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Rolling up the pieces of a puzzle: A systematic review and meta-analysis of the prevalence of toxoplasmosis in Iran

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ABSTRACT

Toxoplasmosis is a neglected parasitic disease with global distribution in warm-blooded vertebrates and high prevalence among different human societies. We contrived a systematic review and meta-analysis on the prevalence of toxoplasmosis in Iran. Following the general methodology recommended for systematic reviews and meta-analysis, four English and three Persian electronic databases were explored up to April 2016. Out of 105,139 examined samples of different hosts, the weighted overall prevalence was 37% (95% CI = 31–43). Due to the significant heterogeneity (I^2 = 81.9%) the random-effects model was used. The pool estimated prevalence of toxoplasmosis in human intermediate hosts, animal intermediate hosts, and definitive hosts was 43% (95% CI = 38–47), 26 (95% CI = 17–35) and, 34% (95% CI = 22–46), respectively. Our results represent that regular inspection in food industries, improved screening programs using standard diagnostic assay as well as distinguishing toxoplasmosis condition in other zoonotic hosts are extremely recommended for better disease management in Iran.

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1. Introduction

An obligate intracellular parasitic protozoan, *Toxoplasma gondii* (*T. gondii*), infects approximately one third of the world's population, and causes a potential zoonotic disease called toxoplasmosis.[1–3] This infection is appointed to be a neglected parasitic disease by CDC (Centers for Disease Control and Prevention), characterized by high prevalence and chronic nature as well, which principally occurs in regions with poor hygiene.[4] The majority of warm-blooded animals as intermediate hosts may be sources of tissue cysts, universal abundance of felines (Family: Felidae) as definitive hosts as well as multiple transmission routes have maintained parasite dissemination in the environment. *T. gondii* gains access to the host's body through several principal pathways, including: vertical transmission, oocyst-contaminated food and water, raw or undercooked meat containing viable tissues cysts, organ transplantation, and blood transfusion.[1,3,5–8] Human populations are dead-end host for toxoplasmosis with up to 80% suffering from chronic asymptomatic infection.[9] Pregnant women and immunocompromised individuals (cancer, transplant and AIDS patients) comprise the two important risk groups for toxoplasmosis.[3,5,10,11] Owing to the *Toxoplasma* predilection to the brain and eye, poor prognosis and complications such as glaucoma, chorioretinitis, retinal detachment, brain abscess and encephalitis can occur during acute or recrudescent infection.[12,13] Furthermore, serious complications such as brain focal lesions, hydrocephaly, microcephaly, deafness, and mental retardation may arise from congenital toxoplasmosis, according to the gestational age.[3,6,10] Additionally cerebral toxoplasmosis may have also a significant correlation to neurodegenerative disorders like schizophrenia, epilepsy, and bipolar disorder.[14–17] Moreover, chronic toxoplasmosis is strongly correlated to autoimmune diseases.[18,19] Routine diagnostic methods for toxoplasmosis generally pertain to serology-dependent experiments such as enzyme-linked immunosorbent assay (ELISA) and indirect immunofluorescence assay (IFA) in order to discern the *T. gondii*-specific antibodies, i.e. IgM or IgG.[20] In addition to the medical significance of toxoplasmosis, this protozoan is of veterinary importance in terms of abortion in sheep herds as well as a relatively high prevalence in domestic animals in Iran such as cat, sheep, goat and cattle.[21–23]

We have designed a systematic review and meta-analysis in order to shed light on the status of *Toxoplasma* infection in both human and animal populations. We hope that the conception derived from this study help us to better understand the epidemiological surveillance of toxoplasmosis in Iran.

2. Materials and methods

2.1. Study area

Covering a wide area in the Middle East (1,648,195 km^2) (Fig. 1), Iran with population of approximately 80 million in 2015, located between 25°3′ and 39°47′N, and 44°5′ and 63°18′E, and bordering Iraq and Turkey in the west, Afghanistan and Pakistan in the east, the Persian Gulf and Oman Sea in the south, as well as Azerbaijan, Armenia and Turkmenistan in the north. Except for a small region on the margin of the Caspian Sea coast with a considerable annual rainfall and covered by dense vegetation, the general climate of Iran is hot and dry, forming the Iranian plateau. It is one of the world's most mountainous countries, its landscape dominated by rugged mountain ranges that separate various basins or plateaux from each other. The populous western part is the most mountainous, with ranges such as the Caucasus, Zagros and Alborz Mountains. Lower temperatures, severe winters and heavy snowfalls exist in the Zagros basin, while in the central and eastern basins there is an arid climate because of high-altitude mountain ranges in the western and northern parts. These mountain ranges are so high that rain clouds cannot reach the central and eastern basins. Annual precipitation is 680 mm in the eastern part of the plain and more than 1700 mm (66.9 in.) in the western part.[24]

2.2. Search strategy

In this systematic review and meta-analysis we sought to determine the epidemiological aspects of toxoplasmosis in both human and animal population in Iran. The search strategy was performed

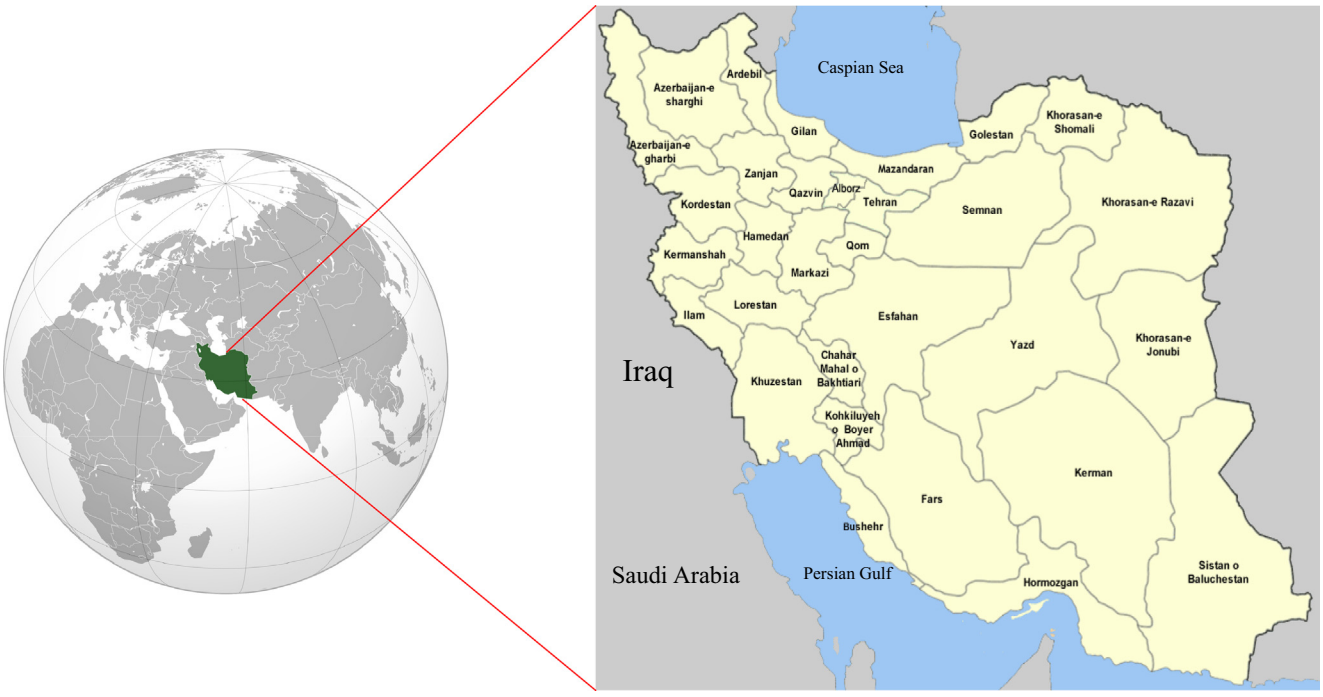

Fig. 1. Location of Iran country.

based on the online literature screening in four English databases (PubMed, Web of Science, Scopus, and Google Scholar) and three Persian databases (Scientific Information Database, Iran Medex, and Magiran) up to April 2016. This review was accomplished using medical subject heading (MeSH) terms and combination of several keywords consisting of: "*Toxoplasma*", "*Toxoplasma gondii*", "Toxoplasmosis", "Prevalence", "Epidemiology", "Iran", "Islamic Republic of Iran", "Systematic review", and "meta-analysis".

2.3. Study selection and data extraction

During initial search, the relevant citations were recorded based on topics and abstracts of them were saved in a world file for next evaluation. Afterwards, based on primary screening the records that seem to be potentially eligible were chosen to download the full-text. The retrieved papers were reviewed precisely by two different reviewers (M. Foroutan and H. Majidiani) to evaluate the final eligibility and inclusion criteria. The selected articles were read carefully and incoherence among studies was clarified by controversy and consensus. The required data were extracted by one author (M. Foroutan) and rechecked by a second (S. Khademvatan). Inclusion criteria were as follows: (1) systematic review and meta-analysis papers; (2) review articles that estimated the prevalence of *T. gondii* in human or animal population; (3) published online up to April 2016; (4) published in English or Persian; (5) full-text articles were available; (6) exact total sample size and positive samples were available. The papers were excluded if they didn't met the above-mentioned criteria. The reference list of selected full-text articles were also meticulously checked manually to find papers not retrieved by the database searching. Finally, a data extraction form was exerted to gather data depending on the study population, number of included studies, number of examined samples, duration of time, number of positive cases, prevalence (95% CI), study methodology, and main findings. The preferred reporting items for systematic reviews and meta-analysis (PRISMA) guideline was used to report our results.[25]

2.4. Meta-analysis

Meta-analysis procedure was performed as previously described.[24,26,61] Briefly, prevalence and its 95% confidence interval (CI) of toxoplasmosis were extracted from each included paper. Then forest plot was drawn to illustrate the meta-analysis outcomes. Cochran's Q and I^2 statistics were employed to quantify the variations and heterogeneity. I^2 values of 25%, 50% and 75% were considered as low, moderate and high heterogeneity, respectively.[27] Besides, in order to evaluate publication bias and small study effects, the funnel plot relied on Egger's regression test was used. Either Der Simonian and Laird's random-effects method or Mantel-Haenszel's fixed-effects method were used to pool the estimations, based on the results of heterogeneity test. Furthermore, we divided the papers by different subgroups (human intermediate host, animal intermediate host, and definitive host) and pool estimation was calculated for them.

3. Results

Herein we summarize the results of the current systematic review and meta-analysis. According to Supplementary Fig. 1, a number of 142 studies were explored during literature review, among which 7 papers were eligible for this systematic review and meta-analysis based on the inclusion criteria.[1–3,5,21–23] Due to the presence of significant heterogeneity (I^2 = 81.9%) the random-effects model was applied. The Egger's regression test was carried out, suggesting that there is no substantial influence for publication bias on overall prevalence estimate (P = 0.9). Also, the forest plot diagram of the current meta-analysis has been depicted in Supplementary Fig. 2. Considering Table 1, the outcomes of literature search and related features of studies, the number of included studies, examined samples and positive cases, prevalence rate and coverage period are shown. The subgroup analysis in different hosts yielded 43% (95% CI = 38–47) and 26% (95% CI = 17–35) prevalence rate in human and animal intermediate hosts, respectively (Table 2). We found that transplant patients category was the most at-risk group regarding toxoplasmosis in human hosts with 702 examined samples, 372 positive cases and a prevalence rate of 55% (95% CI = 43–67). On the contrary, the least at-risk group was blood donors with a prevalence rate of 33% (95% CI = 24–42). Additionally, the pool estimated prevalence of toxoplasmosis in definitive hosts was evaluated 34% (95% CI = 22–46) (Table 2). The most widely-used diagnostic tests to evaluate *Toxoplasma* infection in human hosts were as follows: ELISA in 73 studies and IFA in 40 studies. In animal intermediate and definitive hosts IFA followed by direct agglutination test (DAT) were the most common employed experiments (Table 1).

4. Discussion

Being one of the marvelous parasites, *T. gondii* still possesses a relatively high rate of prevalence in different mankind societies as well as various animal species.[1,3,8,11,21,28–32] The objective of this systematic review and meta-analysis was to estimate the prevalence of *T. gondii* infection in human and animal populations in Iran premised on records obtained from literature review. We searched 7 databases among which 7 papers were included with 105,139 examined samples obtained from different hosts and weighted overall prevalence was 37% (95% CI = 31–43) (Table 2). There have been multiple risk factors involved in the high prevalence of toxoplasmosis in Iran. Suppression of the host immune responses, consumption of oocysts contaminated water and unwashed fruit and vegetables, keeping cats indoors as pet animals, eating raw meat and direct contact with meat or viscera of infected animals are among the risk factors which directly increase the incidence of toxoplasmosis.[2,3,5,23] Regarding climate, any meteorological agent that can facilitate the sporulation of *Toxoplasma* oocysts shed in the cat feces, e.g. appropriate humidity, would entail the protracted survival and spread of infective parasites in the environment, and hence the higher contingency of human and animal infection.[23,33] Meanwhile, some risk factors such as occupation, gender, place of residence, and level of education indirectly influence the above-mentioned behaviors and bias the prevalence of infection. Two risk factors, contact with cat and place of residence, have been significantly correlated to toxoplasmosis in Iranian general population as well as pregnant women[2,3] (Table 1). Abundance of cats and infected prey animals as well as high survival of oocysts in dump soil, high number of rural communities, lack of adequate health literacy and limited access to health resources, would justify 39% (95% CI = 33–46) prevalence of *T. gondii* infection in Iranian general population.[2,23,32] The prevalence is lower in USA, Mexico and China, being 10.8%, 20.26% and 6.31%, respectively, mostly due to the good hygienic measures, successful educational programs to alert people, precise diagnostic tests for women of childbearing age and pregnant women, industrialization of animal husbandry as well as well-established monitoring systems and improved rules in meat inspection.[11,34,35] In Ethiopia, toxoplasmosis prevalence rate of 75% has been observed which may be corroborated by the abundance of infected cats and food animals, low levels of hygiene and living in sub-standard conditions.[28]

Pregnant women are substantial targets of *T. gondii* infection and the seroprevalence of infection among this population in Iran

Table 1
Baseline characteristics of included studies.

References	Group	No. of included studies	Time period	Prevalence 95% CI	Methods	Main findings
Human intermediate host						
(5)	Cancer patients	8	1997–2013	45% (95% CI = 39–51)	ELISA (6 studies) IFA (2 studies)	The Q statistic was 26.11 (df = 7, $P = 0.0005$) with inconsistency ($I^2 = 73.2\%$).
(5)	HIV/AIDS patients	8	1997–2013	50% (95% CI = 37–63)	ELISA (7 studies) IFA (1 study)	The Q statistic was 128.75 (df = 7, $P < 0.0001$).
(5)	Transplant patients	9	1997–2013	55% (95% CI = 43–67)	ELISA (7 studies) IFA (1 study) ELFA (1 study)	The Q statistic was 90.62 (df = 8, $P < 0.0001$).
(2)	General population	35	1978–2013	39% (95% CI = 33–46)	IFA (23 studies) ELISA (11 studies) CLIA (1 study)	Estimated seropositive rate of toxoplasmosis among the different studies has a wide variation, and the Q statistic was very large ($Q = 7319.1$, df = 34, $P < 0.0001$; $I^2 = 99.5\%$). The results showed high seroprevalence in groups including: direct contact with cats ($P < 0.05$), eat uncooked meat ($P < 0.0001$) and raw fruits or vegetables ($P < 0.05$), in farmers and housewife ($P < 0.0001$), low level educated persons ($P < 0.0001$) and elders ($P < 0.0001$).
(3)	Pregnant women	50	1990–2015	41% (95% CI = 36–45)	ELISA (36 studies) IFA (13 studies) CLIA (1 study)	Results of Egger's regression test indicates publication bias might not have a significant influence on overall prevalence estimate ($P = 0.89$). $I^2 = 97.85\%$, $P = < 0.001$ The highest and lowest seroprevalence of toxoplasmosis were observed in south 53% (95% CI = 30–77) and east 33% (95% CI = 23–42%), respectively. Correlation between toxoplasmosis and two risk factors including ‘‘residence ($P = 0.005$)” and ‘‘contact with cat ($P = 0.002$)” was estimated with multivariate analysis.
(1)	Blood donors	7	1980–2015	33% (95% CI = 24–42)	ELISA (6 studies) EIA (1 study)	$I^2 = 96.5\%$ $Q = 171.33$ Seroperevalance of toxoplasmosis in different parts of Iran was between 19.3% and 56.4%. Though the results of this study indicate relatively high prevalence but this does not mean active infection. Also this does not lead to a conclusion that blood donation screening is required.
Animal intermediate host						
(22)	Cattle	22	1983–2102	18% (95% *CI* = 10–28)	IFA (8 studies) MAT (5 studies) LAT (3 studies) DAT (2 studies) SFT (2 studies) ELISA (1 study) IHA (1 study)	There was a wide variation in the cattle toxoplasmosis prevalence among different studies (Q statistic = 1982.9, df = 19, $P < 0.0001$) and $I^2 = 99\%$. Rate of toxoplasmosis in different parts of Iran was between 1.4% and 71.3%.
(21)	Sheep	58	1977–2012	31% (95% CI = 26–35)	DAT (18 studies) IFA (13 studies) LAT (9 studies) IHA (4 studies) MAT (4 studies) ELISA (4 studies) PCR (3 studies) SFT (2 studies) CCIEP (1 study)	Different studies showed a wide variation in prevalence of toxoplasmosis and the Q statistics was 1189.544882 (df = 33), $P < 0.0001$, and $I^2 = 97.2\%$. There was no significant difference in rate of toxoplasmosis between male and female sheep (odds ratio (OR) = 1.002, 95% CI = 0.59–1.696).
(21)	Goats	18	1977–2012	27% (95% CI = 14–42)	LAT (7 studies) IFA (3 studies) DAT (2 studies) MAT (2 studies) ELISA (2 studies) IHA (1 study) PCR (1 study)	Different studies showed a wide variation in prevalence of toxoplasmosis in goats and the Q statistics was 1172.891557 (df = 15), $P < 0.0001$, and $I^2 = 98.7\%$. There was no significant difference in rate of toxoplasmosis between male and female goats (OR = 1.027, 95% CI = 0.685–1.541).

Definitive host						
(23)	Cats	21	1975–2013	34% (95% CI = 22–46)	IFA (5 studies) Flotation (4 studies) MAT (3 studies) LAT (2 studies) DAT (2 studies) ICT (2 studies) SFT (1 study) PCR (1 study) wet smear (1 study)	Results showed a wide variation in the prevalence estimates of different studies (Q statistic = 742.3, df = 20, $P < 0.0001$ and $I^2 = 99\%$) In the various parts of Iran, prevalence of toxoplasmosis in cats was between 1.2% and 89.2%. Overall prevalence rates for stray and domestic cats were 38% (95% CI = 22–55) and 33% (95% CI = 19–47), respectively. Random meta-analysis prevalence rates of infection in males and females were 21% (95% CI = 23–59) and 31% (95% CI = 19–43), respectively.

Abr: EIA, enzyme immunoassay; ELFA, enzyme-linked fluorescent assay; MAT, modified agglutination test; DAT, direct agglutination test; IFA, indirect immunofluorescent assay; LAT, latex agglutination test; ICT, immunochromatography test; SFT, Sabin and Feldman test; PCR, polymerase chain reaction; CLIA, chemiluminescence enzyme immuno assay.

has been assigned 41% (95% CI = 36–45). Congenital cases appear more frequently when infection occurs late in pregnancy causing drastic imperfections of eyes and hearing apparatus. However debilitating outcomes such as mental retardation, deafness, retinochoroiditis, microcephaly, and hydrocephaly mostly take place when infection is encountered in the first trimester. In this case there are plenty of documentations worldwide.[6,10,13] Totally, seroprevalence rates of toxoplasmosis in pregnant women and those in childbearing age illustrated more endemicity in the Americas and Africa, ranging 6.1–77.5% and 25.3–75.2%, respectively. Additionally, in Europe and Asia the seroprevalence trend indicate a range scope between 8.2–63.2% and 0.8–63.9%, respectively.[30] Moreover, in recent systematic review, annual incidence of congenital toxoplasmosis was reported 190,100 cases (95% CI = 179,300–206,300) from global perspective that impose 1.20 million DALYs (Disability-adjusted life year) (95% CI = 0.76–1.90). South America, some Middle Eastern and low-income countries had the highest burden of infection.[6] Higher endemicity of toxoplasmosis in some regions implicates lower primary active infection in gestation period, since pregnant women have encountered *T. gondii* during their childhood or childbearing age, leading to the premunition or concomitant immunity in person's body which extinguishes the pathogenicity of parasites.[6]

The other at risk group for toxoplasmosis is immunocompromised patients. So prevalence of infection is significantly higher in immunocompromised individuals than normal people (50% *vs.* 39%).[2,5] This may be to a great extent due to a relapse originating from the decline of concomitant immunity in persons with a latent *Toxoplasma* infection. The weighted overall seroprevalence of infection in Iranian immunocompromised patients was 50% (95% CI = 44–56). Of this, transplant patients were the most exposed risk group (55%) and AIDS patients (50%) followed by cancer patients (45%) (Table 1). Corresponding to our finding, in China, a remarkable difference was found in cancer patients, representing 20.59% infection seroprevalence compared to the 6.31% in immunocompetent population ($P < 0.001$; OR 3.90).[11] In contrast to infected immunocompetent individuals which are often asymptomatic, toxoplasmosis inflicts awful consequences in persons with disordered immune system particularly in AIDS patients, such as infection reactivation and recrudescence, fulminant disease, pneumonitis, myocarditis, encephalitis and even death.[5,11,12] Furthermore, *Toxoplasma* serologic diagnosis is faced with the obstacle of low immune function in immunosuppressed patients and choosing the best diagnostic method is open to question.[36]

The risk of transmission of *Toxoplasma* infection by blood transfusion from seemingly asymptomatic and healthy individuals who are carrier of infection puts an extra burden on global population especially where toxoplasmosis is more common. *Toxoplasma* seropositive individuals in acute stage of infection may have played a role in transfusion transmitted toxoplasmosis. Africa and Asia enclosed the highest and lowest global burdens of toxoplasmosis in blood donors with prevalence rate of 46% (95% CI = 14–78) and 29% (95% CI = 23–35), respectively.[1] Brazil (75%) and Ethiopia (73%) had the highest seroprevalence of toxoplasmosis.[37,38] The prevalence of toxoplasmosis in Iranian blood donors is 33% (95% CI = 24–42) (Table 1); while lower prevalence was reported by Galvan-Ramirez et al.,[35] in Mexico 17% (95% CI = 15–19). Blood products are often required in thalassemia patients, tissue graft recipients, individuals suffering from anemia as well as hematopoietic disorders. Besides, blood transfusion is a vital need during many operations and surgeries. So allogenic (homologous) blood transfusion may be associated with the high risk of postoperative infectious complications.[39–41] Some complications have been reported following donation of *Toxoplasma*-infected blood such as reactivation of toxoplasmosis in immunocompromised patients (HIV$^+$, transplant individuals) receiving allogenic grafts

Table 2
Subgroup analysis for comparison of prevalence in different hosts.

Host	No. of studies	Prevalence 95% CI	I^2%	Heterogeneity test		Egger test	
				Q	*P*	t	*P*
Human intermediate host	6	43 (38–47)	57.5	11.77	0.038	0.84	0.45
Animal intermediate hosts	3	26 (17–35)	69	6.45	0.040	0.88	0.54
Definitive host	1	34 (22–46)	–	–	–	–	–
Overall	10	37 (31–43)	81.9	49.62	<0.001	0.04	0.97

Test for heterogeneity between sub-groups:
Q: 13.15; *P*-value: 0.001.

particularly suffering from graft-versus-host disease (GVHD) as well as high mortality in cord blood transplantation cases with disseminated toxoplasmosis.[42,43] According to WHO recommendations, screening of donated blood for transfusion-transmitted infections must be performed for human immunodeficiency virus (HIV), hepatitis B virus surface antigen (HBsAg), hepatitis C virus (HCV) and *Treponema pallidum* (causative agent of Syphilis) in all countries. Furthermore, blood screening tests have to be accomplished for Malaria, Chagas disease, human T-cell lymphotropic viruses I/II (HTLV I/II) and human cytomegalovirus (CMV) in some countries and endemic regions.[44] In this case, a pre-transfusion screening for *T. gondii* has not yet been considered; therefore, afore-mentioned groups constitute highly susceptible populations which are predisposed to acute and severe toxoplasmosis by donated bloods. According to Siegel et al. (1971)[45] study, transmission of parasites through leukocytes transfusion from donors infected to chronic myelogenous leukemia (CML) was documented. Additionally, they showed that the parasite survives in citrated blood condition at 5 °C up to 50 days, thus prevention of disease transmission could not be accomplished by refrigeration of blood packs during storage period. The same route of infection was implied by Roth et al. (1971).[46] Also a weird case of acquired retinochoroiditis resulting from toxoplasmosis was reported with platelet transfusion as its possible reason.[47] Nevertheless, based on data from American Association of Blood Banks, transfusion-transmitted toxoplasmosis categorizes as rare (www.aabb.org/tm/eid/Documents/227s.pdf). In our previous systematic review of toxoplasmosis in Iranian blood donors based on molecular methods, only in a low proportion of IgM^+ samples the parasite DNA was identified.[1] This finding suggests high serologic prevalence does not justify donor screening, for two reasons: (1) serology does not imply infectivity; and (2) a high serologic background prevalence (if used to eliminate donors) would result in major limitation on blood availability; thus, causing more harm than toxoplasmosis. It seems a test for the direct presence of the organism in blood (an antigen test or a DNA based test) will be useful. Ideally, provide a method to inactivate *Toxoplasma* infection in blood products. However, for better understanding of this issue, more studies should be designed using molecular techniques in the future.

Toxoplasmosis is recognized as a likely reason of stillbirth, abortion and fetal mummification in small ruminants such as sheep and goat, causing detriments to animal husbandry and substantial economic losses.[48] The risk of human infection is always lurking around in regions that people consume mutton, goat and calf meat regularly.[7,49] *Toxoplasma* has also been found in milk of host animals. Despite of mandatory pasteurization procedure in milk processing industries that kills *T. gondii*, there have been some reports indicative of transmission of infection by raw goat milk and its derivatives such as whey and cheese to humans and pigs, leading to health problems and even serious symptoms.[50–53] Among common food animals in Iran, the highest prevalence was dedicated to sheep with 31% (95% CI = 26–35), followed by goats with 27% (95% CI = 14–42) and cattle with 18% (95% CI = 10–28) (Table 1). Cats which devour on *Toxoplasma*-infected rodents, pass large amounts of oocysts and implicate a pivotal role in disease transmission. The prevalence rate of toxoplasmosis in cats of Iran was 34% (95% CI = 22–46.) (Table 1). This relatively high prevalence probably originates from several factors such as lack of routine treatment, significant exuberance of feline hosts and favorable humid climate.[23] In Ethiopia small ruminants and cat populations were appointed prevalence rates of 35% (95% CI = 21–51) and 88% (95% CI = 79–93), respectively.[28] Up to 59% of sheep and 92% of goats in Brazil had antibodies against *T. gondii*.[29] In Iran, there exist several molecular studies on the prevalence of infection in meat and meat products of food animals which emphasize the danger of food-transmitted toxoplasmosis.[54–58] Also, individuals who are in direct contact with raw meat especially veterinarians, butchers and slaughterhouse staff, have been shown to be more prone to infection.[59,60]

In conclusion, this systematic review and meta-analysis focuses on the distribution and epidemiological aspects of toxoplasmosis in Iran. Regarding geographical climate of Iran, toxoplasmosis proceed to higher rates in Caspian Sea littoral but nipping highland provinces as well as hot territories were substantiated to have lower seroprevalence rates, highlighting the importance of humidity and adequate temperature for oocyst survival and infectivity. Public awareness, training courses and hygienic practice all are valuable to direct people toward cooked meat, washed vegetables, organizing stray cats as well as on time and proper treatment of infected household cats. Intense surveillance system and regular inspection in food production industries, improved hygienic criteria in abattoirs and sanitary disposal of viscera in addition to advanced screening programs using a modulus diagnostic assay particularly in two risk groups in endemic regions, i.e. immunocompromised patients and pregnant women, are very important to harness transmission cycle of the parasite. Although there have been comprehensive and analytical studies on the prevalence of *T. gondii* infection in general population, blood donors, women in pregnancy and childbearing age, immunocompromised patients and animals such as sheep, goat, cattle, and cat in Iran, there is lack of systematic reviews and meta-analysis about toxoplasmosis in consumed meats as well as birds and other hosts of zoonotic potential in the country. We propose to pay more attention on the above-mentioned neglected groups by researchers in future.

Compliance with ethical standards

Authors' contribution: M. Foroutan and H. Majidiani conceived the study; M. Foroutan, H. Majidiani and E. Abbasi designed the study protocol; M. Foroutan and S. Khademvatan searched the literature and extracted the data; S. Dalvand analyzed and interpreted the data; H. Majidiani and M. Foroutan wrote the manuscript; A. Daryani and E. Ahmadpour critically revised the manuscript. All authors read and approved the final manuscript.

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Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.ajme.2017.06.003.

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