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# Toxoplasmosis in Blood Donors: A Systematic Review and Meta-Analysis

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ABSTRACT

Transfusion-transmissible infections include pathogens that may cause severe and debilitating diseases. Toxoplasmosis is a cosmopolitan neglected parasitic infection that can lead to severe complications including death in immune-compromised patients or following infection in utero. Multiple studies have demonstrated the transmission of *Toxoplasma gondii* by blood transfusion. The objective of this review was to comprehensively assess the seroprevalence rate of *Toxoplasma* in blood donors from a worldwide perspective. Seven electronic databases (PubMed, Science Direct, Web of Science, Scopus, Cochrane, Ovid, and Google Scholar) were searched using medical subject headings terms. A total of 43 records met the inclusion criteria in which 20,964 donors were tested during the period from January 1980 to June 2015. The overall weighted prevalence of exposure to toxoplasmosis in blood donors was 33% (95% confidence interval [CI], 28%-39%). The seroprevalences of immunoglobulin (Ig)M and both IgG and IgM antibodies were 1.8% (95% CI, 1.1%-2.4%) and 1.1% (95% CI, 0.3%-1.8%), respectively. The highest and the lowest seroprevalences of toxoplasmosis were observed in Africa (46%; 95% CI, 14%-78%) and in Asia (29%; 95% CI, 23%-35%), respectively. Brazil (75%) and Ethiopia (73%) were identified as countries with high seroprevalence. Because positive serology does not imply infectiousness and because seroprevalence is high in some nations, a positive serology test result alone cannot be used as an effective method for donor screening. Future research for methods to prevent transfusion-transmitted toxoplasmosis may derive benefit from studies conducted in areas of high endemicity.



**Contents**



Although the safety of the blood supply is always under strict control and surveillance, concerns remain regarding transfusion-transmitted diseases [1]. *Toxoplasma gondii* is a transfusion-transmissible infection [2–3]. This unicellular protozoan parasite belongs to the phylum Apicomplexa which is adapted to humans and warm-blooded animals.

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Toxoplasmosis affects one-third of the world's population with prevalence rates in developing countries varying between 30% and 60%. Toxoplasmosis predominantly occurs in tropical and subtropical regions [4–5]. *T gondii* needs 2 hosts to complete its life cycle: the Felidae family as the definitive host and vertebrates like birds and mammals as an intermediate host [5]. The consumption of oocyst-contaminated water, ingestion of raw/undercooked meat containing tissue cysts, and congenital transmission are the main routes of transmission. *Toxoplasma* infection can also be transmitted by blood transfusion and organ transplantation [2,6–12,64].

In general, toxoplasmosis is asymptomatic in immune-competent individuals, whereas severe infection may occur in immune-compromised patients such as transplant recipients, HIV-positive individuals, and cancer patients. In these patients, acute infection or reactivation of latent toxoplasmosis can cause complications with poor prognosis including encephalitis, brain abscess, myocarditis, and chorioretinitis. Acute or recrudescent infections may result in death [13–14].

Transfusion-transmitted toxoplasmosis from asymptomatic donors remains a concern for patients receiving blood transfusions, particularly among immune-suppressed recipients. Because *T gondii* infection is lifelong and most infected individuals are without symptoms, testing is required to identify toxoplasmosis in blood donors [15–20]. During recent years, numerous articles have been published about the epidemiology of toxoplasmosis in blood donors worldwide. The absence of a comprehensive study encouraged us to conduct a global systematic review and meta-analysis to assess the prevalence of antibodies to toxoplasmosis in blood donors.

## Methods

### *Search Strategy*

To evaluate the prevalence of positive serologic test results for toxoplasmosis among blood donors, we performed a systematic review screening literature published online and limited to English full text or abstracts. Records identified through 7 databases (PubMed, Science Direct, Web of Science, Scopus, Cochrane, Ovid, and Google Scholar) and related published articles were restricted to the those published from January 1980 to June 2015 (Fig 1). The current research was performed using medical subject headings terms and a combination of several keywords including *Toxoplasma*, *Toxoplasma gondii*, *Toxoplasmosis*, *T. gondii*, *Prevalence*, *Epidemiology*, *Blood donor*, *Transfusion*, and *Blood pack*.

### *Study Selection and Data Extraction*

We included cross-sectional and case-control studies that estimated the prevalence of toxoplasmosis based on serological techniques in blood donors and blood supplies. To evaluate the eligibility for inclusion, articles were reviewed by 2 independent reviewers. Studies that focused on toxoplasmosis in groups unrelated to blood donors were excluded. Then, the desired data were recorded using a data extraction form which included title, year of publication, country, sample size, number of seropositive cases (immunoglobulin [Ig]$G^+$, $IgM^+$, or both $IgG^+$ and $IgM^+$), and diagnostic methods. Data on risk factors such as residence, sex, contact with animals, education level, raw or undercooked meat consumption, unwashed vegetables or fruits

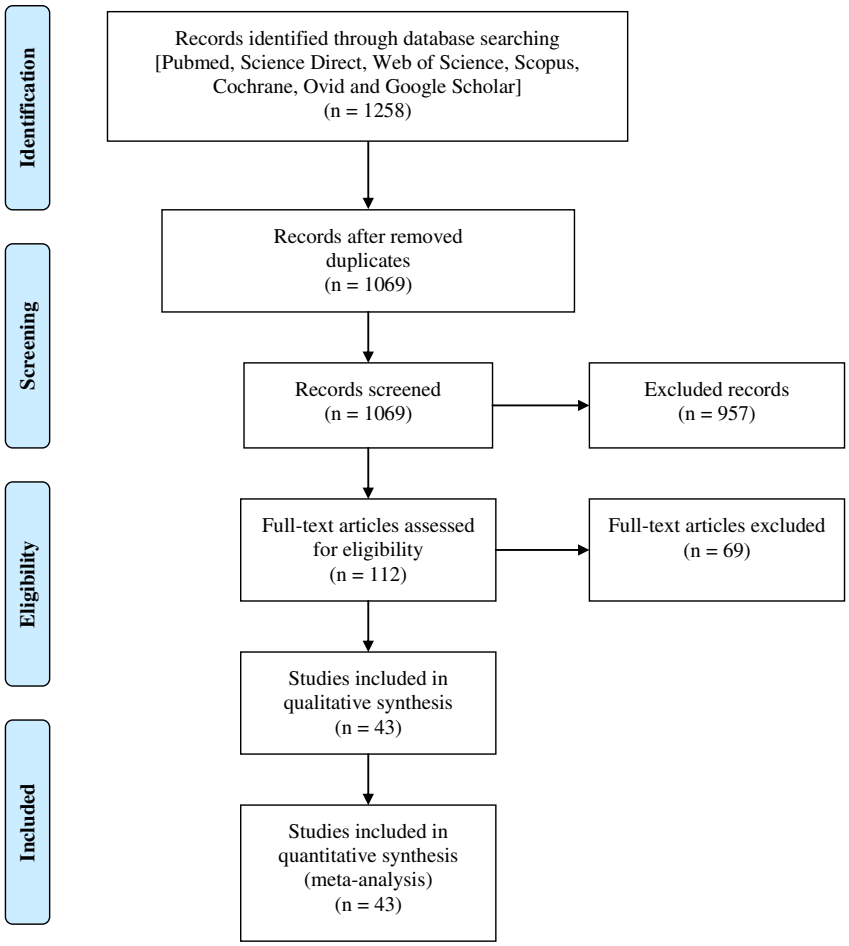


**Fig 1.** Flowchart describing the study design process.

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

| No. | Country | Year | Study population (n) | Seroprevalence, n (%) | | | Total prevalence | Method | Reference |
|---|---|---|---|---|---|---|---|---|---|
| | | | | IgG | IgM | IgG & IgM | | | |
| Asia | | | | | | | | | |
| 1 | Saudi Arabia | 1993 | 1000 | 521 (52.1) | 15 (1.5) | – | 536 (53.6) | ELISA & IHAT | [28] |
| 2 | Saudi Arabia | 1993 | 150 | 74 (49.3) | 3 (2) | – | 77 (51.33) | IFAT | [29] |
| 3 | Saudi Arabia | 1994 | 784 | 294 (37.5) | – | – | 294 (37.5) | IHAT | [30] |
| 4 | Jordan | 2000 | 931 | 387 (41.5) | – | – | 387 (41.5) | IFAT | [31] |
| 5 | Thailand | 2000 | 345 | 14 (4.05) | 15 (4.34) | – | 29 (8.4) | ELISA | [32] |
| 6 | Malaysia | 2002 | 203 | 57 (28.1) | – | – | 57 (28.1) | ELISA | [33] |
| 7 | Jordan | 2004 | 1500 | 532 (35.5) | – | – | 532 (35.5) | ELISA | [34] |
| 8 | China | 2005 | 680 | 49 (7.2) | 2 (0.29) | – | 51 (7.5) | ELISA | [35] |
| 9 | India | 2007 | 1000 | 203 (20.3) | 18 (1.8) | – | 221 (22.1) | ELISA | [27] |
| 10 | India | 2010 | 493 | 240 (48.6) | 9 (1.8) | 16 (3.2) | 265 (53.7) | ELISA | [36] |
| 11 | Iran | 2010 | 250 | 132 (52.8) | 9 (3.6) | – | 141 (56.4) | ELISA | [37] |
| 12 | Iraq | 2010 | 91 | 21 (23.07) | 1 (1.09) | 4 (4.39) | 26 (28.6) | ELISA | [38] |
| 13 | Iraq | 2010 | 464 | 102 (22) | – | – | 102 (22) | LAT | [39] |
| 14 | Saudi Arabia | 2010 | 100 | 40 (40) | – | – | 40 (40) | ELISA | [40] |
| 15 | Iraq | 2011 | 258 | 38 (14.72) | 15 (5.81) | – | 53 (20.54) | ELISA | [41] |
| 16 | China | 2012 | 898 | 44 (4.9) | – | – | 44 (4.9) | ELISA | [42] |
| 17 | Taiwan | 2012 | 1783 | 161 (9) | 0 (0) | 5 (0.28) | 166 (9.3) | EIA | [43] |
| 18 | China | 2013 | 864 | 44 (5.1) | – | – | 44 (5.1) | ELISA | [44] |
| 19 | India | 2013 | 90 | 21 (23.33) | – | – | 21 (23.33) | ELISA | [45] |
| 20 | Iran | 2014 | 1480 | 182 (12.3) | 81 (5.47) | 23 (1.6) | 286 (19.3) | EIA | [46] |
| 21 | Iran | 2014 | 250 | 58 (23.2) | 1 (0.4) | – | 59 (23.6) | ELISA | [47] |
| 22 | Iran | 2014 | 223 | 86 (38.6) | 1 (0.45) | – | 87 (39) | ELISA | [48] |
| 23 | Iran | 2014 | 375 | 94 (25) | 0 (0) | 0 (0) | 94 (25) | ELISA | [49] |
| 24 | Iran | 2014 | 235 | 80 (34.04) | 4 (1.71) | – | 84 (35.7) | ELISA | [50] |
| 25 | Iraq | 2014 | 400 | 121 (30.25) | 10 (2.5) | – | 131 (32.75) | ELISA | [51] |
| 26 | Iran | 2015 | 500 | 144 (28.8) | 11 (2.2) | 5 (1) | 160 (32) | ELISA | [15] |
| Europe | | | | | | | | | |
| 27 | Czech Republic | 1998 | 663 | 213 (32.1) | 16 (2.4) | – | 229 (34.53) | IFAT | [52] |
| 28 | Turkey | 2000 | 520 | 85 (16.3) | 15 (2.88) | – | 100 (19.2) | ELISA | [53] |
| 29 | Turkey | 2006 | 385 | 78 (20.25) | 9 (2.33) | – | 87 (22.59) | ELISA | [16] |
| 30 | Turkey | 2006 | 414 | 176 (42.5) | – | – | 176 (42.5) | SFDT | [54] |
| Africa | | | | | | | | | |
| 31 | Kenya | 1983 | 322 | 174 (54) | – | – | 174 (54) | HA | [55] |
| 32 | Egypt | 2009 | 260 | 155 (59.6) | – | – | 155 (59.6) | ELISA | [17] |
| 33 | Sudan | 2012 | 534 | 235 (44) | – | – | 235 (44) | LAT | [56] |
| 34 | Ethiopia | 2013 | 101 | 71 (70.29) | 3 (2.97) | – | 74 (73.26) | ELISA | [57] |
| 35 | Namibia | 2014 | 312 | 2 (0.64) | 0 (0) | 1 (0.32) | 3 (0.96) | ELISA | [58] |
| America | | | | | | | | | |
| 36 | Brazil | 2003 | 160 | 120 (75) | – | – | 120 (75) | EIA | [59] |
| 37 | Mexico | 2005 | 359 | 104 (29) | 13 (3.6) | – | 117 (32.59) | IFAT | [18] |
| 38 | Mexico | 2007 | 432 | 24 (5.5) | 0 (0) | 8 (1.9) | 32 (7.4) | EIA | [20] |
| 39 | Brazil | 2008 | 132 | 79 (60) | – | – | 79 (60) | ELISA | [60] |
| 40 | Colombia | 2011 | 201 | 60 (29.9) | – | – | 60 (29.9) | ECL | [61] |
| 41 | Cuba | 2012 | 562 | 267 (47.5) | – | – | 267 (47.5) | IFAT | [62] |
| Oceania | | | | | | | | | |
| 42 | New Zealand | 2007 | 140 | 60 (42.9) | – | – | 60 (42.9) | ILAT | [19] |
| 43 | Papua New Guinea | 2012 | 120 | 49 (40.8) | – | – | 49 (40.8) | ELISA | [63] |

ELISA, enzyme-linked immunosorbent assay; IHAT, indirect hemagglutination antibody test; IFAT, indirect fluorescent antibody technique; LAT, latex agglutination test; EIA, enzyme immunoassay; SFDT, Sabin-Feldman dye test; HA, hemagglutination assay; ELC, electrochemiluminescence; ILAT, indirect latex agglutination test.

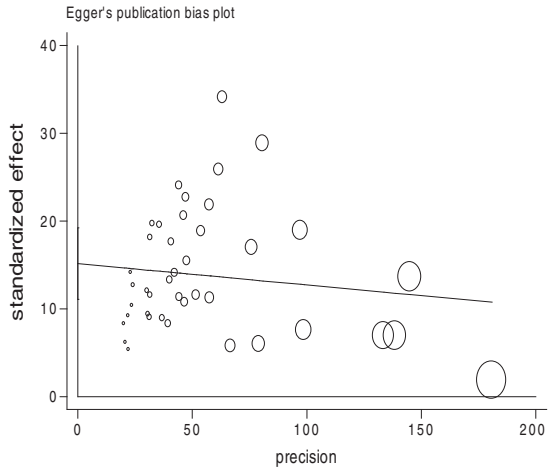


**Fig 2.** Funnel plot to detect publication bias.

consumption, history of blood transfusion, blood group, and Rh factor were also extracted. We used the Preferred Reporting Items for Systematic Reviews and Meta-Analysis guideline for reporting our results [21].

*Meta-Analysis*

Point estimates and their 95% confidence intervals (CIs) for the prevalence rate of antibodies to toxoplasmosis were calculated for each study. Data analysis was performed using the random-effects model (DerSimonian and Laird) to estimate the heterogeneity of effects among included studies. The forest plot was used to provide a comprehensive display of the included studies according to effect size and its CI. For evaluation of heterogeneity and inconsistency among studies, Cochran's $Q$ test and $I^2$ index were used, respectively, to estimate the percentage of variation across included studies [22–23]. Furthermore, we tested the heterogeneity among subgroups using meta-regression analysis. In addition, to assess small study effects and potential population bias, a funnel plot based on the Egger regression asymmetry test

**Table 2**
Subgroup analysis for comparison of prevalence in different continents

| Continent | No. of studies | Prevalence (95% CI) | $I^2$% | Heterogeneity test | | Egger test | |
|---|---|---|---|---|---|---|---|
| | | | | Q | P | t | P |
| Asia | 26 | 0.29 (0.23-0.35) | 99.1 | 2678.85 | .000 | 4.47 | <.0001 |
| Europe | 4 | 0.30 (0.19-0.40) | 96.3 | 80.32 | .000 | 1.10 | .385 |
| Africa | 5 | 0.46 (0.14-0.78) | 99.7 | 1225.40 | .000 | 12.59 | .001 |
| America | 6 | 0.42 (0.21-0.63) | 99.2 | 598.02 | .000 | 3.06 | .038 |
| Oceania | 2 | 0.42 (0.36-0.48) | – | 0.11 | .741 | – | – |
| Total | 43 | 0.33 (0.28-0.39) | 99.2 | 5205.26 | .000 | 6.95 | <.0001 |

Test for heterogeneity between subgroups: Q: 6.512, P value: .164.

was applied. Meta-regression was used to examine the relationship between seroprevalence, the year of publication, and the study sample size. We stratified the included studies by continents (Asia, Europe, Africa, America, and Oceania), estimating the overall prevalence by continents. For the purpose of meta-analysis, we assumed that the included studies were a random sample from each study population. All analysis was carried out with STATA statistical software.

## Results

A total of 1258 articles were found following the initial search of databases. Of these, 43 articles from 22 countries out of 5 continents met the inclusion criteria in the systematic review and meta-analysis (Table 1). A flowchart, shown in Figure 1, represents the study process. The random-effects model was used because of the presence of significant heterogeneity ($I^2 = 99.2\%$). Detecting publication bias using the Egger regression test revealed that publication bias was statistically very significant ($P < .0001$) (Fig 2). A total of 20,964 blood samples were evaluated for toxoplasmosis from January 1980 to June 2015. The overall prevalence of a positive serologic test result for toxoplasmosis in blood donors was estimated to be 33% (95% CI, 28%-39%) (Table 2). The highest and lowest global burdens of *Toxoplasma* infection were found in Africa (46%; 95% CI, 14%-78%) and Asia (29%; 95% CI, 23%-35%), respectively (Table 2). Brazil (75%) and Ethiopia (73%) were identified as the nations with the highest percentage of seropositive results; the lowest prevalence (1%) was found in Namibia.

All of 43 studies estimated the prevalence of IgG antibodies, whereas some articles (24 studies) reported IgM antibodies, and a minority of articles (8 studies) reported both IgG and IgM seropositivity (Table 1). The

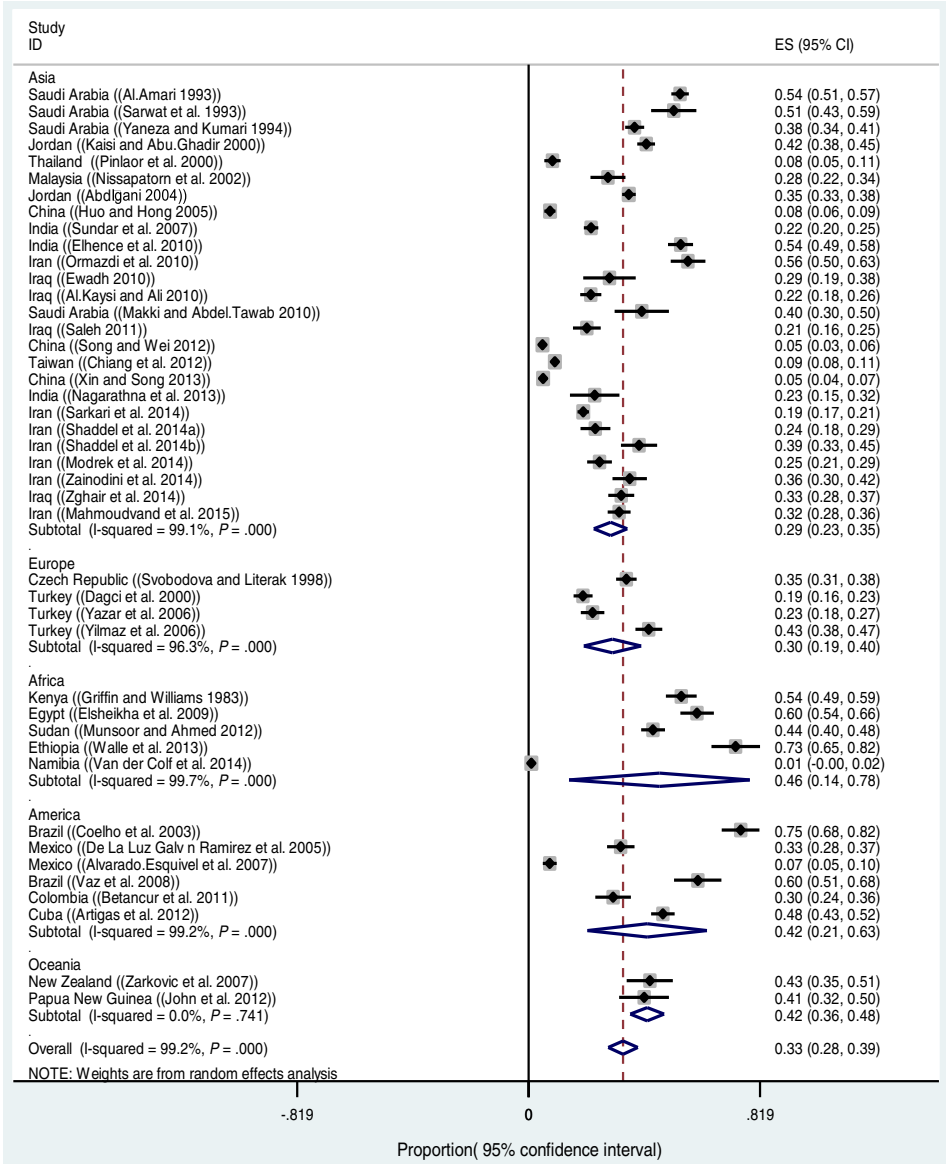


**Fig 3.** Forest plot diagram of the reported prevalence of antibodies to *T gondii*.

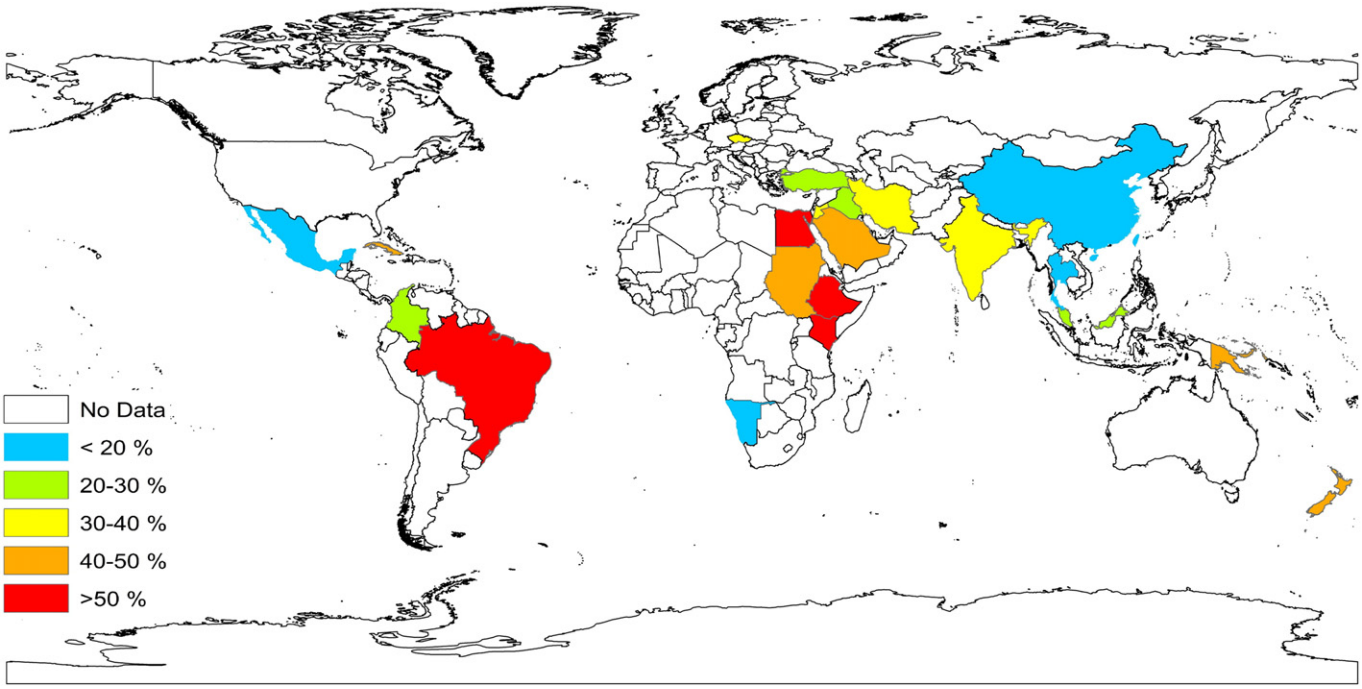


**Fig 4.** Overall prevalence of antibodies to *T gondii* in blood donors of different geographical regions. This map was created using ArcGIS software by Esri (http://www.esri.com).

prevalence of IgM antibodies and both IgG and IgM antibodies in blood donors was evaluated by random-effects model as 1.8% (95% CI, 1.1%-2.4%) and 1.1% (95% CI, 0.3%-1.8%), respectively. The forest plot diagram of the current meta-analysis is presented in Figure 3. Prevalence rates of seropositivity for *T gondii* in blood donors among different geographical locations are shown in Figure 4. According to meta-regression results, the overall prevalence of antibodies against *T gondii* declined in more recent publications, although this was not statistically significant ($P = .105$) (Fig 5). Furthermore, the overall prevalence of antibodies fell with increasing sample size ($P = .03$) (Fig 6). The distribution of antibodies to *Toxoplasma* infection in blood donors was associated with various risk factors. Multivariate analysis showed a statistically significant correlation between seroprevalence for toxoplasmosis and residence ($P < .0001$), sex ($P < .0001$), contact with animals ($P < .0001$), raw or undercooked meat consumption ($P < .0001$), unwashed fruit and vegetables consumption ($P = .028$), and blood group ($P = .011$) (Table 3). Studies based on detection of DNA positivity for *T gondii* are listed in Table 4.

## Discussion

Despite technical improvements in blood donation monitoring, transfusion-transmitted *Toxoplasma* infection remains a potential risk for immune-compromised recipients of transfusions [2–3]. The current study presents a systematic review and meta-analysis of the global seroprevalence of *T gondii* in blood donors. The highest seroprevalence was found in Brazil. Possible reasons include the high prevalence of *T gondii* infection in native animals such as sheep (up to 59%), cats (5%-84%), goats (up to 92%), pigs (up to 90%), as well as a large herbivorous rodent named *capybara* (42%-75%) which is part of the diet of Brazilian people. The seroprevalence of pregnant women in Brazil ranges from 36% to 92% and is considered one of the highest globally [24].

Some reports have documented the transmission of parasites by transfusion of leukocytes [2,25] or platelets [26]. *T gondii* has been shown to survive in citrated blood at 5°C for more than 50 days [2]. Nevertheless, the American Association of Blood Banks categorizes blood transmission of toxoplasmosis as rare: only 4 cases have been definitively demonstrated, and those were associated with transfusion of

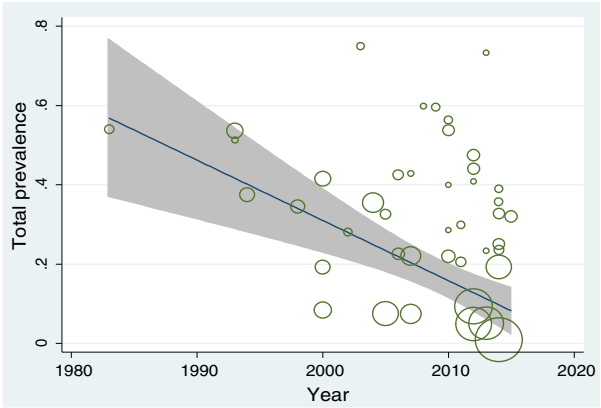


**Fig 5.** Meta-regression plot of antibodies to *T gondii* according to the year of the study.

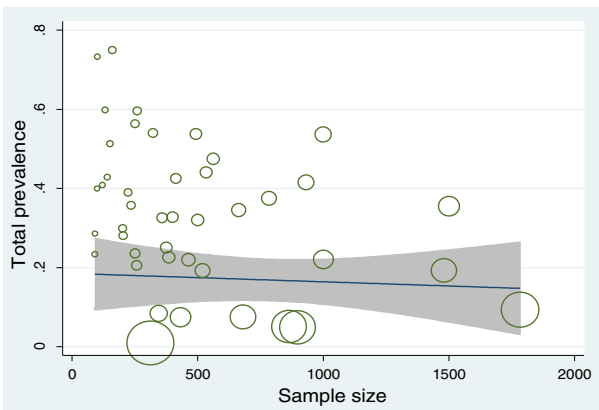


**Fig 6.** Meta-regression plot of antibodies to *T gondii* according to the study sample size.

**Table 3**
Risk factors associated to seroprevalence for *T gondii* in blood donors

| Demographic factors | No. of studies | Categories | Total individuals | Positive cases | Overall prevalence (95% CI) | *P* value | References |
|---|---|---|---|---|---|---|---|
| Residence | 7 | Urban | 1611 | 367 | 0.29 (0.16-0.42) | *P* < .0001 | [15,17,20,41,57–58,62] |
| | | Rural | 807 | 377 | 0.42 (0.16-0.67) | | |
| Sex | 20 | Male | 8891 | 2480 | 0.35 (0.27-0.43) | *P* < .0001 | [15,17,20,30,32–34,36–37,39,41,43, 46,49,53–54,57–59,62] |
| | | Female | 2305 | 627 | 0.38 (0.28-0.49) | | |
| Contact with animals (cat or dog) | 8 | Yes | 1330 | 421 | 0.38 (0.16-0.61) | *P* < .0001 | [15,17,20,33,43,56–58] |
| | | No | 2765 | 462 | 0.27 (0.18-0.36) | | |
| Education level | 2 | Uneducated | 38 | 8 | 0.21 (0.08-0.34) | .11 | [43,46] |
| | | Primary, secondary, and diploma | 1738 | 298 | 0.16 (0.08,0.24) | | |
| | | University level | 1480 | 144 | 0.12 (0.03-0.20) | | |
| Raw or half-cooked meat consumption | 6 | Yes | 1248 | 355 | 0.37 (0.16-0.58) | *P* < .0001 | [15,20,33,43,56–57] |
| | | No | 2300 | 370 | 0.25 (0.15-0.35) | | |
| Uncooked/unwashed vegetables consumption | 5 | Yes | 1913 | 368 | 0.35 (0.16-0.55) | .028 | [15,17,20,43,57] |
| | | No | 1127 | 220 | 0.36 (0.15-0.58) | | |
| History of blood transfusion | 4 | Yes | 213 | 59 | 0.15 (0.001-0.38) | .193 | [15,20,33,57] |
| | | No | 1016 | 263 | 0.26 (0.10,0.45) | | |
| Blood group | 5 | A | 1206 | 240 | 0.29 (0.15-0.43) | .011 | [15,17,43,46,49] |
| | | B | 893 | 184 | 0.34 (0.19-0.50) | | |
| | | AB | 382 | 88 | 0.25 (0.15-0.36) | | |
| | | O | 1876 | 348 | 0.31 (0.17-0.45) | | |
| Rh | 2 | Positive | 1639 | 336 | 0.22 (0.16-0.28) | .83 | [46,49] |
| | | Negative | 205 | 42 | 0.20 (0.15-0.26) | | |

granulocyte concentrates, as well as 1 possible case involving a platelet transfusion (www.aabb.org/tm/eid/Documents/227s.pdf). Overall, the findings suggest that *Toxoplasma* infection can only rarely occur from blood transmission.

Our study was subject to several limitations. First, only a limited number of seroprevalence studies were available, and methodological quality varied among them. Second, the included reports used a variety of diagnostic methods such as enzyme-linked assays, immunofluorescent assays, and hemagglutination assays with different sensitivities, specificities, and cutoff levels used to define a positive result. Third, seroprevalence data were based on sampling from a limited number of participants not necessarily representing national seroprevalence rates. Fourth, in most of the selected articles (up to 70%), related risk factors could not be evaluated. Fifth, published information on the seroprevalence of toxoplasmosis was not available for many parts of the world.

In conclusion, this systematic review and meta-analysis provides information on the prevalence of antibodies to *Toxoplasma* among blood donors in different regions of the world. Although a relatively high prevalence of antibodies to *Toxoplasma* was observed in published studies, this finding does not necessarily represent active infection. DNA-based methods that will allow detection of infectious organisms will likely prove of far greater value for blood donor screening in high-risk areas. Research focused on those parts of the world with high endemicity will clarify the risk factors and epidemiology of toxoplasmosis among blood donors.

## Conflict of Interest Statement

The authors declare no conflict of interests.

## Acknowledgments

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**Table 4**
Molecular epidemiology of *Toxoplasma* infection in blood donors

| No. | Country | Sample size (n) | Positive n (%) | Method | Primer | Ref |
|---|---|---|---|---|---|---|
| 1 | Taiwan | 1783<br>On all samples | 0 (0) | Real-time PCR | 529 bp RE gene<br>5′-CACAGAAGGGACAGAAGT-3′<br>5′-TCGCCTTCATCTACAGTC-3′ | [43] |
| 2 | Iran | 200<br>On selected samples | 14 (7) | Real-time PCR | 355 bp SAG1 gene<br>SAG1F: 5′-GCTGTAACATTGAGCTCCTTGATTCCTG-3′<br>SAG1R: 5′-CCGGAACAGTACTGATTGTTGTCTT-GAG-3′ | [50] |
| 3 | Iran | 104<br>Only on $IgM^+$ samples and both $IgG^+$ and $IgM^+$ samples | 2 (1.9) | Nested PCR | B1 gene<br>Outer primer:<br>5′-CCG TTGGTT CCG CCT CCT TC-3′<br>5′-GCA AAA CAG CGG CAGCGT CT-3′<br>Inner primer:<br>5′-CCG CCT CCT TCG TCCGTC GT-3′<br>5′-GTG GGG GCG GAC CTC TCT TG-3′ | [46] |
| 4 | Iran | 11<br>Only on $IgM^+$ samples | 1 (9.09) | Real-time PCR | 126 bp B1 gene<br>F: 5′-GGAGGACTGGCAACCTGGTGTCG-3′<br>R: 5′-TTGTTTCACCCGGACCGTTTAGCAG-3′ | [15] |

PCR, polymerase chain reaction; bp, base pair; RE, repeat element; F, forward; R, reverse.

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