Abstract

**Background**: Toxoplasmosis is a great public health concern due to its capacity for prenatal transmission. Serologic studies have reported various estimates for seroprevalence of toxoplasmosis among Iranian pregnant women. Estimation of the pooled prevalence of this infection is necessary for policy-making.

**Aims**: The aim of this study was to estimate the prevalence of *Toxoplasma gondii* infection in Iranian pregnant women using systematic review and meta-analysis.

**Methods**: We searched national and international databases to identify relevant studies. To enhance the search sensitivity, we evaluated all references and interviewed relevant
Introduction

Toxoplasma gondii is an obligate intracellular protozoa with a complicated life cycle. This agent causes toxoplasmosis among humans and animals and is one of the most prevalent chronic infections, infecting one-third of the world population (1–5). Three main modes are responsible for fetal: consumption of including raw or semi-cooked meat, eating the oocytes defecated by researchers and research centres. The final studies for meta-analysis were selected according to the quality assessment as well as inclusion/exclusion criteria. Because of the heterogeneity of the primary results, random effects models were used to estimate the pooled prevalence of T. gondii. We included 43 studies with a total sample size of 22 644 in the meta-analysis.

Results: The pooled seroprevalence of overall toxoplasma infection, IgG antibody and IgM antibody was estimated at 41.3% (95% CI: 35.8–46.8), 39.2% (95% CI: 33.3–45.1) and 4.0% (95% CI: 3.1–4.9) respectively.

Conclusions: Our study showed that a considerable proportion of Iranian pregnant women are at high risk for toxoplasmosis.
cats and vertical transmission from an infected pregnant mother to her fetus (6–7).
Considering toxoplasmosis among pregnant women (owing to the risk of maternal transmission) and immunocompromised patients is of great importance for control programmes because infection can lead to serious pathologic outcomes among neonates with congenital toxoplasmosis and patients with immunodeficiency status (8–9). Knowing the burden of this infection will help health systems focus on prevention of risk factors.

A number of serological tests, such as the latex agglutination test, enzyme-linked immunosorbent assay (ELISA) and indirect fluorescence antibody test, have been used in the detection of antibodies against T. gondii in pregnant women. However, ELISA is the most commonly used diagnostic technique (7,9).

Previous research has shown that toxoplasmosis infection was more common among those with history of close contact with cats, raw meat and vegetable consumption, and low education level (3). The most important benefit in the serology of toxoplasma is to detect whether the pregnant woman has acute infection or not, and if so, whether it occurred before pregnancy (10). The main problem in diagnosis among pregnant women is long-term antibody IgM, but T. gondii-specific antibody (IgM) does not necessarily indicate acute infection (11). In many cases, laboratory diagnosis of latent and acute T. gondii is based on detecting T. gondii-specific IgM and IgG antibodies (7). There are several serologic tests for anti-toxoplasma IgM and IgG, among which ELISA has maximum sensitivity and specificity (2). Chronic infection before pregnancy cannot be transmitted to the fetus, but acute untreated infection during pregnancy may lead to congenital toxoplasmosis with neonatal complications (6). The risk of transmission and the severity of fetal disease is based on gestational age and progressive antibody titration (8), so this risk varies between 0–9% (congenital infection during the first trimester) and 35–59% (congenital infection during the third trimester) (12). Although the infection is usually asymptomatic or mild and self-limiting (fever, agitation, lymphadenopathy), infection occurring during pregnancy causes vertical transmission to the fetus (3) leading to pathologic complications such as hydrocephaly (2,3), microcephaly, chorioretinitis (12), blindness (2,3), mental retardation (2,12), epilepsy (12), jaundice (12), abortion (2,3,12) and fetal death (2,3,12). These complications can be accompanied by disabilities, reduced quality of life and a high socioeconomic burden (8).

Prevention of toxoplasmosis by screening is mandatory in some countries and is recommended in some others such as the United States of America and Canada (12). There is no routine screening programme for toxoplasmosis in the Islamic Republic of Iran (8) and there is no agreement on the best strategy for control of congenital toxoplasmosis (11) although treatment is very important, especially among immunocompromised patients and pregnant women (1).
Seroprevalence of toxoplasmosis has been reported as 30–60% in developed and developing countries (3). In an Iranian study, the incidence of congenital infection during pregnancy was reported to vary from 1 to 8 per 1000 pregnancies (8). According to a systematic review, the global annual incidence of congenital toxoplasmosis was estimated at 190,100, equivalent to a burden of 1.20 million disability-adjusted life years. This burden was greater in South America, some Eastern Mediterranean countries and other low-income countries (13).

Various primary studies have been published estimating the prevalence of toxoplasmosis among pregnant women in the Islamic Republic of Iran. Combining the results of these studies using systematic and meta-analytic methods will be of great importance. Therefore, in this study, we used the methods outlined above to estimate the pooled seroprevalence of toxoplasma antibodies among Iranian pregnant women.

Methods

Data sources and search strategy

The current study is a systematic review and meta-analysis of estimation of the seroprevalence of toxoplasmosis among Iranian pregnant women.

All electronic papers published in national and international databases including SID, Iranmedex, Magiran, Irandoc, Pubmed, Google Scholar, Scopus and Science Direct from 1990 until 10 March 2015 were enrolled in this study. The search strategy was performed using the following keywords as well as their Farsi equivalents: “toxoplasmosis”, “Toxoplasma gondii”, “toxoplasma infection”, “T. gondii”, “Iran”, “pregnant”, “seroepidemiology”, “seroprevalence”, “IgG antibody”, “IgM antibody”, “prevalence”.

Searching was done from 11 to 20 March 2015. We used “OR” to identify studies with any of the keywords in their titles, abstracts and full texts. Limiting the search strategy was carried out applying “AND” to select studies with all of the required keywords. To provide more relevant keywords and studies leading to increased search sensitivity, we investigated all references used in these papers. One of the researchers randomly evaluated the search action and found that all required studies had been entered in the systematic review. Moreover, to find unpublished studies, we asked some well-known Iranian parasitologists working in the medical universities and infectious diseases research centres to introduce any relevant manuscripts which had not been published. However, we did not find any evidence during this phase of the search. All stages of the search as well as the follow-up actions were performed by 2 independent researchers. Any disagreement was settled by a third researcher.

Selection of studies
We extracted the full texts or abstracts of all documents collected during our search. During primary screening, repeated studies were excluded by investigation of the title and abstract. Secondary screening was conducted among studies selected during the primary phase to select more relevant studies with evaluation of the full text. In this stage, abstracts and full texts of the papers were investigated to exclude irrelevant and duplicated studies.

**Inclusion criteria**

All studies published in Farsi or English that achieved an adequate quality score (> 8 of 12) during the assessment process and also those estimating seroprevalence of toxoplasmosis, IgG and IgM titration among Iranian pregnant women were selected. These titrations were categorized according to the standards defined by the companies manufacturing the relevant substances (in most studies, antibody titration > 1.1 IU/mL for indirect fluorescence antibody test and ELISA was considered positive).

**Exclusion criteria**

Studies without estimations of IgG or IgM seroprevalence, studies without sample size reporting, abstracts submitted in congresses whose full texts were not available and case–control studies which could not report prevalence estimations were excluded from the study.

**Quality assessment**

After selecting relevant studies based on titles and contents, to select the documents of satisfactory quality, we applied the STROBE checklist (14). This checklist includes 22 items covering various components of the methodology such as sample size estimation and selection, study population, data collection methods, instrument for data collection, statistical analysis, geographical distribution of the study, aims of the study and appropriate illustration of the results based on the study objectives. Scores were determined from 0 to 44. Based on the STROBE checklist assessment, documents were divided into 3 groups: low quality, score