

Triglyceride-Glucose Index predicts type 2 diabetes risk and progression of diabetic nephropathy: a critical appraisal

Rajeev Chawla¹

Published online: 11 April 2025

© The Author(s), under exclusive licence to Research Society for Study of Diabetes in India 2025

The Triglyceride-Glucose (TyG) Index has emerged as a valuable marker in predicting the onset and progression of type 2 diabetes mellitus (T2DM) and its associated complications. The growing body of research underscores its clinical significance, particularly in assessing gender-based risk differentials, diabetic kidney disease (DKD) progression, and the interplay between metabolic and epigenetic factors in diabetes-related nephropathy. By synthesizing findings from recent studies, this editorial aims to highlight the predictive value of the TyG Index, gender-specific variations in its effectiveness, and the broader implications for diabetes management and prevention.

Gender-specific predictive value of TyG Index in T2DM risk

A recent cohort study by Guo and Tong et al. [1] published in this issue involving 48,230 individuals established a significant association between an elevated TyG Index and an increased risk of T2DM in both men and women. However, the predictive strength of the index was markedly higher in women (AUC = 0.812) compared to men (AUC = 0.721). This disparity suggests that women might be more metabolically vulnerable to insulin resistance as measured by the TyG Index, warranting a gender-sensitive approach in diabetes risk assessment and preventive strategies. The adjusted model further indicated that while men with a higher TyG Index had a 1.68 times greater risk of developing T2DM, the risk was considerably elevated in women (3.59 times), reinforcing the need for targeted interventions.

TyG Index and diabetic kidney disease progression

Huang and Liu et al. [2] extended the discussion by investigating the TyG Index's role in diabetic kidney disease (DKD) progression. Their findings emphasized that an elevated TyG Index correlates with a higher risk of DKD progression, particularly in male patients with T2DM. While the mechanisms underlying this gender disparity remain unclear, hormonal and metabolic differences may contribute to the observed variations. These findings underscore the importance of using the TyG Index not only for predicting diabetes onset but also for monitoring disease progression and implementing timely interventions, especially in male patients at risk for DKD.

The burden of poor glycemic control and diabetic nephropathy

Abdulqawi Ali and Al-Shammakh et al. [3] studied a broader epidemiological perspective by examining the prevalence of poor glycemic control and diabetic nephropathy among T2DM patients in Yemen. Alarming, 58% of patients exhibited poor glycemic control, with factors such as combined antihyperglycemic therapy (oral drugs plus insulin), poor dietary adherence, and lack of education contributing to suboptimal glucose regulation. Moreover, diabetic nephropathy was present in 32% of patients, with significant risk factors including advanced age (> 50 years), hypertension, prolonged diabetes duration (> 5 years), and uncontrolled blood glucose levels. These findings highlight the pressing need for comprehensive diabetes management programs that incorporate lifestyle modifications, patient education, and improved access to healthcare resources.

✉ Rajeev Chawla
rajeevaastikchawla@yahoo.com

¹ North Delhi Diabetes and Cardiac Centre, New Delhi, India

Epigenetic insights: the Nrf2-HDAC axis in diabetic nephropathy

Beyond clinical markers and epidemiological insights, diabetes progression is increasingly being understood through the lens of molecular biology. Harith Priya and Juttada's study [4] published in this issue delved into the dysregulation of the Nrf2-HDAC axis in diabetic nephropathy. The significant downregulation of Nrf2 and selective histone deacetylases (HDACs) in DN patients suggests an epigenetic imbalance that exacerbates kidney damage. Interestingly, the upregulation of specific HDACs (HDAC1/2/4/5/6) was negatively correlated with Nrf2, reinforcing the hypothesis that epigenetic modifications play a pivotal role in diabetes-related kidney disease. These findings open new avenues for therapeutic interventions targeting the Nrf2-HDAC pathway to mitigate renal complications in diabetes.

Advancing DKD detection: the role of biomarkers

Early detection remains a cornerstone of effective DKD management, and recent advancements in biomarker research offer promising avenues for improving diagnostic accuracy. Alofa and Avogbe's study [5] in this current issue identified plasma levels of kidney injury molecule-1 (KIM-1) and tumor necrosis factor receptor-1 (TNFR1) as reliable biomarkers for DKD prediction. Their combination with albumin-to-creatinine ratio (ACR) enhanced diagnostic precision, suggesting that a multiparametric approach integrating traditional and novel biomarkers could revolutionize early DKD detection. By refining risk stratification, such strategies can facilitate timely therapeutic interventions, ultimately reducing the burden of diabetic kidney disease.

Clinical implications and future directions

The collective insights from these studies emphasize the multifaceted nature of diabetes and its complications, reinforcing the critical role of the TyG Index, gender-specific risk assessment, and molecular underpinnings of disease progression. Moving forward, several key areas warrant attention:

1. **Gender-specific risk stratification:** Given the differential predictive power of the TyG Index in men and

women, future research should focus on elucidating the underlying biological and lifestyle factors contributing to these disparities. Tailored screening and prevention strategies could significantly enhance early diabetes detection and management.

2. **Comprehensive DKD monitoring:** Integrating the TyG Index with established and novel biomarkers like KIM-1 and TNFR1 could improve the accuracy of DKD risk assessment. Such an approach would enable proactive interventions, particularly for high-risk male patients with T2DM.
3. **Addressing socioeconomic and behavioral determinants:** The findings from Yemen underscore the urgent need for patient-centered education and support programs to enhance glycemic control. Healthcare systems must prioritize interventions addressing dietary habits, medication adherence, and health literacy to mitigate diabetes-related complications.
4. **Therapeutic targeting of epigenetic mechanisms:** The Nrf2-HDAC axis represents a promising target for novel therapeutics aimed at curbing diabetic nephropathy progression. Further exploration of epigenetic modulation could pave the way for innovative treatment strategies in diabetes care.

In conclusion, the TyG Index remains a robust and clinically relevant marker for assessing T2DM and its complications. Gender differences in its predictive value highlight the need for tailored healthcare approaches, while advancements in biomarker research and epigenetic insights offer new hope for improving disease outcomes. As diabetes continues to pose a global health challenge, a multidisciplinary approach integrating epidemiology, molecular biology, and clinical practice will be instrumental in advancing prevention, diagnosis, and treatment strategies.

References

1. Guo R, Tong J, Wang R, Ma S, Wei L, Zhao W. Gender differences in triglyceride glucose index predictive power for type 2 diabetes mellitus: a Chinese cohort study. *Int J Diabetes Dev Countries*. 2025;45:2.
2. Huang J, Liu D, Zeng H, Liu J. Associations between triglyceride-glucose index and risk of diabetic kidney disease progression in type 2 diabetes mellitus. *Int J Diabetes Dev Countries*. 2025;45:2.
3. Al-Shammakh Abdulqawi Ali, Al-Tamimi Abdul Haleem Salem, Robed QaidTaherQaid, Al-Mojahid Faheem Qaid. Prevalence and risk factors of poor glycemic control and diabetic nephropathy among patients with type 2 diabetes mellitus in Dhamar, Yemen. *Int J Diabetes Dev Countries*. 2025;45:2.
4. Harithpriya Kannan, Juttada Udyama, Jayasuriya Ravichandran, Kumpatla Satyavani, Viswanathan Vijay, Ramkumar KunkaMohanam. Comprehensive gene expression analysis of histone deacetylases and the transcription factor Nrf2 in the progression of diabetic nephropathy. *Int J Diabetes Dev Countries*. 2025;45:2.

5. Alofa Carina P. A, Avogbe Patrice H, Kougnimon Espérance F. E, Migan Marcos A. D. F, Amoussou Riel A. N, Fandohan Antoine, Segbo Julien A. G, Akpovi Casimir D. Optimized multiparametric approach for early detection of kidney disease in diabetic patients. *Int J Diabetes Dev Countries*. 2025;45:2.

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.