BMC Pregnancy and Childbirth

RESEARCH

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Assessment of simultaneous IgM, IgG avidity, and IgA testing in diagnosis of acute toxoplasmosis in pregnant women: a systematic review and meta-analysis study

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Abstract

Backgrounds *Toxoplasma gondii* is a relatively common parasite with a global prevalence that can cause toxoplasmosis. This infection usually does not have clear symptoms, so timely and accurate detection plays a major role in the treatment of this disease. This study reviewed *Toxoplasma* antibodies dependent serologic tests in pregnancy, assessing their diagnostic effectiveness to guide healthcare providers, particularly obstetricians and gynecologists.

Methods In this systematic review and meta-analysis, we utilized four different databases for our search and adhered to the PRISMA guidelines to collect pertinent studies in duration of 2000 to April 2024. After carefully evaluating the inclusion/exclusion criteria list, we ultimately selected 67 qualifying studies for our analysis and subjecting the obtained data to statistical scrutiny.

Results Data analysis revealed that the pooled seroprevalence of IgM anti-*T. gondii* among pregnant women tested were 2.1% (95% CI = 1.67 to 3.03). Moreover, the weighted seroprevalence rate estimate of low IgG avidity in IgM-positive pregnant women was 30% (95% CI = 28 to 31) and the seroprevalence of IgA in IgM-positive pregnant women was 43% (95% CI = 18 to 70). Combining the IgG avidity test results with those of IgM and IgA can significantly improve the accuracy of diagnosing recent and past *Toxoplasma* infections.

Conclusions This approach is particularly valuable for pregnant women, as it improves the reliability of serological test outcomes and helps to provide timely treatment and mitigate irreversible complications associated with toxoplasmosis.

Keywords *Toxoplasma gondii*, IgG avidity, Serological tests, Systematic review and meta-analysis

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Backgrounds

Toxoplasmosis is a common disease between humans and animals, which is caused by a eukaryotic parasite from the phylum Apicomplexa called *Toxoplasma gondii* (*T. gondii*). *T. gondii* can cause disease in humans by consuming meat (cysts), water, food, and contaminated soil (oocytes) [1, 2].

About one-third of the world's individuals have anti-*Toxoplasma* antibodies in their blood [3]. *T. gondii* infection can range from asymptomatic disease in individuals with complete immunity to severe cases in individuals with weak immune systems [4]. Also, about 200,000 cases of toxoplasmosis occur during pregnancy [4].

In the initial infection, if *T. gondii* is transmitted through the placenta, it can lead to irreparable consequences in the fetus [5]. The stage of pregnancy at which the infection occurs is the primary determinant of the risk of fetal harm [6]. Past maternal infection with parasites has no effect on fetal development [5]. Fetal infection occurs when the parasite is present in the mother's blood and before the appearance of anti-*T. gondii* antibodies [7].

The most serious consequence of toxoplasmosis occurs in the first and second trimesters during pregnancy and causes vertical transmission to the fetus [8, 9]. The rate of this form of the disease is 1–14 cases per 10,000 pregnancies [10]. Congenital infected babies can show specific signs and symptoms such as hydrocephalus, microcephaly, chorioretinitis, brain calcification, mental disorders, movement, and seizures [11, 12]. The parasite strain can have a great impact on the clinical condition of the baby or fetus [13].

Evaluation of antibodies is common in the diagnosis of toxoplasmosis, but it is relatively difficult to diagnose it quickly and definitively [14, 15]. Serological methods are common in the diagnosis of toxoplasmosis, but the results of these methods collect indirect information that must be interpreted carefully. A positive serological test (IgG, IgM, and IgA) alone does not indicate an existing infection, as *Toxoplasma* antibodies are present in the blood of many humans for various reasons [16]. On the other hand, to prove the acute disease of toxoplasmosis, the high level of toxoplasma antibody in the blood is not enough, although it is a suitable guide for diagnosis evaluations. Sometimes, for various reasons, only antibodies evaluation is not useful for the acute stages of *T. gondii*, including long-term responses, delay in the production of these antibodies, or non-specific polyclonal responses against various factors [17, 18].

In recent years, the discovery of the IgG avidity ELISA method, which only evaluates IgG class antibodies, is a suitable solution for differentiating between acute and chronic *T. gondii* infections. At the beginning of the infection, the affinity of the antibody to bind to the antigen is in a low avidity (Acute toxoplasmosis). With the continuation of the infection, the tendency these antibodies to bind to the antigen of the *T. gondii* parasite increases and is in a high avidity, which is a sign of a long-term infection [10, 19].

This study aims to investigate serology tests related to T. gondii and pregnancy, determine the effectiveness of these tests in diagnosis, and inform healthcare providers, including obstetricians and gynecologists.

Methods

Study design and search strategy

Search based on keywords *Toxoplasma* infection, *Toxoplasma gondii*, *T. gondii*, pregnancy, *Toxoplasma* antibodies (IgG, IgM, and IgA), IgG avidity, congenital, diagnosis and "AND", "OR" operators by two independent reviewers (M.T and B.B) in four databases (PubMed, Scopus, Web of Science and Google Scholar) in duration of 2000 to April 2024 were performed. Based on PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) principles, two independent reviewers screened titles and abstracts against predefined inclusion criteria (Fig. 1). In the case of disagreement on the eligibility of the two authors, the third author made the final decision (S.A.H). Potentially eligible studies were retrieved, and M.T and B.B independently assessed them for final inclusion (Fig. 1). Conflicts were resolved through discussion or consultation with a third reviewer (S.A.H). Furthermore, End Note 21 software was used for initial screening to remove duplicates and assist in title/abstract screening.

Quality assessment

The quality of reporting in the studies was evaluated using the Standardized Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist, which was completed by two authors (M.T and B.B) [20]. The checklist consists of six main sections (Title and Abstract, Introduction, Methods, Results, Discussion, and Other Information) and evaluates various aspects of study design, methods, and reporting, such as sample size, statistical tests, and limitations. Based on the STROBE assessment, we categorized the studies into three quality levels: low (scores below 16.5), moderate (scores ranging from 16.6 to 25.5), and high (scores between 25.6 and 34). The articles included in this study were found to be of acceptable quality.

Inclusion and exclusion criteria

Inclusion criteria included (1) cross-sectional studies on *Toxoplasma* IgG avidity and pregnancy; (2) articles available from 2000 to April 2024; (3) English text of studies; and (4) human studies. Exclusion criteria included (1) Studies in languages other than English; (2) unrelated

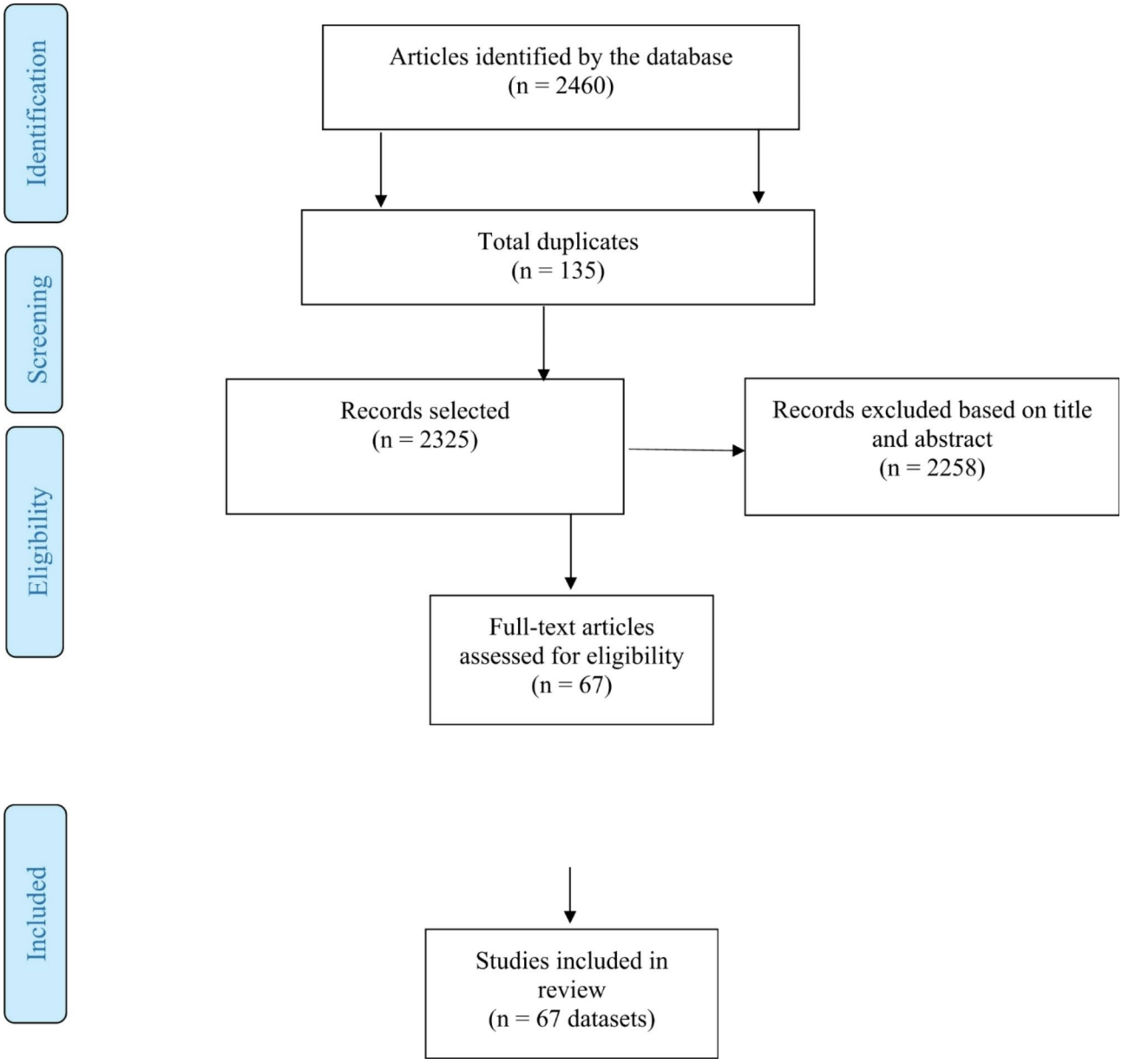

Fig. 1 Flow diagram of the study process based on PRISMA statement

articles on *Toxoplasma* IgG avidity and pregnancy; and (3) lack of access to the full text of the article.

Data extraction

Two authors (M.T and B.B) thoroughly examined the selected articles and extracted relevant data and S.A.H resolved disagreements consensus. Primary outcomes including: The name of first author and the publication year of paper, as well as Secondary outcomes such as country, mean age of participants, total sample, number and percentage of positive IgM, and number of low avidity index. Moreover, no automation tools were used for data extraction. Finally, a baseline table based on study characteristics was designed.

Statistical analysis

In our study, StatsDirect statistical software package version 2.6.1 was used for data meta-analysis. Cochrane test based on $\chi 2$ (Q) test and I^2 index was used to show heterogeneity between studies [21]. The results from the individual studies were combined using a random effects model. A forest plot was utilized to display the low IgG avidity of toxoplasmosis in pregnant women across each study, as well as to calculate the overall pooled seroprevalence estimate of the studies included in the

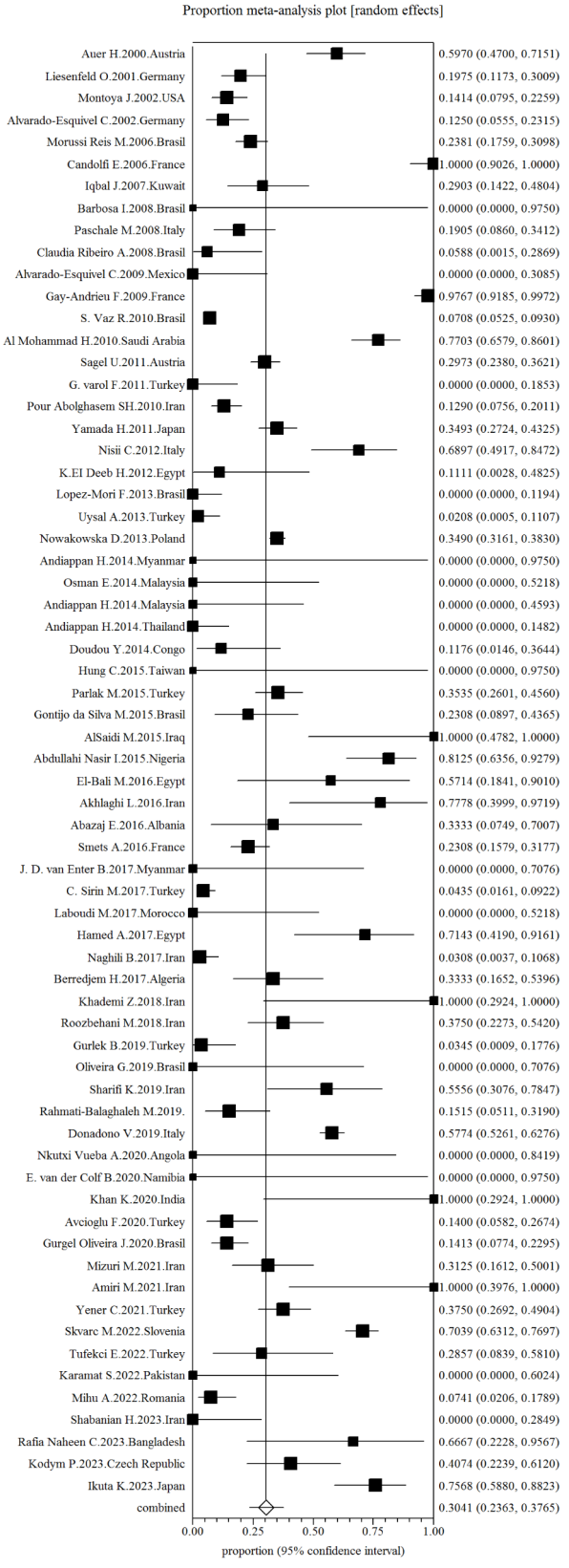

Fig. 2 Forest plot of prevalence of low IgG avidity in pregnant women with suspected acute toxoplasmosis (IgM+)

meta-analysis. Additionally, we performed funnel plots and Egger's regression test to assess publication bias (PB) and statistical significance [22], respectively. This study was registered in the open-access online database PROSPERO (International Prospective Register of Systematic Reviews) with code CRD42024542274.

Results

After an initial search based on keywords from 4 internet databases, a total of 2460 studies were obtained. After screening and removing duplicates, 67 studies were eligible in the study based on inclusion and exclusion criteria. Analysis of heterogeneity (95.7%, 95% CI = 95.2–96.1%, P value < 0.001) demonstrated heterogeneity between included studies in this systematic review since we selected a random effect for obtaining estimation of results. Data analysis in this study, the pooled seroprevalence of low avidity in pregnant women with suspected acute toxoplasmosis (IgM+) was 30% (95% CI = 28 to 31) (Fig. 2). The results of Egger's test (Egger bias = 1.11, 95% CI = -1.79 to 4.02, $P = 0.447$) do not show a significant publication bias in low avidity in IgM-positive pregnant women (Fig. 3). The analysis results in different groups showed that the overall seroprevalence of IgG antibodies in pregnant women in this study was 39% (95% CI = 35 to 43). In addition, the pooled seroprevalence of IgM antibodies in these individuals was 2.3%. (95% CI = 1.67 to 3.03). The pooled seroprevalence of IgA antibodies during pregnancy with suspected acute toxoplasmosis (IgM+) was estimated to be 43% (95% CI = 18 to 70) (Table 1). More information is available in Table 2. The mean age of the individuals involved in the study was 28.2 years. In total, studies were conducted in 36 countries. The number of studies conducted in Asia, Europe, America, and Africa was 25, 23, 10 and 9 studies, respectively. The most studies conducted in Asia, Europe, America, and Africa were in Iran (n = 9), Turkey (n = 8), Brazil (n = 8) and Egypt (n = 3), respectively.

Discussion

T. gondii is a highly significant opportunistic pathogen in humans, posing a silent threat to many populations globally, and the differential diagnosis of recent infection from past infection during pregnancy is a great challenge [7]. Toxoplasmosis presents a notable risk during pregnancy, as it endangers the developing fetus. This parasite breaches the placental barrier, leading to fetal involvement and potentially resulting in adverse outcomes. The likelihood of infection transmission from mother to child escalates with pregnancy stage, underscoring the need for preventive measures and vigilance in monitoring throughout gestation. Scientific studies consistently demonstrate that *Toxoplasma* infection heightens the risk of miscarriage, emphasizing the critical role

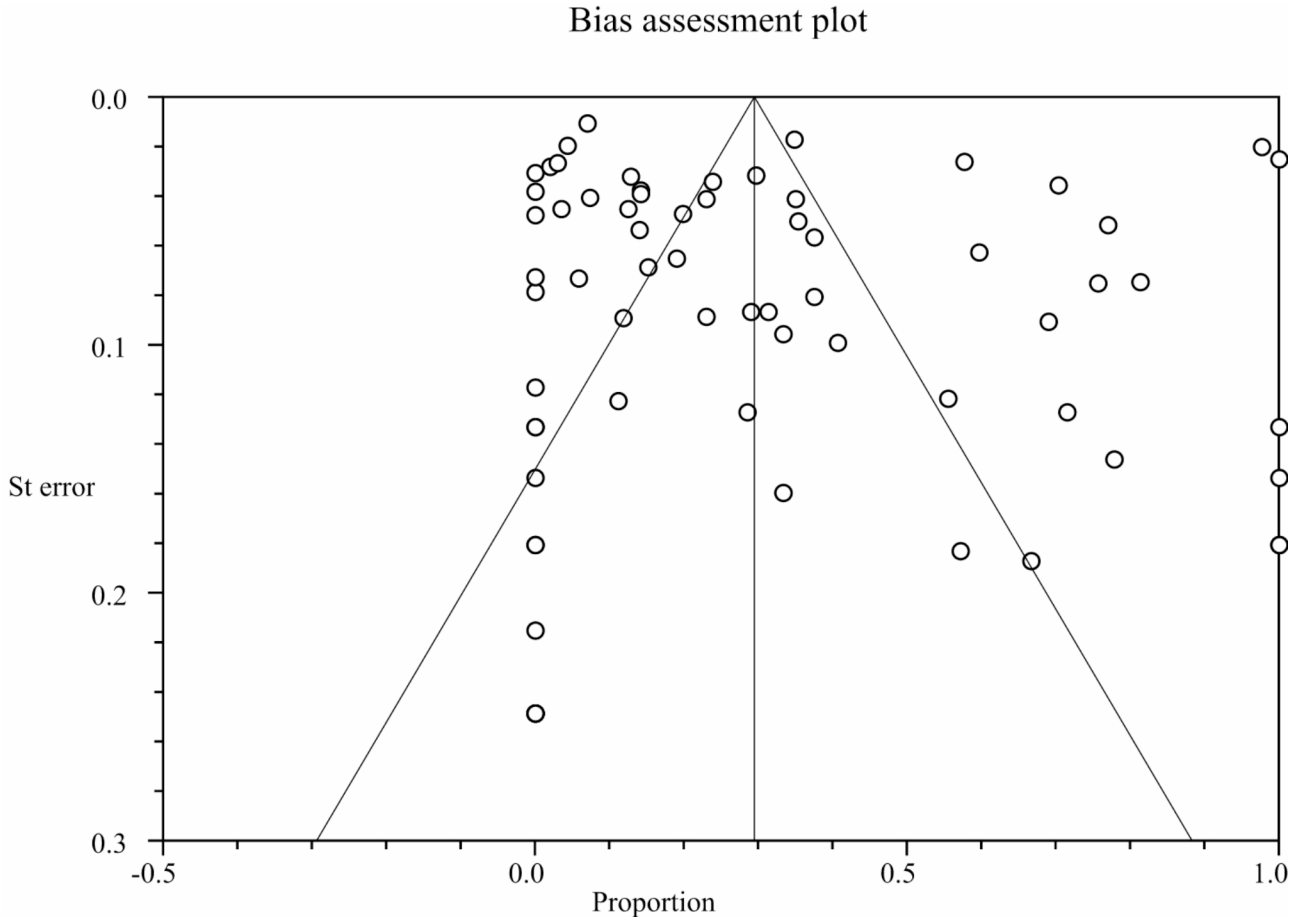

Fig. 3 Bias assessment plot based on standard error in pregnant women with acute toxoplasmosis (low IgG avidity in IgM+)

Table 1 Pooled seroprevalence of acute and chronic toxoplasmosis (IgM+, IgG+, and IgA+) in pregnant women

Pooled seroprevalence	Pos. samples/total samples	Pooled. *P* (95% CI)	Heterogeneity				Publication Bias	
			Q	I^2	df	*P* value	Egger	*P* value
IgG (CT) in pregnant women	63,317/191,413	39.00 (35.00–43.00)	14581.13	99.6%	58	< 0.001	5.11	0.088
IgM (AT) in pregnant women	3099/204,208	2.30 (1.67–3.03)	3829.05	98.7%	48	< 0.001	4.52	< 0.001
IgA in pregnant women with AT	142/370	43.00 (18.00–70.00)	193.06	96.4%	7	< 0.001	5.15	0.326

CT: Chronic toxoplasmosis, AT: Acute toxoplasmosis

of proper prenatal care and condition management [16, 17]. The United Nations (UN) focus on preventing preventable deaths before 2030 is in line with sustainable development programs. By improving the conditions of mother and baby, these programs greatly reduce the mortality and adverse consequences of toxoplasmosis in babies and children. Since the lack of early and accurate diagnosis of toxoplasmosis during pregnancy may have irreparable consequences for the fetus or newborn, it seems that the effort to find a group of serological tests that have the maximum efficiency for distinguishing recent infection from chronic seems necessary. Classification of included studies in this review showed that 67 collected studies were conducted in 36 countries. The low number of countries indicates that the avidity-based toxoplasmosis-screening programs is not widely implemented. Countries have different policies regarding screening for toxoplasmosis in pregnant women. In France, Italy, Austria, Lithuania, and Slovenia, mandatory screening is performed on pregnant women [88], but in some other countries, such as the United States [89] or Canada [90], and other countries, they do not recommend this screening.

Based on the results of this systematic review, it was observed that IgG antibodies were prevalent in 39% of pregnant women. Notably, IgG antibodies typically appear in the bloodstream approximately 14 days after infection, with their maximum concentration occurring at 3 months. Subsequently, the antibody levels often decline but remain detectable throughout an individual's

Table 2 Baseline characteristics of included studies

ID	First author and References	Year	Country	Continent	Mean Age	Quality score	Total sample	*N.* IgG + (%)	*N.* IgM + (%)	*N.* IgA + (%)	*N.* Low IgG avidity (%)
1	Auer et al. [23]	2000	Austria	Europe	N.M	19	138	138 (100)	67 (48.5)	59 (42.7)	40 (28.9)
2	Liesenfeld et al. [24]	2001	Germany	Europe	N.M	20	125	125 (100)	81 (74.4)	N.M	16 (12.8)
3	Montoya et al. [25]	2002	USA	America	N.M	19	127	N.M	99 (77.9)	N.M	14 (11)
4	Alvarado-Esquivel et al. [26]	2002	Germany	Europe	N.M	24	64	64 (100)	64 (100)	N.M	8 (12.5)
5	Reis et al. [27]	2006	Brasil	America	N.M	27	6700	N.M	168 (2.5)	N.M	40 (0.5)
6	Candolfi et al. [28]	2007	France	Europe	N.M	22	91	55 (60.4)	36 (39.5)	24 (26.3)	36 (39.5)
7	Iqbal et al. [29]	2007	Kuwait	Asia	27	25	224	119 (53.1)	31 (13.8)	N.M	9 (4)
8	Barbosa et al. [30]	2009	Brasil	America	29	30	190	126 (66.3)	1 (0.52)	N.M	0 (0)
9	De Paschale et al. [31]	2008	Italy	Europe	N.M	28	3426	737 (21.5)	42 (1.2)	N.M	8 (0.2)
10	Ribeiro et al. [32]	2008	Brasil	America	29	29	832	625 (75.1)	17 (2)	N.M	1 (0.12)
11	Alvarado-Esquivel et al. [33]	2009	Mexico	America	24.5	27	439	36 (8.2)	10 (2.3)	N.M	0 (0)
12	Gay-Andrieu et al. [34]	2009	France	Europe	N.M	31	730	153 (21)	45 (6.1)	N.M	84 (11.5)
13	Vaz et al. [35]	2010	Brasil	America	25.8	24	20,389	10,806 (53)	664 (3.2)	N.M	47 (0.23)
14	Tutarlılığı et al. [36]	2010	Saudi Arabia	Asia	24.8	26	160	118 (73.7)	74 (46.3)	N.M	57 (35.6)
15	Sagel et al. [37]	2011	Austria	Europe	27.8	29	92,365	28,633 (31)	222 (0.2)	N.M	66 (0.07)
16	Varol et al. [38]	2011	Turkey	Europe	27.8	21	1333	426 (31.9)	18 (1.35)	N.M	0 (0)
17	Pour Abolghasem et al. [39]	2011	Iran	Asia	N.M	25	225	168 (65.8)	124 (55.5)	N.M	16 (7.1)
18	Yamada et al. [12]	2011	Japan	Asia	N.M	30	146	146 (100)	146 (100)	N.M	51 (34.9)
19	Nisii et al. [40]	2012	Italy	Europe	36	26	1424	85 (5.9)	29 (2)	20 (1.4)	20 (1.4)
20	El Deeb et al. [41]	2012	Egypt	Africa	26.4	22	323	218 (67.4)	9 (2.8)	N.M	1 (0.3)
21	Lopes-Mori et al. [42]	2013	Brasil	America	25	27	2226	1151 (51.7)	29 (1.3)	N.M	0 (0)
22	Uysal et al. [43]	2013	Turkey	Europe	30	25	4651	1871 (39.9)	48 (2.5)	N.M	1 (0.2)
23	Nowakowska et al. [44]	2014	Poland	Europe	28.7	29	8281	3364 (40.6)	808 (9.7)	N.M	282 (3.4)
24	Andiappan et al. [45]	2014	Myanmar	Asia	29.4	28	215	65 (30.2)	1 (0.4)	N.M	0 (0)
25	Emelia et al. [46]	2014	Malaysia	Asia	N.M	22	281	94 (33.5)	5 (1.8)	N.M	0 (0)
26	Andiappan et al. [45]	2014	Malaysia	Asia	30	26	219	87 (39.7)	6 (2.7)	N.M	0 (0)
27	Andiappan et al. [47]	2014	Thailand	Asia	29.5	28	760	167 (22)	23 (3)	N.M	0 (0)
28	Doudou et al. [48]	2014	Congo	Africa	28	31	781	387 (49.5)	17 (4.4)	N.M	2 (0)
29	Hung et al. [49]	2015	Taiwan	Asia	30.9	30	104	7 (6.7)	1 (0.9)	N.M	0 (0)
30	Parlak et al. [50]	2015	Turkey	Europe	N.M	25	9156	N.M	99 (1.1)	N.M	35 (0.3)
31	Gontijo da Silva et al. [51]	2015	Brasil	America	N.M	28	487	307 (63)	26 (5.3)	4 (0.8)	6 (1.3)
32	AlSaidi et al. [52]	2015	Iraq	Asia	N.M	28	80	77 (96.2)	5 (6.2)	N.M	5 (6.2)
33	Nasir et al.[53]	2015	Nigeria	Africa	30	24	360	144 (40)	32 (8.9)	N.M	26 (7.2)
34	El-Bali et al. [54]	2016	Egypt	Africa	N.M	26	2247	487 (21.7)	7 (0.3)	N.M	4 (0.17)
35	Akhlaghi et al. [55]	2016	Iran	Asia	N.M	30	468	86 (18.3)	9 (1.9)	N.M	7 (1.4)
36	Abazaj et al. [56]	2016	Albania	Europe	27	27	152	48 (31.6)	9 (5.9)	N.M	3 (1.9)
37	Smets et al. [57]	2016	France	Europe	N.M	22	117	117 (100)	117 (100)	9 (7.6)	27 (23)
38	Van Enter et al. [58]	2017	Myanmar	Asia	35	28	199	63 (31.7)	3 (1.5)	N.M	0 (0)
39	Sirin et al. [59]	2017	Turkey	Europe	30.7	25	7513	2427 (32.3)	138 (1.9)	N.M	6 (0.07)
40	Laboudi et al. [60]	2017	Morocco	Africa	N.M	29	128	54 (42.1)	5 (3.9)	N.M	0 (0)
41	Hamed et al. [61]	2017	Egypt	Africa	N.M	28	180	31 (17.2)	14 (7.7)	9 (5)	10 (5.5)
42	Naghili et al. [62]	2017	Iran	Asia	N.M	26	391	267 (68.3)	65 (16.6)	N.M	2 (0.7)
43	Berredjem et al. [63]	2017	Algeria	Africa	32.5	27	143	57 (39.8)	27 (18.8)	7 (4.8)	9 (6.2)
44	Khademi et al. [64]	2019	Iran	Asia	27	22	360	100 (27.8)	3 (0.8)	N.M	3 (0.8)
45	Roozbehani et al. [65]	2018	Iran	Asia	N.M	26	2120	1362 (64.2)	40 (1.9)	N.M	15 (0.7)
46	Gurlek et al. [66]	2019	Turkey	Europe	N.M	30	3490	1176 (33.6)	29 (0.8)	N.M	1 (0.02)
47	Oliveira et al. [67]	2019	Brasil	America	25	28	196	133 (67.9)	3 (1.5)	N.M	0 (0)
48	Sharifi et al. [68]	2019	Iran	Asia	25	26	250	58 (23.2)	18 (7.2)	N.M	10 (4)
49	Rahmati-Balaghaleh et al. [69]	2019	Iran	Asia	N.M	29	208	88 (42.3)	33 (15.8)	N.M	5 (2.4)
50	Donadono et al. [70]	2019	Italy	Europe	N.M	30	1159	778 (67.1)	381 (32.8)	N.M	220 (18.9)
51	Tawfiq et al. [71]	2019	Iraq	Asia	30	25	180	64 (35.5)	N.M	N.M	0 (0)
52	Vueba et al. [72]	2020	Angola	Africa	30	28	878	346 (39.4)	2 (0.2)	N.M	0 (0)

Table 2 (continued)

ID	First author and References	Year	Country	Continent	Mean Age	Quality score	Total sample	*N.* IgG + (%)	*N.* IgM + (%)	*N.* IgA + (%)	*N.* Low IgG avidity (%)
53	van der Colf et al. [73]	2020	Namibia	Africa	27	28	344	9 (2.61)	1 (0.3)	N.M	0 (0)
54	Khan et al. [74]	2020	India	Asia	28	26	594	162 (27)	3 (0.5)	N.M	3 (0.5)
55	Avcioglu et al. [75]	2020	Turkey	Europe	30	25	3607	702 (19.1)	50 (1.3)	N.M	7 (0.19)
56	Oliveira et al. [76]	2020	Brasil	America	26	29	1716	468 (27)	92 (5.3)	N.M	13 (0.75)
57	Sultan et al. [77]	2021	Iraq	Asia	20.4	24	305	32 (10.4)	2 (0.6)	N.M	9 (2.9)
58	Amiri et al. [78]	2021	Iran	Asia	N.M	29	264	79 (28.4)	4 (1.5)	N.M	4 (1.5)
59	Yener et al. [79]	2021	Turkey	Europe	26.4	30	2317	607 (26.1)	80 (3.4)	N.M	30 (1.29)
60	Skvarc et al. [80]	2022	Slovenia	Europe	N.M	28	17,990	2339 (13)	179 (0.9)	N.M	126 (0.7)
61	Tüfekci et al. [81]	2022	Turkey	Europe	27.6	26	1294	263 (20.3)	14 (1.1)	N.M	4 (0.3)
62	Karamat et al. [82]	2022	Pakistan	Asia	26.8	24	336	126 (37.5)	4 (1.2)	N.M	0 (0)
63	Mihu et al. [83]	2022	Romania	Europe	29.4	30	1317	607 (46)	54 (4.1)	10 (0.7)	4 (0.3)
64	Shabanian et al. [84]	2023	Iran	Asia	N.M	28	191	88 (46.1)	11 (5.8)	N.M	0 (0)
65	Naheen et al. [85]	2016	Bangladesh	Asia	N.M	27	39	33 (84)	6 (15.4)	N.M	4 (10.2)
66	Kodym et al. [86]	2023	Czech Republic	Europe	31.5	26	141	81 (57)	27 (19)	N.M	11 (7.8)
67	Ikuta et al. [87]	2023	Japan	Asia	N.M	29	100	70 (70)	37 (37)	N.M	28 (28)

lifetime. In the context of toxoplasmosis screening programs (prevent and control), the absence of IgG antibodies before pregnancy and the positivity of these antibodies during pregnancy can be a warning signal for potentially in the diagnosis of acute toxoplasmosis [91].

Analysis of our study showed that only 30% of pregnant women with positive IgM (suspected acute toxoplasmosis) had low IgG avidity, indicating that the false positives of this test are very significant. IgM antibodies can be measured about 7 days after acute infection, and they are among the first antibodies to appear in the blood. The titer of these antibodies reaches its maximum value after 1–3 months and then slowly decreases until 9 months until it becomes undetectable. However, in 9 to 27% of infected individuals, IgM antibodies persist in the blood for 2 years or more [92, 93].

False-positive outcomes in IgM tests can occur due to various factors, including Autoimmune antibodies, such as rheumatoid factor (RF) and antinuclear antibodies (ANA), acute viral infections, non-specific binding in laboratory conditions, also known as the prozone phenomenon, different sensitivity of diagnostic kits, and severe hemolytic and lipemic samples. Therefore, these reasons can lead to misinterpretation, inappropriate use of medication, and sometimes worry about the decision to have an abortion [1, 3, 7].

A positive result for IgM antibodies suggests the likelihood of an acute infection. Scientific studies consistently show that when IgG avidity measurements are combined with sensitive tests for *Toxoplasma*-specific IgM antibodies, it leads to the most precise diagnoses of acute toxoplasmosis [94]. Measuring IgG avidity is because the affinity of IgG antibodies to their target antigens increases over time after infonecit [95]. The strength of antibody binding can be measured using ELISA with a washing step and neutralizing buffer (such as urea) to remove low-affinity antibodies. The benefits of using this method in pregnant women include reduced need for frequent follow-ups, eliminating the need for PCR testing of amniotic fluid, avoiding unnecessary treatment with spiramycin or other drugs, and lowering costs [96, 97]. Numerous studies have demonstrated that IgG avidity is a valuable tool for distinguishing between acute and chronic toxoplasmosis with high sensitivity and specificity.

One limitation of this method is its ability to accurately diagnose active toxoplasmosis in individuals with compromised immune systems [1, 16]. Also, in some individuals, low or intermediate IgG avidity may remain for months to more than a year due to differences in the maturation of immune system responses [60, 98]. Therefore, the IgG avidity test lonely should not be decisive in the decision for recent infection. Because it may confuse the diagnosis of the stage (acute or chronic) of the disease [95]. To confirm the recent infection, a test panel is essential to make the necessary decisions and management about the conditions of pregnant women. Performing low avidity tests and reports in the early months of pregnancy should be more accurate and sensitive. Recently, numerous researches have been conducted on the design of IgG avidity diagnostic kits using recombinant and chimeric antigens. However, the antigen combination that is a definitive marker for differentiating between acute and chronic toxoplasmosis has not yet been discovered. Nevertheless, studies have emphasized the use of recombinant and chimeric proteins for maximum detection

efficiency. To increase the specificity of the avidity test and eliminate the mentioned disadvantages, it is possible to achieve higher confidence by making changes in the protocols of the test, such as changing different dilution, which affects the results of the avidity test [14, 19, 99].

The analysis of the results of this systematic review showed that the amount of IgA in pregnant women suspected to acute toxoplasmosis (IgM positive) is 43%. The kinetics of IgA production is similar to IgM and after that, it reaches its peak and remains positive for longer time (usually 6–7 months) [100].

The simultaneous presence of anti-*Toxoplasma* IgA with IgM probably indicates an acute infection, because the production of this antibodies during acquired immunity is not common, furthermore, it is rarely seen in chronic toxoplasmosis infection.

Our study shows that the presence of IgA antibodies in pregnant women, in the context of a serological panel, can significantly help in distinguishing between acute and chronic infection compared to patients without these antibodies. Similar to the results reported in this systematic review, several researchers have found that the *Toxoplasma* IgA assay is useful for differentiating the stages of infection during pregnancy [8, 11]. However, in some other studies, they have found that due to insensitivity and long reaction time, IgA assay is not a reliable indicator for detecting the stages of infection [7, 101]. However, the use of *Toxoplasma* IgA in the diagnosing of recent infection is controversial.

A study by Olariu et al. (2019) discovered that women who were positive for both anti-*Toxoplasma* IgA and IgM antibodies were four times more likely to have recently contracted the infection compared to those who were only positive for IgM antibodies [102]. According to these findings, including the *Toxoplasma* IgA antibodies test as part of the standard serological panel used to diagnose toxoplasmosis increases the accuracy of detecting recent infections.

Conclusions

In summary, the findings from this review emphasize the significance of addressing hurdles related to consistent screening practices and accurate differentiation between recent and past *Toxoplasma* infections during pregnancy. By combining IgG avidity assessments with sensitive IgM testing and IgA, we have the potential to precisely identify acute infection stages. Furthermore, ongoing advancements in diagnostic methodologies, especially with molecular technologies and comprehensive antibodies analyses, hold promise for enhancing clinical approaches in managing the complex challenges posed by toxoplasmosis in pregnant women.

Abbreviations

CT Chronic toxoplasmosis
AT Acute toxoplasmosis

Acknowledgements

We extend our sincere appreciation to our colleagues in the Department of Medical Parasitology and Mazandaran University of Medical Sciences, Sari, Iran, for their contributions to this research. We are also grateful for the support provided by the Deputy of Research and Technology of Mazandaran University of Medical Sciences, Sari, Iran and The Higher Education and Science Committee of RA (Research project No. 23RL-1F014). Their support enabled us to conduct this study and we are thankful for their commitment to advancing medical research.

Author contributions

Study concept design, A. D., H.A. O., and S.A.H.; Conduct experiments and acquire data, M. T., B.B., and S.A.; Analysis and interpretation of data, S. A. H.; drafting of the manuscript, A. D., M. S., and M. T.; critical revision of the manuscript for important intellectual content, Sh. Gh., Sh. S., and S. A. A.; statistical analysis, S. A. H.; Study supervision, A. D and S. A. H. All authors participated in reading and endorsing the final version of the manuscript.

Funding

This research received no specific grant from any funding agency, commercial or not-for-profit sectors.

Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Clinical trial number

Not applicable.

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Received: 24 January 2025 / Accepted: 8 April 2025
Published online: 06 May 2025

References

1. Moncada PA, Montoya JG. Toxoplasmosis in the fetus and newborn: an update on Seroprevalence, diagnosis and treatment. Expert Rev Anti Infect Ther. 2012;10(7):815–28. https://doi.org/10.1586/eri.12.58.

2. Sepúlveda-Arias JC, Gómez-Marin JE, Bobić B, Naranjo-Galvis CA, Djurković-Djaković O. Toxoplasmosis as a travel risk. Travel Med Infect Dis. 2014;12(6):592–601. https://doi.org/10.1016/j.tmaid.2014.05.007.
3. Chaudhry SA, Gad N, Koren G. Toxoplasmosis and pregnancy. Can Fam Physician. 2014;60(4):334–6.
4. Torgerson PR, Mastroiacovo P. The global burden of congenital toxoplasmosis: a systematic review. Bull World Health Organ. 2013;91:501–8. https://doi.org/10.2471/BLT.12.111732.
5. Remington JS, Wilson CB, Nizet V, Klein JO, Maldonado Y. Infectious diseases of the fetus and newborn. E-book: Elsevier Health Sciences; 2010.
6. Jenum PA, Stray-Pedersen B, Melby KK, Kapperud G, Whitelaw A, Eskild A, et al. Incidence of *Toxoplasma gondii* infection in 35,940 pregnant women in Norway and pregnancy outcome for infected women. J Clin Microbiol. 1998;36(10):2900–6. https://doi.org/10.1128/jcm.35.8.1972-1977.1997.
7. Dunn D, Wallon M, Peyron F, Petersen E, Peckham C, Gilbert R. Mother-to-child transmission of toxoplasmosis: risk estimates for clinical counselling. Lancet. 1999;353(9167):1829–33. https://doi.org/10.1016/S0140-6736(98)08220-8.
8. Oz HS. Maternal and congenital toxoplasmosis, currently available and novel therapies in horizon. Front Microbiol. 2014;5:385. https://doi.org/10.3389/fmicb.2014.00385.
9. Hoseini SA, Dehgani N, Sharif M, Daryani A, Gholami S, Ebrahimi F, Pagheh AS, Arefkhah N. Serological survey of *toxoplasmosis* in pregnant women. J Maz Univ Med Sci. 2014;24(114):146–50.
10. Jenum PA, Stray-Pedersen B, Gundersen A-G. Improved diagnosis of primary *Toxoplasma gondii* infection in early pregnancy by determination of Antitoxoplasma Immunoglobulin G avidity. J Clin Microbiol. 1997;35(8):1972–7. https://doi.org/10.1128/jcm.36.10.2900-2906.1998.
11. de Souza-e-Silva CH, Vasconcelos-Santos DV, de Andrade GQ, Carellos EVM, de Castro Romanelli RM, de Resende LM, et al. Association between IgG subclasses against *Toxoplasma gondii* and clinical signs in newborns with congenital toxoplasmosis. Pediatr Infect Dis J 2013. 2013;32(1):13–6. https://doi.org/10.1097/INF.0b013e3182703460.
12. Yamada H, Nishikawa A, Yamamoto T, Mizue Y, Yamada T, Morizane M, et al. Prospective study of congenital toxoplasmosis screening with use of IgG avidity and multiplex nested PCR methods. J Clin Microbiol. 2011;49(7):2552–6. https://doi.org/10.1128/JCM.02092-10.
13. Ajzenberg D, Cogné N, Paris L, Bessières M-H, Thulliez P, Filisetti D, et al. Genotype of 86 *Toxoplasma gondii* isolates associated with human congenital toxoplasmosis, and correlation with clinical findings. J Infect Dis. 2002;186(5):684–9. https://doi.org/10.1086/342663.
14. Bahhaj R, Ahmadpour E, Mahami-Oskouei M, Fallah E, Shamsasenjan K, Safaiyan A. *Toxoplasma gondii* infection and related risk factors among blood donors in Northwest Iran. Arch Clin Infect Dis. 2017;2017(2). https://doi.org/10.5812/archcid.62005.
15. Zhang K, Lin G, Han Y, Li J. Serological diagnosis of toxoplasmosis and standardization. Clin Chim Acta. 2016;461. https://doi.org/10.1016/j.cca.2016.07.018.:83– 9.
16. Robert-Gangneux F, Dardé M-L. Epidemiology of and diagnostic strategies for toxoplasmosis. Clin Microbiol Rev. 2012;25(2):264–96. https://doi.org/10.1128/cmr.05013-11.
17. Gharavi M, Ourmazdi H, Roueintan E. A comparative study on sensitivity and specificity of conventional and unconventional IgG and IgM assays for diagnosis of toxoplasmosis. 2008.
18. Petersen E, Borobio MV, Guy E, Liesenfeld O, Meroni V, Naessens A, et al. European multicenter study of the LIAISON automated diagnostic system for determination of *Toxoplasma gondii*-specific Immunoglobulin G (IgG) and IgM and the IgG avidity index. J Clin Microbiol. 2005;43(4):1570–4. https://doi.org/10.1128/jcm.43.4.1570-1574.2005.
19. Hedman K, Lappalainen M, Seppäiä I, Mäkelä O. Recent primary Toxoplasma infection indicated by a low avidity of specific IgG. J Infect Dis. 1989;159(4):736–40. https://doi.org/10.1093/infdis/159.4.736.
20. von Erik M, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. Ann Intern Med. 2007;147(8):573. https://doi.org/10.1016/j.ijsu.2014.07.013.
21. Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. Stat Med. 2002;21(11):1539–58. https://doi.org/10.1002/sim.1186.
22. Egger M, Smith GD, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. BMJ. 1997;315(7109):629–34. https://doi.org/10.1136/bmj.315.7109.629.
23. Auer H, Vander-MoÈse A, Picher O, Walochnik J, AspoÈck H. Clinical and diagnostic relevance of the *Toxoplasma* IgG avidity test in the serological surveillance of pregnant women in Austria. Parasitol Res. 2000;86:965–70. https://doi.org/10.1007/pl00008527.
24. Liesenfeld O, Montoya JG, Kinney S, Press C, Remington JS. Effect of testing for IgG avidity in the diagnosis of *Toxoplasma gondii* infection in pregnant women: experience in a US reference laboratory. J Infect Dis. 2001;183(8):1248–53. https://doi.org/10.1086/319672.
25. Montoya JG, Liesenfeld O, Kinney S, Press C, Remington JS. VIDAS test for avidity of *Toxoplasma*-specific Immunoglobulin G for confirmatory testing of pregnant women. J Clin Microbiol. 2002;40(7):2504–8. https://doi.org/10.1128/jcm.40.7.2504-2508.2002.
26. Alvarado-Esquivel C, Sethi S, Janitschke K, Hahn H, Liesenfeld O. Comparison of two commercially available avidity tests for *Toxoplasma*-specific IgG antibodies. Arch Med Res. 2002;33(6):520–3. https://doi.org/10.1016/S0188-4409(02)00411-3.
27. Reis MM, Tessaro MM, D'azevedo PA. *Toxoplasma*-IgM and IgG-avidity in single samples from areas with a high infection rate can determine the risk of mother-to-child transmission. Rev Inst Med Trop São Paulo. 2006 2006;48:93– 8. https://doi.org/10.1590/S0036-46652006000200007
28. Candolfi E, Pastor R, Huber R, Filisetti D, Villard O. IgG avidity assay firms up the diagnosis of acute toxoplasmosis on the first serum sample in immunocompetent pregnant women. Diagn Microbiol Infect Dis. 2007;58(1):83–8. https://doi.org/10.1016/j.diagmicrobio.2006.12.010.
29. Iqbal J, Khalid N. Detection of acute *Toxoplasma gondii* infection in early pregnancy by IgG avidity and PCR analysis. J Med Microbiol. 2007;56(11):1495–9. https://doi.org/10.1099/jmm.0.47260-0.
30. Barbosa IR, de Carvalho Xavier Holanda CM, de Andrade-Neto VF. Toxoplasmosis screening and risk factors amongst pregnant females in Natal, Northeastern Brazil. Trans R Soc Trop Med Hyg. 2009;103(4):377–82. https://doi.org/10.1016/j.trstmh.2008.11.025.
31. De Paschale M, Agrappi C, Clerici P, Mirri P, Manco M, Cavallari S, et al. Seroseroprevalence and incidence of *Toxoplasma gondii* infection in the Legnano area of Italy. Clin Microbiol Infect. 2008;14(2):186–9. https://doi.org/10.1111/j.1469-0691.2007.01883.x.
32. Ribeiro AC, Mutis MS, Fernandes O. Association of the presence of residual anti-*Toxoplasma gondii* IgM in pregnant women and their respective family groups in Miracema, Northwest Rio de Janeiro, Brazil. Mem Inst Oswaldo Cruz 2008. 2008;103:591–4. https://doi.org/10.1590/S0074-02762008000600013.
33. Alvarado-Esquivel C, Torres-Castorena A, Liesenfeld O, García-López C, Estrada-Martínez S, Sifuentes-Alvarez A, et al. Seroepidemiology of *Toxoplasma gondii* infection in pregnant women in rural Durango, Mexico. J Parasitol. 2009;95(2):271–4. https://doi.org/10.1645/GE-1829.1.
34. Gay-Andrieu F, Fricker-Hidalgo H, Sickinger E, Espern A, Brenier-Pinchart M-P, Braun H-B, et al. Comparative evaluation of the ARCHITECT Toxo IgG, IgM, and IgG avidity assays for anti-*Toxoplasma* antibodies detection in pregnant women Sera. Diagn Microbiol Infect Dis. 2009;65(3):279–87. https://doi.org/10.1016/j.diagmicrobio.2009.07.013.
35. Vaz RS, Thomaz-Soccol V, Sumikawa E, Guimarães ATB. Serological Seroprevalence of *Toxoplasma gondii* antibodies in pregnant women from Southern Brazil. Parasitol Res. 2010;106:661–5.
36. Tutarlılığı A. The accuracy of IgG avidity for detection of acute toxoplasmosis among pregnant Saudi women. TAF Preventive Medicine Bulletin. 2010 2010;9(1):7–14.
37. Sagel U, Krämer A, Mikolajczyk RT. Incidence of maternal *Toxoplasma* infections in pregnancy in upper Austria, 2000–2007. BMC Infect Dis. 2011;11:1–7. https://doi.org/10.1186/1471-2334-11-348.
38. Varol FG, Sayin NC, Soysuren S. Seroprevalance of *Toxoplasma gondii* antibodies in antenatal population of Trakya region. J Turk Soc Obstet Gynecol. 2011;8:93–9. https://doi.org/10.5505/tjod.2011.00533.
39. Pour Abolghasem S, Bonyadi MR, Babaloo Z, Porhasan A, Nagili B, Gardashkhani OA, et al. IgG avidity test for the diagnosis of acute *Toxoplasma gondii* infection in early. Iran J Immunol. 2011;8(4):251–5.
40. Nisii C, Pane S, Liuzzi G, Butera O, Chiappini R, Khouri D, et al. Results of anti-*Toxoplasma gondii* IgG, IgM, IgA and IgG avidity testing in pregnant women in Rome, Italy. Microbiol Med. 2012;27(4). https://doi.org/10.4081/mm.2012.2294.
41. El Deeb HK, Salah-Eldin H, Khodeer S, Allah AA. Seroprevalence of *Toxoplasma gondii* infection in antenatal population in menoufia Governorate, Egypt. Acta Trop. 2012;124(3):185–91. https://doi.org/10.1016/j.actatropica.2012.08.005.

42. Lopes-Mori FMR, Mitsuka-Breganó R, de Barros Bittencourt LHF, Dias RCF, Gonçalves DD, Capobiango JD, et al. Gestational toxoplasmosis in Paraná State, Brazil: Seroprevalence of IgG antibodies and associated risk factors. Braz J Infect Dis 2013. 2013;17(4):405–9. https://doi.org/10.1016/j.bjid.2012.12.003.
43. Uysal A, Cüce M, Tañer CE, Uysal F, Atalay S, Göl B, et al. Seroprevalence of congenital toxoplasmosis among a series of Turkish women. Rev Med Chil. 2013;141(4):471–6. https://doi.org/10.4067/S0034-98872013000400008.
44. Nowakowska D, Wujcicka W, Sobala W, Śpiewak E, Gaj Z, Wilczyński J. Age-associated Seroprevalence of *Toxoplasma gondii* in 8281 pregnant women in Poland between 2004 and 2012. Epidemiol Infect. 2014;142(3):656–61. https://doi.org/10.1017/S0950268813001179.
45. Andiappan H, Nissapatorn V, Sawangjaroen N, Nyunt MH, Lau Y-L, Khaing SL, et al. Comparative study on *Toxoplasma* infection between Malaysian and Myanmar pregnant women. Parasit Vectors. 2014;7:1–8. https://doi.org/10.1186/s13071-014-0564-9.
46. Emelia O, Rahana A, Firdaus AM, Cheng H, Nursyairah M, Fatinah A et al. IgG avidity assay: a tool for excluding acute toxoplasmosis in prolonged IgM titer Sera from pregnant women. 2014.
47. Andiappan H, Nissapatorn V, Sawangjaroen N, Chemoh W, Lau YL, Kumar T, et al. *Toxoplasma* infection in pregnant women: a current status in Songklanagarind hospital, Southern Thailand. Parasit Vectors. 2014;7:1–7. https://doi.org/10.1186/1756-3305-7-239.
48. Doudou Y, Renaud P, Jacqueline F, Hypolite S, Hypolite M, Patrick M, et al. Toxoplasmosis among pregnant women: high seroseroprevalence and risk factors in Kinshasa, Democratic Republic of congo. Asian Pac J Trop Biomed. 2014;4(1):69–74. https://doi.org/10.1016/S2221-1691(14)60211-2.
49. Hung C-S, Su H-W, Lee Y-L, Weng H-W, Wang Y-C, Naito T, et al. Seroseroprevalence, seroconversion, and risk factors for toxoplasmosis among pregnant women in Taipei, Taiwan. Jpn J Infect Dis 2015. 2015;68(4):312–7. https://doi.org/10.7883/yoken.JJID.2014.263.
50. Parlak M, Çim N, Erdin BN, Güven A, Bayram Y, Yıldızhan R. Seroseroprevalence of *Toxoplasma*, *Rubella*, and *Cytomegalovirus* among pregnant women in Van. Turk J Obstet Gynecol. 2015 2015;12(2):79. https://doi.org/10.4274/tjod.35902
51. Gontijo da Silva M, Clare Vinaud M, de Castro AM. Seroprevalence of toxoplasmosis in pregnant women and vertical transmission of *Toxoplasma gondii* in patients from basic units of health from Gurupi, tocantins, Brazil, from 2012 to 2014. PLoS ONE. 2015;10(11):e0141700. https://doi.org/10.1371/journal.pone.0141700.
52. AlSaidi MA, Muslt AH, Hraiga BA. The role of avidity test in the diagnosis of acute and chronic infection with *Toxoplasma gondii*. J Nat Sci Res. 2015;5(14):2225–0921.
53. Nasir IA, Aderinsayo AH, Mele HU, Aliyu MM. Seroprevalence and associated risk factors of *Toxoplasma gondii* antibodies among pregnant women attending Maiduguri teaching hospital, Nigeria. J Med Sci 2015. 2015;15(3):147. https://doi.org/10.3923/jms.2015.147.154.
54. El-Bali M, Zaglool DA, Khodari YA, Al-Harthi SA. Appraisal of prenatal anti-toxoplasma *gondii* (IgG + IgM)-IHA/IgM-ELISA screening in single samples via IgG avidity test. J Egypt Soc Parasitol. 2016;46(1):201–8.
55. Akhlaghi L, Tabatabaie F, Hadighi R, Maleki F, Hajialiani F, Dayer MS, et al. Diagnosis of acute toxoplasmosis in pregnant women referred to therapeutic centers of Alborz Province (Iran) using Immunoglobulin G avidity ELISA technique. Asian Pac J Trop Dis 2016. 2016;6(11):864–7. https://doi.org/10.1016/S2222-1808(16)61147-7.
56. Abazaj E, Ferataj Deliu E, Petri O, Shundi L, Hysaj B, Ali E, et al. IgG avidity test for diagnosis of acute *Toxoplasma gondii* in pregnant women. J Environ Prot Ecol. 2016;17:681–6. https://doi.org/10.1128/jcm.00505-20.
57. Smets A, Fauchier T, Michel G, Marty P, Pomares C. Comparison of *Toxoplasma gondii* IgG avidity architect and Vidas assays with the estimated date of infection in pregnant women. Parasite. 2016;23. https://doi.org/10.1051/parasite/2016056.
58. van Enter BJ, Lau Y-L, Ling CL, Watthanaworawit W, Sukthana Y, Lee W-C, et al. Seroseroprevalence of *Toxoplasma gondii* infection in refugee and migrant pregnant women along the Thailand–Myanmar border. Am J Trop Med Hyg. 2017;97(1):232. https://doi.org/10.4269/ajtmh.16-0999.
59. Sirin MC, Agus N, Yilmaz N, Bayram A, Derici YK, Samlioglu P, et al. Seroseroprevalence of *Toxoplasma gondii*, *Rubella* virus and *Cytomegalovirus* among pregnant women and the importance of avidity assays. Saudi Med J. 2017;38(7):727. https://doi.org/10.15537/smj.2017.7.18182.
60. Laboudi M, Sadak A. Serodiagnosis of toxoplasmosis: the effect of measurement of IgG avidity in pregnant women in Rabat in Morocco. Acta Trop. 2017-08;172:139–42. eng. https://doi.org/10.1016/j.actatropica.2017.04.008
61. Hamed ASM, Omar SH, Basyoni MM, El Antably AS, El Khateeb E, El Kateb AY. Comparative and analytical study on active toxoplasmosis to assess the IgG avidity in correlation to serological profile in a cohort of Egyptian patients. Comp Clin Pathol. 2017;26:1157–63. https://doi.org/10.1007/s00580-017-2501-8.
62. Naghili B, Abbasalizadeh S, Tabrizi S, Rajaii M, Akramiyan M, Alikhah H, et al. Comparison of IIF, ELISA and IgG avidity tests for the detection of anti-*Toxoplasma* antibodies in single serum sample from pregnant women. Infez Med. 2017;25(1):50–6.
63. Berredjem H, Aouras H, Benlaifa M, Becheker I, Djebar MR. Contribution of IgG avidity and PCR for the early diagnosis of toxoplasmosis in pregnant women from the North-Eastern region of Algeria. Afr Health Sci. 2017;17(3):647–56. https://doi.org/10.4314/ahs.v17i3.7.
64. Khademi SZ, Ghaffarifar F, Dalimi A, Davoodian P, Abdoli A. Seroprevalence and risk factors of *Toxoplasma gondii* infection among pregnant women in Hormozgan Province, South of Iran. Iran J Parasitol. 2019 2019;14(1):167. https://doi.org/10.18502/ijpa.v14i1.732
65. Roozbehani M, Gharavi M, Moradi M, Razmjou E. Detection of acute *Toxoplasma gondii* infection in pregnant women by IgG avidity and PCR analysis. 2018.
66. Gurlek B, Colak S, Antenatal. *Toxoplasma gondii*, *rubella* and *cytomegalovirus* infection screening among pregnant women attending tertiary university hospital. Gynecol Obstet Reprod Med. 2019 2019;25(2):74–80. https://doi.org/10.21613/GORM.2019.903
67. Oliveira GMSd, Simões JM, Schaer RE, Freire SM, Nascimento RJM, Pinheiro AMCM, et al. Frequency and factors associated with *Toxoplasma gondii* infection in pregnant women and their pets in Ilhéus, Bahia, Brazil. Rev Soc Bras Med Trop. 2019;52:e20190250. https://doi.org/10.1590/0037-8682-0250-2019.
68. Sharifi K, Farash BRH, Fatemeh T, Khaledi A, Sharifi K, Shamsian SAA. Diagnosis of acute toxoplasmosis by IgG and IgM antibodies and IgG avidity in pregnant women from Mashhad, Eastern Iran. Iran J Parasitol. 2019;14(4):639. https://doi.org/10.18502/ijpa.v14i4.2107.
69. Rahmati-Balaghaleh M, Hosseini Farash BR, Zarean M, Hatami-Pourdehno S, Mirahmadi H, Jarahi L, et al. Diagnosis of acute toxoplasmosis by IgG avidity method in pregnant women referred to health centers in south-eastern Iran. J Parasit Dis. 2019;43:517–21. https://doi.org/10.1007/s12639-019-01120-8.
70. Donadono V, Saccone G, Maruotti GM, Berghella V, Migliorini S, Esposito G, et al. Incidence of toxoplasmosis in pregnancy in Campania: A population-based study on screening, treatment, and outcome. Eur J Obstet Gynecol Reprod Biol. 2019;240:316–21. https://doi.org/10.1016/j.ejogrb.2019.07.033.
71. Tawfiq SK, Rezaig ZS, Al-Jebouri MM. Determination the time of toxoplasmosis among pregnant women by using IgG avidity to various *Toxoplasma gondii* antigens. Kirkuk Univ J-Sci Stud. 2019;14(1):1–12. https://doi.org/10.32894/kujss.2019.14.1.1.
72. Vueba AN, Faria CP, Almendra R, Santana P, Sousa MC. Serological Seroprevalence of toxoplasmosis in pregnant women in Luanda (Angola): Geospatial distribution and its association with socio-demographic and clinical-obstetric determinants. PLoS One 2020. 2020;15(11):e0241908. https://doi.org/10.1371/journal.pone.0241908.
73. Van der Colf BE, Ntirampeba D, Van Zyl GU, Noden BH. Seroseroprevalence of Toxoplasma *gondii* infection among pregnant women in Windhoek, Namibia, in 2016. South Afr J Infect Dis. 2020;35(1):1–7. https://doi.org/10.4102/sajid.v35i1.25.
74. Khan K, Khan W, Khan T, Naaz G, Naheda A, Aqeel S. Seroseroprevalence of low avidity anti-*Toxoplasma* IgG in pregnant women and its relationship with their age and contact with cats. 2020. Trop biomed. https://doi.org/10.47665/tb.37.4.1038
75. Avcioglu F, Behcet M, Kurtoglu MG. Evaluation of *Toxoplasma*, *Rubella*, and *Cytomegalovirus* serological results in women of childbearing age. Rev Assoc Médica Bras. 2020 2020;66:789–93. https://doi.org/10.1590/1806-9282.66.6.789
76. Oliveira JG, Arruda FM, Motoyama PVP, Braga ACS, Porto BM, Carneiro LRE, et al. Seroseroprevalence and classification of cases by probability of acute toxoplasmosis among pregnant women from Northeast Brazil. Braz J Dev 2020. 2020;6(6):33238–51. https://doi.org/10.34117/bjdv6n6-034.
77. Sultan S, Mero WM. Serodiagnosis of Toxoplasmosis by Using ELISA and IgG Avidity Test in Relation to Some Risk Factors among Women at Childbearing Age in Zakho City, Iraq DP. Al-Qadisiyah J Pure Sci. 2021;26(4):1–8. https://doi.org/10.29350/jops. 2021.26. 4.1331.
78. Amiri M, Saki J, Cheraghian B. Study of the Seroprevalence of Toxoplasmosis in pregnant women with diabetes type 1 and type 2 using serological and molecular methods in Abadan and Khoramshahr Counties, Southwest of Iran.

Gene Rep. 2021 2021;25:101276. https://doi.org/10.1016/j.genrep.2021.101276
79. Yener C, Varol F, Uzun I, Sütcü H, Yeşildağ B, Başar B et al. Seroseroprevalence of Toxoplasma *gondii* Antibodies in Pregnant Women in Thrace Region of Turkey-A Tertiary Center Experience. The Medical Journal Of Haydarpaşa Numune Training and Research Hospital. 2021 2021;61(3):0&#8211.
80. Skvarč M. Diagnostic accuracy of adjusted low IgG avidity index to predict acute *Toxoplasma gondii* infection in the first trimester of pregnancy. Folia Parasitol 2022. 2022;69:1–5. https://doi.org/10.14411/fp.2022.023.
81. Tüfekci EF, Duman MY, Çalışır B, Kılınç Ç, Uzel A. Investigation of *Toxoplasma gondii* seropositivity in pregnant women in Kastamonu Province, Turkey. Turkiye Parazitol Derg. 2022;46(4):288–92. https://doi.org/10.4274/tpd.galenos.2022.28247.
82. Karamat S, Khan FA, Saeed S, Jafri A, Langhani SK, Saleem A. Occurrence of seropositivity of *Toxoplasma gondii*, cytomegalovirus, and Rubella infections in pregnant women. Pak J Med Health Sci. 2022;16(9):25–8. https://doi.org/10.53350/pjmhs2216925.
83. Mihu AG, Lupu MA, Nesiu A, Marti DT, Olariu TR. Screening for the detection of *Toxoplasma gondii* IgG, IgM and IgA in females of reproductive age from Western Romania. Life. 2022;12(11):1771. https://doi.org/10.3390/life12111771.
84. Shabanian H, Jafari-Shakib R, Sharifdini M, Atrkar-Roshan Z, Majidi-Shad B. Seroepidemiology of Toxoplasmosis in Pregnant Women Referring to the Pregnancy Care Center of Ramsar. J Guilan Univ Med Sci. 2023 2023;32(2):106–15. https://doi.org/10.32598/JGUMS.32.2.1157.2
85. Naheen CR, Tarafder S, Sattar H, Khan S. *Toxoplasma gondii* specific IgG avidity assay: role and implication in the confirmatory diagnosis of acute toxoplasmosis in seropositive pregnant women. Bangabandhu Sheikh Mujib Med Univ. 2016 2016-08-17;9(2):96. en. https://doi.org/10.3329/bsmmuj.v9i2.29263
86. Kodym P, Kurzová Z, Berenová D, Malỳ M. Detection of persistent low IgG avidity–an interpretative problem in the diagnosis of acute toxoplasmosis. Plos one. 2023 2023;18(4):e0284499. https://doi.org/10.1371/journal.pone.0284499
87. Ikuta K, Kanno R, Bessho T, Koshizuka T, Suzutani T. Evaluation of *Toxoplasma gondii* IgG avidity assays through a comparison of IgM serostatus. Diagn Microbiol Infect Dis 2023. 2023;105(4):115901. https://doi.org/10.1016/j.diagmicrobio.2023.115901.
88. Boubaker K, Raeber P, Vaudaux B, Bucher H, Garweg J, Hoesli I, et al. Toxoplasmosis during pregnancy and infancy. A new approach for Switzerland. Swiss Med Wkly. 2008;138(Suppl 168):49–50. https://doi.org/10.4414/SMW.2008.w30271.
89. Maldonado YA, Read JS, Diseases Col. Diagnosis, treatment, and prevention of congenital toxoplasmosis in the united States. Pediatrics. 2017;139(2). https://doi.org/10.1542/peds.2016-3860.
90. Paquet C, Yudin MH. 285-Toxoplasmosis in pregnancy: prevention, screening, and treatment. J Obstet Gynaecol Can. 2018;40(8):e687–93. https://doi.org/10.1016/j.jogc.2018.05.036.
91. Nichols RA, Jones TB. Treatment of a positive *Toxoplasma* titer in pregnancy. Infectious Diseases: Elsevier; 2017. pp. 517–9.
92. Reiter-Owona I. Laboratory diagnosis of toxoplasmosis–possibilities and limitations die labordiagnose der Toxoplasmose–Möglichkeiten und Grenzen. LaboratoriumsMedizin. 2005;29(6):439–45. https://doi.org/10.1515/JLM.2005.060.
93. Gras L, Gilbert R, Wallon M, Peyron F, Cortina-Borja M. Duration of the IgM response in women acquiring *Toxoplasma gondii* during pregnancy: implications for clinical practice and cross-sectional incidence studies. Epidemiol Infect. 2004;132(3):541–8. https://doi.org/10.1017/s0950268803001948.
94. Dunn D, Wallon M, Peyron F, Petersen E, Peckham C, Gilbert R. Mother-to-child transmission of toxoplasmosis: risk estimates for clinical counselling. Obstet Gynecol Surv. 2000;55(1):6. https://doi.org/10.1016/S0140-6736(98)08220-8.
95. Tork M, Sarvi S, Asgarian-Omran H, Sadeghi M, Basirpour B, Nejad MH, Gholami S, Hosseini SA, Daryani A, Aghayan SA. Design and optimization of IgG avidity test for differentiating acute from chronic human *toxoplasmosis*: A systematic review and meta-analysis. Exp Parasitol. 2024;108883.
96. Sarvi S, Chegeni TN, Sharif M, Montazeri M, Hosseini SA, Amouei A, Hosseininejad Z, Anvari D, Saberi R, Gohardehi S, Daryani A. Congenital toxoplasmosis among Iranian neonates: a systematic review and meta-analysis. Epidemiol Health. 2019;41:e2019021.
97. Hosseini SA, Sharif M, Sarvi S, Abediankenari S, Hashemi-Soteh MB, Amouei A, Montazeri M, Aghayan SA, Gholami S, Shaker D, Mizani A. Genetic characterization of Toxoplasma gondii in Iranian HIV positive patients using multilocus nested-PCR-RFLP method. Parasitology. 2020;147(3):322–8.
98. Cardoso Fonseca Z, Xavier Rodrigues IM, Cruz e Melo N, Boaventura Avelar J, Castro AM, Martins Avelino M. IgG avidity test in congenital toxoplasmosis diagnoses in newborns. Pathogens 2017. 2017;6(2):26. https://doi.org/10.3390/pathogens6020026.
99. Vandenbroucke JP, Von Elm E, Altman DG, Gøtzsche PC, Mulrow CD, Pocock SJ, et al. Strengthening the reporting of observational studies in epidemiology (STROBE): explanation and elaboration—a Korean translation. Ewha Med J. 2024;47(2). https://doi.org/10.12771/emj.2024.e31.
100. Bessieres M, Roques C, Berrebi A, Barre V, Cazaux M, Seguela J. IgA antibody response during acquired and congenital toxoplasmosis. J Clin Pathol. 1992;45(7):605–8. https://doi.org/10.1136/jcp.45.7.605.
101. Hosseininejad Z, Sharif M, Sarvi S, Amouei A, Hosseini SA, Nayeri Chegeni T, et al. Toxoplasmosis seroseroprevalence in rheumatoid arthritis patients: a systematic review and meta-analysis. PLoS Negl Trop Dis. 2018;12(6):e0006545. https://doi.org/10.1371/journal.pntd.0006545.
102. Olariu TR, Blackburn BG, Press C, Talucod J, Remington JS, Montoya JG. Role of *Toxoplasma* IgA as part of a reference panel for the diagnosis of acute toxoplasmosis during pregnancy. J Clin Microbiol. 2019;57(2):01357–18. https://doi.org/10.1128/jcm.

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