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Seroprevalence of *Toxoplasma gondii* in the Iranian pregnant women: A systematic review and meta-analysis

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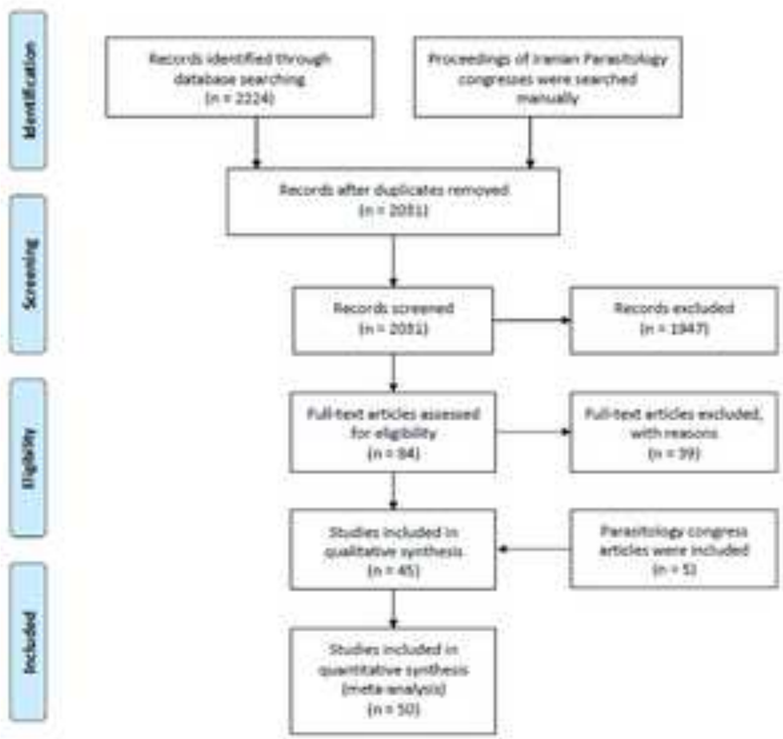
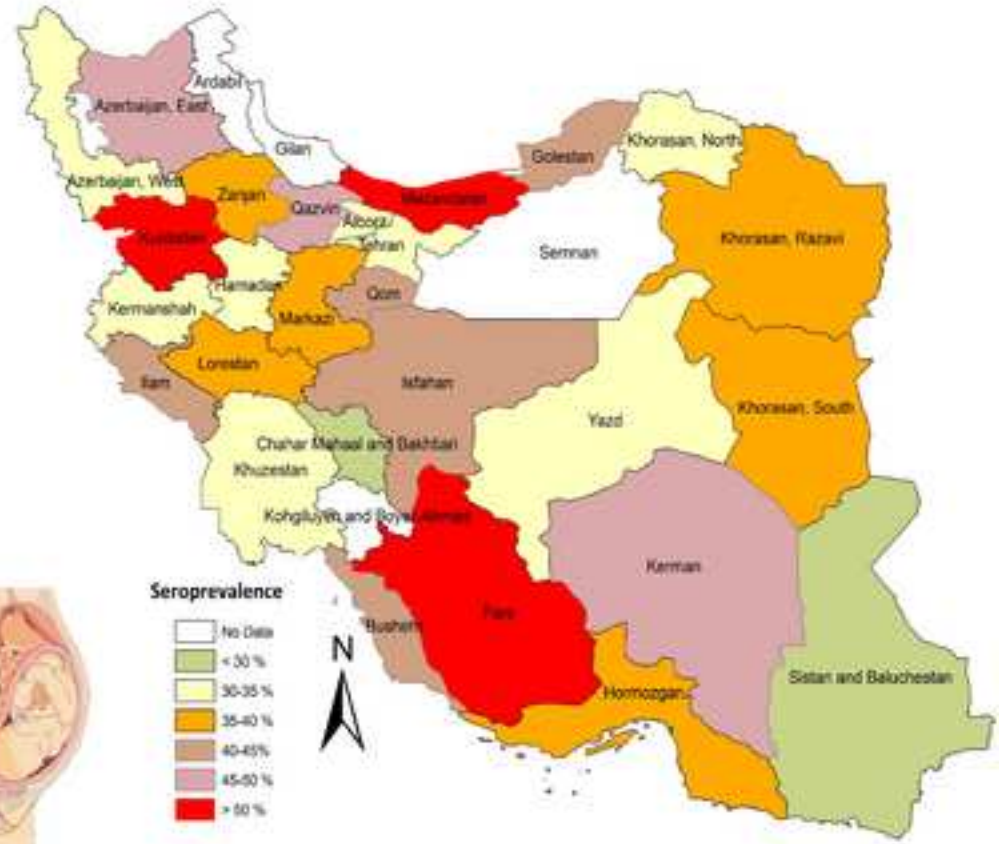
Graphical Abstract





Highlights

- Current study is the first systematic review and meta-analysis that estimated seroprevalence of *Toxoplasma gondii* among the Iranian pregnant women as a high risk group during Jan 1990-June 2015.
- The review provided a comprehensive estimation of *T. gondii* seroprevalence in different geographical regions and provinces of Iran.
- Weighted overall prevalence of toxoplasmosis in pregnant women were obtained using random-effects model, which was estimated 41% (95% CI = 36% – 45%).
- The highest and the lowest seroprevalence of toxoplasmosis in five geographical zones of Iran were observed in South 53% (95% CI = 30% – 77%) and East 33% (95% CI = 23% – 42%), respectively.
- Multivariate analysis showed that there's a statistically significant correlation between toxoplasmosis and two risk factors including "Place of residence" (*P*= 0.005) and "Contact with cat" (*P*= 0.002).

Abstract

Toxoplasmosis is a common and serious parasitic disease with high prevalence and global distribution in human and other warm-blooded vertebrates. Though the infection of *Toxoplasma gondii* is usually asymptomatic in healthy people, it can lead to severe pathological effects to the fetus of infected women and in immunocompromised patients. So pinpointing the risk factors and control procedures are of important works among these populations. In order to reach this goal, we conducted a systematic review and meta-analysis to identify the seroprevalence rate of *T. gondii* infection among Iranian pregnant women population to achieve a comprehensive explanation of the disease condition in Iran for future use. English electronic databases (PubMed, Science Direct, Scopus, Ovid and Cochrane) and Persian language databases (Scientific Information Database, Iran Medex, Magiran and Iran Doc) were searched. Furthermore, the proceedings of Iranian parasitology congresses were explored manually. Our review resulted in a total of 50 publications meeting the inclusion criteria during Jan 1990-June 2015. Totally, 20221 women had been tested during this period of which 7724 women had seropositivity for IgG. According to results of heterogeneity test, either Der Simonian and Laird's random-effects method or Mantel-Haenszel's fixed-effects method were used to pool the estimations. Weighted overall prevalence of toxoplasmosis in pregnant women were obtained using random-effects model, which was estimated 41% (95% CI = 36% – 45%). Also IgG and IgM antibodies was obtained 38% (95% CI = 34% – 42%) and 4% (95% CI = 3% – 5%), respectively. The highest and the lowest seroprevalence of toxoplasmosis in five geographical zones of Iran were observed in South 53% (95% CI = 30% – 77%) and

East 33% (95% CI = 23% – 42%), respectively. In order to detect publication bias, Egger's regression test was done which revealed that publication bias might not have a significant influence on overall prevalence estimate (*P*=0.89). Multivariate analysis showed that there's a statistically significant correlation between toxoplasmosis and two risk factors including "Place of residence" (*P*= 0.005) and "Contact with cat" (*P*= 0.002). There was no significant difference between toxoplasmosis and the other surveyed risk factors. It is highly recommended to further study for the aim of better disease management and developing more efficient diagnostic tests.

Keywords: *Toxoplasma gondii*, Seroprevalence, Pregnant women, Iran, Systematic Review, Meta-analysis

1. Introduction

Toxoplasma gondii, an obligate intracellular parasite belonging to phylum Apicomplexa, is a zoonotic protozoan which can infect many warm-blooded vertebrates such as humans, livestock, birds as well as marine mammals, causing a global disease called toxoplasmosis. This is a neglected parasitic disease (NPD) out of five parasitic infections which have been classified as a concern to public health by CDC. Toxoplasmosis is highly prevalent among humans. This infection is reported to impress one-third of the world's population, specifically in developing and low-income countries (Robert-Gangneux and Darde, 2012). In the Middle East the infection rate is about 30-50%, being amongst the high prevalent regions worldwide (Daryani et al., 2014; Pappas et al., 2009).

The life cycle of *T. gondii* comprises of two hosts: the intermediate host like mammals and birds in which asexual stage occurs and felines (family: Felidae) as definitive host, where the sexual stage takes place. The infection in intermediate host is established through devouring on raw and undercooked flesh in which the infective cysts are formed, consuming food and water impregnated by oocysts released from the feces of infected cats, congenital transmission during pregnancy, organ transplantation as well as blood transfusion by infected persons (Robert-Gangneux and Darde, 2012). In the early acute phase of toxoplasmosis the tachyzoites (rapid-multiplying form) are prevailed. As the infection takes step to the chronic stage, the parasite encysts in many tissues such as muscle and brain cells (especially neurons and neuroglia) and will differentiate into bradyzoites (slow-multiplying form) which persist for many decades or for the life-time, resulting in the seropositivity of the host. Human is a dead-end host for toxoplasmosis. Approximately 80% of individuals suffering from chronic infection are asymptomatic (Sullivan and Jeffers, 2012). The high risk groups for toxoplasmosis are immunocompromised individuals and pregnant women (Ahmadpour et al., 2014; Gharavi et al., 2011; Saki et al., 2013; Saki et al., 2015; Saki et al., 2016). There have been investigations about correlation of this infection to mental disorders such as epilepsy (Ngoungou et al., 2015), bipolar disorder (Khademvatan et al., 2013) and schizophrenia (Khademvatan et al., 2014). Women usually do not manifest any signs for this infection during pregnancy. Upon maternal infection, fetus is likely to be exposed to the congenital transmission. The repetition and severity of vertical transmission and damage to the fetus is absolutely depending on the occurrence time of the infection during gestation period. The more the time is elapsed during pregnancy, the more parasites are able to pass through the placenta. The complications following the congenital transmission are focal necrosis and inflammation plus abnormalities such as brain and eye injuries. In case of such a serious infection, many sequelae may be established including deafness, mental retardation, hydrocephalus and microcephalus (Montoya and Remington, 2008). Additionally eye lesions as retinochoroiditis and its complications such as glaucoma, retinal detachment, etc. are ruling manifestations which could be observed in the infected fetus in any time point of the gestation period (Phan et al., 2008).

Despite of the abundant publications on toxoplasmosis in pregnant women from Iran, there has been no systematic review and meta-analysis describing the status of this congenital long-lasting infection in this country; hence, current systematic review and meta-analysis was aimed to evaluate the weighted seroprevalence of *T. gondii* infection and clarify the epidemiological characteristics of infection in pregnant women from Iran.

2. Methods

2.1. Search strategy

To evaluate the seroepidemiological status of *T. gondii* in Iranian pregnant women, we designed a systematic review based on screening the literature released online both in English and Persian languages. Five English databases (PubMed, Science Direct, Scopus, Ovid and Cochrane) and four Persian databases (Scientific Information Database (SID), Iran Medex, Magiran and Iran Doc) were surveyed for published papers from Jan 1990-June 2015. Furthermore proceedings of Iranian parasitology congresses were explored manually (Fig. 1). Current review was done using medical subject headings (MeSH) terms including: "*Toxoplasma*", "*Toxoplasma gondii*", "Toxoplasmosis", "*T. gondii*", "Prevalence", "Epidemiology", "Iran", "Islamic Republic of Iran", "Pregnancy" and "Pregnant women" alone or combined together.

2.2 Study selection and data extraction

According to inclusion criteria, the cross-sectional studies based on serological techniques in pregnant women that estimate the seroprevalence of *T. gondii* were included. To assess the eligibility and inclusion criteria, all papers were reviewed by two independent reviewers (MFR and SK). Investigations enclosing immunocompromised individuals like transplant recipients, HIV^+ and cancer patients were excluded. Those selected, were read carefully. The contradictions among studies were unraveled by discussion and consensus. Hereafter the desired data were gathered precisely using a data extraction form on the basis of title, province, geographical region (North, East, West, South and Center), sample size, positive cases (IgG^+, IgM^+ or both) and recruitment method. Data on risk factors such as place of residence, contact with cat, education level, raw meat consumption, the type of vegetable/fruit consumption, history of abortion and gestation age were also exploited. Present survey was performed based on PRISMA guideline (Preferred reporting items for systematic reviews and meta-analysis) (Moher et al., 2010).

2.3. Meta-analysis

The prevalence and its 95% confidence intervals (CI) of toxoplasmosis were estimated for each study. The forest plot was used to presenting results of meta-analyses which is exhibited estimates of prevalence and their confidence intervals of individual studies with the summary measure. Heterogeneity and inconsistency was evaluated using the Cochran's Q and I^2 statistics, respectively. Furthermore, funnel plot based on Egger's regression test was designed to assess small study effects and publication bias. According to results of heterogeneity test, either Der Simonian and Laird's random-effects method or Mantel-Haenszel's fixed-effects method were used to pool the estimations. Furthermore, we stratified the studies by regions (North, East, West, South and Center) of Iran country and overall prevalence was estimated in five different regions.

3. Results

Out of 2224 studies from the literature review, 50 had eligibility to be accounted in the systematic review and meta-analysis according to inclusion criteria, as shown in Fig. 1. The results of the literature search and characteristics of each study including, year of publication, sample size, region of country and incidence of selected outcome have been embedded in Table 1. In order to detect publication bias, Egger's regression test was done which revealed that publication bias might not have a significant influence on overall prevalence estimate (*P*=0.89) (Fig. 2). A total number of 20221 women were tested and evaluated for toxoplasmosis from the Jan 1990 till June 2015 in different regions of Iran. Weighted overall prevalence of toxoplasmosis in pregnant women were obtained using random-effects model, which was estimated 41% (95% CI = 36% – 45%). Seroprevalence of toxoplasmosis in five geographical zones of Iran was highly varied which the highest and lowest prevalence were observed in South 53% (95% CI = 30% –77%) and East 33% (95% CI = 23% – 42%), respectively (Table 2). The forest plot diagram of current meta-analysis is shown in Fig. 3. Three different types of diagnostic tests were used to evaluate *Toxoplasma* infection in women from Iran are including: enzyme-linked immunosorbent assay (ELISA), immunofluorescence assay (IFA) and chemiluminescence assay (CLIA). The most employed test to determine the infected pregnant women in different regions of Iran was ELISA (36 studies) followed by IFA (13 studies) and CLIA (1 study). Considering meta-analysis results, 7724 out of 20221 women in different geographical zones were seropositive in terms of IgG 38% (95% CI = 34% – 42%). All 50 studies estimated the prevalence of IgG^+, while in some articles IgM^+ (30 studies) and both

IgG^+/IgM^+ (16 studies) were surveyed which have been listed in Table 1. The seroprevalence of IgM^+ and both IgG^+/IgM^+ using the random effects model in Iranian pregnant women was 4% (95% CI = 3% – 5%) and 5% (95% CI = 3% – 7%), respectively that indicate acute stage of infection.

Comply with these well-reviewed studies and amongst the seven risk factors of interest, only two risk factors showed to be statistically significant in association between toxoplasmosis and pregnant women from Iran which consist of residence ($P= 0.005$) and contact with cat ($P= 0.002$) (Table 3). Rates of seropositivity of women in different geo-locations for *T. gondii* are shown in Fig. 4.

4. Discussion

This systematic review and meta-analysis approximates the prevalence of *T. gondii* infection in Iranian pregnant women, using data documented from the literature review, which have been obtained from different provinces. We searched 9 databases among which 50 records, 20221 pregnant women and 7724 IgG positive individuals were registered overall. Weighted overall prevalence of toxoplasmosis in pregnant women were obtained using random-effects model, which was estimated 41% (95% CI = 36% – 45%) (Table 2). There are many reports which have investigated the prevalence of the infection in pregnant women. For instance, studies in the Americas and Africa have represented more endemicity and higher prevalence of toxoplasmosis among pregnant women, ranging 6.1-77.5% and 25.3-75.2%, respectively. Also the seroprevalence rate in Europe and Asia has a range limit between 9.1-63.2% and 0.8-60.4%, respectively (Pappas et al., 2009).

The climate of various geographical zones is of critical parameters. While having an arid climate, Iran bears a broad weather condition in different regions. Our results showed that from five geographical areas of Iran the highest and lowest prevalence were observed in South 53% (95% CI = 30% –77%) and East 33% (95% CI = 23% – 42%), respectively (Table 2). Also among 27 provinces, Fars province had a prevalence of 77.2% and Sistan and Baluchestan had a prevalence of 22.7%, as the most and the least potent provinces, respectively (Fig. 4). Low prevalence in Sistan and Baluchestan province is justified with hot and dry climate in this region that reduce *T. gondii* oocysts survival in the environment; while in southern and northern part of Iran, due to vicinity to sea and existence of appropriate humidity which considered as suitable condition for oocysts sporulation, higher frequency of toxoplasmosis will be expected than other regions. Our data on the distribution of toxoplasmosis are in accordance with that of Rahimi et al. (Rahimi et al., 2015) and Sarvi et al. (Sarvi et al., 2015) that showed the prevalence of cat and cattle toxoplasmosis is much more frequent in southern regions of Iran than in northern parts. Considering contact with infected animals, these findings may justify the high seroprevalence of pregnant women in these regions. In our study, Mazandaran province stands second of the most prevalence of infection among pregnant women which in Daryani et al.'s (Daryani et al., 2014) on toxoplasmosis in Iranian general population and Sharif et al.'s (Sharif et al., 2015) on sheep and goat toxoplasmosis was mentioned to be top prevalent province; however, overall are in agreement with current results. As it was mentioned, the seroprevalence of IgM^+ and both IgG^+/IgM^+ using the random effects model in Iranian pregnant women was obtained 4% (95% CI = 3% – 5%) and 5% (95% CI = 3% – 7%), respectively. The high titer of IgM indicates the acute phase of the infection.

There are many risk factors on which the prevalence of *Toxoplasma* depends. A single risk factor may have little significance on the seroepidemiology of *T. gondii* on its own, but they can influence the epidemiologic scheme of the disease in different geo-locations. Some of the risk factors were not included in studies or they weren't assessed in some papers at all; but we exploited the important ones and statistically analyzed them in a broader area to reach more accurate evaluation of the status of related risk factors. In our results there were cases of seropositive pregnant women having a history of contact with a cat (*P*= 0.002). The native cats are one of the most important risk factors because they've got a potential to be the final host for *T. gondii*, thus releasing millions of oocysts and finally increasing the likelihood of disease transmission to women who contact with them. Individuals should be aware of cats in rural areas, because they traffic easily into the houses and farms, devouring on tissue cysts of infected small rodents, shedding large amount of oocysts indoors and outdoors by their feces. The oocysts sporulated in the environment (usually moist soil, warm and humid weather) can survive for months and even years (Rahimi et al., 2015). An integrated preventive control programs in cats should be adopted and continued as regular like extirpate of stray cats, periodic veterinary surveillance in household cats, etc. In addition to cats, the livestock (like cattle, sheep and goat) infected by the oocysts are also responsible for the seropositivity cases of individuals (Sarvi et al., 2015; Sharif et al., 2015). For example there were studies having reported the relationship between human toxoplasmosis and drinking goat's milk (Sacks et al., 1982). Hence women in contact with cats, livestock and other animals are at risk.

The "Place of residence" risk factor, also, was statistically meaningful in our results with the prevalence of 39% (28% – 49%) in urban districts and 43% (30% – 55%) in rural areas (*P* value=0.005) (Table 3). So the villagers lifestyle (direct contact with soil and livestock) could make this condition predictable. The third risk factor in our study was "gestational period" (*P*=0.35). We found out that the most positive cases i.e. women infected to toxoplasmosis were in their first trimester of the gestational period. It may be of great concern since the effect of toxoplasmosis infection is more dangerous to the fetus in the first trimester. Results from studies such as Jenum et al. (Jenum et al., 1998) and Andiappan et al. (Andiappan et al., 2014) is consistent with ours; while Almushait et al. (Almushait et al., 2014) and Zemene et al. (Zemene et al., 2012) determined the second trimester in which the most cases occur. We didn't find a statistically significant relation in case of "education" risk factor between toxoplasmosis and pregnant women in published data. Similarly, Ertug et al. (Ertug et al., 2005) reported no correlation between these two. In contrast, de Moura et al. (de Moura et al., 2013) showed that the more the level of education, the less the seroprevalence of *T. gondii*.

Risk factors like "raw meat consumption" and "kind of vegetable/fruit consumption" were not statistically significant in the results of our study. Alvardo-Esquivel et al. (Alvarado-Esquivel et al., 2006) showed that even consumption of meat with different origins could not have an important role to establish the infection in pregnant women. Agmas et al. (Agmas et al., 2015) and Cong et al. (Cong et al., 2015) indicated that the type of consumed fruit and vegetables is not an important risk parameter, according to our results. Finally the data disclosed that there is no significant correlation between "history of abortion" and women infected to toxoplasmosis (*P*=0.59) (Table 3).

It's noteworthy that this systematic review encountered some limitations, comprising: (1) lack of evaluate some of the related risk factors in majority of papers, (2) lack of a suitable method with invariant cut-off values, specificity and sensitivity among studies to determine infection, (3) absence of a standard questionnaire to gather requisite data in most of studies, and (4) lack of studies in some regions of the country. These limitations may have a crucial role on the epidemiologic aspects of this infection in pregnant women. It is highly important to adopt a particular detection method, instead of various assays with different sensitivities, specificities and cut-off values to obtain more precise results.

In conclusion, to the best of our knowledge, this is the first systematic review and meta-analysis providing a general view of the seroprevalence of *T. gondii* infection and its related risk factors in Iranian pregnant women. Regarding to Table 1 & Fig. 4., particularly in high risk areas many procedures such as improvement of hygiene in abattoirs, surveillance on food production units, programs on public health, etc. should be implemented to meet the standard health criteria and prevent the infection and determine the susceptible populations and involved risk factors. Furthermore, alerting pregnant women of transmission routes by means of compulsory educational programs as well as establishing regular screening procedures by an appropriate method is recommended. We propose to design a standard questionnaire containing the demographic data and related risk factors including: place of residence, education level, contact with cat, exposure to soil, history of raw meat consumption, the type of vegetable/fruit consumption, history of abortion and gestation period for future studies. Cracking the parasite seroepidemiology in all regions is also necessary to better recognize the pattern of infection in pregnant women.

Competing interests: The authors declare no conflict of interests.

Authors' contributions: MFR conceived the study; MFR, SK and FR designed the study protocol; MFR and SK searched the literature and extracted the data; FR and ASM analyzed and interpreted the data; HM and MFR wrote the manuscript; MFR, HM, SA and SK critically revised the manuscript. All authors read and approved the final manuscript.

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Tables and Figures legends:

Fig. 1. Flow diagram describing the study design process.

Fig. 2. Assessing the heterogeneity of all sample (A) population and subgroups (Region) (B).

Fig. 3. Forest plot diagram of the present systematic review and meta-analysis based on overall prevalence.

Fig. 4. Seroprevalence of *T. gondii* in Iranian pregnant women in different provinces.

Table 1. Baseline characteristics of included studies based on geographical regions.

Table 2. Subgroup analysis for comparison of prevalence in different geographical regions.

Table 3. Risk factors associated to seroprevalence for *T. gondii* in Iranian pregnant women.

Table 1. Baseline characteristics of included studies based on geographical regions

No.	Province	Sample size (n)	IgG$^+$ n (%)	IgM$^+$ n (%)	Both IgG$^+$ and IgM$^+$ n (%)	Overall prevalence n (%)	Method	Cut off value (Antibody titer)	References
North									
1.	Alborz	400	116 (29)	4 (1)	-	120 (30)	ELISA	>11 IU/ml	(Akhlaghi et al., 2014)
2.	Golestan	555	221 (39.8)	19 (3.4)	8 (1.4)	232 (41.8)	ELISA	>1.1 IU/ml	(Sharbatkhori et al., 2014)
3.	Mazandaran	612	435 (71.07)	-	-	435 (71.07)	ELISA	-	(Saffar et al., 1999)
4.	Mazandaran	1057	739 (69.91)	54 (5.10)	-	793 (75.02)	ELISA	>11 IU/ml	(Panah et al., 2013)
5.	Mazandaran	175	106 (60.6)	-	-	106 (60.6)	ELISA	>11 IU/ml	(Kalantari et al., 2014)
6.	Mazandaran	289	170 (58.8)	7 (2.4)	4 (1.4)	181 (62.6)	ELISA	>1.1 IU/ml	(Hoseini et al., 2014)
7.	Mazandaran	50	28 (56)	-	-	28 (56)	CLIA	-	(Elahian Firouz et al., 2014)
8.	North Khorasan	211	65 (30.8)	3 (1.4)	3 (1.4)	65 (30.8)	ELISA	-	(Jalai et al., 2013)
9.	North Khorasan	350	110 (31.42)	12 (3.42)	-	122 (34.8)	ELISA	-	(Hashemi et al., 2015)
10.	Qazvin	255	160 (62.75)	-	-	160 (62.75)	IFA	≥1:20	(Eskandarian, 2009)
11.	Qazvin	200	58 (29)	4 (2)	-	62 (31)	ELISA	>11 IU/ml	(Tabatabaie et al., 2015)
12.	Tehran	140	48 (34.3)	1 (0.7)	9 (6.4)	49 (35)	ELISA	>1.1 IU/ml	(Noorbakhsh et al., 2002)

13.	Tehran	785	244 (31.1)	-	-	244 (31.1)	ELISA	>1.1 IU/ml	(Ghasemloo et al., 2014)
South									
14.	Bushehr	365	138 (37.8)	21 (5.7)	3 (0.82)	159 (43.6)	ELISA	-	(Fouladvand and Jafari, 2001)
15.	Fars	320	247 (77.2)	-	-	247 (77.2)	IFA	≥1:16	(Alleyassin et al., 1990)
16.	Hormozgan	418	143 (34.21)	33 (7.89)	10 (2.39)	166 (39.71)	ELISA	IgG >40 EU/ml ; IgM >10%	(Setoodeh et al., 2003)
Center									
17.	Chaharmahal and Bakhtyari	394	108 (27.4)	-	-	108 (27.4)	IFA	≥1:50	(Manouchehri Naeini et al., 2004)
18.	Chaharmahal and Bakhtyari	384	106 (27.6)	-	-	106 (27.6)	IFA	≥1:20	(Manouchehri-Naeini et al., 2006)
19.	Isfahan	317	98 (30.9)	4 (1.26)	-	102 (32.17)	IFA	≥1:20	(Talari et al., 2000)
20.	Isfahan	270	72 (26.6)	15 (5.6)	-	87 (32.2)	IFA	≥1:20	(Talari et al., 2003)
21.	Isfahan	127	67 (52.76)	-	-	67 (52.76)	IFA	≥1:20	(Ghasemi et al., 2012)
22.	Isfahan	798	341 (42.7)	5 (0.63)	-	346 (43.35)	ELISA	-	(Rasti et al., 2014)
23.	Isfahan	80	30 (37.5)	3 (3.8)	-	33 (41.25)	ELISA	>1.1 IU/ml	(Josheghani et al., 2015)
24.	Markazi	308	117 (38)	3 (0.98)	-	120 (38.9)	ELISA	-	(Vakil et al., 2014)
25.	Qom	600	257 (42.8)	-	-	257 (42.8)	ELISA	>50 IU/ml	(Mardani and Keshavarz, 2004)
26.	Qom	200	76 (38)	11 (5.5)	-	87 (43.5)	ELISA	>0.343	(Akhlaghi et al., 2013)
27.	Yazd	181	58 (32)	-	-	58 (32)	ELISA	>30 IU/ml	(AnvariTafti and Ghafourzadeh, 2014)

West									
28.	East Azerbaijan	300	79 (26.3)	1 (0.3)	-	80 (26.6)	ELISA	>30 IU/ml	(Dalimiasl and Arshad, 2012)
29.	East Azerbaijan	391	215 (54.99)	65 (16.62)	65 (16.62)	280 (71.61)	IFA	≥1:100	(Rajaii et al., 2015)
30.	West Azerbaijan	346	98 (28.32)	-	-	98 (28.32)	ELISA	>1.1 IU/ml	(Alizadeh et al., 2012)
31.	West Azerbaijan	177	61 (34.46)	1 (0.56)	-	62 (35.02)	ELISA	-	(Abdolah-nezhad et al., 2015)
32.	Hamadan	576	193 (33.5)	-	-	193 (33.5)	IFA	≥1:20	(Fallah et al., 2008)
33.	Hamadan	2523	681 (26.99)	51 (2.02)	-	732 (29.01)	ELISA	≥1:200	(Hamidi et al., 2015)
34.	Ilam	553	247 (44.8)	-	-	247 (44.8)	IFA	≥1:10	(Abdi et al., 2008)
35.	Lorestan	331	95 (28.7)	35 (10.5)	35 (10.5)	130 (39.2)	ELISA	>1:10 IU/ml	(Cheraghipour et al., 2010a)
36.	Lorestan	390	121 (31)	29 (7.4)	29 (7.4)	121 (31)	ELISA	>1:10 IU/ml	(Cheraghipour et al., 2010b)
37.	Lorestan	721	250 (34.7)	65 (9)	-	315 (43.68)	ELISA	>1:10 IU/ml	(Nejad et al., 2011)
38.	Lorestan	496	154 (31.04)	35 (7.05)	35 (7.05)	154 (31.04)	ELISA	>1:10 IU/ml	(Fazeli et al., 2013)
39.	Khuzestan	79	28 (35.4)	-	-	28 (35.4)	ELISA	-	(Sohrabi et al., 2007)
40.	Khuzestan	501	137 (27.3)	7 (1.39)	3 (0.5)	147 (29.35)	ELISA	-	(Yad Yad et al., 2014)
41.	Kermanshah	495	162 (32.7)	-	-	162 (32.7)	IFA	≥1:50	(Athari et al., 1994)
42.	Kurdistan	201	54 (27)	24 (12)	33 (16.5)	111 (55)	ELISA	-	(Parvizpour et al., 2010)
43.	Zanjan	500	186 (37.2)	7 (1.4)	4 (0.8)	189 (37.8)	ELISA	-	(Hajsoleimani et al., 2012)

East									
44.	Kerman	203	98 (48.3)	-	-	98 (48.3)	IFA	≥1:16	(Keshavarz-Valian and Zare-Ranjbar, 1992)
45.	Razavi Khorasan	367	147 (40.05)	-	-	147 (40.05)	ELISA	-	(Yazdanfar et al., 2012)
46.	Razavi Khorasan	419	144 (34.4)	27 (6.44)	27 (6.44)	144 (34.4)	ELISA	>1.1 IU/ml	(Babaie et al., 2013)
47.	South Khorasan	205	78 (38.04)	-	-	78 (38.04)	ELISA	-	(PashaieNaghadah et al., 2012)
48.	Sistan and Baluchistan	200	54 (27)	-	-	54 (27)	IFA	≥1:20	(Sharifi-Mood et al., 2004)
49.	Sistan and Baluchistan	221	65 (29.41)	3 (1.4)	3 (1.4)	68 (30.8)	ELISA	>1.1 IU/ml	(Ebrahimzadeh et al., 2013)
50.	Sistan and Baluchistan	185	19 (10.3)	1 (0.55)	1 (0.55)	19 (10.3)	ELISA	>1.1 IU/ml	(Mousavi et al., 2014)

Table 2. Subgroup analysis for comparison of prevalence in different geographical regions

Region	**No. of studies**	**Prevalence 95%CI**	I^2**%**	**Heterogeneity test**		**Egger test**	
				Q	*P*	t	*P*
North	13	0.48 (0.37 – 0.59)	98.61	864.67	< 0.001	-1.18	0.26
South	3	0.53 (0.30 – 0.77)	98.66	149.47	< 0.001	-0.69	0.61
Center	11	0.37 (0.33 – 0.42)	87.81	82.05	< 0.001	0.18	0.86
West	16	0.38 (0.32 – 0.43)	96.40	416.19	< 0.001	1.46	0.17
East	7	0.33 (0.23 – 0.42)	95.41	130.77	< 0.001	1.52	0.19
Overall	50	0.41 (0.36 – 0.45)	97.85	2276.3	< 0.001	0.14	0.89

Test for heterogeneity between sub-groups:

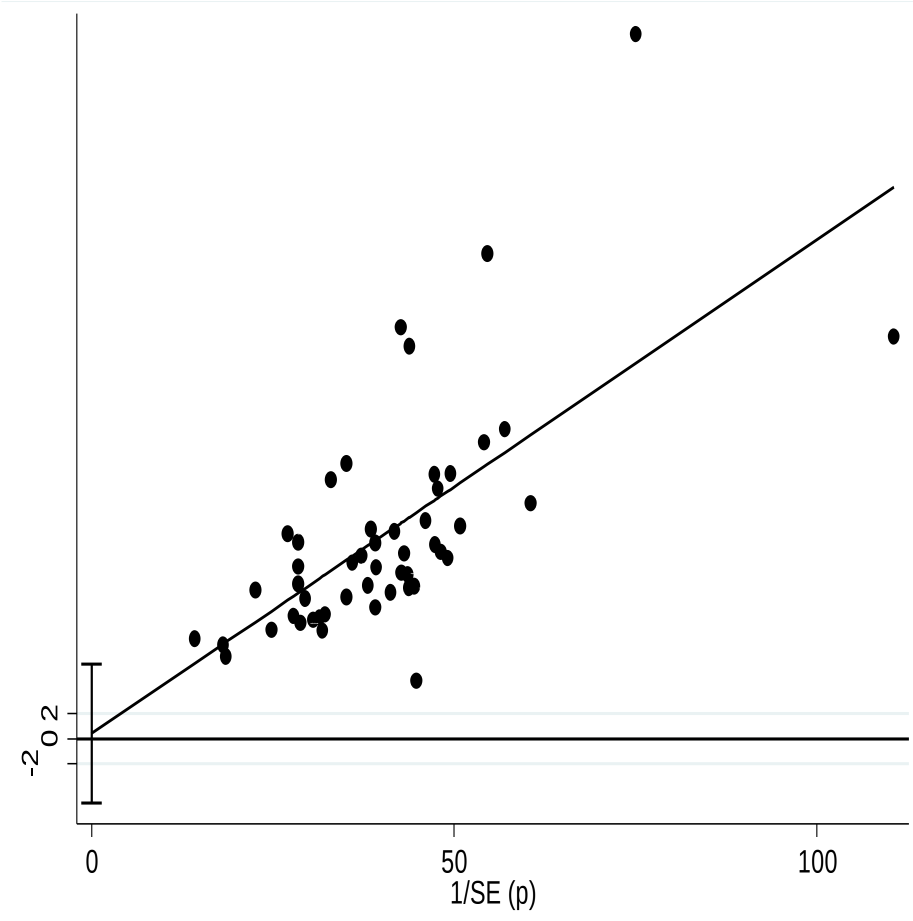
Q: 5.93 **P-value: 0.20**

Table 3. Risk factors associated to seroprevalence for *T. gondii* in Iranian pregnant women

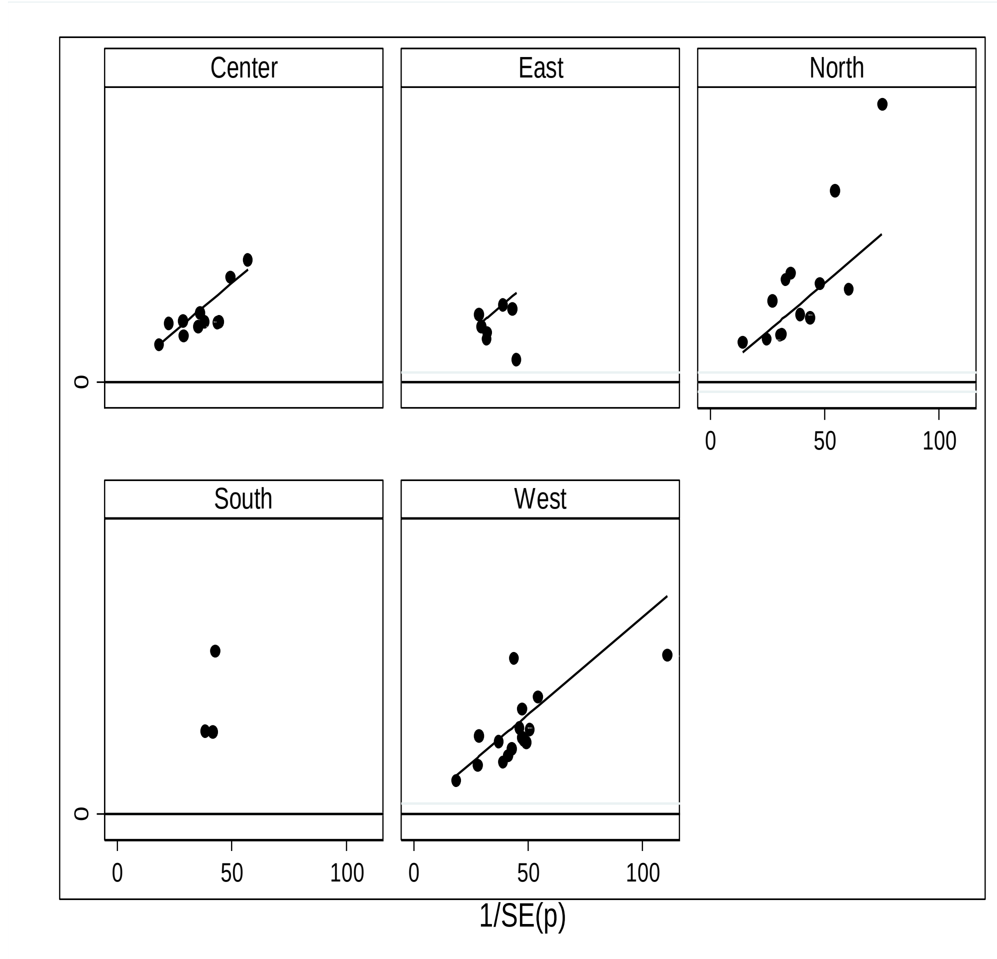
Demographic factors	No. of studies	Categorize	Total individuals	Positive cases	Overall prevalence (%)	*P*-value	References
Residence	9	Urban	1608	663	0.39 (0.28 – 0.49)	0.005	(Hajsoleimani et al., 2012; Hoseini et al., 2014; Jalai et al., 2013; Kalantari et al., 2014; Keshavarz-Valian and Zare-Ranjbar, 1992; Mousavi et al., 2014; Nejad et al., 2011; Sharbatkhori et al., 2014; Yad Yad et al., 2014)
		Rural	1732	613	0.43 (0.30 – 0.55)		
Contact with cat	10	Yes	984	360	0.38 (0.33 – 0.43)	0.002	(AnvariTafti and Ghafourzadeh, 2014; Athari et al., 1994; Babaie et al., 2013; Dalimiasl and Arshad, 2012; Ebrahimzadeh et al., 2013; Fallah et al., 2008; Jalai et al., 2013; Mousavi et al., 2014; Nejad et al., 2011; Parvizpour et al., 2010)
		No	2526	789	0.27 (0.18 – 0.36)		
Education	8	Uneducated	220	75	0.35 (0.23 – 0.49)	0.81	(AnvariTafti and Ghafourzadeh, 2014; Ebrahimzadeh et al., 2013; Fallah et al., 2008; Hajsoleimani et al., 2012; Kalantari et al., 2014; Mousavi et al., 2014; Nejad et al., 2011; Sharbatkhori et al., 2014)
		Primary, secondary and Post-secondary level (till Diploma)	2412	872	0.35 (0.26 – 0.44)		
		University level	482	176	0.33 (0.21 – 0.44)		
Raw meat consumption	4	Yes	525	174	0.30 (0.08 – 0.52)	0.58	(AnvariTafti and Ghafourzadeh, 2014; Ebrahimzadeh et al., 2013; Mousavi et al., 2014; Parvizpour et al., 2010)
		No	263	82	0.31 (0.13 – 0.49)		
Kind of vegetable/fruits consumption	4	Water	500	176	0.39 (0.13 – 0.65)	0.78	(Ebrahimzadeh et al., 2013; Kalantari et al., 2014; Mousavi et al., 2014; Parvizpour et al., 2010)
		detergent	282	128	0.40 (0.20 – 0.61)		
History of abortion	9	Yes	1050	409	0.41 (0.34 – 0.47)	0.59	(AnvariTafti and Ghafourzadeh, 2014; Athari et al., 1994; Babaie et al., 2013; Ebrahimzadeh et

		No	2118	839	0.42 (0.34 – 0.51)		al., 1994; Babaie et al., 2013; Ebrahimzadeh et al., 2013; Eskandarian, 2009; Hajsoleimani et al., 2012; Kalantari et al., 2014; Nejad et al., 2011; Parvizpour et al., 2010)
Gestational age	2	First trimester	375	171	0.46 (0.41 – 0.51)	0. 35	(Hajsoleimani et al., 2012; Sharbatkhori et al., 2014)
		Second trimester	311	128	0.41 (0.36 – 0.46)		
		Third trimester	369	130	0.35 (0.30 – 0.40)		

Figure2



A.



B.

Figure3

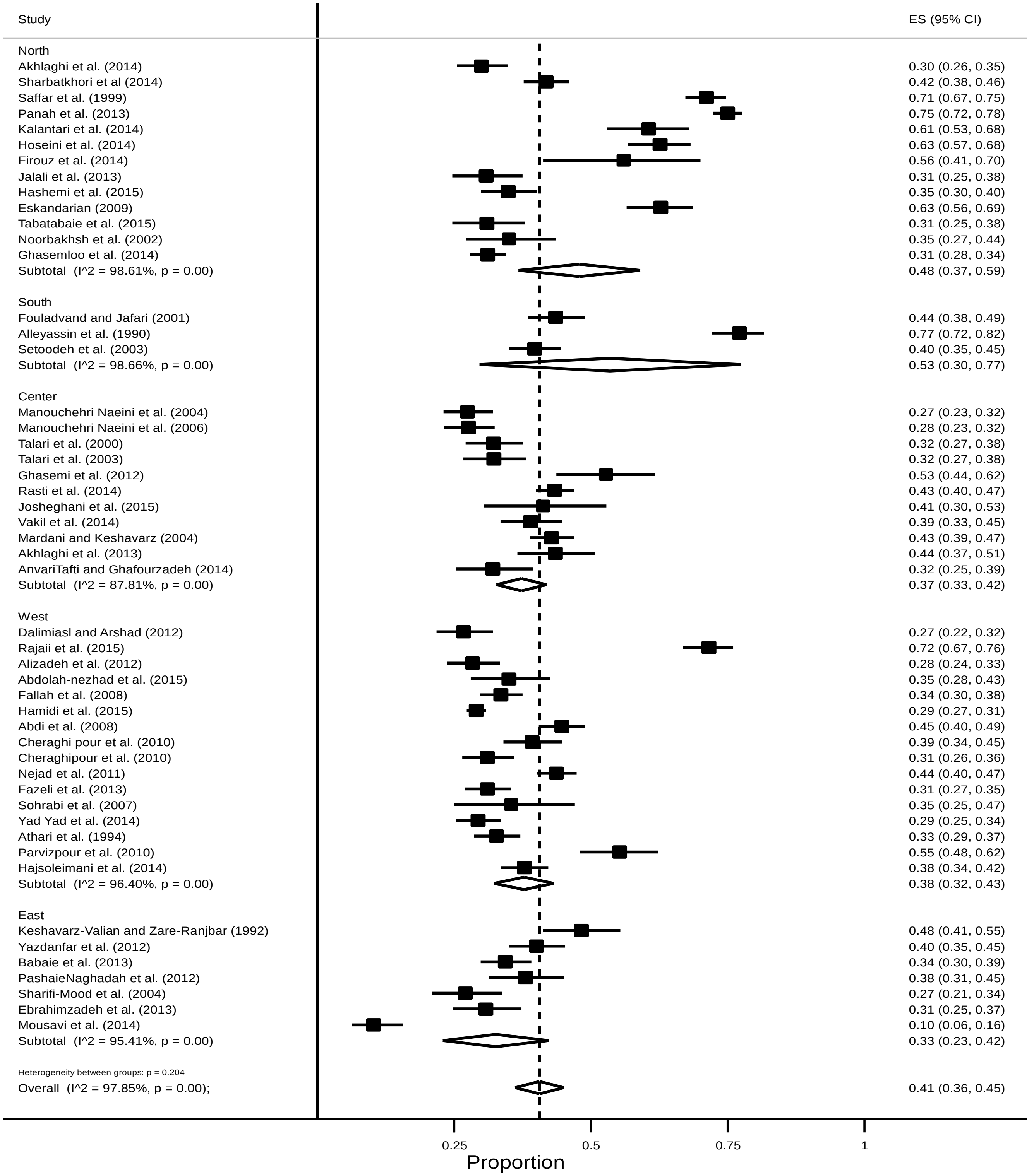
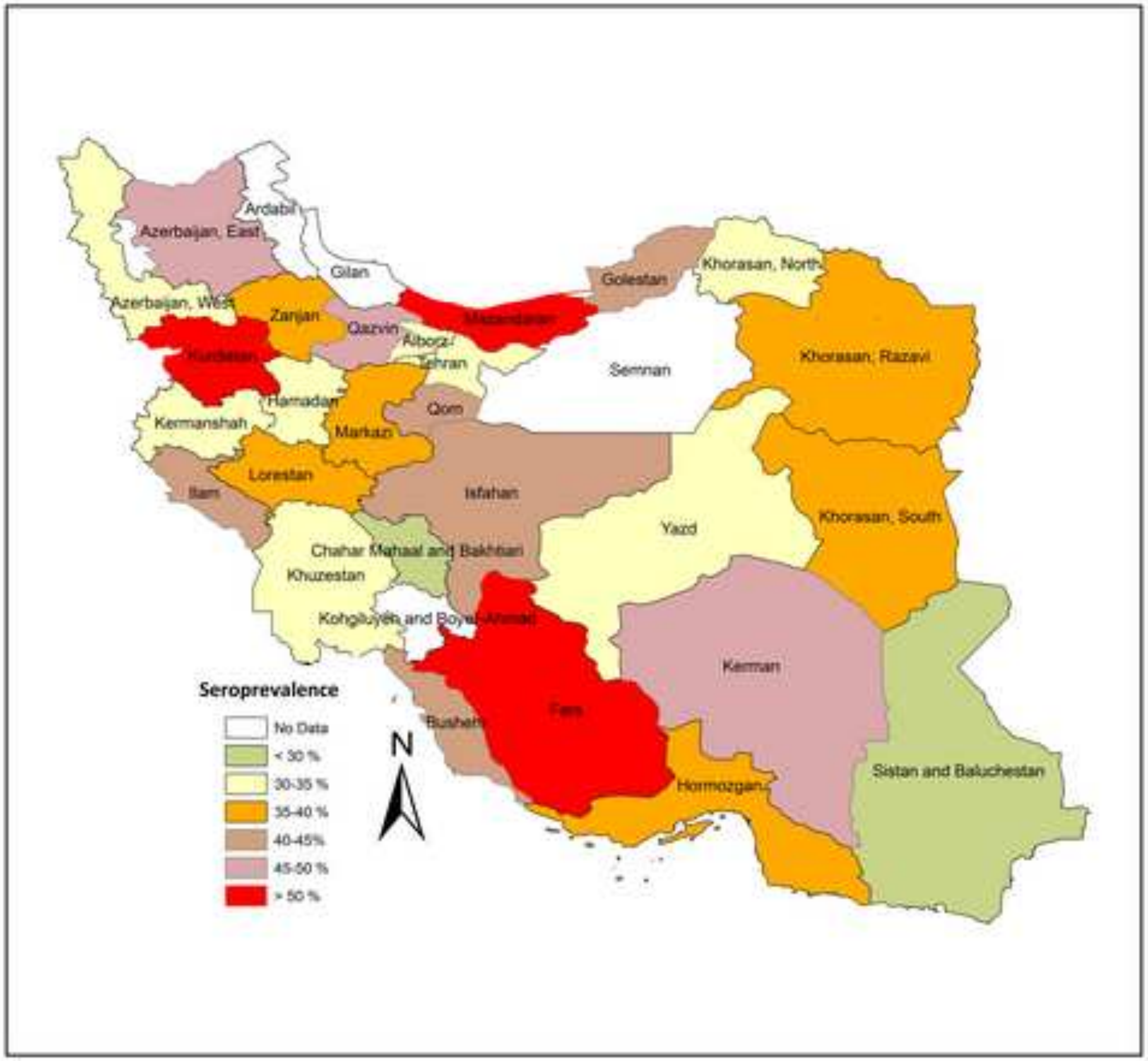
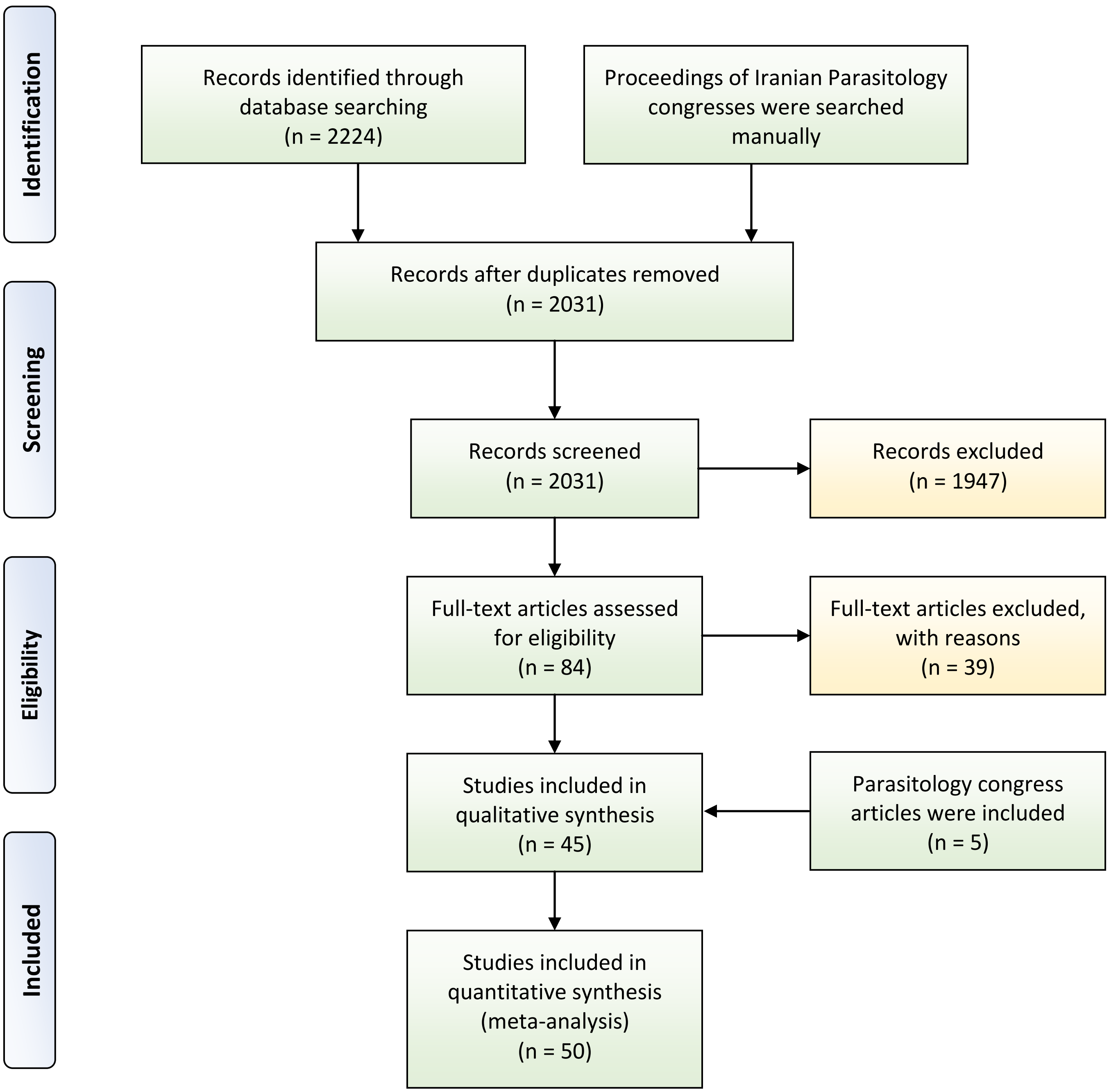

Study
ES (95% CI)
North
Akhlaghi et al. (2014) 0.30 (0.26, 0.35)
Sharbatkhori et al (2014) 0.42 (0.38, 0.46)
Saffar et al. (1999) 0.71 (0.67, 0.75)
Panah et al. (2013) 0.75 (0.72, 0.78)
Kalantari et al. (2014) 0.61 (0.53, 0.68)
Hoseini et al. (2014) 0.63 (0.57, 0.68)
Firouz et al. (2014) 0.56 (0.41, 0.70)
Jalali et al. (2013) 0.31 (0.25, 0.38)
Hashemi et al. (2015) 0.35 (0.30, 0.40)
Eskandarian (2009) 0.63 (0.56, 0.69)
Tabatabaie et al. (2015) 0.31 (0.25, 0.38)
Noorbakhsh et al. (2002) 0.35 (0.27, 0.44)
Ghasemloo et al. (2014) 0.31 (0.28, 0.34)
Subtotal (I^2 = 98.61%, p = 0.00) 0.48 (0.37, 0.59)
South
Fouladvand and Jafari (2001) 0.44 (0.38, 0.49)
Alleyassin et al. (1990) 0.77 (0.72, 0.82)
Setoodeh et al. (2003) 0.40 (0.35, 0.45)
Subtotal (I^2 = 98.66%, p = 0.00) 0.53 (0.30, 0.77)
Center
Manouchehri Naeini et al. (2004) 0.27 (0.23, 0.32)
Manouchehri Naeini et al. (2006) 0.28 (0.23, 0.32)
Talari et al. (2000) 0.32 (0.27, 0.38)
Talari et al. (2003) 0.32 (0.27, 0.38)
Ghasemi et al. (2012) 0.53 (0.44, 0.62)
Rasti et al. (2014) 0.43 (0.40, 0.47)
Josheghani et al. (2015) 0.41 (0.30, 0.53)
Vakil et al. (2014) 0.39 (0.33, 0.45)
Mardani and Keshavarz (2004) 0.43 (0.39, 0.47)
Akhlaghi et al. (2013) 0.44 (0.37, 0.51)
AnvariTafti and Ghafourzadeh (2014) 0.32 (0.25, 0.39)
Subtotal (I^2 = 87.81%, p = 0.00) 0.37 (0.33, 0.42)
West
Dalimiasl and Arshad (2012) 0.27 (0.22, 0.32)
Rajaii et al. (2015) 0.72 (0.67, 0.76)
Alizadeh et al. (2012) 0.28 (0.24, 0.33)
Abdolah-nezhad et al. (2015) 0.35 (0.28, 0.43)
Fallah et al. (2008) 0.34 (0.30, 0.38)
Hamidi et al. (2015) 0.29 (0.27, 0.31)
Abdi et al. (2008) 0.45 (0.40, 0.49)
Cheraghi pour et al. (2010) 0.39 (0.34, 0.45)
Cheraghipour et al. (2010) 0.31 (0.26, 0.36)
Nejad et al. (2011) 0.44 (0.40, 0.47)
Fazeli et al. (2013) 0.31 (0.27, 0.35)
Sohrabi et al. (2007) 0.35 (0.25, 0.47)
Yad Yad et al. (2014) 0.29 (0.25, 0.34)
Athari et al. (1994) 0.33 (0.29, 0.37)
Parvizpour et al. (2010) 0.55 (0.48, 0.62)
Hajsoleimani et al. (2014) 0.38 (0.34, 0.42)
Subtotal (I^2 = 96.40%, p = 0.00) 0.38 (0.32, 0.43)
East
Keshavarz-Valian and Zare-Ranjbar (1992) 0.48 (0.41, 0.55)
Yazdanfar et al. (2012) 0.40 (0.35, 0.45)
Babaie et al. (2013) 0.34 (0.30, 0.39)
PashaieNaghadah et al. (2012) 0.38 (0.31, 0.45)
Sharifi-Mood et al. (2004) 0.27 (0.21, 0.34)
Ebrahimzadeh et al. (2013) 0.31 (0.25, 0.37)
Mousavi et al. (2014) 0.10 (0.06, 0.16)
Subtotal (I^2 = 95.41%, p = 0.00) 0.33 (0.23, 0.42)
Heterogeneity between groups: p = 0.204
Overall (I^2 = 97.85%, p = 0.00); 0.41 (0.36, 0.45)
0.25
0.5
0.75
1
Proportion

Figure4


Ardabil
Azerbaijan, East
Gilan
Golestan
Khorasan, North
Azerbaijan, West
Zanjan
Qazvin
Mazandaran
Alborz
Tehran
Kurdistan
Semnan
Khorasan, Razavi
Hamadan
Qom
Kermanshah
Markazi
Lorestan
Ilam
Isfahan
Yazd
Khorasan, South
Chahar Mahaal and Bakhtiari
Khuzestan
Kohgiluyeh and Boyer-Ahmad
Kerman
Seroprevalence
No Data
< 30 %
30-35 %
35-40 %
40-45%
45-50 %
> 50 %
Fars
Bushehr
N
Hormozgan
Sistan and Baluchestan


Identification
Screening
Eligibility
Included
Records identified through database searching (n = 2224)
Proceedings of Iranian Parasitology congresses were searched manually
Records after duplicates removed (n = 2031)
Records screened (n = 2031)
Records excluded (n = 1947)
Full-text articles assessed for eligibility (n = 84)
Full-text articles excluded, with reasons (n = 39)
Studies included in qualitative synthesis (n = 45)
Parasitology congress articles were included (n = 5)
Studies included in quantitative synthesis (meta-analysis) (n = 50)