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FACULTY OF MEDICINE  
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# **PhD THESIS**

**RESEARCH ON THE EPIDEMIOLOGY OF TOXOPLASMOSIS  
IN PSYCHIATRIC DISORDERS. SEROEPIDEMIOLOGICAL  
CHARACTERISTICS OF *TOXOPLASMA GONDII* INFECTION  
IN PATIENTS WITH SCHIZOPHRENIA**

**ABSTRACT**

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**Timișoara  
2024**

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## ABSTRACT

Toxoplasmosis is a disease caused by infection with a zoonotic intracellular protozoan parasite known as *Toxoplasma gondii* (*T. gondii*). The seroprevalence of toxoplasmosis varies significantly depending on several factors, such as dietary habits, food preparation methods,

climate, and the presence and density of definitive hosts (cats) and intermediate hosts (other mammals and birds).

Humans are accidental hosts of this parasite and can become infected in various ways. Contact with the parasite may occur through the ingestion of tissue cysts in undercooked meat, most commonly pork, lamb, goat, or wild game meat. Another route of contamination involves the consumption of unwashed fruits or vegetables, water contaminated with oocysts, contact with contaminated soil, or cat litter boxes. Toxoplasmosis can also be transmitted transplacentally from mother to fetus. Tachyzoites, the active form of the parasite, can cross the placenta and infect the fetus, leading to congenital toxoplasmosis, which can have severe consequences for the child's development. *T. gondii* can also be transmitted through organ transplants or blood transfusions.

The presence of *T. gondii* infection can be determined using serological tests. Anti-*T. gondii* IgG antibodies reach a plateau within 2-3 months after the onset of infection, then decrease and persist at residual levels throughout life. A positive result for anti-*T. gondii* IgG antibodies indicates a past infection but cannot accurately determine the timing of the infection. Interpreting serological results is a complex process, requiring additional tests to determine the moment of the infection.

*T. gondii* infects approximately one-third of the world population. According to seroepidemiological studies in Europe, the prevalence of *T. gondii* infection in psychiatric patients ranges from 40-76%.

The research conducted in this doctoral thesis contains three studies carried out in Arad and Timiș counties between July 1, 2018, and July 31, 2019, aiming to evaluate for the first time the seroprevalence of *T. gondii* infection and to identify the potential risk factors associated with its prevalence among psychiatric patients in Western Romania.

This doctoral thesis is composed of three parts: the general part, the special part, and the conclusions.

**The general part** begins with an introductory chapter on *T. gondii* infection. The second chapter presents updated epidemiological data regarding *T. gondii* infection, including its prevalence among psychiatric patients from different geographic regions and the main risk factors involved in the occurrence of toxoplasmosis. The third chapter focuses on toxoplasmosis in psychiatric patients, particularly those with schizophrenia. The final chapter of the general part covers serological diagnosis of toxoplasmosis.

**The special part** of the thesis includes the motivation, aim, and objectives of the research, as well as the materials and methods, including the selection criteria for study groups, collection and preservation of biological samples, and bioethical considerations. The special part continues with the presentation of results from the three epidemiological studies conducted in Western Romania and their correlation with existing literature data.

**The conclusions** highlight the originality of the research, its impact on psychiatric patients, and directions for future research.

## Motivation and aim of the research

Currently, the international medical community has limited data regarding the seroprevalence and associated risk factors of *T. gondii* infection in psychiatric patients. Given that in the scientific literature is discussed a potential correlation between *T. gondii* infection and psychiatric disorders, this doctoral thesis investigates the possible link between *T. gondii* infection and certain psychiatric conditions.

The aim of this work was to assess the seroprevalence of IgG anti-*T. gondii* antibodies and to identify the potential risk factors associated with seroprevalence among psychiatric patients in Western Romania.

## Research Objectives

The objectives of this research were:

1. to determine the seroprevalence of IgG anti-*T. gondii* antibodies in psychiatric patients admitted to the Psychiatry Department of the Arad County Emergency Clinical Hospital;
2. to determine the seroprevalence of IgG anti-*T. gondii* antibodies and identify potential risk factors associated with seroprevalence in psychiatric patients;
3. to evaluate the prevalence of *T. gondii* infection and associated risk factors in patients with schizophrenia.

To achieve these objectives, three seroepidemiological studies were conducted among psychiatric patients diagnosed in Arad County.

## Evaluation of *Toxoplasma gondii* infection seroprevalence in psychiatric patients from Western Romania

The first study included 308 psychiatric patients aged 19-63, admitted to the Psychiatry Department of the Arad County Emergency Clinical Hospital and a control group of 296 consecutive voluntary blood donors aged 19-63 without psychiatric disorders, from the Regional Blood Transfusion Center in Timisoara. The presence of anti-*T. gondii* IgG antibodies were determined using chemiluminescence.

The overall seroprevalence of anti-*T. gondii* IgG antibodies was significantly higher in psychiatric patients (67.86%; 209/308) compared to the control group (54.05%; 160/296;  $p < 0.001$ ; OR: 1.79; 95% CI: 1.29–2.50).

An analysis of the seroprevalence of anti-*T. gondii* IgG antibodies in psychiatric patients and the control group based on gender revealed a significantly higher seroprevalence in female psychiatric patients compared to the corresponding subjects in the control group (73.49%, 122/166 vs. 54.25%, 83/153;  $p < 0.001$ ; OR: 2.33; 95% CI: 1.46–3.74).

Following the analysis of anti-*T. gondii* IgG antibody seroprevalence in psychiatric patients based on the psychiatric pathology for which they were admitted to the Psychiatry Department of the Arad County Emergency Clinical Hospital, a significantly higher prevalence of anti-*T. gondii* IgG antibodies was observed in patients with schizophrenia (69.77%;  $p = 0.009$ ; OR = 1.96; 95% CI: 1.17–3.28), organic disorders (personality and behavioural disorders) (76.74%;  $p = 0.005$ ; OR = 2.81; 95% CI: 1.33–5.90), and mental disorder concerning alcohol abuse (84.62%;  $p = 0.043$ ; OR = 4.68; 95% CI: 1.02–21.46), compared to the control group.

### **Assessment of anti-*Toxoplasma gondii* IgG antibodies seroprevalence and risk factors associated with seroprevalence in psychiatric patients from Western Romania**

This study was conducted on a cohort of 464 adult psychiatric patients, aged 19 to 97 years, who were admitted to the Psychiatry Department of the Arad County Emergency Clinical Hospital. The presence of anti-*Toxoplasma gondii* IgG antibodies were assessed using chemiluminescence.

The overall seroprevalence of anti-*T. gondii* IgG antibodies in psychiatric patients was 70.04%. Among female psychiatric patients, the seroprevalence of *T. gondii* infection was 74.29% (182/245), while in male patients, it was 65.3% (143/219). The seroprevalence of anti-*T. gondii* IgG antibodies increased with age among psychiatric patients, from 37.50% in the 19–29 age group to 83.87% in the over-70 age group.

Patients with intellectual disabilities exhibited the highest seroprevalence of anti-*T. gondii* IgG antibodies (85.71%), followed by those with delusional disorders (85.19%), dementia (82.76%), alcohol abuse (78.57%), other personality and behavioural disorders (70.83%), schizophrenia (70.75%), and depression (70.43%). Significant levels of seroprevalence were also noted in patients with somatic symptom disorders, bipolar disorder, mood disorders, impulse control disorders, and adjustment disorders (**Table 1**).



**Table 1. Seroprevalence of anti-*T. gondii* IgG antibodies in the study group stratified by psychiatric disorders**

Mental Disorder	Diagnosis*	Number of Investigated Patients	Number of Patients with Detectable <i>T. gondii</i> Antibodies (%)
Adjustment Disorder	F43.2	5	1 (20)
Bipolar Disorder	F31.9	27	17 (62.96)
Delusional Disorder	F05.8	27	23 (85.19)
Dementia	F03.90	29	24 (82.76)
Depression	F33.0	115	81 (70.43)
Impulse Control Disorder	F63.9	13	7 (53.85)
Alcohol Abuse	F10.1	14	11 (78.57)
Intellectual Disabilities	F78.8	7	6 (85.71)
Mood Disorder	F06.3	46	27 (58.7)
Other Personality and Behavioural Disorders	F07.8	72	51 (70.83)
Schizophrenia	F20.9	106	75 (70.75)
Somatic Symptom Disorder	F45.1	3	2 (66.67)
<b>Total</b>	-	464	325 (70.04)

\* diagnosis established according to ICD-10, the International Classification of Disease, 10th Revision

This study also highlighted correlations between *T. gondii* infection and risk factors such as soil contact, low income, and low educational level. However, other factors such as contact with pets (cats and/or dogs), hand hygiene before food preparation, consumption of potable water, consumption of meat (including undercooked meat), unwashed fruits and vegetables, and various types of alcohol were not associated with the presence of anti-*T. gondii* antibodies.

### **Assessment of anti-*Toxoplasma gondii* IgG antibodies and risk factors associated with seroprevalence in patients with schizophrenia from Western Romania**

This study included 98 patients diagnosed with schizophrenia, aged 20 to 64 years, admitted to the Psychiatry Department of the Arad County Emergency Clinical Hospital, and 98 voluntary blood donors aged 20 to 63 years, without a history of psychiatric disorders, from the Regional Blood Transfusion Center in Timisoara. The chemiluminescence technique was used to detect anti-*Toxoplasma gondii* IgG antibodies.

The overall seroprevalence of *T. gondii* infection was 69.39% (68/98) in the schizophrenic patient group, compared to 51.02% (50/98) in the control group. The study results showed varying

seroprevalence rates of anti-*T. gondii* IgG antibodies across different age groups, indicating an increase in toxoplasmosis prevalence with age. In both groups, female subjects had a higher seroprevalence of anti-*T. gondii* IgG antibodies compared to male subjects.

Schizophrenic patients who consumed raw or undercooked meat had a significantly higher seroprevalence of *T. gondii* infection compared to the control group ( $p = 0.02$ ; OR: 3.75; 95% CI: 1.25–11.21). Furthermore, the seroprevalence of anti-*T. gondii* antibodies was higher in schizophrenic patients with a low level of education (77.59%; 45/58) compared to control subjects with the same educational level (50%; 34/68) ( $p = 0.002$ ; OR: 3.5; 95% CI: 1.59–7.54) (**Table 2**).

**Table 2. Potential risk factors for *T. gondii* infection in the investigated groups**

Risk factor*	Number of participants with detectable <i>T. gondii</i> antibodies/ Total participants tested (%)		OR	95% CI	<i>p</i> value
	Study group	Control group			
	(n = 98)	(n = 98)			
Contact with soil	30/46 (65.22)	21/36 (58.33)	1.34	0.55-3.29	0.65
Contact with cats	52/79 (65.82)	15/22 (68.18)	0.9	0.32-2.47	1
Contact with dogs	39/54 (72.22)	20/31 (64.52)	1.43	0.56-3.68	0.47
Contact with either cats or dogs	63/92 (68.48)	21/32 (65.63)	1.13	0.49-2.67	0.83
Consumption of raw/uncooked meat	25/31 (80.65)	20/38 (52.63)	3.75	1.25-11.21	<b>0.02</b>
Low educational attainment	45/58 (77.59)	34/68 (50)	3.5	1.59-7.54	<b>0.002</b>
High educational attainment	23/40 (57.5)	16/30 (53.33)	1.18	0.46-3.07	0.8

\* = participants who answered "Yes" were included in statistical analysis

CI, confidence interval

OR, odds ratio

n, number of the participants included in this study

The results of this research highlight that the seroprevalence of toxoplasmosis among psychiatric patients in Western Romania is among the highest in Europe.

## CONCLUSIONS AND PERSONAL CONTRIBUTIONS

This scientific work represents the first study in Romania that analyse the seroprevalence and the risk factors associated with *T. gondii* infection in psychiatric patients from Western Romania. The findings of this research provide a clear perspective on the seroprevalence of *T. gondii* infection in psychiatric patients in this region and emphasize the importance of monitoring risk factors in this population.

The general conclusions drawn from this study are as follows:

1. the overall seroprevalence of IgG anti-*T. gondii* antibodies is significantly higher in psychiatric patients compared to the control group;
2. the seroprevalence of IgG anti-*T. gondii* antibodies shows a significant increase with age in psychiatric patients, likely due to prolonged exposure to the parasite;
3. female psychiatric patients, including those with schizophrenia, exhibit a significantly higher seroprevalence of IgG anti-*T. gondii* antibodies compared to the control group, suggesting that *T. gondii* infection may have a different impact on women;
4. the prevalence of IgG anti-*T. gondii* antibodies is significantly higher in patients diagnosed with schizophrenia, organic personality and behaviour disorders, and mental disorder concerning alcohol abuse compared to the control group;
5. there is a significant association between the presence of IgG anti-*T. gondii* antibodies and certain psychiatric disorders; patients with intellectual disability had the highest seroprevalence of IgG anti-*T. gondii* antibodies, followed by those with delusional disorders and dementia; significant seroprevalence levels of this parasitic infection were also observed in patients suffering from somatic symptom disorders, bipolar disorder, depression, mood disorders, impulse control disorders, and adjustment disorders;
6. psychiatric patients with activities involving contact with soil have higher rates of *T. gondii* infection compared to those who reported not engaging in such activities;
7. socio-economic status plays an important role in exposure and susceptibility to *T. gondii* infection, with psychiatric patients of lower income showing a higher prevalence of IgG anti-*T. gondii* antibodies compared to those with higher incomes;
8. the prevalence of *T. gondii* infection is higher among psychiatric patients and those with schizophrenia with a low educational attainment compared to those with a high educational attainment;
9. the seroprevalence of *T. gondii* infection is significantly higher among patients with schizophrenia who consume raw or undercooked meat compared to the control group.

The studies conducted in this doctoral thesis provide a comprehensive perspective on the importance of assessing the seroprevalence of *T. gondii* infection in psychiatric patients from Western Romania, contributing to the understanding of its spread and the development of effective strategies for the prevention and management of this infection in the affected population.

This research offers new insights into the risk factors associated with *T. gondii* infection in psychiatric patients from Western Romania, serving as a foundation for future research and the development of prevention strategies for this parasitic infection. Additionally, new data are presented regarding the seroprevalence of *T. gondii* infection and the potential risk factors associated with this infection in patients diagnosed with schizophrenia, contributing significantly to the advancement of knowledge at both national and international levels.