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# A meta-analysis of the prevalence of *Toxoplasma* gondii in animals and humans in Ethiopia

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#### **Abstract**

**Background:** Toxoplasmosis is a worldwide zoonosis. The objectives of this study were to estimate the prevalence and assess the potential risk factors of *Toxoplasma gondii* infections in animals and humans in Ethiopia by using meta-analytical methods.

**Methods:** Published studies on *T. gondii* in animals and humans in Ethiopia were searched in Medline, Google Scholar and the lists of references of articles. Eligible studies were selected by using inclusion and exclusion criteria. The risks of within and across study biases, and the variations in prevalence estimates attributable to heterogeneities were assessed. Pooled prevalence was estimated by the DerSimonian and Laird random effects model.

**Results:** Thirty two studies were eligible and data from 5689 animals and 5718 humans were used for quantitative syntheses. The pooled IgG seroprevalence in cats, small ruminants and humans were estimated at 87.72 % (95 % CI = 78.63, 93.28), 34.59 % (95 % CI = 21.08, 51.12) and 74.73 % (95 % CI = 61.85, 84.36), respectively. The odds of infections were higher in pregnant than in non pregnant women (OR = 3.96), in individuals that had contact with cats than those with no contact (OR = 2.53), and in urban than in rural inhabitants (OR = 2.06).

**Conclusions:** Toxoplasmosis is highly prevalent and could be a cause of considerable reproductive wastage in small ruminants and multiple diseases in humans in Ethiopia. Public education on preventive measures could help reduce the transmission of the parasite to humans.

Keywords: Animals, Ethiopia, Humans, Prevalence, Toxoplasma gondii

#### **Background**

Toxoplasma gondii is a widespread zoonotic parasite that infects all warm-blooded animals and humans [1]. Felids are its definitive hosts and excrete oocysts in their feces [2, 3], and the oocyst burden in areas where cats selectively defecate is high [4]. Animals and humans acquire infections mainly by ingesting food or water contaminated with sporulated oocysts and tissue cysts [5]. Although most infections are asymptomatic, reproductive losses in animals [6] and multiple disorders, that include cognitive impairment and fatal encephalitis in humans could come about [7, 8]. Additionally, there are reports of associations between *T. gondii* infections with schizophrenia [9, 10], bipolar disorder [11, 12], suicide [13], epilepsy [14] and traffic accidents [15, 16].

Despite *T.gondii* being an important zoonotic pathogen, there is no national survey that addressed the multiple disorders it causes in humans, its impact in animal production, its temporal and spatial distribution and the risk factors associated with the occurrence of the disease in Ethiopia. The objectives of this study were to estimate the prevalence of *T. gondii* infection in cats, food animals and humans in Ethiopia, and assess the potential risk factors of infection.

#### **Methods**

The study was conducted according to the PRISMA guideline (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) [17]. The PRISMA checklist was used to ensure inclusion of relevant information in the analysis (see Additional file 1).

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#### Literature search

Published studies were searched in Medline. Non-Medline indexed articles were searched in Google Scholar and the lists of references of articles. Toxoplasm\* and Ethiopia were the main MeSH terms used in electronic searches. Additional searches were done by using the main MeSH terms, Boolean operators, prevalence, incidence, cats, cattle, sheep, goats, camels, pigs, chicken and humans. The last search was done on December 23, 2014. Full text articles were downloaded or obtained from the library of the school of Medicine, College of Health Sciences, Addis Ababa University, and from Dr. Jitender P. Dubey.

#### Selection of studies

A study was eligible for quantitative analyses if (i) it was published in English, (ii) it was cross-sectional, (iii) the methods were coprological and/or serological [Sabin Feldman dye test (SFT), modified agglutination test (MAT), modified direct agglutination test (MDAT), direct agglutination test (DAT), enzyme linked immunosorbent assay (ELISA) and latex agglutination test (LAT)], and (iv) the sample size was greater than 35. Studies were excluded if the titles and abstracts were not relevant to the outcomes of interest or did not fulfill the eligibility criteria.

# Data extraction

From each eligible study, the following data were extracted: the first author, year of publication, year of study, location, climatic zone, altitude, study design, sample size, species, sex, age group, test methods and the number of positive samples. In addition, from studies on humans, the following were extracted: setting (hospital/non-hospital), pregnancy status (pregnant/non pregnant), HIV status (HIV positive/HIV negative), residence (urban/rural), behavior (apparently normal/abnormal), raw meat (consumer/non consumer), raw vegetable (consumer/non consumer), presence of cats in the household/contact (yes/no) and water source (pipe/others).

#### Data analysis

Data on cats, food animals and humans were analyzed separately. The study level estimates were transformed to logit event estimates [18, 19] by the following formula: lp = ln [p/ (1-p)], where lp = logit event estimate; ln = natural logarithm; p = study level estimate. The variances of the estimates were calculated by the following formula: v (lp) = 1/(np) + 1/[n(1-p)], where v = variance and n = sample size.

# Bias and heterogeneity analyses

The qualities of the study methods (study design and serological tests) were used to assess the within study biases. The across study bias (small study effects) was examined by funnel plots, and the statistical significance was assessed by the Egger's regression asymmetry test [20]. The Duval and Tweedie non-parametric 'fill and trim' linear random method was used to calculate unbiased estimates [21]. The heterogeneities of study level estimates were assessed by Galbraith plot [22] and Cochran's Q test. A non significant heterogeneity was accepted if the ratio of Q and the degree of freedom (Q/df) was less than one. The percentage of the variation in prevalence estimates attributable to heterogeneity was quantified by the inverse variance index (I<sup>2</sup>), and I<sup>2</sup> values of 25 %, 50 % and 75 % were considered as low, moderate and high heterogeneity, respectively [23]. Subgroup analyses were done if the heterogeneities were moderate to high. A study was included in a subgroup analysis if the number of individuals (n) was more than 25 % of the mean of the subgroup.

#### Pooling and sensitivity tests

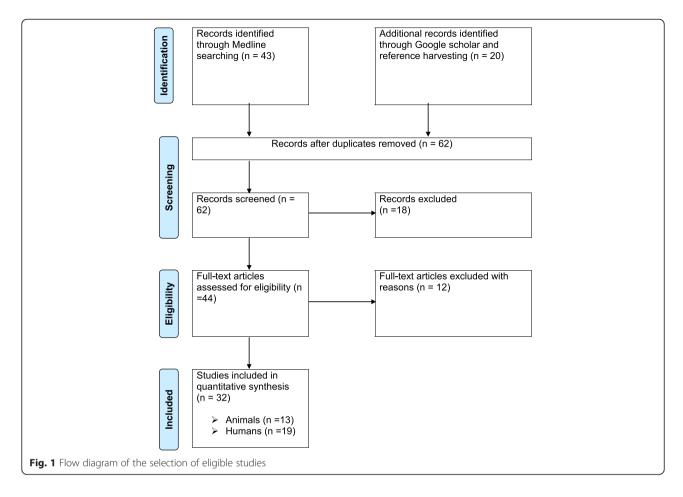
The DerSimonian and Laird random effects model was used to pool logit event estimates [24]. Pooled logit estimates were transformed to prevalence estimates (p) by the following formula:  $p = e^{lp}/(e^{lp} + 1)$ : where e = the base of natural logarithm. Single study omitted influence analyses were done to test the robustness of a pooled estimate, and a study was considered to have no influence if the pooled estimate without it was within the 95 % confidence limits of the overall mean. The Z test was used to test whether a pooled estimate significantly differs from zero or not. The Yates corrected Chi Square test was used to test the significance of a difference between estimates [25, 26]. Alpha was set at 0.05.

Microsoft Office Excel 2007 was used to transform study level estimates to logit event estimates, and to back transform pooled logit event estimates to prevalence estimates. Epi info<sup>TM</sup> (Version 3.5.1, Center for Disease Control, CDC, USA) was used to compare groups. Stata (Version 11.1, Stata Corp, College Station, Texas) was used in all other analyses.

# Results

# Search results and eligible studies

Figure 1 shows the search results. A total of 63 studies were found of which 18 were excluded based on the titles and abstracts. Of the studies screened for eligibility, 12 were excluded due to the following reasons: one was not available; two were abstracts; the sample size was 20 in one; the data was inconsistent in one; the diagnosis was established on the basis of clinical signs in one; IHAT was used in three, and the methods were not described in three studies. A total of 32 full-text studies were used for quantitative analyses [27–58].



## Characteristics of the eligible studies

On the whole, data from 5689 animals (124 cats, 1950 sheep, 2102 goats, 726 chickens, 402 pigs and 385 camels) and 5718 humans from several regions of Ethiopia were analyzed (Table 1).

# Bias and heterogeneity assessment

All studies on animals were cross-sectional, and the serological tests were ELISA, DAT, MDAT and MAT. All studies on humans were cross-sectional and IgG seroprevalence was examined by using ELISA, LAT, SFDT and MDAT. According to the manufacturers of the kits, the sensitivities and specificities of the tests were > = 92 %, and > = 95 %, respectively. As the sensitivity and specificity of LAT was lower than those of the other tests, a subgroup analysis of the estimates of human studies that used LAT vs. other tests did not yield a statistically significant difference (p > 0.05). The funnel plots (Fig. 2) and the bias coefficients in both food animal [b = 0.54 (95 % CI = -19.27, 20.35; p > 0.05), and human [b = 5.45 (95 % CI = -4.67, 15.57; p > 0.05)studies did not suggest the presence of bias, and no theoretical missing study was incorporated by the Duval and Tweedie non-parametric method. The percentages of the variations in prevalence estimates attributable to heterogeneities were zero, 97.6 % and 98.6 % in cat, food animal and human studies, respectively.

# **Pooled prevalence estimates**

# Cats

The pooled prevalence of seropositive cats was 87.72 % (95 % CI = 78.63, 93.28; p < 001),  $I^2$  = 0. The pooled prevalence of oocyst shedder cats was 17.51 % (95 % CI = 9.77, 29.36; p < 001),  $I^2$  = 19 %.

#### Food animals

Figure 3 shows a forest plot of the IgG logit event estimates in food animals. The pooled estimates by potential risk factors are presented in Table 2. The overall prevalence of *T. gondii* infection was 35.5 % (95 % CI = 25.96, 46.36), and the estimates for ruminants and non-ruminants did not differ significantly (p > 0.05). In subgroup analyses, the pooled seroprevalence of *T. gondii* in small ruminants was 34.59 % (95 % CI = 21.08, 51.12; p > 0.05),  $I^2$  = 98.9 %, with a higher occurrence in sheep than in goats, in females than in males, and in adults than in young animals. All single study omitted estimates lie within the 95 % confidence intervals of the respective overall means of each group.

**Table 1** Characteristics of the eligible studies

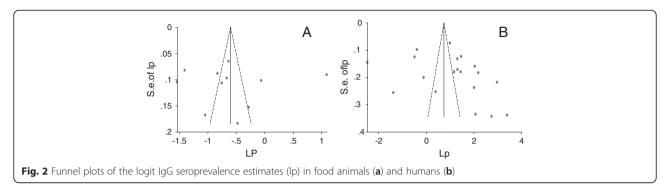
Author	Year of study	Location	Host	Method	Number	Positive (%)
Zewdu et al. [27]	2010–2011	CE	Goat	ELISA	927	183 (19.74)
Gebremedhin et al. [28]	2010–2011	CE	Sheep	ELISA	1030	357 (34.66)
Teshale [29]	2005-2006	CSE	Sheep, goat	MDAT	641	480 (74.88)
Demissie and Tilahun [30]	2000-2001	CE	Sheep, goat	MDAT	468	159 (33.97)
Negash et al. [31]	1999–2000	CE	Sheep, goat	MDAT/ELISA	174	75 (43.10)
Gebremedhin and Gizaw [32]	2013-2014	SE	Sheep, goat	ELISA	184	48 (26.09)
Gebremedhin et al. [33]	2011–2012	CE	Sheep, goat	DAT	628	111 (17.68)
Gebremedhin et al. [34]	2012-2013	CE	Camel	MAT	385	187 (48.57)
Tilahun et al. [35]	2012	CE	Chicken	MAT	125	48 (38.40)
Gebremedhin et al. [36]	2012–2013	CE	Chicken	MAT	601	183 (30.45)
Gebremedhin et al. [37]	2014	CE	Pig	DAT	402	129 (32.09)
Dubey [38]	2011	CE	Cat	MAT	36	33 (91.67)
Tiao [39]	2012	CE	Cat	MAT	48	41 (85.42)
Negash et al. [31]	1999–2000	CE	Cat	Coprology	40	5 (12.5)
Dubey [38]	2011	CE	Cat	Coprology	36	8 (22.22)
Mellbin and Vahlquist [40]	nr	WCSE	human	SFT	267	102 (38.20)
De Roever-Bonnet [41]	nr	CE	human	SFT	99	47 (47.47)
Guebre Xabier et al. [42]	1990	CSE	human	ELISA	919	673 (73.23)
Eshete et al. [43]	nr	CE	human	ELISA	94	19 (20.21)
Woldemichael et al.[44]	1995–1996	CE	human	SFT/LAT	340	268 (78.82)
Negash et al. [45]	1999–2000	CE	human	MDAT	65	39 (60.00)
Yimer et al. [46]	nr	CE	human	ELISA	279	270 (96.77)
Shibre et al. [47] <sup>a</sup>	2005	CE	human	ELISA	90	80 (88.89)
Shimelis et al. [48]	2007	CE	human	ELISA	330	297 (90.00)
Tedla et al. [49] <sup>a</sup>	2009	CE	human	ELISA	456	434 (95.18)
Zemene et al. [50]	2011	SE	human	ELISA	201	163 (81.09)
Gebremedhin et al. [51]	2010–2011	CE	human	ELISA	425	346 (81.41)
Aleme et al. [52]	2011–2012	CE	human	ELISA	150	141 (94.00)
Walle et al. [53]	nr	NE	human	ELISA	204	161 (78.92)
Muluye et al. [54]	2012-2013	NE	human	LAT	170	130 (76.47)
Tadesse et al. [55]	2012	NE	human	LAT	422	171 (40.52)
Endris et al. [56]	2010–2011	NE	human	LAT	385	341 (88.57)
Zeweld et al. [57]	2012–2013	NE	human	ELISA	651	51 (7.83)
Yohannes et al. [58]	2013	SE	human	ELISA	170	150 (88.24)

CE, Central Ethiopia; CSE, Central and Southern Ethiopia; DAT, direct agglutination test; ELISA, enzyme linked immunosorbent assay; LA, latex agglutination test; MAT, modified agglutination test; MDAT, modified direct agglutination test; MDAT/ELISA, modified direct agglutination test and enzyme linked immunosorbent assay; n, sample size; NE, Northern Ethiopia; nr, not reported; SE, Southern Ethiopia; SFT, Sabin-Feldman dye test; WCSE, Western, Central and Southern Ethiopia aData on T.gondii infection was collected before the trials

# Humans

Figure 4 shows a forest plot of the logit estimates in humans. The pooled prevalence estimates by potential risk factors are presented in Table 3. The overall pooled prevalence was 74.73~% (95 % CI = 61.85, 84.36). The pooled estimate was affected by sex, age, pregnancy, status, cat contact/ possession and residential area but not

by raw meat and raw vegetable consumption habits, and source of water. The pooled seroprevalence in patients with behavioral disorders (schizophrenia/bipolar disorder) was 93.88 % (95 % CI = 81.47, 98.16; p < 001),  $I^2$  = 88.2 %. All single study omitted estimates lie within the 95 % confidence intervals of the respective overall means of each group.



## **Discussion**

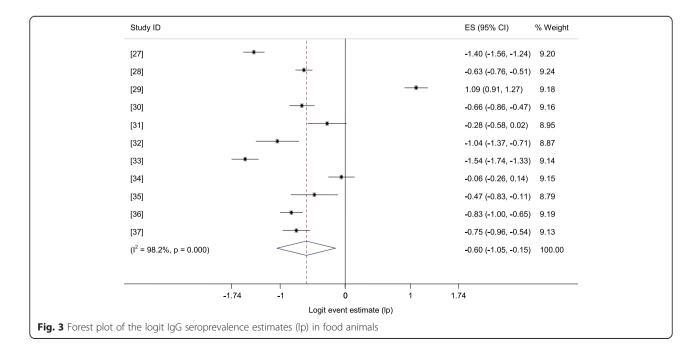
The moderate to high inverse variance indexes of the study level estimates in food animals and humans reported here are suggestive of potential variations that could have been due to cat densities, environmental and societal factors [59, 60].

The prevalence of *T. gondii* in cats in Ethiopia was high. Ethiopian cats live outdoors, hunt, feed on scraps and garbage-thus more exposed to the parasite [3]. In a study from California, USA, the annual environmental burden per square meter was estimated to be in the range of 94 to 4671 oocysts, based on a low prevalence (0.9 %) of oocysts in cat feces [61]. Therefore, if we assume 17.51 % oocyst shedder cats in Ethiopia, and 100 million oocysts per shedder [1], the environmental burden in urban residential areas where cats abound is apparently high.

The overall pooled estimate in small ruminants was considerable (34.59 %), and the odds of infection was three times greater in adults than in young small ruminants. The

higher occurrence of *T.gondii* infection in adults compared to young animals is in agreement with results of studies carried out elsewhere [62, 63]. The estimate demonstrates the potential of *T. gondii* as a cause of reproductive wastage in small ruminants, and the risk associated with the consumption of raw products derived from small ruminants [64, 65].

The substantially high prevalence of *T. gondii* infections in humans could be due to the uncontrolled movement of cats, the substandard living circumstances, and the unhygienic life styles and habits that favor the transmission of the parasite from either felids or food animals. Comparison of the present estimate with estimates for sub-Saharan African countries (SSA) is difficult because national survey reports or meta-analytical studies are scarce. However, the prevalence of *T. gondii* infection in Ethiopian women is apparently higher than estimates for most developed countries (4 % in South Korea to 11 % in USA) [60]. Therefore, assuming three million live births each year [66], and a conservative estimate of 0.1 % birth



**Table 2** Pooled estimates of *T. gondii* in food animals by potential risk factors

Risk factors		p (95 % CI)	Z-p	Q/df	Q-p	l <sup>2</sup>	$\chi^2$	Y-p	OR (95 % CI)
All animals	Overall	35.50 (25.96,46.36)	0.009	56.97	0.000	98.2			
	Ruminant	32.54 (22.51,44.47)	0.005	32.41	0.000	98.1	0.01	0.933	1.01 (0.87,1.16)
	Non-ruminant	32.34 (28.88,35.99)	0.000	1.5	0.223	33.4			
Small Ruminants	Overall	34.59 (21.08, 51.12)	0.067	88.69	0.000	98.9			
	Sheep	33.51 (26.06, 41.90)	0.000	10.71	0.000	90.7	10.24	0.001	1.25 (1.09,1.43)
	Goat	28.80 (11.17, 56.54)	0.129	100.39	0.000	99			
	Female	29.38 (23.06, 36.63)	0.000	9.73	0.000	89.7	23.95	0.000	1.70 (1.37,2.12)
	Male	19.67 (10.80, 33.09)	0.000	11.48	0.000	91.3			
	Adult	34.30 (24.96, 45.07)	0.005	18.79	0.000	94.7	100.50	0.000	3.06 (2.43,3.86)
	Young	14.62 (10.93, 19.26)	0.000	2.35	0.070	57.4			
	Midland <sup>a</sup>	53.32 (36.12, 69.76)	0.710	16.09	0.000	93.8	45.43	0.000	2.27 (1.78,2.91)
	Highland	33.45. (29.78, 37.36)	0.000	0.28	0.597	0			
	Lowland	14.99 (8.0, 26.39)	0.000						

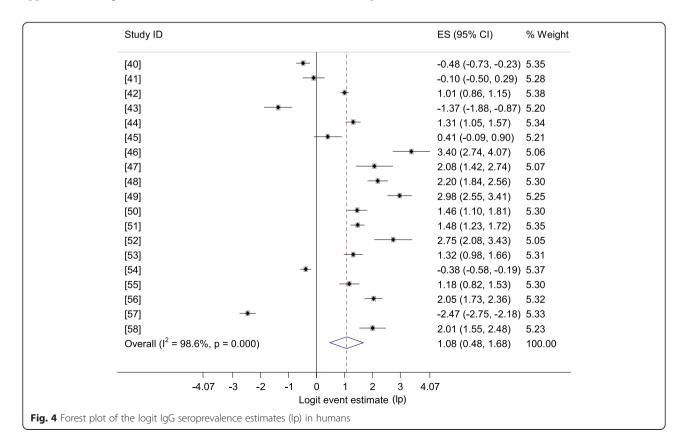
I<sup>2</sup>, inverse variance index; OR, odds ratio; Q, Cochran's X<sup>2</sup>; Y-p, probability of Yates test; Z-p, probability of Z test

prevalence of congenital infections [67, 68], the number of congenitally infected neonates per annum could be about 3000.

*T.gondii* infection was higher in urban than in rural inhabitants and in individuals with cats in the household or had contact with cats. The cat population per unit area appears to be higher in the urban than in the rural areas

because of the relatively better feed resource in the former than the latter, and as cats roam in search of food a single cat could be a source of infection to several neighboring urban households.

The high prevalence of *T.gondii* in HIV positive individuals suggests the risk of cerebral toxoplasmosis in patients that do not have access to HIV treatment.



<sup>&</sup>lt;sup>a</sup>The comparison was between midland and highland estimates

**Table 3** Pooled estimates of *T. gondii* in humans by potential risk factors

Risk factors		p (95 % CI)	Z-p	Q/df	Q-p	l <sup>2</sup>	$\chi^2$	Ү-р	OR (95 % CI)
	Overall	74.73 (61.85,84.36)	0.000	70.4	0.000	98.6			
Sex	Male	73.54 (41.95, 91.44)	0.137	51.1	0.000	98	37.17	0.000	1.65 (1.40,195)
	Female	62.74 (40.08,80.91)	0.269	69.4	0.000	98.6			
Age	Adults	69.87 (47.50,85.59)	0.080	80.2	0.000	98.8	51.06	0.000	1.95 (1.62,2.36)
	Children	54.34 (24.81,81.11)	0.790	54.8	0.000	98.2			
Pregnancy	Pregnant	62.55 (29.88, 86.74)	0.462	56.8	0.000	98.2	152.83	0.000	3.96 (3.15,4.97)
	Non-pregnant	29.59 (0.75, 95.87)	0.672	197.8	0.000	99.5			
Cat	Contact	85.96 (74.12, 92.90)	0.000	13.6	0.000	92.6	64.10	0.000	2.53 (2.00,3.20)
	No contact	70.70 (53.74, 83.37)	0.018	27.4	0.000	96.4			
Residence	Urban	82.58 (73.63, 88.93)	0.000	2.7	0.000	96.3	64.04	0.000	2.06 (1.71,2.47)
	Rural	69.80 (52.40, 82.91)	0.027	19.8	0.000	94.9			
Meat	Raw C <sup>a</sup>	77.22 (63.85, 86.68)	0.000	18.3	0.000	94.5	0.65	0.421	1.10 (0.88,1.36)
	Raw NC <sup>b</sup>	75.58 (51.22.90.11)	0.040	36.0	0.000	97.2			
Vegetable	Raw C <sup>a</sup>	75.44 (53.00, 89.33)	0.028	31.8	0.000	96.9	1.45	0.229	1.19 (0.90,1.56)
	Raw NC <sup>b</sup>	72.23 (35.92, 92.34)	0.222	36.6	0.000	97.3			
Water	Non pipe	86.65 (82.17, 90.13)	0.000	0.54	0.585	0	1.36	0.243	1.30 (0.85,2.00)
	Pipe	83.45 (76.73, 88.52)	0.000	6.4	0.000	84.2			
HIV	Positive	81.06 (50.07, 94.81)	0.05	77.7	0.000	98.7	0.26	0.609	1.06 (0.87,1.29)
	Negative	80.17 (72.47, 86.13)	0.000	6.7	0.000	85.0			

 $I^2$ , inverse variance index; OR, odds ratio; Q, Cochran's  $X^2$ ; Y-p, probability of Yates test; Z-p probability of Z test

Cerebral toxoplasmosis is one of the sequels of *T.gondii* in HIV patients [69–71], and in the absence of chemoprophylaxis against HIV, up to 40 % of patients co-infected with *T. gondii* may develop fatal *Toxoplasma* encephalitis [6]. Before the start of the highly active anti-reteroviral therapy (HAART) in Ethiopia, neural toxoplasmosis was one of the complications [72] with mortality in more than a third of the patients [72, 73], and after the initiation of HAART, immune reconstitution inflammatory syndrome (IRIS) was one of the sequels of toxoplasmosis [74–76].

To date, there have been only two studies that reported the prevalence of T.gondii in patients with schizophrenia/bipolar disorders and the study level estimates were greater than 88 % [47, 49]. Meta-analytical studies have also shown higher odds of schizophrenia (OR = 2.73) [77, 78], and epilepsy (OR = 4.8) [13] in T.gondii seropositive than in seronegative individuals, and positive associations of T.gondii seroprevalence with traffic accidents [79–81], and suicide attempts and success [82] have been recorded elsewhere.

## Implications and limitations

This study demonstrates the importance of toxoplasmosis in small ruminant production and its public health impact. The control of the disease in a country where most cats are stray, and the food animal management system is mainly of an extensive type is difficult. Therefore, public education as regards the value of cooked meat and washed vegetables, and hygienic practice could reduce the transmission of the parasite and the consequences of infection in humans. Secondly, although a large scale neonatal screening program and treatment of infected neonates at a national level is not an economically viable strategy against congenital infections, initiation of such a program at least in urban areas where there are individuals who afford the medical costs could somehow reduce the impacts of the disease to a limited extent.

As the numbers of eligible studies in each stratum were small and all regions of the country have not been covered in the studies, the estimates and the predictive values of the risk factors may vary depending on factors that may involve animal, environmental and societal variables. However, the pooled estimates highlight the overall magnitude of *Toxoplasma* infections in animals and humans in Ethiopia; the heterogeneity statistics show the variability of the study level estimates and potential areas of research, and the crude odds ratios depict the relative importance of the risk factors.

## **Conclusions**

Toxoplasmosis is highly prevalent in Ethiopia, and could be a cause of considerable reproductive wastage in small

<sup>&</sup>lt;sup>a</sup>Consumers

<sup>&</sup>lt;sup>b</sup>Non-consumers

ruminants and multiple diseases in humans. Educational programs, and serological screening and treatment of neonates when possible could help to reduce the national impacts of the disease. Further studies are needed to describe the epidemiology of the disease at a national level in Ethiopia.

#### **Additional file**

#### Additional file 1: PRISMA Checklist.

#### Competing interests

The authors declare that they have no competing interests.

#### Authors' contributions

EZG searched the literature and extracted the data; TG designed the study and analyzed the data; EZG and TG have participated in drafting the manuscript. Both authors have read and approved the manuscript.

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