Green Medical Journal Vol.6 Issue: 3 (December, 2024): 100-108
E-ISSN: 2686-6668
DOI: 10.33096/gmj.v6i3.195

Green Medical Journal
Volume 6 Issue 3

Literature Review Open Access

Correlation between Triglyceride Glucose Index and Diabetic Kidney in Type 2 Diabetic: Literature Review

Rizki Fajar Utami[1*], Atien Nur Chamidah[2]

[1]Department of Biochemistry, Faculty of Medicine, Universitas Negeri Yogyakarta, Yogyakarta, Indonesia
[2]Department of Public Health, Faculty of Medicine, Universitas Negeri Yogyakarta, Yogyakarta, Indonesia

*Corresponding Author. E-mail: rizkifajarutami@ac.id Mobile number: +628197979977

ABSTRACT

Introduction: One marker of insulin resistance in type 2 diabetes is the triglyceride index (TyG), which has been studied to predict the development of diabetic kidney disease (DKD). This study investigates the correlation between the triglyceride glucose index and diabetic kidney disease in type 2 diabetes mellitus.
Methods: A comprehensive search was conducted in PubMed, Proquest, ScienceDirect, Taylor and Francis, Cochrane Library and Google Scholar search using search terms including (‘‘Triglyceride Glucose Index or TyG’’) and (‘‘Diabetic Kidney or Diabetic Nephropathy’’) and ("Diabetes Mellitus" OR "Diabetes Mellitus Type II" OR "Type 2 Diabetes Mellitus").
Results: A total of 8 studies were screened based on titles and abstracts, of which 7 studies were included in the analysis of TyG and DKD. A prediction model including the TyG index demonstrated excellent calibration and discrimination for the probability of DKD in research involving patients recently diagnosed with type 2 diabetes mellitus (T2DM). This approach has potential applications in clinical practice. DKD and metabolic diseases are independently correlated with the TyG index. Recently, one sensitive method for identifying DKD with insulin resistance has been the TyG index. The TyG index is a readily available, affordable, and simple marker for identifying of microvascular problems in T2DM patients.
Conclusion: In our review, TyG and DKD were significantly positively correlated in patients with type 2 diabetic mellitus. TyG index has potential as a practical tool for determining insulin resistance and predicting the probabilities that individuals with type 2 diabetes are related to diabetic kidney disease.

Keywords: Triglyceride glucose (TyG) index; diabetic kidney disease (DKD); type 2 diabetes mellitus

GREEN MEDICAL JOURNAL
E-ISSN 2686-6668

Published by:
Faculty of Medicine
Universitas Muslim Indonesia

Address:
Jl. Urip Sumoharjo Km. 5, Makassar
South Sulawesi, Indonesia

Email:
greenmedicaljournal@umi.ac.id

Article history:
Received: 9 August 2024
Accepted: 23 September 2024
Published: 30 September 2024

Introduction

Diabetes mellitus (DM) is a chronic illness that affects people all over the world. There are 537 million adults with diabetes globally as of right now, based on data from the International Diabetes Federation Atlas Diabetes 2021.[1] One of the microvascular complications of diabetes mellitus is diabetic kidney disease (DKD) approximately 50 % of DM patients.[2] The risk of cardiovascular disease, end-stage renal disease (ESRD), and mortality has increased over the years in conjunction with the increased risk of chronic kidney disease (CKD). Kidney illness can be prevented or postponed with an early diagnosis and thorough treatment.[3,4]

In populations with diabetes mellitus, there is a strong correlation between kidney disease risk and insulin resistance (IR).[5] There is variation in the relationship between insulin resistance and the progression of CKD. For instance, in non-diabetic individuals with mild-to-moderate CKD, a study found no significant correlation between HOMA-IR, HbA1c, or C-peptide and CKD development.[6] Insulin resistance is commonly assessed in clinical practice utilizing fasting state measures and the homeostasis model assessment for insulin resistance (HOMA-IR).[7] Unfortunately, the plasma insulin assay has low repeatability, is costly, and is not readily available in many laboratories. New biomarkers that are less expensive and simpler to identify are therefore required. IR is frequently associated with abnormal fasting blood glucose (FBG) and triglyceride (TG) levels. The triglyceride–glucose index (TyG) has proved to be a useful marker for insulin resistance (IR) and its related problems, according to recent research. An indicator of insulin resistance and a predictor of DKD individuals with type 2 diabetes has been investigated is the Triglyceride Glucose (TyG) index.[8,9] The result of this review is to explore the correlation between the triglyceride glucose index and diabetic kidney disease in type 2 diabetic mellitus.

Methods

This review was carried out by the literature review reporting item (PRISMA ScR). Inclusion criteria included observational, cohort, and cross-sectional studies in adult subjects (18 years or older), type 2 diabetes mellitus with diabetic kidney disease and, measurement of TyG index. There is no exclusion criteria based on the language or country of publication. A comprehensive search was conducted in PubMed, Proquest, ScienceDirect, Taylor and Francis, Cochrane Library, and Google Scholar search using search terms including (‘‘Triglyceride Glucose Index or TyG’’) and (‘‘Diabetic Kidney or Diabetic Nephropathy’’) and ("Diabetes Mellitus" OR "Diabetes Mellitus Type II" OR "Type 2 Diabetes Mellitus"). Data extraction was carried out using a Google Sheet-based template to extract key data variables which included title, year, study design, study population, age of subjects, measured outcomes, and main findings. Then, we compiled the study according to the appropriate criteria, and the results are

included in this review.

Result

Based on the database, a total of 8 records were found. Seven papers were considered in this review after the titles and abstracts of the seven records were screened. Seven full-text articles were then evaluated for eligibility. The literature search and study selection process are summarized in Figure 1.

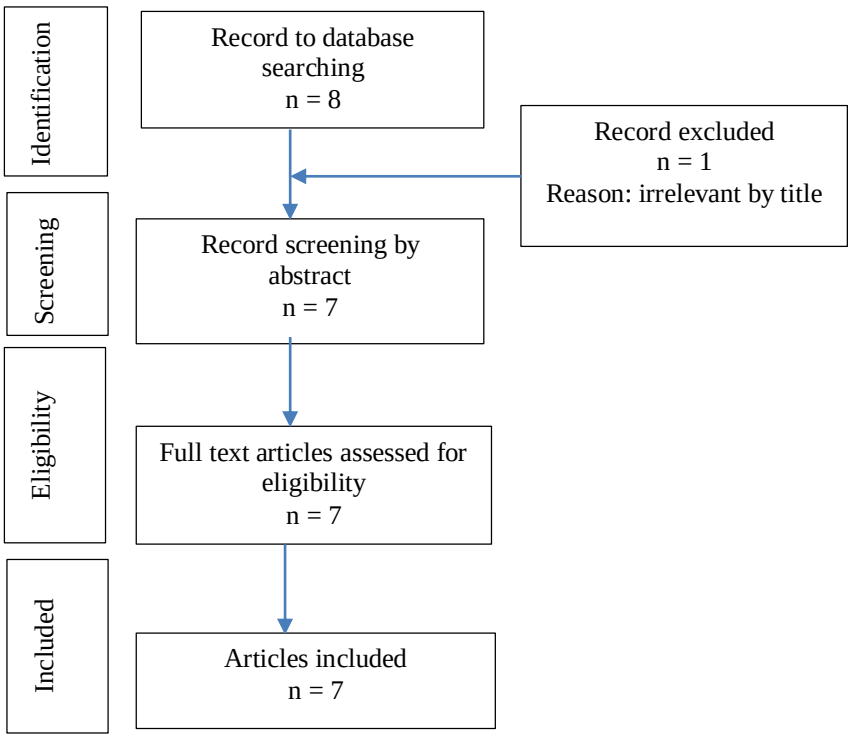

Figure 1. Flowchart of the study selection process

Triglyceride Glucose (TyG) Index

The TyG index was calculated as follows, TyG = Ln [fasting triglycerides (mg/dL) × fasting plasma glucose (mg (dL)/2]. There is a significant correlation between the TyG index and DKD. Li et al studies show the mean of TyG index in the the non-DKD DM group was 9,051±0.757, the DM group with DKD 9,312±0.831 with p<0.001. Lv et al studies show the mean total of TyG is 9.17 (8.73-9.71). Tu et al studies showed, the non-DKD DM group 7.38 (6.89-7.92), DM group with DKD 7.53 (7.07-8.09). Jiang and Lai, 2024 studies show the average TyG of the the non-DKD DM group was 9.77±1.06, the DM group with DKD 10.01±1.02 (p=0.005). Lui et al, 2020 studied that the average TyG of the the non-DKD DM group was 9.10±0.358, the DM group with DKD 9.42±0.74 (p<0.001). While there is evidence linking elevated TyG indices to increased risks of both DM and DKD, specific consensus on cut-off values remains unclear and varies by study. However, all studies show that the mean of the TyG index is higher in the DM group with DKD (table 1).

Table 1. Comparison of TyG index between control and DM+DKD: (mean±SD)

No	Authors	Year	DM	DM+DKD	p
1	Li et al	2023	9,051±0.757	9,312±0.831	p<0.001
2	Lv et al	2021	Mean=9.17 (8.73-9.71)		
3	Tu et al	2024	7.38 (6.89-7.92)	7.53 (7.07-8.09)	
4	Jiang and Lai	2024	9.77±1.06	10.01±1.02	p=0.005
5	Lui et al	2021	9.10±0.358	9.42±0.74	p<0.001

The DKD parameters

Kidney Disease Improving Global Outcomes (KDIGO) states that a decrease in estimated glomerular filtration rate (eGFR < 60 ml/min/1.73 m2) and an increase in urine albumin excretion (≥ 30 mg/g creatinine) over three months is required for the diagnosis of DKD.[10] DKD parameters include a decrease of eGFR and an increase the urine microalbuminuria: creatinine ratio (UACR). Based on journals in this review, eGFR for the non-DKD DM group 90,876±15,442, DM group with DKD 81,017±22,702 (p<0.001); the non-DKD DM group 123.36±25.56, DM group with DKD 108.46±36.90 (p<0.001); eGFR of the non-DKD DM group 94.93 (90.17-108.39), DM group with DKD 35.79 (14.35-53.42) mL/min/1.73m^2 (p<0.001) and eGFR of the non-DKD DM group 128.9 (100.7-157.7), and DM group with DKD 76.1 (38.0-121.8) mL/min/1.73m^2 (p<0.001). Other parameters of DKD are UACR for the non-DKD DM group 11.8 (7.70-18.20), DM group with DKD 88.8 (46.50-215.40). Whereas in other journals, the value of UACR for the non-DKD DM group was 20.65+45.04, DM group with DKD 156.73±438.94 (p<0.001).

Correlation of TyG index with DKD

The correlation between TyG with DKD parameters based on this review, UACR was r=0.172 (p<0.001) and albumin r=0.102 (p<0.008), and correlation between TyG with DKD (OR=1.693; 95% CI=1.002-2.803; p=0.041). After performing a binary logistic regression analysis, another publication demonstrated the relationship between the TyG Index and DKD. The low tertile in this model of the TyG Index is set as a reference, the TyG Index in the upper terminus is associated with a higher OR for microalbuminuria (OR=2.342; 95% CI=1.744–3.144; p< 0.001), eGFR (OR=1.696; 95% CI=1.096–2.625; p=0.018) and DKD (OR=2.728; 95% CI=2.030–3.661; p<0.001) determined by sex and age.

The triglyceride-glucose (TyG) index has been investigated for its association with diabetic kidney

disease (DKD), but consensus on specific cut-off values is still evolving across different studies. A TyG index cut-off value of ≥ 8.31 has been linked to a higher risk of type 2 diabetes, but values between 8.7 and 8.9 indicate a 54% sensitivity and a 71% specificity in predicting the disease.[11] Higher values were associated with higher risk, and a TyG index cut-off of 9.5 was found to be meaningful in categorized risk for ESRD in individuals with T2DM and Chronic kidney Disease (CKD).[12]

Multiple regression analysis based on the evaluation of the included article showed that the occurrence of DKD in patients with T2D was correlated with SBP, DBP, BMI, HbA1c, TG, TyG index (OR=1.57; 95% CI=1.26–1.94; p<0.001), and TyG-BMI after controlling for confounding factors like age and sex. According to other journals, the TyG index has a good correlation with both albuminuria and eGFR, a DKD marker. The TyG index and lnAER had a positive association, per the correlation analysis (r = 0.190, p = 0.003). After adjusting for several factors, such as age, sex, duration of illness, weight, prevalence of hypertension, HbA1C, and serum uric acid, this link persisted (r = 0.173, p = 0.006). There was no correlation between the TyG index and lneGFR (r = -0.095, p = 0.138) or without (r = -0.016, p = 0.805) after confounding factors were considered. Subjects with normoalbuminuria showed a lower TyG index than patients with macro- and microalbuminuria (p < 0.05). Between DKD patients with eGFR <30, 30-59, 60-89, and ≥90 mL/min/1.73 m2, there was no difference in the TyG index (p = 0.786).

Table 2. Correlation of TyG index with DKD

No	Author	Results	Main findings
1	Li et al, 2023	UACR r=0.172, p<0.001	The TyG index were independently related to DKD and related metabolic disorders
2	Lv et al, 2021	Microalbuminuria (OR = 2.342, 95% CI =1.744–3.144, p < 0.001), eGFR (1.696, 1.096–2.625, 0.018) and DKD (2.728, 2.030–3.661, <0.001)	The TyG Index is a potential predictor for DKD in T2DM patients.
3	Tu et al, 2024	Univariate logistic regressions: risk of DKD (OR = 1.842, [95% CI] 1.317–2.578, p < 0.01). Multivariable logistic regression: risk of DKD (OR = 1.581, [95% CI] 1.031–2.424, p < 0.05)	Elevated the TyG was significantly associated with an increased risk of DKD in T2D
4	Wang et al, 2024	TyG index was identified as a prominent clinical risk factor for DKD, showing the highest odds ratio (OR 1.57 (1.26 - 1.94), P<0.001).	The DKD risk presented a threshold effect with the increase of TyG index, initially stable at a low level, and then gradually rising when the TyG index is above 9.35.
5	Jiang and Lai, 2024	Logistic regression revealed that TyG index (odds ratio [OR] 1.232, 95% confidence interval [CI] 1.064–1.428, p = 0.005) and TyG-BMI (OR 1.003, 95% CI	Among newly diagnosed T2D patients, the risk of DKD increases with the increase of TyG index and the TyG-BMI, with their respective cut-off values being 9.68 and 243. Both the TyG index and the TyG-BMI

		1.000–1.006, p = 0.021) were risk factors for DKD.	have poor diagnostic values for the risk of DKD.
6	Shang et al, 2019	A non-linear relationship was identified between TyG index and the risk of newly diagnosed biopsy-proven diabetic nephropathy with a potential threshold of TyG at 9.05–9.09.	In people with type 2 diabetes, the TyG index above 9.05–9.09 could be a prognostic threshold to identify individuals at high risk of diabetic nephropathy.
7	Lui et al, 2020	The TyG index positively correlated with lnAER (r = 0.190, p = 0.003).	The TyG index was independently associated with DN in patients with type 2 diabetes and was a better marker than HOMA2-IR for the identification of DN in type 2 diabetes patients.

Discussion

Based on the seven studies the reseachers reviewed, the biomarker of insulin resistance, the TyG index, relates to DKD parameters such as UACR and eGFR. Insulin resistance has multiple effects on diabetes-related kidney disease (CKD), contributing to the incidence and progression. Hyperinsulinemia can lead to glomerular hyperfiltration, which raises the rate of renal filtration and may eventually cause injury. Moreover, hyperinsulinemia promotes blood vessel permeability, which can lead to renal inflammation and oxidative stress. Insulin resistance affects podocytes as well, and maintaining the structural integrity of the glomerular filtration barrier depends on it. Reduced insulin action can lead to glomerulosclerosis and albuminuria by thickening the base membrane of the glomerulus, removing leg processes, and triggering apoptosis in the podocit. Insulin resistance can be found in various chronic kidney diseases (CKD) in addition to diabetic nephropathy. The impairment of glucose, lipid, and protein metabolism caused by CKD could contribute to systemic insulin resistance, a condition that progressively decreases kidney function.[13,14]

A study conducted by Li et al. showed that the TyG index had a positive correlation with the urinary albumin-creatinine ratio (UACR) and was closely associated with DKD. The risk factor is independent of the DKD increase of 1,699 times on each increase in the TyG index. A TyG index higher than 9.25 showed a significant difference in the eGFR value (60-89.9 mL/min/1.73 m2).[15] Lv et al (2024) reported that an increase in the TyG Index was associated with an increased risk of microalbuminuria and a decrease in eGFR. Longitudinal studies also show that the TyG Index can effectively predict DKD. The TyG index also often interferes with insulin resistance (IR) conditions, so it can be used as a substitute for IR.[16]

After adjusting for confounding factors, Tu et al. (2024) found a strong correlation between TyG and DKD (OR=1.581; 95% CI=1.031–2.424). According to univariate logistic regression, an increase in the TyG index is associated with an increased risk of DKD. Various metabolic conditions can affect the TyG

index. Therefore, some variables associated with TyG can be identified through quantitative regression. These variables include age, gender, SBP, HbA1c, FCP, TC, HDL-C, LDL-C, and drinking habits. In patients with T2D, this indicator is mainly associated with the metabolic impairment associated with TyG and microvascular complications. After confounding is controlled, the risk of diabetic kidney disease (CKD) increases.[17]

Research by Wang et al. (2024) used a cross-sectional design to investigate the threshold between the TyG index and DKD risk. The results showed that even though the confounding factor was removed, the risk of DKD remained stable at a lower level in patients with a TyG index of less than 9.35, but in patients with a TyG index of more than 9.35, an increase of one unit of the TyG index led to a 94% increase in the risk of DKD. The results of this study can be used to place risk and management interventions in DKD patients with type 2 diabetes (T2D). [5]

This review also included the TyG index as a marker of insulin resistance associated with the risk of newly diagnosed DKD in people with type 2 diabetes mellitus. Jiang and Lai's study examined the relationship between the TyG index and the presence of DKD in patients with newly diagnosed T2D. The results show that the TyG index is an important risk factor for DKD. This relationship proved significant after adjusting for confounding variables based on nonlinear correlations. The risk of DKD increases as the TyG index increases greater than 9.68, which indicates that the TyG index is a potential indicator of DKD risk. [8] The research by Shang et al. (2019), the threshold value of the TyG index was obtained 9.07 (9.05–9.09). People with type 2 diabetes who are newly diagnosed with DKD as evidenced by a biopsy have a much higher risk with a TyG index value above 9.07. This conclusion is in line with previous findings, a high TyG index (specifically a TyG index above 9.07) is associated with a high risk of CKD, which is the main cause of end-stage kidney disease in diabetics.[9] These results suggest that the TyG index may be useful for finding and monitoring the risk of DKD in patients with newly diagnosed T2D.

In a study conducted by Liu et al (2021), patients with type 2 diabetes and DKD showed greater insulin resistance compared to patients without DKD, as indicated by the TyG index and higher HOMA2-IR scores. To identify DKD in type 2 diabetic patients, the TyG index showed a higher AUC ROC score (AUC 0.67, p=0.002) compared with HOMA2-IR (AUC 0.61, p=0.029). With a cut-off point of more than 9.66, the TyG index has a sensitivity of 61.7% and a specificity of 76.0%. In addition, the TyG index was positively correlated with levels of metabolic indicators such as weight, HbA1C, triglycerides, total cholesterol, serum uric acid, fasting glucose, and HOMA2-IR ($p < 0.05$ for each) but not with lneGFR values. According to multiple regression analysis, the TyG index as a marker of insulin resistance substitution is independently associated with the diagnosis of type 2 diabetes complications (OR=1.91; p= 0.001).[18]

The present review demonstrates that the TyG index is a useful tool for detecting DKD in T2D patients. A new indicator that has been proposed recently, the TyG Index, has shown to be a simple and dependable marker to replace IR.[12] This review also showed that in patients with type 2 diabetes, elevated FBG and TG have been linked to the development of DKD. A high TyG index has been linked to an increased risk of type 2 diabetes in the general population.[9]

The etiology of DKD is linked to insulin resistance, however, incompletely understood mechanisms underlie the association.[19] Increased renal vascular permeability and, eventually, glomerular hyperfiltration are linked to insulin resistance and increased glomerular hydrostatic pressure. Additional routes and mechanisms that may connect diabetes-related kidney disease (DKD) with insulin resistance include increased lipotoxicity, oxidative stress, metabolic acidosis, and inflammation, which can result in microangiopathy.[4,20]

This review has some limitations. There are certain restrictions on this review. A broad spectrum of scientific literature is typically included in reviews, which can be obtained via several techniques such as manual searches, electronic databases, internet search engines, and gray literature, among others. Nevertheless, because this review's search techniques were restricted to electronic databases, it is likely that fewer papers were examined than it would have if other search methods had been included.

Conclusion

We concluded that among patients with type 2 diabetes mellitus, TyG and DKD significantly correlated positively in our review. The TyG index has been proposed as a marker of insulin resistance as a simple and clinically reliable substitute for predicting the risk of diabetic kidney disease in type 2 diabetes mellitus.

Conflicts of Interest

There is no conflict of interest.

Funding sources

There is no funding source.

Acknowledgments

There is no acknowledgments

References

1. International Diabetes Federation. IDF Diabetes Atlas 10th edition. n.d.
2. Hoogeveen EK. The Epidemiology of Diabetic Kidney Disease. Kidney and Dialysis 2022;2:433–42. https://doi.org/10.3390/kidneydial2030038.
3. Poloni JAT, Rotta LN. Diabetic kidney disease: Pathophysiological changes and urinalysis contribution to diagnosis-a narrative review. J Lab Precis Med 2022;7. https://doi.org/10.21037/jlpm-21-20.
4. Jha R, Lopez-Trevino S, Kankanamalage HR, Jha JC. Diabetes and Renal Complications: An Overview on Pathophysiology, Biomarkers and Therapeutic Interventions. Biomedicines 2024;12. https://doi.org/10.3390/biomedicines12051098.
5. Wang H, Chen G, Sun D, Ma Y. The threshold effect of triglyceride glucose index on diabetic kidney disease risk in patients with type 2 diabetes: unveiling a non-linear association. Front Endocrinol (Lausanne) 2024;15. https://doi.org/10.3389/fendo.2024.1411486.
6. Schrauben SJ, Jepson C, Hsu JY, Wilson FP, Zhang X, Lash JP, et al. Insulin resistance and chronic kidney disease progression, cardiovascular events, and death: Findings from the chronic renal insufficiency cohort study. BMC Nephrol 2019;20. https://doi.org/10.1186/s12882-019-1220-6.
7. Freeman AM, Acevedo LA, Pennings N. Insulin Resistance . Ncbi 2023. https://www.ncbi.nlm.nih.gov/books/NBK507839/ (accessed September 5, 2024).
8. Jiang Y, Lai X. Association between the triglyceride glucose index, triglyceride-glucose body mass index and diabetic kidney disease in adults with newly diagnosed type 2 diabetes. Front Med (Lausanne) 2024;11. https://doi.org/10.3389/fmed.2024.1328601.
9. Shang J, Yu D, Cai Y, Wang Z, Zhao B, Zhao Z, et al. The triglyceride glucose index can predict newly diagnosed biopsy-proven diabetic nephropathy in type 2 diabetes: A nested case control study. Medicine 2019;98:e17995. https://doi.org/10.1097/MD.0000000000017995.
10. KDIGO. Official JOurnal Of the internatiOnal SOciety Of nephrOlOgy KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. 2013.
11. Flake CC, Morales-Valenzuela M, Tiongco RE, Navarro A. Profiling triglyceride-glucose index in Filipinos with type 2 diabetes mellitus: a single-center study. Egypt J Intern Med 2024;36. https://doi.org/10.1186/s43162-024-00294-9.
12. Gao YM, Chen WJ, Deng ZL, Shang Z, Wang Y. Association between triglyceride-glucose index and risk of end-stage renal disease in patients with type 2 diabetes mellitus and chronic kidney disease. Front Endocrinol (Lausanne) 2023;14. https://doi.org/10.3389/fendo.2023.1150980.
13. Thomas SS, Zhang L, Mitch WE. Molecular mechanisms of insulin resistance in chronic kidney disease. Kidney Int 2015;88:1233–9. https://doi.org/10.1038/ki.2015.305.
14. Whaley-Connell A, Sowers JR. Insulin Resistance in Kidney Disease: Is There a Distinct Role Separate from That of Diabetes or Obesity. Cardiorenal Med 2017;8:41–9. https://doi.org/10.1159/000479801.
15. Li HF, Miao X, Li Y. Influence of Insulin Resistance on Diabetes Nephropathy. Medical Science Monitor 2023;29. https://doi.org/10.12659/MSM.939482.
16. Lv L, Zhou Y, Chen X, Gong L, Wu J, Luo W, et al. Relationship between the tyg index and diabetic kidney disease in patients with type-2 diabetes mellitus. Diabetes, Metabolic Syndrome and Obesity 2021;14:3299–306. https://doi.org/10.2147/DMSO.S318255.
17. Tu Z, Du J, Ge X, Peng W, Shen L, Xia L, et al. Triglyceride Glucose Index for the Detection of Diabetic Kidney Disease and Diabetic Peripheral Neuropathy in Hospitalized Patients with Type 2 Diabetes. Diabetes Therapy 2024;15:1799–810. https://doi.org/10.1007/s13300-024-01609-3.
18. Liu L, Xia R, Song X, Zhang B, He W, Zhou X, et al. Association between the triglyceride–glucose index and diabetic nephropathy in patients with type 2 diabetes: A cross-sectional study. J Diabetes Investig 2021;12:557–65. https://doi.org/10.1111/jdi.13371.
19. Galicia-Garcia U, Benito-Vicente A, Jebari S, Larrea-Sebal A, Siddiqi H, Uribe KB, et al. Pathophysiology of type 2 diabetes mellitus. Int J Mol Sci 2020;21:1–34. https://doi.org/10.3390/ijms21176275.
20. Antar SA, Ashour NA, Sharaky M, Khattab M, Ashour NA, Zaid RT, et al. Diabetes mellitus: Classification, mediators, and complications; A gate to identify potential targets for the development of new effective treatments. Biomedicine and Pharmacotherapy 2023;168. https://doi.org/10.1016/j.biopha.2023.115734.