How to Cite:
Al-Shabani, Z. K., & Al-Waaly, A. B. M. (2022). Effect of Toxoplasma gondii infection in causing psychiatric diseases in Al-Diwaniyah governorate, Iraq. *International Journal of Health Sciences*, *6*(S6), 10279–10288. https://doi.org/10.53730/ijhs.v6nS6.12588

Effect of *Toxoplasma gondii* infection in causing psychiatric diseases in Al-Diwaniyah governorate, Iraq

Zahra K. Al-Shabani
Department of Biology, College of Science, University of AL- Qadisiyah

Ali B. Mohsen Al-Waaly
Department of Biology, College of Science, University of AL- Qadisiyah
*Corresponding author email: ali.alwaaly@qu.edu.iq

Abstract---The serological examination for specific antibodies to *T. gondii*included 335 patients who were confirmed by the specialist doctor for a mental and neurological disease (Depression, anxiety, schizophrenia, addiction) who were attending Al-Diwaniyah Teaching Hospital, the outpatient clinics and the nursing home in Al-Diwaniyah Governorate for the period from the beginning of the month February until the end of June 2022. The information data on age and gender was recorded, and the control group included 50 people with toxoplasmosis and no history of any of the psychiatric and neurological diseases included in the current study, to study the effect of infection with the parasite *T. gondii* in causing mental and neurological diseases. The results of the examination showed that they were infected with toxoplasmosis with a total infection rate of 27.26%, where the highest percentage of infection was recorded in schizophrenia patients by 32%, then depression by 30%, then addiction by 25.17%, and the lowest percentage of infection in patients with anxiety with an infection rate of 20%.

Keywords---*T. gondii*, Alzheimer, depression, anxiety, schizophrenia.

Introductions

Toxoplasmosis is caused by infection with a protozoan parasite that is transmitted from infected animals (such as a cat) to humans, and if caught by a pregnant woman, it can lead to severe harm to the fetus, as it may develop into non-pregnancy, abortion and sometimes birth defects in the context of toxoplasmosis. congenital, infection with the parasite *Toxoplasma gondii* is widespread throughout the world (Al-Malki, 2021). Most people who become

infected with *T.gondii* are not aware of it because they have no symptoms at all. Initially, patients with influenza feel swollen lymph nodes or muscle pain that lasts for a month, then develops into acute toxoplasmosis, which causes damage to the brain, eyes, or other organs(CDC, 2020).

It was found that approximately one third of people with congenital toxoplasmosis show severe neurological changes, including hydrocephalus, and mental retardation (El-Beshbishi*et al.*,2020). In adults, latent infection of *T. gondii* is associated with an increased risk of psychiatric disorders, such as schizophrenia, anxiety, mixed depression, personality disorders, and obsessive-compulsive disorder (Xiao et al.,2018). However, little is known about the potential link between latent *T. gondii* infection and neurodegenerative disease, and the results of studies are somewhat conflicting (Prandota*et al.*, 2014). The aim of the study was to evaluate the incidence of toxoplasmosis and its effect on psychiatric conditions such as depression, anxiety, schizophrenia and addiction.Toxoplasmosis is very important especially in pregnant women and in immunocompromised patient (Al-Gharibawi and Al-waaly,2021). This study came to assess the relationship between infection with *T. gondii* and its effect on some psychological diseases

Material and Methods

Study community

335 psychiatric patients (schizophrenia,depression and anxiety) with *T.gondii* were selected from the nursing home and auditors of Al-Diwaniyah Teaching Hospital for psychiatric and psychiatric diseases and outpatient clinics. For the period from the beginning of February until the end of May 2021 until the end of December 2021, and clinical diagnoses were recorded according to the pre-prepared diagnostic and epidemiological manual. The control group included 50 control group, and all participants ranged in age from 75-86 years and provided written initial consent (research ethics) after explaining the study procedures.

Serological analysis

Blood samples were collected in ethylenediaminetetraacetic acid (EDTA) vials from patients and controls using Venipuncture drawers. Serum was separated from whole blood immediately after blood collection by centrifugation at 3500 × g for 5 min, and stored at −70°C until analysis. Specific anti-Toxoplasma IgM and IgG antibodies in serum samples were quantitatively measured by mini VIDAS® assays (Renard et al., 2021; Al-Hassani& Al-Mayali,2020).

Statistical analysis

Multivariate logistic regression models were used to estimate the association between *T.gondii* infection and mental disorders by means of adjusted odds ratios (OR) with a 95% confidence interval (CI) with adjustment for age and gender among others. All tests were divided and considered as ($P< 0.05$). Statistically significant. Data management and analysis were performed using SPSS software (version 24.0; SPSS).

Results

Toxoplasma gondii infection inpsychiatric diseases

The results of the examination of 335 patients who were diagnosed with some psychiatric diseases by specialized doctors in Al-Diwaniyah Governorate, and as in Table (1), showed that they were infected with toxoplasmosis, with a total infection rate of 27.16%, where the highest rate of toxoplasmosis was recorded among patients with schizophrenia by 32%, then depression patients by 30%, and then 25.71% of addiction patients, and the lowest in anxiety patients, with a percentage of 20%, respectively. The results of the statistical analysis also showed significant differences (P.value = 0.00) in the incidence of toxoplasmosis and the type of mental illness. The results of the current study revealed an association between Toxoplasmosis infection and an increased risk of mental and neurological diseases compared to the control group, where toxoplasmosis plays an important role in causing mental health disorders in patients with schizophrenia (OR=2.47), which is the strongest association after depression (OR =2.27), while the lowest correlation value for odds ratio (OR = 1.81) was recorded in addictive patients and (OR = 1.31) in anxiety patients.

Table 1
Toxoplasma gondii infection causes in some psychiatric diseases

psychiatric diseases	No. tested	No. infected	Prevalence%	Odds Ratio (OR)
Schizophrenia	100	32	32	2.47
Depression	100	30	30	2.25
addiction	35	9	25.71	1.81
anxiety	100	20	20	1.31
total	335	91	27.16	
control	50	8	16	------
X^2	P . Value =0.00			

Prevalence of *Toxoplasma condii* on schizophrenia patients by age

The results of our study indicated the role of infection with the Toxoplasma parasite in schizophrenia. The results did not record any significant differences according to the age group, and the group (20-30) years recorded the highest infection rate of 34.28%, followed by the category (31-40) years with a rate of 33.33% and the category (41-50) years 30% (Table 2).

Table 2
Prevalence of*T.gondii* among schizophrenia patients by age groups

Age group	No. tested	No. infected	Prevalence%
30 – 20	35	12	34.28

40 – 31	30	10	33.33
50 – 41	20	6	30
60 – 51	15	4	26.66
total	100	32	32
X^2	p.value = 0.952*		

Prevalence of *Toxoplasma condii* on schizophrenia patients by gender

The results of the study indicated, as in Table (3) which shows the role of infection with *Toxoplasma condii* in schizophrenia patients according to gender, as the results did not record any significant differences according to (P>0.05) and that the female gender recorded an infection rate of 34% compared to With male gender 30%.

Table 3
Prevalence of*T.gondii* among schizophrenia patients by gender

Gender	No. tested	No. infected	Prevalence%
male	50	15	30
female	50	17	34
total	100	32	32
X^2	0.668*		

Prevalence of *Toxoplasma condii* on depression patients by gender

The results of the study indicated, and as Table (4) shows, the Prevalence of *T.gondii*infection in depression, the results did not record any significant differences according to (P>0.05), and the age group 51-60 years recorded the highest infection rate of 33.33%, followed by the group 20-30 years with 31.42% and the least 31-40 years with 26.66%.

Table 4
Prevalence of*T.gondii*among depressed patients by age groups

Age group	No. tested	No. infected	Prevalence%
30 - 20	35	11	31.42
40 - 31	30	8	26.66
50 - 41	20	6	30
60 - 51	15	5	33.33
Total	100	30	30
X^2	P . Value =0.965		

Prevalence of *Toxoplasma condii* on depression patients by gender

The results of the study indicated, as in Table (5), which shows the role of *T.gondii* infection among depression by gender, as the results did not record any

significant differences according to (P>0.05) and that the female gender recorded an infection rate of 31.66% compared with Male gender 27.5%.

Table 5
Prevalence of*T.gondii* among depressed patients by gender

Gender	No. tested	No. infected	Prevalence %
male	40	11	27.5
female	60	19	31.66
total	100	30	30
X^2	p.value = 0.656		

Prevalence of *Toxoplasma condii* on anxiety **patients by gender**

The results of the study indicated, as shown in Table (6), the role of anxiety in the physical predisposition to infection with the *T.gondii*, the results did not record any significant differences according to (P > 0.05), and the age group 20-30 years recorded an infection rate of 22.5%, followed by the group 41- 50 and 51-60 years with 20% each, respectively.

Table 6
Patients infected with the *T.gondii* among anxious patients by age groups

Age group	No. tested	No. infected	Prevalence %
30 - 20	40	9	22.5
40 - 31	30	5	16.66
50 - 41	20	4	20
60 - 51	10	2	20
Total	100	20	20
X^2	0.947*		

Prevalence of *Toxoplasma condii* on anxiety **patients by gender**

The results of the study indicated, as in Table (7), which shows the role of infection with the Toxoplasma parasite in the occurrence of anxiety disease according to the gender of the patient, as the results did not record any significant differences according to (P>0.05) and that the male sex recorded a higher infection rate of 23.07% compared to With female gender 14.28%.

Table 7
Patients infected with the *T.gondii* among anxious patients by gender

Gender	No. tested	No. infected	Prevalence %
male	65	15	23.07
female	35	5	14.28
total	100	20	20
X^2	p.value = 0.295		

Discussions

Flegr & Horacek (2020) Infection with the parasite Toxoplasma, which infects about 33% of the world's population, is associated with an increased risk of several mental health disorders, the most severe of which is schizophrenia. It is not known whether schizophrenia is strongly associated with this infection, or whether This association was an extensive family history study that used data from 367 people tested for toxoplasmosis who participated in an online survey looking for associations of this infection with 24 mental health disorders and evidence of poor mental health. The typical symptoms associated with toxoplasmosis were are anxiety, and the disorders associated with toxoplasmosis were autism (OR = 4.78), schizophrenia (OR = 3.33), attention deficit hyperactivity disorder (OR = 2.50), obsessive-compulsive disorder (OR = 1.86), antisocial personality disorder (OR = 1.86), 1.63), learning disabilities (OR = 1.59), and anxiety disorder (OR = 1.48), toxoplasmosis can play an important role in the pathogenesis of mental health disorders and its association with schizophrenia is the second strongest association after autism.

The study agreed with Carter(2013) in not only the role of the parasite Toxoplasma gondii in schizophrenia and neurological disorders, but also in Alzheimer's disease or Parkinson's disease, cancer, cardiomyopathy and autoimmune disorders, as shown through the life cycle of the parasite, the pathogen interacts With about 3,000 host genes or proteins, including genes for multiple sclerosis, Alzheimer's disease, schizophrenia, bipolar disorder and depression. The researcher Burgdorf*et al.* (2019) indicated that exposure to the parasite T. gondii may be a causative factor contributing to the development of schizophrenia and that exposure to cytomegalovirus (CMV) may be a causative factor contributing to serious mental disorders, and that changes in dopamine levels have a role in Causing the behavioral changes associated with toxoplasmosis in humans. These include prolonged reaction time, decreased long-term focus, decreased cognition and specific changes in neurodegenerative and psychiatric disorders.

A recent large-scale study conducted in Denmark revealed that seropositivity for *T. gondii*is associated with schizophrenia (OR = 1.47) but a stronger association (OR = 2.78) was observed after exclusion of diagnosed participants. Blood samples were collected beforehand, indicating that *T. gondii* infection may be a causative agent of schizophrenia (Burgdorf*et al.*, 2019). Several mechanisms have been suggested to link *T. gondii* to psychiatric disorders. Toxoplasmosis infection, especially in schizophrenia, represents that the association of toxoplasmosis with schizophrenia is due to dysregulation of dopamine and modulation of dopamine signaling by the parasite. Some researchers have suggested that hyperactive dopamine signal transduction may It plays a role in the pathophysiology of schizophrenia (McConkey*et al.*, 2013).

Hinze-Selch*et al.* (2017) reported that T. gondii infection is more common in schizophrenia. The lifelong interaction of the parasite with the host's immune system includes T-cell-induced tryptophan degradation/IFN-gamma and provides a challenge to the host beyond a potential role in the etiology of T. gondii. Schizophrenia. The results agreed with Khademvatan*et al.* (2014), which

confirmed that *T. gondii* as a risk factor for schizoaffective disorder in females only, and the differences in latent toxoplasmosis were not statistically significant between age groups. The results differed with Kezai*et al.* (2020) by recording a relationship with toxoplasmosis in patients with schizophrenia with age groups, as toxoplasmosis was previously associated with an increased risk of schizophrenia in several epidemiological studies.

The study agreed with Kezai*et al.* (2020) that no significant differences were recorded between Toxoplasmosis sufferers with schizophrenia and its relationship to sex, as the males recorded an immune level of IgG 41 (73.2%) positive and IgG negative 15 (26.8%) compared with the positive control 30. (53.6%) and negative 26 (46.4%). In Wang et al. (2014) assessed the relationship between different infectious agents and depression, no significant association was found, and the OR was calculated as 1.36. The study agreed with (Suvisaari*et al.*, 2017) that it did not record statistical differences in seropositivity of *T. gondii* and its association with depression, anxiety, alcohol use for 12 months and current depressive symptoms. The results of the study of Nayeri*et al.* (2019) indicated that based on the results of the immunological analysis, depressed patients had a lower seroprevalence of *T. gondii* compared to the control, as major depression did not show any association with anti-toxoplasma IgG and anti-toxoplasma IgM. This is consistent with our results That evaluates the relationship between toxoplasmosis and mental disorders

Our study agreed with the study of NayeriChegeni*et al.* (2019) that there is no association between sex factor, Toxoplasmosis infection and depression.A study Hlaváčová*et al.* (2021) indicated that Effect of toxoplasmosis on depression in a specific group of men and women attending fertility clinics, based on BDI scores between women and men, found higher levels of depression in women than in men. These results are consistent with studies that have shown higher levels of depression in older women who are toxoplasma positive and in pregnant women, it did not find a significant difference in levels of depression between toxoplasma positive women and negative women diagnosed with fertility problems, as the depression scores in these two groups were similar to those in those in In women with toxoplasmosis without fertility problems, female infertility is associated with increased depression (Duffy *et al.*, 2015; Groër*et al.*, 2011).

Hlaváčová et al, (2021) found a significant difference in depression levels between T-positive and T-negative men and also indicated that T-positive men can be protected from depression, as host infection is characterized by elevated levels of IL-10, which can reduce depression through Its immunosuppressive and anti-inflammatory activities. The study agreed with Bak*et al.* (2018) that it did not record any significant differences in the anti-*T. gondii* Ab antibodies between Toxoplasma gondii infection in anxiety patients and age groups, as the age group less than 30 years recorded 3% and the age group 30- 35 years 26.5% and over 51 years 10% in a study to determine whether *T. gondii*seroprevalence is associated with suicidal behavior and other psychiatric symptoms such as anxiety Coccaro*et al.* (2016) reported increased status and trait anxiety scores in *T. gondii* seropositive patients. Alvarado-Esquivel *et al.* (2016) demonstrated the association between *T. gondii* infection and mixed anxiety and depressive disorder and Markovitz et al (2015) reported that the *T. gondii* serogroup had a higher risk

of developing generalized anxiety disorder. *T. gondii*(Mitra*et al.*, 2013; Cook *et al.*, 2015).

Alvarado-Esquivel *et al.* (2016) noted that the association of *T. gondii* infection, mixed anxiety and major depressive disorder is affected by gender and age. A strong association was recorded in females and patients aged 31-50 years. The study agreed with Sapma*zet al.* (2019) that there were no statistically significant differences between anxious patients with Toxoplasma gondii. Identification of the structural causes of depression is important for the treatment process, and toxoplasmosis may be related to mental disorders. The aim was to assess the relationship between the positivity of *Toxoplasma gondii*seropositivity and depression in children and adolescents.

References

Al-Gharibawi, Y. K., &Alwaaly, A. B. (2021). Pregnant Women With Toxoplasmosis In Al-Hai City, Wasit Governorate, Iraq. *NVEO-NATURAL VOLATILES & ESSENTIAL OILS Journal| NVEO*, 5431-5440.

Al-Hassani, M. K. K., & Al-Mayali, H. M. H. STUDY OF VARIATIONS IN INTERLEUKIN-6 AND TNFa LEVELS OF SERUM IN LABORATORY ANIMALS EXPERIMENTALLY INFECTED WITH CUTANEOUS LEISHMANIASIS.

Al-Malki, E. S. (2021). Toxoplasmosis: stages of the protozoan life cycle and risk assessment in humans and animals for an enhanced awareness and an improved socio-economic status. Saudi Journal of Biological Sciences, 28(1), 962-969.

Alvarado-Esquivel, C., Sanchez-Anguiano, L. F., Hernandez-Tinoco, J., Berumen-Segovia, L. O., Torres-Prieto, Y. E., Estrada-Martinez, S., . . . Garcia, I. B. (2016). Toxoplasma gondii infection and mixed anxiety and depressive disorder: a case-control seroprevalence study in Durango, Mexico. Journal of clinical medicine

Attias, M., Teixeira, D. E., Benchimol, M., Vommaro, R. C., Crepaldi, P. H., & De Souza, W. (2020). The life-cycle of Toxoplasma gondii reviewed using animations. Parasites & vectors, 13(1),

Bak, J., Shim, S.-H., Kwon, Y.-J., Lee, H.-Y., Kim, J. S., Yoon, H., & Lee, Y. J. (2018). The association between suicide attempts and toxoplasma gondii infection. Clinical Psychopharmacology and Neuroscience, 16(1), 95.

Burgdorf, K. S., Trabjerg, B. B., Pedersen, M. G., Nissen, J., Banasik, K., Pedersen, O. B., . . . Erikstrup, C. (2019). Large-scale study of Toxoplasma and Cytomegalovirus shows an association between infection and serious psychiatric disorders. Brain, behavior, and immunity, 79, 152-158.

Carter, C. (2013). Toxoplasmosis and polygenic disease susceptibility genes: extensive Toxoplasma gondii host/pathogen interactome enrichment in nine psychiatric or neurological disorders. Journal of pathogens, 2013.

CDC, Page last reviewed: September 3, 2020 https://www.cdc.gov/parasites/toxoplasmosis/gen_info/faqs.html.

Coccaro, E. F., Lee, R., Groer, M. W., Can, A., Coussons-Read, M., & Postolache, T. T. (2016). Toxoplasma gondii infection: relationship with aggression in psychiatric subjects. The Journal of clinical psychiatry, 77(3)

Dubey, J. P., Lindsay, D. S., & Speer, C. (1998). Structures of Toxoplasma gondii tachyzoites, bradyzoites, and sporozoites and biology and development of tissue cysts. Clinical microbiology reviews, 11(2), 267-299.

Duffy, A. R., Beckie, T. M., Brenner, L. A., Beckstead, J. W., Seyfang, A., Postolache, T. T., & Groer, M. W. (2015). Relationship between Toxoplasma gondii and mood disturbance in women veterans. Military medicine, 180(6), 621-625.

El Mouhawess, A., Hammoud, A., Zoghbi, M., Hallit, S., Haddad, C., El Haddad, K., Halabi, M. A. (2020). Relationship between Toxoplasma gondii seropositivity and schizophrenia in the Lebanese population: potential implication of genetic polymorphism of MMP-9. BMC psychiatry, 20(1), 1-9.

El-Beshbishi, S., Elzeky, S., Atia, R., Abdalaziz, K., & El-Tantawy, N. (2020). Toxoplasmosis among Egyptian children with neurological disorders: developmental and risk factors analysis. Parasitologists United Journal, 13(3), 190-196.

Hinze-Selch, D., Däubener, W., Eggert, L., Erdag, S., Stoltenberg, R., & Wilms, S. (2017). A controlled prospective study of Toxoplasma gondii infection in individuals with schizophrenia: beyond seroprevalence. Schizophrenia bulletin, 33(3), 782-788

Hlaváčová, J., Flegr, J., Fiurašková, K., & Kaňková, Š. (2021). Relationship between latent toxoplasmosis and depression in clients of a center for assisted reproduction. Pathogens, 10(8), 1052.

Kezai, A. M., Lecoeur, C., Hot, D., Bounechada, M., Alouani, M. L., & Marion, S. (2020). Association between schizophrenia and Toxoplasma gondii infection in Algeria. Psychiatry Research, 291, 113293.

Khademvatan, S., Saki, J., Khajeddin, N., Izadi-Mazidi, M., Beladi, R., Shafiee, B., & Salehi, Z. (2014). Toxoplasma gondii exposure and the risk of schizophrenia. Jundishapur Journal of Microbiology, 7(11).

Khandaker, G.M., Dalman, C., Kappelmann, N., Stochl, J., Dal, H., Kosidou, K., Jones,P.B., Karlsson, H., 2018. Association of childhood infection with IQ and adult nonaffective psychosis in Swedish men a population-based longitudinal cohort and corelative study. JAMA Psychiatry 75, 356–362..

Markovitz, A. A., Simanek, A. M., Yolken, R. H., Galea, S., Koenen, K. C., Chen, S., & Aiello, A. E. (2015). Toxoplasma gondii and anxiety disorders in a community-based sample. Brain, behavior, and immunity, 43, 192-197.

McConkey, G. A., Martin, H. L., Bristow, G. C., & Webster, J. P. (2013). Toxoplasma gondii infection and behaviour–location, location, location? Journal of Experimental Biology, 216(1), 113-119.

Nagineni, C.N., Pardhasaradhi, K., Martins, M.C., Detrick, B., Hooks, J.J., (1996). Mechanisms of interferon-induced inhibition of Toxoplasma gondii replication in human retinal pigment epithelial cells. Infect Immun. 64, 4188–4196.

Nayeri, T., Sarvi, S., Sharif, M., & Daryani, A. (2021). Toxoplasma gondii: A possible etiologic agent for Alzheimer's disease. Heliyon, 7(6), e07151.

Prandota, J. (2014). Possible link between Toxoplasma gondii and the anosmia associated with neurodegenerative diseases. American Journal of Alzheimer's Disease & Other Dementias®, 29(3), 205-214.

Renard, N., Daniel, S., Cayet, N., Pecquet, M., Raymond, F., Pons, S., ... & Berthier, F. (2021). Performance characteristics of the Vidas SARS-CoV-2 IgM and IgG serological assays. Journal of clinical microbiology, 59(4), e02292-20.

Rizkiyati, I., Ahmad, M., Syarif, S., & Ahmar, H. (2021). Analysis of motivation and behavior of midwives in using digital partographs. International Journal of Life Sciences, 5(2), 48–58. https://doi.org/10.29332/ijls.v5n2.1234

Sah, R. P., Dey, A. R., Rahman, A. A., Alam, M. Z., &Talukder, M. H. (2019). Molecular detection of Toxoplasma gondii from aborted fetuses of sheep, goats and cattle in Bangladesh. Veterinary Parasitology: Regional Studies and Reports, 18, 100347.

Sangole, M. K., & Gandhe, S. T. (2022). Malaria diagnosis using microscopic imaging. International Journal of Health Sciences, 6(2), 880–897. https://doi.org/10.53730/ijhs.v6n2.8735

Suryasa, I. W., Rodríguez-Gámez, M., & Koldoris, T. (2021). The COVID-19 pandemic. *International Journal of Health Sciences*, *5*(2), vi-ix. https://doi.org/10.53730/ijhs.v5n2.2937

Suvisaari, J., Torniainen-Holm, M., Lindgren, M., Härkänen, T., & Yolken, R. H. (2017). Toxoplasma gondii infection and common mental disorders in the Finnish general population. Journal of Affective Disorders, 223, 20-25.

Tenter, A. M., Heckeroth, A. R., & Weiss, L. M. (2000). Toxoplasma gondii: from animals to humans. International journal for parasitology, 30(12-13), 1217-1258.

Tong, W. H., Pavey, C., O'Handley, R., & Vyas, A. (2021). Behavioral biology of Toxoplasma gondii infection. Parasites & Vectors, 14(1), 1-6.

Wang, Z. T., Verma, S. K., Dubey, J. P., & Sibley, L. D. (2017). The aromatic amino acid hydroxylase genes AAH1 and AAH2 in Toxoplasma gondii contribute to transmission in the cat. PLoS pathogens, 13(3), e1006272.

Xiao, J., Prandovszky, E., Kannan, G., Pletnikov, M. V., Dickerson, F., Severance, E. G., &Yolken, R. H. (2018). Toxoplasma gondii: biological parameters of the connection to schizophrenia. Schizophrenia bulletin, 44(5), 983-992.