

Original Article

The Correlation between Anti-Cytomegalovirus and Anti-Toxoplasma gondii Antibodies with the Plasma Level of Glycosylated Hemoglobin

Mehrdad Haghighi¹, Mehdi Goudarzi², Mohammad Sistanizad^{3, 4}, Elham Pourheidari^{3*}

¹Infectious Diseases and Tropical Medicine Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran

²Department of Microbiology, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

³Department of Clinical Pharmacy, School of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran

⁴Prevention of Cardiovascular Disease Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran

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Abstract

Background: Viral infections play an important role in the pathogenesis of diabetes mellitus (DM). The association between some viral infections, including cytomegalovirus (CMV) and the development of DM was reported by some articles, but about *T. gondii* data is limited. We aimed to evaluate the correlation between anti-CMV and anti-Toxoplasma gondii (*T. gondii*) antibodies with the plasma level of glycosylated hemoglobin (HbA1C).

Materials and Methods: This is a cross-sectional retrospective study conducted on the medical records of women who tested for pre-pregnancy checkups and had antibody levels against CMV and/or *T. gondii*, and plasma level of HbA1C.

Results: During 4 years, data from 117 patients with anti-CMV IgG, and 186 with anti-*T. gondii* IgG was finally analyzed. According to the data, we did not detect any correlation between the plasma levels of HbA1C and IgG levels against CMV (Correlation Coefficient 0.150, $p = 0.108$) and *T. gondii* (Correlation Coefficient 0.076, $p = 0.300$).

Conclusion: In conclusion, we recommended a large-scale controlled clinical trial to compare the plasma level of HbA1C between patients with confirmed CMV or *T. gondii* infection and the control group.

Keywords: Diabetes Mellitus, Cytomegalovirus, *Toxoplasma gondii*, Antibodies, Glycosylated hemoglobin

***Corresponding Author:** Elham Pourheidari, Department of Clinical Pharmacy, School of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran. Email: e.pourheidari@gmail.com

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Introduction

Diabetes mellitus (DM) is a multifactorial disease, and many factors, including viral infections, are suggested

to be involved in its pathogenesis¹⁻³.

Cytomegalovirus (CMV) is a universal herpes group virus that causes life-long chronic infection and several complications in affected patients⁴. Some articles

reported the association between CMV and the development of DM. The infection can lead to an increased risk of developing type 1 DM due to inducing or accelerating the auto-destructive process of insulin-producing β -cells^{1,3-6} and new-onset type 2 DM due to beta-cell dysfunction, impaired insulin release, and insulin resistance^{7,8}.

Toxoplasma gondii (*T. gondii*) is a coccidian parasite that can cause infection via two main routes: contaminated food or water with oocysts shed by infected cats and raw or undercooked meat containing tissue cysts. It also may be transmitted vertically when a primary infection occurs during pregnancy⁹. Data about the association between toxoplasmosis and DM is not enough. Some articles reported the lack of association between them⁹, whereas some others recommended that *T. gondii* be considered a possible contributing factor in the development of DM¹⁰⁻¹³.

We aimed to evaluate the association between anti-CMV and anti- *T. gondii* antibodies with the plasma level of glycosylated hemoglobin (HbA1C).

Methods

Setting and subjects: This was a cross-sectional retrospective study conducted on the medical records of women who tested in Negaresh pathobiology laboratory in Tehran, Iran, between January 2017 and April 2021, for pre-pregnancy checkups. Approval of this study was obtained from The Medical Ethical Committee (Approval no: IR.SBMU.RETECH.REC.1400.509) at Shahid Beheshti University of Medical Sciences, Tehran, Iran.

Eligibility criteria: Inclusion criteria were patients who had antibody levels against CMV and/or *T. gondii* and plasma levels of HbA1C. Body mass index (BMI) ≥ 30 , immunocompromised state or using any immunomodulatory drugs, presence of fever or any acute inflammatory sign or symptom, substance abuse, and using any glucose-lowering agents were considered as not inclusion criteria.

Data gathering: We recorded age, body mass index, anti-CMV IgG and IgM, and anti-*T. gondii* blood levels. *T. gondii* IgG and IgM, and the serum level of HbA1C. Anti-CMV and anti-*T. gondii* antibodies titer were evaluated quantitatively via ELISA microplate reader

(DA-32000).

Analysis: The records were analyzed using SPSS version 24 (IBM, New York, USA). Kolmogorov–Smirnov test was used to evaluate the normal distribution of data. The correlation was assessed using the Spearman test. $P < 0.05$ was considered as significance correlation.

Results

During 4 years, 500 medical records were registered and evaluated. After excluding records with missing data or other exclusion criteria, data from 117 patients with anti-CMV IgG, and 186 with anti-*T. gondii* IgG was finally analyzed. The mean age $\pm$ SD of participants in each group was 33.50 ± 3.30 and 31.71 ± 4.55 , respectively.

According to the data, we did not detect any correlation between the plasma levels of HbA1C and IgG levels against CMV (Correlation Coefficient 0.150, $p = 0.108$) and *T. gondii* (Correlation Coefficient 0.076, $p = 0.300$).

Discussion

Viral infections play an essential role in the pathogenesis of DM¹⁻³. The association between some viral infections like human *enteroviruses*, *rotavirus*, *mumps*, *rubella*, and CMV, and the development of DM was reported by some articles^{1,3,4,8,14}. Although we detected no correlation between IgG levels against CMV and the plasma levels of HbA1C, Chen S. et al. suggested CMV as a risk factor to developing type 2 DM according to their founding that was a significantly higher CMV seropositivity among old patients with type 2 DM and who had high levels of HbA1C compared with the control group¹⁴. Seul GY. also reported a significantly higher frequency of new-onset type 2 DM in patients with CMV disease than in the control group⁸. The significant association between CMV infection and increased risk of type 1 DM was also shown by some articles in children^{4,6}.

Data about the association between *T. gondii* and the development of DM is limited. We detected no correlation between IgG levels against CMV and the plasma levels of HbA1C. Whereas, Shirbazu et al. showed a two-fold higher risk of toxoplasmosis infection in patients with diabetes compared to healthy

controls¹². Seropositivity of anti-T. gondii IgG was also significantly higher among patients with type 1 DM (86.37%) than in the control group (60%) by Engy et al.¹³. This significant association between chronic toxoplasmosis and increased risk of type 2 DM was also reported by some other studies^{10,15}. Same as our finding, Alvarado EC. et al. did not obtain any serological evidence for the association between T. gondii infection and DM in their case-control study⁹.

The single-center experience and small sample size were the main limitations of our study. Considering the limitations of this study, a large-scale clinical trial is needed to evaluate this correlation.

Conclusion

In conclusion, we revealed no correlation between IgG levels against CMV and T. gaondii with the plasma levels of HbA1C. We recommended a large-scale controlled clinical trial to compare the plasma level of HbA1C between patients with confirmed CMV or T. gondii infection and the control group.

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