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TRIGLYCERIDE-GLUCOSE INDEX: A REPLACEMENT MEASURE OF HOMEOSTASIS TO ASSESS INSULIN ESISTANCE AND FORECAST OF DIABETIC NEPHROPATHY

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ABSTRACT

BACKGROUND: The World Health Organization estimates that diabetes killed almost 1.5 million people in 2019. Diabetic nephropathy (DN) is the most common underlying cause of end-stage renal disease in people with diabetes. About 40% of people on Earth have DN. Albuminuria or a decrease in glomerular filtration rate (GFR) indicate chronic renal impairment, which accounts for 31% of all cases of diabetic kidney disease (DN) in Pakistan.

OBJECTIVE: In order to predict diabetic nephropathy, the current study sought to determine whether the TyG index is related to UACR or HOMA-IR in people with type 2 diabetes.

STUDY DESIGN: A cross-sectional study

PLACE AND DURATION: This study was conducted in Liaquat University of Medical and Health Sciences Jamshoro from January 2023 to January 2024

METHODOLOGY: The sample size was calculated using the formula Z2 (pq)/e2, with Z=1.96, p=prevalence of T2DM in Pakistan 17.1%, Using a non-probability sequential selection approach, a sample of patients visiting the diabetic clinic was selected. Included were known T2DM patients who had been diagnosed for one to five years and had a fasting plasma glucose (FPG) of 126 mg/dl or above. Venous blood samples (5 ml) were taken using special tubes for different parameters after a 10- to 12-hour overnight fast, and they were then refrigerated at -20°C. For HOMA-IR evaluation, the concentrations of insulin and FPG were measured. A spot urine sample was collected in order to calculate the ACR.

RESULTS: Among the 180 patients, 48.7±7.56 years was the average age. The average BMI for everyone was 28.63±4.56. When comparing Q4 to the other quartiles, there was a substantial increase in fasting plasma glucose, triglycerides, total cholesterol, low-density lipoprotein (LDL) cholesterol, and HOMA-IR ($p<0.05$

CONCLUSION: In T2DM patients, the TyG index outperformed HOMA-IR in predicting DN, exhibiting a substantial correlation with the latter. In T2DM patients, it accurately predicted the probability of micro-albuminuria and diabetic nephropathy at an early stage.

Keywords: Diabetic nephropathy,Homeostasis model assessment, Triglyceride-glucose index

INTRODUCTION

Diabetes mellitus (DM) is characterized by hyperglycemia, irregularities in the metabolism of proteins, lipids, and carbohydrates, and progressive damage, malfunctions, and failures of several critical organs, such as the kidneys, heart, blood vessels, eyes, and nerves [1, 2]. In 2021, it is anticipated that over 537 million people, or 10.5% of the world's population, will suffer from diabetes. This was expected to expand at rates of 643% by 2030 and 783% by 2045 [3]. The most recent statistics from the International Diabetes Federation (2022) shows that the incidence of diabetes in adults in Pakistan has risen to 26.7%, meaning that there are over 33,000,000 cases overall [4, 5].

About 1.5 million people died from diabetes in 2019, making it the leading cause of death. [6]. Pakistan is among the countries most vulnerable to diabetes-related deaths because the condition is more prevalent in low- and middle-income countries. Adults with diabetes are mostly at risk for the disease due to genetics and leading an unhealthy lifestyle. These include living a sedentary lifestyle, which contributes to obesity, and consuming more processed foods with added sugar [4]. Pakistan's overall weighted prevalence of generalized obesity was 57.9% (42% in men and 58% in women) based on WHO Asia-Pacific cutoffs, while central obesity was 73.1% (37.3% in men and 62.7% in women) [7].

Globally about 40% of individuals have DN [8]. A total of 31% of all instances of diabetic kidney disease (DN) in Pakistan are due to chronic renal impairment, as shown by albuminuria or a decline in glomerular filtration rate (GFR) [9, 10].

Patients should be screened for DN both at the time of diagnosis and once a year since type 2 diabetes (T2DM) develops slowly. After determining the spot urine albumin-to-creatinine ratio (UACR) from blood creatinine, urinary creatinine, and albumin in a spot urine test, screening must determine estimated GFR (eGFR) [11].

In Pakistani, pertinent data has proven elusive. A novel, easily available, reasonably priced, and trustworthy marker is required to forecast early-stage diabetic nephropathy in the Pakistani population. The purpose of the current study was to ascertain if the TyG index is associated with HOMA-IR in patients with type 2 diabetes and whether it is associated with UACR in order to predict diabetic nephropathy.

METHODOLOGY

The sample size was calculated using the formula Z2 (pq)/e2, with Z=1.96, p=prevalence of T2DM in Pakistan 17.1%, q=1-p, and margin of error e=5%, after receiving clearance from the institutional ethical review committee [19].

Using a non-probability sequential selection approach, a sample of patients visiting the diabetic clinic was selected. Included were known T2DM patients who had been diagnosed for one to five years and had a fasting plasma glucose (FPG) of 126 mg/dl or above. Individuals afflicted with type 1 diabetes (T1DM), long-term medical conditions, smoking, pregnancy, and dialysis were not allowed-to-participate.

After obtaining the patients' informed consent and guaranteeing their confidentiality, data was gathered. Age, gender, length of diabetes, waist circumference (WC), height, weight, blood pressure (BP), and body mass index (BMI) were among the demographic and clinical data. Venous blood

samples (5 ml) were taken using special tubes for different parameters after a 10- to 12-hour overnight fast, and they were then refrigerated at -20°C. For HOMA-IR evaluation, the concentrations of insulin and FPG were measured. A spot urine sample was collected in order to calculate the ACR. The individuals were split into 4 quartiles based on their TyG index scores: Q1=4.5–5, Q2=5.1–5.5, Q3=5.6–6, and Q4=>6.

We used the SPSS version 26 for data analysis. The TyG index, HOMA-IR, UACR, eGFR, anthropometric indices, and biochemical data were analyzed using Pearson correlation. The predictive ability of the TyG index and the HOMA-IR for the assessment of eGFR and UACR was evaluated using linear regression analysis. P value less than 0.05 was regarded as significant.

RESULTS

Among the 180 patients, 48.7±7.56 years was the average age. The average BMI for everyone was 28,63±4.56. Table I includes information on the mean age, BMI, waist circumference, SBP, DBP, and mean length of diabetes. When comparing Q4 to the other quartiles, there was a notable variation in age, diastolic blood pressure (DBP), and time spent with type 2 diabetes.

Table I Socio-Demographic distribution according to triglyceride-glucose (TyG) index quartiles.

Demographic Characteristics	Quartile 1 (4.5-5) n=47	Quartile 2 (5.1-5.5) n=72	Quartile 3 (5.6-6) n=38	Quartile 4 (>6) n=23
Age (years)	48.65±7.21	42.93±8.91	46.470±8.79	49.21.±6.89
Body Mass Index (BMI)	27.3124±2,65	28.45±3.11	27.65±3.11	29.01±3.09
Waist circumference (inches)	31.55±4.12	32.44±3.99	31.67±3.51	31/83±8.09
Systolic blood pressure (SBP) (mmHg)	137±10.5	130±14.3	134±13.78	131±13.54
Diastolic blood pressure (DBP) (mmHg)	79.±10.5	82±9.0	78±8.5	87±12.5
Duration of type 2 diabetes mellitus (Years)	4.56±0.92	4.1±2.01	4.3±2.12	5.2±2.01

When comparing Q4 to the other quartiles, there was a substantial increase in fasting plasma glucose, triglycerides, total cholesterol, low-density lipoprotein (LDL) cholesterol, and HOMA-IR ($p<0.05$). Urinary albumin and high-density lipoprotein (HDL) cholesterol were considerably lower in Q4 than in the other three quartiles ($p<0.05$). (As shown in Table II)

Table II Triglyceride-glucose (TyG) index quartiles Based distribution of Biochemical parameters

Biochemical Parameters	Quartile 1 (n=47) (4.5-5)	Quartile 2 (n=72) (5.1-5.5)	Quartile 3 (n=38) (5.6-6)	Quartile 4 (n=23) (>6)
Fasting plasma glucose (mg/dl)	162.43±23.5	211±34.7[a]	224±56.5	322.4±58.7
Fasting serum insulin (µIU/mL)	3.43±0.98	3.12±1.02	2.89±1.43	4.23±1.78
Serum cholesterol (mg/dL)	166.3±36.6	177.78±36.2	188.89±61.4	225±34.1
Serum triglyceride (mg/dL)	145.43±41.56	212.65±67.2	312.98±60.8	520.76±110.5
HDL-C (mg/dL)	38.45±5.6	34.54±6.75	32.6±5.97	32.4±5.67
LDL-C (mg/dL)	132.4±41.3	139.9±33.3	146±37.2	156.88±16.12
HOMA-IR	1.67±0.12	1.72±0.69	1.97±0.75	2.10.9±0.88
Urinary albumin (mg/dL)	5.95±2.29	5.89±3.1	6.34±3.12	5.17±3.42

DISCUSSION

In order to forecast diabetic nephropathy, the association between the UACR and TyG index was assessed. The TyG index has been examined in many research as a possible indicator of heart disease, diabetes, and metabolic problems. However, it hasn't received as much attention as other techniques for evaluating IR [18, 20].

The definition of insulin resistance (IR) is decreased sensitivity to insulin in tissues, which raises the risk of hyperglycemia, hypertension, and dyslipidemia. Lipid levels have been studied as a major parameter to evaluate the insulin action to determine IR. Overweight and obese individuals with greater triglyceride levels are more likely to have increased IR and lipoprotein metabolic abnormalities, such as raised levels of triglyceride-rich lipoprotein remnants, remnant-like particle cholesterol, and apolipoprotein B [21]. Higher triglyceride levels have been associated with lower insulin sensitivity, and vice versa. It has been demonstrated that muscles with elevated triglyceride levels have poor glucose utilization. In the current investigation, it was discovered that triglycerides and FPG were independently linked to DN [17].

In Pakistan, a 2018 study investigated the relationship between the TyG index and DN and IR. When compared to other markers such fasting triglycerides, HOMA-IR, and HDL-C, the TyG index showed a greater linear link with BMI, atherogenic dyslipidemia, HbA1c, and IR. The research found no evidence linking the TyG index to DN and concluded that the TyG index was a more accurate measure of MSm [21].

The TyG index, HOMA-IR, and UACR were observed to significantly negatively correlate with eGFR in the current investigation. However, a research conducted on a Chinese population found no evidence of a significant correlation ($p=0.786$) between the TyG index and eGFR. Nonetheless, it discovered a high correlation ($r=0.173$, $p=0.006$) between an increased TyG index and type 2 DN, which is in line with the current findings [16].

DN and HOMA-IR have also been connected in earlier studies. The new results supported previous research by showing that high HOMA-IR levels were common in diabetic nephropathy patients. In particular, the current study discovered that the TyG index showed a stronger correlation with DN than HOMA-IR (AUC 0.37, 95% CI: 0.27-0.46, $p<0.01$), with sensitivity of 59% and specificity of 65%. The TyG index also had a higher area under the curve (AUC) (0.51, 95% confidence interval [CI]: 0.28-0.47, $p<0.01$) with sensitivity of 67% and specificity of 85%. When compared to HOMA-IR, the TyG index was clearly a more reliable diagnostic tool for predicting type 2 diabetes and albuminuria.

Similar to this study, a 2020 study conducted in India investigated the relationship between TyG index and DN, diabetic neuropathy, and diabetic retinopathy. The study found that albuminuria was correlated with a higher level of TyG index, but it did not include eGFR. FPG and triglycerides were found to be independently associated with DN [17]. The present study, however, differs from the others in that it uses spot urine ACR rather than 24-hour albumin excretion rate.

CONCLUSION

In T2DM patients, the TyG index outperformed HOMA-IR in predicting DN, exhibiting a substantial correlation with the latter. In T2DM patients, it accurately predicted the probability of micro-albuminuria and diabetic nephropathy at an early stage.

CONFLICT

No conflict of interest

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ETHICAL APPROVAL

It was taken

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