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Review On: Seroprevalence of *Toxoplasma gondii* Infection in Women of Child-Bearing Age

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ABSTRACT

Toxoplasmosis is a zoonotic disease transmitted by the protozoan parasite *Toxoplasma gondii*. The disease is common worldwide due to its ability to infect a wide range of warm-blooded animals including humans. Areas with poor hygiene and infrastructure along with climatic conditions where the parasites tend to exist and most importantly unawareness of the presence of asymptomatic condition has caused a persistent prevalence of infection in women of childbearing age. This persistency later becomes the principal cause for congenital toxoplasmosis. Since more than 80% of immunocompetent individuals remain asymptomatic or exhibit only flu-like symptoms, a measure of seroprevalence can help to find any exposure to infection by identifying specific IgG and IgM antibodies. So, this review has been summarized to assess the prevailing seropositivity of *T. gondii* infection among women who are going through childbearing age of 15- 49 years and the possible associated factors behind this prevalence rate.

Keywords: Toxoplasma gondii; Congenital Toxoplasmosis; Seroprevalence; IgG; IgM Antibodies; Child-Bearing Age; Seropositivity; Rural Residency

Introduction

Toxoplasmosis is a disease caused by the protozoan *Toxoplasma gondii*, which affects practically all warm-blooded animals, including humans, domestic animals, and terrestrial and marine wild animals. Susceptible hosts can be infected by *T. gondii* through the following primary forms: transplacental transmission, ingestion of animal tissues containing infective cysts, and the ingestion of water and food contaminated with cat feces containing sporulated oocysts. Toxoplasma gondii has a complex, facultatively heteroxenous life cycle that involves several stages of development and a range of hosts and environments. In humans, toxoplasmosis is often subclinical in immunocompetent adults; however, in immunosuppressed individuals, it can cause encephalitis and retinochoroiditis. In pregnant women, the parasite can be transmitted to the fetus, causing miscarriage or the development of chorioretinitis, intracranial calcifications and hydrocephalus in the fetus. In animals, *T. gondii* is responsible for causing miscarriage, fetal mummification, stillbirth and congenital disease, leading to economic losses and increasing production costs (Deganich, et al. [1]). It can also occur subclinically in immunocompetent animals. This characteristic, in addition to making diagnosis difficult, puts human health at risk since it allows the presence of chronically infected animals and facilitates the slaughter of infected animals for human consumption. The consumption of raw or undercooked meat and raw milk is a source of infection for humans.

Because of this, it is important to know the spread of this protozoan, which can be identified through seroprevalence surveys. Furthermore, the description of the genetic variability of *T. gondii* with genotypic characterization studies is also very important for understanding its pathogenicity and virulence. The importance of this genetic knowledge is justified to try to establish a relationship between the genotype and the clinical manifestations, as well as possible associations such as the biological potential of the species, virulence, infectivity, and drug and vaccine resistance. One of the most successful intracellular apicomplexan protozoan parasites is *Toxoplasma gondii*, responsible for causing the worldwide zoonotic infection toxoplasmosis. The parasite is capable of infecting warm-blooded animals with more than 30 species of birds and 300 species of mammals (Flegr, et al. [2]) as well as humans. All of them serve as intermediate hosts while cats and other animals belonging to the family Felidae act as the definitive hosts. The non-infectious oocysts shed by the felids in their

feces become infectious after sporulation and persist in water or soil for a prolonged period of time (Schluter, et al. [3]). Infection occurs from ingestion of contaminated soil, water or plant material by the intermediate hosts that helps the oocysts to settle in the neural and muscular tissue where they transform into tissue cysts. Cats acquire infections by consuming the intermediate hosts or directly by ingesting the sporulated oocysts.

This heteroxenous life cycle of *T. gondii* has created quite a number of routes for transmission in humans. Another principal route of infection is transplacental transmission from a newly infected pregnant woman to her fetus resulting in congenital toxoplasmosis (WHO, [4,5]). Congenital toxoplasmosis has devastating effects on the unborn child if left untreated. Miscarriage still births or congenital defects in the eye and the central nervous system are the potential consequences of primary infection in pregnant women (Montoya, et al. [6]) which occurs due to colonization of tachyzoite stages of *T. gondii* in placental tissues that make their way to the fetal compartment in nearly 30% cases (Robert-Gangneux, et al. [7]). Congenital diseases can later result in cerebral calcification, hydrocephaly, chorioretinitis and mental retardation (Koppe, et al. [8]). More than 80% of immune-competent individuals remain asymptomatic or only show flu like symptoms when they come across an infection (Robert-Gangneux, et al. [7]). So, a measure of seroprevalence can reflect the exposure to infections. Seroprevalence is the detection of the percentage of individuals in a population having antibodies against an infectious pathogen by testing their blood serum. The samples that come out positive for specified antibodies imply the occurrence of previous exposure to that particular pathogen (CDC, [9]). The specific IgG and IgM antibodies are indicative of detecting Toxoplasma infection. Repetitive serological screening for IgG and IgM distinguishes between acute and chronic infections (Robert-Gangneux, et al. [7]).

Centre for Disease Control & Prevention recommends to run a test for IgG antibodies first for detecting immune status as a positive result points out infections of past exposure. Recent infection frequently forms IgM antibody first (Fricker-Hidalgo, et al. [10]) but the lack of specificity in IgM testing makes it difficult to diagnose the precise time of infection acquired. The extent of persistency of IgM antibody can be up to 18 months which lead to the false positive interpretation unless additional specific IgG antibody tests are done (Montoya, et al. [6]). 1-3 weeks later, an IgG antibody test is thus required to follow (Fricker-Hidalgo, et al. [10]). Vaccines for toxoplasmosis are still inaccessible due to a very high degree of antigenic polymorphism displayed by *T. gondii*. The only commercially licensed is the live attenuated Toxovax vaccine from S48 strain against congenital infection in sheep (Buxton, et al. [11]). But the maximum shelf-life limit of this costly vaccine is 10 days only (Dubey, [12]) with the potential to revert into its virulent form (Chu, et al. [13]). The trials undergone have demonstrated promising results towards the possibility of an effective vaccine development (Liu, et al. [14]). Usual medication guideline involves the use of a combination of Pyrimethamine and Sulfadiazine drugs along with Folinic acid (CDC, [15]). But the gradual increasing tendency of drug resistance is drawing concerns for treatment failure (Montazeri, et al. [16]). So, the best option left is to maintain preventive measures to reduce the chance of infection.

One such measure is the early diagnosis of infected women going through child-bearing age to prevent or monitor the probable congenital toxoplasmosis. The global estimation shows an approximation of 1.5 neonatal cases of congenital toxoplasmosis per 1000 births (Torgerson, et al. [17]). Though gestation period determines the risk and severity of infection (Robert-Gangneux, et al. [7]) in cases of maternal exposure, the asymptomatic nature of the infection leaves most of the women unaware whether they have acquired *T. gondii* infection or not. This signifies the necessity of prior detection of infection in women of childbearing age (Myla, et al. 2023).

Material & Methods

The articles were searched primarily in Google Scholar by using the review title "Seroprevalence of *Toxoplasma gondii* in women of childbearing age" and other keywords "*Toxoplasma gondii* prevalence in women", "Toxoplasmosis status in women", which later directed to sites BMC infectious diseases, International Journal of Infectious Diseases, Journal of Parasitic Diseases, Parasite Journal, PubMed, Research Gate etc. A total of 10 articles have been reviewed from the publishing year of 2011-2021 and relevant data on seropravelence were collected. Most of these research articles also included associated risk factors and socioeconomic infrastructure related to the prevailing seroprevalence of the infection.

Results

Data extracted from the articles selected for review have been summarized in the following tables of next page. The data have been categorized on the basis of the detected antibody type IgG, IgM or presence of both IgG and IgM in the samples along with statistically significant variables which have been considered to be potential associated factors. An estimation of overall prevalence of the studied areas have been tabulated as well. Seroprevalence data detected in the highest age category has been demonstrated in a separate table (Tables 1 & 2).

Table 1: Global overview of seroprevalence of *Toxoplasma gondii* in women of childbearing age.

Author	Location	Study Period	Sample Size	Age Range	Overall Seropositive Prevalence	Prevalence Based On Detected Antibody Type			Differences In the Seropositive Prevalence BetweenStatistically Significant Factors (95% CI, P < 0.05
						IgG	IgM	IgG+IgM	Variables
									Prevalence
(Lopes, et al. [26])	North Portugal	January2009-December2010	401	16-45yrs.	24.4%	22.9%	0.5%	1%	Consumers of Unwashed Vs. Washed vegetables
									58.1% Vs. 18.3%
									Consumers of cured & smoked processed pork products Vs. Non-consumers of processed pork products 36.2% Vs. 14.5%
									Participants of soil related works without gloves Vs. Non- participants of soil related works
									64.3% Vs. 17.1%
(Gebremedhin, et al. [24])	Debre-Zeit, Metehara ofCentral Ethiopia	March 2011- September 2011	212 (Non-pregnant)	15-49 yrs.	76.4%	74.1%	1.4%	2.4%	Non-pregnancy Vs.Pregnancy condition
			213 (Pregnant)	15-49 yrs.	86.4%	82.6%	0.5%	3.8%	76.4% Vs. 86.4%
									Consumer Vs. Non-consumer of raw vegetable
									87.7% Vs. 81.9%
(Singh, et al. 2014)	Karnataka, Gujarat, Assam, Delhi NCR of India	October 2011-October 2012	1464	18-45 yrs.	22.43% (all IgG positives were also IgM positive except for one)	21%	0.07%	1.36%	Single Vs. Marriedwomen
									4.3% Vs. 25.8%
									Highest (South India,Karnataka) Vs. Lowest IgG status (West India, Assam)
									31.3% Vs. 8.8%
Doni, et al. [21]	Adiyaman, Batman, Diyarbakir, Gaziante, Kilis, Mardin, Siirt, Sanliurfa, Sirnak Provinces OfTurkey	January – April 2013	684	15-45 yrs.	58.3%	57.28%	0.29%	0.73%	Family farmers Vs.Seasonal farmers
									52.8% Vs. 68.6%
									Living in Under-developed Vs. Developed provincial. development
									55.9% Vs. 66.1%
									Women with historyof Two or fewer Vs. Three or morepregnancies
									41.5% Vs. 61.8%

(Obaidat, et al.[29])	Jordan University of Science andTechnology, Jordan	September 2013- July 2014	202	18-23 yrs.	66.5%	66%	-	0.5%	Women living in apartment Vs. Houseswith open backyards
									52% Vs. 92%
									Family income ≤750US$/month Vs. >750 US$/month
									45% Vs. 63%
									Consumer of tap water Vs. Spring water
									49% Vs. 57%
									Women living in dry (<300mm rainfall) Vs.Wet area (≥300 mm rainfall
									57% Vs. 92%
(Kareshk, et al. [25])	Kerman City, Southeast Iran	January – April 2015	300	16-39 yrs.	12.6%	10.3%	2%	0.33%	Urban Vs. RuralResidency
									11.26% Vs.17.9%
(Alvarado-Esquivel, et al. [20])	University of Sonora, Hermisillo City, Northwestern Mexican City, Mexico	May 2015 – June2017	445	13-46 yrs.	3.6%	3.15%	-	0.45%	Working group: business, professional,agriculture Vs. Non- working group: housewife, student, none
									12.5% Vs. 2.9%
									With Vs. Without history of pregnancy
									9.1% Vs. 2.6%
									With Vs. Without history of miscarriage
(Mihu, et al. [27])	Arad County, Romania	January2016- December2018	2626	15-45 yrs.	41.16%	41.16%	Test not done	Test not done	25% Vs. 3.2%
									Rural Vs. Urban residency
									46.06% Vs. 36.11%
(Fanigluilo, etal. [22])	Sienna province. Italy	2013, 2014, 2016	409	36-45 yrs.	41.16%	41.16%	Test not done	Test not done	Differences in 15-25 yrs. age group Sienna Vs. Bari
									4.2% Vs.18.8%
									Differences in 26-35 yrs. age group Sienna Vs. Bari
									9.4% Vs. 18.3%
	Bari Province, Italy	2015-2016	398	36-45 yrs.	12.4%	12.4%	Test not done	Test not done	Differences in 36-45yrs. age group Sienna Vs. Bari
									17.6% Vs. 30.7%
	Bari Province, Italy	2016-2017	232 (Pregnant)	36-45 yrs.	13.8%	13.8%	Test not done	Test not done	Pregnant Vs. Non-pregnant women ofBari
									30.7% Vs. 16.2%
(Olarinde, et al. [30])	Osun State, Nigeria	May - December2019	415	18-49 yrs.	76.63%	44.1%	6.02%	26.51%	Primary education or none Vs. Secondary ortertiary education
									86.9% Vs. 74%

Table 2: Seroprevalence based on the highest detected age group.

Author	Total Sample Size	Highest Age Group Detected	Prevalence of *T. gondii* (Positive/Total No. Of Individuals In The Age Group)
(Doni, et al. [21])	684	35-45 yrs.	61.2% (244/371)
(Kareshk, et al. [25])	300	31-39 yrs.	17% (6/35)
(Alvarado-Esquivel, et al. [20])	445	31-46 yrs.	13% (6/46)
(Mihu, et al. [27])	2626	40-45 yrs.	61.53% (48/78)
(Fanigliulo, et al. [22])	409	36-45 yrs.	17.6% (34/193)
	398	36-45 yrs.	30.7% (39/127)
	232	36-45 yrs.	16.2% (12/74)

Discussion

Most of the participants in these studies did not have prior knowledge about toxoplasmosis. Women living in the rural facilities were more exposed to infection for their involvement in agricultural work and lack the maintenance of proper hygiene and sanitation. The humid climate in some geographical locations is another important fact explaining the persistency of cysts in the environment. Women with history of miscarriage had a high prevalence depicting the severe effect of congenital infection. Socioeconomic infrastructure, lifestyle, housing type, food habits are some influencing factors for rate dissimilarities in different regions. One common issue was high seroprevalence with increasing age. Long time of exposure has been predicted to be the possible reason behind it (Myla et al. 2023). Molan, et al. [18] have estimated an overall range of global seroprevalence of human *T. gondii* infection as 0.5% to 87.7% with highest average rate of 61.4% in African countries. The chronological average seroprevalence rate for other continents are as follows: Oceania 38.5%, South America 31.2%, Europe 29.6%, North America 17.5% & Asia 16.4%. Maximum study sample included women with pregnancy status and child-bearing age. Only a handful number of works on human toxoplasmosis has been published in Bangladesh half of which date back to the 90's. The most recent studies conducted had a sample size of less than 100. All the researches were narrowed into specified status like pregnancy and gyneco-obstetric problems. None of these fully included all categories of women of the childbearing age range (Rahman, et al. [19-31]).

Conclusion

Most of the studies included sample populations on a small scale and without continuous screening. So the data obtained doesn't exactly demonstrate the crucial factors behind such seroprevalence. A trend to an increasing age related seropositivity has been observed over recent years but except for long exposure period, other prime cause has not been detected yet. Future studies need to address these points to overcome the knowledge gap. Bangladesh is lagging far behind on human toxoplasmosis research. There was no constant continuation among the works published until now so reliable data on the seroprevalence status of Bangladeshi women are unavailable which needs attention of the researchers.

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