

Serum Uric Acid HDL-Cholesterol Ratio (UHR): An Index of Cardiovascular Risk Among Diabetes Mellitus Subjects

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ABSTRACT

The search for a better and effective biomarker for early diagnosis of cardiovascular events in Diabetes mellitus is a continuous process. The growing burden of cardiovascular disease (CVD) among diabetic populations has necessitated the development of novel, integrative, and cost-effective indicators for early diagnosis and risk stratification. Hence this study investigates serum uric acid (SUA) to high-density lipoprotein - cholesterol (HDL-C) ratio as a potential biomarker for cardiovascular risk assessment in diabetes mellitus (DM). Two hundred (200) participants comprising one hundred and sixty (160) diabetic subjects and forty (40) apparently healthy subjects were enrolled in this study. Fasting blood glucose (FBG), serum uric acid (SUA), high density lipoprotein cholesterol (HDL-C), and calculated SUA/HDL-C ratio were evaluated. Statistical package for social sciences (SPSS) version 25 was used and student's t test was employed for comparison and Pearson correlation was used for association at $p < 0.05$ significance. Results shows that Diabetic subjects had significantly higher ($p < 0.05$) SUA and FBG levels, with lowered HDL-C, when compared with apparently healthy subjects. Likewise, SUA/HDL-C ratio was significantly higher in diabetic subjects, and a positive correlation between FBG and SUA as well as SUA/HDL-C ratio, but negative correlation was observed between FBG and HDL-C levels. These findings showed that SUA/HDL-C ratio may be deployed as reliable, effective, and affordable biomarker for cardiovascular risk assessment, especially in resource-limited settings where advanced diagnostic tools are inaccessible.

Keywords: Uric acid, high density lipoprotein, Diabetes mellitus, cardiovascular risk index

INTRODUCTION

Diabetes mellitus is a chronic, multifactorial metabolic disorder characterized by sustained hyperglycemia due to impaired insulin secretion, action, or both (American Diabetes Association, 2023). Globally, diabetes has reached epidemic proportions, with a significant share of the morbidity and mortality burden stemming from its vascular complications, particularly cardiovascular disease (Ye et al., 2022). The interplay between chronic hyperglycemia, oxidative stress, endothelial dysfunction, and dyslipidemia forms the foundation of atherosclerosis development in diabetic patients

(Caturano et al., 2025). Evidence has shown that there is a significant association between serum uric acid and lipid abnormalities (dyslipidemia) such as elevated triglycerides, low density lipoprotein cholesterol and reduced high density lipoprotein cholesterol (Zhang et al., 2021)

Traditionally, risk stratification for CVD in diabetes has relied on measurements of fasting blood glucose, blood pressure, LDL-C, and total cholesterol. However, these markers have not sufficiently accounted for the complexities of cardiovascular risk in diabetic populations, resulting in under diagnosis or late diagnosis of cardiovascular disorders. This limitation has prompted research into emerging biomarkers that integrate metabolic disturbances and inflammatory mechanisms (Wong et al., 2022).

Serum uric acid (SUA), a byproduct of purine metabolism, is often elevated in diabetes mellitus and has pro-inflammatory and pro-oxidative properties under hyperuricemic conditions (Kimura et al., 2021; Du et al., 2024). In an earlier study by Adu (2022), it was observed that serum uric acid correlate positively with glycemic indices among diabetes mellitus subjects. Conversely, HDL cholesterol (HDL-C), regarded as "good cholesterol," facilitates reverse cholesterol transport and exhibits anti-inflammatory and antioxidant properties (Julve & Escolà-Gil, 2021; Madaudo et al., 2024). Lower level of HDL-C is common feature in diabetic dyslipidemia, and is an indicator of increased cardiovascular risk in such subjects (Adu et al., 2015).

The SUA/HDL-C ratio is a mathematically derived ratio and novel marker obtained by dividing serum uric acid with high density lipoprotein, and it serves as composite marker encompassing oxidative stress through serum uric acid (SUA) and protective lipid function through high density lipoprotein cholesterol (HDL-C). In an earlier study, Huang et al., (2024); Yin et al., (2025), observed that this ratio is a more sensitive indicator of cardiovascular risk than either serum uric acid or HDL-C alone, particularly in individuals with type 2 diabetes mellitus (T2DM). However, this new biomarker has not been fully deployed into the clinical setting for therapeutic decision for early detection of cardiovascular risk especially among diabetes mellitus. A search through the literature shows paucity of data on this new biomarker in this study area. Therefore, this study sought to evaluate serum uric acid to high density lipoprotein cholesterol ratio as an index of cardiovascular risk in diabetes mellitus subjects.

MATERIALS AND METHODS

Study Area and Design

The study took place at Central Hospital, Agbor, in Delta State, Nigeria. This healthcare facility was selected due to its accessibility, availability of a diverse diabetic mellitus subject population, and appropriate laboratory facilities. It serves a vast array of communities in Ika land including the nearby state of Edo.

Study Population

Two hundred (200) volunteers were randomly recruited in the study comprising of one hundred and sixty (160) diagnosed type 2 diabetes mellitus (T2DM) subjects for at least six months, and forty (40) apparently healthy age and sex matched control subjects. Inclusion criteria included adults aged 30–65 years, non-pregnant, and free from kidney disease, liver disease, or gout. The study was conducted in line with Helsinki declaration

of 2024 with informed consent obtained verbally while ethical clearance was given by institutional ethical committee of Central Hospital, Agbor.

Sample Collection

Fasting venous blood samples (5 mL) was collected from participants under aseptic conditions and divided into fluoride oxalate and plain container. Blood in plain container was allowed to clot, centrifuged, and serum was separated for analysis. All samples were stored at -20°C until biochemical analysis. However, the fluoride oxalate sample was used to estimate glucose to confirm the status of the participants.

Biochemical Analysis

Serum Uric Acid (SUA) was measured using enzymatic colorimetric uricase-peroxidase method while HDL Cholesterol (HDL-C) was determined after precipitation of LDL and VLDL using phosphotungstic acid and magnesium chloride. Fasting Blood Glucose (FBG) was evaluated using the glucose oxidase-peroxidase (GOD-POD) method. Serum uric acid HDL-C ratio (SUA/HDL-C Ratio) was calculated mathematically by dividing serum uric acid by HDL-C. In all analysis, quality control samples were included in the assay and manufacturer's instruction was strictly adhered to during analysis.

Statistical Analysis

Data obtained were analyzed with statistical package for social science (SPSS) version 25 using student's t-test and Pearson correlation to evaluate relationships. Results were presented as mean \pm SEM, and graphs with level of significance at $p < 0.05$.

RESULTS

The results of this study shows that 80% of the participants are diabetic while 20% are apparently healthy as shown in Figure 1. The 80% diabetic subjects, has 32.5% as male subjects while 67.5% as female subjects as shown in Figure 2.

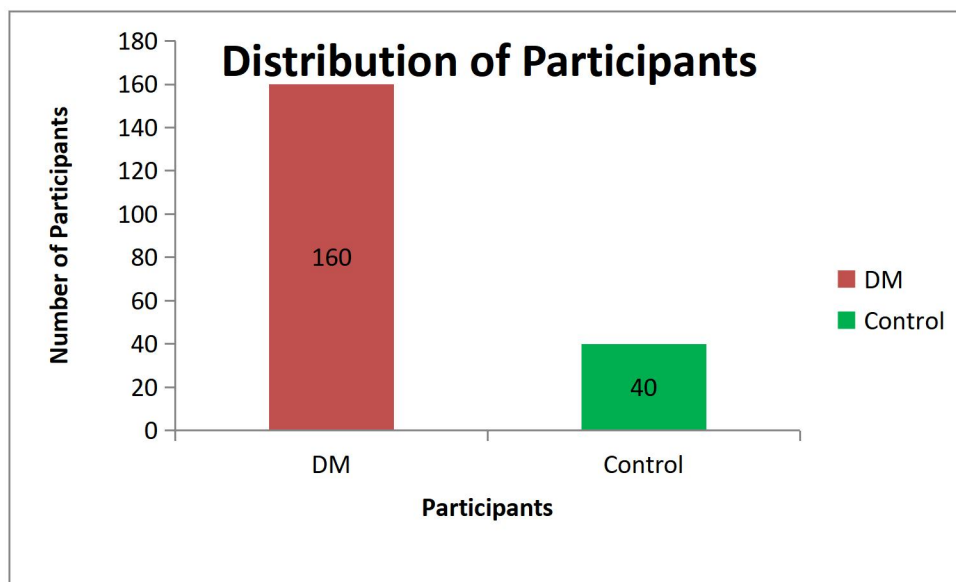


Fig.1; Distribution of Participants

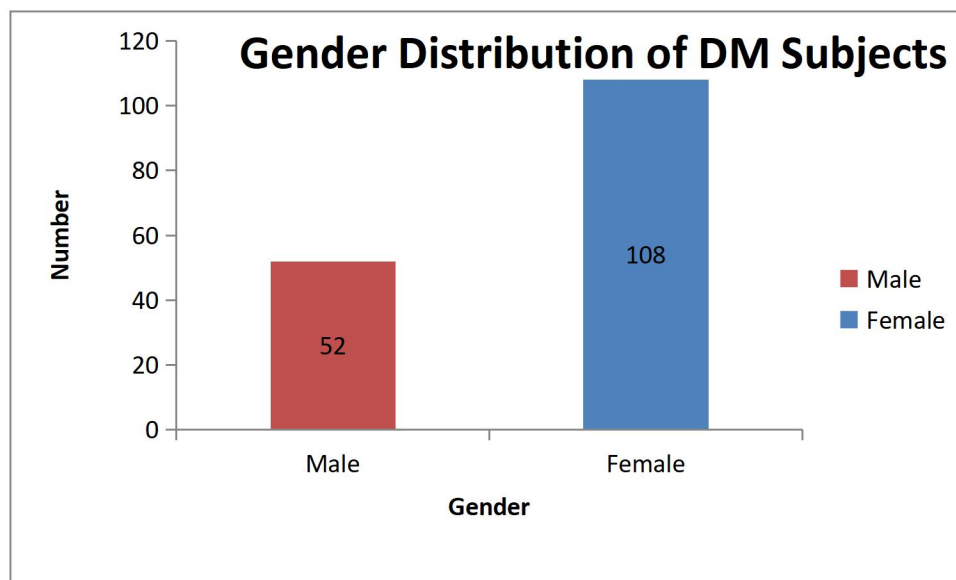


Fig.2: Gender distribution of diabetes mellitus subjects

There was a significantly higher ($p < 0.05$) age among diabetes mellitus subjects when compared with apparently healthy subjects. Similarly, there was significantly higher ($p < 0.05$) fasting blood glucose, serum uric acid and uric acid HDL ratio (UHR) in diabetes mellitus subjects than apparently healthy subjects when compared. However, there was significantly lower ($p < 0.05$) HDL-C in diabetes mellitus subjects than in apparently healthy subjects when compared as shown in table 1.

Table 1: Mean \pm SEM of Age, Fasting Blood Glucose, Serum uric acid, HDL-C, and serum uric acid HDL-C ratio of diabetes and apparently healthy subjects.

Parameter	DM (N=160)	Control (N=40)	tvalue	pvalue
Age (Years)	54.25 \pm 1.93	49.10 \pm 0.35	9.004	0.000*
FBG (mg/dl)	154.45 \pm 8.80	98.10 \pm 2.84	3.168	0.003*
SUA (mg/dl)	7.24 \pm 0.17	5.70 \pm 0.12	4.527	0.000*
HDL-C (mg/dl)	39.23 \pm 0.44	49.60 \pm 0.90	-10.522	0.000*
SUA/HDL	0.19 \pm 0.01	0.11 \pm 0.00	6.679	0.000*

Table 2: Mean \pm SEM of Fasting Blood Glucose, Serum uric acid, HDL-C and serum uric acid HDL-C ratio of male and female diabetes mellitus subjects.

Parameter	Male DM (N=52)	Female DM (N=108)	tvalue	pvalue
Age (Years)	52.53 \pm 3.64	55.07 \pm 2.30	-0.609	0.546 [†]
FBG (mg/dl)	163.62 \pm 20.79	150.04 \pm 8.58	0.718	0.477 [†]
SUA	7.73 \pm 0.43	7.00 \pm 1.12	2.156	0.037*
HDL-C	40.00 \pm 0.76	38.85 \pm 0.53	1.232	0.225 [†]
SUA/HDL-C	0.20 \pm 0.01	0.18 \pm 0.00	1.270	0.212 [†]

*Significant [†]Not Significant. **KEY:** FBG =Fasting Blood Glucose, SUA = Serum uric acid,

There was a positive correlation between fasting blood glucose and serum uric acid but there was a negative correlation between fasting blood glucose and HDL-C as shown in Figure 3 and 4 respectively. There was also, positive correlation between uric acid HDL-C ratio and fasting blood glucose as shown in Figure 5.

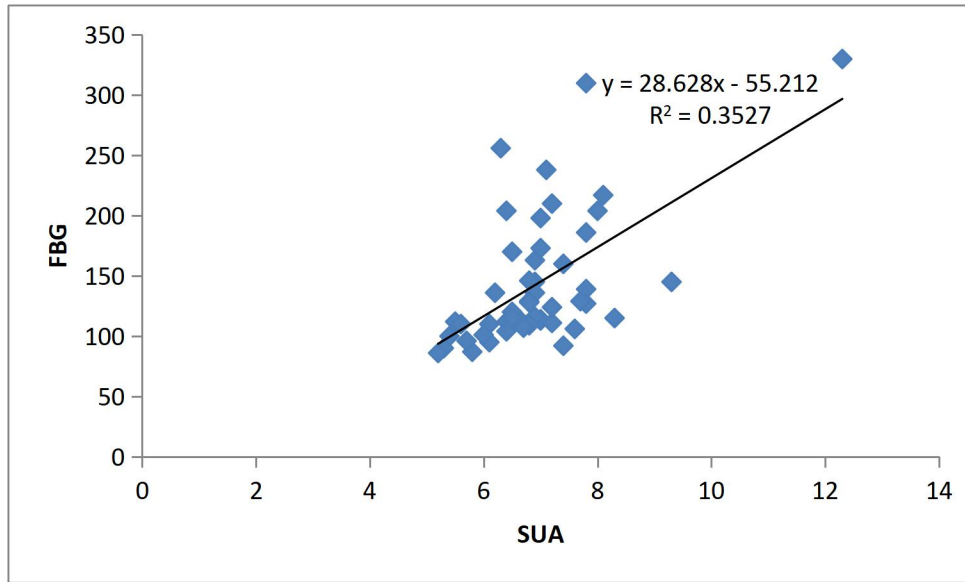


Fig. 3: Positive correlation of fasting blood glucose (FBG) and serum uric acid (SUA)

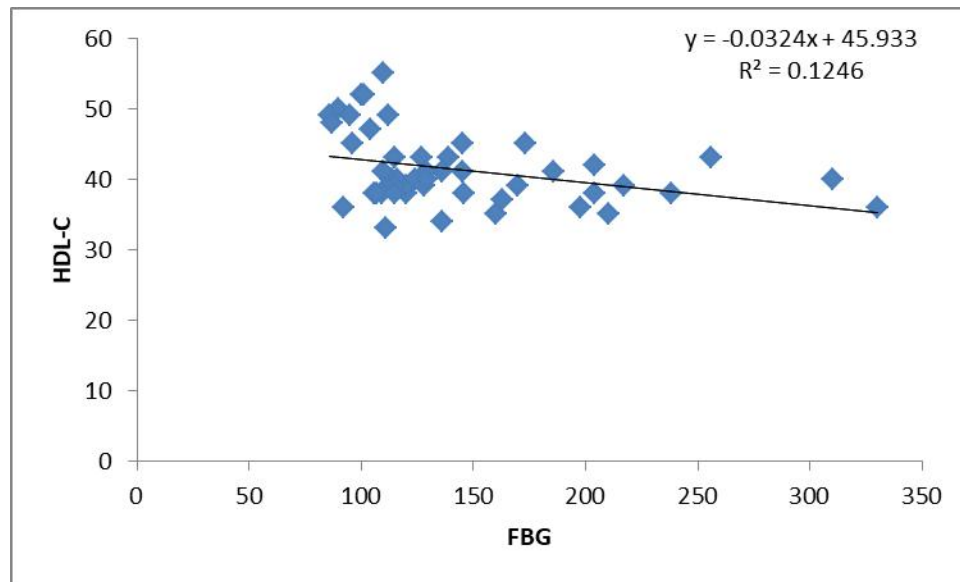


Fig.4: Negative correlation of fasting blood glucose and HDL-C

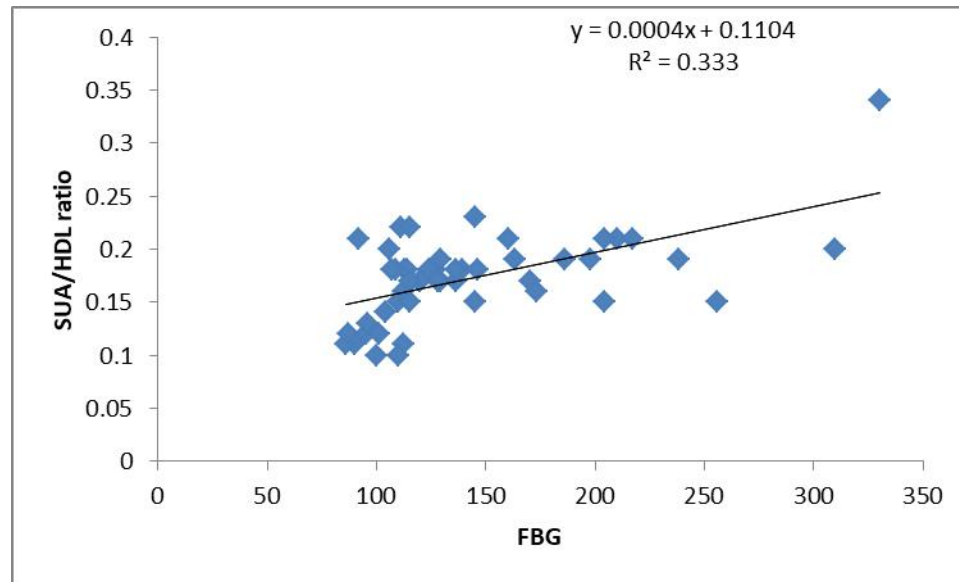


Fig.5: Positive correlation between fasting blood glucose and serum uric acid HDL-C ratio

DISCUSSION

Diabetic complications are so severe that new biomarkers are being sought for in order to have a better diagnosis of the disease. The uric acid HDL ratio (UHR) is a new composite marker that encompasses oxidative stress and protective lipid component. This study observed a higher level of SUA in diabetic subjects which aligns with literature indicating that hyperuricemia contributes to oxidative stress, insulin resistance, and vascular inflammation (Kimura et al., 2021; Adu 2022; Du et al., 2024). Lower HDL-C levels in diabetics also support existing data associating low HDL-C with impaired cholesterol transport and heightened cardiovascular risk (Adu et al, 2015; Julve & Escolà-Gil, 2021).

There was a significantly higher SUA/HDL-C ratio in diabetic individuals in this study. This provides a composite indicator that reflects both metabolic insult and diminished cardio-protection in these subjects (Huang et al., 2024; Obirikorang et al., 2025). The correlation between FBG and SUA, and SUA/HDL-C ratio, emphasizes that poor glycemic control fuels metabolic imbalance, supporting the utility of the ratio as a predictor of cardiovascular risk.

The absence of significant differences in HDL-C between male and female diabetic participants, despite differences in SUA, suggests that the ratio normalizes gender differences and provides a consistent risk marker. The integration of SUA and HDL-C into a singular ratio offers enhanced predictive value for cardiovascular disease in diabetes, particularly in settings where traditional risk assessments may be insufficient or unavailable as earlier reported by Yin et al., (2025). Correlation analysis revealed a positive relationship between FBG and both SUA and the SUA/HDL-C ratio. There was a significant negative correlation between FBG and HDL-C, supporting the hypothesis that poor glycemic control exacerbates oxidative stress and lipid imbalances in diabetic individuals (Adu, 2022; Tjitradinata et al., 2025).

CONCLUSION

Conclusively, this study affirms the clinical significance of the serum uric acid to HDL-C ratio as a reliable and practical biomarker for cardiovascular risk in diabetic subjects. Elevated SUA and reduced HDL-C are common in diabetes and jointly amplify cardiovascular risks. The SUA/HDL-C ratio encapsulates these effects, offering a simplified, yet effective tool for clinicians, especially in resource-constrained settings. It is therefore recommended that UHR being incorporated into routine diabetes care protocols, and being included in the national diabetes mellitus management guidelines to facilitate early intervention.

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None

CONFLICT OF INTEREST

None

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