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Comparison of Serum Uric Acid-to-HDL Ratio and Triglyceride Glucose Index in Relation to Glycemic Control Among Patients with Type 2 Diabetes Mellitus

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ABSTRACT

Diabetes mellitus, which is a case of impaired metabolism related to insulin production or resistance occurs. Serum uric acid levels elevating to some extent were related to diabetes and metabolic syndrome. Hyperuricemia is a serious health risk that may underlie metabolic disorders, such as type 2 diabetes and metabolic syndrome. **Objective:** To investigate the correlation of uric acid and triglyceride variables with glycemic control in patients with Type 2 Diabetes Mellitus (T2DM). **Methods:** A Comparative cross-sectional study was conducted on 167 patients categorized into non-diabetic (n=59), diabetic with good glycemic control (n=41), and diabetic with poor glycemic control (n=62) groups. Sociodemographic data and serum variables were recorded. Statistical analysis was performed using SPSS version 26.0, employing one-way ANOVA and Pearson correlation tests. **Results:** Patients with poor glycemic control exhibited significantly higher fasting blood sugar levels and triglyceride glucose index compared to non-diabetic and well-controlled diabetic individuals. However, there were no significant differences in serum uric acid levels and UHR among the study groups. A positive correlation was observed between the triglyceride glucose index and HbA1c, highlighting the association between intermittent blood glucose rises and worse glycemic outcomes. **Conclusion:** The triglyceride glucose index revealed the potential to be an inexpensive indicator to evaluate blood sugar levels and should be taken into consideration together with the other generally used indicators like HbA1c to strengthen diabetes management.

INTRODUCTION

Diabetes mellitus, which is a case of impaired metabolism related to insulin production or resistance occurs [1]. The case of diabetes is evidenced worldwide in 2022 at the rate of 10.5%, about 500 million people are affected worldwide [2]. There are quite close to half of patients with diabetes who are not aware of their situation, which is about 49.7% [3]. Though this disease is primarily a problem in developed countries, it is quickly becoming a significant issue in developing nations, and the number of affected people may rise to 80 percent of the total number [4]. Of the total population of Pakistan, as many as 26.7%, meaning the number is as high as 33 million people. Timely glycemic control is so instrumental in Bangladesh whereby it would reduce associated morbidity and mortality from diabetes [5]. Glycemic control monitoring role is crucial and the blood glucose level self-monitoring using the Simple Blood Glucose Meter (SMBG) is the best solution accompanied by the glycated hemoglobin (HbA1c) test [6]. HbA1c, rigorous

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as it may be, still has some limitations that are time-consuming, costly, and not available in the developing world [7]. Research indicates that pulsatile rises of blood-glucose levels are very impactful as compared to prolonged hyperglycemia. However, in chronic hyperglycemia, pulsatile rises of glucose levels cannot overcome the continuous hyperglycemia in the progression of the disease. The patients with variable blood glucose levels, concurrently with HbA1c, the use of SMBG and Continuous Glucose Monitoring (CGM) is considered appropriate to assess glycemic control [6]. Lowering HbA1c to less than 7% diminishes the risk for micro and macrovascular complications in diabetes by a large margin [8]. Besides, as for the rise of one percent in HbA1c, the cardiovascular risk is expected to endure by 18 percent [2]. Nevertheless, the majority of diabetic (20% to 30%) patients cannot satisfy the stringent HbA1c goal. LAS or elevated low-density lipoprotein (LDL) cholesterol are predetermining factor, especially for endothelial dysfunction and cardiovascular disorders out of diabetes. Elevated levels of triglyceride (TG) in diabetes mellitus and lower high-density lipoproteins (HDL)-C mainly cause insulin resistance and raise the possibility of cardiovascular disease [9]. Glucose levels in the blood interact with the components of the lipid profile in a refined manner, and good glycemic control has a positive influence on the total cholesterol and HDL levels. Optimal regulation of both parts of a blood glucose and lipid complex is the number one priority when dealing with type 2 diabetes mellitus [10]. Serum uric acid levels elevating to some extent are related to diabetes, NAFLD, and metabolic syndrome. Hyperuricemia is a serious health risk that may underlie metabolic disorders, such as type 2 diabetes and metabolic syndrome [8]. However low uric acid levels are also associated with higher triglycerides, metabolic syndromes, and cardiovascular disease as well. The presence of high levels (hyper) of uric acid in the body generates an acidic condition, which can result in the development of several metabolic problems [7]. Moreover, it is linked to small vessel complications in type 2 diabetes-like retinopathy and neuropathy among others. An experimental use of uric acid-lowering medicine may help to improve insulin sensitivity and development of the type 2 diabetes. About type 1 diabetes, hyperuricemia which is linked to the development of renal dysfunction and microalbuminuria is an accurate reflection [8, 9]. Moreover, a marker of glycemic control is needed and it must be able to be easily available and comprise no or minimal cost. The UHCR and TG are the new are being considered as biomarkers, because of their simplicity. UHR is a marker of metabolic worsening and is also related to having decreased metabolic status [10]. The triglyceride index is obtained by multiplying the fasting blood glucose level with that of the fasting triglyceride level and is a better predictor for insulin resistance, blood glucose control, hypertension development, and undesirable cardiovascular outcomes than conventional indicators of metabolic syndrome.

The current investigation focused on establishing the association of either the UHR and triglyceride glucose index values with glycemic control in metropolis patients with diabetes mellitus.

METHODS

A comparative cross-sectional study was conducted at Central Park Teaching Hospital in collaboration with Mansoorah Teaching Hospital after getting ethical approval from the institutional review board of Central Park Medical College Lahore (CPMC/IRB-no/1395) from March 2023 to September 2023. A sample size of 166 was calculated by using the WHO sample size calculator at the prevalence of hyperuricemia at 12.4 percent in diabetics with a confidence interval of 95 percent and a margin of error of 5 percent [11]. After getting ethical approval, a total of 167 patients with type 2 diabetes with an age range of 30 to 70 years were recruited for assessment of the Uric acid to HDL ratio and Triglyceride glycemic index. Study participants were grouped into 3 groups; group 1 (non-diabetic; n=60), group 2 (diabetic with good glycemic control; n=42), and group 3 (diabetic with poor glycemic control; n=64). A non-random convenient sampling method was adopted and the patients presenting in OPDs of both hospitals were enrolled after getting written informed consent. Those patients who had type 1 diabetes, ischemic heart disease, previous tuberculous infection, and any malignancy were excluded from the study. Sociodemographic details were recorded like gender, age, weight, height, BMI, systemic diseases, and duration of disease. For assessment of serum uric acid, serum HDL, fasting blood glucose levels and HbA1c, LDL cholesterol, VLDL cholesterol, and serum triglycerides, 5 cc venous blood was taken under aseptic conditions after applying tourniquet while patients sitting comfortably. That blood was centrifuged at 5000 rpm for 30 minutes and serum was separated for assessment of lab variables. These labs were done on commercially available ELISA kits. Data were entered into Microsoft Excel and were dully checked for errors and omissions after cross-verifying data were exported into SPSP version 26. Qualitative data were presented in terms of frequencies and percentages and were presented as charts and graphs. The normality of the data was checked using the Shapiro-Wilk test and the mean/median was computed depending upon normality. One-way ANOVA was employed for comparison between the groups and within-group analysis was done using Post Hoc Tukey analysis. For the assessment of correlation, person correlation was employed. For significant results, a cut of 0.05 p value was set.

RESULTS

The mean age for group 1 (non-diabetic; n=59) was 51.15 ±

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16.96 years, for group 2 (diabetic with good glycemic control; n=41) was 55.17 ± 10.02 and in group 3 (diabetic with poor glycemic control; n=62) mean age was 51.737 ± 10.08 with a p value of 0.239, no significant age difference was observed in study groups by applying one-way ANOVA. In group 1, there were 40 percent males (n=23) and 60 percent females (n=36), in group 2 there were 41 percent males (n=17) and 59% females (n=26) and in group 3 there were 46% males (n=29) and 54% females (n=35). Hypertension was majorly prevalent comorbid in all the study groups as in group 1; 56% (n=33), in group 2; 63% (n=26) and in group 3; 63% (n=40) were hypertensive as explained in table 1.

Table 1: Gender and Comorbidities of Study Population (n=166)

Variables	N (%)		
	Group 1	Group 2	Group 3
Male	23 (40%)	17 (41%)	29 (46%)
Female	36 (60%)	26 (59%)	35 (54%)
Hypertension	33 (56%)	26 (63%)	40 (63%)
Smokers	17 (29%)	12 (28%)	25 (39%)

One-way ANOVA was employed to assess and compare mean differences among study groups. Significant mean difference for fasting blood sugar levels, serum HbA1c and triglyceride glucose index was noted in study groups as explained in table 1 with the p-values of 0.0001, 0.0001 and 0.001 suggesting that poor glycemic control leads to derangement of blood sugar and triglyceride glucose index. Afterwards, variables of fasting lipid profile were compared among study groups, but no significant mean differences were notes as explained in table 2. Similarly, no significant mean difference was noted for serum uric acid and uric acid to HDL ratio among study groups.

Table 2: Assessment and Comparison of Study Variables among Study Groups (n=166)

Variables	Mean ± SD			p-Value
	Group 1	Group 2	Group 3	
Fasting BSI (mg/dL)	101.88 ± 8.70	123.49 ± 29.87	175.50 ± 63.23	<0.001*
HbA1c	5.70 ± 0.36	6.37 ± 0.41	9.03 ± 1.61	<0.001*
TAG Glucose Index	4.89 ± 0.21	4.88 ± 0.21	5.06 ± 0.32	0.001*
Serum Cholesterol (mg/dL)	192.64 ± 35.20	174.17 ± 58.44	174.02 ± 39.17	0.80
Serum TAG (mg/dL)	191.36 ± 77.76	163.10 ± 78.58	168.44 ± 74.438	0.20
Serum LDL (mg/dL)	109.42 ± 32.96	99.37 ± 41.65	103.61 ± 30.05	0.538
Serum VLDL (mg/dL)	46.69 ± 34.74	40.53 ± 23.69	41.81 ± 33.18	0.571
Serum HDL (mg/dL)	42.98 ± 8.1	45.02 ± 11.41	41.79 ± 9.33	0.294
Serum Uric Acid (mg/dL)	5.12 ± 1.14	4.81 ± 1.06	4.82 ± 1.21	0.234
Uric Acid to HDL Ratio	0.12 ± 0.03	0.11 ± 0.03	0.12 ± 0.04	0.287

*Difference is Significant at 5% level of Significance

Within group analysis was done by appliance of Post Hoc Tukey's analysis for three variables that had significant mean differences by ANOVA as explained in Table 1. In fasting BSI, significant group differences were noted between group 1 and group 2 (101.88 ± 8.70 versus 123.49 ± 29.87) with a mean difference (i-j) of -21.607 with a p-value of 0.032 suggestive of significantly lower blood sugar levels in non-diabetics when compared to diabetics. Similarly, on comparing groups 2 and 3 (123.49 ± 29.87 versus 175.50 ± 63.23), a significant mean difference (i-j) of -52.012 mg/dl with p p-value of 0.0001 was noted. Similarly, a significant mean difference in comparing groups 1 and 3 (101.88 + 8.70 versus 175.50 ± 63.23) was noted with i-j of -73.619 and p value of 0.0001 as explained I table 3. Correspondingly, similar sort of significant mean differences (i-j) can be appreciated for comparison of HbA1c in study groups as explained in Table 2. On the assessment of triglyceride glucose index, a significant mean difference between group 1 and group 3 (4.89 ± 0.21 versus 5.06 ± 0.32) with a mean difference (i-j) of -0.1599 with a p value of 0.003 suggesting increased triglyceride glucose index in diabetics with poor compliance when compared to non-diabetics as explained in table 2 and 3. Similarly, a significant mean difference for groups 2 and 3 (4.88 ± 0.21 versus 5.06 ± 0.32) with a mean difference (i-j) of -0.1471with p-value of 0.014 suggesting a lower triglyceride glucose index in controlled diabetics when compared to non-diabetics. No significant group difference was noted between groups 1 and 2 with a p-value of 0.968 suggesting controlled diabetics have a similar triglyceride glucose index as non-diabetics Table 3.

Table 3: Assessment and Comparison of Fasting Blood Sugar Levels, HbA1c and TAG Glucose Index with in Study Groups

Variables	Groups	Comparison Group	Mean Difference	p-Value
Fasting BSI	Groups 1	Groups 2	-21.607*	0.032*
		Groups 3	-73.619*	<0.001*
	Groups 2	Groups 1	21.607*	0.032*
		Groups 3	-52.012*	<0.001*
	Groups 3	Groups 1	73.619*	<0.001*
		Groups 2	52.012*	<0.001*
HbA1c	Groups 1	Groups 2	-0.6885*	0.003*
		Groups 3	-2.6812*	0.0001*
	Groups 2	Groups 1	0.6885*	0.003*
		Groups 3	-2.6812*	<0.001*
	Groups 3	Groups 1	3.3697*	<0.001*
		Groups 2	2.6812*	0.001*
TAG Glucose Index	Groups 1	Groups 2	-0.0128	0.968
		Groups 3	-0.1599*	0.003*
	Groups 2	Groups 1	0.0128	0.968
		Groups 3	-0.1471*	0.014*
	Groups 3	Groups 1	0.1599*	0.003*
		Groups 2	0.1471*	0.014*

*Within-group analysis using Post Hoc Tukey analysis, p-value<0.05 was considered as significant

On appliance of Pearson correlation between triglyceride glucose index and HbA1c, a positive correlation was noted

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with an R-value of 0.306 and p-value of 0.0001 suggestive of a weak positive but significant correlation as explained in figure 1. While a positive correlation was noted between triglyceride index and uric acid to HDL ratio with an r value of 0.165 and p-value of 0.033, the greater the uric acid to HDL ratio more the triglyceride glucose index, the greater the triglyceride glucose index more the HbA1c levels thus high uric acid to HDL ratio can lead to raised serum HbA1c.

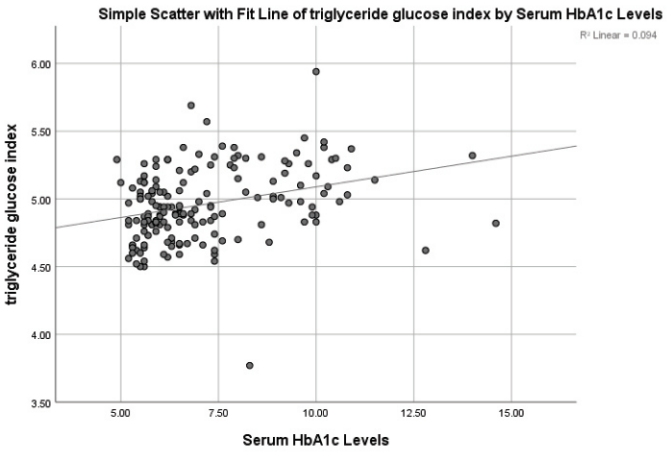

Figure 1: Graphical Illustration of Correlation between Triglyceride Glucose Index and HbA1c

DISCUSSION

The research objective for the present study was to discover the association between UHR and triglyceride indices regarding glycemic control in the T2DM population. The results of the research presented some correlations between these variables and glycemic control, the contribution of which to the discovery of cheap mouth-to-mouth markers for managing diabetes was quite significant. Those with poor glycemic control showed a marked increase in fasting blood glucose and triglyceride glucose index, which was significantly higher than the figures of the non-diabetic as well as the well-controlled. Nevertheless, the serum uric acid levels and UHR showed no statistically significant difference between the study groups. The present results imply that triglyceride glucose index may be a marker for regulating glycemic control and hence a higher value represents poor control of the glycemic level. On the other hand, the positive correlation between the triglyceride glucose index and HbA1c points to this association between the rises in the blood glucose level which were not consistent, and worse long-term outcomes of the glycemic values. Firstly, the obtained results point out that tighter glycemic control in patients with T2DM was mandatory, which was signified by lower HbA1c and TG/HDL-C levels [11, 12]. This was one of the best measures to be taken to slow the development of diabetic micro and macrovascular complications. Such a positive association between the triglyceride glucose index and HbA1c underlines the importance of measuring and controlling blood glucose levels continuously not HbA1c, especially in those whose blood glucose was frequently changing [13, 14]. It was worth noting that no major differences emerged in serum uric acid levels and UHR trends across the study groups, a rather unusual finding [15-17]. Although some earlier research indicated associations between hyperuricemia and metabolic disorders, recent research proposed that these variables do not act as such a direct linkage to the glycemic control of T2DM [18-20]. The reasons may be the cross-sectional pattern of the study or something else that cannot be eliminated in the study model. In the same manner, the positive correlation between triglyceride glucose index and HbA1c shows the high importance of wasting irregular blood glucose spikes in diabetes management. Continuous Glucose Monitoring (CGM) devices can particularly help patients with fluctuating blood sugar levels, as they give very concrete, real-time data and insights into daily glucose levels. The implementation of CGM along with the more traditional markers such as the triglyceride glucose index and HbA1c, can allow health care providers to determine precise treatment plans based on the individual needs of their patients. The cross-sectional design makes it difficult to establish a community between the independent and dependent variables. Longitudinal studies would be certainly a good solution to determining the causality between glycosylated hemoglobin (HbA1c) and lipid profiles. Secondly, there was a question in the method of the study, convenient sampling which can result in making a certain sample that can be affected by any kind of selection bias and can make it difficult to generalize the findings of the study.

CONCLUSIONS

The triglyceride glucose index reveals the potential to be an inexpensive indicator to evaluate blood sugar levels and should be taken into consideration together with the other generally used indicators like HbA1c to strengthen diabetes management. Longitudinal studies with larger and more representative populations should be the subject of further research to confirm the current findings and find new ways to improve glucose control in people with T2DM.

Authors Contribution

Conceptualization: HFM, HNL, BRM, K
Methodology: QA, FUS, MZS, SF
Formal analysis: QA, FUS, MZS, SF
Writing, review and editing: HFM, QA, HNL, BRM, FUS, K, MZS, SF

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

All the authors declare no conflict of interest.

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