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Global status of *Toxoplasma gondii* infection: systematic review and prevalence snapshots

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Abstract. Our group sought to determine the global status of *T. gondii* infection and to evaluate any continental and geographical trends by systematically examining the currently available epidemiological data on the prevalence of *T. gondii* infection. A comprehensive literature search was conducted from 10 electronic databases (Google Scholar, Science Direct, Embase, PubMed, PLOS ONE, Web of Knowledge, SciELO, MyAIS, Free Medical Journals, and Scopus) without date or language restrictions. Specific medical subject heading terms were used to search for human *T. gondii* seroprevalence studies that recruited subjects from general apparently healthy populations. The data were collated and analysed for both continental and global trends. The search identified 152 published studies that examined a total of 648,010 subjects. From these, 166,255 were seropositive for *T. gondii* infection indicating an average global seroprevalence rate of 25.7% (95% CI: 25.6 – 25.8%). The overall range of seroprevalence was determined to be 0.5 – 87.7%. African countries had the highest average seroprevalence rate of 61.4%, followed by Oceania with 38.5%, South America with 31.2%, Europe with 29.6%, USA/Canada with 17.5%, and Asia with 16.4%. Numerous environmental and human factors affect the differences in *T. gondii* seroprevalence rates observed between the various countries and continents. Monitoring the source and transmission may assist public health authorities to clarify the risk factors involved, as well as focus on implementing optimal state-specific health policies targeting *T. gondii* transmission control.

INTRODUCTION

The obligate protozoan parasite *Toxoplasma gondii* belongs to the phylum Apicomplexa which includes intracellular parasites that have a unique polarised cell structure and a complex cytoskeletal arrangement at their apical end (Dupey *et al.*, 1998). This parasite infects approximately one third of the world's population and is considered one of the most successful human parasites (Peng *et al.*, 2011; CDC, 2015). In fact, the Centers for Disease Control have prioritised *T. gondii* as one of the top "Five Neglected Parasitic Infections" due to the severity of illness, high incidence, and potential for prevention (Pappas *et al.*, 2009). Humans acquire *T. gondii* infection by the ingestion of food, water, or soil contaminated by oocysts from the definitive hosts, cats (genera *Felis* and *Lynx*). *Toxplasma gondii* is also transmitted vertically via placenta and horizontally via blood transfusion and sexual contact (Halonen *et al.*, 2013; CDC, 2017; Flegr *et al.*, 2014; Parlog *et al.*, 2015). This parasite has the ability to infect all warm-blooded animals and its infection is one of considerable public health impact. The global prevalence rates of this parasite ranging from less than 10% to over 90% depending on social habits, climate condition, hygienic standards, and geographical regions (Albuquerque *et al.*,

2009; Prandota, 2013). Although *T. gondii* has a worldwide distribution and possibly the widest host range of any parasite, there is only one species (*T. gondii*) in the genus Toxoplasma (Kankova *et al.*, 2015), and cats are the only definitive host in which sexual development is known to occur (Tenter *et al.*, 2000). It is perhaps not surprising that many epidemiological studies have been conducted to determine the prevalence and burden of disease; and explore prevention and control strategies in various populations and clinical states: pregnancy, congenital toxoplasmosis; mental health states such as Alzheimer's disease; cancers; diabetes; food-borne illnesses; mood disorders; AIDS and transplant-related conditions (Dupey, 2008). In addition, another area of active research is examining the prevalence and genotyping of *T. gondii* strains from definitive- and intermediate-hosts such as household, pets, sheep, goats, turkeys, chickens, rats, mice, swine, and cattle to better understand the role of the different strains in human *T. gondii* infection (Guo *et al.*, 2016; Gebremedhin *et al.*, 2015; Dong *et al.*, 2018; Shuralev *et al.*, 2018; Ibrahim *et al.*, 2017). The purpose of this study was to determine the global status of *T. gondii* infection and to evaluate any global and geographical trends. Our group systematically reviewed and collated the currently available epidemiological data on the global prevalence of *T. gondii* from human studies recruiting subjects from general apparently healthy populations. Awareness of these seroprevalence trends may assist public health authorities focus on implementing appropriate health policies targeting *T. gondii* transmission control.

MATERIALS

Strategy for literature search

To identify relevant published studies, our group conducted a systematic search on published literature with no language or date restrictions (from inception until February 2019) from 10 electronic databases (Google Scholar, Science Direct, Embase, PubMed, PLOS ONE, Web of Knowledge, SciELO, MyAIS, Free Medical Journals, and Scopus). The Medical Subject Heading search terms used in the search were: "Toxoplasma" OR "*Toxoplasma gondii*" OR "toxoplasmosis" OR "*T. gondii*" OR "TORCH" combined with (AND) "seroprevalence" OR "seropositivity" OR "prevalence".

Selection of studies

Potentially relevant articles were initially selected based on title content followed by abstract content. The retained human articles were read in full and screened for eligibility using a checklist of inclusion-exclusion criteria. All selected studies had to meet the following inclusion criteria: (i) human observational studies using apparently healthy subjects; (ii) the sample sizes must be suitably estimated; (iii) recruited subjects must to be selected to reflect a representative portion of the general population; (iv) diagnosis of *T. gondii* infection must be based on the following standard laboratory detection methods: serological examination of *T. gondii* IgG and/or IgM antibodies, indirect fluorescent antibody test (IFAT), immunohistochemical (IHC) staining, or molecular methods detecting *T. gondii* DNA; where positive results were characterised by the presence of IgG and/or IgM; or a positive IFAT test; or a positive IHC stain; or the detection of *T. gondii* DNA; and negative results were defined as a lack of IgG or IgM antibodies; a negative IFAT test; a negative IHC stain; or no detection of *T. gondii* DNA. Likewise, studies were excluded if they were repeated studies and/or abstracts. Any discrepancies with the final selection of studies were resolved by discussion and consensus with the author panel.

Data collection and Statistical Analysis

The following information was extracted from each study: author details; year of publication; location of the study; characteristics of the study population including collection criteria, numbers of subjects, and diagnostic methods used in the detection of *T. gondii* infection; and seroprevalence results. Additionally, we also examined the reference lists of full text publications and text books to identify any additional studies not retrieved by the initial database search.

Confidence intervals (CI) at the 95% level were derived from each study. The studies were grouped and tabulated by country and continent (Africa, Asia, Europe, USA/Canada, South America, and Oceania). Continental seroprevalence were calculated and the 95% CIs estimated using the freely available online Confidence Interval Calculator for Proportions (Alto Consulting: https://www.allto.co.uk/tools). This data was then superimposed onto the map of the world to assess geographical trends.

RESULTS

From the 10 databases searched (Google Scholar, Science Direct, Embase, PubMed, PLOS ONE, Web of Knowledge, SciELO, MyAIS, Free Medical Journals, and Scopus), a total of 152 published papers were eligible under the pre-defined search terms that met the inclusion criteria. The references of these articles did not add any new studies. Consequently, 152 studies were retained and analysed. The majority of these studies were conducted within the last decade and report data from woman who were pregnant or of child bearing age. Asian and European countries had the highest research output of 61 and 38 studies, respectively, followed by 27 papers from South America, 17 from Africa, five from Oceania, and lastly four from USA/Canada.

Africa

A total of 14,309 subjects were included from 17 studies conducted between 1995 and 2017 (Table 1). From these studies, four recruited subjects from the general adult population in comparison to the remaining studies that utilised pregnant woman or those of child bearing age. Benin had the highest seroprevalence of 87.7% reported from a 1995 study evaluating *T. gondii* infection from a group of 211 pregnant women (Rodier *et al.*, 1995). An Ethiopian study conducted in 2015 study (Gelaye *et al.*, 2015) also reported a high *T. gondii* seroprevalence of 85.4% from pregnant women (n = 288). This matched a similar but larger (n = 5,718) Ethiopian study, conducted in 2015, that found 74.73% of the recruited adults from the general population had *T. gondii* infection (Gebremedhin *et al.*, 2017). The lowest seroprevalence rate (20.8%) was reported from Nigeria in 2005 (Uneke *et al.*) from a small group of adults (n = 144). A subsequent Nigerian study conducted by Nasir *et al.* in 2015 reported a seroprevalence figure of 40.0% from a group of 360 pregnant women. The latest study to be published from Africa comes from Egypt and reported a seropositivity rate of 33.79% from pregnant women (n = 364) in 2017 (Ibrahim *et al.*, 2017). This is significantly lower than the 67.5% reported from a similar Egyptian study conducted by El Deeb *et al.* in 2012 looking at *T. gondii* infection in 323 pregnant women. The remaining study to report *T. gondii* seroprevalence from an adult population was conducted in Tanzania (Swai *et al.*, 2009) and found that 46.0% of the 199 subjects had detectable levels of *T. gondii* IgG antibodies. Overall, African countries reported the highest global *T. gondii* seroprevalence rate of 61.4% (95% CI: 60.6 – 62.1%) with a range of 20.8 – 87.7% (Table 7, Fig. 1).

Asia

A total of 204,710 subjects were included from 61 studies conducted between 1996 and 2018 (Table 2). The majority of studies reported figures from women whom were pregnant or of childbearing age. Lebanon reported the highest *T. gondii* seroprevalence of 82.6% in 2017 from a study that examined 2,456 pregnant women (Nahouli *et al.*, 2017). No other Lebanese studies have been published. The lowest seroprevalence rate (0.8%) was reported from Korea in 2005 from a large group of pregnant women (n = 5,175) (Song *et al.*, 2005). The other two Korean studies (Shin *et al.*, 2009; Han *et al.*, 2008) examining *T. gondii* seropositivity from 1,265 adults and 351 pregnant women also reported low figures of 6.7% and 3.7%, respectively. China had the largest research output with 19 studies which all showed relatively low *T. gondii* seroprevalence rates (0.5 – 25.5%). This was followed by Iran from which 10 studies were conducted and all reported moderate *T. gondii* seroprevalence rates (29.4 – 63.9%). The largest Asian study was

Table 1. *Toxoplasma gondii* seroprevalence snapshot in Africa - data from human studies

Study	Country	Year	Subjects	n tested	Results	Remarks
Rodier *et al.*	Benin	1995	Pregnant woman	211	87.7%	
Simpore *et al.*	Burkina Faso	2006	Pregnant woman	336	25.3%	95%CI: 20.7-29.9
Ibrahim *et al.*	Egypt	2017	Pregnant women	364	33.79%	
Deeb *et al.*	Egypt	2012	Pregnant woman	323	67.5%	95%CI: 62.39-72.61
Gebremedhin & Tadesse	Ethiopia	2015	Humans	5,718	74.73 %	95%CI: 61.85-84.36
Gelaye *et al.*	Ethiopia	2015	Pregnant woman	288	85.4%	
Nabias *et al.*	Gabon	1998	Pregnant woman	767	71.2%	
Adou-Bryn *et al.*	Ivory Coast	2004	Childbearing age	1,025	60.0%	95%CI: 57.0-63.0
Lelong *et al.*	Madagascar	1995	Pregnant woman	599	83.5%	
El Mansouri *et al.*	Morocco	2007	Pregnant woman	2,456	50.6%	95% CI: 48.6-52.6
Uneke *et al.*	Nigeria	2005	Adults	144	20.8%	95%CI: 14.20-27.46
Kamani *et al.*	Nigeria	2009	Adults	180	23.9%	
Nasir *et al.*	Nigeria	2015	Pregnant woman	360	40.0%	
Faye *et al.*	Senegal	1998	Pregnant woman	353	40.2%	
Hung *et al.*	Soa Tome and Principe	2007	Pregnant woman	499	75.2%	95%CI: 71.4-79.0
Elnahas *et al.*	Sudan	2003	Pregnant woman	487	34.1%	95% CI: 29.9-38.3
Swai & Schooman	Tanzania	2009	Adults	199	46.0%	
			Summary	**14,309**	**61.4%**	

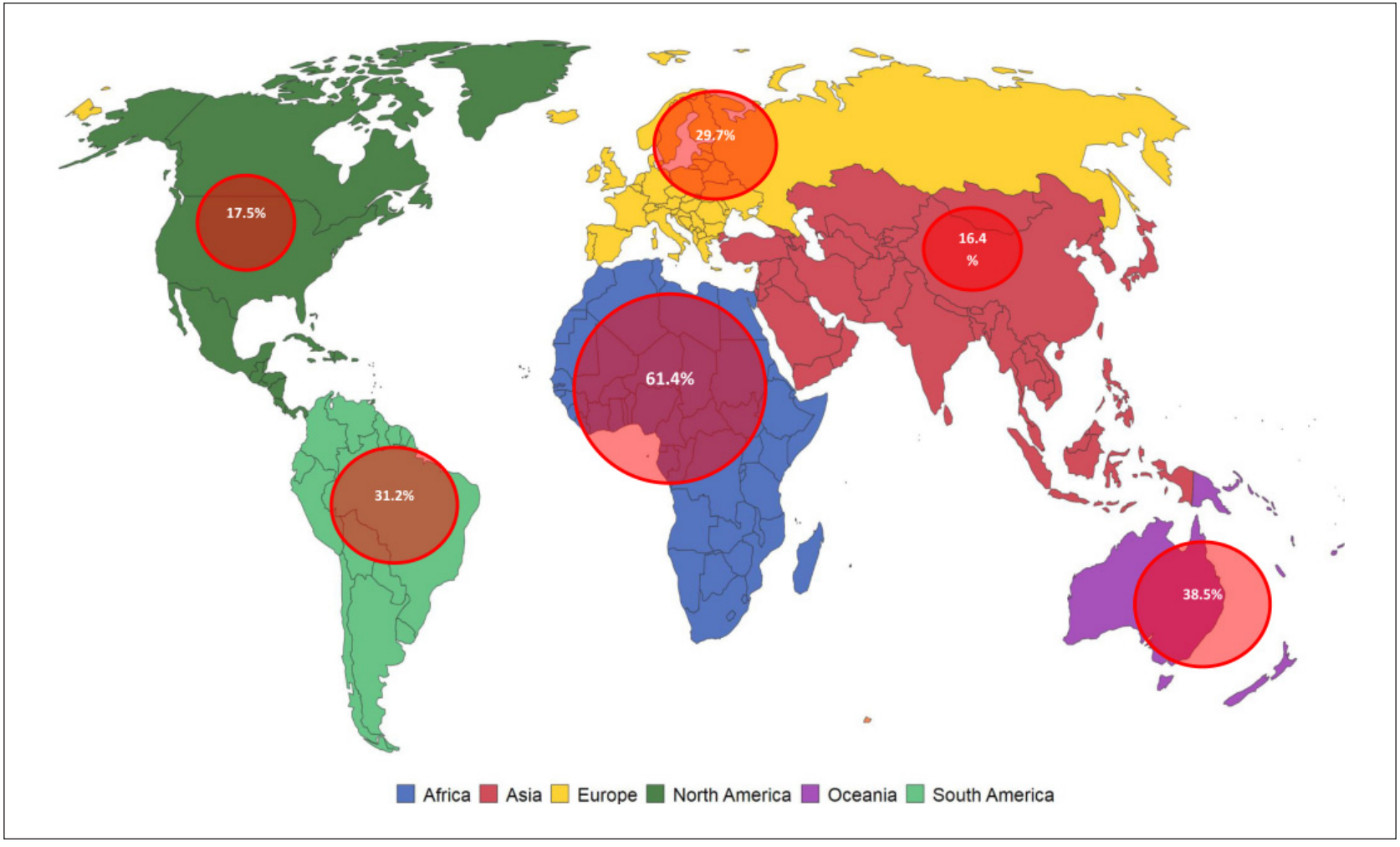

Figure 1. Graphical summary of global *Toxoplasma gondii* infection by continent- data from human studies.

Table 2. *Toxoplasma gondii* seroprevalence snapshot in Asia - data from human studies

Study	Country	Year	Subjects	n tested	Results	Remarks
Tabbara & Saleh	Bahrain	2005	Childbearing age	3,499	23.0%	95%CI: 18.3-26.7
Cheng *et al.*	China	2006	Pregnant woman	2,425	0.5%	
Yue *et al.*	China	2004	Pregnant woman	1,820	0.8%	
Li *et al.*	China	2003	Pregnant woman	2,184	2.2%	
Fan *et al.*	China	2004	Pregnant woman	550	2.7%	
Jiang *et al.*	China	2003	Pregnant woman	1,075	3.3%	
Li *et al.*	China	2006	Pregnant woman	3,500	3.6%	
Liu *et al.*	China	2008	Pregnant woman	3,559	5.0%	
Chen *et al.*	China	2003	Pregnant woman	298	6.0%	
Su *et al.*	China	1996	Pregnant woman	1,495	7.0%	
Buchy *et al.*	China	2003	-Drug users -Pregnant woman	300 300	7.7% 11.2%	
Ji *et al.*	China	2008	Pregnant woman	1,491	7.9%	
Dong *et al.*	China	2018	Humans	103,383	8.2%	95%CI: 8.06-8.39%
Liu *et al.*	China	2005	Pregnant woman	196	9.7%	
Lu *et al.*	China	2002	Pregnant woman	228	10.1%	
Liu *et al.*	China	2009	Pregnant woman	235	10.6%	95%CI: 6.7-14.5
Xiao *et al.*	China	2010	Adults	2,634	12.5%	
Suo *et al.*	China	2007	Pregnant woman	18,127	13.2%	
Han *et al.*	China	2008	Pregnant woman	172	15.1%	
Tang *et al.*	China	2006	Pregnant woman	769	16.5%	

Zhong *et al.*	China	2005	Pregnant woman	1,332	25.5%	
Dhumne *et al.*	India	2007	Humans	23,094	24.3%	
Kaur *et al.*	India	1999	Pregnant woman	120	11.6%	95%CI: 5.9-17.3
Stephen *et al.*	India	2017	Pregnant woman	193	15.54%	
Borkakoty *et al.*	India	2007	Pregnant woman	180	41.6%	95%CI: 34.4-48.8
Akoijam *et al.*	India	2002	Pregnant woman	503	41.7%	95%CI: 37.4-46.0
Singh & Pandit	India	2004	Pregnant woman	180	45.0%	95%CI: 37.7-52.3
Terazawa *et al.*	Indonesia	2003	Childbearing age	399	>60%	
Youssefi *et al.*	Iran	2007	Woman	241	63.9%	
Yad Yad *et al.*	Iran	2013	Pregnant woman	501	29.35%	
Pashazadeh *et al.*	Iran	2008	Pregnant woman	197	29.4%	95%CI: 23.0-35.8
Taravati & Sadegkhalili	Iran	2003	Childbearing age	300	32.8%	95%CI: 27.5-38.7
Fallah *et al.*	Iran	2008	Pregnant woman	576	33.5%	95%CI: 29.7-37.3
Sagha & Diryani	Iran	2004	Childbearing age	504	34.7%	95%CI: 30.5-38.9
Soltani *et al.*	Iran	2018	Adults	496	37.9%	
Adbi *et al.*	Iran	2008	Pregnant woman	553	44.8%	95%CI: 40.7-48.9
Saeedi *et al.*	Iran	2007	Pregnant woman	300	48.3%	95%CI: 42.7-53.9
Gharavi *et al.*	Iran	2017	10- to 18-year-old students	882	56.3%	95%CI: 55.4-59.2 The CASPIAN III Study
Mahdi & Sharief	Iraq	2002	Pregnant woman	254	49.2%	95%CI: 43.1-55.3
Jumaian	Jordan	2005	Pregnant woman	280	31.7% at 15-24 years to 90.0% at 35-45 years	
Song *et al.*	Korea	2005	Pregnant woman	5,175	0.8%	95%CI: 0.6-1.0
Han *et al.*	Korea	2008	Pregnant woman	351	3.7%	

Shin *et al.*	Korea	2009	Adults	1,265	6.7%	
Iqbal *et al.*	Kuwait	2003	Pregnant woman	225	45.7%	95%CI: 39.2-52.2
Iqbal & Khalid	Kuwait	2007	Pregnant woman	224	53.1%	
Nahouli *et al.*	Lebanon	2017	Pregnant woman	2,456	82.6%	
Nissapatorn *et al.*	Malaysia	2003	Pregnant woman	200	49.0%	95%CI: 42.1-55.9
Abu-Madi *et al.*	Qatar	2008	Adults	1,625	29.8%	
Aqeely *et al.*	Sadia Arabia	2014	Pregnant woman	195	24.1%	
Amer *et al.*	Saudi Arabia	2015	Pregnant woman	5,537	9.8%	
Alghamdi *et al.*	Saudi Arabia	2016	Pregnant woman	203	32.5%	
Wong *et al.*	Singapore	2000	Pregnant woman	120	17.2%	95%CI: 10.5-23.9
Lin *et al.*	Taiwan	2008	Pregnant woman	426	31.0%	95%CI: 26.6-35.4
Wanachiwanawin *et al.*	Thailand	2001	Pregnant woman	831	5.3%	95%CI: 3.5-6.8
Sukthana *et al.*	Thailand	2000	Pregnant woman	1,200	13.2%	95%CI: 11.3-15.1
Tantivanich *et al.*	Thailand	2001	Pregnant woman	200	21.5%	95%CI: 15.8-27.2
Bourabtine *et al.*	Tunisia	2001	Adults	1,421	58.4%	
Ocak *et al.*	Turkey	2007	Pregnant woman	1,652	52.6%	95%CI: 50.2-55
Ertug *et al.*	Turkey	2005	Pregnant woman	389	30.1%	95%CI: 25.5-34.7
Harma *et al.*	Turkey	2004	Pregnant woman	1,149	60.4%	95%CI: 57.6-63.2
Buchy *et al.*	Vietnam	2003	Pregnant woman	300	11.2%	95%CI: 7.6-14.8
			Summary	**204,710**	**16.4%**	

conducted in China in 2018 (Dong *et al.*, 2018) and examined 103,383 adults and found that 8.2% had detectable *T. gondii* IgG antibodies. Overall, Asian countries reported the lowest global *T. gondii* seroprevalence rate of 16.4% (95% CI: 16.2 – 16.5%) with a range of 0.5 – 82.6% (Table 7, Fig. 1).

Europe

A total of 299,174 subjects were included from 38 studies conducted between 1999 and 2018 (Table 3). The majority of studies reported figures from women whom were pregnant or of childbearing age. The German study conducted by Fiedler *et al.* in 1999 reported the highest *T. gondii* seroprevalence rate of 59.0% from 4,854 subjects. In contrast, the lowest reported seroprevalence of 8.2% was reported from a Swiss study (Zufferey *et al.*, 2007) examining 1,000 women of childbearing age. Greece had the largest amount of study output and all eight studies conducted from 2002 to 2008 reported comparable *T. gondii* seroprevalence figures ranging from 20.0 – 36.4%. Similarly, the five Italian studies also reported a similar trend from pregnant women (17.5 – 34.4%). The only three studies that recruited subjects other than pregnant women and those of childbearing age reported moderate *T. gondii* seropositivity rates: Germany, 2016, n = 6,564, 55.0% (Wilking *et al.*, 2016); France, 2009, n = 273, 47.0% (Fromont *et al.*, 2009); and Germany, 1999, n = 59.0% (Fiedler *et al.*, 1999). The largest study, conducted in 1999 in Denmark (Lebech *et al.*, 1999), examined 89,873 subjects and found that 27.8% had detectable levels of *T. gondii* IgG antibodies. Overall, European countries had an average *T. gondii* seroprevalence rate of 29.7% (95% CI: 29.5 – 29.9%) with a range of 8.2 – 59.0% (Table 7, Fig. 1).

USA/Canada

A total of 46,795 subjects were included from four studies conducted between 2001 to 2018 (Table 4). Three studies were conducted in the USA with two being by Jones *et al.* The 2003 (Jones *et al.*, 2001) study looking at 27,145 humans over the age of 12 years found a seroprevalence rate of 22.5%. In comparison, a similar study conducted in 2018 examining 13,509 adults reported a lower figure of 10.4% indicating *T. gondii* seroprevalence has decreased in the USA over the last decade (Liu *et al.*, 2018). Overall, USA/Canada had an average *T. gondii* seroprevalence rate of 17.5% (95% CI: 17.2 – 17.8%) with a range of 10.4 – 22.5% (Table 7, Fig. 1).

South America

A total of 68,764 subjects were included from 27 studies conducted between 1992 and 2015 (Table 5). All but one studies utilised samples from pregnant women or those of childbearing age. The highest *T. gondii* seroprevalence (74.7%) was reported by Porto *et al.* (1992) from Brazil from a study looking at 503 pregnant women. The lowest seroprevalence of 7.3% was also reported from a 2008 Brazilian study that examined the largest cohort of 37,961 subjects (Cabral *et al.*, 2008). Over half (14, 52%) of the South American studies were conducted in Brazil and apart from the Cabral *et al.* study, all reported high *T. gondii* seroprevalence figures (59% and above). The only study examining subjects other than pregnant women and those of childbearing age was conducted in Costa Rica in 2005 in which 58.0% of the 400 subjects were found to be infected with *T. gondii* (Zapata *et al.*, 2005). Overall, South American countries had an average *T. gondii* seroprevalence rate of 31.2% (95% CI: 30.8 – 31.5%) with a range of 7.3 – 74.7% (Table 7, Fig. 1).

Oceania

A total of 14,357 subjects were included from 5 studies conducted between 1982 and 2004 (Table 6). All studies utilised samples from pregnant women. The New Zealand study conducted in 1982 reported the highest *T. gondii* seroprevalence figure of 60.0% from a cohort of 566 subjects (Cursons *et al.*, 1982). The more recent New Zealand study observed a much lower seroprevalence rate of 35.4% from a group of 500 subjects examined in 2004 (Morris *et al.*, 2004). In comparison, the lowest reported seroprevalence figure of 23.0% was from an Australian study conducted in 2001 examining 308 subjects (Karunajeewa *et al.*,

Table 3. *Toxoplasma gondii* seroprevalence snapshot in Europe - data from human studies

Study	Country	Year	Subjects	n tested	Results	Remarks
Breugelmans *et al.*	Belgium	2004	Pregnant woman	16,541	48.7%	95%CI: 47.9-49.5
Punda-Polic *et al.*	Croatia	2000	Childbearing age	1,109	38.1%	95%CI: 35.2-41.0
Kankova & Flegr	Czech Republic	2007	Pregnant woman	1,053	19.8%	95%CI: 17.4-22.2
Lebech *et al.*	Denmark	1999	Pregnant woman	89,873	27.8%	95%CI: 27.5-28.1
Fromont *et al.*	France	2009	Adults	273	47.0%	95%CI: 41.0-53.0
Wilking *et al.*	Germany	2016	Adults	6,564	55.0%	95%CI: 46.92-51.23
Fiedler *et al.*	Germany	1999	Adults	4,854	59.0%	
Kansouzidou *et al.*	Greece	2008	Childbearing age	273	21.2%	95%CI: 16.4-26.0
Baka *et al.*	Greece	2006	Pregnant woman	1,466	20.1%	95%CI: 18.1-22.2
Diza *et al.*	Greece	2005	Childbearing age	150	20.0%	95%CI: 13.6-26.4
Glynou *et al.*	Greece	2005	Childbearing age	3,016	25.4%	95%CI: 23.9-26.9
Antoniou *et al.*	Greece	2004	Pregnant woman	5,532	29.4%	95%CI: 28.2-30.6
Mela *et al.*	Greece	2004	Childbearing age	318	22.0%	95%CI: 17.5-26.5
Alexandrou *et al.*	Greece	2002	Pregnant woman	2,794	24.1%	95%CI: 22.5-25.7
Farsaraki *et al.*	Greece	2002	Childbearing age	8,100	36.4%	95%CI: 35.4-37.4
Ferguson *et al.*	Ireland	2008	Pregnant woman	20,252	24.6%	95%CI: 24.0-25.2
De Paschale *et al.*	Italy	2008	Pregnant woman	3,462	22.7%	95%CI: 21.3-24.1
Masini *et al.*	Italy	2008	Pregnant woman	1,345	19.8%	95%CI: 17.7-21.9
Beccara *et al.*	Italy	2005	Pregnant woman	1,801	17.5%	95%CI: 15.8-19.2
Ricci *et al.*	Italy	2003	Pregnant woman	8,061	34.4%	95%CI: 33.4-35.4

Russo *et al.*	Italy	1999	Pregnant woman	9,029	23.0%	95%CI: 22.1-23.9
Kortbeek *et al.*	Netherlands	2004	Childbearing age	7,521	35.2%	95%CI: 32.9-38.6
Nowakowska *et al.*	Poland	2006	Pregnant woman	4,916	41.3%	95%CI: 39.9-42.7
Niemiec *et al.*	Poland	2002	Pregnant woman	2,016	35.8%	95%CI: 33.7-37.9
Paul *et al.*	Poland	2001	Pregnant woman	2,656	43.7%	95%CI: 41.8-45.6
Olariu *et al.*	Romania	2008	Childbearing age	328	57.6%	95%CI: 52.3-62.9
Shuralev *et al.*	Russia	2018	Humans	181	30.9%	
Bobic *et al.*	Serbia	2007	Childbearing age	765	33.0%	95% CI: 29.7-36.3
Studenicova *et al.*	Slovakia	2008	Pregnant woman	656	22.1%	95% CI: 18.9-25.3
Logar *et al.*	Slovenia	2002	Pregnant woman	21,270	34.0%	95% CI: 33.4-34.6
Bartolome Alvarez *et al.*	Spain	2008	Pregnant woman	2,626	21.0%	95% CI: 19.4-22.6
Gutierrez-Zufiaurre *et al.*	Spain	2004	Pregnant woman	2,929	18.8%	95% CI: 17.4-20.2
Munoz Batet *et al.*	Spain	2004	Pregnant woman	16,362	28.6%	95% CI: 27.9-29.3
Pujol-Rique *et al.*	Spain	2000	Childbearing age	7,090	43.8%	95% CI: 42.7-44.9
Evengard *et al.*	Sweden	2001	Pregnant woman	40,978	18%	95% CI: 17.4-20.2
Zufferey *et al.*	Switzerland	2007	Childbearing age	1,000	8.2%	95% CI: 6.5-9.9
Signorell *et al.*	Switzerland	2006	Pregnant woman	Not specified	35.0%	
Nash	UK	2005	Pregnant woman	1,897	9.1%	
			Summary	**299,075**	**29.7%**	

Table 4. *Toxoplasma gondii* seroprevalence snapshot in USA/Canada - data from human studies

Study	Country	Year	Subjects	n tested	Results	Remarks
Scuhaiber *et al.*	Canada	2003	Adults	141	14.2%	95%CI: 8.4-19.9
Jones *et al.*	USA	2003	Humans >12years	27,145	22.5%	95%CI: 21.1-23.9
Jones *et al.*	USA	2007	Childbearing age	>6,000	11.0%	95%CI: 10.2-11.8
Liu *et al.*	USA	2018	Adults	13,509	10.4%	95%CI: 9.2-11.8
			Summary	**46,795**	**17.5%**	

2001). Overall, countries in this region had an average *T. gondii* seroprevalence rate of 38.5% (95% CI: 37.7 – 39.3%) with a range of 23.0 – 60.0% (Table 7, Fig. 1).

DISCUSSION

In the present study, we aimed to collate the currently available global data on *T. gondii* prevalence in order to assess global trends. From the 152 studies identified suitable for inclusion in the analysis, the average global *T. gondii* seroprevalence was calculated to be 25.7% (95% CI: 25.6 – 25.8%). This figure is consistent with the many previous reports that have estimated that one third of the world's population is infected with *T. gondii* (Tenter *et al.*, 2000; Dupey, 2008). However, the overall range of *T. gondii* seroprevalence varied widely from 0.5 – 87.7% making it difficult to establish solid trends. African countries had the highest average seroprevalence rate of 61.4% (17 studies examining 14,309 subjects); followed by Oceania with 38.5% (five studies examining 14,357 subjects); South America with 31.2% (27 studies examining 68,764 subjects); Europe with 29.7% (38 studies examining 299,075 subjects); USA/Canada with 17.5% (four studies examining 46,795 subjects); and Asia with 16.4% (61 studies examining 204,710 subjects). Although there are significant intercontinental differences between the *T. gondii* seroprevalence rates, intracontinental ranges also vary extensively: Africa, 20.8 – 87.7%; Asia, 0.5 – 82.6%; Europe, 8.2 – 59.0%; USA/Canada, 10.4 – 22.5%; South America, 7.3 – 74.7%; and Oceania, 23.0 – 60.0%. Many inherent human and environmental factors have been proposed as possible contributors for the observed differences in *T. gondii* seroprevalence rates between different regions of the world: diet (Lai *et al.*, 1975; McCarthy and Davis, 2003); climate (Yan *et al.*, 2016; Meerburg and Kijlstra, 2009; Patz *et al.*, 2000); human activities such as the degree of interaction with animals, animal welfare standards, urbanisation, social cultures, and anthropogenic activities (Yan *et al.*, 2016).

Although the consumption of raw or under cooked meat products has been well documented and established as a risk factor for *T. gondii* infection (Pappas *et al.*, 2009; CDC, 2017; Dupey, 2008; Dong *et al.*, 2018; Tenter *et al.*, 2000), another area warranting further research is the protective effect of certain diets against *T. gondii* infection. The 1975 study by Lai *et al.* established the notion that diet may have a protective effect against *T. gondii* infection in mice. It was shown that this effect was a result of a dietary deficiency para-aminobenzoic acid. A similar but more recent study was conducted to determine the effects of selenium and vitamin E supplementation on a murine model with *T. gondii* infection (McCarthy and Davis, 2003). The results showed that the complete absence of vitamin E and selenium in the diet had a protective effect in that mice with a diet deficient in these elements had the lowest numbers of tissue cysts and very little evidence of tissue pathology during chronic infection. The authors concluded that a pro-oxidant diet provides protection during infection with *T. gondii*. If the same trends are applicable to humans, specific foods we

Table 5. *Toxoplasma gondii* seroprevalence snapshot in South America - data from human studies

Study	Country	Year	Subjects	n tested	Results	Remarks
Marquez & Etcheverry	Argentina	2003	Pregnant woman	1,007	48.7%	95%CI: 45.6-51.8
Rickard *et al.*	Argentina	1999	Pregnant woman	650	53.4%	95%CI: 49.6-57.2
Avelino *et al.*	Brazil	2004	Childbearing age	2,242	51.2%	95%CI: 49.1-53.3
Cabral *et al.*	Brazil	2008	Childbearing age	37,961	7.3%	95%CI: 7.0-7.6
Caerllos *et al.*	Brazil	2008	Pregnant woman	420	61.2%	95%CI: 56.5-65.9
da Silva *et al.*	Brazil	2015	Pregnant woman	487	68.37%	95%CI: 64.62-72.86
Lago *et al.*	Brazil	2009	Pregnant woman	2,424	67.0%	95%CI: 65.1-68.9
Leao *et al.*	Brazil	2004	Pregnant woman	205	70.6%	95%CI: 64.4-76.8
Olbrich Neto & Meira	Brazil	2004	Pregnant woman	478	60.0%	95%CI: 55.6-64.4
Porto *et al.*	Brazil	1992	Pregnant woman	503	74.7%	95%CI: 73.9-81.1
Reiche *et al.*	Brazil	2000	Pregnant woman	1,559	67.0%	95%CI: 64.7-69.3
Reis *et al.*	Brazil	2006	Pregnant woman	10,468	61.1%	95%CI: 60.2-62.0
Rey & Ramalho	Brazil	1999	Pregnant woman	186	71.3%	95%CI: 64.8-77.8
Spalding *et al.*	Brazil	2005	Pregnant woman	2,126	74.5%	95%CI: 72.7-76.3
Sroka *et al.*	Brazil	2010	Pregnant woman	963	68.6%	95%CI: 65.6-71.6
Varella *et al.*	Brazil	2003	Pregnant woman	1,261	59.8%	95%CI: 57.1-62.5
Barrera *et al.*	Colombia	2002	Pregnant woman	637	63.5%	95%CI: 43.1-50.9
Castro *et al.*	Colombia	2008	Pregnant woman	300	48.7%	95%CI: 60.3-66.7
Rosso *et al.*	Colombia	2008	Pregnant woman	955	71.3%	95%CI: 45.5-51.9

Zapata *et al.*	Costa Rica	2005	20-40 year old	283	58.0%	95%CI: 49.2-60.8
Acosta-Bas *et al.*	Cuba	2001	Pregnant woman	207	61.8%	95%CI: 53.6-67.0
Martinez *et al.*	Cuba	2005	Pregnant woman	160	55.0%	95%CI: 36.3-51.7
Sanchez-Gutierrez *et al.*	Cuba	2003	Pregnant woman	1,210	44.0%	95%CI: 59.1-64.5
Asthana *et al.*	Grenada	2006	Pregnant woman	534	60.3%	95%CI: 52.8-61.2
Alvarado-Esquivel *et al.*	Mexico	2006	Pregnant woman	343	57.0%	95%CI: 3.6-8.6
Ramsewak *et al.*	Trinidad and Tobago	2008	Pregnant woman	450	42.9%	95%CI: 38.3-47.5
Triolo-Mieses & Traviezo-Valles	Venezuela	2006	Pregnant woman	446	38.0%	95%CI: 33.5-42.5
			Summary	**68,764**	**31.2%**	

Table 6. *Toxoplasma gondii* seroprevalence snapshot in Oceania - data from human studies

Study	Country	Year	Subjects	n tested	Results	Remarks
Walpole *et al.*	Australia	2001	Pregnant woman	10,207	35.0%	
Karunajeewa *et al.*	Australia	2001	Pregnant woman	308	23.0%	
Breurec *et al.*	New Caledonia	2004	Pregnant woman	2,415	56.7%	95%CI: 54.7-58.7
Morris & Croxon	New Zealand	2004	Pregnant woman	500	35.4%	95%CI: 31.2-39.6
Curson *et al.*	New Zealand	1982	Pregnant woman	566	60.0%	
			Summary	**14,357**	**38.5%**	

Table 7. Summary of global *Toxoplasma gondii* infection by continent - data from human studies

	No. of studies	No. of subjects	No. positive	Seroprevalence	95%CI	Range
Asia	61	204,710	33,484	**16.4%**	16.2 – 16.5%	0.5 – 82.6%
USA/Canada	4	46,795	8,193	**17.5%**	17.2 – 17.8%	10.4 – 22.5%
Europe	38	299,075	88,828	**29.7%**	29.5 – 29.9%	8.2 – 59.0%
South America	27	68,764	21,441	**31.2%**	30.8 – 31.5%	7.3 – 74.7%
Oceania	5	14,357	5,530	**38.5%**	37.7 – 39.3%	23.0 – 60.0%
Africa	17	14,309	8,779	**61.4%**	60.6 – 62.1%	20.8 – 87.7%
Total	**152**	**648,010**	**166,255**	**25.7%**	25.6 – 25.8%	0.5 – 87.7%

consume could partly explain the large differences in *T. gondii* seroprevalence between different countries and continents.

Changes in environmental conditions, perhaps as a result of global warming and urbanisation, have already altered the ecology, transmission, and distribution of *T. gondii* (Yan *et al.*, 2016). The complex life-cycle of *T. gondii* is sensitive to environmental changes primarily as a result of the infectivity and survival time of the oocysts (Meerburg and Kijlstra, 2009). The distribution, survival, and transmission of *T. gondii* is effected by climatic conditions in three ways: i) the ability of the viable oocysts to sporulate specifically with respect to temperature and humidity (Patz *et al.*, 2000); ii) the impact of climate change on patterns and habits of the definitive and intermediate hosts that play a vital role in the survival and distribution on *T. gondii* (Dhimal *et al.*, 2014; Elmore *et al.*, 2012; Afonso *et al.*, 2013); and, iii) seasonal rainfall and its influence on humidity and river flow which in turn delivers oocysts from land to water, leading to water-borne *T. gondii* infection (Mazzillo *et al.*, 2013; Ribeiro *et al.*, 2015). It has been established that even minute changes in temperature can have a significant effect on the prevalence of *T. gondii* (Laaksonen, 2010). For example, Yan *et al.* (2016) found a positive relationship between average annual temperature in different areas in Sweden and the incidence of *T. gondii* in pregnant women. Many other studies conducted in different countries support this observation (Ljungström *et al.*, 1995; Ahlfors *et al.*, 1989; Caballero-Ortega *et al.*, 2012). Furthermore, rain fall creates a humid environment that increased oocyst survival in addition to increasing the food availability to support definitive and intermediate hosts (Afonso *et al.*, 2013). It has been demonstrated that during years of increased rain fall or in areas subjected to heavy rain, the incidence of *T. gondii* in cats' increases, especially when the average 10-day rainfall exceeds 25mm (Afonso *et al.*, 2010). This suggests that rainfall may influence the exposure of cats to *T. gondii*. Equally, low rain fall or drought can result in poor hygiene and a reduced food supply, thereby increasing contamination leading to increased transmission rates of *T. gondii* (Patz *et al.*, 2000). Considering the above wide ranging variables, it is perhaps not surprising that the *T. gondii* seroprevalence rates vary significantly between continents, countries, and even within countries. This is simply because each region has its own unique combination, or signature, of environmental factors that participates in the ecology and epidemiology of *T. gondii* infection. Therefore, general environmental conditions that in theory allow for *T. gondii* survival and consequently increased human seroprevalence do not always apply, a trend observed in the present study.

With the current, and increasing, rates of urbanisation, travel, immigration, emigration, and environmental degradation, there is little doubt that human activities are directly changing the global environment. An active area of research is currently examining the impact of human activities like deforestation and urbanisation on habitat loss and fragmentation of animal populations that reduces biological diversity and provides favourable conditions for the occurrence and spread of parasitic zoonosis such as *T. gondii* (Yan *et al.*, 2016; Patz *et al.*, 2000). The flipside of these interconnected activities, which can be summarised as social and economic globalisation, is that it will become increasingly more difficult to monitor the source, spread, and risk factors of *T. gondii* infection. This will only reveal the gaps in our knowledge on the evolution, epidemiology, and ecology of *T. gondii* infection and its relationship with the environment. Therefore, it may be prudent for public health authorities to consider the implementation of molecular based techniques to monitor and track the origin and transmission route of *T. gondii* in the environment. Furthermore, genetic characterisation studies will aid in determining the sources of infection and the genotypes/strains involved, as well as establishing the impact of human genetic variation on the incidence and seroprevalence of *T. gondii*.

In order to achieve a geographically representative data set, the current study applied flexible inclusion criteria. There are weaknesses to using this process therefore the results of the present study should be interpreted with caution. For a study to be truly representative, one would expect a sophisticated study design with a thorough selection process from a large sample size. However, many studies included in our review focus only on a limited number of women whom were pregnant or of childbearing age (clinical heterogeneity). Furthermore, some regions had skewed data favouring certain countries therefore there may be a risk of over-representation from either subjects considered high risk or vice versa. Lastly, the lack of consistency in the diagnostic methods used to determine *T. gondii* infection introduced some degree of methodical heterogeneity. While difficult to execute, there is a need for a form of standardisation in regards to the methods used to diagnose *T. gondii* infection.

CONCLUSION

Toxoplasma gondii global seroprevalence varies significantly with no clear inter- and intra-continental trends. This is due to complex interplay of evolving environmental and human factors. Monitoring the source and transmission may assist public health authorities clarify the risk factors involved, as well as focus on implementing optimal state-specific health policies targeting *T. gondii* transmission control.

Declarations

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