BioSocial Health J 2024; 1(2): 59-60
doi:10.34172/bshj.19
https://biosocialhealthjournal.com

BioSocial
Health Journal

Letter to Editor

Treatment of prediabetes by gliflozins: Risk of infection

Ali Shayanfar*

Faculty of Pharmacy, Tabriz University of Medical Sciences, Tabriz, Iran

***Corresponding Author:** Ali Shayanfar, Email: shayanfara@tbzmed.ac.ir

Received: May 3, 2024, **Accepted**: June 12, 2024, **ePublished**: July 4, 2024

To Editor,

An interesting review article by Echouffo-Tcheugui and colleagues about the diagnosis and management of prediabetes has been published in *JAMA*.[1] The lifestyle change that includes exercise and weight loss was proposed as first-line therapy with a superior advantage over than metformin. Recently, a letter was published in which sodium-glucose co-transporter-2 (SGLT2) inhibitors (gliflozins) were suggested as the treatment of prediabetes because of the anti-diabetic effects and weight-reduction benefits of SGLT2 inhibitors.[2] This comment was replied by Dagogo-Jack,[3] and some concerns were declared because of no evidence of gliflozins effect on insulin and β-cell actions and their efficacy on people without type 2 diabetes. Therefore, further studies were recommended to verify the effectiveness of gliflozins in the management of prediabetes. In addition, adverse effects of gliflozins are another issue should be considered.

Gliflozins have several beneficial effects in managing diabetes and cardiovascular disease.[4] However, clinical studies have shown an increased risk of certain infections. The most common infection associated with SGLT2 inhibitors is urinary tract infection (UTI). They work by increasing the excretion of glucose through the urine, which can create an environment favorable for bacterial growth. In addition, osmotic diuresis, by maintaining urinary flow, is another mechanism of UTI in patients treated with gliflozins.[5] They may also enhance the risk of genital yeast infections and vulvitis.[6]

A retrospective cohort study reported that genitourinary infection is common within six months of treatment among patients on gliflozins.[7] McGovern et al[8] reported significantly increased risk of genital infections in 21 004 people with type 2 diabetes starting gliflozins and compared with 55 471 patients initiating dipeptidyl peptidase-4 inhibitors (DPP4i).

A meta-analysis of randomized placebo-controlled trials about renal efficacy and cardiovascular safety of gliflozins in non-diabetic patients concluded an increased risk for genital and UTIs.[9] Bapir et al,[10] also designed a systematic review and meta-analysis, and an increase in the risk of urogenital infections was obtained in patients without diabetes. In another meta-analysis with 77 randomized controlled trials involving 50 820 participants, a significant difference has been reported in genital infections between SGLT2 inhibitors versus control.[11]

According to available evidence, UTI and genital yeast infections are possible adverse effects of SGLT2 inhibitors and may be considered in their administration for prediabetic conditions. Thus, I also believe that more randomized controlled trials are necessary to establish strong evidence for the application of gliflozins in prediabetic patients and monitoring their adverse effects i.e., infections.

Competing Interests
None reported.

Data Availability Statement
Not applicable.

Ethical Approval
Not applicable.

Funding
No funding.

References
1. Echouffo-Tcheugui JB, Perreault L, Ji L, Dagogo-Jack S. Diagnosis and management of prediabetes: a review. Obstet Gynecol Surv. 2023;78(7):408-9. doi: 10.1097/ogx.0000000000001177.
2. Entezari-Maleki T. Review of prediabetes. JAMA. 2023;330(6):563-4. doi: 10.1001/jama.2023.9956.
3. Dagogo-Jack S. Review of prediabetes-reply. JAMA. 2023;330(6):564-5. doi: 10.1001/jama.2023.9964.
4. Talha KM, Butler J, Greene SJ, Aggarwal R, Anker SD, Claggett BL, et al. Population-level implications of sodium-glucose cotransporter-2 inhibitors for heart failure with preserved ejection fraction in the US. JAMA Cardiol. 2023;8(1):66-73. doi: 10.1001/jamacardio.2022.4348.
5. Tanrıverdi M, Baştemir M, Demirbakan H, Ünalan A, Türkmen M, Tanrıverdi G. Association of SGLT-2 inhibitors with bacterial urinary tract infection in type 2 diabetes. BMC Endocr Disord. 2023;23(1):211. doi: 10.1186/s12902-023-01464-6.
6. Mounsey SJ, Teo YX, Calonje JE, Lewis FM. Gliflozin (SGLT2 inhibitor) induced vulvitis. Int J Dermatol. 2023;62(1):62-5.

doi: 10.1111/ijd.16449.
7. Caro MK, Cunanan EC, Kho SA. Incidence and factors associated with genitourinary infections among type 2 diabetes patients on SGLT2 inhibitors: a single retrospective cohort study. Diabet Epidemiol Manag. 2022;7:100082. doi: 10.1016/j.deman.2022.100082.
8. McGovern AP, Hogg M, Shields BM, Sattar NA, Holman RR, Pearson ER, et al. Risk factors for genital infections in people initiating SGLT2 inhibitors and their impact on discontinuation. BMJ Open Diabetes Res Care. 2020;8(1):1238. doi: 10.1136/bmjdrc-2020-001238.
9. Tsai WC, Hsu SP, Chiu YL, Yang JY, Pai MF, Ko MJ, et al. Cardiovascular and renal efficacy and safety of sodium-glucose cotransporter-2 inhibitors in patients without diabetes: a systematic review and meta-analysis of randomised placebo-controlled trials. BMJ Open. 2022;12(10):e060655. doi: 10.1136/bmjopen-2021-060655.
10. Bapir R, Bhatti KH, Eliwa A, García-Perdomo HA, Gherabi N, Hennessey D, et al. Risk of urogenital infections in non-diabetic patients treated with sodium-glucose cotransporter-2 (SGLT2) inhibitors. Systematic review and meta-analysis. Arch Ital Urol Androl. 2023;95(2):11509. doi: 10.4081/aiua.2023.11509.
11. Liu J, Li L, Li S, Jia P, Deng K, Chen W, et al. Effects of SGLT2 inhibitors on UTIs and genital infections in type 2 diabetes mellitus: a systematic review and meta-analysis. Sci Rep. 2017;7(1):2824. doi: 10.1038/s41598-017-02733-w.