Institute of Parasitology, Biology Centre CAS
Folia Parasitologica 2023, 70: 004
doi: 10.14411/fp.2023.004

Folia Parasitologica
http://folia.paru.cas.cz

Research Article OPEN ACCESS

A large-scale study on the seroprevalence of *Toxoplasma gondii* infection in humans in Iran

Reza Kalantari[1,2], **Mahsa Esmaeilifallah**[1,2], **Rasool Jafari**[3], **Hossein Mirhendi Esfahani**[1,4] and **Hossein Yousofi Darani**[1]

[1] Department of Parasitology and Mycology, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran;

[2] Student Research Committee, Isfahan University of Medical Sciences, Isfahan, Iran;

[3] Department of Medical Parasitology and Mycology, School of Medicine, Urmia University of Medical Sciences, Urmia, Iran;

[4] Acquired Immunodeficiency Research Centre, Isfahan University of Medical Sciences.

Abstract: It is estimated that nearly one-third of the world's human population is infected with *Toxoplasma gondii* (Nicolle et Manceaux, 1908). Human infection is commonly asymptomatic, multifaceted, and can manifest in severe pathological forms in congenital toxoplasmosis and immunocompromised individuals. This study attempted to recognise the seroprevalence of *T. gondii* infection in Iranian residents referred to medical laboratories for toxoplasmosis tests throughout the country. This retrospective cross-sectional study was conducted from 2015 to 2019 on individuals referred to diagnostic laboratories in 26 provinces, and these laboratories sent their samples to the referral centres. Accordingly, data associated with serodiagnosis of toxoplasmosis, age, sex, anti-*T. gondii* IgG, and IgM status in Iranian residents were collected from two referral diagnostic laboratories. All individuals were evaluated using the antibody immunocapture-chemiluminescence assay (CLIA) method with the Immulite®2000s XPi system. In this study, the first large-scale assay of *T. gondii* infection in Iran, an overall seroprevalence of 30.4% was among 35,047 patients examined. The highest IgM seropositivity rate was in the 10–20 years old patients. In addition, this study showed a very different prevalence of *T. gondii* across the country, highest in the humid areas, such as the Caspian Sea basin in the North, and the North West with seroprevalence of 48.6%.

Key words: Prevalence, toxoplasmosis, IgG/IgM, chemiluminescence, antibody, public health

Toxoplasma gondii (Nicolle et Manceaux, 1908) is an obligatory apicomplexan intracellular parasite that infects about a third of humans worldwide and can infect all warm-blooded animals (Molan et al. 2019). Felids are definitive hosts for this parasite, shedding up to millions of oocysts per day in their faeces, which sporulate and become infective in the environment. Ingestion of these sporulated oocysts, which contaminate vegetables, soil and water sources, together with eating bradyzoites from raw or undercooked meat, comprise the two major horizontal transmission routes (Hill and Dubey 2018, Attias et al. 2020). Indeed, these parasite stages are responsible for a substantial burden of postnatally acquired infections, potentially causing sporadic outbreaks of acute or mild disease in immunocompetent people and severe toxoplasmosis in immunocompromised individuals, including HIV/AIDS patients, and cases of congenital infection during pregnancy, following reactivation of bradyzoites into disseminating tachyzoites (Nayeri et al. 2020, Thebault et al. 2021).

Infection with *T. gondii* in pregnancy is associated with foetal loss and foetal and newborn abnormalities in humans and livestock. This parasite also causes infections in the eye (retina) and brain, necessitating the use of drugs that cross the placenta, brain and eye barriers for penetration (Aguirre et al. 2019). In addition, given the growing number of cancer and immunocompromised patients and organ transplant recipients, *T. gondii*, as an opportunistic parasite, can drive acute life-threatening conditions for those patients (Aguirre et al. 2019). Owing to the tropism of *T. gondii* for the central nervous system (CNS) and eye, poor prognosis and complications such as glaucoma, chorioretinitis, retinal detachment, brain abscess and encephalitis can occur during acute or recrudescent infection (Weiss and Dubey 2009, Kalogeropoulos et al. 2021).

Furthermore, congenital toxoplasmosis may cause serious complications such as focal brain lesions, microcephaly, hydrocephaly, deafness and mental retardation (Daher et al. 2021). Cerebral toxoplasmosis may also cause neuropsychological effects, such as obsessive-compulsive

Address for correspondence: Hossein Yousofi Darani, Department of Parasitology and Mycology, School of Medicine, Isfahan University of Medical Sciences, Hezar Jerib St. Isfahan, 8174673461, Iran. E-mail: yousofi@med.mui.ac.ir

Table 1. Anti-*Toxoplasma* IgG and IgM seropositivity in different parts of Iran with different variables. The total column shows that infants and child-bearing women were the most frequent patients referred to the studied laboratories for testing antibodies against *Toxoplasma gondii* (Nicolle et Manceaux, 1908).

Variables	IgG				IgM			
	Positive	**Negative**	**Total**	***p***	**Positive**	**Negative**	**Total**	***p***
Mean age (years) ± SD	32.1 ± 13.3	27.6 ± 11.6	-	< 0.001*	25.9 ± 11.1	29.5 ± 11.3	-	< 0.001*
Male	31.2 ± 21	18.6 ± 17.4	-	< 0.001*	22.2 ± 9.9	23.7 ± 19.2	-	0.73*
Female	32.3 ± 11.5	29.0 ± 9.7	-	< 0.001*	27.4 ± 11.3	30.2 ± 9.7	-	< 0.001*
Sex								
Male	787 (31.8%)	1687 (68.2%)	2,474	0.09	73 (3.8%)	1,851 (96.2%)	1,924	< 0.001
Female	4,695 (30.1%)	10,879 (69.9%)	15,574		177 (1.2%)	14,898 (98.8%)	15,075	
Age groups								
< 1 month	270 (38.5%)	432 (61.5%)	702	< 0.001	8 (1.7%)	462 (98.3%)	470	< 0.001
< 1 years	286 (33.7%)	562 (66.3%)	848		8 (1.3%)	596 (98.7%)	604	
1–10 years	80 (9.0%)	806 (91.0%)	886		12 (1.8%)	656 (98.2%)	668	
10–20 years	280 (22.0%)	993 (78.0%)	1273		54 (4.9%)	1,038 (95.1%)	1,092	
20–30 years	1,657 (25.5%)	4,851 (74.5%)	6,508		98 (1.5%)	6,301 (98.5%)	6,399	
30–40 years	2,221 (33.3%)	4,445 (66.7%)	6,666		59 (0.9%)	6,596 (99.1%)	6,655	
40–50 years	578 (47.9%)	628 (52.1%)	1,206		12 (1.1%)	1,032 (98.9%)	1,044	
50–60 years	207 (54.3%)	174 (45.7%)	381		5 (1.6%)	314 (98.4%)	319	
60–70 years	110 (56.4%)	85 (43.6%)	195		2 (1.3%)	150 (98.7%)	152	
>70 years	63 (74.1%)	22 (25.9%)	85		0 (0.0%)	66 (100%)	66	

* Estimated by Mann-Whitney test (the age distribution was not normal; $p < 0.001$ estimated by One-Sample Kolmogorov-Smirnov Test)

disorder (OCD), autism, Alzheimer's disease, Parkinson's disease, schizophrenia, epilepsy, multiple sclerosis, headache/migraine, bipolar disorder, depression, and suicide (Hlaváčová et al. 2021, Inceboz and Inceboz 2021, Mendoza-Larios et al. 2021, Nayeri et al. 2021).

Several factors such as parasite strains, number of ingested organisms, genetic background, immunity status, and sex of the host are crucial in the progression of infection (Montoya and Liesenfeld 2004). Infection with *T. gondii* has severe socioeconomic effects on individuals. Families incur many costs while caring for sick children, especially those with mental retardation and blindness (Roberts et al. 1994, Ben-Harari and Connolly 2019).

In highly endemic areas, such as parts of Africa and continental Europe and Central and South America, seroprevalence can reach around 90%, whereas in some European areas it can reach 60%, and ranges from 8 to 22% in the United States (Dubey and Jones 2008, Aguirre et al. 2019, Molan et al. 2019). The prevalence of the infection fluctuates depending on the region, climate, diet, hygiene and host susceptibility (Almeria et al. 2021).

In Iran, several studies with various serological methods were performed on different human populations (Nayeri et al. 2020, Sobati 2020), particularly high-risk demographic groups, such as people undergoing chemotherapy (Hosseini et al. 2021), ophthalmic disorders (Saki et al. 2020), transplant, immunocompromised and hemodialysis patients (Ahmadpour et al. 2014, Rasti et al. 2016), diabetic patients (Asgari et al. 2021), pregnant women (Ben-Harari and Connolly 2019, Khademi et al. 2019, Nayeri et al. 2020), neonates (Nahvi et al. 2019), blood donors (Moshfe et al. 2018), and occasionally healthy human population (Mousavi-Hasanzadeh et al. 2020). The seroprevalence ranged from 13% to 73% and varied among gender, province and lifestyle (Daryani et al. 2014).

As a cosmopolitan strategy, the One Health concept has emphasised the need for an interdisciplinary effort to seek optimal human, animal and ecosystem health. This approach suggested zoonotic infection monitoring for *T. gondii* prevalence by integrating data on humans, domestic animals and wildlife in the same area for better management (Aguirre et al. 2019). Standard diagnostic methods for toxoplasmosis generally pertain to immunology-dependent examinations such as enzyme-linked immunosorbent assay (ELISA) and indirect immunofluorescence assay (IFA) to detect the *T. gondii*-specific antibodies, i.e., IgM or IgG (Robert-Gangneux and Darde 2012).

Numerous seroprevalence studies show that the different results reported from a particular area can vary due to the selected target human population and the applied laboratory methods and diagnostic kits (Daryani et al. 2014, Khademi et al. 2019, Saki et al. 2020). Therefore, restricting these variables can better express the existing real situation. In Iran, serological and immunological tests in diagnostic laboratories are usually performed by kits with varying characteristics and performance levels on the Iranian market. To the best of our knowledge, this study is the first extensive and non-local evaluation of the *T. gondii* seroprevalence in Iran with the susceptible and specific reliable technique allowing for comfort and safety in serological interpretation.

In this study, we determined the seroprevalence of *T. gondii* based on the test performed previously using *T. gondii* Quantitative IgG/IgM Kits (Siemens Healthcare Diagnostics Products, Marburg, Germany) with an automated assay Immulite® 2000s analyser (Euro/Diagnostic Products Corporation, Siemens Medical, Gwynedd, UK) recently placed on the Iran market. The objective of this study was to evaluate the large-scale *T. gondii* seroprevalence in the human population throughout the country

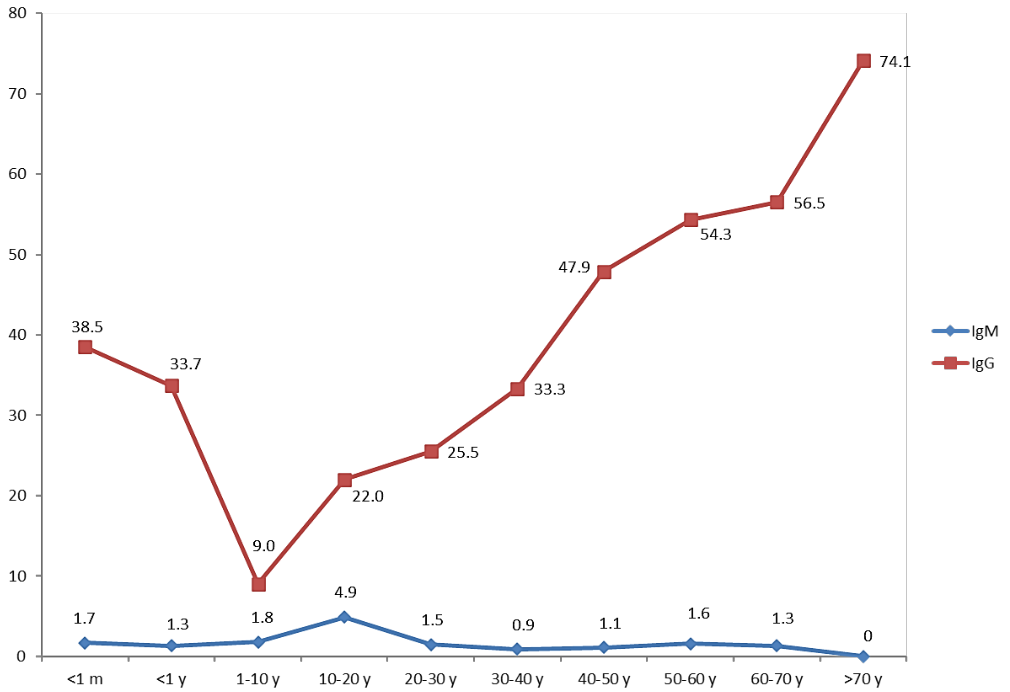

Fig. 1. The seroprevalence plot of *Toxoplasma gondii* (Nicolle et Manceaux, 1908) in Iran in different age groups (m-month; y-year).

with a single sensitive technique (antibody immunocapture-chemiluminescence assay).

MATERIALS AND METHODS

Study design and sample collection

A large-scale retrospective cross-sectional study was carried out in 26 of 31 provinces in Iran – East Azerbaijan, Zanjan, Ardabil, Gilan, Mazandaran, Golestan, Qazvin, Alborz, Tehran, Semnan, Markazi, Ilam, Kurdistan, Kermanshah, Hamedan, Lorestan, Qom, Isfahan, Yazd, Kohgiluyeh and Boyer-Ahmad, Fars, Kerman, Sistan and Balochistan, Hormozgan, Khuzestan and Bushehr – between September 2015 and March 2020. To diagnose toxoplasmosis, the recorded data of the 35,047 sera samples of the human population, including 16,999 anti-*T. gondii* IgM and 18,048 anti-*T. gondii* IgG tests. Medical Laboratories Noor Lab in Tehran and Pooyesh Lab in Isfahan, Iran, processed the samples in a determined way and used *Toxoplasma gondii* Quantitative IgG/IgM kits (Siemens Healthcare Diagnostics Products, Marburg, Germany) in the following section. About three to five ml of blood samples were obtained from the median cubital and cephalic veins. Sera were separated from cell pellets in a different tube to limit the interference of fibrin that may lead to false-positive results using automated immunoassay. The individuals were classified into ten age groups: < 1 month, < 1 year, 1–10 years, 10–20 years, 20–30 years, 30–40 years, 40–50 years, 50–60 years, 60–70 years, > 70 years (Table 1).

Diagnostic analysis

According to the manufacturer's instructions, DPC Immulite®2000s *Toxoplasma* Quantitative IgG/IgM Kits were used. Antibody immunocapture-chemiluminescence assay (CLIA) method with Immulite®2000s XPi System (Euro/Diagnostic Products Corporation, Siemens Medical, Gwynedd, UK) was used. The positivity threshold with the Immulite®2000s technique was considered 8 IU/ml, with an uncertain and equivocal area from 6.5 to 8 IU/ml, and below 6.5 IU/ml was deemed negative.

Statistical analysis

IBM SPSS 22.0 software (Armonk, New York, USA) was used for statistical analyses. The prevalence of IgG and IgM antibodies against *T. gondii* was estimated from the ratio of positive samples to the total number of samples tested, with a 95% confidence interval (CI). Associations between *T. gondii* seroprevalence and the explanatory variables (age, sex and sampling area) were initially screened using the Chi-square test or Fisher's test. All statistical variables with a p-value < 0.05 were considered significant. A geographic information system (GIS) map was created for anti-*T. gondii* IgM and IgG seropositivity for studied provinces of the country, using ESRI ArcGIS 10.4 software (Esri, Redlands, California).

RESULTS

In total, 35,047 samples of human sera were referred to Medical Laboratories for *T. gondii* IgG and IgM tests, 87.45% (n = 30,649) tests were related to females, and 12.54% (n = 4,398) tests were for males (Table 1). The mean age of the studied patients was 29.2 years (from 1 day up to 99 years old; median 30 years). The mean age of anti-*T. gondii* IgM seropositive patients were significantly lower (25.9 years) than that of negative patients (29.5 years) ($p < 0.001$).

In people who were anti-*T. gondii* IgG seropositive, the mean age was significantly higher (32.1 years) than

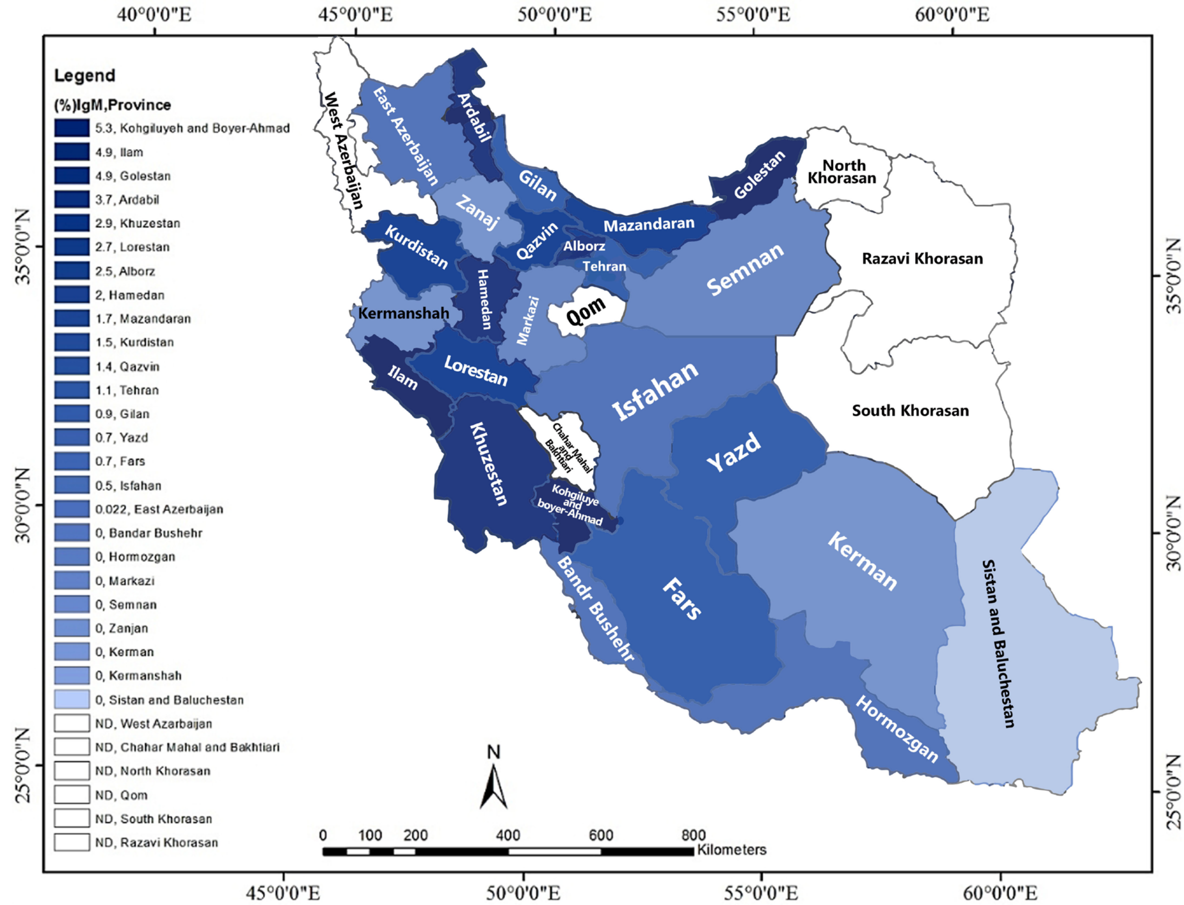

Fig. 2. A GIS map of IgM seroprevalence of *Toxoplasma gondii* (Nicolle et Manceaux, 1908) in different provinces of Iran, during 2015–2020 (ND – no data).

the mean age in negative patients (27.6 years) ($p < 0.01$). The anti-*T. gondii* IgG seropositivity showed a high prevalence in neonates < 1-month-old (38.5%) and < 1-year-old (33.7%) and then declined to 9.0% and continued with a significant increase by age ($p < 0.001$). However, considering IgM, it starts with low seropositivity in neonates < 1-month-old (1.7%) and < 1-year-old (1.3%) and a continuous with a significant increase ($p < 0.001$) until 10–20 years old patients, then it shows a mild decrease in seropositivity by the increasing age (Fig. 1; Table 1).

The results showed that 250 (1.5%) out of 16,999 and 5,482 (30.4%) out of 18,048 individuals were anti-*T. gondii* IgM and IgG seropositive, respectively. There was no significant relationship between sex and IgG seropositivity ($p = 0.094$). The risk of infection in men compared to women was 1.055, which shows an almost equal risk for both sexes. However, the prevalence was significantly higher in men with IgM seropositivity ($p < 0.001$), as well as the risk of infection (IgM) in men was 3.23 × higher than in women (Table 1; Fig. 2).

Since the majority of the studied population were women of childbearing ages, we divided the ages into some age groups, and the results of IgG and IgM seropositivity in females were as follows: anti-*T. gondii* IgG seropositivity in < 1-year-old 34.1%, 1–10 years 10.5%, 10–20 years 20.5%, 20–30 years 25%, 30–40 years 32.8%, 40–50 years 46.1%, 50–60 years 53.9%, 60–70 years 62%, and > 70 years 71.2%. Anti-*T. gondii* IgM seropositivity in < 1 year-old 2.1%, 1–10 years 1.2%, 10–20 years 3.2%, 20–30 years 1.3%, 30–40 years 0.7%, 40–50 years 1.3%, 50–60 years 1.9%, 60–70 years 2.2%, and >70 years 0%. Values of the overall prevalence of *T. gondii* antibodies in different age groups are in Table 1.

The highest number of studied samples was from Tehran province, and the lowest number was from Hormozgan province (Table 2). The association between the seroprevalence and the geographic location was statistically significant ($p < 0.001$). The highest prevalence of anti-*T. gondii* IgM was observed in Kohgiluyeh and Boyer-Ahmad (5.3%), and the lowest rate in Bushehr, Zanjan, Semnan, Sistan and Baluchestan, Kerman, Kermanshah, Markazi, and Hormozgan provinces (0%) (Fig. 2). The highest prevalence of anti-*Toxoplasma* IgG was found in East Azerbaijan and Mazandaran (48.6%), and the lowest rate was in samples from Sistan and Baluchistan provinces (10.6%) (Fig. 3).

DISCUSSION

Understanding the status of infection with *Toxoplasma gondii* in each community's population is critical (Dubey and Jones 2008). Most epidemiological surveys in Iran are based on IgG titres and the ELISA method (Daryani et al. 2014, Foroutan et al. 2019). There is limited knowledge of

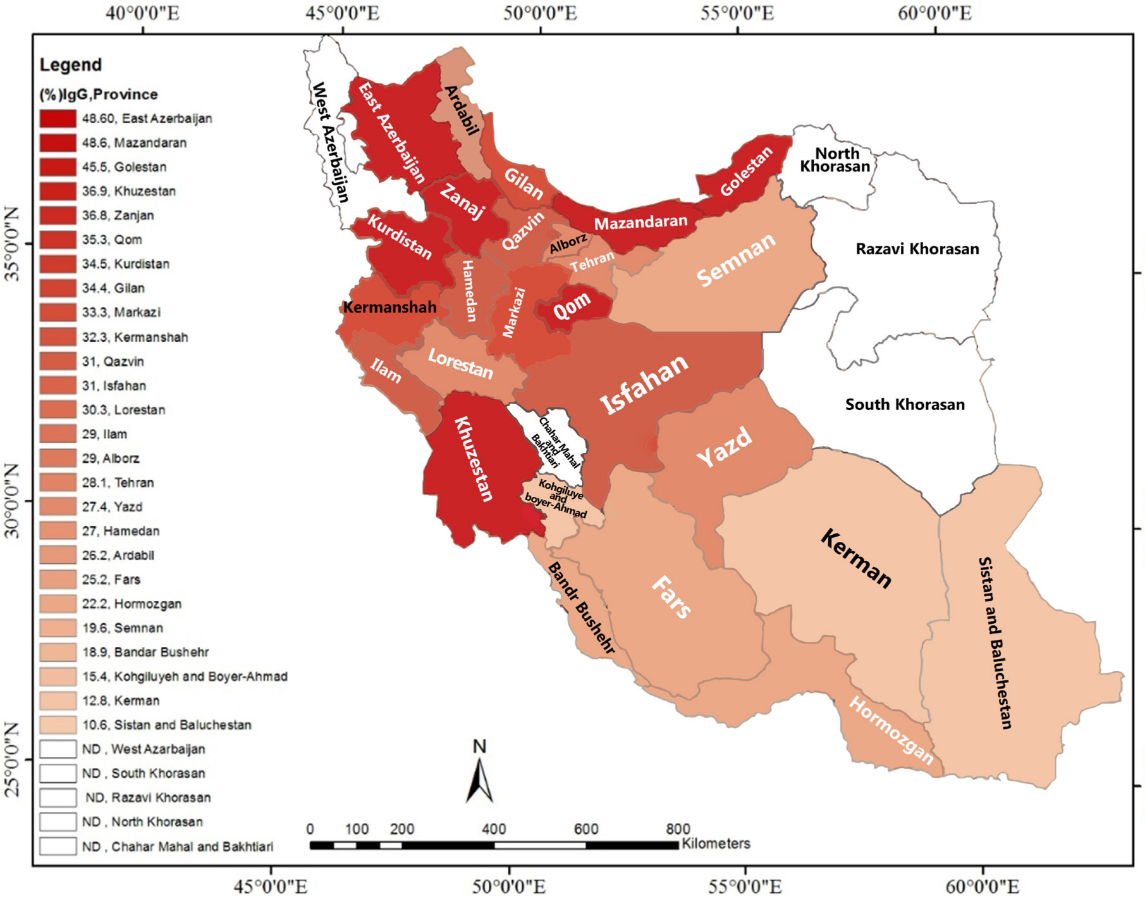

Fig. 3. A GIS map of IgG seroprevalence of *Toxoplasma gondii* (Nicolle et Manceaux, 1908) in different provinces of Iran, during 2015–2020.

the seroepidemiology of *T. gondii* in the human population of Iran, and most of the research was conducted on high-risk groups at a local level (Ahmadpour et al. 2014, Saki et al. 2020).

The major limitations of other studies were avoided in this study, such as the absence of studies in some regions of Iran and different methods without similar sensitivities and specificities (Foroutan et al. 2019). The present retrospective cross-sectional survey estimated the seroprevalence of *T. gondii* infection in the Iranian population referred to medical laboratories for *T. gondii* infection tests, using a large number of sera samples over five years.

IgG-positive-antibody titres can be detected 2–3 weeks after infection, reaching a maximum titre within two months. It then diminishes to a baseline level that persists throughout life. In contrast, IgM titres appear within a few days after infection and reach a maximum level within four weeks. It is necessary to detect both the IgG and IgM antibodies simultaneously to establish a chronic or acute phase of infection (Robert-Gangneux and Darde 2012).

Our results estimate that the seroprevalence of *T. gondii* infection in the human population of Iran is 30.4%. In other studies in Iran, slightly higher seroprevalence rates of 33–46% and 38–47% have been reported for *T. gondii* infection (Daryani et al. 2014, Foroutan et al. 2019). The difference in infection rate may be related to the study populations.

In this research, the target population was humans requested for anti-*T. gondii* IgG and IgM. The prevalence is lower in the USA/Canada, Europe, and China, being 17.5%, 29.6%, and 16.4%, respectively, primarily due to the good hygienic conditions, successful learning and cultural plans to alert people, precise diagnostic tests for women of childbearing age and pregnant women, industrialisation of animal husbandry as well as well-established monitoring systems and enhanced laws in meat inspection. In African countries, a 61.4% prevalence of *T. gondii* infection has been observed, which may be settled by the abundance of infected cats and food animals, low levels of hygiene, and living in sub-standard conditions (Molan et al. 2019).

In our work, a considerable number of the studied population were women, especially between 20 and 40 years old (women of childbearing age), and infants tested for screening, monitoring or diagnosis of toxoplasmosis. The IgG seropositivity for women in the 20–30 and 30–40 age groups was registered as 25.0% and 32.8%, respectively, and for the IgM as 1.3% and 0.7%, respectively. Notably, we observed the highest IgM seropositivity in the females in the 10–20 year-old age group (3.2%), which is very im-

Table 2. The prevalence of anti-*Toxoplasma* IgG and IgM in males and females referred from different provinces in Iran.

Province	IgG positive n (%)			IgG negative n (%)			IgM positive n (%)			IgM negative n (%)		
	Male	**Female**	**Total**	**Male**	**Female**	**Total**	**Male**	**Female**	**Total**	**Male**	**Female**	**Total**
1. East Azerbaijan	3 (17)	15 (83)	18	2 (11)	17 (90)	19	1	0 (0.0)	1	4 (9)	42 (91)	46
2. Zanjan	3 (21)	11 (79)	14	4 (17)	20 (83)	24	-	-	-	6 (18)	28 (82)	34
3. Ardabil	9 (28)	23 (72)	32	13 (14)	77 (86)	90	2 (40)	3 (60)	5	20 (15)	111 (85)	131
4. Gilan	26 (21)	101 (80)	127	47 (19)	195 (81)	242	1 (33)	2 (67)	3	60 (19)	261 (81)	321
5. Mazandaran	44 (11)	368 (89)	412	59 (14)	376 (86)	435	4 (22)	14 (78)	18	96 (9)	922 (91)	1,018
6. Golestan	1 (3)	34 (97)	35	2 (5)	40 (95)	42	2 (67)	1 (33)	3	2 (3)	56 (97)	58
7. Qazvin	10 (29)	25 (71)	35	5 (6)	73 (94)	78	1 (50)	1 (50)	2	11 (8)	133 (92)	144
8. Alborz	17 (9)	177 (91)	194	44 (9)	432 (91)	476	5 (21)	19 (79)	24	55 (6)	890 (94)	945
9. Tehran	380 (14)	2,403 (86)	2,783	740 (10)	6,386 (90)	7126	30 (27)	82 (73)	112	916 (9)	8,887 (91)	9,803
10. Semnan	0 (0)	9	9	8 (22)	29 (78)	37	-	-	-	6 (15)	34 (85)	40
11. Markazi	1 (10)	9 (90)	10	3 (15)	17 (85)	20	-	-	-	6 (16)	32 (84)	38
12. Ilam	6 (14)	36 (86)	42	23 (22)	80 (78)	103	4 (67)	2 (33)	6	18 (16)	98 (85)	116
13. Kurdistan	38 (13)	246 (87)	284	97 (18)	441 (82)	538	5 (56)	4 (44)	9	87 (14)	519 (86)	606
14. Kermanshah	1 (10)	9 (907)	10	2 (10)	19 (91)	21	-	-	-	8 (9)	79 (91)	87
15. Hamedan	14 (13)	95 (877)	109	45 (15)	249 (85)	294	2 (29)	5 (71)	7	42 (12)	301 (88)	343
16. Lorestan	88 (22)	306 (78)	394	211 (23)	697 (77)	908	9 (35)	17 (65)	26	166 (18)	764 (82)	930
17. Qom	26 (9)	252 (91)	278	24 (5)	485 (95)	509	1 (14)	6 (86)	7	21 (5)	436 (95)	457
18. Isfahan	19 (28)	48 (72)	67	34 (23)	115 (77)	149	0 (0)	1	1	48 (24)	150 (76)	198
19. Yazd	20 (18)	94 (83)	114	66 (22)	236 (78)	302	0 (0)	2	2	72 (25)	222 (76)	294
20. Kohgiluyeh & Boyer-Ahmad	1 (13)	7 (88)	8	6 (14)	38 (86)	44	0 (0)	2	2	5 (14)	31 (86)	36
21. Fars	8 (21)	31 (80)	39	19 (16)	97 (84)	116	0 (0)	1	1	23 (17)	116 (84)	139
22. Kerman	0 (0)	11	11	8 (11)	67 (89)	75	-	-	-	6 (11)	50 (89)	56
23. Sistan & Baluchistan	2 (12)	15 (88)	17	35 (24)	109 (76)	144	-	-	-	37 (23)	123 (77)	160
24. Hormozgan	0 (0)	4	4	3 (21)	11 (79)	14	-	-	-	3 (23)	10 (77)	13
25. Khuzestan	66 (16)	359 (85)	425	178 (25)	548 (76)	726	6 (29)	15 (71)	21	125 (18)	578 (82)	703
26. Bushehr	3 (43)	4 (57)	7	8 (27)	22 (73)	30	-	-	-	8 (24)	25 (76)	33
Total	**786 (14)**	**4,692 (86)**	**5,478**	**1,686 (13)**	**10,876 (87)**	**12,562**	**73 (29)**	**177 (71)**	**250**	**1,851 (11)**	**14,898 (89)**	**16,749**

portant, showing a possibly higher risk of congenital toxoplasmosis in pregnancies that occur before 20 years of age. The prevalence of acute toxoplasmosis in pregnant women worldwide is estimated between 0.1 and 0.8% (Torgerson and Mastroiacovo 2013), close to our findings in women 20 to 40 years of age.

The seroprevalence in infants under one month and one year were 38.5%, 33.7% for IgG, and 1.7% and 1.3% for IgM, respectively. Because *T. gondii*-specific IgG may have been passively transplacentally transferred, our estimate was close to the overall population (30.4%). Of course, as *T. gondii* has been requested from the physician for infants, naturally occurring infections in the studied infants are also not unlikely. Khosravi et al. (2016) reported a prevalence of acute toxoplasmosis in neonates from Tehran, Isfahan, and Kashan of 1.5–28.6%, 39%, and 0.6%, respectively. Nahvi et al. (2019) reported the prevalence of toxoplasmosis in neonates as 19.8% seropositive for anti-*T. gondii* IgG in Tehran. This difference may be due to the number of populations studied and the methods used.

The prevalence of *T. gondii*-specific IgM in the present study in neonates may be related to the origin of the sera we used. They may be suspected of congenital toxoplasmosis that made physicians request a toxoplasmosis test. Congenital toxoplasmosis substantially burdens health globally (Torgerson and Mastroiacovo 2013), and the corresponding data should be used to finance public health interventions to reduce the disease burden. On the other hand, a sharp decrease in prevalence in the age group of 1–10 years (9.0%) may indicate a reduction in maternal IgG. With the increasing age, the infection (IgG) prevalence is also increased and reached the highest rate, 74.1%, in > 70 years old.

The significant linear trend of increasing prevalence by increasing age is simple; more exposure occurs, as frequently reported in other studies. Nevertheless, the IgM seropositivity trend is somehow different. It starts with the minimum rate in infants and has its highest rate in the 10–20 age group (4.9%). Then it shows a decreasing trend by age and finally reaches 0% in age patients older than 70 years old. These results show that acute infection occurs more frequently in teenagers; this may be because they are more exposed to the environment.

This survey estimates the seroprevalence of *T. gondii* infection rate in the Iranian population using the sera sample, which were collected from different provinces. Although Iran has an arid climate in large areas, the weather condition is subject to variability. Due to geographic location and urbanisation, *T. gondii* seroprevalence in some provinces such as Tehran, Kerman, Khuzestan and Fars varies widely. A very variable prevalence of *T. gondii* showed the highest in humid areas, such as the Caspian Sea littoral in the North and the North West with 48.6%, and the South West of Iran with 36.9%. At the same time, the lower prevalence is registered in hot and dry areas of the country, especially in the South East with 10.6%.

In reality, any meteorological factor, like suitable humidity, that can help the sporulation of oocysts of *T. gondii* shed in the cat faeces would occasion prolonged survival and the spread of infective parasites in the environment, increasing the possibility of human and animal infection (Attias et al. 2020). The provinces with seroprevalence of toxoplasmosis that differed significantly from previous assessments were: East Azerbaijan, Ardabil, Gilan, Golestan, Qazvin, Tehran, Kermanshah, Isfahan, Kohgiluyeh and Boyer-Ahmad, Fars, Kerman, Sistan and Balochistan, and Khuzestan, respectively, in the study of Daryani et al. 2014. Due to economic problems, migration from rural to urban areas has been reversed in recent years.

However, migration from neighbouring countries with different climates and health conditions and cooking due to war and insecurity can complicate our assessment of metropolitan areas because IgG antibody titres persist throughout one's life. However, there was no significant difference between the sera prevalence of men and women in this evaluation, as in many studies (Daryani et al. 2014).

To the best of our knowledge, this is the first large-scale seroprevalence study that provides a comprehensive view of the seroepidemiology of *T. gondii* in the Iranian population (from 26 of 31 provinces). In conclusion, an overall seroprevalence of 30.4% was detected. Thus, about one-third of Iranian people have been infected with *T. gondii*. Accordingly, two-thirds of the human population is seronegative and susceptible to infection. Therefore, individuals at high risk should be monitored. Several measures will aid in the prevention and control of *T. gondii* infection. These include health policies targeting the promotion of public educational programs, training courses for childbearing age and pregnant women, an inspection of food production industries, improvement of hygienic standards of abattoirs, and sanitary disposal of viscera.

Acknowledgements. The present study was carried out at the Department of Parasitology and Mycology, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran and has been carried out alongside a PhD thesis in Medical Parasitology (ethical code: IR.MUI.MED.REC.1398.267; grant no. 49003). The authors would like to thank the Noor and the Pooyesh labs' supervisors for their help and contributions.

Author Contributions. RK: The design of the study, data collection and write-up. ME: Performed research and contributed to 1st draft. RJ: Analysis and interpretation of data. HM-E and HY-D: Supervised the research, supported this study's implementation, provided feedback during the write-up, and final approval of the version to be submitted. All the authors read and gave final approval of the version to be submitted.

REFERENCES

Aguirre A.A., Longcore T., Barbieri M., Dabritz H., Hill D., Klein P.N., Lepczyk C., Lilly E.L., McLeod R., Milcarsky J., Murphy C.E., Su C., VanWormer E., Yolken R., Sizemore G.C. 2019: The One Health approach to toxoplasmosis: epidemiology, control, and prevention strategies. Ecohealth 16: 378–390.

Ahmadpour E., Daryani A., Sharif M., Sarvi S., Aarabi M., Mizani A., Rahimi M.T., Shokri A. 2014: Toxoplasmosis in immunocompromised patients in Iran: a systematic review and meta-analysis. J. Infect. Dev. Ctries. 8: 1503–1510.

Almeria S., Cano-Terriza D., Prieto P., Dubey J.P., Jimenez-Martin D., Castro-Scholten S., Paniagua J., Garcia-Bocanegra I. 2021: Seroprevalence and risk factors of *Toxoplasma gondii* infection in wild ungulates that cohabit in a natural park with human-animal interaction in the Mediterranean ecosystem. Zoonoses Public Health 68: 263–270.

Asgari Q., Motazedian M.H., Khazanchin A., Mehrabani D., Naderi Shahabadi S. 2021: High prevalence of *Toxoplasma gondii* infection in type I Diabetic patients. J. Parasitol. Res. 2021: 8881908.

Attias M., Teixeira D.E., Benchimol M., Vommaro R.C., Crepaldi P.H., De Souza W. 2020: The life-cycle of *Toxoplasma gondii* reviewed using animations. Parasit. Vectors 13: 588.

Ben-Harari R.R., Connolly M.P. 2019: High burden and low awareness of toxoplasmosis in the United States. Postgrad. Med. J. 131: 103–108.

Daher D., Shaghlil A., Sobh E., Hamie M., Hassan M.E., Moumneh M.B., Itani S., El Hajj R., Tawk L., El Sabban M., El Hajj H. 2021: Comprehensive overview of *Toxoplasma gondii*-induced and associated diseases. Pathogens 10:1351.

Daryani A., Sarvi S., Aarabi M., Mizani A., Ahmadpour E., Shokri A., Rahimi M.T., Sharif M. 2014: Seroprevalence of *Toxoplasma gondii* in the Iranian general population: a systematic review and meta-analysis. Acta Trop. 137: 185–194.

Dubey J.P., Jones J.L. 2008: *Toxoplasma gondii* infection in humans and animals in the United States. Int. J. Parasitol. 38: 1257–1278.

Foroutan M., Dalvand S., Daryani A., Ahmadpour E., Majidiani H., Khademvatan S., Abbasi E. 2019: Rolling up the pieces of a puzzle: a systematic review and meta-analysis of the prevalence of toxoplasmosis in Iran. Alexandria J. Med. 54: 189–196.

Hill D.E., Dubey J.P. 2018: *Toxoplasma gondii*. In: Y.R. Ortega and C.R. Sterling (Eds.), Foodborne Parasites. Springer, Cham, pp. 119–138.

Hlaváčová J., Flegr J., Fiurašková K., Kaňková S. 2021: Relationship between latent toxoplasmosis and depression in clients of a center for assisted reproduction. Pathogens 10: 1052.

Hosseini S.A., Sharif M., Sarvi S., Janbabai G., Keihanian S., Abediankenari S., Gholami S., Amouei A., Javidnia J., Saberi R., Shekarriz R., Daryani A. 2021: Toxoplasmosis among cancer patients undergoing chemotherapy: a population study based on the serological, molecular and epidemiological aspects. Trans. R. Soc. Trop. Med. Hyg. 115: 677–686.

Inceboz M., Inceboz T. 2021: Toxoplasmosis and neuropsychological effects. Turkiye Parazitol. Derg. 45: 49–55.

Kalogeropoulos D., Sakkas H., Mohammed B., Vartholomatos G., Malamos K., Sreekantam S., Kanavaros P., Kalogeropoulos C. 2021: Ocular toxoplasmosis: a review of the current diagnostic and therapeutic approaches. Int. Ophthalmol. 42: 295–321.

Khademi S.Z., Ghaffarifar F., Dalimi A., Davoodian P., Abdoli A. 2019: Prevalence and risk factors of *Toxoplasma gondii* infection among pregnant women in Hormozgan province, south of Iran. Iran. J. Parasitol. 14: 167–173.

Khosravi S, Eslamirad Z., Rafiei F. 2016: The overview on studies related to the prevalence of neonatal toxoplasmosis in Iran. Iran. J. Clin. Infect. Dis. 3: 91–96.

Mendoza-Larios L.A., Garcia-Dolores F., Sanchez-Anguiano L.F., Hernandez-Tinoco J., Alvarado-Esquivel C. 2021: Association between suicide and *Toxoplasma gondii* seropositivity. Pathogens 10: 1094.

Molan A N.K., Hunter M, Wang W. 2019: Global status of *Toxoplasma gondii* infection: systematic review and prevalence snapshots. Trop. Biomed. 36: 898–925.

Montoya J.G., Liesenfeld O. 2004: Toxoplasmosis. Lancet 363: 1965–1976.

Moshfe A., Arefkhah N., Sarkari B., Kazemi S., Mardani A. 2018: *Toxoplasma gondii* in blood donors: a study in Boyer-Ahmad county, southwest Iran. Interdiscip. Perspect. Infect. Dis. 2018: 3813612.

Mousavi-Hasanzadeh M., Sarmadian H., Ghasemikhah R., Didehdar M., Shahdoust M., Maleki M., Taheri M. 2020: Evaluation of *Toxoplasma gondii* infection in western Iran: seroepidemiology and risk factors analysis. Trop. Med. Health 48: 35.

Nahvi M., Shojaee S., Keshavarz H., Salimi M., Mohebali M. 2019: Detection of *Toxoplasma gondii* in cord blood samples from neonates in Tehran, Iran. Iran. J. Public Health 48: 912–916.

Nayeri T., Sarvi S., Moosazadeh M., Amouei A., Hosseininejad Z., Daryani A. 2020: The global seroprevalence of anti-*Toxoplasma gondii* antibodies in women who had spontaneous abortion: a systematic review and meta-analysis. PLOS Negl. Trop. Dis. 14: e0008103.

Nayeri T., Sarvi S., Sharif M., Daryani A. 2021: *Toxoplasma gondii*: a possible etiologic agent for Alzheimer's disease. Heliyon 7: e07151.

Rasti S., Hassanzadeh M., Soliemani A., Hooshyar H., Mousavi S.G., Nikoueinejad H., Abdoli A. 2016: Serological and molecular survey of toxoplasmosis in renal transplant recipients and hemodialysis patients in Kashan and Qom regions, central Iran. Ren. Fail. 38: 970–973.

Robert-Gangneux F., Darde M.L. 2012: Epidemiology of and diagnostic strategies for toxoplasmosis. Clin. Microbiol. Rev. 25: 264–296.

Roberts T., Murrell K.D., Marks S. 1994: Economic losses caused by foodborne parasitic diseases. Parasitol. Today 10: 419–423.

Saki J., Eskandari E., Feghhi M. 2020: Study of toxoplasmosis and toxocariasis in patients suffering from ophthalmic disorders using serological and molecular methods. Int. Ophthalmol. 40: 2151–2157.

Sobati H. 2020: Chemiluminescent microparticle immunoassay-based detection and prevalence of *Toxoplasma gondii* infection in childbearing women (Iran). J. Parasit. Dis. 44: 273–280.

Thebault A., Kooh P., Cadavez V., Gonzales-Barron U., Villena I. 2021: Risk factors for sporadic toxoplasmosis: a systematic review and meta-analysis. Microb. Risk Anal. 17: 100116.

Torgerson P.R., Mastroiacovo P. 2013: The global burden of congenital toxoplasmosis: a systematic review. Bull. World Health Organ. 91: 501–508.

Weiss L.M., Dubey J.P. 2009: Toxoplasmosis: a history of clinical observations. Int. J. Parasitol. 39: 895–901.

Received 12 December 2022 Accepted 20 September 2022 Published online 1 February 2023

Cite this article as: Kalantari R., Esmaeilifallah M., Jafari R., Esfahani H.M. and Darani H.Y. 2023: A large-scale study on the seroprevalence of *Toxoplasma gondii* infection in humans in Iran. Folia Parasitol. 70: 004.