

Seroepidemiology of *Toxoplasma gondii* in kidney transplant patients

Marzieh Latifi (PhD) ¹
 Habib Rahban (MD) ^{2,3}
 Elahe Pourhosein ⁴
 Tannaz Hajjalireza Tehrani ⁴
 Parisa Mahjoobi ⁵
 Sanaz Dehghani (MD) ^{4,6*}

1. Department of Public Health, School of Health and Safety, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
2. Creighton University School of Medicine, St. Joseph Hospital and Medical Center, Department of Cardiovascular Disease, Phoenix, Arizona.
3. Cardiovascular Research Foundation of Southern California, Beverly Hills, CA, USA
4. Organ Procurement Unit, Sina Hospital, Tehran University of Medical Sciences, Tehran, Iran.
5. Department of Medical Parasitology and Mycology, Medicine, Alborz University of Medical Sciences, Alborz, Iran.
6. Iranian Tissue Bank & Research Center, Tehran University of Medical Sciences, Tehran, Iran

* Correspondence:

Sanaz Dehghani, Organ Procurement Unit, Sina Hospital, Tehran University of Medical Sciences, Tehran, Iran

E-mail:

Sanaz_dehghani2002@yahoo.com
 Tel: +98 2166348563

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Abstract

Background: Opportunistic infection after transplantation is a serious problem, with *Toxoplasma Gondii* (*T.gondii*) and cytomegalovirus being the most concerning infections. The objective of this research was to examine the seroepidemiology of the *T. gondii* virus among kidney transplant recipients at Sina Hospital in Tehran from 2017 to 2021.

Methods: A total of 342 kidney transplant patients participated in this cross-sectional study using the census method after obtaining consent. Data were collected by reviewing medical records and the transplant database, including demographic characteristics and infectious tests related to kidney transplantation. The collected information was entered into SPSS18 software.

Results: The age of the subjects ranged from 10 to 73 years, with 125 patients having kidney failure due to ERDS. The rate of exposure to *T. gondii* in kidney transplant patients was 54.2%. 125 patients experiencing kidney failure due to ERDS. In kidney transplant patients, the exposure rate to *T. gondii* was 54.2%. There is a positive correlation between *TOX IgG* and age ($r = 0.12$, $P = 0.02$). There is a positive correlation between *CMV IgG* and the time elapsed since kidney transplantation ($r = 0.11$, $P = 0.03$) and *TOX IgG* ($r = 0.13$, $p < 0.01$). Gender was found not to predict *EBV.IgG* ($\beta = 0.787$, $p < 0.21$), *CMV.IgG* ($\beta = 4.752$, $p < 0.071$), *TOX.IgG* ($\beta = 1.154$, $p < 0.256$) based on regression tests.

Conclusion: Physicians should be aware of preventive measures and should consider early diagnosis in cases of compatible symptoms. Screening for anti-Toxoplasma IgM antibodies in potential donors is recommended.

Keywords: Seroepidemiology, Kidney transplant, *EBV*, *IgG*, *CMV.IgG*, *TOX.IgG*.

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One of the most severe opportunistic infections occurring after transplantation is *Toxoplasma gondii* (*T.gondii*), which has a high mortality rate in recipients who receive a delayed diagnosis (1). This zoonotic infection affects humans and other warm-blooded animals globally, with differences in prevalence and clinical severity based on geographic location (2). *T.gondii* transmission occurs through the prolonged viability and infectivity of oocysts in soil and water; a minimal quantity of oocysts can be enough to transmit the infection (3). The main way that humans become infected is through consuming food or water that has been contaminated with oocysts from the feces of infected felids or undercooked meat that contains cysts (2, 4). In some countries, the prevalence of *T.gondii* infection in the normal population exceeds 50% (5). Based on the study, *T.gondii* is a well-known opportunistic pathogen in heart transplant recipients; it remains a rare but significant pathogen in kidney recipients. According to previous studies, asymptomatic infection of *T.gondii* in kidney recipients reports in 2 to 8% (6, 7). Based on the World Health Organization (WHO), *T.gondii* is an important public health problem (8).



The prevalence of *T.gondii* among adults in Germany was reported to be 49.1% (9). *T.gondii* is frequently asymptomatic in individuals (10). It has been proposed as a significant opportunistic infection in immunocompromised individuals (11), including kidney recipients. *T.gondii* transmitted from the donor has also been identified post liver and kidney transplantation, albeit less commonly (12, 13). Several complications, such as encephalitis, pneumonitis, chorioretinitis, meningitis, and disseminated *T.gondii* with multi-organ involvement, are present in transplantation patients, as opposed to the self-limiting spectrum in immunocompetent individuals (14).

After solid organ transplantation, it has been recognized as a potential infection transmitted from donor to host, and the diagnosis of *T.gondii* is typically made one month after transplantation (7, 15). High mortality rates of 50% have been reported in published cases, underscoring the critical importance of identifying at-risk patients and diagnosing the condition early (12). Tissue encystment in the muscle is a common complication of *T.gondii* infection after transplantation, particularly when a recipient lacking antibodies receives a donor heart with antibodies (16, 17). The main goal of this study was to investigate the seroepidemiology of the *T.gondii* virus in kidney transplant patients at Sina Hospital in Tehran from 2017 to 2022.

Methods

The research ethics committee of Sina Hospital and Tehran University of Medical Sciences (TUMS) approved the study. (Protocol no. IR. TUMS. Sina hospital. REC. 1401.078). It was conducted according to the principles of the Helsinki Declaration. The informed consent form was signed by kidney recipients before the entrance to the evaluation. The patients were assured about the confidentiality of the information and stated that the information would be used only for research purposes and

that the results would be published in general. In this study, a comprehensive investigation was conducted on all deceased kidney transplant patients who had received transplants at Sina Hospital from 2017 until 2022 using a census sampling. Those who did not undergo the required laboratory tests were excluded from the study. Over all, we analyzed data from 341 kidney patients. The presence of the IgG antibody was confirmed by IgG and IgM Trinity kit according to the manufacturer's recommendations (Trinity, USA) (18). The levels of *anti-toxoplasma IgG*, *EBV IgG*, and *CMV IgG* were measured 1 week after kidney transplant in accordance with the manufacturer's instructions.

Statistical analysis: The data was assessed for normality using the Kolmogorov-Smirnov test. Descriptive and analytical statistics, such as frequency, mean \pm SD, were used for analysis. Multivariate logistic regression analyses were conducted to investigate the relationship between gender and levels of *EBV.IgG*, *CMV.IgG*, *TOX.IgG*. Pearson correlation was used to assess the association between quantitative variables and levels of *Cr*, *SGOT*, *CMV IgG*, *TOX IgG*, and *EBV IgG*. Statistical analyses were performed using SPSS Version 18, with a significance level set at $p < 0.05$.

Results

Demographic and clinical characteristics: During the 5 years under review, 341 patients had kidney transplants in the Sina Organ Procurement Unit (OPU), and were determined to be eligible for this study. The sample covered a wide range of ages, from 10 years to 73 years. The median age of the respondents was 43 years. Overall, the majority of patients were males (135, 68.2%) with an average age of 42.11 ± 13.96 years. Altogether, 125 cases of ESRD were due to hypertension, followed by diabetes mellitus, with 40 cases due to other causes. The clinical and demographical data of the participants are shown in table 1.

Table 1. The participants' characteristics, total (n = 341)

Variables		Total (n = 341)
Age, years		42.11 \pm 13.96 (43: Median)
Months of transplantation		31.84 \pm 15.37 (35: Median)
Marital Status	Single	56 (16. 4%)
	Married	285 (83.6%)
Gender	Female	102 (29.9%)
	Male	239 (70.1%)

Variables Total (n = 341)		
Level of Education*	Primary	42 (12.3%)
	Under diploma & Diploma	274 (80.4%)
	BSc/ Associate	23 (6.7%)
	Master & Higher than	2 (0.6%)
Cause of ESRD	Hypertension	125 (36.7%)
	Diabetes Mellitus	49 (14.4%)
	Infection	10 (2.9%)
	Polycystic	26 (7.6%)
	Kidney stone	18 (5.3%)
	Proteinuria	19 (5.6%)
	Congenital	7 (2.1%)
	ESRD	8 (2.3%)
	Others	40 (11.7%)
Smoking	Unknown	39 (11.4%)
	Yes	13 (3.8%)
	No	323 (94.74%)
EBV IgG*	Quitted	5 (1.46%)
	Negative	42 (12.6%)
	Equivocal	12 (12.6%)
TOX IgG*	Positive	280 (83.8%)
	Negative	180 (54.2%)
	Equivocal	14 (4.2%)
CMV IgG*	Positive	138 (41.6%)
	Negative	42 (12.6%)
	Equivocal	12 (3.6%)
	Positive	280 (83.8%)

Missing data (EBV IgG, CMV IgG: 7 Missing and TOX IgG: 9 missing data). EBV IgG: Epstein-Barr virus Immunoglobulin G, TOX IgG: Toxoplasma gondii (T.gondii) Immunoglobulin G, CMV IgG: Cytomegalovirus Immunoglobulin G.

According to Pearson's correlation test, there is a positive correlation between *EBV IgG* and the time elapsed since kidney transplantation ($r = 0.16$, $P = 0.002$). In addition, this test showed that there is a positive correlation between *TOX IgG* and age ($r = 0.12$, $P = 0.02$). Based on this test, there is a positive correlation between *CMV IgG* and the time elapsed since kidney transplantation ($r = 0.11$, $P = 0.03$) and *TOX IgG*

($r = 0.13$, $p < 0.01$). And also, a positive correlation was seen between SGOT and serum creatinine ($r = -0.16$, $p < 0.001$). As shown in table number 3, after control variables (age, marital status, education level) and gender were added, and the results reveal that gender had not a significant impact on *EBV.IgG* ($\beta = 0.787$, $p < 0.21$), *CMV.IgG* ($\beta = 4.752$, $p < 0.071$), *TOX.IgG* ($\beta = 1.154$, $p < 0.256$).

Table 2. Pearson's correlation coefficient test between the investigated variables in kidney transplant patients

	1	2	3	4	5	6	7	8
Age (1)	1							
Time after transplant (2)	r=-0.05 P=0.28	1						
EBV IgG (3)	r=0.06 P=0.23	r=0.16 P=0.002	1					
TOX IgG (4)	r=0.12 P=0.02	r=0.07 P=0.17	r=-0.03 P=0.47	1				
CMV IgG (5)	r=0.03 P=0.56	r=0.11 P=0.03	r=-0.02 P=0.59	r=0.13 P=0.01	1			
Cr (5)	r=-0.08 P=0.12	r=-0.06 P=0.22	r=-0.02 P=0.59	r=0.04 P=0.37	r=0.06 P=0.27	1		
SGOT (6)	r=0.07 P=0.18	r=-0.07 P=0.17	r=0.07 P=0.15	r=-0.04 P=0.46	r=0.04 P=0.41	r=-0.16 P=0.00	1	
SGPT (7)	r=0.04 P=0.41	r=0.01 P=0.85	r=0.03 P=0.48	r=-0.03 P=0.51	r=0.07 P=0.20	r=-0.07 P=0.20	r=0.65 0	1

EBV IgG: Epstein-Barr virus Immunoglobulin G, TOX IgG: Toxoplasma gondii Immunoglobulin G, CMV IgG: Cytomegalovirus Immunoglobulin G, Cr: Creatinine, SGOT: Serum Glutamic-Oxaloacetic Transaminase, SGPT: Serum Glutamic Pyruvic Transaminase

Table 3. Regression test to predict gender on EBV.IgG, CMV.IgG, TOX.IgG

	B	Sig.	Exp (B)	95% C. I	
				Lower	Upper
EBV.IgG.	-0.239	0.217	0.787	0.539	1.150
CMV.IgG	1.559	0.071	4.752	0.876	25.766
TOX.IgG	0.144	0.256	1.154	0.901	1.479

EBV IgG: Epstein-Barr virus Immunoglobulin G, TOX IgG: Toxoplasma gondii Immunoglobulin G, CMV IgG: Cytomegalovirus Immunoglobulin G

Discussion

Transmission of *T.gondii* through kidney transplantation has already been proven in previous studies. This transmission is more common after a heart or bone marrow transplant (7, 19). Most infections are donor related. Multiple case studies show that most organ recipients develop symptoms within 3 months of transplantation, usually with fever, pneumonia, and neurological disturbances (20). This study is the first to ascertain the prevalence and predictors of known *T.gondii* infection among kidney transplant recipients in Iran. The overall seroprevalence of *T.gondii* infection reported by this study was 54.2%, and the rate of exposure to *EBV* was reported to

be 12.4% in these people, while the rate of exposure to *CMV* was reported to be 0.9%. Similar to our study, in 2016, Wilking et al. investigated the seroprevalence of *T.gondii* in adults in Germany and found it was about 49.1% (9). Walpore et al. showed that the worldwide seroprevalence of this infection ranges from 75% of people in France at age 40 to 22% of adults in the United States. They also reported that it increases with age. Seroprevalence in Australia has not been documented recently, although a study of pregnant women showed IgG antibodies in 35% of patients (21).

According to our results, there is no statistically significant relationship between the level of education, marriage, and contracting toxoplasmosis. In the present

study, there were no significant differences between gender and toxoplasmosis. The results were similar to those of Flegr et al., who showed that although a small difference was recorded in the relationship between toxoplasmosis infection in men and women, the findings did not show a significant difference in the rate of infection in women compared to men (22). Shah et al. demonstrated that women were highly infected as compared to men (23), however, in other studies men were more frequently infected than women (24, 25). This study had some limitations, including a small sample size due to the prevalence of the COVID - 19 disease in recent years, leading to a decrease in organ transplants in all countries including Iran and Tehran, as well as incomplete information on some patients in their medical records.

In summary, *T. gondii* in kidney transplant recipients who test negative for antibodies poses a serious risk of morbidity and mortality. The results of this study found that 54.2% of kidney transplant patients had *T. gondii* infections, which can lead to serious complications in immunocompromised patients receiving hemodialysis. Physicians should be aware of this possibility, take preventive measures, and make an early diagnosis if compatible symptoms are present (7). All potential donors should be screened for anti-toxoplasma IgM antibodies. In addition, all recipients who test positive for *Toxoplasma* should go on drug therapy for 6 months to reduce the likelihood of acute transmission or reactivation of *T. gondii* (18).

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Conflict of interests: None.

Authors' contribution: M.L. Supervisor & Design of the work, H.R. Review draft & English edit E.P. Methodologo & Data analysis T.H and P.M. Data curation, S.D. Writing the final draft, all authors have approved the final article.

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