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The global seroprevalence of *Toxoplasma gondii* infection in bovines: a systematic review and meta-analysis

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Abstract

Bovines, especially cattle, are considered as one of the main sources of *Toxoplasma gondii* infection for humans. A more comprehensive understanding of the occurrence of *T. gondii* is needed to provide a global perspective on the prevalence of *T. gondii* in bovines. Here, we present the results of the first systematic review and meta-analysis on the global *T. gondii* seroprevalence in bovines. Six databases (PubMed, ScienceDirect, Web of Science, Scopus, ProQuest and Google Scholar) were comprehensively searched for relevant studies published between 1 January 1967 and 30 May 2019. Among 7691 publications searched, 178 studies (from 50 countries) with 193 datasets were included in the meta-analysis. The global pooled and weighted seroprevalence of *T. gondii* among bovines was 17.91% [95% confidence interval (CI): 15.32–20.6]. Weighted prevalence based on the host was as follows: cattle 16.94% (95% CI: 14.25–19.81), buffalo 22.26% (95% CI: 16.8–29), yak 23% (95% CI: 14–33) and bison 8.1% (95% CI: 3.9–13.7). Continued monitoring on the status of *T. gondii* seroprevalence in bovines is essential. Study on the prevalence of *T. gondii* in the products of bovines such as milk, meat, etc., which are considered as the source of transmission of infection to humans, is recommended.

Introduction

Toxoplasma gondii is the only obligatory intracellular protozoan infecting almost all warm-blooded animals. Approximately one-third of the world's population is estimated to be infected with this parasite (Guo *et al.*, 2015). *Toxoplasma gondii* infection in the general population can remain asymptomatic, but could be fatal in the immunocompromised patients. Pregnant women are a very important group, because this parasite may lead to miscarriage or neurological disorders in the fetus (Dong *et al.*, 2018*b*). The route of transmission of *T. gondii* to humans could be vertical or horizontal *via* the consumption of resistant oocysts from the environment or uncooked meat of infected animals (Belluco *et al.*, 2018). Approximately, 60% of toxoplasmosis occurs horizontally, which varies from country to country. Intermediate hosts, such as livestock animals play an important role as reservoirs of infection for humans. Studies in six major European cities, estimated that, 30–63% of the infections in pregnant women are meat-borne (Cook *et al.*, 2000). Direct microscopic observations, polymerase chain reaction (PCR), bioassay and antibody detection by serological techniques are common methods of diagnosing *T. gondii*. But, in epidemiological studies, serological methods are preferred for the diagnosis of *T. gondii* infection in animals. It is because other methods are not suitable for the analysis of a large sample size (Montoya, 2002; Ferra *et al.*, 2015).

However, bovines do not appear to be a suitable host for *T. gondii*, but cattle are considered as one of the sources of *T. gondii* infection for humans (Hoffmann *et al.*, 2017). In fact, the meat and milk contaminated with *T. gondii* are the risk factor for *T. gondii* infection (Dubey and Thulliez, 1993; Hill and Dubey, 2013; Kalita and Sarmah, 2015). Further research is needed to determine the prevalence of *T. gondii* infection in bovines worldwide and the associated factors to help control it in these animals. Since *T. gondii* is a common important pathogen in humans and livestock, a more comprehensive understanding of the occurrence of *T. gondii* in the animal is essential. Although numerous valuable studies have been performed on the seroprevalence of *T. gondii* worldwide, to our knowledge, no global meta-analyses have been performed based on the systematic review of the literature. Therefore, the present systematic review and meta-analysis has been accomplished to draw a global perspective on the

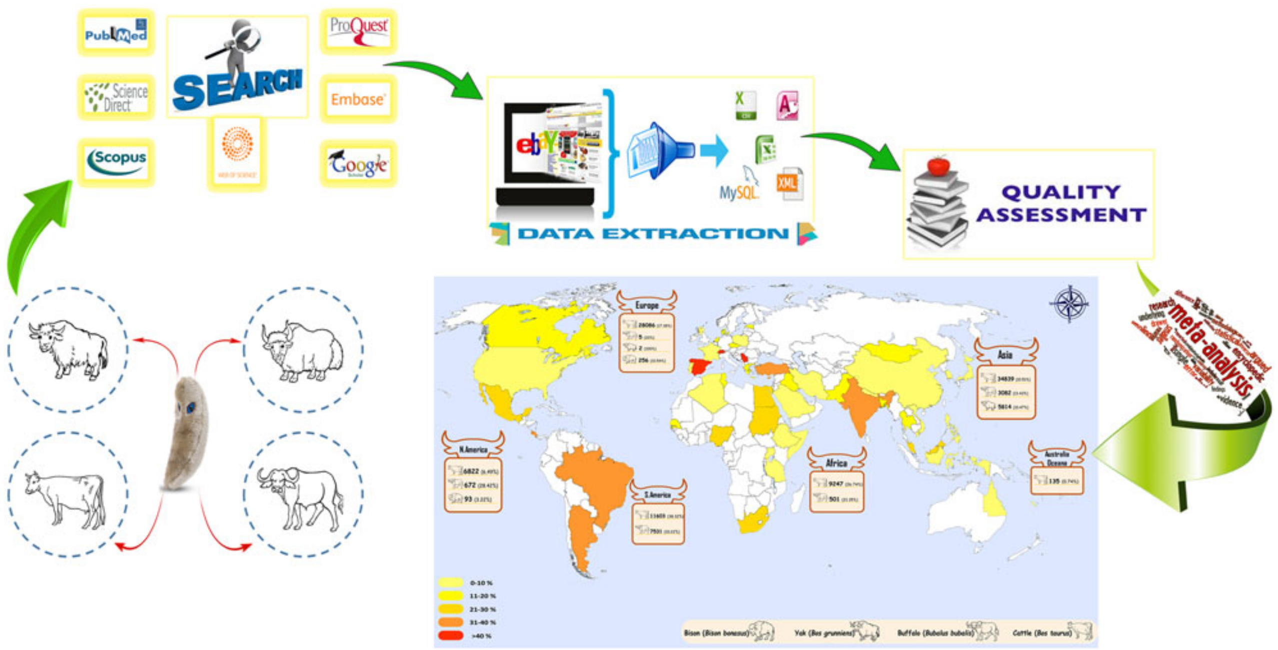

Fig. 1. Graphical summary of this study on global seroprevalence of bovine *Toxoplasma* infection.

seroprevalence of *T. gondii* in bovines to better understand the global seroprevalence and importance of the bovine *T. gondii* infection.

Methods

Design and protocol registration

The present systematic review and meta-analysis followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISMA) as described previously (Shamseer *et al.*, 2015). The details of the study protocol are available on the website of the International Prospective Register of Systematic Reviews with the identifier Central Registration Depository of CRD42019107442 (Daryani *et al.*, 2018).

Search strategy

Seroprevalence of *T. gondii* in bovines including cattle (*Bos taurus*), buffalo (*Bubalus bubalis*), yak (*Bos grunniens*) and bison (*Bison bonasus*) were of interest in this global review. To begin, we searched scientific databases for all the articles on the prevalence of bovine *T. gondii* infection published up to 30 May 2019. These keywords used alone or in combination were as follows: '*Toxoplasma gondii*', '*T. gondii*', 'toxoplasmosis', 'seroprevalence', 'prevalence', 'serological test', 'bovine', 'cattle', 'heifer', 'calf', 'buffalo', 'yak' and 'bison'. The searching process of articles was carried out using English language databases including 'Web of Science', 'Scopus', 'PubMed', 'Science Direct', 'ProQuest' and 'Google Scholar'. The systematic search of articles was conducted from 20 April to 30 May 2019 by two researchers independently (SAS and ASP).

Inclusion and exclusion criteria

Abstracts and full texts were assessed independently by the two researchers using a piloted form. The final decisions about the inclusion or exclusion of studies were made separately. Disagreements were resolved through arbitration by another author. Following the removal of duplicate entries, articles were evaluated according to the following criteria: (1) cross-sectional studies about the prevalence of *T. gondii* infection in bovines, (2) studies conducted only on cattle, buffalo, yak and bison and (3) studies where *T. gondii* infection in bovines was diagnosed by detecting immunoglobulin G (IgG) and/or IgM antibodies against *T. gondii*. The exclusion criteria comprised of: (1) case-control studies, review articles, dissertations, letters and animal models, (2) studies provided unclear data, (3) articles that were not available in the English language, (4) studies conducted on human and other animals and (5) conference abstracts.

Data extraction and the study quality assessment

All necessary information on the studies was recorded using Microsoft Excel software. The following data were collected for each study: the first author's name, publication year, country, continent, location, sample size, number of positives and negatives cases, bovine species, gender and age of each animal and type of serological method.

The Joanna Briggs Critical Evaluation Checklist was implemented to assess the quality of included records (Munn *et al.*, 2014). This checklist contains ten questions with four options designated as yes, no, unclear and not-applicable, regarding study quality. The papers with total scores of <5, 6 and 7–10 were considered to be of low, moderate and high quality, respectively. Our decisions to include or exclude the articles were influenced by the score of quality assessment and the articles with a quality score <5 were deleted.

Data synthesis and statistical analysis

In this study, the pooled rate seroprevalence of *T. gondii* with a 95% confidence interval (CI) was calculated using the random-effects model using StatsDirect software, version 2.8.0 (http://statsdirect.com). Heterogeneity among included studies was examined by Cochran's Q and I^2 statistics test. I^2 values of 50% or more were considered heterogeneous. A forest plot in the random effects model was used to calculate the pooled seroprevalence of *T. gondii* in bovines. To determine the source of heterogeneity, subgroup analyses were carried out. In a subgroup

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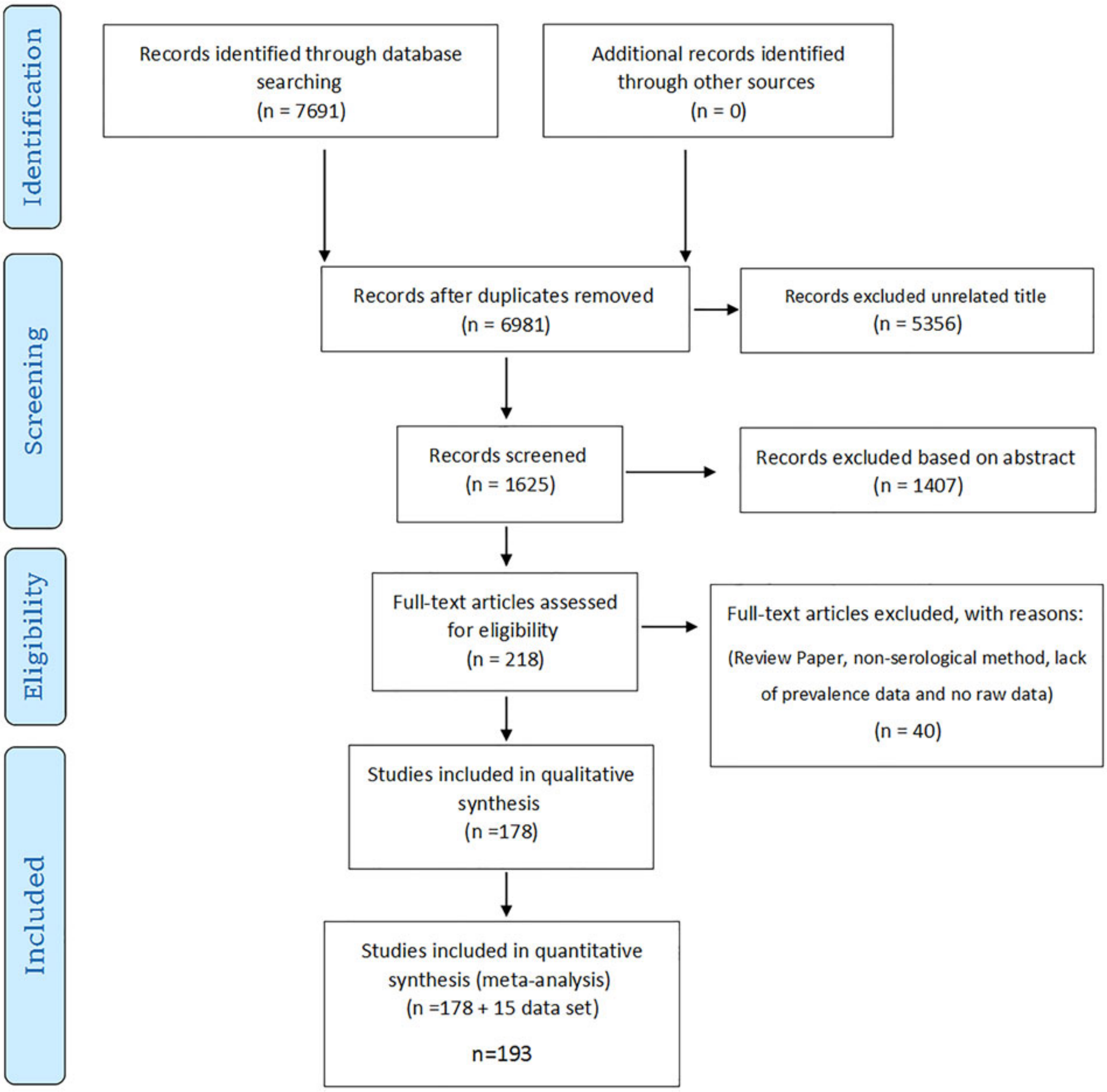

Fig. 2. Flow chart of the study selection process showing inclusion and exclusion of studies identified.

analysis, the seroprevalence of *T. gondii* was estimated based on year, gender, the continent of origin, type of animal, type of diagnostic method and sample size. Publication bias was evaluated graphically and statistically by applying Egger's and Begg's tests. In all statistical analyses, P value <0.05 was considered significant.

Results

A graphical summary of this study on global seroprevalence of bovine *Toxoplasma* infection is shown in Fig. 1. Our preliminary search of seven databases yielded 7691 articles but 710 were excluded from the study due to duplication. After a primary screening of the titles of the articles based on keywords, 5356 studies were extracted. In the next step, by screening the abstracts of the articles and based on the inclusion/exclusion criteria, 1407 of them were excluded. After reading the full text of the articles, 40 other papers were excluded. Finally, 178 (overall, 108 688 bovines, including 90 732 cattle, 11 791 buffaloes, 5816 yaks and 349 bison) of these articles (total data: 193) were entered into the meta-analysis with respect to the inclusion/exclusion criteria (Fig 2). The publication date of the studied articles was from 1967 to 2019.

Overall, there were 25 studies (28 349 bovines) in Europe, 84 studies (43 735 bovines) in Asia, 31 studies (9748 bovines) in Africa, 36 studies (26 721 bovines) in America and 2 studies (135 bovines) in Australia/Oceania. Among the included articles in this systematic review, enzyme-linked immunosorbent assay (ELISA) was the most common diagnostic method (53 studies), followed by modified agglutination test (MAT) in 24 studies, indirect immunofluorescence antibody test (IFAT) in 41 studies, direct agglutination test (DAT) in seven studies, latex agglutination test (LAT) in 30 studies, Sabin–Feldman dye test (SFDT) in 8 studies, indirect haemagglutination (IHA) in 25 studies, 2-mercaptoethanol (2ME) in one study, complement fixation test (CFT) in one study, Lateral flow chromatographic immunoassay (LFCIA) in one study, Indirect agglutination test (IAT) in one study and Micro precipitation in agar gel (MPA) in one study.

The main characteristics of the included studies are given in Table 1. In the studies, seroprevalence of *T. gondii* among bovines varied (from 0 to 100%) and a heterogeneity in the papers was observed (Cochran $Q = 28\,162.82$; $I^2 = 99.3\%$; $df = 192$;

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Table 1. Baseline characteristics of the included studies in this systematic review and meta-analysis based on years

No.	Author (Ref)	Hosts	Country	Diagnostic methods	Total individuals (*n*)	Seroprevalence *n* (%)	Quality score
1	Work (1967)	Cattle	Denmark	SFDT	211	24 (11.4)	6
2	Maronpot and Botros (1972)	Cattle-buffalo	Egypt	IFAT	418	111 (6.5)	5
3	Chhabra and Mahajan (1978)	Cattle	India	IHA	219	52 (23.7)	5
4	Costa *et al.* (1978)	Cattle	Brazil	IFAT	204	66 (32.3)	5
5	Riemann *et al.* (1978)	Cattle	United States	IHA	33	67 (18.1)	5
6	Tizard *et al.* (1978)	Cattle	Canada	SFDT	1759	309 (7.5)	7
7	Aganga *et al.* (1981)	Cattle	Nigeria	IHA	200	6 (3)	5
8				IFAT	200	6 (3)	
9	Makinde and Ezeh (1981)	Cattle	Nigeria	IHA	638	416 (5.2)	6
10	McColm *et al.* (1981)	Cattle	Scotland	SFDT	250	7 (2.8)	6
11	van Knapen *et al.* (1982)	Cattle	Netherlands	ELISA	180	8 (6.6)	5
12	Chhabra *et al.* (1985)	Cattle-buffalo	India	IHA	351	64 (18.2)	6
13	Dubey (1985)	Cattle-bison	United States	MAT	2632	84 (3.1)	8
14	Zain Eldin *et al.* (1985)	Cattle	Sudan	IHA	175	70 (40)	5
15	Bekele and Kasali (1989)	Cattle	Ethiopia	IHA	785	55 (7)	7
16	Norton *et al.* (1989)	Cattle	Queensland	IHA	105	0 (0)	5
17	Rajamanickam *et al.* (1990)	Cattle	Malaysia	IHA	132	0 (0)	5
18	Moreno *et al.* (1991)	Cattle	Spain	IFAT	304	122 (0.1)	5
19				2ME	304	125 (1.1)	
20	Hejlicek and Literak (1992)	Cattle	Czech	SFDT	218	49 (22.4)	5
21				CFT	176	6 (3.4)	
22				MPA	209	1 (0.5)	
23	Garcia-Vazquez *et al.* (1993)	Cattle	Mexico	ELISA	397	47 (11.8)	7
24	Hoghooghirad and Afraa (1993)	Cattle	Iran	LAT	142	21 (14.8)	5
25	Samad *et al.* (1993)	Cattle	Bangladesh	LAT	205	33 (16.1)	7
26	Arias *et al.* (1994)	Cattle	Costa Rica	IFAT	601	206 (4.4)	7
27	van Knapen *et al.* (1995)	Cattle	Netherland	ELISA	13256	1947 (0.7)	7
28	Zaki (1995)	Cattle	Pakistan	LAT	100	25 (25)	5
29	Adesiyun and Cazabon (1996)	Cattle	Trinidad	DAT	55	15 (27.3)	5
30	HashemiFesharki (1996)	Cattle	Iran	LAT	2000	0 (0)	6
31				IHA	2000	0 (0)	
32	Matsuo and Husin (1996)	Cattle	Indonesia	LAT	200	18 (9)	6
33	Dubey *et al.* (1998)	Buffalo	Egypt	MAT	75	0 (0)	6
34	Huong *et al.* (1998)	Cattle-buffalo	Vietnam	DAT	400	27 (6.7)	6
35	Navidpour and Hoghooghi-Rad (1998)	Buffalo	Iran	IFAT	385	34 (8.8)	5
36	Gondim *et al.* (1999)	Cattle-Buffalo	Brazil	LAT	298	6 (2)	7
37	Mirdha *et al.* (1999)	Cattle	India	IHA	50	26 (52)	5
38	El-Metenawy (2000)	Cattle	Saudi Arabia	IHA	60	1 (1.7)	5
39	de Souza *et al.* (2001)	Buffalo	Brazil	IFAT	411	205 (9.9)	6
40	Sroka (2001)	Cattle	Poland	DAT	262	141 (3.8)	7
41	Nalbantoğlu *et al.* (2002)	Cattle	Cyprus	SFDT	98	34 (34.7)	5
42				IFAT	98	30 (30.6)	
43	Joshua and Akinwumi (2003)	Cattle	Nigeria	LAT	586	99 (16.9)	5

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Table 1. (*Continued.*)

No.	Author (Ref)	Hosts	Country	Diagnostic methods	Total individuals (*n*)	Seroprevalence *n* (%)	Quality score
44	Tutuncu *et al.* (2003)	Cattle	Turkey	IHA	104	8 (7.6)	5
45	Diakou *et al.* (2005)	Cattle	Greece	ELISA	105	21 (20)	6
46	Dubey *et al.* (2005)	Cattle	United States	ELISA	2094	0 (0)	10
47	Ogawa *et al.* (2005)	Cattle	Brazil	IFAT	385	102 (6)	8
48	Chaudhary *et al.* (2006)	Cattle	Pakistan	LAT	50	11 (22)	5
49	Ghazaei (2006)	Cattle	Iran	ELISA	200	18 (9)	6
50	Klun *et al.* (2006)	Cattle	Serbia	MAT	611	466 (6.3)	9
51	Sedlak and Bartova (2006)	Cattle	Czech	IFAT	46	17 (37)	8
52	Hamzavi *et al.* (2007)	Cattle	Iran	IFAT	125	6 (4.8)	5
53	Selvaraj *et al.* (2007)	Buffalo	India	MAT	99	99 (100)	5
54	Sharif *et al.* (2007)	Cattle	Iran	IFAT	290	0 (0)	6
55	Sroka *et al.* (2007)	Cattle	Poland	DAT	259	139 (3.7)	6
56	Yu *et al.* (2007)	Cattle	China	IAT	263	6 (2.3)	9
57	Acici *et al.* (2008)	Cattle	Turkey	SFDT	96	52 (54.1)	6
58	Chandrawathani *et al.* (2008)	Cattle	Malaysia	IFAT	126	8 (6.3)	5
59	Jittapalapong *et al.* (2008)	Cattle	Thailand	ELISA	186	23 (12.4)	6
60	Konnai *et al.* (2008)	Cattle	Philippines	ELISA	96	5 (5.2)	6
61	Liu *et al.* (2008)	Yak	China	LAT	946	112 (1.8)	8
62	More *et al.* (2008)	Cattle	Argentina	IFAT	90	82 (91)	7
63				MAT	90	13 (14.4)	
64	Nematollahi and Moghddam (2008)	Cattle	Iran	IFAT	490	78 (15.9)	7
65	Sharma *et al.* (2008)	Cattle-buffalo	India	ELISA	186	5 (2.6)	5
66	Ergin *et al.* (2009)	Cattle	Turkey	LAT	50	12 (24)	5
67	Gilot-Fromont *et al.* (2009)	Cattle	France	MAT	1329	103 (.8)	8
68	Ibrahim *et al.* (2009)	Cattle	Egypt	ELISA	93	10 (10.7)	5
69	Santos *et al.* (2009)	Cattle	Brazil	IFAT	2000	1420	6
70	Yildiz *et al.* (2009)	Cattle	Turkey	SFDT	557	138 (4.7)	6
71	Akca and Mor (2010)	Cattle	Turkey	ELISA	216	202 (3.5)	7
72	Asgari *et al.* (2010)	Cattle	Iran	IFAT	588	119 (0.2)	6
73	Hamidinejat *et al.* (2010b)	Cattle	Iran	MAT	450	71 (15.8)	7
74	Hamidinejat *et al.* (2010a)	Buffalo	Iran	MAT	300	43 (14.3)	7
75	Inpankaew *et al.* (2010)	Cattle	Thailand	LAT	700	66 (9.4)	7
76				ELISA	700	119 (7)	
77	Panadero *et al.* (2010)	Cattle	Spain	DAT	178	13 (7.3)	7
78	Schoonman *et al.* (2010)	Cattle	Tanzania	LAT	654	22 (3.36)	7
79	Shaapan *et al.* (2010)	Buffalo	Egypt	MAT	160	36 (22.5)	5
80	Silva *et al.* (2010)	Buffalo	Brazil	IFAT	374	4 (1.1)	6
81	Sroka *et al.* (2010)	Cattle	Poland	DAT	74	25 (33.8)	6
82	Albuquerque *et al.* (2011)	Cattle	Brazil	IFAT	589	87 (14.8)	6
83	Al-Mohammed (2011)	Cattle	Saudi Arabia	ELISA	130	6 (4.6)	5
84	Persad *et al.* (2011)	Buffalo	Trinidad	LAT	333	26 (7.8)	9
85	Berger-Schoch *et al.* (2011)	Cattle	Switzerland	ELISA	406	185 (5.6)	7
86	Chikweto *et al.* (2011)	Cattle	India	MAT	119	10 (8.4)	5
87	Costa *et al.* (2011)	Cattle	Brazil	IFAT	50	9 (18)	7

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Table 1. (*Continued.*)

No.	Author (Ref)	Hosts	Country	Diagnostic methods	Total individuals (*n*)	Seroprevalence *n* (%)	Quality score
88	Song *et al.* (2011)	Cattle	South Korea	LAT	105	4 (3.8)	5
89	Frazao-Teixeira and de Oliveira (2011)	Cattle	Brazil	ELISA	77	38 (49.3)	6
90	Khalil and Elrayah (2011)	Cattle	Sudan	LAT	50	16 (32)	5
91	Lee *et al.* (2011)	Cattle	China	ELISA	368	25 (6.8)	5
92	Liu *et al.* (2011)	Yak	China	IHA	650	228 (5.1)	6
93	Luciano *et al.* (2011)	Cattle	Brazil	IFAT	459	9 (1.9)	6
94	Raeghi *et al.* (2011)	Cattle	Iran	MAT	120	2 (1.6)	5
95	Rahman *et al.* (2011)	Cattle	Malaysia	IFAT	116	3 (2.6)	5
96	Roqueplo *et al.* (2011)	Cattle	New Caledonia	ELISA	30	1 (3.3)	5
97	Shahiduzzaman *et al.* (2011)	Cattle	Bangladesh	LAT	25	3 (12)	5
98	Sroka *et al.* (2011)	Cattle	Poland	MAT	865	111 (2.8)	6
99				ELISA	865	126 (4.6)	
100	Bao *et al.* (2012)	Cattle	China	IHA	350	24 (6.8)	6
101	Costa *et al.* (2012)	Cattle	Brazil	IFAT	100	3 (3)	5
102	de Macedo *et al.* (2012b)	Cattle	Brazil	IFAT	60	29 (48.3)	7
103	de Macedo *et al.* (2012a)	Cattle	Brazil	IFAT	120	35 (29.1)	5
104	Garcia *et al.* (2012)	Cattle	Brazil	IFAT	169	44 (26)	6
105	Qiu *et al.* (2012)	Cattle	China	IHA	1803	46 (2.6)	9
106	Shabbir *et al.* (2012)	Cattle-buffalo	Pakistan	LAT	90	0 (0)	5
107	Swai and Schoonman (2012)	Cattle	Tanzania	LAT	51	6 (12)	6
108	Wang *et al.* (2012)	Yak	China	IHA	1603	133 (.3)	9
109	Wiengcharoen *et al.* (2012)	Cattle	Thailand	IFAT	389	100 (5.7)	7
110	Liu *et al.* (2012)	Cattle	China	IHA	646	39 (6)	7
111	Xu *et al.* (2012)	Cattle	China	IHA	875	120 (3.7)	7
112	Yang *et al.* (2012)	Cattle	China	ELISA	572	19 (3.3)	6
113	Zhou *et al.* (2012)	Cattle	China	IHA	350	20 (5.7)	8
114	Asgari *et al.* (2013)	Cattle	Iran	MAT	80	44 (55)	5
115	de Santos *et al.* (2013)	Cattle-buffalo	Brazil	IFAT	290	67 (23.1)	6
116	Dehkordi *et al.* (2013)	Cattle-buffalo	Iran	ELISA	364	11 (3)	9
117	Elfahal *et al.* (2013)	Cattle	Sudan	ELISA	181	24 (13.3)	6
118	Fajardo *et al.* (2013)	Cattle	Brazil	IFAT	1195	32 (2.7)	10
119	Garcia-Bocanegra *et al.* (2013)	Cattle	Spain	ELISA	504	420 (3.3)	5
120	Holec-Gasior *et al.* (2013)	Cattle	Poland	ELISA	4033	127 (.1)	9
121	Konrad *et al.* (2013)	Buffalo	Argentina	IFAT	500	127 (5.4)	7
122	Lopes *et al.* (2013)	Cattle	Portugal	MAT	161	12 (7.5)	7
123	Nagwa *et al.* (2013)	Cattle	Egypt	ELISA	94	44 (46.8)	6
124	Ndou *et al.* (2013)	Cattle	South Africa	ELISA	178	37 (20.8)	5
125	Singh *et al.* (2013)	Cattle	India	ELISA	45	13 (28.9)	5
126	Tasawar *et al.* (2013)	Cattle	Pakistan	LAT	200	87 (43.5)	6
127	Ahmad and Qayyum (2014)	Cattle-buffalo	Pakistan	ELISA	822	143 (7.4)	7
128	Alvarado-Esquivel *et al.* (2014)	Buffalo	Mexico	MAT	339	165 (8.7)	7
129	Anees *et al.* (2014)	Buffalo	Pakistan	LAT	50	7 (14)	5
130	Beyhan *et al.* (2014)	Buffalo	Turkey	SFDT	131	115 (9.7)	6
131	Da Silva *et al.* (2014)	Buffalo	Brazil	ELISA	4796	1982 (.3)	9

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Table 1. (*Continued.*)

No.	Author (Ref)	Hosts	Country	Diagnostic methods	Total individuals (*n*)	Seroprevalence *n* (%)	Quality score
132				IFAT	4796	1715 (0.8)	
133	Davoust *et al.* (2014)	Cattle	Senegal	MAT	103	13 (13)	6
134	Elfahal *et al.* (2014)	Cattle	Sudan	LAT	181	39 (21.5)	6
135				ELISA	181	24 (13.3)	
136	Ge *et al.* (2014)	Cattle	China	ELISA	1040	133 (2.8)	7
137	Gharekhani (2014b)	Cattle	Iran	ELISA	1406	32 (2.3)	6
138	Gharekhani (2014a)	Cattle	Iran	ELISA	85	5 (5.9)	5
139	Ibrahim *et al.* (2014a)	Cattle	Sudan	LAT	1216	497 (0.9)	7
140	Ibrahim *et al.* (2014b)	Cattle	Sudan	ELISA	744	371 (9.9)	7
141	Kadle (2014)	Cattle	Somalia	LAT	28	2 (7.1)	6
142	Li *et al.* (2014)	Yak	China	IHA	1641	410 (5)	8
143	Matsuo *et al.* (2014)	Cattle	Japan	LAT	422	31 (7.3)	6
144	Rahman *et al.* (2014)	Cattle	Bangladesh	LAT	37	10 (27)	5
145	Yagci Yucel *et al.* (2014)	Cattle	Turkey	MAT	132	74 (56.1)	6
146	Bartova *et al.* (2015)	Cattle	Czech Republic	ELISA	546	53 (9.7)	6
147	Brasil *et al.* (2015)	Buffalo	Brazil	IFAT	136	17 (12.5)	8
148	Dechicha *et al.* (2015)	Cattle	Algeria	IFAT	332	13 (3.9)	6
149	Furtado *et al.* (2015)	Cattle	Brazil	IFAT	1245	10 (0.8)	9
150	Ibrahim *et al.* (2015)	Cattle	Sudan	LAT	1216	497 (0.9)	8
151	Ichikawa-Seki *et al.* (2015)	Cattle	Indonesia	ELISA	598	44 (7.4)	8
152	Kalita and Sarmah (2015)	Cattle	India	MAT	60	16 (26.6)	5
153	Lahmar *et al.* (2015)	Cattle	Tunisia	MAT	25	3 (12)	5
154	Onyiche and Ademola (2015)	Cattle	Nigeria	ELISA	210	29 (13.8)	6
155	Qin *et al.* (2015)	Yak	China	MAT	974	155 (5.9)	7
156	Singh *et al.* (2015)	Cattle	India	ELISA	45	29 (64.4)	5
157	Sudan *et al.* (2015)	Cattle	India	ELISA	252	181 (1.8)	6
158	Sun *et al.* (2015)	Cattle	China	IHA	4487	470 (0.5)	9
159	Tan *et al.* (2015)	Cattle	China	MAT	1657	80 (4.8)	7
160	Zou *et al.* (2015)	Buffalo	China	IHA	427	32 (7.5)	7
161	de Souza *et al.* (2016)	Cattle	Brazil	IFAT	1000	53 (5.3)	7
162	Fereig *et al.* (2016)	Cattle	Egypt	LAT	301	88 (29.2)	7
163				ELISA	301	85 (28.2)	
164	Kuraa and Malek (2016)	Cattle-buffalo	Egypt	ELISA	111	82 (73.9)	7
165				LAT	111	39 (35.1)	
166	Magalhães *et al.* (2016)	Cattle	Brazil	IFAT	140	15 (10.7)	7
167	Oh *et al.* (2016)	Cattle	South Korea	ELISA	568	3 (0.5)	6
168	FK and Shah (2016)	Cattle	Pakistan	LAT	250	35 (14)	6
169	Portella *et al.* (2016)	Buffalo	Brazil	IFAT	220	37 (16.8)	6
170	Zhou *et al.* (2016)	Cattle	Turkey	ELISA	377	15 (4)	7
171	Ayinmode *et al.* (2017)	Cattle	Nigeria	ELISA	174	13 (7.5)	7
172	Bartova *et al.* (2017)	Yak-buffalo-bison	Czech Republic	IFAT	23	5 (21.7)	7
173				ELISA	23	3 (13)	
174	da Silva *et al.* (2017)	Cattle-buffalo	Brazil	IFAT	1000	464 (6.4)	7
175	Do Carmo EL do Carmo et al. (2017)	Cattle	Brazil	IFAT	500	203 (0.6)	7

(*Continued*)

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Table 1. (*Continued.*)

No.	Author (Ref)	Hosts	Country	Diagnostic methods	Total individuals (*n*)	Seroprevalence *n* (%)	Quality score
176	Jokelainen *et al.* (2017)	Cattle	Estonia	DAT	3991	743 (8.6)	8
177	Luo *et al.* (2017)	Cattle-buffalo	China	IHA	595	98 (16.4)	8
178	Almeria *et al.* (2018)	Cattle	Spain	MAT	199	37 (18.6)	7
179	De Oliveira *et al.* (2018)	Cattle-buffalo	Brazil	ELISA	2070	741 (5.8)	9
180				IFAT	2070	934 (5.1)	
181	Dong *et al.* (2018a)	Cattle	China	MAT	5292	102 (0.93)	9
182	Kakooza *et al.* (2018)	Cattle	Uganda	ELISA	52	2 (3.8)	6
183	Khames *et al.* (2018)	Cattle	Algeria	MAT	295	13 (4.4)	7
184	Krzysiak *et al.* (2018)	Bison	Poland	ELISA	240	25 (10.4)	8
185	Majeed and Abbas (2018)	Cattle-buffalo	Iraq	ELISA	200	39 (19.5)	8
186	Pagmadulam *et al.* (2018)	Cattle	Mongolia	ELISA	1438	269 (8.7)	10
187	Sah *et al.* (2018a)	Cattle	Nepal	LFCIA	92	8 (8.7)	6
188	Sah *et al.* (2018b)	Cattle	Bangladesh	ELISA	252	21 (8.3)	9
189	Shadia Ahmed (2018)	Cattle	Sudan	LAT	96	6 (6.2)	6
190	Tilahun *et al.* (2018)	Cattle	Ethiopia	ELISA	326	35 (10.7)	10
191	Udonsom *et al.* (2018)	Cattle	Thailand	ELISA	250	52 (20.8)	8
192	Deng *et al.* (2020)	Cattle	China	IHA	535	33 (6.2)	9
193	Sudan *et al.* (2019)	Cattle	India	ELISA	258	115 (61.5)	8

ELISA, enzyme-linked immunosorbent assay; MAT, modified agglutination test; IFAT, indirect immunofluorescence antibody test; DAT, direct agglutination test; LAT, latex agglutination test; SFDT, Sabin–Feldman dye test; CFT, complement fixation test; LFCIA, lateral flow chromatographic immunoassay; IAT, indirect agglutination test; MPA, micro precipitation in agar gel; IHA, indirect haemagglutination.

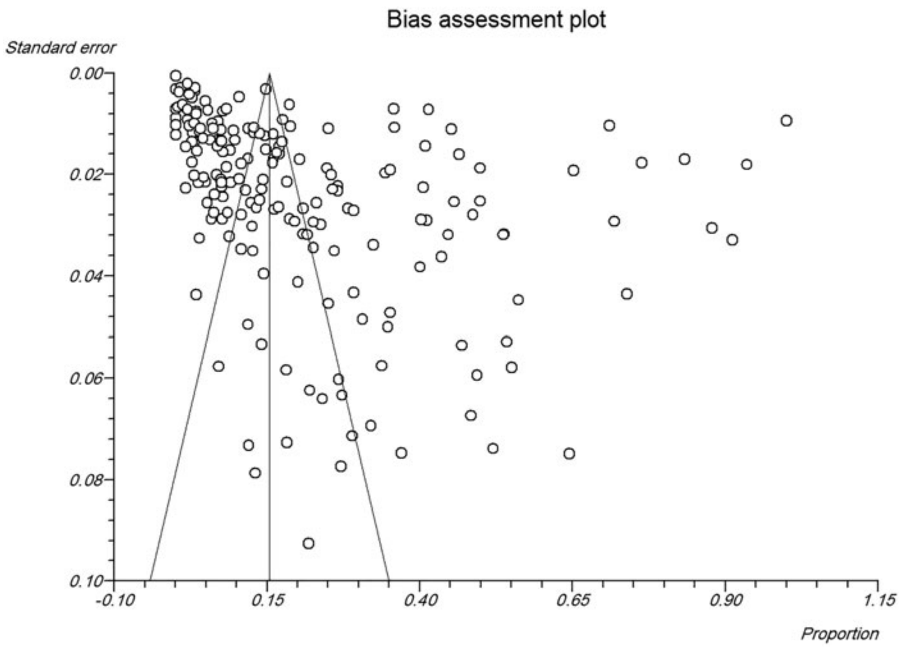

Fig. 3. Bias assessment plot from the Egger's test based on standard error.

$P < 0.001$). Moreover, the results of the Begg–Mazumdar and Egger's regression test conducted to determine publication bias indicated no considerable effect on the total prevalence estimate (Begg–Mazumdar: 7.34×10^{-3}, Egger's bias = 10.56, $P = 0.88$ and $P < 0.001$) (Fig 3).

The global pooled and weighted seroprevalence of *T. gondii* among bovines was 17.91% (95% CI: 15.32–20.6). The forest plot diagram of the present systematic review is illustrated in Fig 4. Moreover, the weighted prevalence of this parasite in bovines based on the host was as follows: cattle 16.94% (95% CI: 14.25–19.81), buffalo 22.26% (95% CI: 16.8–29), yak 23% (95% CI: 14–33) and bison 8.1% (95% CI: 3.9–13.7). Significant geographic differences in pooled *T. gondii* seropositivity rates among bovine were estimated. The seroprevalence was higher in America and Europe, where the *T. gondii* seropositivity rate was 22.2% (95% CI: 15.2–30.1) and 21.93% (95% CI: 15.98–28.53),

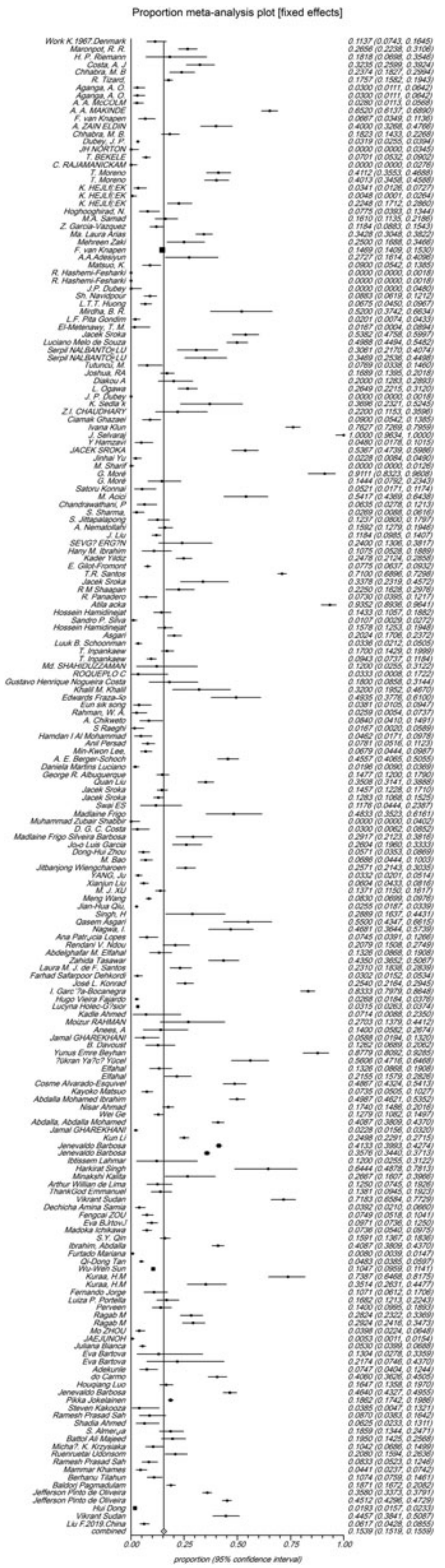

Fig. 4. Forest plot displaying the global seroprevalence of *Toxoplasma gondii* in bovines.

respectively. The lowest seroprevalence was estimated in Australia/Oceania with the rate of 1.36% (95% CI: 0.02–7.65). A geographical map summarizing the seroprevalence of *T. gondii* among bovine in the world is shown in Fig 5.

The pooled seroprevalences of *T. gondii* in male and female bovine were 18.9% (95% CI: 13.8–24.7) and 17.78% (95% CI: 13.2–22.86), respectively. In a subgroup analysis based on diagnostic methods, the highest *T. gondii* seroprevalence detected by SFDT was 30% (95% CI: 17–45), followed by DAT 27% (95% CI: 13–43), IFAT 20.3% (95% CI: 13.9–27.6), MAT 19.7% (12.3–28.5), ELISA 18.52% (95% CI: 13.74–23.84), LAT 14.7% (95% CI: 8.9–21.8) and IHA 12.81% (95% CI: 7.82–18.81). The seroprevalence was higher in 2001–2005 and 2005–2010, whereas the *T. gondii* seropositivity rates were approximately 23.5% (95% CI: 6.8–46.3) and 23.5% (95% CI: 14.4–34.1), respectively. The lowest seroprevalence was estimated in ⩽2000 with the rate of 12.36%% (95% CI: 8.19–17.24). In a subgroup analysis based on sample size, the highest *T. gondii* seroprevalence was detected in sample size of 601–900 with the prevalence of 23% (95% CI: 13–35) followed by ⩽300 with the prevalence of 19.23% (95% CI: 15.17–23.63), 301–600 with the prevalence of 16.4% (95% CI: 11.7–21.8) and ⩾901 with the prevalence of 13.6% (95% CI: 8.3–19.9).

Table 2 summarizes the results of subgroup analysis and its details. Based on subgroup analysis, a statistically significant difference was observed in the overall prevalence of *T. gondii* in bovine based on year ($\chi^2 = 1346.94$, $P < 0.001$), continent ($\chi^2 = 4145.1$, $P < 0.001$), bovine species ($\chi^2 = 2632.73$, $P < 0.001$), gender ($\chi^2 = 4.62$, $P = 0.032$), method ($\chi^2 = 2833.23$, $P < 0.001$) and sample size ($\chi^2 = 363$, $P < 0.001$).

Discussion

Toxoplasmosis is one of the most common parasitic diseases in warm-blooded animals and in livestock poses a risk to the general public health, as the consumption of raw or uncooked meat can facilitate *T. gondii* transmission to humans (Tilahun *et al.*, 2018). Therefore, it is difficult to implement the prevention and control programmes without sufficient information on the prevalence of *T. gondii* infection in animals, because they are the main source of zoonosis. Bovines are one of the most important sources of meat for humans in the world. However, the clinical symptoms of toxoplasmosis in bovines are much milder or more unknown than in the sheep, goats and pigs. However, it seems that accurate estimation on the prevalence of the infection in bovines for large-scale screening is essential in order to elucidate the role of bovines as carriers of *T. gondii* tissue cysts and to clarify the role of beef and milk in transmitting *T. gondii* to humans for health. The purpose of the analysis and interpretation presented in this review is to better understand the global prevalence of *T. gondii* among bovines. Overall, 108 688 bovines including 90 732 cattle, 11 791 buffaloes, 5816 yaks and 349 bisons were investigated by various serological methods. The data demonstrate that the weighted global seroprevalence in bovines was 17.91% and the prevalence range was between 0 and 100. There are numerous differences in the seroprevalence of bovine *T. gondii* infection in the world that could be categorized as follows: (i) biological aspects of parasites including geographical location, climate change, humidity and temperature, which can be effective in the parasitic life cycle and facilitate transmission, (ii) behavioural aspects including animal husbandry industry, the diet in different nations, especially the type of cooking, and public health management, which are considered as important variables in the prevalence of the infection in different communities and (iii) investigative aspects including study population, sample size, type of sampling and diagnostic method, which influences different findings in each study.

To investigate the causes of heterogeneity in the findings of studies included in this systematic review, the subgroup analysis was performed on various variables such as year, continent, and bovine species, gender, diagnostic methods and sample size. Our findings indicated a significant difference between the seroprevalence of *T. gondii* and the bovine species. The pooled seroprevalence of *T. gondii* in yak, buffalo, cattle and bison were 23,

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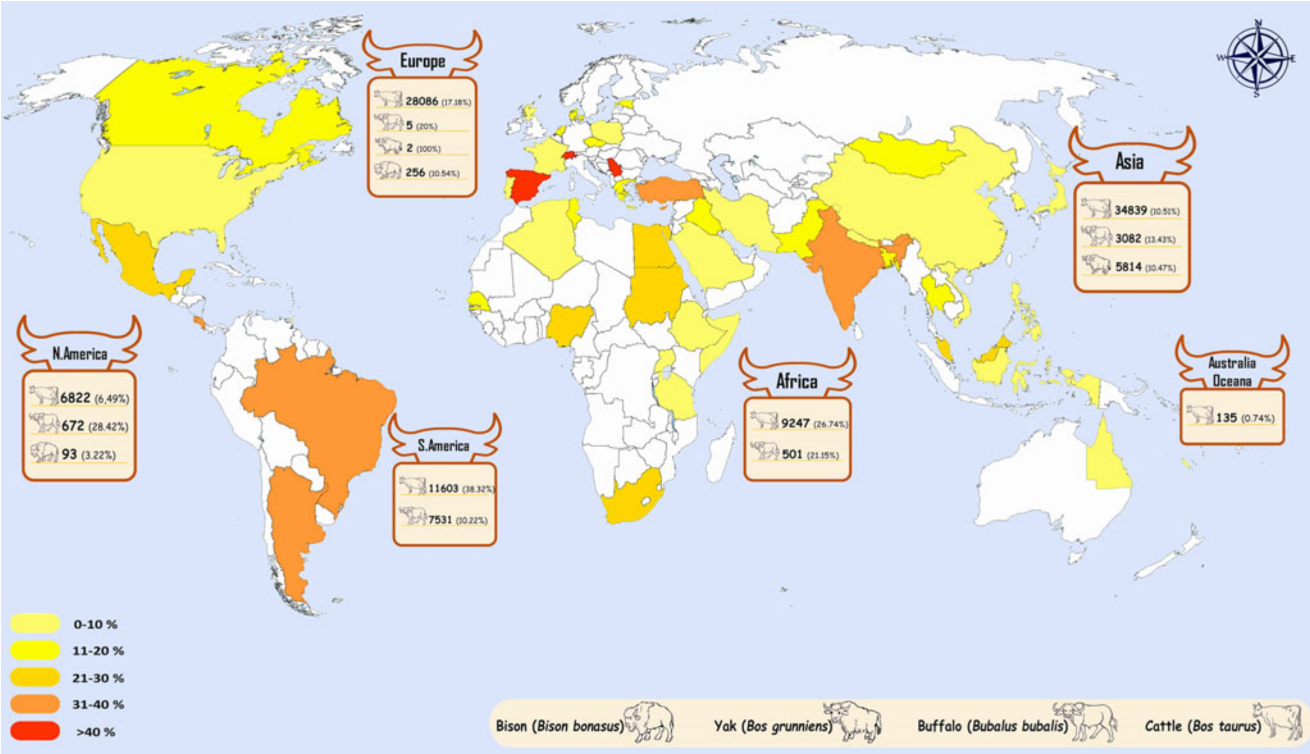

Fig. 5. Global distribution map of seroprevalence of *T. gondii* in bovines worldwide.

22.26, 16.9, and 8.1%, respectively. The most prevalent rate was noted in yaks because the animals are free-grazing bovines that live with other wild and domestic animals. Yak (*B. grunniens*) is a long-haired male bovine species that lives in Afghanistan, the Himalayas, the Tibetan Plateau and Mongolia (Liu *et al.,* 2008). Yaks graze in pastures that are exposed to more *T. gondii* oocysts followed by the consequences of increasing the risk of infection (Qin *et al.,* 2015). Also, the investigated population in various studies on yaks (6 data) is less than cattle (155 data) and buffalo (31 data). In the case of buffaloes, although they are similar to yaks in grazing, perhaps this less common difference than in the yaks is related to the more studied population of buffaloes (Alvarado-Esquivel *et al.,* 2014). The prevalence of toxoplasmosis among buffaloes and yaks were almost similar, which is related to their way of life and breeding. These types of livestock are not bred centrally at all and are fed on open grazing in pastures, but cattle are usually kept centrally and are raised industrially. Obviously, in this type of breeding, the animals have much less access to free water or oocyst-contaminated forage. Although in traditional breeding, livestock has high and easy access to pastures, forage and the oocyst-contaminated water. The low prevalence of *T. gondii* in bison (8.1%) could be attributed to the fact that they are less exposed to cats and in contact with less occurrence of parasite life cycle, as a result, less risk of contamination. Of course, the number of studies on bison is much less compared to other bovines. Perhaps, if the population of this animal had been examined in greater numbers, the prevalence could have been changed as well (Wang *et al.,* 2012; Alvarado-Esquivel *et al.,* 2014; Brasil *et al.,* 2015).

Among the studies, there was a slight difference in the rate of infection by sex; therefore, the rate of infection in males (18.9%) was higher than that in the females (17.78%). Although in most studies the seroprevalence is higher in females. It could be attributed to the low immune system in females for the reasons, such as pregnancy and lactation. In most studies, the population of industrial dairy cattle was investigated (Bao *et al.,* 2012; FK and Shah, 2016). When the study population is higher in the industrial farms where cattle are usually not in contact with pastures and are less exposed to the parasites present in pastures. Under this condition, the lower percentage of infection in the male is more reasonable. Differences in the prevalence of *T. gondii* infection in females compared to males may be attributed to differences in sex hormones. Some researchers believe that female bovines are more resistant to infection compared to males, because the female hormones such as oestrogen strengthen and boost the immune system compared to androgen in males. Androgens make males more susceptible to infection due to a weakening immune system (Diakou *et al.,* 2005; Albuquerque *et al.,* 2011; FK and Shah, 2016).

Based on our analysis, the most prevalence rate of *T. gondii* infection in cattle was observed in studies that used the Sabin–Feldman, DAT, IFAT, MAT, ELISA, LAT and IHA, respectively. MAT is more accurate and suitable compared to other agglutination methods but is unsuitable for investigation in the field, because it requires a large number of tachyzoites of *T. gondii* (Jones and Dubey, 2012). ELISA is a simple method for *T. gondii* diagnosis, but it requires species-specific combinations and an ELISA reader device. The sensitivity and specificity of serological assays are varied. Seroprevalence of *T. gondii* in cattle can be up to 90%, while isolation of live *T. gondii* from cattle has generally been unsuccessful (Dubey and Beattie, 1988). Serological tests, especially MAT, IFAT and ELISA are the most common methods for diagnosing *T. gondii* infection in animal products and meat. Serological methods are often used as the first screening method to identify infected animals. The selection of a reliable and precise method can effectively interpret the results of *T. gondii* serological studies (Sharma *et al.,* 2008; Sroka *et al.,* 2011; Fereig *et al.,* 2016).

The prevalence of *T. gondii* in bovines varied in different years. It seems that since the beginning of 2000, with the introduction of different methods, the prevalence has increased slightly compared to the reports prior to 2000. However, this prevalence rate of infection has decreased in the last 5 years, despite numerous

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Table 2. Subgroup meta-analysis (variables such as year, continent, bovine species, gender, method and sample sizes) of global seroprevalence of *Toxoplasma gondii* in bovine

		Heterogeneity			Publication bias		Chi square test	
Variables	Pooled prevalence (95% CI)	Cochran *Q*	I^2 (%)	*P* value	Egger	*P* value	χ^2	*P* value
Year								
⩽2000	12.36 (8.19–17.24)	4302.99	99.1	<0.001	8.15	<0.001	1346.94	<0.001
2001–2005	23.5 (6.8–46.3)	1588.89	99.5	<0.001	10.11	0.002		
2006–2010	23.5 (14.4–34.1)	5755.3	99.4	<0.001	12.21	0.05		
2011–2015	18.1 (14.21–22.26)	10 507.56	99.3	<0.001	8.55	<0.001		
⩾2015	17.5 (11.9–24)	4493.87	99.3	<0.001	9.4	<0.001		
Continent								
Africa	18.8 (12.9–25.5)	2338.66	98.5	<0.001	6.93	0.023	4145.1	<0.001
Asia	14.89 (11.94–18.11)	7369.87	98.8	<0.001	9.23	<0.001		
Australia/Oceania	1.36 (0.02–7.65)	2.77	–	0.096	–	–		
Europe	21.93 (15.98–28.53)	4172.42	99.3	<0.001	7.78	0.014		
America	22.2 (15.2–30.1)	10 201.28	99.6	<0.001	15.02	<0.001		
Bovine species								
Cattle	16.94 (14.25–19.81)	22 435.56	99.3	<0.001	9.23	<0.001	2632.73	<0.001
Yak	23 (14–33)	327.93	98.2	<0.001	7.6	0.127		
Buffalo	22.26 (16.8–29)	2619.12	98.7	<0.001	−1.38	0.805		
Bison	8.1 (3.9–13.7)	5.76	47.9	0.124	0.29	0.881		
Gender								
Male	18.9 (13.8–24.7)	928.13	96.3	<0.001	4.7	<0.001	4.62	0.032
Female	17.78 (13.2–22.86)	9123.3	99.3	<0.001	9.51	<0.001		
Method								
DAT	27 (13–43)	369.87	98.6	<0.001	5.33	0.398	2833.23	<0.001
ELISA	18.52 (13.74–23.84)	8634.2	99.4	<0.001	11.39	<0.001		
IFAT	20.3 (13.9–27.6)	6404.92	99.4	<0.001	11.77	<0.001		
IHA	12.81 (7.82–18.81)	2803.51	99.2	<0.001	9.64	<0.001		
LAT	14.7 (8.9–21.8)	2523.96	98.9	<0.001	6.8	<0.001		
MAT	19.7 (12.3–28.5)	3495.77	99.3	<0.001	11.68	0.058		
SFDT	30 (17–45)	465.39	98.5	<0.001	10.96	0.137		
Sample size								
⩽300	19.23 (15.17–23.63)	4728.75	97.8	<0.001	6.39	<0.001	363	<0.001
301–600	16.4 (11.7–21.8)	3434.93	98.8	<0.001	15.47	<0.001		
601–900	23 (13–35)	2455.8	99.5	<0.001	41.91	<0.001		
⩾901	13.6 (8.3–19.9)	17 020.23	99.8	<0.001	24.64	<0.001		

ELISA, enzyme-linked immunosorbent assay; MAT, modified agglutination test; IFAT, indirect immunofluorescence antibody test; DAT, direct agglutination test; LAT, latex agglutination test; SFDT, Sabin–Feldman dye test.

studies with higher sample sizes, which may be related to the improvement of health index in animal husbandry, especially industrial breeding of livestock, more attention to animal health, the development of animal and veterinary sciences in the case of chronic diseases in large livestock (De Oliveira *et al.,* 2018). The trend of global climate change, the reduction of rainfall, declining groundwater levels and numerous droughts in different parts of the world had an effective role in this declining trend since the beginning of the 20th century. Environmental and geographical factors, such as temperature, rainfall and geographical coordination can change the prevalence of infection in different populations (de Souza *et al.,* 2016; De Oliveira *et al.,* 2018).

Based on subgroup meta-analysis, there was a significant relationship between sample size and the prevalence of *T. gondii* infection, therefore increase of sample size, is followed by increase of the infection prevalence (Table 2). In the studies with a sample size above 900, the prevalence of *T. gondii* was lower than the other groups under study (Table 2). Most studies that had a sample size of more than 900 were conducted in a wider geographical area (e.g. a country or a vast province or the Tibetan Plateau, etc.) than the other three groups. However, when more livestock are studied in a large area (province or country, etc.), that study naturally notices more geographical and climatic diversity, and as a result, the chances of finding positive cases may be lower (Dubey *et al.*, 2005; Santos *et al.*, 2009; Gharekhani, 2014*b*)

The strengths of this systematic review include the quality assessment by a checklist for incidence and prevalence study (the Joanna Briggs Critical Appraisal Checklist for Studies Reporting Prevalence Data), the high sample size in the global area, diversity of studies and analysis of subgroups according to geographical location, sex, sample size, year and type of serological method. In this study, we tried to pay attention to the maximum datasets in the article, despite the existence of 178 studies, the number of datasets reached 194, which indicates the accuracy of data extraction.

The main limitation expressed in the included articles was related to the selection of only English-language studies. For example, in Brazil which is one of the largest producers and exporters of beef in the world due to our limited access to local Brazilian journals, the number of included studies in this systematic review was lower than the number of studies conducted in the country.

On the contrary, the prevalence of *T. gondii* infection in bovines has been evaluated with different serological methods, while the gold standard method for diagnosing *T. gondii* infection in bovines is the bioassay method (Dehkordi *et al.*, 2013). The use of different laboratory diagnostic methods with varying sensitivity and specificity can affect the test results. It is better for researchers to use a reliable and precise serological test to measure the prevalence of *T. gondii* in bovines (Khames *et al.*, 2018). It seems that in order to better understand the prevalence of *T. gondii* in bovines, it is necessary to use more sensitive and accurate methods such as PCR along with demographic screening methods, such as serological methods (Majeed and Abbas, 2018). Although the serological methods have many advantages, but the variation in the cut-off value of each method cannot be a definitive indicator to estimate the infection in the animal population (Sharma *et al.*, 2019). The data presented, showed significant heterogeneity among the included studies based on livestock habitat. Some of these studies investigated the prevalence rate of *T. gondii* in industrial livestock that had fencing and protection and was less access to cats as a final host of this parasite, but other studies used domestic livestock with open grazing and with traditional breeding methods, which were more exposed to feces of cats. Some studies carried out on free-ranging wild bovines, such as bison. These animals not only live next to domestic cats but are also exposed to the wild cat's life cycle.

The type of sampling in most studies is not carried out uniformly or randomly or clustered. In fact, in most studies, it is not clear whether the study population represents the entire community in the region or not. In some studies on industrial livestock sampling, the sampling was performed only from livestock in a farm, the correct sampling or an acceptable estimate of the sample size was not mentioned.

Finally, due to the incomplete data in the included studies, our meta-analysis could not evaluate risk factors, such as breed, storage location, feeding age, type of breeding, etc. Evaluating these risk factors could provide a more comprehensive analysis with better dimensions of the problem.

Conclusion

To the best of our knowledge, this is the first systematic review and meta-analysis that provides a comprehensive view of the global seroepidemiology of bovine toxoplasmosis. The obtained result of this review showed that the global seroprevalence of bovine *T. gondii* infection is relatively high and it emphasizes the need for implementing screening and management of large animal meat products. This type of review analysis gives us an estimation on the prevalence in the world and completes the puzzle of the challenges facing one of the most important slogans of the World Health Organization, entitled 'Food safety from farm to fork'. Finally, investigation on the role of bovine products, such as milk, meat and oral viscera, known as the source of transmission of infection be examined in detail on a global scale to clear the data on bovine toxoplasmosis and its role in humans.

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Conflict of interest. The authors declare no conflicts of interest.

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