

# TORCH Infection Status in Women of Childbearing Age in China: A Meta-Analysis

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**Abstract:** *Objective:* This paper presents a systematic review and meta-analysis of comprehensive information on the epidemiology of toxoplasmosis (TOX), rubella virus (RV), cytomegalovirus (CMV), and herpes simplex (HSV) also known as TORCH infection in women of childbearing age. Besides, the positive rates of TORCH-Immunoglobulin G (TORCH-IgG) and Immunoglobulin M (IgM) antibodies in women of childbearing age in different regions of China were statistically analyzed, so as to highlight the issue of TORCH infection in women of childbearing age. *Methods:* A total of 12,694 articles were retrieved by keyword searching. The works were screened according to the inclusion criteria, and 25 studies were included totaling 531,617 women of childbearing age. The OpenMeta[Analyst] software was used to perform a heterogeneity test, and a random-effects model was used for system analysis. *Results:* The results of the meta-analysis showed that the positive rates of TORCH-IgG antibodies in women of childbearing age nationwide were 3.2% for TOX-IgG, 73.4% for RV-IgG, 73.8% for CMV-IgG, and 57.4% for HSV-IgG. The positive rates of IgM antibody infection in TORCH were 1.3% for TOX-IgM, 6.1% for RV-IgM, 9.5% for CMV-IgM, 7.6% for HSV-IgM, 2.0% for HSV-1-IgM, and 1.9% for HSV-2-IgM. All meta-analyses had  $I^2 \geq 98\%$  and  $P < 0.001$ , which meant that the results were statistically significant. *Conclusions:* A meta-analysis of the positive rates of IgG and IgM antibodies of TORCH infection in women of childbearing age found that the early infection rate of HSV was the highest, and the previous infection rate of RV was the highest. This result can provide epidemiological basis for the prevention and treatment of TORCH infection.

**Keywords:** TORCH; Women of childbearing age; IgG; IgM; Meta-analysis

**Online publication:** November 27, 2023

## 1. Introduction

TORCH is an acronym for toxoplasmosis (TOX), other pathogenic microorganisms (O), rubella virus (RV), cytomegalovirus (CMV), and herpes simplex virus type 1/2 (HSV). TORCH infects women of childbearing age and the disease can be transmitted to the fetus or newborn through the placenta or the birth canal, making it one of the most important factors leading to miscarriage, preterm delivery, stillbirth, intrauterine growth retardation, congenital developmental anomalies, neonatal central nervous system damage, and other adverse outcomes

in women of childbearing age <sup>[1]</sup>. Women of childbearing age who are infected with TORCH usually have no specific manifestations or symptoms, and once the infection is established, it can lead to adverse maternal and infant outcomes. Immunoglobulin G (IgG) and immunoglobulin M (IgM) are commonly used to diagnose TORCH infection. In the early stages of infection, IgM rises rapidly for 2–3 months, followed by elevated IgG, which can remain lifelong. Therefore, IgM is commonly used as an indicator of early infection, and IgG is an indicator of a previous infection.

Although there are many papers on TORCH, there are almost no cross-sectional studies on TORCH infection in Chinese women of childbearing age. In this paper, we systematically reviewed and meta-analyzed the comprehensive information on the epidemiology of TORCH infection in women of childbearing age, and statistically analyzed the positive rates of TORCH-IgG and IgM antibodies among women of childbearing age of different ages in different regions of China, so as to highlight the issue of TORCH infection among women of childbearing age. The objective of this analysis is to encourage women of childbearing age to pay attention to and prevent TORCH infection.

## **2. General information and methodology**

### **2.1. Data inclusion criteria**

#### **2.1.1. Types of research**

Studies at home and abroad that are related to analyzing the status of TORCH infection among Chinese women of childbearing age.

#### **2.1.2. Inclusion criteria for study subjects**

(1) Chinese or English publications related to the analysis of TORCH infection in women of childbearing age in various regions of China; (2) literature regarding the IgM or IgG of TORCH-infected women of childbearing age and the positive rate of TORCH-IgM and or TORCH-IgG antibodies; and (3) studies involving women of childbearing age who are not pregnant. Exclusion criteria: Literature that does not meet the inclusion criteria.

### **2.2. Search strategy**

We searched PubMed, China National Knowledge Infrastructure (CNKI), WANFANG, and VIP databases for studies related to the analysis of TORCH infection in Chinese women of childbearing age published in the years 2005–2019. The literature was screened by reading the abstract of the literature, and the full text of the selected literature was searched. Keywords: “TORCH,” “*Toxoplasma gondii* (TOX),” “rubella virus (RV),” “cytomegalovirus (CMV),” “herpes simplex virus (HSV) type 1/2,” etc.

### **2.3. Data extraction and processing**

Two evaluators independently searched the literature, extracted the data, and cross-checked. When the opinions were inconsistent, they were resolved by discussion or soliciting third-party opinions. Firstly, the data of all works were extracted and summarized according to the virus types (TOX, RV, CMV, HSV) and IgM and/or IgG. The OpenMeta[Analyst] software was used to calculate the antibody positive rate, with a 95% confidence interval (95% CI) (Lower CL–Upper CL), and a forest map was drawn.

### **2.4. Statistical analysis**

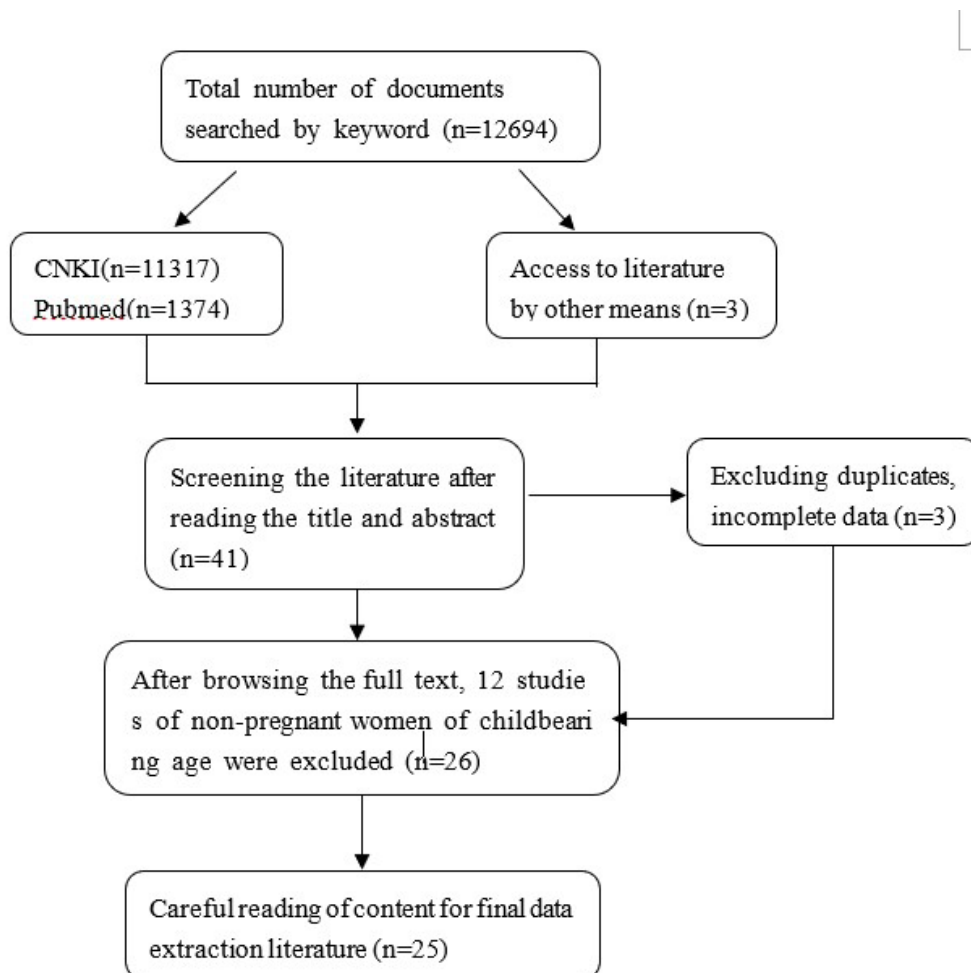
Meta-analysis was performed using the OpenMeta[Analyst] software. The heterogeneity across the studies was examined using the  $I^2$ -test, and the degree of heterogeneity was determined by the value of  $I^2$ ;  $I^2 = 0$  indicated

that the variation between studies was only caused by sampling error;  $I^2 < 0.25$  indicated mild heterogeneity;  $0.25 < I^2 < 0.5$  indicated moderate heterogeneity; a fixed effect model was used for  $I^2 < 0.5$ .  $I^2 > 0.5$  indicated high heterogeneity, in which a random-effects model was used, with 95% CI. The results of the meta-analysis were represented by forest plots.

### 3. Results

#### 3.1. Literature search results

A total of 12,694 articles were retrieved from PubMed, CNKI, WANFANG, and VIP databases. Duplicate articles were excluded. By reading the title and abstract, 41 articles were obtained: CNKI ( $n = 33$ ), PubMed ( $n = 5$ ), and other methods ( $n = 3$ ). After reading the full texts, 3 documents were excluded due to incomplete data, and 12 studies were excluded because they did not include pregnant women of childbearing. Through careful reading and comparison, 1 article showed variations in the number of women of childbearing age with TORCH-IgG and IgM with each virus. A total of 25 articles<sup>[2-26]</sup> were included in the Meta-analysis study after filtering according to the inclusion and exclusion criteria, including 531617 women of childbearing age in China. The literature screening process is shown in **Figure 1**.



**Figure 1.** Flowchart of literature screening

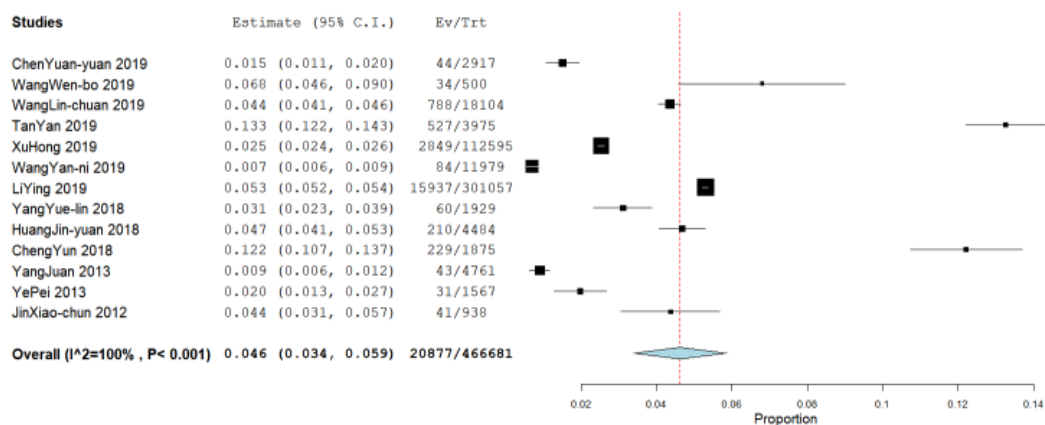
### 3.2. Basic information of the included studies

A total of 25 papers studied the serum levels of TORCH-IgG and TORCH-IgM antibodies in Chinese women of childbearing age, and these papers were published between 2005 and 2020. The subjects were from 13 provinces in China (Fujian, Zhejiang, Hubei, Yunnan, Jiangsu, Chongqing, Beijing, Shaanxi, Henan, Inner Mongolia, Shandong, Liaoning, and Jilin). The studies involved women of childbearing age of different ages and geographic areas. The studies involved a total of 531,617 people, with sample sizes ranging from 500 to 301,057 per study, and the subjects were women of childbearing age between 18 and 49 years old. The enzyme-linked immunosorbent assay (ELISA) kit was used to detect TORCH-IgG (TOX-IgG, RV-IgG, CMV-IgG, HSV-1/2-IgG) and TORCH-IgM (TOX-IgM, RV-IgM, CMV-IgM, HSV-1/2-IgM) antibody levels in the serum of the patients. The details of the studies included are shown in **Table 1**.

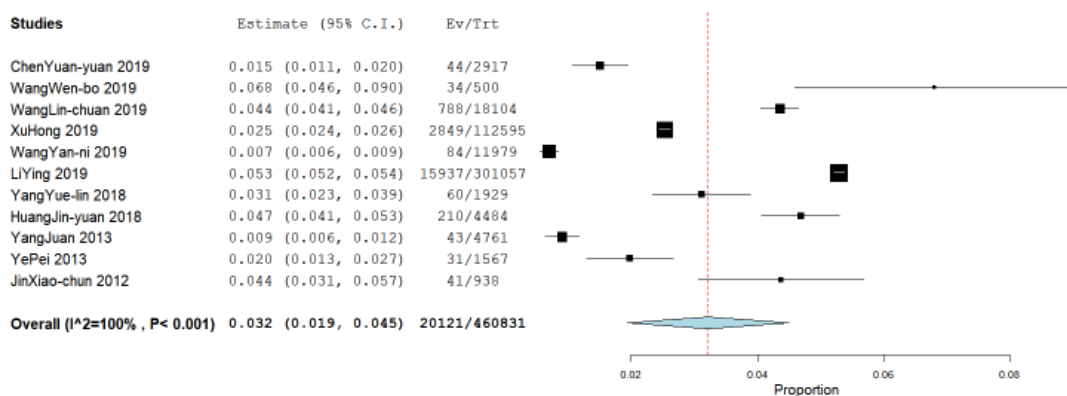
### 3.3. TORCH-IgG antibody positivity rate

#### 3.3.1. Positive rate of IgG antibodies to TOX infection

Thirteen studies reported the positive rate of IgG antibodies to TOX infection in women of childbearing age, including 466,681 patients. 2 studies with high heterogeneity were excluded, and the rate of TOX-IgM antibody positivity in women of childbearing age in 11 studies was statistically analyzed, including 460,831 patients. The studies showed an  $I^2$  of 100%, indicating the presence of heterogeneity. Therefore, meta-analysis was carried out using a random-effects model, and the pre-and post-censoring estimates and 95% CI confidence interval were calculated. The antibody positivity estimates and 95% CI confidence interval after exclusion, and forest plots of TOX-IgG are shown in **Figure 2** and **Figure 3**. The results found that the TOX-IgG antibody positivity rate was 3.2% (95% CI = 0.019–0.045).



**Figure 2.** Forest plot analysis of TOX-IgG antibody positivity (before exclusion)



**Figure 3.** Forest plot analysis of TOX-IgG antibody positivity (after exclusion)

**Table 1.** TORCH detection in women of childbearing age

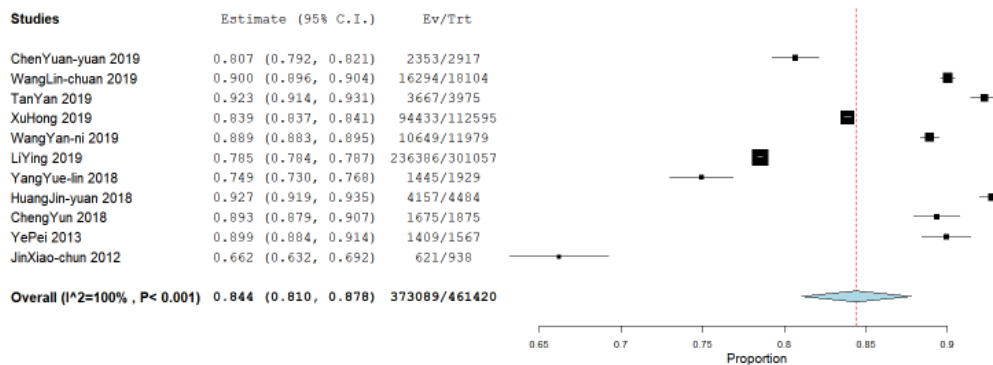
Serial number	Title of document	First author	Year	City	Sample size (cases)	HSV-1 (HSV)		HSV-2		RV		CMV		TOX	
						IgG	IgM	IgG	IgM	IgG	IgM	IgG	IgM	IgG	IgM
1	Analysis of TORCH Screening Results of 2,917 Women of Childbearing Age in Fuzhou, Fujian	Chen Yuanyuan	2019	Fuzhou	2917	91.84% (Total)	10.56% (Total)	80.67%	1.71%	97.15%	0.55%	1.51%	0.10%		
2	Clinical Application and Significance of TORCH Testing in Preconception Eugenic Health Screening	Wang Wenbo	2019	Xiamen	500	16.0% (Total)	16.2% (Total)	18.0%	3.0%	17.6%	1.8%	6.8%	1.0%		
3	TORCH Screening Used Appropriately in China?—Three Years Results from a Teaching Hospital in Northwest China	Lin-Chuan Wang	2019	Xi'an	18104	81.11%	0.14%	6.1%	0.19%	90%	0.63%	96.79%	0.97%	4.35%	0.35%
4	A Study on TORCH Infections in Women of Reproductive Age in the Wanzhou District of the City of Chongqing	Tan Yan	2019	Chongqing Wanzhou	3975	70.48%		17.56%		92.26%	1.76%	98.32%	6.92%	13.27%	1.45%
5	Clinical Analysis of TORCH Infection in Women of Childbearing Age	Bai Jie	2019	Xi'an	1788		0.2%		0.2%		0.5%		2.0%		0.5%
6	Analysis of TORCH Screening Results in 112,595 Women Preparing for Pregnancy in Hangzhou	Xu Hong	2019	Hangzhou	112595					83.87%		96.96%	0.22%	2.53%	0.14%
7	Analysis of TORCH Test Results in 22,063 Women of Childbearing Age	Wang Yann	2019	Chongqing	11979					88.9%	1.1%	3.5%	94.4%	0.7%	6.4%
8	Analysis of the TORCH Infection Status of 301057 Women Undergoing Pre-Pregnancy Health Examination in the Hubei Province	Li Ying	2019	Hubei	301057					78.52%		72.73%	0.17%	5.29%	0.13%
9	Analysis of Serum IgG and IgM Antibodies Against TORCH-Related Pathogens	Yang Yuelin	2018	Kunming	1929	90.77% (Total)	9.9% (Total)		8.19%	74.91%	3.47%	97.51%	0.88%	3.11%	1.3%
10	Analysis of the TORCH Infection Status in 4484 Women Undergoing Pre-Pregnancy Examination in Chongqing	Huang Jinyuan	2018	Chongqing	4484					92.7%	0.65%	90.1%	0.49%	4.68%	0.02%
11	Seasonal Influence on TORCH Infection and Analysis of Multi-Positive Samples with Indirect Immunofluorescence Assay	Chen Lu	2018	Beijing	10669		6.30%		1.94%		2.55%		1.24%		0.67%
12	Investigation on TORCH Infection Among Mongolian Women of Childbearing Age in Baotou	Cheng Yun	2018	Baotou	1875	77.97% (Total)	0.80% (Total)			89.33%	2.03%	93.65%	1.44%	12.21%	1.12%
13	Investigation and Analysis of TORCH Infection Status Among Women of Childbearing Age in Shandong	Song Huanjing	2017	Shandong	5743		2.86%		0.54%		2.79%		0.24%		0.16%
14	Exploring the Clinical Significance of TORCH Testing Before Pregnancy in Married Women of Childbearing Age	Yang Mingxia	2016	Dalian Zhongshan	756		0.66% (Total)				2.25%		0.53%		0.79%

**Table 1. (continued)**

Serial number	Title of document	First author	Year	City	Sample size (cases)	HSV-1 (HSV)		HSV-2		RV		CMV		TOX	
						IgG	IgM	IgG	IgM	IgG	IgM	IgG	IgM	IgG	IgM
15	Analysis of TORCH Infection in 5985 Premarital Women of Childbearing Age in Haicang District, Xiamen	Luo Yulan	2016	Fujian Xiamen	5985			0.27%		0.65%		0.40%			0.58%
16	Analysis of TORCH Testing Results of 4761 Cases of Women of Childbearing Age in Wuxi	Yang Juan	2013	Wuxi	4761			0.63%		0.38%		0.04%		0.90%	0.19%
17	Analysis of 1185 Cases of TORCH Infection in Women of Childbearing Age in Lishui City, Zhejiang Province	Ye Pei	2013	Zhejiang Lishui	1567		0.26%		0.13%	89.92%	0.16%	98.72%	0.64%	1.98%	0.26%
18	Analysis of Preconception Eugenic Test Results of 938 Women of Childbearing Age	Jin Xiaochun	2012	Jilin Baishan	938	10.4% (Total)	0.6% (Total)		0.3%	66.2%	0.3%	95.1%	0.8%	4.4%	0.6%
19	Statistical Analysis of TORCH Infection Among Women of Reproductive Age in Shanyang District, Jiaozuo City	Zhang Xiaocui	2012	Henan Jiaozuo	4095	6.42% (Total)			1.54%			1.17%			6.23%
20	Investigation and Analysis of 3327 Cases of TORCH Infection in Women of Childbearing Age	Chen Ruihong	2011	Zhengzhou	3327			0.75%		1.23%		1.56%			1.29%
21	Statistical Analysis of TORCH Infection Among Women of Childbearing Age in the Region	Jiang Shiqin	2011	Shandong Guangrao, Lijin	4095	6.42% (Total)			1.54%			1.17%			6.23%
22	Detection and Analysis of TORCH Infection in Women of Normal Childbearing Age	Zhang Xuzhen	2010	Shandong Ningjin	5062			1.86%		8.22%		2.39%			2.09%
23	Analysis of Pre-Pregnancy TORCH Infection Status Among Women of Childbearing Age in Kuancheng District, Changchun City	Chen Tingting	2009	Jilin Changchun	2726			18.60%		92.37%		97.07%			8.29%
24	Analysis of Pre-Pregnancy TORCH Screening Results in 20,000 Women of Childbearing Age in Jiangsu Province	Liu Qilan	2008	Jiangsu	20000		2.11%		1.17%		4.13%		2.12%		2.09%
25	Screening for TORCH Infection in Pre-Pregnant Women	Liu Xiangping	2005	Yunnan Lincang	690		19.71% (Total)			8.98%		17.97%			5.36%

### 3.3.2. Positive rate of IgG antibodies to RV infection

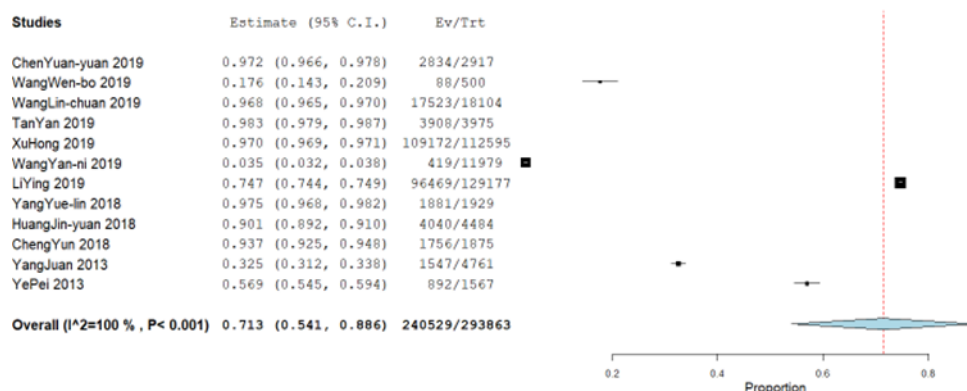
Thirteen studies explored the rate of RV-IgG antibody positivity in women of childbearing age, including 466,982 patients. 2 studies with high heterogeneity were excluded, and 11 studies were statistically analyzed, including 461,420 patients. The studies showed an  $I^2$  of 100%, indicating the presence of heterogeneity. Therefore, meta-analysis was carried out using a random effects model. It was found that the estimated positivity rate of RV-IgG antibodies was 84.4% (95% CI = 0.810–0.878). Further details are shown in **Figure 4**.



**Figure 4.** Forest plot analysis of RV-IgG antibody positivity rate

### 3.3.3. Positive rate of IgG antibodies to CMV infection

Thirteen studies reported the positive rate of IgG antibodies in CMV-infected women of childbearing age, including 465,247 patients. 2 studies with high heterogeneity were excluded, and in women of childbearing age in 11 studies were statistically analyzed, including 461,420 patients. The studies showed an  $I^2$  of 100%, indicating the presence of heterogeneity. Therefore, meta-analysis was carried out using a random effects model (**Figure 5**). The results revealed a CMV-IgG antibody positivity rate of 71.3% (95% CI = 0.541–0.886) in women of childbearing age.



**Figure 5.** Forest plot analysis of CMV-IgG antibody positivity rates

### 3.3.4. Positive rate of IgG antibodies to HSV infection

Five studies reported a positive rate of IgG in HSV-infected women of childbearing age, including 8,159 patients. The OpenMeta[Analyst] software was used to calculate HSV-IgG antibody positivity with 95% CI, and a forest plot was drawn (**Figure 6**). The results showed that the HSV-IgG antibody positivity rate was found to be 57.4% (95% CI = 0.273–0.875) in women of childbearing age.

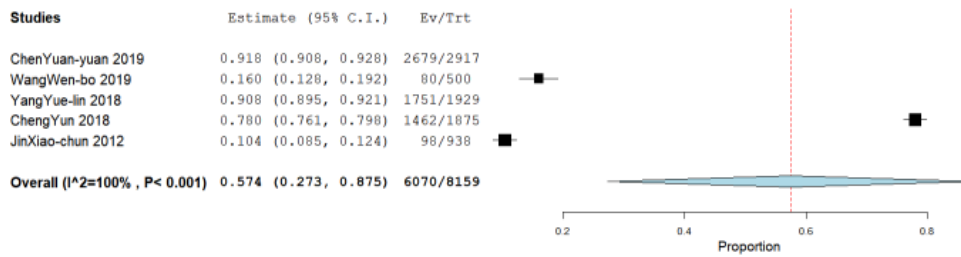


Figure 6. Forest plot analysis of HSV-IgG antibody positivity rate

### 3.4. TORCH infection IgM antibody positivity rate

#### 3.4.1. TOX infection IgM antibody positivity rate

A total of 25 studies involving 531,617 patients reported the rate of IgM antibody positivity for TOX infection in women of childbearing age, and substantial heterogeneity was observed ( $I^2 = 99\%$ ). A meta-analysis, utilizing a random-effects model, was conducted to estimate the rate of TOX-IgM antibody positivity in women of childbearing age, resulting in a rate of 1.3% (95% CI= 0.012–0.015), as shown in **Figure 7**.

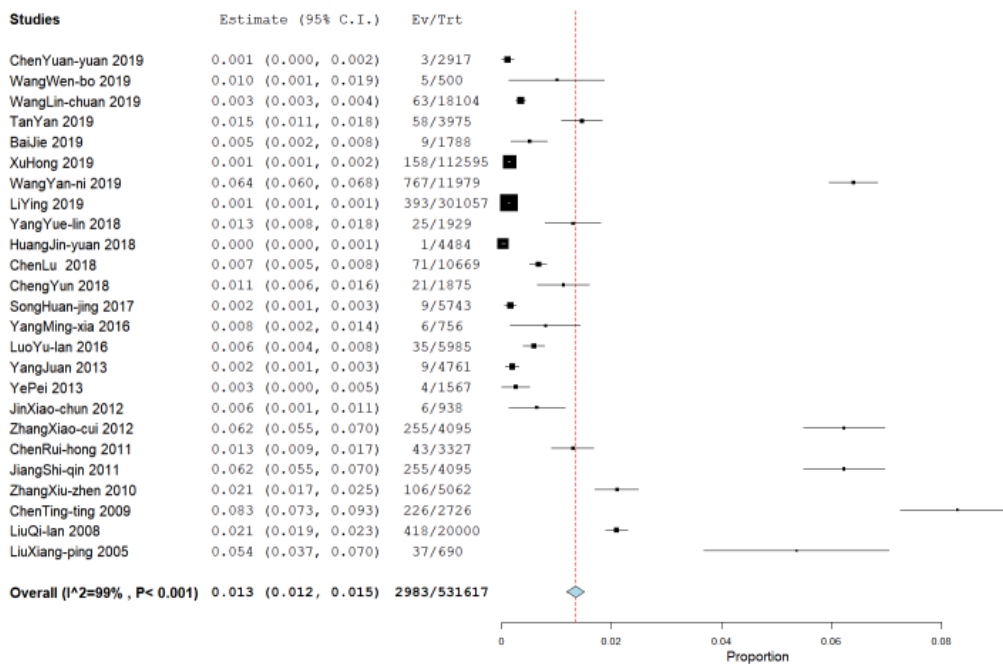


Figure 7. Forest plot analysis of TOX-IgM antibody positivity rate

#### 3.4.2. IgM antibody positivity rate of RV infection

Twenty-two studies investigated the rate of RV-IgM antibody positivity in women of childbearing age, encompassing 112,903 patients. After excluding the two studies with substantial heterogeneity, a statistical analysis was performed on the rate of RV-IgM antibody positivity in women of childbearing age using data from 20 studies, involving 109,487 patients. Heterogeneity was high ( $I^2 = 98\%$ ), and a meta-analysis employing a random-effects model determined that the rate of RV-IgM antibody positivity was 1.6% (95% CI = 0.011–0.020), as illustrated in **Figure 8**.



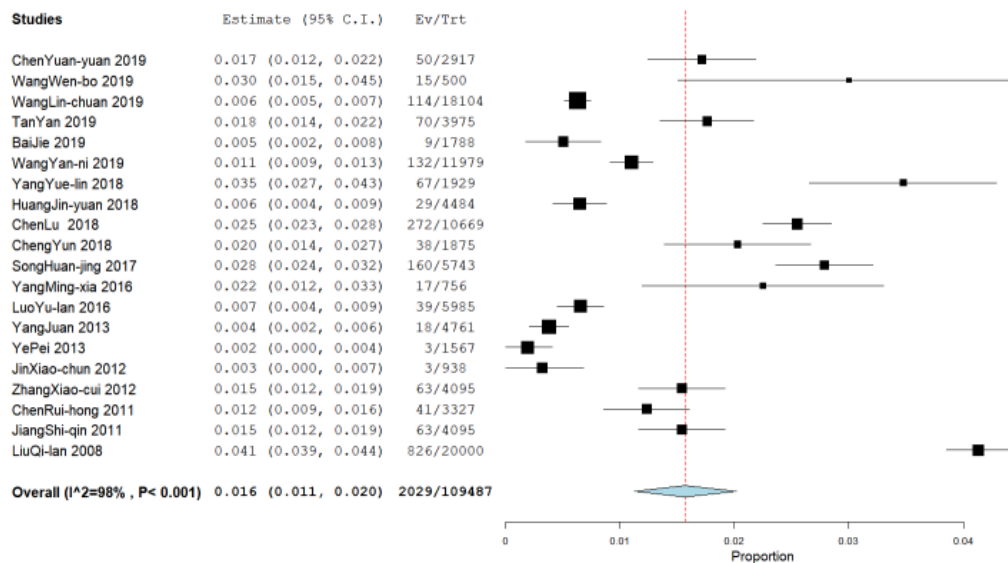


Figure 8. Forest plot analysis of RV-IgM antibody positivity rate

### 3.4.3. Positive rate of IgM antibodies to CMV infection

A total of twenty-five studies investigated the rate of CMV-IgM antibody positivity in women of childbearing age, involving 531,617 patients. The rates of CMV-IgM antibody positivity in each study were aggregated and subjected to statistical analysis. High heterogeneity was observed ( $I^2 = 100\%$ ). Utilizing a random-effects model, a meta-analysis revealed that the rate of CMV-IgM antibody positivity in women of childbearing age was 9.5% (95% CI = 0.075–0.114), as depicted in Figure 9.

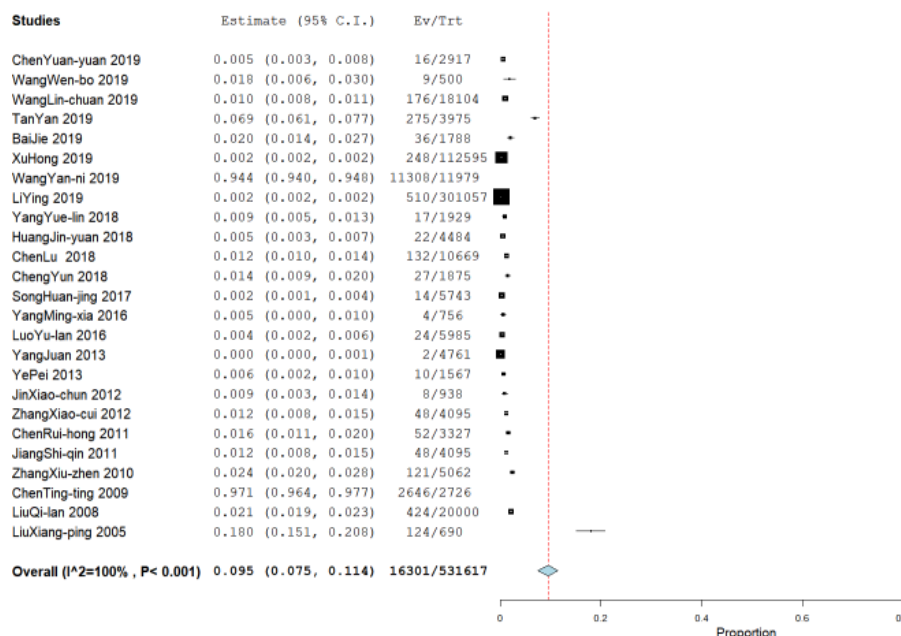
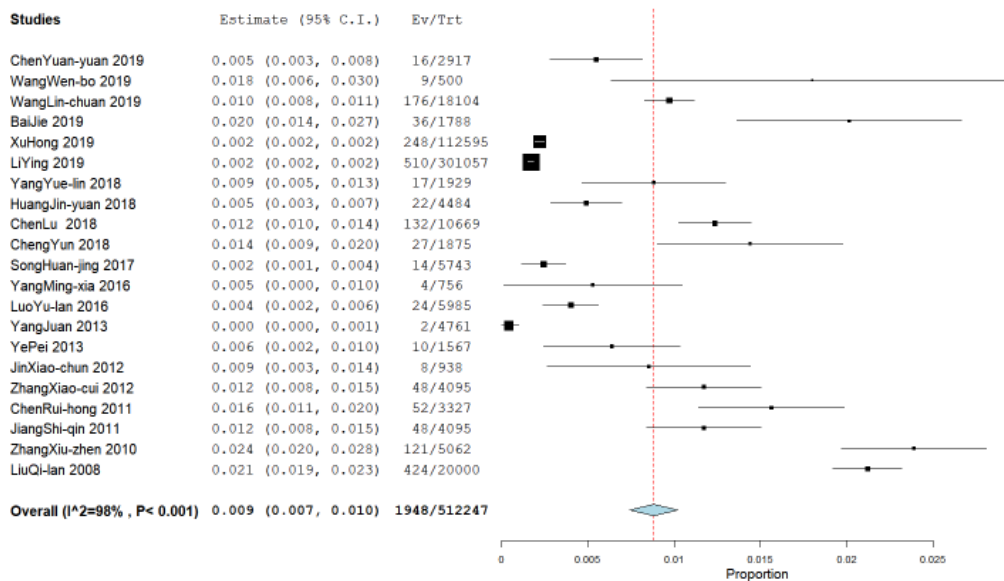


Figure 9. Forest plot analysis of CMV-IgM antibody positivity rate

After excluding four studies with substantial heterogeneity, a revised statistical analysis for CMV-IgM antibody positivity in women of childbearing age was conducted using the data from 21 studies, comprising

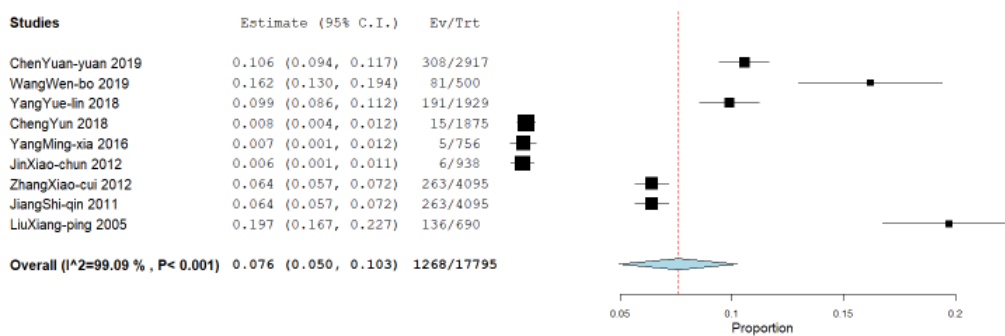
512,247 patients. Despite a remaining heterogeneity with  $I^2 = 98\%$ , a meta-analysis employing a random-effects model determined that the CMV-IgM antibody positivity rate in women of childbearing age was 0.9% (95% CI = 0.007–0.010), as illustrated in **Figure 10**.



**Figure 10.** Forest plot analysis of CMV-IgM antibody positivity rate

### 3.4.4. IgM antibody positivity rate for HSV infection

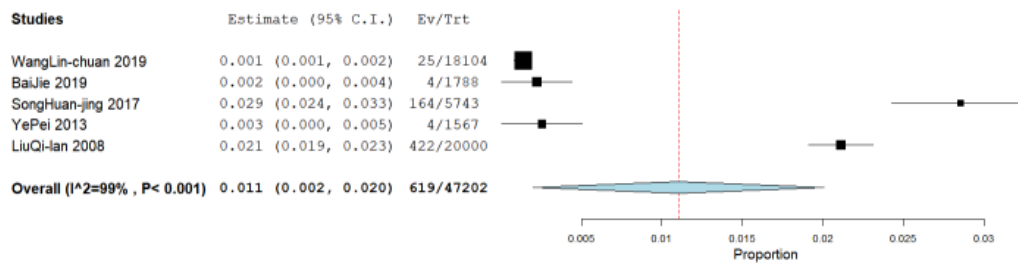
Nine studies reported the rate of IgM antibody positivity for HSV infection in women of childbearing age, including 17,795 patients,  $I^2 = 99.09\%$ , indicating substantial heterogeneity. Utilizing a random-effects model for meta-analysis, the HSV-IgM antibody positivity rate in women of childbearing age was determined to be 7.6% (95% CI = 0.050–0.103), as shown in **Figure 11**.



**Figure 11.** Forest plot analysis of HSV-IgM antibody positivity rate

### 3.4.5. HSV-1 infection IgM antibody positivity rate

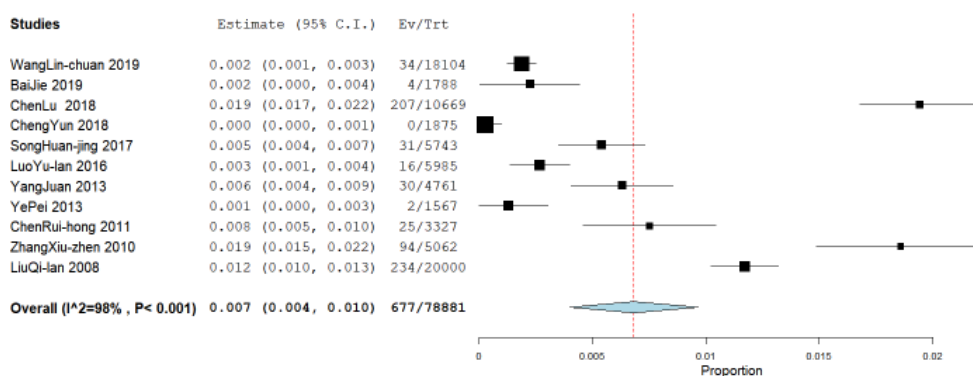
Six studies reported the IgM antibody positivity rate for HSV-1 infection in women of childbearing age, involving 57,871 patients. After excluding one study with substantial heterogeneity, the positivity rate of HSV-1-IgM antibodies in women of childbearing age from the remaining five studies, encompassing 47,202 patients, was statistically analyzed. The analysis revealed substantial heterogeneity with an  $I^2$  value of 99%. Employing a random-effects model for meta-analysis, the rate of HSV-1-IgM antibody positivity in women of childbearing age was found to be 1.1% (95% CI = 0.002–0.020), as shown in **Figure 12**.



**Figure 12.** Forest plot analysis of HSV-1-IgM antibody positivity rate

### 3.4.6. IgM antibody positivity rate of HSV-2 infection

Thirteen studies included data on HSV-2 IgM antibody positivity rates in women of childbearing age, with a total of 83,536 participants. After excluding two studies with significant heterogeneity, a statistical analysis was conducted on the remaining eleven studies, which comprised 78,881 patients. These studies exhibited substantial heterogeneity ( $I^2 = 98\%$ ). Using a random-effects model, the HSV-2 IgM antibody positivity rate in women of childbearing age was determined to be 0.7% (95% CI = 0.004–0.020). The results can be seen in **Figure 13**.



**Figure 13.** Forest plot analysis of HSV-2-IgM antibody positivity rate

## 4. Discussion

TORCH infections are usually asymptomatic and of relatively low virulence, so they are easily overlooked and difficult to diagnose, which may lead to miscarriage, intrauterine fetal death, and congenital malformations. Therefore, testing for TORCH infection is important to prevent adverse fetal outcomes.

Detection of serological evidence of IgM and IgG antibodies to TORCH is the preferred method of identifying TORCH infection. IgM antibodies are elevated rapidly as soon as a viral infection occurs, but disappear quickly. IgG antibodies are produced later and persist for a long time, so they can be used as an indicator of a distant infection. The detection of IgM antibodies is considered to be the main way of acute infection with the virus at present and is also the key to the diagnosis of early infection. IgM antibody test is considered to be the main way of acute viral infection, which is also the key to early diagnosis of infection.

A total of 25 studies on the status and analysis of TORCH infection in women of childbearing age were reviewed in this paper, and IgM (TOX-IgM, RV-IgM, CMV-IgM, HSV 1/2-IgM and IgG (TOX-IgG, RV-IgG, CMV-IgG, HSV-1/2-IgG) antibody positivity rates of TORCH diseases were studied separately. pooled analyses

were performed using the OpenMeta[Analyst] software, and the heterogeneity of the findings was assessed by the  $I^2$  test, which showed that TORCH-IgG (TOX-IgG, RV-IgG, CMV-IgG, HSV 1/2-IgG) and TORCH-IgM (TOX-IgM, RV-IgM, CMV-IgM, HSV-1/2-IgM) antibody positivity rate had high heterogeneity,  $I^2 \geq 98\%$ , and the results were statistically significant when analyzed by random effect model,  $P < 0.001$ .

The results of the meta-analysis showed that the early infection rate of TORCH infection early IgM antibody level of HSV was the highest at 7.6%, with a sample size of 17,795; followed by RV-IgM at 1.6%; then TOX-IgM at 1.3%, which had the largest sample size of 531,617; and lastly, CMV-IgM at 0.9%, with a sample size of 512,247. It was also found that RV had the highest previous infection rate of 84.4%, with a sample size of 466,982; followed by CMV-IgG at 71.3%; then HSV-IgG at 57.4%, with a minimum sample size of 8,159; and lastly, TOX-IgG at 3.2%, with a sample size of 460,831.

Thirteen of the 25 studies were distributed in six southern provinces and cities (Fujian, Zhejiang, Hubei, Yunnan, Jiangsu, and Chongqing) and 12 studies were distributed in seven northern provinces and cities (Beijing, Shaanxi, Henan, Inner Mongolia, Shandong, Liaoning, and Jilin), which covered both northern and southern China, with a total of 531,617 people. Hence the sample range holds a certain significance.

## 5. Conclusion

In summary, this paper included 25 studies on IgG and or IgM antibody levels of TORCH infection in women of childbearing age in various regions of China published from 2005 to 2020 according to the nadir criteria for meta-analysis. TORCH infection is prevalent in women of childbearing age. A person can be cryptically infected with *Toxoplasma gondii* for a long time. RV and CMV can be latent, but their latency periods are relatively short, while HSV is often latent in ganglia. These infections are often asymptomatic and require attention. Seroepidemiological surveys of TORCH infection can help to understand the status of TORCH infection in women of childbearing age, which is important for assessing the risk of TORCH infection in women of childbearing age as well as the adverse outcomes after pregnancy.

## Funding

Matching fund project of the First Affiliated Hospital of Xi'an Medical University (XYFYPT-2022-02)

## Disclosure statement

The authors declare no conflict of interest.

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