Does the prevalence of latent toxoplasmosis and frequency of Rhesus-negative subjects correlate with the nationwide rate of traffic accidents?

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Abstract: Latent toxoplasmosis is probably the most common protistan parasitic disease with many indirect negative impacts on human health. One of the important impacts is impaired psychomotor function leading to reduced driving efficiency in Toxoplasmaseropositive subjects. Numerous case-control studies have established a positive relation between the seroprevalence of Toxoplasma gondii (Nicolle et Manceaux, 1908) and probability of traffic accidents in study populations. The prevalence of toxoplasmosis varies between populations according to local geographical conditions, hygienic practices and kitchen habits. Similarly, we see a striking variation in the incidence of traffic accidents across countries. Hence, we compiled the largest ever data set on the seroprevalence of toxoplasmosis and tried to understand its role in traffic accident-related deaths and disabilities across 87 countries. Simple nonparametric analysis showed a positive and strong relation of T. gondii seroprevalence and traffic accident related disabilities. Further, we conducted multivariate analysis to control for confounding factors. After controlling for wealth, geographical latitude, health of population, length of roads and number of vehicles, the correlation disappeared. When the frequency of RhD negativity and its interaction with toxoplasmosis were included into the model, the effects of toxoplasmosis seemingly returned. However, the analysed data suffered from the problem of multicollinearity. When a proper method of analysis, ridge regression, was applied, the effects of toxoplasmosis prevalence and RhD negativity frequency disappeared again. The existence of a strong correlation between the prevalence of toxoplasmosis and health of population in particular countries, which was the probable cause of multicollinearity and possible reason for the negative result of the present study, suggests that 'asymptomatic' latent toxoplasmosis could have a large impact on public health.

Keywords: parasite, Toxoplasma, manipulation hypothesis, correlation study, ecological regression, Disability Adjusted Life Years

Toxoplasma gondii (Nicolle et Manceaux, 1908), a highly successful protistan parasite that reproduces sexually in the intestine of cats and many multiply asexually in the tissues of any homeothermic animal, infects about 30% of humans in the world population (Tenter et al. 2000, Pappas et al. 2009). Intrauterine infection of the fetus produces severe form of the disease, whereas latent toxoplasmosis, which is the most common form of the infection, was believed to be relatively harmless. However, studies conducted during last decades have thrown light on the ability of Toxoplasma Nicolle et Manceaux, 1909 to exert a plethora of effects on humans like impairment of the psychomotor performance (Havlíček et al. 2001), increased risk of schizophrenia (Torrey et al. 2012), tendency for suicide (Pedersen et al. 2012), incidence of epilepsy (Stommel et al. 2001), and brain tumors (Thomas et al. 2012).

A noteworthy effect has been reported by four retrospective (Flegr et al. 2002, Yereli et al. 2006, Kocazeybek et al. 2009, Galvan-Ramirez et al. 2013) and one prospective (Flegr et al. 2009) case-control studies showing that *Toxoplasma*-infected subjects have higher risk of traffic and workplace accidents (Alvarado-Esquivel et al. 2012). The results of the prospective study also indicate that subjects with a Rhesus-negative blood group (RhD-negative subjects) were responsible for increased probability of traffic accidents in *Toxoplasma*-infected drivers (Flegr et al. 2009).

Due to climatic conditions, hygiene practices and kitchen habits that influence *Toxoplasma* survival and infection, the prevalence of toxoplasmosis varies largely across populations (Table 1). These factors play a crucial role in oocyst survival in soil and consumption of raw or undercooked infected meat, which increases the chances of contact with the infective stages of *Toxoplasma* – see Tenter et al. (2000) and Pappas et al. (2009). Similarly, there is a cross country variation in traffic accident-related deaths and injuries influenced by numerous environmental and socioeconomic factors (WHO 2008).

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Table 1. Prevalence of latent toxoplasmosis in WHO member countries.

Country	Toxo ¹	RhD^2	References	Period ³	No. ⁴
Albania	49 (42)	NA	Maggi et al. (2009)	2004-2005	496
Argentina	60 (53)	9.1	Rickard et al. (1999)	NA	1007
Australia	23 (16)	19	Karunajeewa et al. (2001)	NA	308
Austria	42 (36)	19	Moese and Vander-Moese (1998)	1997	4601
Bahrain	22 (16)	5.89	Tabbara and Saleh (2005)	2000-2003	3 4 9 9
Bangladesh	38 (38)	4.3	Ashrafunnessa et al. (1998)	1995–1996	286
Belgium	49 (42)	15.3	Breugelmans et al. (2004)	1991-2001	16541
Benin	54 (47)	NA	Rodier et al. (1995)	1993	211
Brazil	50 (50)	20	Fonseca et al. (2012)	2007-2008	2136
Burkina Faso	25 (25)	NA	Simpore et al. (2006)	2004-2005	336
Cameroon	77 (70)	3.1	Ndumbe et al. (1992)	1989–1990	1014
Canada	20 (17)	15	Many and Koren (2006)	NA	NA
Colombia	54 (54)	NA	Rosso et al. (2008)	2006	630
Congo	60 (60)	NA	Makuwa et al. (1992)	1990	2897
Costa Rica	76 (76)	NA	Arias et al. (1996)	1991	1234
Croatia	29 (24)	NA	Punda-Polic et al. (2000)	1994–1995	1109
Cuba	55 (55)	NA	Sanchez-Gutierrez et al. (2003)	2001	526
Czech Republic	20 (16)	15	Kaňková and Flegr (2007)	1996–2004	1053
Denmark	28 (20)	16	Lebech et al. (1999)	1992–1996	89873
Egypt	42 (36)	7.8	Attia et al. (1995)	NA	62
Estonia	68.6 (45)	16	Birgisdottir et al. (2006)	1999–2000	1277
Ethiopia	74 (66)	7	Dubey et al. (2012)	1990–1991	1016
Finland	20 (17)	13	Koskiniemi et al. (1992)	1989	16733
France	54 (47)	15	Ancelle et al. (2003)	1995	13459
Gabon	71 (71)	NA	Nabias et al. (1998)	1997	767
Germany	63 (50)	15	Fiedler et al. (1999)	1994–1996	4854
Greece	25 (21)	NA	Antoniou et al. (2004)	1998–2003	5532
Grenada	57 (50)	NA	Asthana et al. (2006)	1995	534
Hungary	45 (39)	NA	Szenasi et al. (2005)	2000	31759
Chile	39 (33)	NA	Contreras et al. (2009)	1996	7536
China	11 (11)	NA	Liu et al. (2009)	2006	235
Iceland	13 (8)	15	Birgisdottir et al. (2006)	1998	440
India	35 (35)	4	Borkakoty et al. (2007)	2003	180
Indonesia	53 (46)	0.5	Konishi et al. (2000)	1999–2000	17735
Iran	39 (33)	NA	Fallah et al. (2008)	2007	576
Iraq	49 (42)	9.9	Mahdi and Sharief (2002)	NA	254
Ireland	34 (25)	NA	Ferguson et al. (2008)	NA	20252
Israel	21 (17)	10	Franklin et al. (1993)	1989	213
Italy	23 (16)	15	De Paschale et al. (2008)	2004	3 4 2 6
Jamaica	57 (57)	7	Prabhakar et al. (1991)	1986	1604
Japan	10 (8)	0.6	Sakikawa et al. (2012)	2011	4466
Jordan	47 (40)	NA	Jumaian (2005)	2000-2001	280
Kuwait	46 (53)	NA	Iqbal et al. (2003)	NA	225
Libya	45 (34)	12.81	Mousa et al. (2011)	2007	143
Lithuania	40 (34)	NA	Rockiene (1997)	1991	NA
Macedonia	22 (18)	NA	Bobic et al. (2011)	2005	NA
Madagascar	84 (84)	0.5	Lelong et al. (1995)	1992	599
Malaysia	49 (42)	0.5	Nissapatorn et al. (2003)	NA	200
Mexico	49 (49)	4.7	Caballero-Ortega et al. (2012)	2000	3 599
Montenegro	27 (23)	NA	Bobic et al. (2011)	2007	NA
Morocco	51 (44)	NA	El Mansouri et al. (2007)	NA	2456
Mozambique	19 (13)	NA	Sitoe et al. (2010)	2008	150
Nepal	55 (55)	0.8	Rai et al. (1998)	NA	345
Netherlands	35 (26)	16.3	Kortbeek et al. (2004)	1995–1996	7 5 2 1
New Zealand	35 (26)	18	Morris and Croxson (2004)	2000	500
Nigeria	78 (71)	NA	Onadeko et al. (1992)	NA	352
Norway	11 (9)	15.3	Jenum et al. (1998)	1992–1993	35940
Pakistan	33 (28)	10.85	Ahmed and Hafiz (1997)	NA	105
Papua New Guinea	18 (15)	NA	Klufio et al. (1993)	1990	197
Peru	39 (33)	2.2	Cantella et al. (1974)	NA	262
Poland	40 (34)	15	Nowakowska et al. (2006)	2003	4916

(continued)

Table 1. Continued.

Country	Toxo ¹	RhD ²	References	Period ³	No. ⁴
Portugal	24 (17)	14.2	Lopes et al. (2012)	2011	401
Qatar	35 (30)	NA	Abu-Madi et al. (2010)	2005-2008	1857
Romania	44 (38)	NA	Crucerescu (1998)	1990	184
Sao Tome & Principe	75 (68)	NA	Hung et al. (2007)	2003-2004	499
Saudi Arabia	32 (27)	7	el Hady (1991)	NA	921
Senegal	40 (34)	NA	Faye et al. (1998)	1993	353
Serbia	31 (26)	NA	Bobic et al. (2011)	2007	765
Singapore	17 (14)	NA	Wong et al. (2000)	1997–1998	120
Slovakia	22 (18)	NA	Studenicova et al. (2008)	NA	656
Slovenia	25 (21)	NA	Logar et al. (2002)	1996–1999	21270
South Korea	4 (3)	0.72	Lim et al. (2012)	2000	NA
Spain	32 (23)	20	Munoz Batet et al. (2004)	1999	16362
Sudan	42 (36)	NA	Elnahas et al. (2003)	2000	487
Sweden	18 (13)	16	Evengard et al. (2001)	1997–1998	40978
Switzerland	35 (26)	17	Signorell et al. (2006)	2006	NA
Tanzania	35 (35)	NA	Doehring et al. (1995)	1991	549
Thailand	13 (11)	0.5	Signorell et al. (2006)	2001	1 2 0 0
Togo	75 (68)	NA	Deniau et al. (1991)	1990	620
Trinidad and Tobago	43 (43)	NA	Ramsewak et al. (2008)	NA	450
Tunisia	43 (37)	NA	Ndong-Obame and Ayadi (1997)	1994–1996	2231
Turkey	54 (47)	12	Harma et al. (2004)	NA	1149
UK	9 (6)	17	Nash et al. (2005)	1999–2001	1897
United Arab Emirates	23 (19)	8.8	Dar et al. (1997)	NA	1 503
USA	11 (9)	15	Jones et al. (2007)	1999–2004	5515
Venezuela	38 (38)	9.1	Triolo-Mieses and Traviezo-Valles (2006)	2001-2004	446
Vietnam	11 (9)	NA	Buchy et al. (2003)	NA	NA

¹ prevalence (%) of toxoplasmosis; the numbers in parentheses represent the prevalence adjusted to a standard age of 22 years to account for variation in childbearing age across countries using the formula $Prevalence_{adj} = 1 - (1 - Prevalence)^{(22/childbearing age)}$ (Lafferty 2006); ² frequency of RhD-negative subjects (%); ³ year(s) of toxoplasmosis data collection; ⁴ number of women in the sample; NA – information not available.

In the present study, we investigate whether the prevalence of latent toxoplasmosis correlates with the nationwide rate of traffic accidents. We present the results of the statistical analysis of relations between *Toxoplasma* seroprevalence and traffic accidents. To prevent selection bias, we compiled and used a large worldwide dataset containing information about *Toxoplasma* seroprevalence (Table 1).

MATERIALS AND METHODS

Toxoplasma prevalence

Most of toxoplasmosis prevalence (seroprevalence) data are available for women in childbearing age. All available prevalence data published mostly between 1995 and 2008 for 87 countries were compiled. The seroprevalence was adjusted to a standard age of 22 years to eliminate differences in the prevalence caused by different childbearing ages across populations (Barber 2004) using the formula of Lafferty (2006):

$Prevalence_{adi} = 1 - (1 - Prevalence)^{(22/childbearing age)}$.

Data on traffic accidents

Estimated road traffic fatal injury deaths per 100000 population for the year 2010 were retrieved from the World Health Organization (WHO, https://www.destatis.de/EN/FactsFigures/CountriesRegions/InternationalStatistics/Topic/Tables/Basic-Data_RoadTrafficDeaths.html).

The missing 2010 figure for Libya was substituted with the 2008 figure. Summary tables present the best estimates of WHO – based on the evidence available in mid-2008 – rather than the official estimates of the member states. Methods and data sources are summarised in the Annexes of (WHO 2008), and the methodology used is described in more detail elsewhere (Lopez et al. 2006); also available at: http://www.dcp2.org/pubs/GBD; accessed July 2013.

Confounding factors

The number of traffic accidents could be directly influenced by the number of vehicles and length of the road networks. Toxoplasma survival depends on latitude due to variation in climate factors. Wealth can reduce the incidence of toxoplasmosis as well as traffic accidents as it can be used to implement control measures. Further, a healthy population will be less prone to acquire toxoplasmosis and will have lower incidence of traffic accidents. To account for these confounding factors, we included the number of vehicles per 1000 inhabitants, length of roads, gross national income (GNI), latitude and population health status for the study populations. The number of vehicles per 1000 inhabitants covers motor vehicles like cars, buses and freight vehicles but do not include two-wheelers. Population refers to midvear population in the year for which data are available. Data for the period 2003 to 2007 were taken from the International Road Federation (World Road Statistics and data files) and were used for computing the arithmetic mean for the whole period. The length of roads indicates total road network size of both paved and unpaved in the country. Data

for the years 1999–2012 were taken from the Central Intelligence Agency (CIA) https://www.cia.gov/library/publications/ the-world-factbook/rankorder/2085rank.html.

Gross national income per capita based on purchasing power parity (GNI, averaged 2002 to 2008) was used as a measure of wealth. GNI, calculated in national currency, is usually converted to U.S. dollars (USD) at official exchange rates for comparisons across economies. GNI data were taken from the World Bank. Values were log transformed for normality. Latitude values for nations were obtained from the CIA World Factbook and numerical values were used irrespective of direction.

To measure health, we used five World Health Organization indicators: health adjusted life expectancy (HALE), adult mortality rate, maternal mortality ratio, under-five mortality rate and infant mortality rate. They were reduced by principle component analysis to obtain a single variable that provides a complete picture about the health of population. The utility of this indicator as well as detailed methods have been presented elsewhere (Dama 2012). Health adjusted life expectancy adds up the expectation of longevity for different health states and predicts the average number of years that a person can expect to live in full health by taking into account years lived in less than full health due to disease and/or injury. While the infant mortality rate and maternal mortality ratio are the actual numbers of deaths of infants (during the first year of life per 1 000 live births in a given year) and mothers (per 100000 live births in a given year), the under 5 and adult mortality rates are the probabilities of dying before reaching the age of five and between the ages of 15 and 65, respectively.

The frequency of RhD-negative subjects was taken from the internet compilation by RhesusNegative.net available at http://www.rhesusnegative.net/themission/bloodtypefrequencies/ on 22 December 2013.

Statistical methods

The association between the prevalence of toxoplasmosis or frequency of RhD-negative subjects and the number of deaths caused by traffic accidents was calculated using univariate general linear modeling (GLM) and the nonparametric Spearman test. Furthermore, we used multiple regression and ridge regression to understand the influence of all confounders (GNI, latitude, health factor, length of road network and number of vehicles per 1 000 inhabitants) on the relation between *Toxoplasma* and the number of deaths due to traffic accidents. All confounding variables except latitude (distance from the equator) were log-transformed before GLM analyses to better approach normal distributions. Type VI variance decompositions were used in the GLM analyses.

RESULTS

Toxoplasma prevalence was positively correlated with the number of deaths owing to traffic accidents across 87 countries (parametric: p = 0.002, $eta^2 = 0.110$; non-parametric: Spearman R = 0.407, p = 0.0001) (Fig. 1). However, when wealth, latitude, health factor, length of roads and number of vehicles per inhabitant were included into the model, the effect of *Toxoplasma* prevalence disappeared (Table 2).

Case-control studies suggest that RhD positivity protects against the effect of *Toxoplasma* infection on the



Fig. 1. Correlation between the prevalence of toxoplasmosis and incidence of traffic accident deaths.

Table 2. Association of the traffic accident burden with the prevalence of latent toxoplasmosis after controlling for the five potential confounding factors.

N = 87	Death in traffic accidents				
	F	р	Partial eta ²	Partial beta	
Intercept	1.149	0.287	0.014	-	
Wealth	0.047	0.830	0.001	-0.024	
Latitude	20.31	< 0.001	0.202	-0.450	
Health	29.53	< 0.001	0.270	0.519	
Roads	2.518	0.116	0.031	0.175	
Vehicles	6.796	0.011	0.078	0.280	
Тохо	3.00	0.087	0.036	-0.190	

The wealth, latitude, health, roads, vehicles and Toxo represent log GNI in USD per capita, distance from the equator in degrees, log health factor computed with principal component analysis, log total length of roads in km, log number of vehicles per 1 000 inhabitants, and prevalence of toxoplasmosis in percentage, respectively.



Fig. 2. Correlation between the frequency of RhD-negative inhabitants and incidence of traffic accident deaths.

		М	ultiple regression	Ridge regression		
N = 49	F	р	Partial eta ²	Partial beta	р	Partial beta
Intercept	8.18	0.007	0.170	-	0.047	_
Wealth	4.05	0.051	0.092	-0.303	0.413	-0.130
Latitude	6.046	0.018	0.131	-0.362	0.011	-0.388
Health	20.43	< 0.001	0.338	0.581	0.002	0.462
Roads	0.470	0.497	0.012	0.108	0.403	0.132
Vehicles	12.34	0.001	0.236	0.486	0.121	0.243
RhD	6.470	0.015	0.139	-0.373	0.134	-0.235
RhD × Toxo	5.575	0.021	0.126	0.355	0.301	0.163
Тохо	15.23	< 0.001	0.170	-0.525	0.065	-0.287

Table 3. Association of the traffic accident burdens with the prevalence of latent toxoplasmosis and frequency of RhD negative inhabitants after controlling for the five potential confounding factors.

Wealth, latitude, health, roads, vehicles, RhD, RhD \times Toxo and Toxo represent log GNI in USD per capita, distance from the equator in degrees, log health factor computed with principal component analysis, log total length of roads in km, log number of vehicles per 1 000 inhabitants, frequency of RhD (Rhesus)-negative subjects in percentage, multiple of toxoplasmosis prevalence and frequency of RhD-negative subjects and prevalence of toxoplasmosis in percentage, respectively.

risk of traffic accidents and against impairment of reaction times. The frequency of RhD-negative subjects was available for 48 countries in our data set. When we also included the frequency of RhD negativity and RhD-toxoplasmosis interaction (multiple of Toxoplasma prevalence and frequency of RhD-negative subjects in particular country) into the model, the effects of toxoplasmosis, RhD and RhD-toxoplasmosis interaction were significant, together explaining more than 55% of the variability in the incidence of deaths due to traffic accidents between countries (Table 3, Fig. 2). However, the negative partial correlation coefficient for toxoplasmosis and visual inspection of the correlation matrix of independent variables suggested that multicollinearity, the nearly linear correlation between certain independent variables, could be responsible for the observed effect. Therefore, we also performed a ridge regression analysis. The comparison of the results of the multiple regression and ridge regression analyses (Table 3) suggested that the prevalence of toxoplasmosis and RhD did not correlate with the traffic accident rate in our set of 48 countries.

DISCUSSION

In a simple univariate test, the prevalence of latent toxoplasmosis correlated positively with the traffic accident burden estimated from the number of deaths due to traffic accidents. This association, however, disappeared when the variables that influence the risk of deaths in traffic accidents, such as wealth, latitude, health of population, length of roads and number of vehicles, were controlled. Even when two more variables, namely frequency of RhD (Rhesus)-negative subjects and multiple of *Toxoplasma* prevalence and frequency of RhD-negative inhabitants were included into the model, and the problem of multicollinearity was solved by ridge regression, all three focal effects (toxoplasmosis, RhD, toxoplasmosis-RhD interaction) remained non-significant.

Up to now, five independent studies have shown that latent toxoplasmosis is a potential risk factor for traffic accidents (Flegr et al. 2002, 2009, Yereli et al. 2006, Kocazeybek et al. 2009, Galvan-Ramirez et al. 2013). Another study has reported a similar influence on the risk of workplace accidents (Alvarado-Esquivel et al. 2012). Moreover, several studies have observed that Toxoplasma-infected subjects have prolonged reaction times and impaired ability to concentrate for a long duration (Havlíček et al. 2001, Flegr et al. 2008a, Novotná et al. 2008, Pearce et al. 2013). Infected subjects have lower consciousness (Lindová et al. 2012), and infected male subjects have lower superego strength (Flegr and Hrdý 1994, Flegr et al. 1996), i.e. lower willingness to follow any rules, probably including traffic rules, possibly due to their increased concentration of free testosterone (Flegr et al. 2008b,c). Given these results, the absence of correlation between the traffic accident-associated burden and prevalence of toxoplasmosis is surprising.

A recent ecological regression study showed that the prevalence of toxoplasmosis can explain a large part of between-country variability in disease burden expressed either as the mortality rate per 100000 population or as DALY (Disability Adjusted Life Year – lost years of 'healthy' life) (Flegr et al. 2014). If the health factor used as a covariate expresses a very strong correlation with the prevalence of toxoplasmosis and the health data are estimated more precisely than the toxoplasmosis prevalence data, then statistical tests could easily provide false negative results.

The negative slope of non-significant correlation between the frequency of RhD-negative subjects in the population and the number of deaths due to traffic accidents agreed with the observation that among *Toxoplasma*-free subjects, RhD-negative individuals have better reaction times than their RhD-positive peers (Flegr et al. 2008a, Novotná et al. 2008). It was even suggested that this in-

creased psychomotor performance was the primary reason for the spread of the RHD gene deletion in Europe in prehistoric times (Novotná et al. 2008). The number of wild cats, the definitive hosts of Toxoplasma, and probably also the prevalence of toxoplasmosis, was low in this region in comparison with Africa and Asia before the very recent advent of the domestic cat (Torrey and Yolken 1995). While the prevalence of RhD-negative subjects in Caucasian populations is about 16%, it is much lower in the population of people of Asian and African origin (Mourant 1954). It must be admitted, however, that RhD-negative individuals are subject to stronger negative effects of aging and smoking on health estimated on the basis of the self-rated number of common viral and bacterial diseases in the past year, regardless of Toxoplasma infection status, and that RhD positivity probably protects against a broader spectrum of negative factors than just the Toxoplasma infection (Flegr et al. 2010, 2012). A possible physiological mechanism of physiological and behavioural effects of RhD phenotype that was based on RhD negativity-associated anoxia in certain parts of nervous system was suggested by Prandota (2012).

Limitation of the present study

It is possible that the published data on the seroprevalence of toxoplasmosis in women in childbearing age are unreliable or only poorly reflect the actual prevalence of toxoplasmosis in the population of drivers. Similarly, many traffic accidents are unregistered and fraction of unregistered accidents probably varies between countries. It must be stressed that in many countries, the prevalence of toxoplasmosis has dramatically changed, mostly decreased, in the past 20 years (Tenter et al. 2000, Pappas et al. 2009). Similarly, the rate of traffic accident-related deaths has also been on the decline during this period. In such a dynamic system, the risk of traffic accidents is likely to reflect the prevalence of toxoplasmosis in a (unknown and country-specific) past rather than in the present. It is not clear whether our prevalence data collected mostly in 1995-2005 should be matched to the traffic accident data for the same period of time or for a later period of time. All these potential problems could result in Type II error, i.e. they can be responsible for false negative results of statistical tests.

Conclusions

The present study demonstrated neither a positive correlation between the prevalence of toxoplasmosis and traffic accident-associated death rate nor a negative correlation between the frequency of the RhD-negative phenotype and traffic accident-associated death rate in the large data set from WHO member countries. However, it showed that positive results can be easily obtained when simple univariate statistical methods are used for the analysis of the same data set. We suggest that the study should be repeated on other data sets, for example on regional data from a large country, e.g. the USA, Mexico or France, for which the traffic accident as well as toxoplasmosis prevalence and RhD negativity frequency data are probably available. The existence of a strong correlation between the prevalence of toxoplasmosis and health of population in particular countries, which was the probable cause of multicollinearity and possible reason for the negative result of the present study, suggests that 'asymptomatic' latent toxoplasmosis could have a large impact on public health.

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