53)
2021	Khouzestan	Cancer	127	9	7.1	Different	ELISA	Cross-sectional	(54)
2021	Sistan & Baluchestan	Malignancy	154	61	39.61	16-72	ELISA	Cross-sectional	(55)
2021	Mazandaran	Cancer	350	264	75.43	17-86	ELISA	Cross-sectional	(56)
2021	Guilan	HIV/AIDS	121	72	59.50	7-74	ELISA	Cross-sectional	(57)
2022	Kohgiluye & Boyer-Ahmad	HIV	64	11	17.19	NA	ELISA	Case-control	(58)

*NA: not available

Pooled prevalence of T. gondii infection (IgG) in immunocomprised patients

The IgG seroprevalence rates of *T. gondii* in immunocompromised patients from Iran was 45.1% (95% CI, 37.4-52.9). The Cochrane Q test was 1981.48; I^2=97.68% and P<0.0001.

The pooled seroprevalence in 12 studies that included 2279 cancer patients were 43.6% (95% CI, 30.2-57.0) (Fig. 2). In this group, the Q statistic was 683.39 (P<0.0001) with inconsistency (I^2=98.15%).

The pooled seroprevalence in 19 studies that included 2565 HIV/AIDS patients were 45.9% (95% CI, 34.8-57.1) (Fig. 3). In this group, the Q statistic was 1267.87 (P<0.0001) with inconsistency (I^2=97.89%).

The pooled seroprevalence in 3 studies that included 200 *Transplant* recipients were 45.8% (95% CI, 32.5-59.0) (Fig. 4). In this group, the Q statistic was 7.67 (P=0.022) with inconsistency (I^2=71.63%). Subgroup analysis based on geographical area is shown in Fig. 5. The highest IgG seroprevalence rates is related to

region 1 (61.2% (95% CI, 49.8-73.3)) and the lowest is related to region 2 (20.6% (95% CI, 13.5-27.8)).

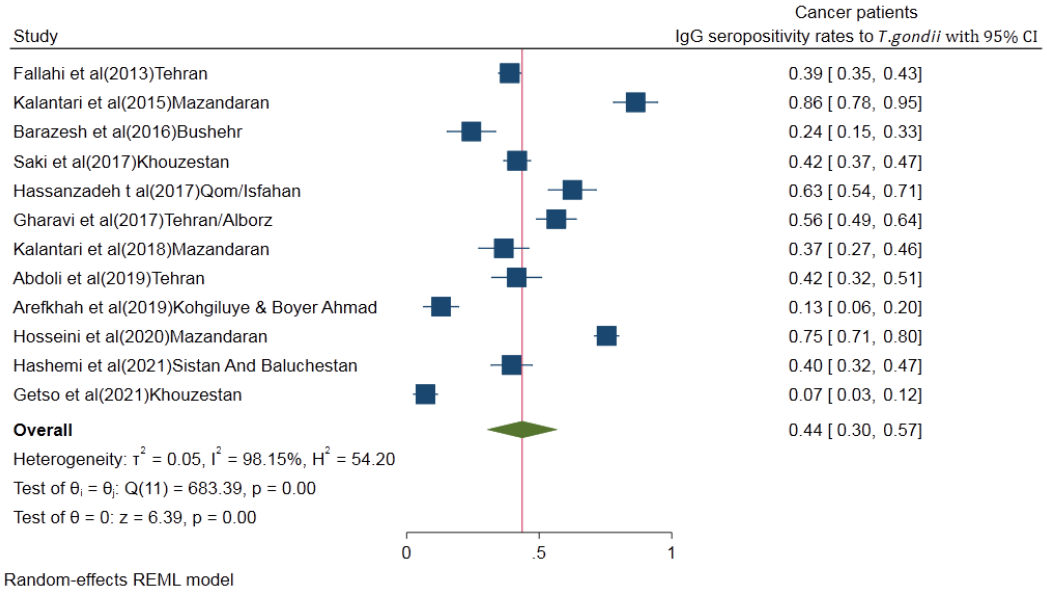

Fig. 2: Forest plot diagram of studies showing IgG seropositivity rates to *T. gondii* in cancer patients from Iran

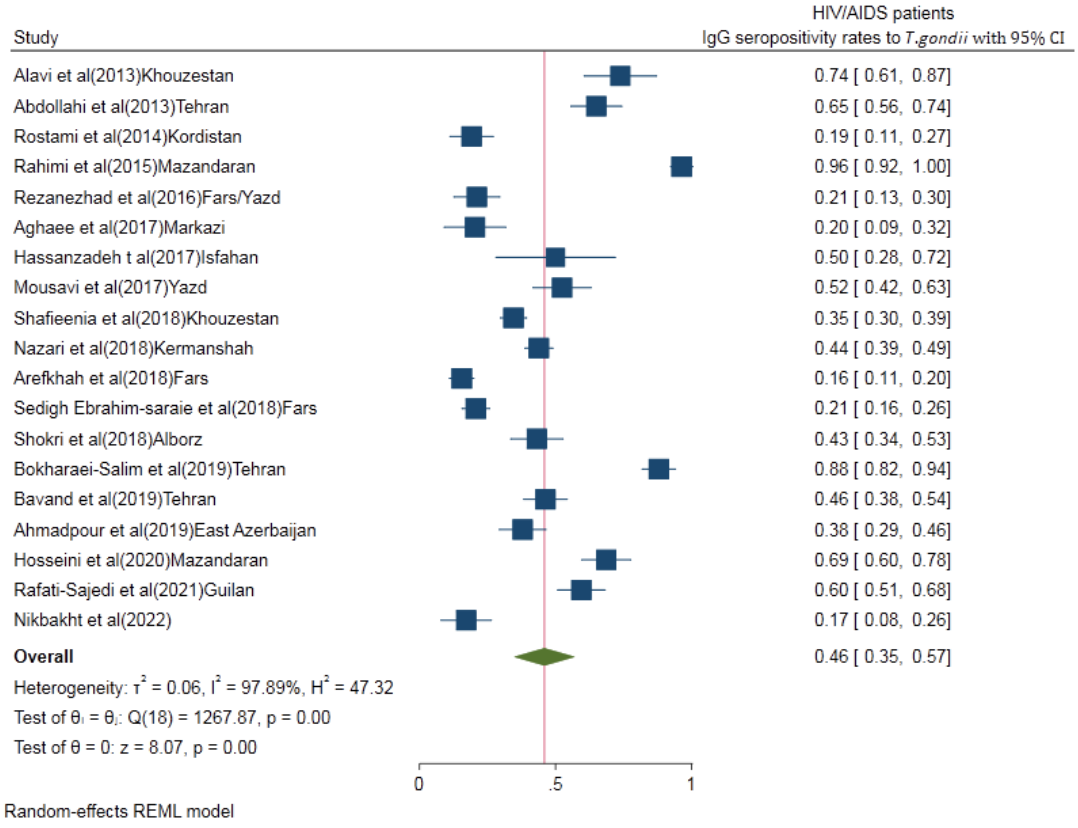

Fig. 3: Forest plot diagram of studies showing IgG seropositivity rates to *T. gondii* in HIV/AIDS patients from Iran

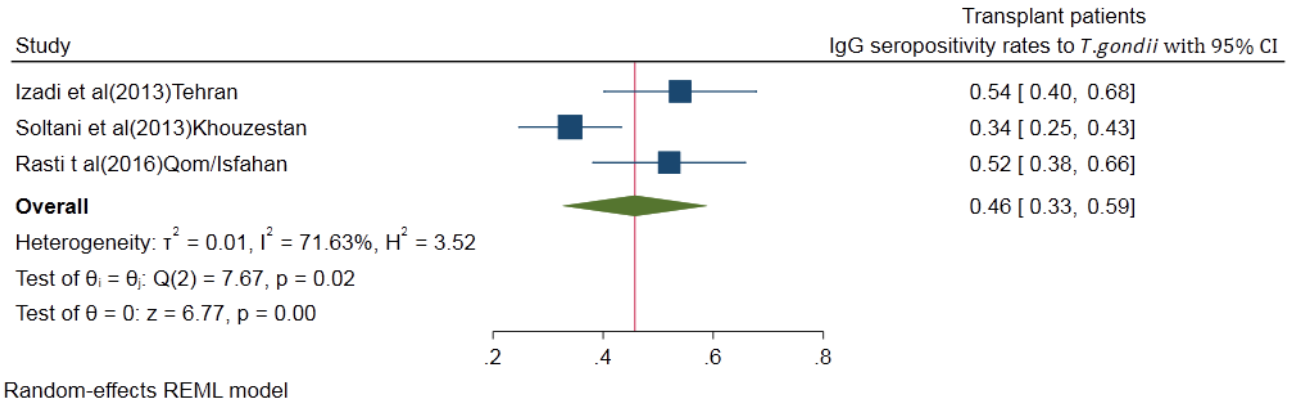

Fig. 4: Forest plot diagram of studies showing IgG seropositivity rates to *T. gondii* in transplant recipients from Iran

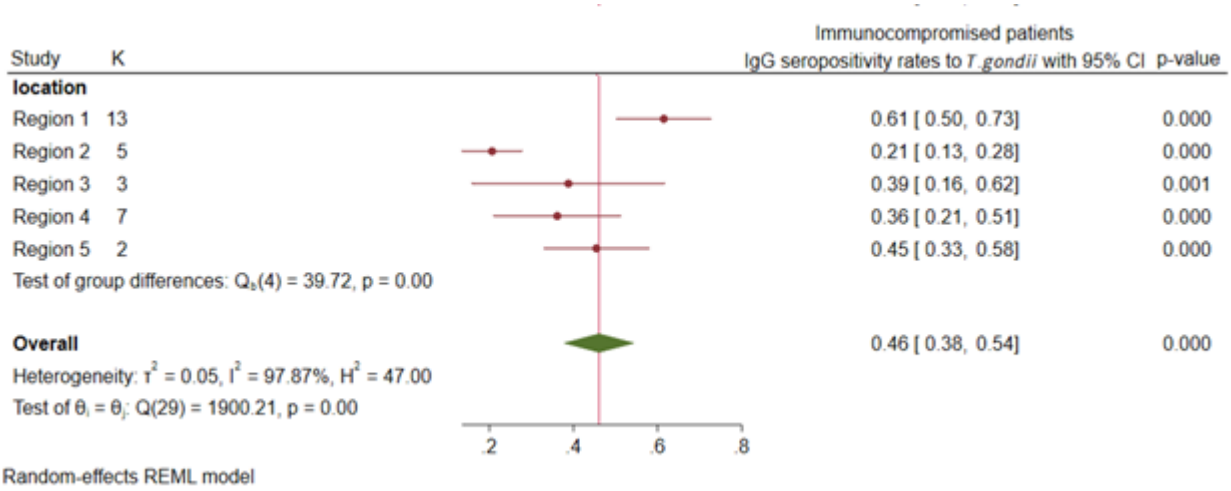

Fig. 5: Forest plot diagram of studies showing IgG seropositivity rates to *T. gondii* in immunocompromised (country divisions of provinces) patients from Iran (Region 1: Provinces of Tehran, Qazvin, Mazandaran, Semnan, Golestan, Alborz, Qom, Region 2: Provinces of Isfahan, Fars, Bushehr, Chaharmahal Bakhtiari, Hormozgan, Kohkiluyeh & Boyer-Ahmad, Region 3: Provinces of East Azerbaijan, West Azerbaijan, Ardabil, Zanjan, Guilan, Kurdistan, Region 4: Kermanshah, Ilam, Lorestan, Hamedan, Markazi, Khuzestan, Region 5: Provinces of Razavi Khorasan, South Khorasan, North Khorasan, Kerman, Yazd, Sistan & Baluchestan)

Pooled prevalence of T. gondii infection (IgM) in immunocomprised patients

Table 2 presents the characteristics of the 26 eligible studies meta-analyzed. The IgM seroprevalence rates of *T. gondii* in immunocompromised patients from Iran was 2.6% (95% CI, 1.4-3.7). The Cochrane Q test was 123.99; I^2=84.82% and *P*<0.0001.

The pooled seroprevalence in 11 studies that included 2167 cancer patients was 3.1% (95% CI, 1.0-5.1) (Fig. 6). In this group, the *Q* statistic was 60.68 (*P*<0.0001) with inconsistency (I^2=84.61%).

The pooled seroprevalence in 12 studies that included 1889 HIV/AIDS patients was 1.3% (95% CI, 0.06-2.1) (Fig. 7). In this group, the *Q* statistic was 22.13 (*P*=0.023) with inconsistency (I^2=41.85%).

The pooled seroprevalence in 3 studies that included 200 Transplant patients was 7.1%

(95% CI, 0.00-17.5) (Fig. 8). In this group, the Q statistic was 14.09 (P=0.001) with inconsistency (I^2=87.98%). Subgroup analysis based on geographical area is shown in Fig. 9. The highest IgM seroprevalence rates is related to region 4 (4.5% (95% CI, 0.2-8.8) and the lowest is related to region 5 (0.0% (95% CI, 0.0-2.0).

Publication bias

The funnel plots showed no publication bias, which was also confirmed from Egger's test which revealed that publication bias might not have a significant influence on overall prevalence estimates.

Sensitivity tests

The sensitivity tests indicated that all single-study omitted estimates lay within the 95% CI of the respective overall effect. This suggested that the pooled effect was not substantially influenced by any single study. The stability of such results validated the rationality and reliability of our analysis.

Table 2: Baseline characteristics of included studies (based on IgM assessment)

Year	*Province*	*Patient group*	*Number of cases*	*IgM-positive cases*	*Seroprevalence (%)*	*Age range*	*Serological test*	*Design*	*Ref*
2013	Tehran	Transplant	50	2	4	Different	ELISA	Cross-sectional	(28)
2013	Khouzestan	Renal Transplant	100	18	18	16-80	ELISA	Case-control	(29)
2014	Tehran	Cancer	535	51	9.53	Children	ELISA	Comparative study	(30)
2015	Mazandaran	Cancer	66	5	7.57	20-50	ELISA	Cross-sectional	(32)
2015	Mazandaran	HIV/AIDS	82	0	0	Different	ELISA	Cross-sectional	(33)
2016	Bushehr	Malignancy	86	0	0	Different	ELISA	Cross-sectional	(34)
2016	Qom/Isfahan	Transplant	50	0	0	Different	ELISA	Case-control	(35)
2017	Markazi	HIV/AIDS	49	1	2.04	NA	ELISA	Cross-sectional	(36)
2017	Tehran/Alborz	Leukemia	170	10	5.88	10-60	ELISA	Cross-sectional	(37)
2017	Khouzestan	Cancer	372	24	6.45	Children	ELISA	Cross-sectional	(40)
2018	Fars	HIV	251	3	1.19	14-83	ELISA	Cross-sectional	(41)
2018	Mazandaran	Blood cancer	101	0	0	<18	ELISA	Case-control	(42)
2018	Kermanshah	HIV	358	10	2.79	3-68	ELISA	Cross-sectional	(43)
2018	Khouzestan	AIDS	379	11	2.9	NA	ELISA	Cross-sectional	(45)
2019	Tehran	Cancer	106	0	0	NA	ELISA	Cross-sectional	(46)
2019	East Azerbaijan	HIV	124	2	1.61	Different	Chemiluminescence	Cross-sectional	(47)
2019	Kohgiluye & Boyer-Ahmad	Cancer	100	2	2	Different	ELISA	Cross-sectional	(48)
2019	Tehran	HIV	149	4	2.68	18-74	ELISA	Cross-sectional	(49)
2019	Alborz	HIV	102	0	0	20-60	ELFA	Cross-sectional	(51)
2020	Tehran	HIV/AIDS	108	1	0.92	5-60	ELISA	Cross-sectional	(52)
2020	Mazandaran	HIV	102	0	0	Different	ELISA	Cross-sectional	(53)
2021	Khouzestan	Cancer	127	2	1.57	Different	ELISA	Cross-sectional	(54)
2021	Sistan & Baluchestan	Malignancy	154	0	0	16-72	ELISA	Cross-sectional	(55)
2021	Mazandaran	Cancer	350	9	2.57	17-86	ELISA	Cross-sectional	(56)
2021	Guilan	HIV/AIDS	121	6	4.96	7-74	ELISA	Cross-sectional	(57)
2022	Kohgiluye & Boyer-Ahmad	HIV	64	5	7.81	NA	ELISA	Case-control	(58)

*NA: not available

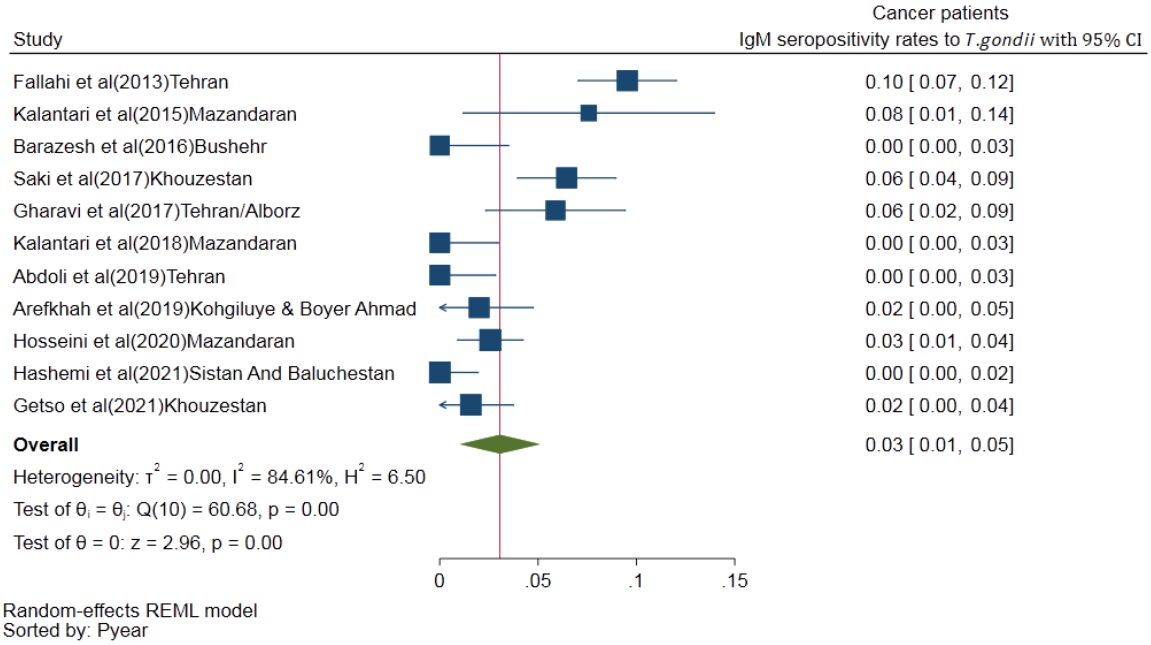

Fig. 6: Forest plot diagram of studies showing IgM seropositivity rates to *T. gondii* in cancer patients from Iran

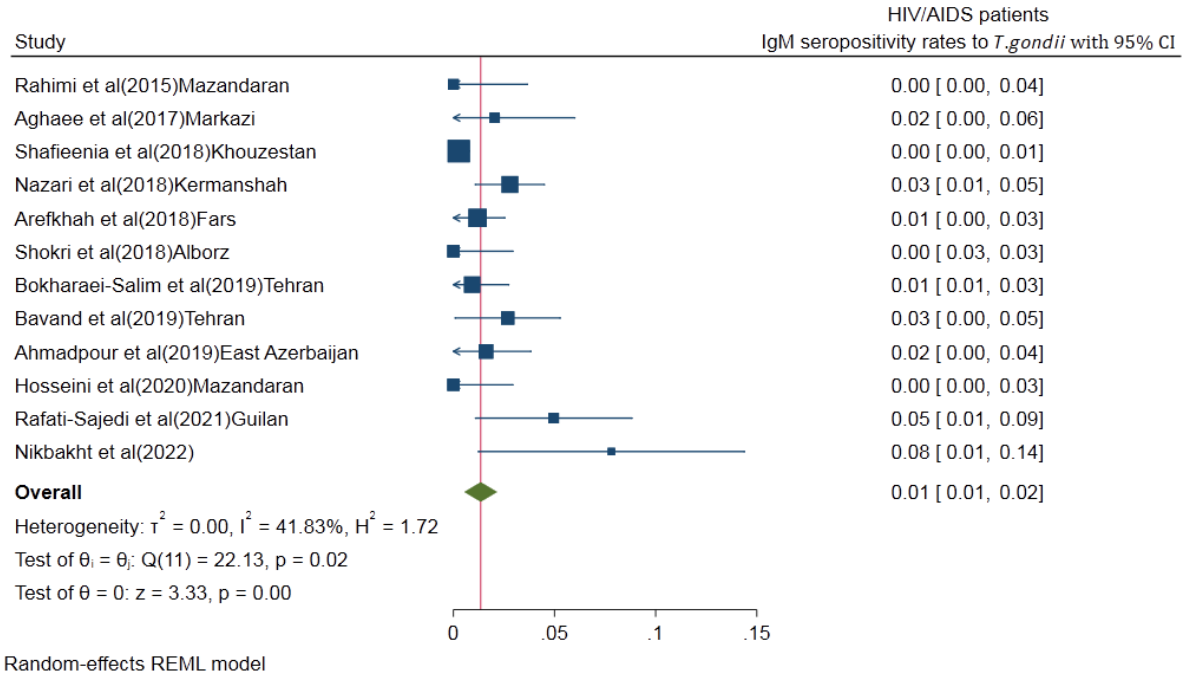

Fig. 7: Forest plot diagram of studies showing IgM seropositivity rates to *T. gondii* in HIV/AIDS patients from Iran

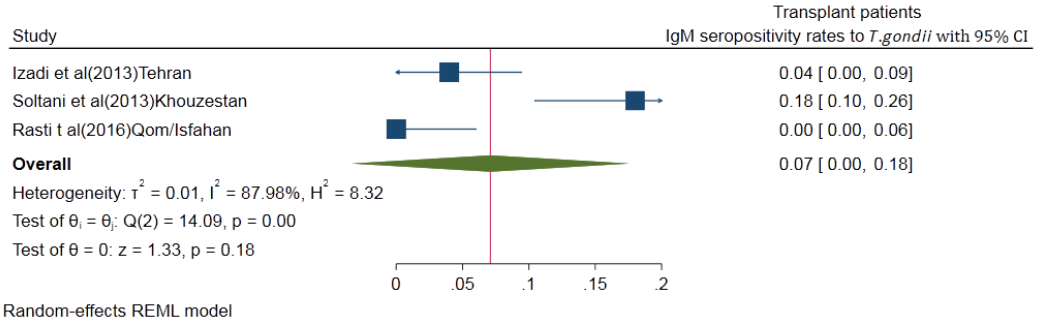

Fig. 8: Forest plot diagram of studies showing IgM seropositivity rates to *T. gondii* in transplant recipients from Iran

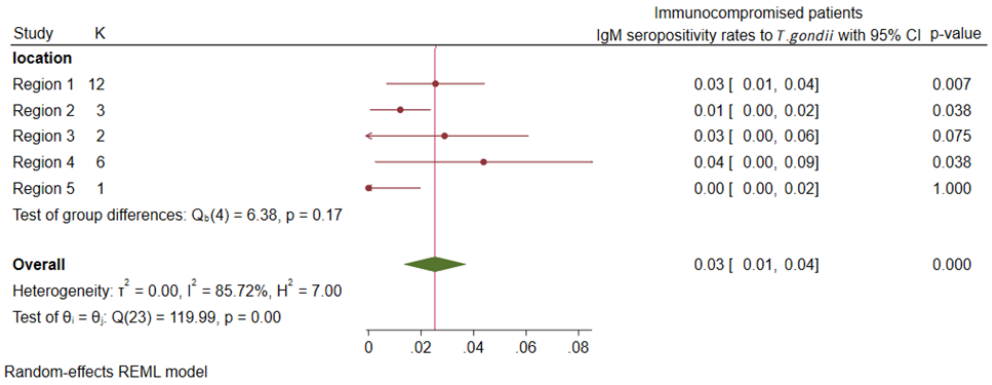

Fig. 9: Forest plot diagram of studies showing IgM seropositivity rates to *T. gondii* in immunocompromised (country divisions of provinces) patients from Iran (Region 1: Provinces of Tehran, Qazvin, Mazandaran, Semnan, Golestan, Alborz, Qom, Region 2: Provinces of Isfahan, Fars, Bushehr, Chaharmahal Bakhtiari, Hormozgan, Kohkiluyeh & Boyer-Ahmad, Region 3: Provinces of East Azerbaijan, West Azerbaijan, Ardabil, Zanjan, Guilan, Kurdistan, Region 4: Kermanshah, Ilam, Lorestan, Hamedan, Markazi, Khuzestan, Region 5: Provinces of Razavi Khorasan, South Khorasan, North Khorasan, Kerman, Yazd, Sistan & Baluchestan)

Discussion

Considering the importance of toxoplasmosis in immunocompromised population, the present systematic review and meta-analysis was carried out. The overall seroprevalence of toxoplasmosis among Iranian immunocompromised patients from 2013 to 2022 was investigated, which demonstrated a noticeable seroprevalence of 45.1%. The prevalence is comparable with the similar previous meta-analysis in Iran among the same population from 1997 to 2013 (50.01%) (59). Given the global prevalence of *T. gondii* in immunocompromised individuals (35.9%) (60), new measurements are essential for better management of the disease in our country.

Our meta-analysis of 2565 HIV/AIDS patients in Iran showed that less than half (45.9%) of them were estimated to be seropositive for *T. gondii*, as the previous meta-analysis of published studies from 1997 to 2013 in Iran had reported a similar prevalence (50.05%), as well (59). However, considering global and regional studies, HIV/AIDS patients in North Africa and the Middle East have the highest seroprevalence (60.7%) among all other regions (61), with a pooled worldwide seroprevalence of 35.8 to 42.1% (60, 61). The lowest global seroprevalence of HIV positive individual co-infected with *T. gondii* was found in Asia and the Pacific (25.1%) (61). Included studies of the present review from north of Iran, for example Ma-

zandaran and Tehran provinces, have reported co-infection of *T. gondii* and HIV as high as 96.3 and 88% (33, 52), while in the central and south Iran, 20.7 and 15.5% co-infection, were reported respectively (41, 44). Similarly, in previous studies in Iran, the highest prevalence of HIV and *T. gondii* co-infection was in Mazandaran (77.4%) and Tehran (65%) provinces and lowest prevalence (18.2%) was in Fars provinces (26,62,63). These studies support the fact that the seroprevalence of antibodies to *T. gondii* among patients with HIV/AIDS follows the regional patterns of seropositivity in the general population. Moreover, most of HIV/AIDS patients have been infected previously in sometime, probably before they become immunocompromised (7). This was depicted by our meta-analysis of 1889 HIV/AIDS patients tested for IgM anti-*Toxoplasma* antibody, a marker of acute infection. We showed that the majority of HIV/AIDS patients have been infected previously, while only a very small percentage of them (1.3%) were infected recently. Comparing to cancer patients and organ transplant recipients, HIV positive individual had the lowest positive IgM seroprevalence in our study.

Serological evidence of *T. gondii* infection among patients with all types of cancers is 26 to 30.8% worldwide (61, 64). However, our results of meta-analysis in Iran indicated that 43.6% of patients with cancer are seropositive for *Toxoplasma*, which is the lowest seroprevalence among the studied immunocompromised populations of the present study. Two previous meta-analysis in Iran reported 45% and 51% seroprevalence in these patients (59, 64). A number of studies have stated that patients with different cancers from similar geographic areas had significantly different seropositivity rates for toxoplasmosis. For instance, in a 2019 worldwide meta-analysis, positive serology for toxoplasmosis was as high as 81% in breast cancer patients, as compared to those with liver cancer (24.1%) (60). Similarly, in North Iran (Mazandaran), 88.24% of the patients with leukemia were seropositive for *T. gondii*, while patients with colon cancer showed 67.6% seropositivity (56). Therefore, it could be hypothesized that apart from regional and geographic patterns, the seroprevalence of *Toxoplasma* among cancerous patients may be affected by the patient's immune system state, which is in turn determined by the type of cancer, its clinical stage and treatment regimens. By taking immune system-related factors as well as lifestyle and environmental risk factors into account, future studies may be able to estimate a more accurate seroprevalence and uncover possible risk factors in these patients. Interestingly, the prevalence of recently infected cancerous patients with *Toxoplasma*, which was assessed by the presence of IgM antibody, was higher than that of HIV/AIDS patients (3.1% vs. 1.3%). However, determining risk factors of this higher prevalence of acute infection among patients with cancer is difficult. Analysis of geographic distribution of IgM seroprevalence as well as age, sex, immune system state, dietary and environmental risk factors between HIV/AIDS and cancerous patients may be helpful, although the majority of the studies lack enough data regarding most of these variables.

Another group of immunocompromised patients is recipients of Hematopoietic stem cell transplant (HSCT) or solid organ transplant (SOT). Both of these scenarios place the patient at a great risk of toxoplasmosis, whether through reactivation of encysted parasites in a seropositive recipient after immunosuppression or graft transmission from a seropositive donor (65, 66). The global seroprevalence of toxoplasmosis in transplant patients is 42.1% (60). This prevalence was estimated to be 55.1% in Iran, by a meta-analysis of 702 patients from 1997 to 2013 (59). Our results from 2013 to 2022 showed 45.8% seropositivity for toxoplasmosis in Iranian transplant patients. Considering the infection source, HSCT recipients more commonly develop

toxoplasmosis by reactivation of latent infection in their course of immunosuppression, while transmission through contaminated transplanted organ is primarily encountered in cases of SOT (65, 66).

By subgroup analysis of geographic areas, we demonstrated a widely regional variation in *Toxoplasma* seroprevalence. Due to better survival of the *T. gondii* oocytes in areas with lower altitudes, hot and humid climates (4), the highest IgG seroprevalence (61.2%) of the infection in immunocompromised population was seen in the North provinces (region 1) and the lowest one (20.6%) was observed in Central and South-Western provinces of Iran (region 2). Regarding the IgM seroprevalence, Western and Northeastern areas of Iran (region 4) have shown the highest seroprevalence. Since these prevalence rates reflect the general population seropositivity, the importance of environmental health promotion and educational measurements, especially in high prevalence areas, is highlighted.

This climate-dependent distribution of the infection, may at least in part be responsible for Iran's higher seroprevalence for *T. gondii* (45.1%) in immunocompromised patients, compared to its worldwide seroprevalence (35.9%) (60). Aside from climate factors, another element, which possibly affected this geographical distribution and high prevalence of *T. gondii* in our country, is agriculture and animal husbandry (67). However regarding to this matter limited data are available and more investigations are required.

This meta-analysis has a number of limitations that could possibly affect the results of study. First, most of the identified studies lack important data regarding risk factors of toxoplasmosis. As an example, although demographic data such as age, sex, rural or urban residency and dietary and environmental risk factors have a dramatic effect on probability of getting infection, these factors were not investigated in the included studies. Thus, subgroup analysis based on these demographic data, except for geographic area, was not performed. Secondly, apart from the type of the cancer, its pathological grade and clinical stage, chemotherapy regimens and even radiotherapy may alter patient's level of immunosuppression and hence affect greatly on the potential of the latent infection reactivation. Immunosuppressive drugs prescribed for transplant patients are also a relevant risk factor, which were missed in the identified studies. Finally, the gold standard in the diagnosis of toxoplasmosis is tissue biopsy and detection of the parasite under the microscope (68). However, the serological methods were the only tests to identify *Toxoplasma* infection in all of the included studies. Since antibody production in immunocompromised patients may be impaired (13), use of serological tests without clinical correlation and pathological studies, may underestimate the actual prevalence of toxoplasmosis in immunocompromised patients. Future studies should consider clinical and para-clinical parameters, as well as serological investigations.

Conclusion

The high seroprevalence of toxoplasmosis among immunocompromised patients necessitates routine and appropriate serological and clinical assessment, with provision of proper prophylaxis and treatments. Acute infection is relatively uncommon among immunocompromised patients and the geographic distribution of toxoplasmosis seroprevalence in these patients matches that of the general population. Thus, health improvement and education toward prevention of toxoplasmosis is of great importance.

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Conflicts of interest

Non-declared

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