CARBOHYDRATE METABOLISM PARAMETERS IN PATIENTS WITH MASLD DEPENDING ON THE PRESENCE OF RENAL DYSFUNCTION

Prof. L.T. Daminova[1], PhD, DSc, N.Z. Muxiddinova[2], MD, D.Sh. Adilova[3], PhD, S.U. Muminova[4] MD, PhD
Tashkent State Medical University. Tashkent, Uzbekistan[1, 2, 3, 4]
https://doi.org/10.5281/zenodo.18464076

Abstract. *Objective: To investigate carbohydrate metabolism parameters in patients with metabolic dysfunction–associated fatty liver disease (MAFLD) depending on the presence of renal dysfunction. The study assessed kidney functional status in young patients with metabolic dysfunction–associated fatty liver disease (MAFLD). A total of 105 patients aged 18–45 years with ultrasound-confirmed hepatic steatosis were included and divided into two groups: MAFLD (n = 81) and MAFLD + chronic kidney disease (CKD) (n = 24). Patients with MAFLD and renal dysfunction demonstrated significantly higher levels of fasting glucose, insulin, HbA1c, and metabolic indices—HOMA-IR, TyG, and METS-IR—compared with MAFLD patients without renal impairment. The integral indices of insulin resistance showed significant correlations with eGFR and albuminuria: HOMA-IR, TyG, and METS-IR were inversely associated with eGFR and positively associated with the albumin-to-creatinine ratio (A/Cr). Young patients with concomitant MAFLD and CKD exhibit a marked exacerbation of metabolic disturbances, including increases in HOMA-IR, TyG, and METS-IR, indicating more pronounced insulin resistance. Integral insulin resistance indices—HOMA-IR, TyG, and METS-IR—demonstrate significant correlations with eGFR and albuminuria.*

Keywords: *insulin resistance, CKD, HOMA-IR, TyG, METS-IR.*

Introduction

Metabolic dysfunction–associated steatotic liver disease (MASLD) is one of the most prevalent chronic liver diseases and is currently regarded as a key component of the cardiometabolic continuum [1–3]. The transition from the term non-alcoholic fatty liver disease (NAFLD) to MASLD emphasizes the dominant role of metabolic dysfunction, insulin resistance, and systemic inflammation in disease pathogenesis [1]. Contemporary studies demonstrate that the presence of MASLD significantly increases the risk of developing chronic kidney disease (CKD), with the magnitude of risk closely correlating with the severity of hepatic fibrosis and the degree of metabolic impairment [2–4].Given the close interrelationship between MASLD, insulin resistance (IR), and renal dysfunction, the assessment of carbohydrate metabolism parameters and integrated indices of insulin resistance in patients with MASLD according to the presence of CKD represents a highly relevant research objective with substantial prognostic and clinical significance. Aim of the work to evaluate parameters of carbohydrate metabolism in patients with MASLD depending on the presence of renal dysfunction.

Materials and Methods

The study included 105 young adult patients (aged 18–45 years) with ultrasound-confirmed hepatic steatosis. Inclusion criteria were the absence of alcohol abuse, previously diagnosed chronic kidney disease, diabetes mellitus, and arterial hypertension. Stratification based on renal

function revealed that 22.9% of patients (n = 24) with hepatic steatosis exhibited impaired renal function, defined by reduced estimated glomerular filtration rate (eGFR) and increased albumin-to-creatinine ratio (ACR), corresponding to CKD stages G1–G2, A2 according to KDIGO criteria. All patients with MASLD were divided into two groups according to renal functional status: Group 1 (MASLD) – 81 patients with preserved renal function; Group 2 (MASLD + CKD) – 24 patients with varying degrees of renal dysfunction. Integrated indices of insulin resistance were calculated: HOMA-IR (Homeostasis Model Assessment of Insulin Resistance), TyG (Triglyceride–Glucose Index), and METS-IR (Metabolic Score for Insulin Resistance) using the following formulas:

- **HOMA-IR** = [fasting glucose (mmol/L) × fasting insulin (μIU/mL)] / 22.5
- **TyG** = ln [triglycerides (mg/dL) × glucose (mg/dL) / 2]
- **METS-IR** = ln [2 × glucose (mg/dL) + triglycerides (mg/dL)] × BMI / ln (HDL-cholesterol)

All data were entered into Microsoft Excel spreadsheets. For parametric variables, mean values and standard errors were calculated. Correlation analysis was performed using Pearson's correlation coefficient, with statistical significance determined accordingly.

Results and Discussion

The results demonstrated moderate disturbances of carbohydrate metabolism in patients with MASLD. Mean fasting glucose levels remained within reference ranges but were higher than in healthy controls, reflecting a tendency toward reduced tissue insulin sensitivity (Table 1). In the presence of CKD, fasting glycemia increased significantly to 5.61 ± 0.24 mmol/L ($p < 0.05$), indicating impaired glucose tolerance.

A parallel significant increase in fasting insulin levels was observed in MASLD patients ($p < 0.05$) and was even more pronounced in the MASLD + CKD group ($p < 0.01$) compared with controls. Correspondingly, elevated HbA1c levels in both MASLD and MASLD + CKD groups ($p < 0.01$) confirmed a trend toward chronic hyperglycemia and disturbances in carbohydrate homeostasis. Although absolute values of glycemic parameters formally remained within normal ranges, their elevation relative to healthy individuals indicates early metabolic alterations characteristic of subclinical insulin resistance. These findings are consistent with contemporary data describing early insulin resistance in MASLD [1,5].

In patients with MASLD and concomitant renal dysfunction, all pathological trends were amplified, including higher glucose and insulin levels, reflecting progressive metabolic imbalance. Statistically significant differences between the two clinical groups underscore the mutual aggravation of renal dysfunction and hepatic steatosis in the development and progression of metabolic syndrome. These observations reflect more profound insulin resistance associated with chronic kidney disease, driven by persistent low-grade inflammation and impaired insulin clearance and utilization [10–11].

Table 1.

Parameters of carbohydrate metabolism in patients with MASLD according to renal function status

Parameter	MASLD (n = 81)	MASLD+ CKD (n = 24)	Control group (n = 20)
Fasting glucose, mmol/L	5,20 ± 0,25	5,61 ± 0,24*	4,40 ± 0,16
Fasting insulin, μIU/mL	8,22 ± 3,74*	14,4 ± 2,14**#	5,50 ± 2,10
HbA1c, %	5,3 ± 0,18*	5,7 ± 0,14**	4,6 ± 0,11

Note: Statistical significance was assessed using Student's *t*-test: $p < 0.05$; ** $p < 0.01$ versus the control group;

In recent years, increasing attention has been focused on the non-invasive assessment of metabolic disturbances using integrated indices such as HOMA-IR (Homeostasis Model Assessment of Insulin Resistance), TyG (Triglyceride–Glucose Index), and METS-IR (Metabolic Score for Insulin Resistance). The HOMA-IR index is widely used to quantify the degree of insulin resistance, reflecting reduced tissue sensitivity to insulin. It allows indirect evaluation of the effectiveness of insulin–receptor interaction and pancreatic β-cell function.

In the control group, the mean HOMA-IR value was 1.07 ± 0.15, corresponding to physiological insulin sensitivity. In patients with MASLD, the index was significantly elevated to 1.91 ± 0.42 ($p < 0.001$), indicating the development of early insulin resistance, although values remained within borderline limits (< 2.5). In the presence of CKD, HOMA-IR increased further to 3.72 ± 0.14 ($p < 0.001$), reflecting overt insulin resistance caused by impaired insulin homeostasis and reduced renal insulin clearance. Thus, patients with concomitant MASLD and CKD exhibited an almost two-fold increase in HOMA-IR compared with isolated MASLD, highlighting the amplification of metabolic dysfunction in the setting of renal impairment.

The TyG index is a direct surrogate marker of insulin resistance, reflecting the interplay between lipid and carbohydrate metabolism. In the control group, TyG was 7.30 ± 0.08, which is within the normal range (< 8.5). In patients with MASLD, TyG increased significantly to 8.77 ± 0.10 ($p < 0.001$), indicating subclinical insulin resistance even when individual biochemical parameters remain within reference limits. In the MASLD + CKD group, TyG reached 9.09 ± 0.09 ($p < 0.001$), reflecting severe dysregulation of glucose–lipid metabolism and correlating with an increased risk of cardiovascular complications.

METS-IR is an integrated metabolic index reflecting the degree of insulin resistance and overall metabolic impairment. This index shows a strong correlation with insulin sensitivity assessed by the euglycemic clamp technique (gold standard). In the present study, healthy individuals demonstrated a mean METS-IR value of 30.2 ± 1.1, consistent with normal insulin sensitivity. In patients with MASLD, METS-IR was significantly higher at 40.7 ± 1.2 ($p < 0.001$), indicating metabolic imbalance and enhanced tissue lipid infiltration. In patients with combined MASLD and CKD, METS-IR reached 54.8 ± 1.4 ($p < 0.001$), exceeding control values by nearly 1.8-fold. This finding reflects severe metabolic decompensation characteristic of patients with chronic renal dysfunction and advanced metabolic syndrome.

Table 2.

Integrated indices of carbohydrate metabolism in patients with MASLD according to renal function status

Parameters	MASLD (n = 81)	MASLD+CKD (n = 24)	Control group (n = 20)
HOMA-IR	1,91 ± 0,42*	3,72 ± 0,14***##	1,07 ± 0,15
METS-IR	40,7 ± 1,2***	54,8 ± 1,4***##	30,2 ± 1,1
TyG	8,77 ± 0,10***	9,09 ± 0,09***#	7,30 ± 0,08

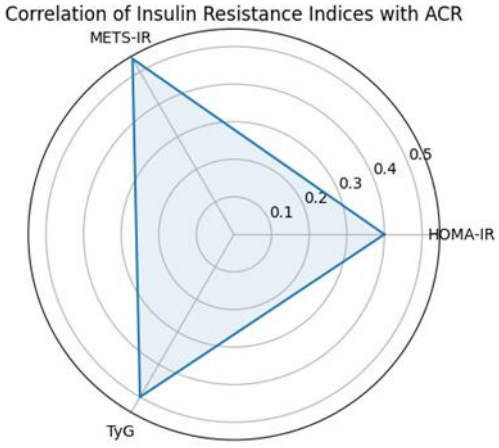
Note: Statistical significance was assessed using Student's *t*-test: $p < 0.05$; ** $p < 0.01$ versus the control group;

Correlation Analysis

A correlation analysis was performed to evaluate the associations between insulin resistance indices and renal functional parameters in patients with MASLD. The data demonstrated significant correlations between integrated metabolic indices (HOMA-IR, METS-IR, and TyG) and key markers of renal function, including estimated glomerular filtration rate (eGFR) and the albumin-to-creatinine ratio (ACR).

A statistically significant inverse correlation was identified between HOMA-IR and eGFR ($R = –0.31$; $p < 0.05$), as well as between METS-IR and eGFR ($R = –0.31$; $p < 0.01$). The TyG index, reflecting combined glucose–lipid dysregulation, showed an even stronger negative association with eGFR ($R = –0.41$; $p < 0.05$), suggesting higher sensitivity to early metabolic disturbances affecting renal function.

A significant positive correlation was observed between insulin resistance indices and ACR levels (Figure 1). HOMA-IR correlated moderately with ACR ($R = +0.40$; $p < 0.01$), whereas stronger associations were observed for METS-IR ($R = +0.54$; $p < 0.01$) and TyG ($R = +0.50$; $p < 0.01$), indicating a close relationship between metabolic dysregulation and early renal injury in patients with MASLD.



Elevated HOMA-IR in patients with MASLD, particularly in the MASLD + CKD group, is consistent with large-scale studies demonstrating an independent association between HOMA-IR, albuminuria, and reduced eGFR [11,12]. According to Li et al., a HOMA-IR threshold > 2.5 is associated with an increased risk of CKD [13], supporting the pivotal role of insulin resistance in early nephron injury.

The TyG index exhibited pronounced intergroup differences and high diagnostic value. Its elevation in MASLD + CKD patients aligns with findings by Wang Z. and Li X., reporting associations between TyG, microalbuminuria, and declining eGFR [14,15]. Recent cohort studies have demonstrated that both TyG and METS-IR independently predict CKD onset and progression even in non-diabetic populations [6,10], highlighting METS-IR as a valuable integrated metabolic marker.

The observed inverse correlations between HOMA-IR, METS-IR, TyG and eGFR, together with positive correlations with albuminuria, are consistent with the concept of a “metabolic nephropathic continuum.” These findings indicate that increasing insulin resistance is closely linked to the development of albuminuria, reflecting enhanced glomerular permeability and early glomerular injury [3,4]. The strongest associations with eGFR were observed for METS-IR and TyG, consistent with reports suggesting that these indices may outperform HOMA-IR in assessing cardiometabolic and renal risk [9,10].

Conclusions

Young adults with MASLD exhibit moderate disturbances of carbohydrate metabolism consistent with early-stage insulin resistance. Concomitant CKD is associated with a significant amplification of metabolic abnormalities, including elevated HOMA-IR, TyG, and METS-IR, indicating more pronounced insulin resistance. Integrated insulin resistance indices demonstrate significant correlations with eGFR and albuminuria, supporting their potential utility as non-invasive markers for early identification of renal dysfunction and cardiometabolic risk in patients with MASLD.

REFERENCES

1. Tilg H., Eslam M., George J. MAFLD and the paradigm shift in fatty liver disease. *Nat Rev Gastroenterol Hepatol*. 2020;17(8):387–388.
2. Byrne C.D., Targher G. NAFLD as a driver of chronic kidney disease. *J Hepatol*. 2020;72(4):785–801.
3. Mantovani A., et al. Steatotic liver disease and risk of chronic kidney disease. *Diabetes Metab*. 2024;50(1):101506.
4. Gao J., et al. Severity and remission of MAFLD and CKD risk. *J Am Heart Assoc*. 2024;13:e032604.
5. Assani M.Z., et al. Comparative evaluation of insulin resistance indices. *Life (Basel)*. 2025;15(12):1845.
6. Zhang Y., et al. Triglyceride–glucose index and risk of chronic kidney disease. *Kidney Blood Press Res*. 2025.
7. Musso G., et al. NAFLD and insulin resistance: meta-analysis. *Diabetes Care*. 2019;42(12):2301–2311.
8. Shi Y., et al. HOMA-IR and NAFLD severity. *Metabolism*. 2020;108:154–165.
9. Ma X., et al. METS-IR as a marker of NAFLD. *Front Endocrinol*. 2024.
10. Sharifi M., et al. TyG index and CKD risk: NHANES 1999–2020. *Int Urol Nephrol*. 2024;56(11):3605–3616.
11. Koppe L., Fouque D. Insulin resistance in CKD. *Clin Nutr*. 2019;38(2):484–494.
12. Lin C.-A., Liu Y.-P., Chen Y.-C. et al. Gender-specific and age-specific associations of the HOMA-IR with albuminuria and renal impairment // BMJ Open. 2021. Vol. 11. e053649.
13. Li J., Zhou Q., Liu Z. et al. Association of insulin resistance with chronic kidney disease in individuals without diabetes // BMC Nephrology. 2024. Vol. 25. 437.
14. Wang Z., Qian H., Zhong S. et al. Relationship between triglyceride–glucose index and albuminuria // Frontiers in Endocrinology. 2023. Vol. 14. 1215055.
15. Li X., Li T., Liu D. et al. Triglyceride-glucose index and diabetic kidney disease // PLOS ONE. 2024. 19(3): e0299864.