Review Article

Seroprevalence of toxoplasma gondii infection: An umbrella review of updated systematic reviews and meta-analyses

Vahid Rahmanian[1], Karamatollah Rahmanian[1], Abdolreza Sotoodeh Jahromi[1], Saied Bokaie[2]

[1]Zoonoses Research Center, Jahrom University of Medical Sciences, Jahrom, [2]Epidemiology and Zoonosis Division, Department of Food Hygiene, Faculty of Veterinary Medicine, University of Tehran, Tehran, Iran

Abstract

Objectives: Toxoplasmosis is one of the neglected parasitic disease in humans and animals that produced via toxoplasma gondii. This study we implemented an umbrella review of all existing systematic reviews, meta-analyzing studies to apprise, and summarize seroprevalence of human toxoplasmosis in worldwide. **Methods:** The search was carried out in databases including: Pub Med, Google Scholar, Science Direct, Scopus, Web of Science, Cochrane, and global health from their start dates until December 2018 in Persian and English language. A total of 21 systematics review and meta-analysis met the inclusion criteria of umbrella review. The Q test and the I^2 statistic were used to evaluate heterogeneities. Quality assessment were performed and made use of the AMSTAR tool. **Results:** The estimated pooled seroprevalence of T. gondii infection in blood donors, Immunocompromised patients, childbearing age women, general population, newborns and children, pregnant women and overall was 33% (95% CI, 29.0–38.0%), 42.0% (95 CI, 34.0–49.0%), 32.0% (CI, 26.0–38.0%), 42.0% (CI, 38.0–45.0%), 4.0% (CI, 2.0–5.0%), 40.0% (CI,37.0–44.0%), and 36% (CI, 24.0–48.0%), respectively. **Conclusion:** The results of our umbrella review show a higher seroprevalence of T. gondii infection in immunocompromised patients, general population, pregnant women, blood donors, childbearing age women, and newborn groups, respectively. Routine serologic screening test and health education by primary care physicians for Toxoplasmosis is recommended to be conducted in high-risk groups in the endemic region.

Keywords: Meta-analysis, prevalence, review, toxoplasma gondii, toxoplasmosis

Introduction

Toxoplasmosis is one of the neglected parasitic disease in humans and animals that produced via Toxoplasma *gondii*.[1-3]

Address for correspondence: Dr. Saied Bokaie, Epidemiology and Zoonosis Division, Department of Food Hygiene, Faculty of Veterinary Medicine, University of Tehran, Tehran, Iran.
E-mail: sbokaie@ut.ac.ir

Received: 02-05-2020 **Revised:** 11-06-2020
Accepted: 03-07-2020 **Published:** 25-08-2020

Access this article online

Quick Response Code:

Website: www.jfmpc.com

DOI: 10.4103/jfmpc.jfmpc_753_20

Felids are the definitive hosts and repel oocysts in their feces. The oocyst load in areas where cats selectively excrete feces is high.[4,5]

Seroprevalence of *T. gondii* fluctuates from 30% to 60%, as at least one third of the world's population is infected, which predominantly happens in districts with poor sanitation.[6]

Human are dead-end host for T. *gondii* with up to 80% given chronic asymptomatic disease.[7,8] Women during pregnancy and immunocompromised persons (cancer, Rheumatoid arthritis,

How to cite this article: Rahmanian V, Rahmanian K, Jahromi AS, Bokaie S. Seroprevalence of toxoplasma gondii infection: An umbrella review of updated systematic reviews and meta-analyses. J Family Med Prim Care 2020;9:3848-55.

transplant, and HIV/AIDS infected) include the high risk groups for T. *gondii*.[9-12]

There have been research about association of T. *gondii* with mental disorders for example epilepsy,[13,14] bipolar disorder, and schizophrenia.[15,16]

Because of the toxoplasma propensity to the brain and eye, poor prognoses, and sequels for example glaucoma, chorioretinitis, retinal detachment, brain abscess, and encephalitis can happen during severe or recurrent infection.[17,18]

Prevention of T.*gondi* infection via screening is compulsory in some countries and is suggested in some others such as the United States and Canada.[19,20]

The seroprevalence of toxoplasmosis in human is diverse in different district relevant on variables such as sex, age, immunity status, food behaviors, culture, keeping the cat at home, geographic area, the percentage, and humidity.[19,21]

In recent years, several systematic review and meta-analysis studies have been published exploring the seroprevalence of T. *gondii* in different country and various groups such as: blood donors, immunocompromised patients, psychosis patients, pregnant women, girls, newborn, and general population and their results indicate different findings.

Therefore, in this study, we implemented an umbrella review of all existing systematic reviews, meta-analyzing studies to apprise and summarize seroprevalence of human toxoplasmosis worldwide. We thus hope to provide both primary care physicians and policy makers with strong data in an easy-to-access and inclusive format to inform guidelines for control and prevention practice.

Methods

Study design

Umbrella reviews (also known as overview of reviews)[22] are a newly developed technique to précis, and analyze systematic reviews. Umbrella review is based on a planned and designed complete search, parallel to traditional systematic reviews, but it searches systematic reviews instead of observational or clinical research (e.g., Cross-Sectional or Clinical Trials).[23]

Now, no generally used guidelines exist to do this type of review. Nevertheless, we followed the references of the PRISMA statement for search approach scheme and made use of the Assessing the Methodological Quality of Systematic Reviews (AMSTAR) tool for quality assessment.[24]

Search strategy

The search was carried out in databases including: Pub Med, Google Scholar, Science Direct, Scopus, Web of Science, Cochrane, and global health from their start dates until December 2018 in Persian and English language. Duplicates and animal-based studies were excluded. All systematic review and meta-analysis studies in human toxoplasmosis were concerned. We included systematic reviews and meta-analyses of observational studies that gave a seroprevalence of Toxoplasmosis. The process is shown in Figure 1.

This umbrella review was accomplished using medical subject heading (MeSH) terms and combination of numerous keywords including: "Toxoplasma", "Toxoplasma gondii", "Toxoplasmosis," "Prevalence," "Seroprevalence," "Epidemiology," individually in combination with "meta-analysis," "systematic review."

Quality assessment

Rahmanian(V) and Bokaie(S) evaluated quality for totally included papers separately using the AMSTAR checklist.[24] A third author removed disagreement. The assessment base on the AMSTAR tool was done as follow: if the answer is "Yes", a grade was stated, if "No" or "Can't answer" were signed no grade was stated. When "Not applicable" was signed, no grade was stated but the item was removed from the feasible maximum score.

"If the ultimate score was 80-100% quality was marked as 3 (high quality or very low risk of bias), 65-80% as 2 (acceptable quality or low risk of bias), 50-65% as 1 (low quality or high risk of bias), and ≤50% as 0 (unacceptable quality or very high risk of bias)."[22]

Data collection

Based on the mentioned strategy, the search was performed in

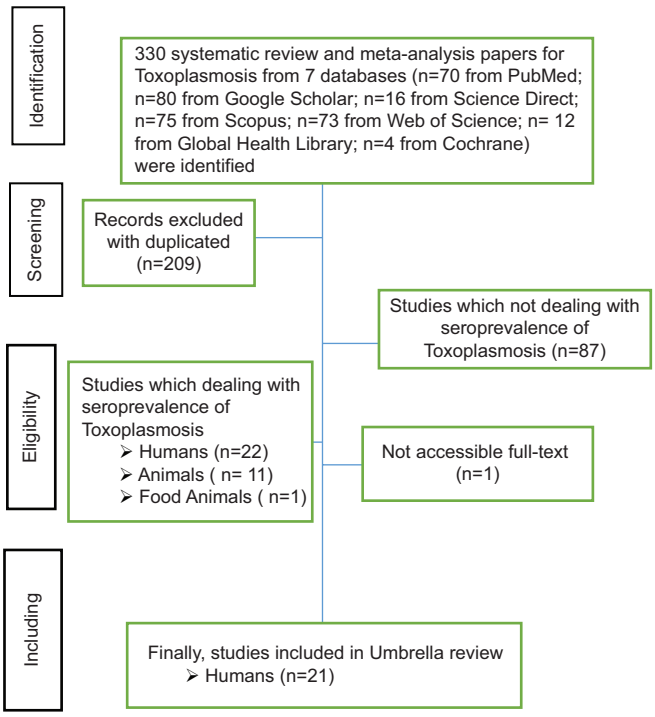

Figure 1: Flowchart showing the selection of studies analyzed in Umbrella review

six databases. Subsequently, the collected systematics review and meta-analysis were carefully evaluated for epidemiological parameters; finally, 21 reviews had study inclusion criteria, including the accessibility of full text, the study of human toxoplasmosis seroprevalence. Exclusion criteria were data inconsistencies, the use of inappropriate statistical methods, low-quality based on the AMSTAR tool and toxoplasmosis in non-human cases. The data extracted from the review were the name of the author, date of study, demographic information such as types of study groups as well as the geographical area of the study, the number of subjects examined, the seropositive number, and the seroprevalence and the laboratory method used to study [Table 1].

Statistical analyses

Point estimates and their 95% confidence intervals of seroprevalence of all included studies were calculated. The seroprevalence (P) and standard error (Se) of each study estimated with respect of binomial distribution and studies combined according to sample size and variance. Forest plot was employed to visualize the heterogeneity

Table 1 Baseline features of included studies in umbrella review of seroprevalence of Toxoplasma gondii and Quality assessment using the AMSTAR checklist

Study/ authors	Place of study	study group	Number of studies included in the meta-analysis	Population	%Seroprevalence, (95% CI)		% seroprevalence (95% CI)	Quality score	References
					IgG	IgM			
Mansouri *et al.* 2017	Iran	Blood donor	10	4538	31.84 (20.61-43.08)	2.74 (0.55-4.92)	34.4 (24.9-43.9)	3	[25]
Foroutan-Rad *et al.* 2016	worldwide	Blood donor	43	20964	NA	1.8 (1.1-2.4)	33 (28-39)	3	[26]
Jiang *et al.* 2015	china	Population with Cancer	19	4493	NA	NA	20.59 (20.11-21.06)	3	[11]
Borna *et al.* 2013	Iran	childbearing age women	22	13480	34.5 (28.5-40.5)	NA	39.9 (26.1-53.7)	3	[27]
Gebremedhin and Tadesse. 2015	Etiopia	general population	19	5718	74.73 (61.85-84.36)	NA	NA	3	[28]
Daryani *et al.* 2014	Iran	general population	35	52294	NA	NA	39.3 33-45.7	2	[29]
Mizani *et al.* 2017	Iran	childbearing age women	38	17512	31 21-41	5 3.00-6.00	33 23-43	3	[30]
Wang *et al.* 2017	worldwide	HIV-infected	74	25989	NA	NA	35.8 (30.8-40.7)	3	[31]
Foroutan *et al.* 2018	Iran	hemodialysis patients	10	1048	58 (46-70)	2 (0-6)	NA	3	[32]
Ahmadpour *et al.* 2014	Iran	immunocompromised patients	22	2805	NA	NA	50.01 (43.85-56.17)	1	[33]
Wang *et al.* 2017	worldwide	Immunocompromised patients	72	17780	NA	NA	35.9 (31-40.8)	3	[34]
Foroutan *et al.* 2017	Iran	general population	117	105139	NA	NA	43 (38-47)	3	[35]
Ramirez *et al.* 2012	Mexico	general population	132	70123	NA	NA	19.27 (18.97-19.56)	2	[36]
Ramirez *et al.* 2012	Mexico	Newborns and Children	10	5728	NA	NA	3.63 (2.29-4.935)	2	[37]
Deng *et al.* 2017	China	pregnant women	72	NA	4.37 (2.22-8.1)	NA	NA	2	[38]
Malary *et al.* 2018	Iran	pregnant women	43	22644	39.2 (33.3-45.1)	3.1-4.9	41.3 (35.8-46.8)	3	[39]
Wang *et al.* 2018	China	Blood donor	40	49784	6.26 (4.62-8.13)	NA	NA	3	[40]
Foroutan-Rad *et al.* 2016	Iran	pregnant women	50	20221	38 (34-42)	4 (3-5)	41 (36-45)	3	[41]
Hosseininejad *et al.* 2018	worldwide	rheumatoid arthritis patients	9	4168	NA	NA	46 (37-56)	3	[9]
Azadi *et al.* 2015	Iran	pregnant women	28	12818	NA	NA	34.2 (23-45.3)	1	[42]
Alzaheb. 2018	Saudi Arabia	women of reproductive age	20	13597	NA	NA	27.8 (20.6-36.3)	2	[43]

among studies. The heterogeneity was expected in advance, and statistical methods, I^2 and Q test (with significance of $P < 0.05$) were used to quantify the variations. All systematic review and meta- analyses included this umbrella review were used a random effects model, and thus a random effects model was employed. Proportions of individual studies and overall seroprevalence were presented by forest plots. Statistical analyses were implemented using Stata, version 12.0 (Stata Corp, College Station, TX, USA). Furthermore, the Arc GIS 10.3 software was applied to map the distribution of *T.gondi* infection.

Results

In total, 330 systematics review and meta-analysis were obtained by searching the databases referred to in the period from their start dates until December 2018; after reviewing the inclusion criteria and their study, 21 systematics review and meta-analysis met the inclusion criteria of umbrella review. All 21 studies included in the umbrella review evaluated the seroprevalence of *T.gondi* infection in blood donors, immunocompromised patients, pregnant women, childbearing age women, newborns, and children and general population. A total of 470,843 people were evaluated in 885 primary study in 21 systematics review and meta-analysis met the inclusion criteria of this Umbrella review [Table 1].

Pooled seroprevalence estimates of (IgM + IgG) *T. gondii* Infection by study groups

The estimated pooled seroprevalence of T. *gondii* infection in immunocompromised patients and general population were highest 42% and newborns and children were lowest 4%, respectively [Table 2]. There was high degree of heterogeneity in estimating the seroprevalence of studies in meta-analysis, in which the heterogeneity was $I^2 = 83.4\%$ (Q test: $P < 0.001$) in Immunocompromised patient groups and $I^2 = 98.8\%$ (Q test: $P < 0.001$) in overall, but there was no heterogeneity in estimated pooled seroprevalence in blood donor, childbearing age women, general population, newborn, and pregnant women groups ($P > 0.05$) [Figure 2].

Pooled seroprevalence estimates of IgG antibodies by study groups

The estimated pooled seroprevalence of IgG in immunocompromised patient was highest %48 and blood donors

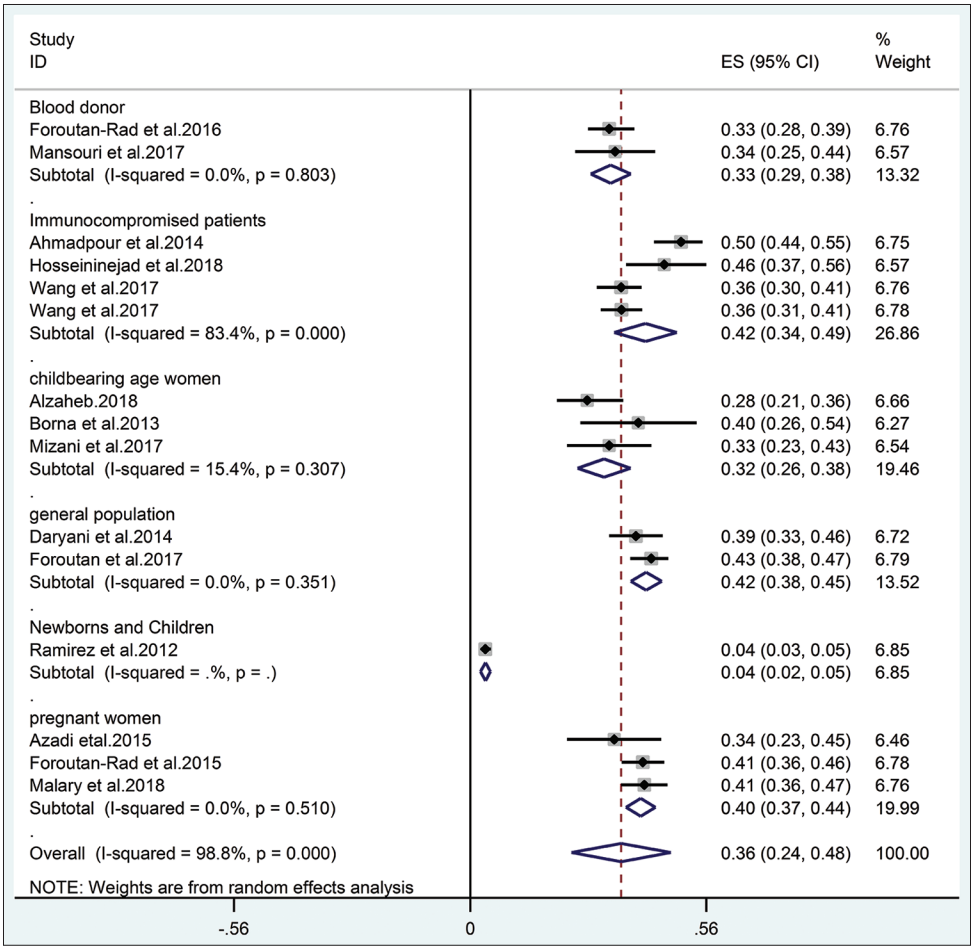

Figure 2: Forest plot diagram of Systematic Reviews and Meta‐Analyses studies showing seroprevalence (IgM + IgG) of human toxoplasmosis by group population Three meta-analyses reported the seroprevalence of T. gondi infection worldwide and not shown in the map

was lowest 18%, respectively [Table 2]. There was high degree of heterogeneity in estimating the seroprevalence of studies in meta-analysis, in which the heterogeneity was $I^2 = 94.90\%$ (Q test: $P < 0.001$) in blood donors' groups, $I^2 = 86.4\%$ (Q test: $P = 0.007$) in Immunocompromised patients, $I^2 = 98.90\%$ (Q test: $P < 0.001$) in pregnant women and $I^2 = 98.6\%$ (Q test: $P < 0.001$) in overall, but there was no heterogeneity in estimated pooled seroprevalence in childbearing age women ($P > 0.05$).

Pooled seroprevalence estimates of IgM antibodies by study groups

The estimated pooled seroprevalence of IgM in pregnant women was highest 4% and blood donors and immunocompromised patients were lowest 2%, respectively [Table 2].

Table 2: Pooled seroprevalence estimates of T. gondii Infection by study groups

study groups	seroprevalence of T. gondii with positive antibody (%)		
	IgG	IgM	IgM +IgG
blood donors	18 (8 -43)	2 (1-2)	33 (29-38)
Immunocompromised patients	48 (31-66)	2 (1-5)	42 (34-49)
childbearing age women	34 (28 -39)	5 (4-6)	32 (26-38)
general population	-	-	42 (38-45)
newborns and children	-	-	4 (2-5)
pregnant women	29 (10-48)	4(3-5)	40 (37-44)
overall	35 (24-47)	4 (3-5)	36 (24-48)

There was no heterogeneity in estimated pooled seroprevalence in blood donor and pregnant women groups ($P > 0.05$), but the heterogeneity was $I^2 = 85.9\%$ (Q test: $P < 0.001$) in overall.

In addition, a schematic image of the T *gondii* distribution has been made based on studies conducted over the past years among different geographical locations are shown in Figure 3.

Discussion

We have presented an overview of seroprevalence from 21 meta-analyses based on over 470,843 individuals. To our knowledge, this is the first quantitative umbrella review of updated systematic reviews and meta-analyses of the field.

T. *gondii* infection has been known as a significant opportunistic pathogen in immunocompromised patients.[44] This infection in healthy individuals (immunocompetent) is commonly self-limited and subclinical Infection, consequential in chronic infection of tissue cysts that can status latent, possibly for the full lifetime of the hosts. But, immunocompromised patients, such as HIV-infected, cancer patients with chemotherapy, hemodialysis patients, transplant recipients, rheumatoid arthritis patients with consuming immunosuppressive drugs are at risk of increasing, myocarditis, or pneumonitis, Toxoplasma encephalitis due to recrudescence of the chronic infection.[45] For instance, almost 30-40% of HIV co-infected immunocompromised persons with T. *gondii* expand encephalitis.[46]

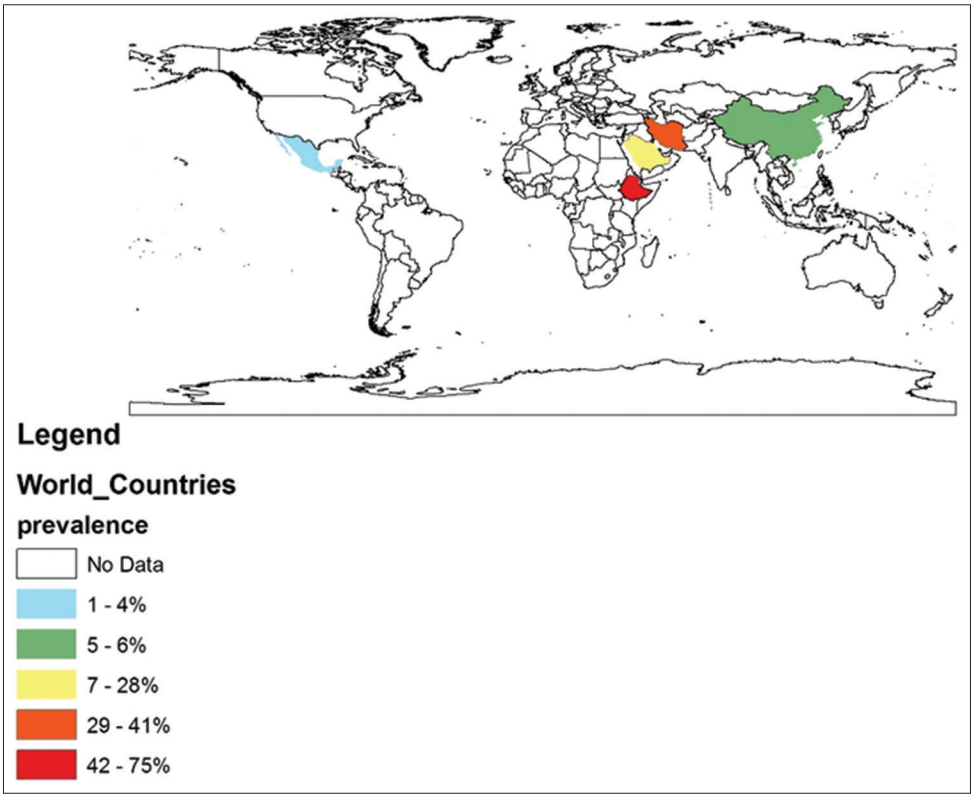

Figure 3: Pooled percentage seroprevalence of Toxoplasma gondii Infection in human of different geographical regions in this umbrella review. This map was created using ArcGIS software by Esri (http://www.esri.com)

This current study showed that pooled seroprevalence, seroprevalence of IgG and IgM anti-Toxoplasma *gondii* antibodies in immunocompromised patients was 42%, 48%, and 2%, respectively. Toxoplasmosis is an opportunistic infection in immunocompromised patients with a high mortality rate, causing encephalitis, pneumonitis, and myocarditis due to relapses and chronic reactivation (latent) disease followed by rupture of the cyst of the tissue.

Jiang *et al.* reported in a systematic review and meta-analysis 20.59% (95% CI: 20.11-21.06%) seroprevalence of T. *gondii* in the population with cancer in China.[47] Also, Wang *et al.*[48] and Hosseininejad *et al.*[9] reported 35.8% and 46% in a meta-analysis of HIV-infected and rheumatoid arthritis patients in worldwide, respectively. In a meta-analysis of IgG antibodies of T. *gondii* infection in hemodialysis patients was 58% in Iran.[49]

Females commonly do not appear any symptom for Toxoplasmosis infection within pregnancy. In maternal infection, the fetus is possible to be exposed to the mother-to-child transmissions. The complications resulting the mother-to-child transmissions are focal necrosis and inflammation plus congenital abnormalities like eye and brain injuries. In the event of such a serious infection, many sequelae may be created containing deafness, mental retardation, hydrocephalus, and microcephalus.[17]

This umbrella review indicated pooled seroprevalence, seroprevalence of IgG and IgM anti-Toxoplasma *gondii* antibodies in pregnant women was 40%, 29%, and 4%, respectively. Deng *et al.*[1] and Malary *et al.*[39] reported in a systematic review and meta-analysis of pregnant women that 4.37% and 39.2% seroprevalence of IgG anti-Toxoplasma *gondii* antibodies in china and Iran, respectively.

Two different studies, reported the seroprevalence of Korean pregnant women as 3.7%[50] and 0.8%.[51] Seroprevalence of IgG and IgM among Indian pregnant women was 45% and 3.3%, respectively[52] corresponding values for 1149 Turkish pregnant women were 60.4% and 3.0%, respectively.[53]

Seroprevalence of Toxoplasmosis in Iranian pregnant women like its seroprevalence in other pregnant women around the world is dependent on many factors such as keeping a cat at home or contact with stray infected cats, varied eating habits such as eating raw meat, failing to comply with hygiene principles of storing fruits and vegetables. These factors that directly and indirectly cause of toxoplasmosis in individuals and especially in the sensitive group of pregnant women.

Also, women in childbearing age are the most important group to pay attention to toxoplasmosis infection. This study showed pooled seroprevalence and seroprevalence of IgG anti-Toxoplasma *gondii* antibodies in women in reproductive age was 32.0% and 34.0%, respectively. Alzaheb reported in a systematic review and meta-analysis that 27.8 seroprevalence of T. *gondii* in women of reproductive age in Saudi Arabia.[43]

It is necessarily important to realize the status of T. *gondii* infection in the general population because this infection has heavy socioeconomic effects on people. Families suffer many costs during the care of sick children, particularly those with mental retardation and blindness.[21,54]

Ramirez *et al.* in one systematic review and meta-analysis reported that 3.63% seroprevalence of Toxoplasma *gondii* infection in Mexican Newborns and Children.[37]

This overview of reviews indicated pooled seroprevalence of Toxoplasma *gondii* infection in general population was 42%. Gebremedhin and Tadessein a systematic review and meta-analysis of the general population in Etiopia reported that 74.73% seroprevalence of IgG anti-Toxoplasma *gondii* antibodies.[28] The Significant high seroprevalence of T. *gondii* infection in Ethiopian humans can be due to uncontrolled cat movement, abnormal living conditions, and lifestyle and unsanitary behaviors that favor the transmission of parasites from cats or food animals.[28]

Furthermore Ramirez *et al.*[36] and Foroutan *et al.*[35] in the two study of systematic review and meta-analysis studies in Mexico and Iran population reported that 19.27% and 43% seroprevalence of T *gondii* infection, respectively.

Despite the fact that technical betterment in blood donation monitoring and evaluation, transfusion-transmitted T *gondii* infection remains a possible risk for immune-compromised recipients of transfusions. This study showed that pooled seroprevalence, seroprevalence of IgG and IgM anti-Toxoplasma *gondii* antibodies in blood donors was 33%, 18.0% and 2%, respectively. Mansouri *et al.*[25] and Foroutan-Rad *et al.*[55] in systematic review and meta-analysis in Iran and worldwide reported seroprevalence 34.4% and 33%. Also, Wang *et al.*[40] reported in a systematic review and meta-analysis that 6.26% seroprevalence of IgG antibodies of T. *gondii* in blood donors in china.

A limitation of our analyses is the often high levels of doubtful heterogeneity (I^2). In our 21 meta-analysis, one study did not report heterogeneity and fourteen meta-analyses had I^2 values greater than 60%, which meta-regression of sample size only partly explained in five of these 14 cases. Heterogeneity can be addressed via means of a meta-regression, and sub-group or sensitivity analyses.[56,57] Nevertheless, meta-regressions failed to recognize a factor that could describe the observed heterogeneity,[22] suggesting that the cause was a non-described variable.

This is the first umbrella review of updated systematic reviews and meta-analyses that provides a general view of the seroepidemiology of Toxoplasmosis in the worldwide subgroups population. The results of our umbrella review show a higher seroprevalence of *T. gondii* infection in immunocompromised patients, general population, pregnant women, blood donors,

childbearing age women, and newborn groups, respectively. So, Health education and health promotion, especially toward avoiding consumption raw and uncooked meat and avoiding contact with felines' feces advised. Furthermore, the screening and monitoring for Toxoplasmosis by primary care physicians is recommended to be conducted in high-risk groups in the endemic region.

Ethics in Systematic Reviews

The authors of this study followed the ethical principles of Systematic Reviews, including guidance on authorship, avoiding redundant (duplicate) publication, avoiding plagiarism, transparency, ensuring accuracy that potential complications.

Acknowledgments

The authors hereby would like to express their gratitude and appreciation to Dr. Mohammad Heidari, Assistant Professor of Epidemiology at Urmia University of Medical Sciences, to advise and collaborate on implementing this study in different stages and sections.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Deng H, Devleesschauwer B, Liu M, Li J, Wu Y, van der Giessen JWB, *et al.* Seroprevalence of Toxoplasma gondii in pregnant women and livestock in the mainland of China: A systematic review and hierarchical meta-analysis. Sci Rep 2018.;8:6218.
2. Davami MH, Pourahmad M, Baharlou R, Jahromi AS, Vasmejani AA, Solhjoo K, *et al.* Seroepidemiology of Toxoplasma infection in blood donors in Jahrom District, Southern Iran. Asian Pac J Trop Biomed 2015;5:1060-4.
3. Davami MH, Pourahamd M, Jahromi AR, Tadayon SM. Toxoplasma seroepidemiology in women who intend to marry in Jahrom, Islamic Republic of Iran. East Mediterr Health J 2014;19(Suppl 3):S71-5.
4. Fux B, Covre K, Estevan Nazar Lopes R, Bresciani Salaroli L, Wagner De almeida Vitor R, *et al.* Seroprevalence of toxoplasmosis in cats in Espirito Santo State, Brazil. Curr Devel Nutr 2020;4:186.
5. Brennan A, Hawley J, Dhand N, Boland L, Beatty JA, Lappin MR, *et al.* Seroprevalence and risk factors for Toxoplasma gondii infection in owned domestic cats in Australia. Vector-Borne Zoonotic Dis 2020;20:275-80.
6. Wei HX, Wei SS, Lindsay DS, Peng HJ. A systematic review and meta-analysis of the efficacy of anti-toxoplasma gondii medicines in humans. PLoS One 2015;10:e0138204.
7. Desmettre T. Toxoplasmosis and behavioural changes. J Fr Ophtalmol 2020;43:89-93.
8. Molan A, Nosaka K, Hunter M, Wang W. Seroprevalence and associated risk factors of Toxoplasma gondii infection in a representative Australian human population: The Busselton health study. Clin Epidemiol Global Health 2020;8:1-7
9. Hosseininejad Z, Sharif M, Sarvi S, Amouei A, Hosseini SA, Nayeri Chegeni T, *et al.* Toxoplasmosis seroprevalence in rheumatoid arthritis patients: A systematic review and meta-analysis. PLoS Negl Trop Dis 2018;12:e0006545.
10. Huang Y, Huang Y, Chang A, Wang J, Zeng X, Wu J. Is toxoplasma gondii infection a risk factor for leukemia? An evidence-based meta-analysis. Med Sci Monit 2016;22:1547-52.
11. Jiang C, Li Z, Chen P, Chen L. The seroprevalence of Toxoplasma gondii in Chinese population with cancer a systematic review and meta-analysis. Medicine (United States) 2015;94:e2274.
12. Ahmadpour E, Daryani A, Sharif M, Sarvi S, Aarabi M, Mizani A, *et al.* Toxoplasmosis in immunocompromised patients in Iran: A systematic review and meta-analysis. J Infect Dev Ctries 2014;8:1503-10.
13. Palmer BS. Meta-analysis of three case controlled studies and an ecological study into the link between cryptogenic epilepsy and chronic toxoplasmosis infection. Seizure 2007;16:657-63.
14. Ngoungou EB, Bhalla D, Nzoghe A, Dardé ML, Preux PM. Toxoplasmosis and epilepsy — systematic review and meta analysis. PLoS Negl Trop Dis 2015;9:e0003525.
15. Sutterland AL, Fond G, Kuin A, Koeter MW, Lutter R, van Gool T, *et al.* Beyond the association. Toxoplasma gondii in schizophrenia, bipolar disorder, and addiction: Systematic review and meta-analysis. Acta Psychiatr Scand 2015;132:161-79.
16. de Barros JLVM, Sutterland AL, Fond G, Kuin A, Koeter MW, Lutter R, van Gool T, *et al.* Is there any association between Toxoplasma gondii infection and bipolar disorder? A systematic review and meta-analysis. J Affect Disord 2017;209:59-65.
17. Montoya JG, Boothroyd JC, Kovacs JA. 280 - Toxoplasma gondii. In: Bennett JE, Dolin R, Blaser MJ, editors. Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases (Eighth Edition). Philadelphia: Content Repository Only!; 2015. p. 3122-53.
18. Bresciani KDS, Da Costa AJ. Congenital Toxoplasmosis in Humans and Domestic Animals. Bentham Science Publishers; 2018.
19. Daryani A, Sarvi S, Aarabi M, Mizani A, Ahmadpour E, Shokri A, *et al.* Seroprevalence of Toxoplasma gondii in the Iranian general population: A systematic review and meta-analysis. Acta Tropica 2014;137:185-94.
20. Makiani MJ, Davoodian P, Golsha R, Dehghani M, Rajaee M, Mahoori K, *et al.* Seroepidemiology and risk factors of toxoplasmosis in the first trimester among pregnant women. Int Electron J Med 2012;1:12-7.
21. Roberts T, Frenkel J. Estimating income losses and other preventable costs caused by congenital toxoplasmosis in people in the United States. J Am Vet Med Assoc 1990;196:249-56.
22. Martin-Saavedra JS, Vergara-Mendez LD, Talero-Gutierrez C. Music is an effective intervention for the management of pain: An umbrella review. Complement Ther Clin Pract 2018;32:103-14.
23. Grant MJ, Booth A. A typology of reviews: An analysis of 14 review types and associated methodologies. Health Info Libr J 2009;26:91-108.
24. Shea BJ, Grimshaw JM, Wells GA, Boers M, Andersson N,

Hamel C, *et al.* Development of AMSTAR: A measurement tool to assess the methodological quality of systematic reviews. BMC Med Res Methodol 2007;7:10.

25. Mansouri A, Adhami Mojarad MR, Badfar G, Abasian L, Rahmati S, Kooti W, *et al.* Epidemiology of Toxoplasma gondii among blood donors in Iran: A systematic review and meta-analysis. Transfusion Apheresis Sci 2017;56:404-9.
26. Foroutan-Rad M, Majidiani H, Dalvand S, Daryani A, Kooti W, Saki J, *et al.* Toxoplasmosis in blood donors: A systematic review and meta-analysis. Transfus Med Rev 2016;30:116-22.
27. Borna S, Majidiani H, Dalvand S, Daryani A, Kooti W, Saki J. Prevalence of immunity to toxoplasmosis among Iranian childbearing age women: Systematic review and meta-analysis. Iran J Reprod Med 2013;11:861-8.
28. Gebremedhin EZ, Tadesse G. A meta-analysis of the prevalence of Toxoplasma gondii in animals and humans in Ethiopia. Parasites Vectors 2015;8.
29. Daryani A, Sarvi S, Aarabi M, Mizani A, Ahmadpour E, Shokri A, *et al.* Seroprevalence of Toxoplasma gondii in the Iranian general population: A systematic review and meta-analysis. Acta Tropica 2014;137:185-94.
30. Mizani A, Alipour A, Sharif M, Sarvi S, Amouei A, Shokri A, Rahimi MT, *et al.* Toxoplasmosis seroprevalence in Iranian women and risk factors of the disease: A systematic review and meta-analysis. Trop Med Health 2017;45:7.
31. Wang ZD, Wang SC, Liu HH, Ma HY, Li ZY, Wei F, *et al.* Prevalence and burden of Toxoplasma gondii infection in HIV-infected people: A systematic review and meta-analysis. Lancet HIV 2017;4:e177-88.
32. Foroutan M, Rostami A, Majidiani H, Riahi SM, Khazaei S, Badri M, *et al.* A systematic review and meta-analysis of the prevalence of toxoplasmosis in hemodialysis patients in Iran. Epidemiol Health 2018;40:e2018016.
33. Ahmadpour E, Daryani A, Sharif M, Sarvi S, Aarabi M, Mizani A, *et al.* Toxoplasmosis in immunocompromised patients in Iran: A systematic review and meta-analysis. J Infect Dev Ctries 2014;8:1503-10.
34. Wang ZD, Liu HH, Ma ZX, Ma HY, Li ZY, Yang ZB, *et al.* Toxoplasma gondii infection in immunocompromised patients: A systematic review and meta-analysis. Front Microbiol 2017;8:389.
35. Foroutan M, Dalvand S, Daryani A, Ahmadpour E, Majidiani H, Khademvatan S, *et al.* Rolling up the pieces of a puzzle: A systematic review and meta-analysis of the prevalence of toxoplasmosis inIran. Alexandria journal of medicine2018;54:189-96.
36. Galvan-Ramirez Mde L, Troyo R, Roman S, Calvillo-Sanchez C, Bernal-Redondo R. A systematic review and meta-analysis of Toxoplasma gondii infection among the Mexican population. Parasit Vectors 2012;5:271.
37. Galvan-Ramírez Mde L, Troyo-Sanroman R, Roman S, Bernal-Redondo R, Vázquez Castellanos JL. Prevalence of toxoplasma infection in Mexican newborns and children: A systematic review from 1954 to 2009. ISRN Pediatr 2012;2012:501216.
38. Deng H, Devleesschauwer B, Liu M, Li J, Wu Y, van der Giessen JWB, *et al.* Seroprevalence of Toxoplasma gondii in pregnant women and livestock in the mainland of China: A systematic review and hierarchical meta-analysis. Sci Rep 2018;8:6218.
39. Malary M, Hamzehgardeshi Z, Moosazadeh M, Afshari M, Ahmadi I, Moghaddasifar I, *et al.* Seroprevalence of Toxoplasma gondii infection among Iranian pregnant women: A systematic review and meta-analysis. East Mediterranean Health J 2018;24:488-96.
40. Wang T, Han Y, Pan Z, Wang H, Yuan M, Lin H. Seroprevalence of Toxoplasma gondii infection in blood donors in mainland China: A systematic review and meta-analysis. Parasite 2018;25:36.
41. Foroutan-Rad M, Khademvatan S, Majidiani H, Aryamand S, Rahim F, Malehi AS. Seroprevalence of Toxoplasma gondii in the Iranian pregnant women: A systematic review and meta-analysis. Acta Tropica 2016;158:160-9.
42. Azadi T, Darabi M, Sayehmiri F, Sayehmiri K. Investigating the prevalence of toxoplasmosis in Iranian pregnant women: A Systematic review and meta-analysis. Sci J Ilam Univ Med Sci 2017;25:148-58.
43. Alzaheb RA. Seroprevalence of Toxoplasma gondii and its associated risk factors among women of reproductive age in Saudi Arabia: A systematic review and meta-analysis. Int Jf Women's Health 2018;10:537-44.
44. Ahmadpour E, Daryani A, Sharif M, Sarvi S, Aarabi M, Mizani A, *et al.* Toxoplasmosis in immunocompromised patients in iran: A systematic review and meta-analysis. J Infect Dev Ctries 2014;8:1503-10.
45. Machala L, Kodym P, Malý M, Geleneky M, Beran O, Jilich D. Toxoplasmosis in immunocompromised patients. Epidemiol Mikrobiol Imunol 2015;64:59-65.
46. Snydman DR, Walker M, Zunt JR. Parasitic central nervous system infections in immunocompromised hosts. Clin Infect Dis 2005;40:1005-15.
47. Jiang C, Li Z, Chen P, Chen L. The seroprevalence of Toxoplasma gondii in Chinese population with cancer: A systematic review and meta-analysis. Medicine 2015;94:e2274.
48. Wang ZD, Wang SC, Liu HH, Ma HY, Li ZY, Wei F, *et al.* Prevalence and burden of Toxoplasma gondii infection in HIV-infected people: A systematic review and meta-analysis. Lancet HIV 20174:e177-88.
49. Foroutan M. A systematic review and meta-analysis of the prevalence of toxoplasmosis in hemodialysis patients in Iran. PLoS Negl Trop Dis 2018;40:e2018016.
50. Han K, Shin DW, Lee TY, Lee YH. Seroprevalence of Toxoplasma gondii infection and risk factors associated with seropositivity of pregnant women in Korea. J Parasitol 2008;94:963-5.
51. Song K-J, Shin JC, Shin HJ, Nam HW. Seroprevalence of toxoplasmosis in Korean pregnant women. Korean J Parasitol 2005;43:69.
52. Singh S, Pandit AJ. Incidence and prevalence of toxoplasmosis in Indian pregnant women: A prospective study. Am J Reprod Immunol 2004;52:276-83.
53. Harma M, Gungen N, Demir N. Toxoplasmosis in pregnant women in Sanliurfa, Southeastern Anatolia City, Turkey. J Egypt Soc Parasitol 2004;34:519-25.
54. Roberts T, Murrell KD, Marks S. Economic losses caused by foodborne parasitic diseases. Parasitol Today. 1994;10:419-23.
55. Foroutan-Rad M, Majidiani H, Dalvand S, Daryani A, Kooti W, Saki J, *et al.* Toxoplasmosis in blood donors: A systematic review and meta-analysis. Transfus Med Rev 2016;30:116-22.
56. Cornell JE, Liao JM, Stack CB, Mulrow CD. Annals understanding clinical research: Evaluating the meaning of a summary estimate in a meta-analysis. Ann Internal Med 2017;167:275-7.
57. Bigby M. Understanding and evaluating systematic reviews and meta-analyses. Indian J Dermatol 2014;59:134-9.