Seroprevalence and associated risk factors of *Toxoplasma gondii* infection in psychiatric patients: a case-control study in eastern China

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SUMMARY

In recent years, the effect of *Toxoplasma gondii* infection on the cerebrum and neuropsychiatric patients has been increasingly highlighted. However, there is limited information about the epidemiology of *T. gondii* infection in psychiatric patients in Shandong province, eastern China. Therefore, through a case-control study, 445 patients hospitalized for diacrisis or treatment in Weihai, eastern China, and 445 control subjects from the general population of the same region matched by gender, age, and residence were examined with enzyme-linked immunoassays for the presence of IgG and IgM antibodies to *T. gondii* and associated sociodemographic and behavioural characteristics in a population of psychiatric patients. Seroprevalence of IgG antibodies to *T. gondii* in psychiatric patients (77/445, 17·30%) was significantly higher than in control subjects (55/445, 12·36%) (*P* = 0·038). Fourteen (3·15%) psychiatric patients and 10 (2·25%) control subjects had IgM antibodies to *T. gondii* (*P* = 0·408). Multivariate analysis using logic regression showed that *T. gondii* infection was associated with cats at home and consumption of raw/undercooked meat in psychiatric patients. Considering that most psychiatric patients usually have lower cognitive functioning and additional transmission routes related to their inappropriate behaviours that could enhance the risk of infection, psychiatric patients should be considered as a specific group of *T. gondii* infection.

Key words: Eastern China, psychiatric patients, seroepidemiology, *Toxoplasma gondii*, toxoplasmosis.

INTRODUCTION

Toxoplasma gondii is an opportunistic protozoan parasite that can infect almost all warm-blooded animals throughout the world, including humans [1–3]. It is estimated that *T. gondii* has infected about one-third of the human population in the world [1]. Human infection is mainly by consumption of undercooked or raw meat containing tissue cysts from an infected intermediate host, as well as unwashed vegetables and fruit or drinking water containing oocysts, polluted by the faeces of infected cats [4].

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In most adults with a normal immune system, *T. gondii* does not cause serious diseases, and clinical symptoms are usually not apparent. Blindness and mental deficiency can be caused in congenitally infected children and the disease can be severe in immunocompromised individuals [5]. Moreover, reactivation and replication of *T. gondii* in immunocompromised individuals can cause neurological or psychiatric symptoms [6]. Studies performed in various countries showed increased seroprevalence of toxoplasmosis in psychiatric patients, and increasing evidence supports the hypothesis that psychosis may be related to *T. gondii* infection [7].

Currently, several epidemiological investigations on the relationship between *T. gondii* infection and psychosis have been performed in different areas in China [7], which were originally published in local Chinese journals (with limited accessibility to international readers). However, most of these investigations simply estimated the seroprevalence of *T. gondii* infection and did not evaluate the risk factors and possible contamination routes of *T. gondii* infection in psychiatric patients. Therefore, we conducted this case-control study in order to estimate the seroprevalence of *T. gondii* infection, and identify risk factors and possible contamination routes of *T. gondii* infection in a population of psychiatric patients in Shandong province, eastern China.

MATERIALS AND METHODS

Study site and study populations

The present investigation was conducted in Weihai, eastern China from June 2011 to July 2013. Weihai is located in a coastal region in the east of China (36° 41′–37° 35′ N, 121° 11′–122° 42′ E) at 200–300 m above sea level and has a typical temperate monsoon climate. Weihai has an average annual rainfall of 730·2 mm and an average annual temperature of 11·9 °C. Most inhabitants of Weihai are of Han ethnicity, and some residents are of Korean ethnicity. During the study period, 445 patients hospitalized for diacrisis or treatment were invited to participate in the study. All patients were included in the study based on the following inclusion criteria: (1) psychiatric patients, (2) aged ⩾16 years, and (3) agreed to participate in the study. Control subjects (*n* = 445), matched with psychiatric patients by age, gender, and residence, were included in the study. Serum samples were obtained from the general population of Weihai, eastern China.

Sample collection and transportation

About 5 ml of venous blood was drawn from each participant. Blood samples were kept overnight at room temperature to allow clotting and centrifuged at 1000 *g* for 10 min. The sera were collected in Eppendorf tubes and stored at 4 °C for 24–72 h until transportation in an icebox to State Key Laboratory of Veterinary Etiological Biology, Key Laboratory of Veterinary Parasitology of Gansu Province, Lanzhou Veterinary Research Institute, Chinese Academy of Agricultural Sciences, Lanzhou, Gansu Province where they were kept at −20 °C until tested.

Sociodemographic, clinical and behavioural data

Sociodemographic data including age, birth place, residence and race were obtained for all patients. Clinical data explored in patients included the type of the mental disorder. Behavioural data included animal contact, presence of cats and dogs at home, consumption of raw/undercooked meat, consumption of raw vegetables and fruit, source of drinking water and exposure to soil. These variables were selected based on the literature. Data were obtained from the patients, medical examination records, and informants. Patients were invited to provide veridical information and they were informed that data were used in a confidential manner. Classification of mental illnesses was performed according to the ICD-10 criteria [8].

Serological assay

Sera were analysed for the presence of IgG and IgM antibodies to *T. gondii* using commercially available enzyme immunoassay kits (Demeditec Diagnostics GmbH, Germany) [9] according to the manufacturer's instructions. Positive and negative serum controls were included in every plate.

Statistical analysis

Results were analysed with SPSS v. 19.0 software (SPSS Inc., USA). For comparison of the frequencies in the groups, the Mantel–Haenszel test, and when indicated Fisher's exact test, were used. Bivariate and multivariate analyses were used to assess the association between the characteristics of the subjects and *T. gondii* infection. Variables were included in the multivariate analysis if they had a *P* value of ⩽0·25 in the bivariate analysis. Adjusted odd ratios

Table 1. *Seroprevalence of IgG antibodies to* Toxoplasma gondii *in psychiatric patients and controls according to age group*

Age group (years)	Psychiatric patients			Controls			P value
	No. tested	*T. gondii* infection		No. tested	*T. gondii* infection		
		No.	%		No.	%	
⩽19	44	9	20·45	47	8	17·02	0·675
20–29	128	13	10·16	114	11	9·65	0·895
30–39	113	18	15·93	119	10	8·40	0·079
40–49	80	15	18·75	82	9	10·98	0·164
50–59	40	10	25·00	40	4	10·00	0·078
60–69	9	1	11·11	9	1	11·11	1·00
70–79	14	6	42·86	15	6	40·00	0·876
⩾80	17	5	29·41	19	6	31·58	0·888
Total	445	77	17·30	445	55	12·36	0·038

(ORs) and 95% confidence intervals (CIs) were calculated by multivariate analysis using multiple, unconditional, logistic regression. $P \leqslant 0.05$ was considered statistically significant.

Ethical consideration

This study was approved prior to commencement by the ethical committee of Weihaiwei People's Hospital, Wendeng Municipal Hospital and Wendeng People's Hospital. The purpose and procedures of the study were explained to the participants, and a written informed consent was obtained from all participants. The sera were collected with agreement from the volunteers.

RESULTS

In the present study, psychiatric patients were aged 16–91 years. There were 238 females and 207 males. All psychiatric patients resided in Weihai, eastern China. IgG antibodies to *T. gondii* were detected in 77 (17·30%) of the 445 psychiatric patients, and in 55 (12·36%) of the 445 controls. The difference in these seroprevalences was statistically significant ($P = 0.038$); IgM antibodies to *T. gondii* were found in 14 patients and in 10 controls (3·15% *vs.* 2·25%, respectively, $P = 0.408$). Table 1 shows the seroprevalences of latent *T. gondii* infection in the populations studied according to age group. Seroprevalence in patients and controls increased with age (Table 1). In addition, the seroprevalences of *T. gondii* infection in patients according to their psychiatric disorder are shown in Table 2. The highest prevalence of latent *T. gondii* infection was found in schizophrenia patients (11/34, 32·35%).

Bivariate analysis showed a number of sociodemographic characteristics and behavioural characteristics with $P \leqslant 0.25$, including cats at home, dogs at home, contact with cats and dogs, consumption of raw vegetables and fruit, consumption of raw/undercooked meat and exposure to soil (Table 3). Multivariate analysis of these sociodemographic and behavioural characteristics showed that cats at home [adjusted OR (aOR) 5·060, 95% CI 2·814–9·100, $P < 0.001$] and consumption of raw/undercooked meat (aOR 2·438, 95% CI 1·167–5·096, $P = 0.018$) were significantly associated with *T. gondii* infection in psychiatric patients (Table 4). Other behavioural characteristics did not show an association with *T. gondii* infection.

DISCUSSION

According to prevalence projections conducted by some authoritative medical institutions, the number of psychiatric patients numbers more than 100 million in China [10]. Psychiatric patients have become a serious social public problem in China. In recent years, a number of researchers showed interest in studying the effect of *T. gondii* infection on the cerebrum and in neuropsychiatric patients [7]. *T. gondii* has a highly substantial connection with brain tissue where tachyzoites may develop into tissue cysts and persist for the individual's entire life. Some psychiatric clinical signs such as schizophrenia and mental deficiency may be motivated by *T. gondii* infection [4, 7]. In this study, we found a 17·30% prevalence of *T. gondii* infection in psychiatric patients compared to 12·36%

Table 2. *The types of psychiatric disorder and seroprevalence of IgG antibodies to* Toxoplasma gondii *antibodies in 445 psychiatric patients*

Type of psychiatric disorder	ICD-10 diagnosis	Patients with anti-*T. gondii* IgG antibodies			
		No. tested	No.	% (95% CI)	*P* value*
Epilepsy	G40	49	10	20·41 (9·12–31·69)	0·114
Affective disorder	F30, F39	13	2	15·39 (0·00–35·00)	0·745
Somatoform disorder	F45	36	3	8·33 (0·00–17·36)	0·476
Schizophrenia	F20	34	11	32·35 (16·63–48·08)	0·001
Mental and behavioural disorders due to use of alcohol	F10, F18	53	10	18·87 (8·33–29·40)	0·184
Mental and behavioural disorders due to use of drugs	F13, F15, F19	26	3	11·54 (0·00–23·82)	0·901
Obsessive-compulsive disorder	F42	29	7	24·14 (8·56–39·71)	0·068
Mild depression	F32·051	23	3	13·04 (0·00–26·81)	0·923
Moderate depression	F32·151	52	8	15·39 (5·58–25·19)	0·535
Major depressive disorder	F32·251	39	3	7·69 (0·00–16·06)	0·390
Mental retardation	F71–37, F78	40	9	22·50 (9·56–35·44)	0·070
Alzheimer's disease	G30	33	5	15·15 (2·92–27·39)	0·640
Dementia in Alzheimer's disease with early onset	F00·0	18	3	16·67 (0·00–33·88)	0·588
Total		445	77	17·30 (13·79–20·82)	0·038

* Compared to 12·36% seroprevalence of IgG antibodies to *T. gondii* antibodies in controls (55/445).

in controls. A statistically significant difference between psychiatric patients and controls was found in this study (*P* = 0·038), this difference in prevalence between psychiatric patients and controls might be caused, at least in part, by differences in the sanitary conditions between the groups. In fact most psychiatric patients were from the lower socioeconomic level. In addition, they had worse housing conditions and poorer sanitation compared to controls.

Regarding demographic characteristics, the *T. gondii* seroprevalence found in the present study was not significantly associated with any of the sociodemographic characteristics of the psychiatric patients. It has been reported that seropositivity to *T. gondii* is related to age [11–13]; however, in the present investigation, *T. gondii* infection in psychiatric patients was not significantly influenced by age. Although high seropositivity to *T. gondii* was found in the 70–79 and ⩾80 years age groups of psychiatric patients, the number of subjects in age groups 60–69, 70–79 and ⩾80 years was limited in this study. The difference was not considered to be statistically significant in age groups for psychiatric patients.

Of the types of psychiatric disorder, the highest prevalence of latent *T. gondii* infection was found in schizophrenia patients (11/34, 32·35%). Schizophrenia is a serious, chronic, and often debilitating neuropsychiatric disorder. Its causes are still poorly understood [14].

Moreover, there are conflicting reports concerning the association of *T. gondii* infection and schizophrenia in humans. However, previous studies [3, 14–17] and our case-control study provides evidence to clarify the controversial information on the association of *T. gondii* infection and schizophrenia.

With respect to behavioural characteristics, multivariate analysis showed that cats at home and consumption of raw/undercooked meat were associated with *T. gondii* seropositivity. As the definitive hosts for *T. gondii*, cats play a vital role in maintaining *T. gondii* in nature [18]. In China, cats are prevalently kept as pets because they are very easy to take care of and provide company that enriches people's home life. However, little attention has been focused on their potential to pollute the environment with *T. gondii* [19]. In this study, we found that keeping cats at home was highly associated with *T. gondii* seropositivity (aOR 5·060, 95% CI 2·814–9·100, *P* < 0·001). Some previous reports have indicated that humans can become infected with *T. gondii* through ingesting tissue cysts in undercooked or raw meat from an infected intermediate host, or by ingestion of oocytes via unwashed vegetables and fruit or drinking water polluted by the faeces of an infected cat [4, 20–22]. Similarly, our study found that consumption of raw/undercooked meat was highly associated with *T. gondii* seropositivity (aOR 2·438, 95% CI

Table 3. *Bivariate analysis of selected characteristics with* Toxoplasma gondii *infection in psychiatric patients and controls in China*

Variable	Category	Psychiatric patients (*n* = 445)				Controls (*n* = 445)				Total (*n* = 890)			
		No. tested	*T. gondii* infection			No. tested	*T. gondii* infection			No. tested	*T. gondii* infection		
			No.	%	*P* value		No.	%	*P* value		No.	%	*P* value
Sex	Male	207	32	15·46	0·337	207	27	13·04	0·683	414	59	14·25	0·650
	Female	238	45	18·91		238	28	11·76		476	73	15·34	
Race	Han	382	68	17·80	0·494	382	45	11·78	0·360	764	113	14·79	0·933
	Korean	63	9	14·29		63	10	15·87		126	19	15·08	
Residential area	Urban	315	56	17·78	0·681	297	32	10·77	0·150	612	88	14·38	0·573
	Suburban or rural	130	21	16·15		148	23	15·54		278	44	15·83	
Cat at home	Yes	67	30	44·78	<0·001	76	28	36·84	<0·001	143	58	40·56	<0·001
	No	378	47	12·43		369	27	7·32		747	74	9·91	
Dog at home	Yes	88	21	23·86	0·069	92	22	23·91	<0·001	180	43	23·89	<0·001
	No	357	56	15·69		353	33	9·35		710	89	12·54	
Contact with cat and dog	Yes	309	60	19·42	0·076	307	38	12·38	0·986	616	98	15·91	0·175
	No	136	17	12·50		138	17	12·32		274	34	12·41	
Consumption of raw vegetables and fruit	Yes	345	55	15·94	0·141	340	42	12·35	0·994	685	97	14·16	0·303
	No	100	22	22·00		105	13	12·38		205	35	17·07	
Consumption of raw/undercooked meat	Yes	314	62	19/75	0·035	334	43	12·87	0·567	648	105	16·20	0·060
	No	131	15	11·45		111	12	10·81		242	27	11·16	
Exposure to soil	Yes	279	56	20·07	0·045	261	36	13·79	0·274	540	92	17·04	0·022
	No	166	21	12·65		184	19	10·32		350	40	11·43	
Source of drinking water	Tap	317	57	17·98	0·552	297	35	11·78	0·602	614	92	14·98	0·849
	Well + river	128	20	15·63		148	20	13·51		276	40	14·49	

Table 4. *Multivariate analysis of characteristics of the psychiatric patients and their association with* Toxoplasma gondii *infection*

Characteristic*	aOR†	95% CI	*P* value
Cats at home	5·060	2·814–9·100	<0·001
Dogs at home	1·619	0·870–3·014	0·128
Contact with cats and dogs	0·883	0·438–1·781	0·728
Consumption of raw vegetables and fruit	0·561	0·298–1·056	0·073
Consumption of raw/undercooked meat	2·438	1·167–5·096	0·018
Exposure to soil	1·697	0·932–3·090	0·084

aOR, Adjusted odds ratio; CI, confidence interval.
* The variables included were those with a value of *P* < 0·25 obtained in the bivariate analysis.
† Adjusted by age and the rest of characteristics included in this Table.

1·167–5·096, *P* = 0·018). Therefore, it is very important to publicize the knowledge of disease prevention to the public, with particular emphasis on the important role cats play in the transmission of *T. gondii* and the association between *T. gondii* infection and behavioural characteristics.

CONCLUSION

Through a case-control study, the present study revealed, for the first time, that infection with *T. gondii* in psychiatric patient is common in Weihai, eastern China. Psychiatric patients (17·30%) have a significantly higher prevalence of *T. gondii* infection than controls (12·36%). Moreover, keeping cats at home and consumption of raw/undercooked meat are important risks for the acquisition of *T. gondii* infection in psychiatric patients. Considering that most psychiatric patients usually have lower cognitive functioning and additional transmission routes related to their inappropriate behaviours that could enhance the risk of infection, psychiatric patients should be considered as a specific group of *T. gondii* infection.

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DECLARATION OF INTEREST

None.

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