

WITHDRAWN: Sero-epidemiology of *Toxoplasma gondii* and risk factors among pregnant women in Africa

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EDITORIAL NOTE:

The full text of this preprint has been withdrawn by the authors while they make corrections to the work. Therefore, the authors do not wish this work to be cited as a reference. Questions should be directed to the corresponding author.

Abstract

Introduction Infections caused by *Toxoplasma gondii* is a great public health concern worldwide. *Toxoplasma gondii* infection in pregnant women may result in abortion, stillbirth, or lifelong disabilities of the fetus. Serologic studies have reported various estimates for seroprevalence of toxoplasmosis among African pregnant women. Estimation of the pooled seroprevalence of this infection is necessary for policy-making and target intervention.

Methods We conducted this systematic review and meta-analysis according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. A rigorous literature selection was performed by using the databases of PubMed, Google Scholar, and ScienceDirect for the period Jan 1, 2001, to July 31, 2019. Sero-prevalence with 95% CI was presented for each study, and point estimates and their 95% CIs of pooled seroprevalence was then calculated.

Findings The search process resulted in the inclusion of a total of 36 studies in the systematic review and meta-analysis. The pooled seroprevalence of *Toxoplasma gondii* Immunoglobulin G (IgG) in Africa was found to be 46.7% (95%CI: 37.0, 56.4). Geographical-based subgroup analysis showed that the seroprevalence of *T. gondii* among pregnant women was found to be 65.1% (95% CI: 44.7, 85.5), 50.2% (95% CI: 32.0, 68.3), 47.8% (95% CI: 31.7, 63.8), 38.3% (95% CI: 25.2, 51.4) and 5.8% (95% CI: 3.6, 8.1) in Central, Eastern, Northern, Western and Southern Africa respectively. The most common risk factors for *T. gondii* were living or contact with cat and consumption of raw vegetables or fruits.

Conclusion The current systematic review and meta-analysis revealed a high seroprevalence of *Toxoplasma gondii* infection among pregnant women. There is a need to establish prevention and control measures that should be directed to educational programs. We recommend that periodic screenings for *Toxoplasma gondii* infection among pregnant women should be incorporated into routine clinical care in order to avoid serious clinical complications of mother and fetus.

Introduction

Toxoplasma gondii (*T. gondii*) an apicomplexan, unicellular parasite, is one of the most common zoonoses around the world, affecting warm-blooded animals, including humans [1].

It is approximated that up to one-third of the world's human population is infected with *T. gondii* [2]. Moreover, *T. gondii* is considered as the third most common food-borne pathogen of which patients are infected [3].

Human can be infected with *T. gondii* through one of three ways: 1) by eating raw or undercooked meat containing *T. gondii* tissue cysts or eating food that has been cross-contaminated with raw/undercooked meat; 2) by ingesting oocysts from soil (through gardening, handling/eating unwashed vegetables, or infected cat feces); or 3) by acquiring congenital infection through the placenta [4,5] when a woman gets an infection during pregnancy [6,7]

In most cases, infection in humans is asymptomatic or mild symptoms including malaise, swelling of lymph nodes and fever [8], however, when infection occurs in pregnant women several health problems can affect the fetuses, including mental retardation, blindness, epilepsy, abortion and death [1,9]. Moreover, In a systematic review and meta-analysis, it was reported that *T. gondii* causes severe encephalitis via acute infection or reactivation of latent infection among immune-suppressed individuals, including those with acquired immunodeficiency syndrome (AIDS), immunosuppressive cancer, and transplant recipients on immunosuppressive drugs [10].

In Africa, the prevalence of *T. gondii* among pregnant women varies greatly, the lowest prevalence has been reported in Zambia (0.6%) [11] and the highest in Ghana (92.5%)[12].

The wide prevalence range might be due to the different factors that might influence the probability of infection by *T. gondii* among pregnant women, these factors include environmental, socioeconomic, geographical location, health care facilities, individuals factors such as behavioral and habits [13–15]. The present systematic review and meta-analysis were therefore carried out to establish *T. gondii* seroprevalence among pregnant women, and to evaluate the possible risk factors associated with *T. gondii* seroprevalence among pregnant women across diverse settings and sampling time periods in Africa. For public health actions, understanding the prevalence and associated risk factors can aid in the analysis of the epidemiological pattern of disease among pregnant women and in Africa.

Methods

Search strategy

This study was a systematic review and meta-regression analysis of the seroprevalence of *T. gondii* and the risk of infection among pregnant women. We searched for studies in PubMed, Google Scholar, and ScienceDirect for the period Jan 1, 2001, to July 31, 2019. Checklist for Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [16] was followed. We used the search term "*Toxoplasma gondii*","Toxoplasmosis"pregnant women", "prevalence" and seroprevalence" with the search restricted to records in English.

Selection of studies

DCK and MRM independently screened the abstracts in the search list for potentially relevant studies. Both authors compared the list of potential articles independently. DCK retrieved the full texts of the selected studies. Both DCK and MRM independently assessed published studies for inclusion, using an eligibility form based on the inclusion and exclusion criteria. Studies that met all of the eligibility criteria were included. The disagreements were resolved through discussions, or by contacting a third person who is among the authors (MA, AM, OR JJM).

Data extraction and management

For data extraction, the detailed characteristics of each published study were extracted using a data-collection form. Information was recorded as follows: study characteristics such as the first author, year of publication, year of study, country, study design sample size; the number of the positives cases and seroprevalence of *T. gondii* of each study.

Data analysis

We analyzed data within sub-regions of sub-Saharan Africa: eastern Africa, southern Africa, and west and central Africa. Data were entered in Microsoft Excel and then exported to OpenMeta [Analyst] advanced software (<http://www.cebm.brown.edu/openmeta>) for analyses of a pooled estimate of outcome measures, as well as subgroup analysis. Heterogeneity was checked by using an I^2 test statistic. Forest plots were used to visualize the presence of heterogeneity. To confirm the results, two authors independently computed the statistical analyses and checked for uniformity. The effect size estimates were converted to odds ratios. A statistical test with a p-value less than 0.05 (one-tailed) was considered statistically significant.

Findings

Characteristics of Included Studies

The search information is summarized in Figure 1 following PRISMA guidelines [16]. We identified 161,589 articles, with 107 articles plus 11 additional articles found via reference proceeding to full-text review and finally 36 meets the inclusion criteria. Most of the studies included in this systematic review and meta-analysis had cross-sectional study design (n = 25), and one was retrospective and in other studies (n = 10) the design was not stated. The minimum sample size was 110 participants in a study conducted in Cameroon [17], while the highest sample size was 718 in a study conducted in DRC [18].

The studies qualified for the review were conducted in 12 countries in Africa. Thirteen (36.1%) of these studies were from eastern Africa [19–31], 12 (33.3%) from western Africa [12,32–42], 5 (13.9%) from northern Africa [43–47], five (13.9%) from central Africa [17,18,48–50] and one (2.8%) were from southern Africa [11]. The overall number of study participants included in this meta-analysis was 10,701 and 4,242 pregnant women for IgG and IgM respectively.

The pooled prevalence of Toxoplasmosis based in IgG measurement

Thirty-six published studies were included in this systematic review and meta-analysis and all of these studies were used to estimate the pooled prevalence of *T. gondii* among pregnant women as measured by IgG. The minimum prevalence of anti- *T. gondii* IgG was 0.6% and it was found in Zambia [11]. On the other hand, the maximum *T. gondii* prevalence was found to be 92.5% in a study conducted in Ghana [12]. Using the random effect analysis, the pooled prevalence of *T. gondii* among pregnant women in Africa was 46.7% (95% CI (37.0, 56.4)). The I^2 test result showed high heterogeneity (I^2 99.3%, $P = <0.000$), Figure 1

Sub-group analysis showed that the seroprevalence of *T. gondii* among pregnant women was found to be 50.2% (95% CI: 32.0, 68.3), 38.3% (95% CI: 25.2, 51.4), 65.1% (95% CI: 44.7, 85.5), 5.8% (95% CI: 3.6, 8.1) and 47.8% (95% CI: 31.7, 63.8) in Eastern, Western, Central, Southern and Northern Africa respectively, (Figure 2).

The pooled prevalence of Toxoplasmosis based in IgM measurement

Eighteen published studies were included in the meta-analysis to estimate the pooled prevalence of *T. gondii* among pregnant women as measured by IgM. Likewise, the minimum prevalence of anti- *T. gondii* IgM was 0.7% in a study conducted in Tanzania [19] while the maximum *T. gondii* seroprevalence was found to be 76.1% in a study conducted in Ghana [12]. The pooled prevalence of *T. gondii* among pregnant women in Africa was 8.40% (95% CI (5.20, 11.6). The I^2 test result showed high heterogeneity (I^2 96.7%, $P = <0.000$), Figure 3

Subgroup analysis showed varied seroprevalence of *T. gondii* in four geographical zones of Africa with the highest and lowest prevalence observed in Western 14.8% (95% CI: 5.6, 24.0) and Central 2.7% (95% CI: 0.3%–5.8), respectively (Figure 4).

Discussion

The objective of the present systematic review and meta-analysis was to assess the seroprevalence of *T. gondii* infection and associated risk factors among pregnant women in Africa. *T. gondii* infection during pregnancy results in mental retardation, premature birth, low birth weight, blindness, epilepsy, and death [9]. Moreover a number of published studies have shown that *T. gondii* infection in pregnancy is associated with increased risk of miscarriages, hearing loss, hematological abnormalities and death as a major determinant of infant mortality and increased risk of maternal morbidity and mortality [51–53].

Pooled Prevalence

In a meta-analysis, the pooled prevalence of IgG against *T. gondii* infections among pregnant women in Africa was 46.7%. This is higher than the study conducted in China and Iran which showed a seroprevalence of 5.0% [54] and 38% [55] respectively among pregnant women. However, relatively similar seroprevalence (41.3%) has been reported in Iranian pregnant women [56]. The high seroprevalence of *T. gondii* among pregnant women could be due to decreased immunity and physiological changes during pregnancy, decreased awareness, as well as increased risk of exposure.

Risk factors

In this review, a number of studies reported the assessment of risk factors of *T. gondii* infection in pregnant women. Cat is the final host of *T. gondii* and various warm-blooded animals and humans are the intermediate hosts. It is reported that the sexual multiplication of *T. gondii* takes place in cats and hence cats excrete the unsporulated oocysts with faeces in the environments [4,57]. Living or contact with

cat were found to be the independent predictors of *T. gondii* infection ($p < 0.05$) [11,21,23,27,29,34]. Whereas only one study did not find any association of living or contact with domestic animals such as cat and being infected with *T. gondii* among pregnant women [45]. As per the WHO recommendations on the prevention of *T. gondii* infections; hygiene including hand-washing and the use of clean water in food production and preparation is critical. Pregnant women should avoid undercooked meat [58]. Moreover, it is advisable that pregnant women wear gloves when gardening and during contact with soil or sand because they might be contaminated with cat feces that contain *Toxoplasma* [58].

In this review, other predictors of *T. gondii* seropositivity were the consumption of raw vegetables or fruits. A significant association was observed between *T. gondii* seropositivity and eating raw or unwashed vegetables or fruits [20,21,28,30,35,37,44].

Continue Health Education for toxoplasmosis control

Reviewed studies concluded that there is the need of implanting a community education among pregnant women [11,21,22,27–30,33,35,44,46,50]. Since there is no vaccine against *T. gondii*, prevention depends only on increasing the pregnant women's knowledge about toxoplasmosis, its origin, transmission and prevention. Education programs are inevitably needed for the improvement of basic concepts of toxoplasmosis control and prevention. More importantly, continued and improved knowledge and access to reliable information about sources of infection are suitable to consequently change women's behavior during pregnancy [59,60] and also in their everyday life.

Limitation

This review contains some limitations, which should be discussed. Some studies had limited sample size that may not necessarily have represented the country or national seroprevalence. Studies used a variety of serological diagnostic methods that have a different range of sensitivities and specificities, and they used different cutoff levels in defining positive results. Most of the studies in this review employed cross-sectional study designs, which means that it is hard to establish a causal relationship between the risk factors they identified and *T. gondii* infection among pregnant women.

Implications for policy practice

Based on the current review, pregnant women still have a greater risk of *T. gondii* infection. *T. gondii* infection is often ignored or not diagnosed or insufficiently reported in many African countries. In addition to the effort of improving women and child health, policymakers may wish to consider improving diagnosis of *T. gondii* in African settings. Thus, community education of pregnant women and general population would effectively combat *T. gondii* in Africa.

Implication for Research

Different risk factors particularly consumption of raw or unwashed/ not well-washed vegetables or fruits, staying or contact with cats are highly correlated and influence on *Toxoplasma gondii*. Future studies

may collect data on follow-up studies and develop a comprehensive valid and reliable measure to be used for analyzing the cause of risk factors on *Toxoplasma gondii*. Moreover, intervention studies that involve provision of health education about *Toxoplasma gondii* and evaluation any changes in the risk of infection that might be observed.

Conclusion

The current systematic review and meta-analysis showed that the pooled prevalence of *T. gondii* in Africa among pregnant women is relatively higher compared with the other review and meta-analysis conducted in other parts of the world. Therefore, there is a need to establish prevention and control measures that should be directed to educational programs. We recommend that periodic screenings for *T. gondii* infection among pregnant women should be incorporated into routine clinical care in order to avoid serious clinical complications of mother and fetus.

List of Abbreviations

AIDS: acquired immunodeficiency syndrome

IgG: Immunoglobulin G

IgM: Immunoglobulin M

PRISMA: Systematic Reviews and Meta-Analyses

WHO: World health organization

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and materials

Data will be available upon request to the corresponding author.

Competing interests

None to declare

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No funding was obtained for this study.

Authors' contributions

DCK developed the protocol and involved in the design, selection of study, data extraction, statistical analysis and developing the initial drafts of the manuscript.

MRM Involved in data extraction, quality assessment, statistical analysis.

JJM prepared and revising subsequent drafts

AM prepared and revising subsequent drafts

MA prepared and edited the final draft of the manuscript.

All authors read and approved the final draft of the manuscript.

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Figures

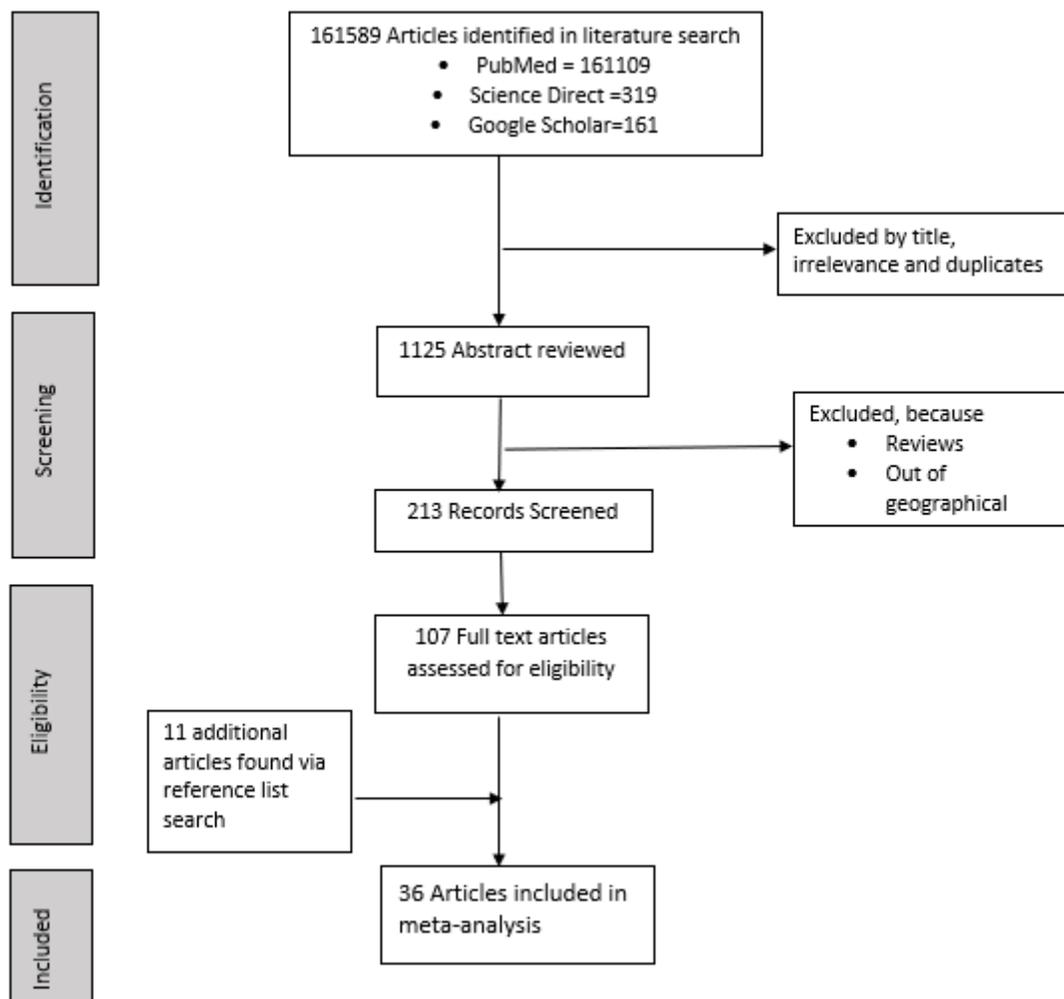


Figure 1

Flow chart of the selection process

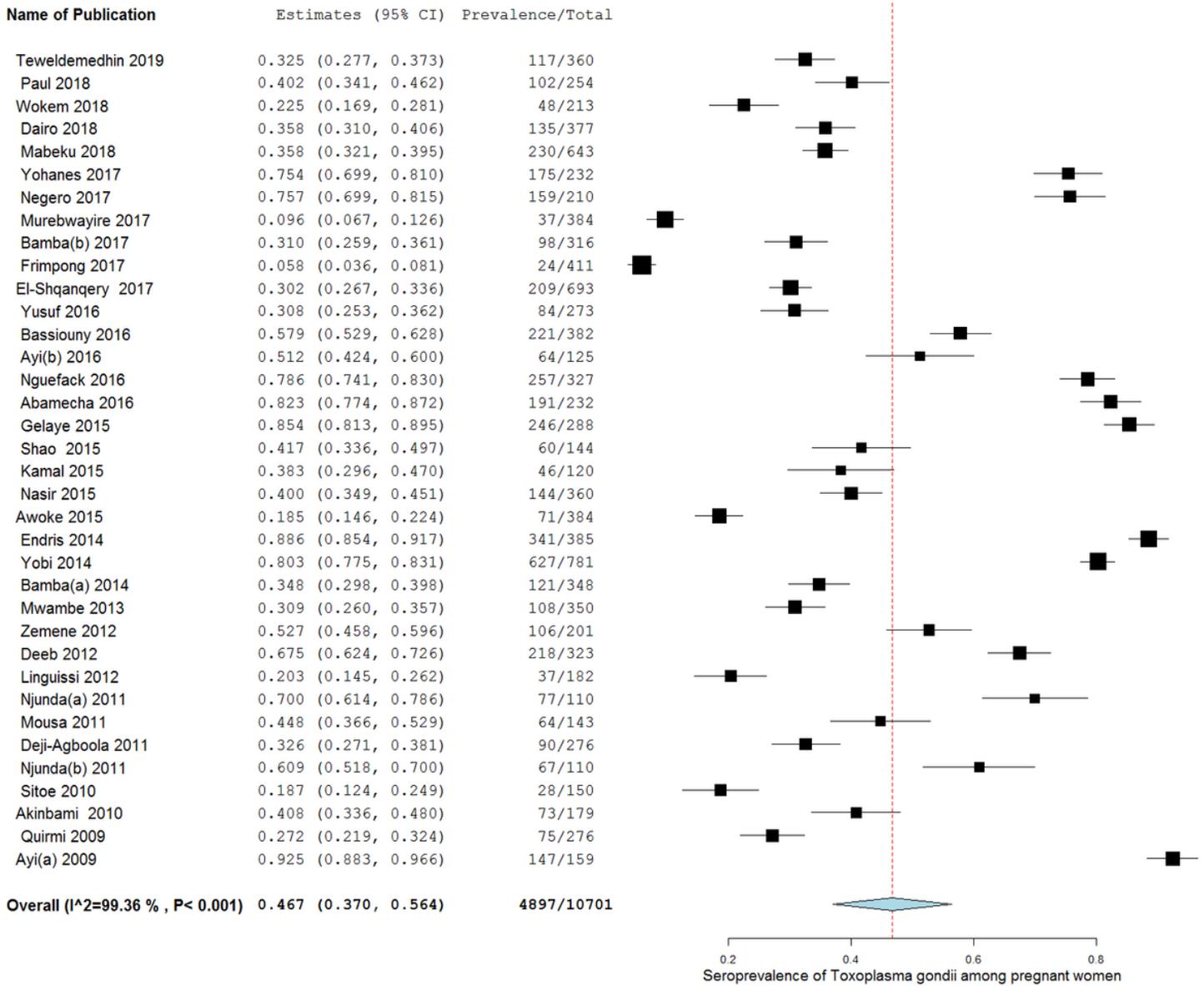


Figure 2

Forest Plot depicting the pooled analysis of 36 studies reporting Seroprevalence of *T. gondii* among pregnant women measured by IgG

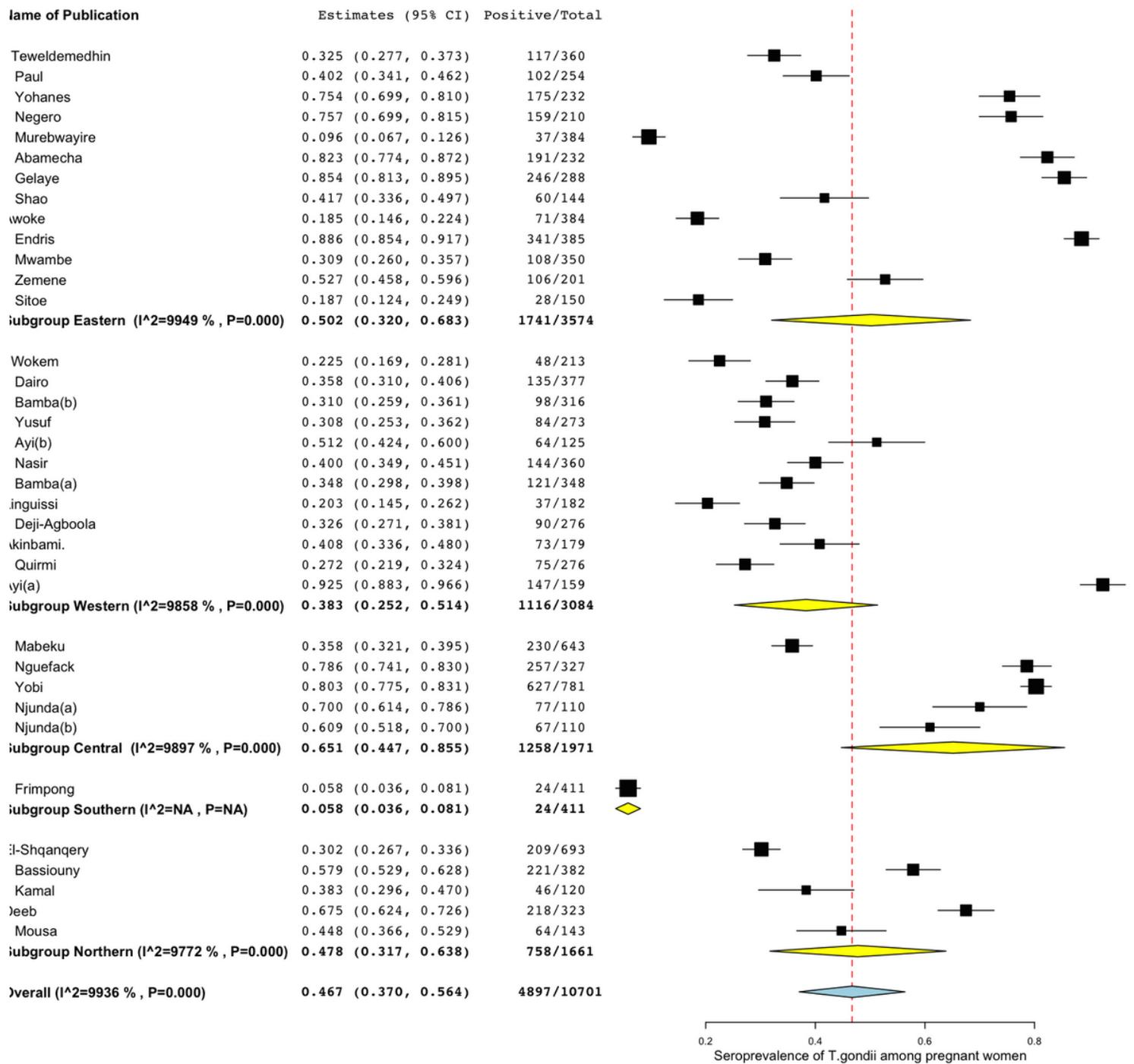


Figure 3

Forest plot depicting sub-group analysis of *T. gondii* among pregnant women measured by IgG

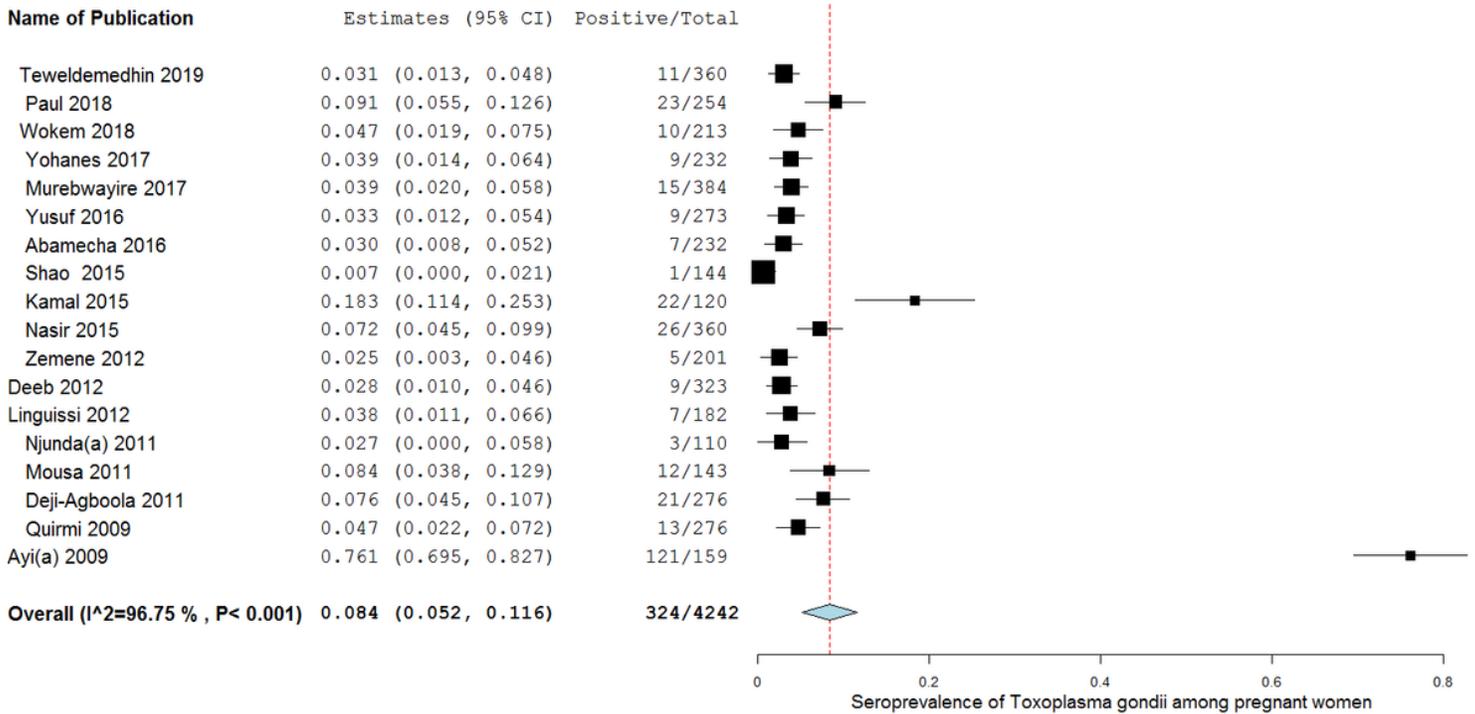


Figure 4

Forest Plot depicting the pooled analysis of 18 studies reporting sero-prevalence of *T. gondii* among pregnant women measured by IgM

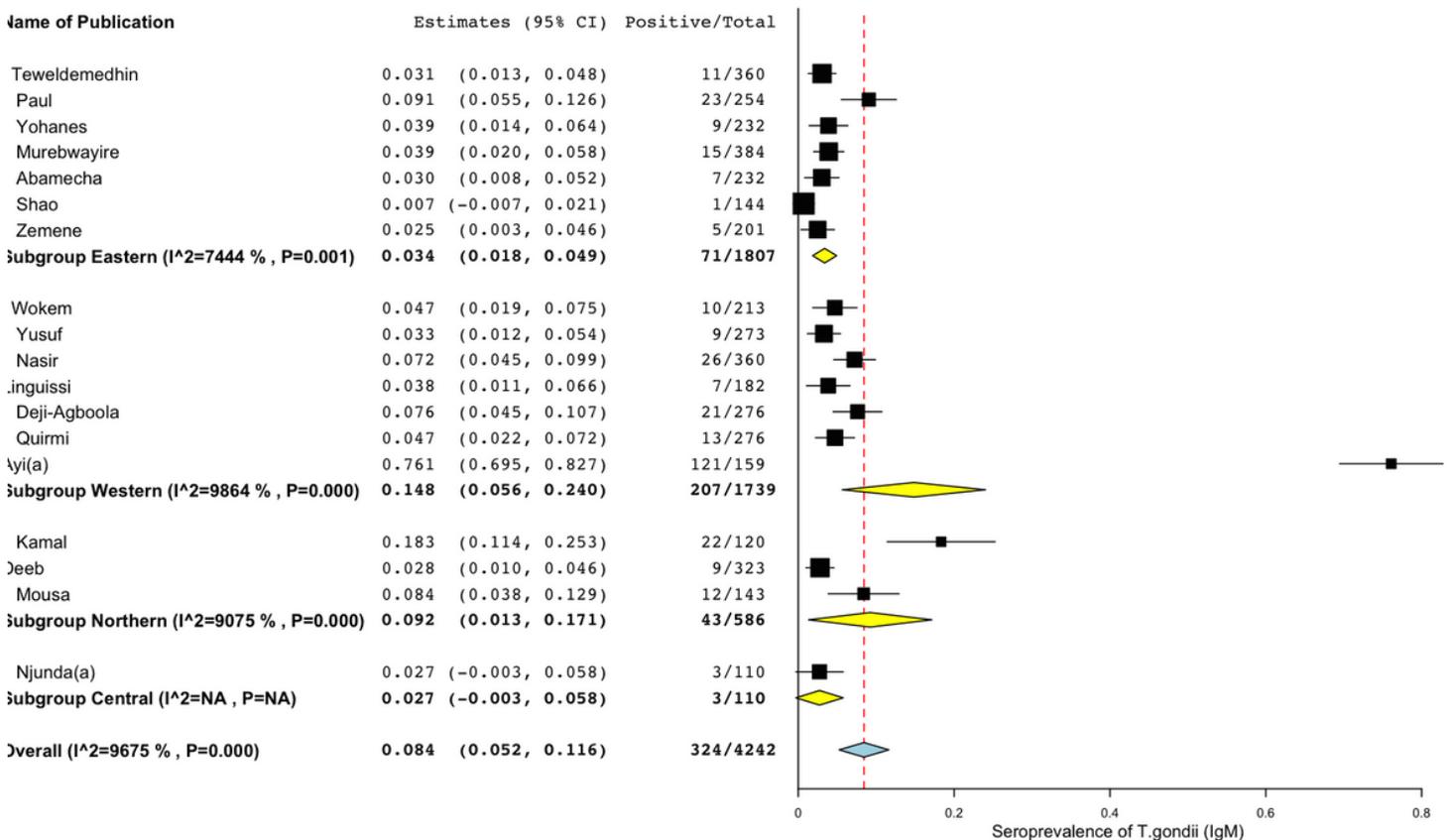


Figure 5

Forest plot depicting sub-group analysis of *T. gondii* among pregnant women measured by IgM