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SEROPREVALENCE OF *TOXOPLASMA GONDII* INFECTION AND ITS ASSOCIATED RISK FACTORS IN NEUROPSYCHIATRIC PATIENTS IN JAZAN PROVINCE, SAUDI ARABIA

By
WAFAA M. ZAKI[1,2], RASHA Y. HOFDI[2], AISHA A. SHEBILEY[2], ZAKI A. SAADI[3], and ALI H. AGEEL[3]
Department of Medical Parasitology[1], Faculty of Medicine, Suez Canal University, Egypt, Department of Medical Laboratory Technology[2,3], Faculty of Applied Medical Science, Jazan University[2] and Al-Amal Hospital for Psychiatric Health[3], Jazan, Saudi Arabia (*Correspondence: wafaa_zaki@hotmail.com)

Abstract

Toxoplasma gondii has worldwide distribution in nearly one-third of the human population. It is a neurotropic protozoan parasite so a potential role of *T. gondii* infection for some neuropsychiatric disorders was postulated. Patients with psychiatric disorders had high toxoplasmosis seroprevalence. Limited information about toxoplasmosis seroprevalence in psychiatric patients was known in southern area of Saudi Arabia.

The current cross sectional case control study aims at determination of the prevalence of *T. gondii* IgG & IgM in neuropsychiatric patients in Jazan Province. A total of 162 neuropsychiatric patients from Al-Amal hospital for psychiatric health and 162 subjects without neuropsychiatric manifestations from Jazan General Hospital, Jazan City, KSA. were enrolled in the study. Psychiatric diagnosis was based on the International Classification of Diseases-10 (ICD-10 classification). Serological analysis for latent toxoplasmosis (IgG) and active toxoplasmosis (IgM) was done using Enzyme Linked Immunosorbent Assay (ELISA). Investigations for the association with socio-demographic, clinical and behavioral characteristics in psychiatric patients were also done.

The serofrequency of IgG antibodies among neuropsychiatric patients was significantly higher than that of the controls (35.8% vs 14.8%) P = 0.0022. OR 3.2 with 95% CI= (1.4952 to 6.8774). However; serofrequency of toxoplasma IgM antibody between neuropsychiatric patients and controls was not statistically significant ($P > 0.05$). Bivariate and multivariate analysis for socio-demographics and possible associated risk factors showed that contact to cats and/or dogs, eating under cooked meat, and contact to soil were significantly higher in neuropsychiatric patients than controls.

Keywords: *Toxoplasma gondii*, Neuropsychiatric patients, ELISA.

Introduction

Toxoplasma gondii is an obligate opportunistic intracellular protozoan parasite which belongs to the phylum Apicomplexa, order Coccidia (Rorman *et al,* 2006). It can infect almost all warm-blooded animals, including humans (Zhou *et al,* 2011). *T. gondii* infection was estimated to be about one-third of the human population in the world (Dubey *et al,* 2010). Human infection is mainly acquired by special routes which include ingestion of contaminated food or water and eating undercooked or raw meat that contains tissue cysts. Less commonly, it is associated with blood transfusion or organ transplantation (Alvarado-Esquivel *et al,* 2010). Meanwhile infection in immunocompetent persons does not cause serious illness; it is kept in its latent stage by the host's immune system and clinical manifestations are often not apparent. However; in congenital infection, blindness and mental retardation in children can result (Hamidinejat *et al,* 2010). The disease can be severe in immunocompromised patients e.g., AIDS patients, patients after transplantation and patients under corticosteroids or anticancer therapy. Latent toxoplasmosis can be transformed into its active form resulting in toxoplasmic encephalitis, which is often fatal (Jones *et al,*

2001).

Toxoplasma gondii has a neurotropic nature, this nature and other features may help in pathogenic mechanisms implicating in mental and behavioural disorders (Flegr, 2015). *T. gondii* uses a complex mechanism to gain access to the brain with preferred sites at cerebral hemispheres, basal ganglia, cerebellum and brain stem (Carruthers and Suzuki, 2007). Once enters CNS, it invades various brain cells, including astrocytes and neurons, where it forms cysts containing bradyzoites. Then, it can establish a continuous infection within the CNS, influencing host behaviour, and can cause neurological and psychiatric symptoms in some infected individuals (Fabiani *et al,* 2013). Many toxoplasmic immunological reactions and reactivation mechanisms led to behavioral disorders in man (Fekadu *et al,* 2010). Subjects with various neuropsychiatric disturbances, as schizophrenia (Alvarado-Esquivel *et al,* 2006) personality disorders, obsessive compulsive disorder (Alvarado-Esquivel *et al,* 2015b), bipolar disorder, unipolar depression, drug abuse disorder, suicides, homicides, generalized anxiety, panic disorders and mood disturbances, have been reported to be more often infected with *Toxoplasma* than normal controls (Flegr, 2015). Behavioral disorders due to psychoactive substances are also reported in toxoplasmosis patients (Alvarado-Esquivel *et al,* 2015a). *T. gondii* infection proved to have a role in traffic accidents, work accidents, and mental illnesses (Alvarado-Esquivel *et al,* 2015b).

This present study was conducted to estimate the seroprevalence of *T. gondii* infection, and identify its risk factors and possible contamination routes in a population of psychiatric patients in Jazan, KSA.

Subjects, Materials and Methods

This is a cross-sectional, case control study examining the serofrequency of *T. gondii* among patients with neuropsychiatric disorders. A total of 162 patients suffering from psychological and/or neurological disorders attended Al-Amal hospital for psychiatric health, Jazan were investigated for presence of *T.gondii* IgG and IgM antibodies. Furthermore, the correlation between *T. gondii* infection and the socio-demographic, clinical and behavioral characteristics of the patients was also investigated.

A uniformly structured questionnaire was fulfilled by the patients to obtain their socio-demographic, clinical, and behavioral features. The socio-demographic data included age, gender, residence, urban or rural habitation, marital status, educational level, occupation, and socioeconomic status. Regarding the clinical features, the following data were investigated: health status, history of lymphadenopathy, blood transfusions, transplantation and surgeries, presence of frequent headache, dizziness, and impairments in vision, hearing, memory and reflexes. In female patients, obstetric history was also obtained. In addition, history of aggressiveness, suicidal ideation and suicide attempt were also collected from each study subject. Psychiatric diagnosis was based on the ICD-10 classification (WHO, 1992). Information on potential risk factors such as direct contact with cats or dogs or litter's box, contact with other animals, eating behavior like consumption of raw or undercooked meat and its frequency, consumption of unwashed raw vegetables and fruits, contact with soil, and type of flooring at home.

Five mL of venous blood was collected aseptically from 162 neuropsychiatric patients (subjects) from Al- Amal hospital for psychiatric health, Jazan and 162 subjects without neuropsychiatric manifestations (controls) from Jazan General Hospital during the period between September 2015 to May 2016. The serum was separated from the whole blood by centrifugation at 3000 rpm for ten minutes at room temperature. The separated serum was labeled and kept at −20◦C until tested for anti-*T. gondii* IgG and IgM antibodies using ELISA test kit (Human Gesllschaft for biochemical and diagnostic, Max Plank, Germany) following the

manufacturer's instruction. Samples absorbance were read using microtiter plate reader at absorbance of 450/620 nm. The sera of both patients and controls were obtained from blood at the time of interviews. Each sample was tested in duplicate to ensure reliability. All experiments were done in strict sterile conditions.

Statistical analysis: Results were analyzed using Statistical Package for Social Sciences (SPSS) version 20 (Chicago, Illinois, USA). Sserofrequency of *T. gondii* IgG & IgM antibodies were calculated by descriptive statistics (frequencies), and the differences between the groups were calculated using the Chi-square, Student's t-test or Fisher's exact test. Odd ratio (OR) and its 95% Confident Interval (CI) were used to estimate the association between *T. gondii* and neuropsychiatric disorder. Bivariate and multivariate logistic regression analysis was done for demographic data and associated risk factors.

Ethical considerations: All enrolled participants were informed with the aim of the study and an approval form was used to obtain written informed consent from each of them or their guardians. Seropositive patients were informed with their results and appropriate treatment was prescribed by the concerned physician.

Results

Individuals with neuropsychiatric disorder had significantly increased levels of serum IgG antibodies to *T. gondii* 58/162 (35.8%) when compared to controls 24/162 (14.8%), $P = 0.0022$. The OR for this association was 3.2 with 95% CI = 1.4952 to 6.8774. Meanwhile, the IgM antibody was found in 10/162 (6%) of patients with neuropsychiatric disorders and 6 subjects (3.7%) in control group. The difference is statistically insignificant, $P= 0.497$; OR 1.7105, CI 0.3949 to 7.4085 (Tab. 1). The demographic profiles of the patients with neuropsychiatric disorders and controls were compared (Tab. 2). The mean ages of patients and controls were 35.3± 9.1 years (range; 19-67 years) and 34.7± 8.9 years (17-64 years) respectively. The duration of illness for patients was 3.6 ±1.4 years (1.0-9.0 years). Non-working status was significantly higher ($P = 0.005$) among IgG positive patients (42.5%) compared to IgG positive controls (18.9%).

The majority of IgG positive patients (45.9%) had duration of education less than 12 years and (47.5%) belonged to low socioeconomic state. However, both gender and marital status have no significant differences between patients and control $P = 0.643$ and $P = 0.566$ respectively. The most prevalent neuropsychiatric disorder was schizophrenia patients (Tab. 3).

Bivariate analysis (Tab. 4) showed association between some sociodemographic characteristics and some behavioural characteristics in neuropsychiatric patients, including pet cats or dogs, consumption of raw vegetables and fruit, consumption of raw/ undercooked meat and exposure to soil. Multivariate analysis of sociodemographic and behavioral characteristics (Tab. 5) showed that exposure to soil led to highly significant differences between cases and control [adjusted OR (aOR) 7.31; 95% CI 3.6-15.1; $P= 0.001$]. Also, cats indoors showed [(aOR) 6.17, 95% CI 3.411-10.715, $P= 0{\cdot}001$] and the consumption of raw/undercooked meat [aOR 0.26; 95%CI 0.10-0.63; $P= 0{\cdot}002$] were significantly associated with increased *Toxoplasma* IgG seroprevalence in neuropsychiatric patients. Other behavioral characteristics did not show association with *T. gondii* infection.

Table1: Seroprevalence of IgG & IgM antibodies to *T. gondii* in neuropsychiatric patients & controls.

Immunogloblin	Neuropsyciatric patients (n=162)		Control (n=162)		P value	OR (95% confidence interval)
	No	%	No	%		
IgG positive	58	35.8	24	14.8	0.0022	3.2067 (1.4952 to 6.8774)
IgG negative	104	64.1	138	85.2		
IgM positive	10	6	6	3.7	0.497	1.7105(0.3949 to 7.4085)
IgM negative	152	94	156	96.3		

Table 2: Socio-demographic characters and seroprevalence of *T. gondii* IgG antibodies in studied subjects.

Demographic data		Neuropsyiacatric patients				Controls				P value
		n=162	%	IgG +ve	%	N=162	%	IgG +ve	%	
Age	≤19	12	7.4	1	8.3	12	7.4	0	0	0.4288
	20-29	22	13.6	3	13.6	24	14.8	2	8.3	0.5677
	30-39	24	14.8	6	25	23	14.2	2	8.7	0.1415
	40-49	41	25.3	15	36.6	47	29	8	17	0.0379
	50-59	36	22.2	18	50	30	18.5	6	20	0.0123
	60-69	23	14.2	13	56.5	23	14.2	5	21.7	0.6638
	≥70	4	2.5	2	50	3	1.9	1	33.3	0.6825
	Total	162	100	58	35.8	162	100	24	14.8	0.0022
Sex	Male	94	58	34	36.2	94	58	16	67	0.643
	Female	68	42	24	35.3	68	42	8	33	
Working status	Working	89	55	27	30.3	109	67.3	14	12.8	0.005
	Not working	73	45	31	42.5	53	32.7	10	18.9	
Marital status	Married	108	66.7	37	34.3	119	73.5	15	42	0.5661
	Single/widow/divorced	54	33.3	21	38.9	43	26.5	9	58	
Educational level	(>12years education	75	46.3	18	24	114	70.4	13	11.4	0.003
	(≤12years education)	87	53.7	40	45.9	48	29.6	11	22.9	
socioeconomic state	High	8	4.9	2	25	10	6.2	1	10	0.002
	Medium	93	57.4	27	29	104	64.2	9	8.7	
	Low	61	37.7	29	47.5	48	29.6	14	29.2	
Illness duration in years		1-9 3.6±1.4				-------				
Age	M±SD Range	35.3± 9.1 19-67				34.7±8.9 17-64				

Table 3: Seropositivity of anti-*T. gondii* IgG in 162 neuropsychiatric patients according to clinical diagnosis

Neuropsychiatric disorder	ICD-10	Patients No.	IgG +ve (%)	95% CI	P value
Schizophrenia	F20	52	18 (34.6 %)	0.6343 - 40.8180	0.022
Drug induce Psychosis	F19	34	12 (35.3 %)	2.6818 - 47.7685	0.048
Mild depression	F32.051	24	4 (16.7 %)	15.5931- 34.3951	0.864
Moderate depression	F32.151	10	6 (60 %)	1.1485 - 8.6073	0.010
Obsessive compulsive disorder	F42	8	2 (25 %)	6.0034 - 16.2164	0.582
Major depressive disorder	F32.251	6	2 (33.3 %)	15.3619 - 76.1724	0.387
Epilepsy	G40	6	6 (100 %)	17.6000- 37.5683	0.001
Mental retardation	F70-F71	4	2 (50 %)	14.4846 - 54.4301	0.178
Mental and behavioral disorders due to drug	F19	4	1 (25 %)	36.4171-45.2742	0.656
Alzheimer's disease	G30	4	2 (50 %)	14.4846 - 48.4301	0.178
Unspecified mental disorder	F99	4	1 (25 %)	36.4171-45.2742	0.656
Drug induce Parkinsonism	G21.1	4	2 (50 %)	14.4846 - 48.4301	0.178
Depressive conduct disorder	F92.0	2	0 (0%)	24.4316-52.9449	0.679
Total		162	58 (35.8 %)	1.4952 to 6.8774	0.0022

as compared with 14.8% seroprevalence of anti-*T. gondii* IgG antibodies in controls (24/162).

Table 4: Bivariate logistic regression analysis of risk factors associated with *T. gondii* among studied subjects.

Character		Neuropsychaitric patients				Control subjects				Total			
		No	IgG +ve	%	P	No	IgG +ve	%	P	No	IgG +ve	%	P
Residence	Urban	94	37	39.4	0.267	91	15	16.5	0.501	185	52	28.1	0.184
	Rural	68	21	30.9		71	9	12.7		139	30	21.6	
Contact with cat/dog	Yes	97	45	46.4	0.006	80	19	23.8	0.001	177	64	36.2	<0.0001
	No	65	13	20		82	5	6.1		147	18	12.2	
Eating raw undercooked vegetables or fruits	Yes	91	36	39.6	0.259	89	14	15.7	0.722	180	50	27.8	0.250
	No	71	22	31		73	10	13.7		144	32	22.2	
Eating raw/undercooked meat	Yes	86	38	44.2	0.018	78	17	21.8	0.016	164	55	33.5	0.005
	No	76	20	26.3		84	7	8.3		160	27	16.9	
Contact with soil	Yes	104	49	47.1	0.001	98	19	19.4	0.043	202	68	33.7	<0.0001
	No	58	9	15.5		64	5	7.8		122	14	11.5	
Past history of surgery	Yes	59	19	32.2	0.467	53	8	15.1	0.984	112	27	24.1	0.6989
	No	103	39	37.9		109	16	14.7		212	47	22.2	
History of blood transfusion	Yes	29	17	58.6	0.048	24	6	25	0.345	53	23	43.4	0.001
	No	133	41	30.8		138	18	13.0		271	59	21.8	

Table 5: Multivariate logistic regression analysis of psychiatric patients' characteristics & *T. gondii* infection.

Characteristics	Adjusted Odd ratio	95 % C.I.	P value
Residence area	0.89	0.429 – 1.812	0.691
Contact with cat and/or dog	6.17	3.411- 10.715	0.001
Eating raw /undercooked meat	0.26	0.10 – 0.63	0.002
Contact with soil	7.31	3.6 – 15.1	0.001
History of blood transfusion	0.94	0.61 – 1.67	0.83

Discussion

The mental and behavioral disorders have major public health problem. It affects about 10% to 16% of the population in any given year (Wang *et al,* 2007). Twelve percent of the global disease burden was shared by these disorders (WHO, 2001). The treatment is mostly symptomatic because the etiology is still obscure. Although it is hypothesized to be multifactorial and related to genetic and environmental mediation, there is a great assumption for the role of microbial agents in the causation of psychiatric disorders. The infectious agents take major part in attention, such as *Toxoplasma gondii*, *herpes simplex virus*, *cytomegalovirus* and *influenza virus* (Fekadu *et al,* 2010).

In the present study, a significant difference was found between neuropsychiatric patients 35.8% and controls 14.8 % for *T. gondii* IgG. Regional variations in the incidence of *T. gondii* infection rates from one country to another or even within the same country, has been well documented. In different areas in Saudia Arabia, there was a diversity between levels, it was lower than our study in some areas: 21.3% in Almadinah Almunawwarah (Immam *et al,* 2016), 22.4% in Riyadh (Ahmed, 1992), 24.1% in Jazan (Aqeely *et al.,* 2014), 29.4% in Makkah Al-Mukkaramah (Al-Harthi *et al,* 2006), 32.3% in Najran were seropositive for toxoplasmosis by ELISA-IgG (El-Shahawy *et al,* 2014). On the contrary, some studies showed higher levels of seroprevalence than the current study: 42.1% in Dammam District (Abbas *et al,* 1986) and 52.1% in Asir Region (Al-Amari, 1994). In a study by Al-Hussainya *et al.* (2015) in Jeddah, *T. gondii*-IgG was 31.75% among schizophrenic patients and 25.64% in patients with major depressive disorders compared to an incidence of 14.55% in healthy ones.

Regarding other Arab Countries, Morsy *et al.* (1978) in Jordan reported positive toxoplasmin skin tests in children in the Royal Institute for Mentally Retarded Children.

Wishahy *et al.* (1975) in Egypt reported toxoplasmosis in children with some neurological manifestations and Rifaat *et al.* (1975) reported infantile toxoplasmosis and some neurological disorders. Mabrouk and Dahawi (1991) studied 42 meningoencephalitis patients with negative CSF cultures for common pathogenic bacteria. The seropositive *Toxoplasma*-IgG by IFA were 10/42 (26%). Clinical presentation and CSF changes were found with high antibody titers. They incriminated toxoplasmosis as an etiologic agent for meningo-encephalitis.

In United Arab Emirates, seroprevalance was 34% in blood donors (Uduman *et al,* 1998), 29.8% seropositives in Doha, Qatar (Abu-Madi *et al,* 2008). In Libya *T. gondii* IgG antibodies in psychiatric patients was 50.3%, & 33% in control volunteers (Elsaid *et al,* 2014).

In Aden City, Yemen seropositive rate was 64.3% (Muqbil and Alqubatii, 2014). Seroprevalences variability from an area to another, not only depended on climatic and geographical localities but also on cultural behaviors (Pappas *et al,* 2009).

In other studies comparing *T. gondii* in psychiatry patients to controls, great varieties were noted; at Durango City, Mexico, the prevalence of *T. gondii* infection in psychiatric inpatients was 18.2% which is significantly higher than in controls 8.9 % (Alvarado-Esquivel *et al,* 2006). In Chinese psychiatric patients, it was 17·3% while it was 12·36% in controls (Cong *et al,* 2015). Koshy and Cabral (2014) in USA stated that brain-*Toxoplasma* interaction is critical to the symptomatic disease produced by *Toxoplasma*, but with little understanding of the cellular or molecular interaction between cells of the CNS and the parasite. All of the above mentioned studies showed evidence that *T. gondii*-IgG in neuropsychiatric patients was significantly higher than *T. gondii*-IgG in controls which agreed with the present data.

Some reports are linking *Toxoplasma* infection to psychiatric disorders with the fact

that *Toxoplasma* infection alters the host's immunological status with oxidative stress producing toxic free radicals like reactive oxygen species and nitric oxide. These free radicles are involved in the pathophysiology of many psychiatric and neurodevelopmental disorders (Meyer *et al,* 2011). Nevertheless, there was no statistical difference between seroprevalence of IgM in neuropsychiatric patients and controls $P = 0.497$. This was in accordance with the study of Cong *et al,* 2015 which found that no relation between them. This confirmed the assumption of the role for latent and not recent infection of toxoplasmosis in neuropsychiatric disorder.

There is no significant difference when comparing each age group between studied and controls except for age group 40-49 and 50-59. The increase in patients' age went side by side with increase in the prevalence of *Toxoplasma* IgG (Cong *et al,* 2015; Owakowska *et al,* 2014). On the other hand; a Mexican study did not find any relation between age and prevalence of *Toxoplasma* IgG (Alvarado-Esquivel *et al,* 2006).

Working, education and socioeconomic status showed significant differences between the two groups. Being not working and having a low level of education is usually coexisting in most of the neuropsychiatric patients. This is mostly linked to patient infections exposure as these people might live in a poor environmental and sanitary condition which triggers their infections. When specific diagnoses of psychiatric diseases were analyzed, we found that most prevalent disease was schizophrenia. The prevalence of *Toxoplasma* IgG was statistically significant among schizophrenic patients compared to control group. This is in accordance with forty two studies analysis that carried out in 17 countries and reported that schizophrenia patients had increased seroprevalence of *T. gondii* than controls (Torrey *et al,* 2007).

In the present study, significant differences of *Toxoplasma* IgG were found in moderate depression and drug induced psychosis. Al-Hussainya *et al.* (2015) reported that the level of *Toxoplasma* IgG was higher in depressed patients compared to controls. Interestingly all epileptic patients had positive IgG-antibodies against *T. gondii* with highly significant differences than controls. The relation between epilepsy and toxoplasmosis was strongly postulated. A previous study on this relation concluded that chronic toxoplasmosis infection might be an etiological factor for cryptogenic epilepsy (Yazar *et al,* 2003).

Linear regression bivariate analysis revealed that contact to cats and/or dogs and contact to soil were associated with high seroprevalence rate of *Toxoplasma* IgG than others. Eating raw or under cocked meat and positive history of blood transfusion were also correlated to increased serofrequency rate of *Toxoplasma* IgG. This finding is in accordance to other studies which prove the role of cats in disease transmission (Zemene *et al,* 2012). Contact with incriminated soil transmitted toxoplasmosis, mainly in Jazan (Aqeely *et al,* 2014) as that oocyst might present in soil which may be spread along with dusty winds (Seasonal Ghubrah) that is predominantly present in Jazan District.

Saleh *et al*. (2016) in Egypt reported several means of acquiring toxoplasmosis in humans: 1- Through vertical transmission from an infected mother to her fetus (Congenital). 2- Ingestion of infectious oocysts from the environment (usually from soil contaminated with feline feces), 3- Cleaning cat litter boxes. 4- Drinking unpasteurized goat milk or equine milk. 5- Ingestion of tissue cysts in meat from an infected animal, 6- Eating unwashed raw vegetables or fruits. 7- Blood transfusion or organ transplantation from an infected donor, (Acquired infection). 8- By needle-stick injuries that occurs accidentally as well as handling specimens that may contain viable organisms during laboratory investigations and experimental work.

Conclusion

Toxoplasmosis is a worldwide distributed disease with a complex epidemiology. The risk of infection for humans depends on their contact with infective oocysts in a contaminated environment and on the amount of tissue cysts located within consumed meat.

In the present study, the psychiatric patients in Al-Amal Neuropsychiatry hospital, Jazan, had a significantly higher seroprevalence of *T. gondii* IgG than the controls. Thus, there might be a causal relationship between toxoplasmosis and the etiology of psychiatric diseases. The outcome data suggested that the contact with cat and/dogs indoors or outdoors and also contaminated soil contact might be the most important routes of *T. gondii* transmission in the studied psychiatric patients.

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References

Abbas, SA, Basalamah, A, Serebour, F, Alfonso, M, 1986: The prevalence of *Toxoplasma gondii* antibodies in Saudi women and the outcome of congenital infection among newborns in Saudi Arabia. Saudi Med. J. 7:346-54.

Abu-Madi, MA, Al-Molawi, N, Behnke, JM, 2008: Seroprevalence and epidemiolo-gical correlates of *Toxoplasma gondii* infections among patients referred for hospital-based serological testing in Doha, Qatar, Parasites and Vectors, 1, 39-44.

Ahmed, MM, 1992: Seroepidemiology of *Toxoplasma* infection in Riyadh, Saudi Arabia. J. Egypt. Soc. Parasitol. 22, 2:407-13.

Al-Amari, OM, 1994: Prevalence of antibodies to *Toxoplasma gondii* among blood donors in Abha, Asir Region, south-western Saudi Arabia. J. Egypt. Publ. Hlth. Assoc. 69, 1/2:77-88

Al-Harthi, SA, Jamaoom, MB, Ghazi, HO, 2006: Seroprevalence of *Toxoplasma gondii* among pregnant women in Makkah, Saudi Arabia.2006 Umm Al-Qura Univ. J. Sci. Med. Eng. 18, 2:217-27

Al-Hussainya, NH, Al-Saedib, AM, Al-lehaibib, JH, Al-lehaibib, YA, Al-Sehlib, YM, *et al*, 2015: Serological evidences link toxoplasmosis with schizophrenia and major depression disorder J. Microsc. Ultrastruct. 3:148-53.

Alvarado-Esquivel, C, Alanis-Quiñones, OP, Arreola-Valenzuela, MA, Rodríguez-Briones, A, Piedra-Nevarez, LJ, *et al*, 2006: Seroepidemiology of *Toxoplasma gondii* infection in psychiatric inpatients in a northern Mexican City. BMC Infect. Dis. 6:178-84.

Alvarado-Esquivel, C, Liesenfeld, O, Márquez-Conde, JA, Estrada-Martínez, S, Dubey, J P, 2010: Seroepidemiology of infection with *Toxoplasma gondii* in workers occupationally exposed to water, sewage, and soil in Durango, Mexico. J. Parasitol. 96, 5:847-50.

Alvarado-Esquive, C, Arrillo-Oropeza, D, Pacheco-Vega, SJ, Hernández-Tinoco, J, Salcedo-Jaquez, M, *et al*, 2015a: *Toxoplasma gondii* exposure in patients suffering from mental and behavioral disorders due to psychoactive substance use. BMC Infect. Dis. 15:172-8.

Alvarado-Esquivel, C, Sánchez-Anguiano, L F, Hernández-Tinoco, J, Arreola-Cháidez, E, López, J, Salcido-Meraz, KI, ***et al*, 2015b:** High seroprevalance of *Toxoplasma gondii* infection in female sex workers: A case control study Europ. J. Microbiol. Immunol. 5, 4:285-92

Aqeely, H, El-Gayar, EK, Perveen Khan, D, Najmi, A, Alvi, A, *et al*, 2014: Seroepidemiology of *Toxoplasma gondii* amongst pregnant women in Jazan Province, Saudi Arabia J Trop Med, doi.org/10.1155/2014/913950.

Carruthers, VB, Suzuki, Y, 2007: Effects of *Toxoplasma gondii* infection on the brain. Schizophr. Bull. 33:745-51.

Cong, W, Dong, W, Bai, L, Wang, TX, Ni, X T, *et al*, 2015: Seroprevalence and associated risk factors of *Toxoplasma gondii* infection in psychiatric patients: a case-control study in eastern China Epidemiol. Infect. 143, 3103-9.

Dubey, JP, 2010: Toxoplasmosis of Animals and Humans, 2nd edn. Boca Raton, Florida: CRC Press.

Elsaid, MMA, Azbedah, AG, El-Alem, DE, Alkout, A, 2014: The prevalence of *Toxoplasma gondii* infection in psychiatric patients in Tripoli, Libya. J. Amer. Sci. 10, 5: http://www.Jofamericanscience. Org.

El-Shahawy, IS, Khalil, MI, Bahnass, MM, 2014: Seroprevalence of *Toxoplasma gondii* in women in Najran City, Saudi Arabia. Saudi Med. J. 35, 9:1143-6.

Fabiani, S, Pinto, B, Bruschi, F, 2013: Toxoplasmosis and neuropsychiatric diseases: can

serological studies establish a clear relationship? Neurol. Sci. 34:417-25

Fekadu, Al, Shibre, T, Cleare, AJ, 2010: Toxoplasmosis as a cause for behavior disorders--overview of evidence and mechanisms. Folia Parasitol (Paraha) 57, 2:105-13.

Flegr, J, 2015: Neurological and neuropsychiatric consequences of chronic *Toxoplasma* infection. Curr. Clin. Mic. Reports 2, 4:163-72.

Hamidinejat, H, Ghorbanpoor, M, Hosseini, H, Alavi, SM, Nabavi, L, *et al*, 2010: *Toxoplasma gondii* infection in first-episode and inpatient individuals with schizophrenia Int. J. Infect. Dis. 14, 11:978-81.

Immam, NFA, Azzam, EAA, Attia, AA, 2016: Seroprevalence of *Toxoplasma gondii* among pregnant women in Almadinah Almunawwarah KSA. J. Taibah Univ. Med. Sci. 11, 3:255-9.

Jones, JL, Kruszon-Moran, D, Wilson, M, McQuillan, G, Navin, T, McAuley, JB, 2001: *Toxoplasma gondii* infection in the United States: Seroprevalence and risk factors. Am. J. Epidemiol, 154, 4:357- 65.

Koshy, AA, Cabral, CM, 2014: 3-D imaging and analysis of neurons infected in vivo with *Toxoplasma gondii*. J. Vis. Exp. Dec 9;(94). doi: 10.3791/52237.

Meyer, U, Feldon, J, Dammann, O, 2011: Schizophrenia and autism: both shared and disorder-specific pathogenesis via perinatal inflammation. Pediatr. Res. 69:26-33.

Mabrouk, MA, Dahawi, HS, 1991: *Toxoplasma* antibodies in patients with meningoencephalitis. J. Egypt. Soc. Parasitol. 21, 2:547-51.

Morsy, TA, El Dasouqi, ST, Michael, SA, 1978: Toxoplasmin skin tests in mentally retarded children in Jordan. J. Egypt. Pub. Hlth. Assoc. 53, 1/2:87-90.

Muqbil, NA, Alqubatii, MA, 2014: Seroprevalence of toxoplasmosis among women in Aden city, Yemen. Arch. Biomed. Sci. 2, 2:42-50.

Nowakowska, D, Wujcicka, W, Sobala, W, Spiewak, E, Gaj, Z, *et al*, 2014: Age-associated prevalence of *Toxoplasma gondii* in 8281 pregnant women in Poland between 2004 and 2012. Epidemiol. Infect. 142, 3:656-61.

Pappas, G, Roussos, N, Falagas, ME, 2009: Toxoplasmosis snapshots: global status of *Toxoplasma gondii* seroprevalence and implications for pregnancy and congenital toxoplasmosis. Int. J. Parasitol. 39:1385-94.

Rifaat, MA, Wishahy, AO, Morsy, TA, Sadek, MSM, Hussein, D, 1975: Toxoplasmosis and some neurological disorders in Egypt. J. Egypt. Pub. Hlth. Assoc. 50, 1:1-10.

Rorman, E, Zamir, CS, Rilkis I, Ben-David, H, 2006: Congenital toxoplasmosis—prenatal aspects of *Toxoplasma gondii* infection. Reprod. Toxicol. 21:458-72.

Saleh, AMA, Al-Agroudi, MA, Morsy, TA, 2016: Occupational, nosocomial or hospital acquired toxoplasmosis. J. Egypt. Soc. Parasitol. 46, 2:407-18.

Torrey, EF, Bartko, JJ, Lun, ZR, Yolken, RH, 2007: Antibodies to *Toxoplasma gondii* in patients with schizophrenia: A meta-analysis. Schizophr. Bull. 33, 3:729-36.

Uduman, SA, Mohamed, HN, Bener, A, Dar, FK, 1998: The prevalence of *Toxoplasma gondii* specific IgG and IgM antibodies in blood donors in Al Ain, United Arab Emirates indicates a potential risk to recipients. J. Commun. Dis. 30, 4: 237-9.

Wang, PS, Aguilar-Gaxiola, S, Alonso, J, Angermeyer, MC, Borges, G, *et al*, 2007: Use of mental health services for anxiety, mood, and substance disorders in 17 countries in the WHO world mental health surveys. Lancet 8, 370 (9590):841-50.

WHO, 1992: The ICD-10 Classification of Mental and Behavioral Disorders: Clinical Descriptions and Diagnostic Guidelines. Geneva, Switzerland.

WHO, 2001: World Health Report 2001. Mental Health: New Understanding, New Hope; World Health Organization, Geneva, 178, Switzerland.

Wishahy, AO, Rifaat, MA, Morsy, TA, El Naggar, BA, 1975: Toxoplasmosis in children with some neurological manifestations. J. Trop. Med. Hyg. 75, 12:255-6.

Yazar, S, Arman, F, Yalçin, S, Demirtaş, F, Yaman, O, *et al*, 2003: Investigation of probable relationship between *Toxoplasma gondii* and cryptogenic epilepsy. Seizure 12, 2:107-9.

Zemene, E, Yewhalaw, D, Abera, S, Belay, T, Samuel, A, *et al*, 2012: Seroprevalence of *Toxoplasma gondii* and associated risk factors among pregnant women in Jimma town, Southwestern Ethiopia, BMC Infect. Dis. 12, 337, doi: 10. 1186/1471-2334-12-337

Zhou, P, Chen, Z, Li, H, Zheng, H, He, S, *et al*, 2011: *Toxoplasma gondii* infection in humans in China. Parasites Vectors 4, 1:165) doi: 10.1186/1756-3305-4 -165.