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(Original Article)

Effect of Serum Triglycerides/HDL Cholesterol Ratio on Aminotransferases and Alkaline Phosphatase in Type 2 Diabetes Mellitus Patients

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ABSTRACT

Background: The prevalence of type 2 diabetes mellitus (DM) is increasing, mainly due to the increased prevalence of an inactive lifestyle and obesity; therefore, it can be prevented by lifestyle changes for subjects with impaired glucose tolerance. Type 2 DM is associated with several liver disorders, which are considered part of insulin resistance (IR).

Objectives: This study aimed to correlate serum triglycerides with the high-density lipoprotein cholesterol ratio, and to assess the association between AST, ALT, and ALP enzyme levels and the high-density lipoprotein cholesterol ratio in Sudanese patients diagnosed with type 2 DM.

Materials and Methods: This descriptive cross-sectional study was conducted in Khartoum State on 122 randomly selected Sudanese patients with type 2 DM. Blood samples were drawn from the participants and tested for triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), AST, ALT, ALP, and HbA1c levels using the Cobas Integra 400 Plus. Triglyceride and high-density lipoprotein cholesterol levels were used to calculate the TG/HDL ratio.

Results: The study revealed no correlation between the TG/HDL-C ratio and AST or ALT levels among all participants (P-values> 0.05). However, there was a moderate positive correlation between the TG/HDL-C ratio and the ALP level in all participants (r = 0.312) (P-value = 0.000).

Although the study revealed that there was no association between the different groups of TG/HDL ratio and the levels of AST and ALT, a significant difference in the level of ALP enzyme existed between patients with TG/HDL ratio ≤ 2 (normal TG/HDL) and patients with a ratio > 2 (high TG/HDL ratio) (P-value < 0.05).

Conclusion: The TG/HDL-C ratio was weakly correlated with the ALP enzyme level.

1. INTRODUCTION

Diabetes mellitus (DM) is a major global health challenge, affecting individuals across all nations, age groups, and genders (Global, regional, and national burden of diabetes 2023). Presenting these findings underscores the importance of understanding DM's impact, which can inspire healthcare professionals to prioritize research and intervention efforts.

Type 2 DM is the predominant form of diabetes, constituting about 90% of all cases. The global surge in unhealthy habits, the aging population, and the rising prevalence of obesity in both adults and children are contributing factors to the widespread occurrence of diabetes (Elisa et al., 2019). The development of T2DM results from a multifaceted interplay between genetic and environmental factors. Genetic factors that impact insulin secretion and insulin resistance, along with lifestyle choices such as obesity, excessive eating, and physical inactivity, contribute to the onset of T2DM (Shojima & Yamauchi, 2023). The International Diabetes Federation (IDF) has estimated that in 2017, diabetes accounted for 425 million cases and is forecasted to be 629 million by 2040. Indeed, 9·3% is prevalent in North Africa and the Middle East (Global, regional, and national burden of diabetes 2023, Elisa, et al.2019) In 2014, the IDF reported that in Sudan, the prevalence of diabetes among adults is estimated to be between 9 and 12% (Hussein & Menasri, 2019).

In the liver, insulin maintains glucose homeostasis by suppressing hepatic glucose production; however, during IR, blood glucose tends to increase due to the action of other antagonizing hormones, such as glucagon, which promotes gluconeogenesis and glycogenolysis (Armandi et al., 2021; Laakso, 2019).

TG/HDL-C ratio as a marker of insulin resistance: An adjusted TG/HDL ratio has been linked to IR, suggesting that understanding this relationship could improve early detection and management of insulin resistance, motivating clinicians to consider lipid ratios in patient assessments.

An adjusted TG/HDL ratio was reported to be associated with IR, with higher ratios associated with lower insulin sensitivity. The hypothesis underlying this finding is that fatty acids are returned to the liver for reutilization in TG synthesis, and that, subsequently, more free fatty acids will be formed. These free fatty acids impair the release of sufficient insulin, forcing pancreatic β-cells to secrete more insulin. Finally, it concludes with the development of IR and DM (Liu et al., 2022).

In metabolic syndrome, high TG and low HDL-C levels are common; consequently, several studies recommend using lipid indicators (e.g., the RC/HDL-C ratio) as IR surrogates. However, compared with other lipid parameters, the TG/HDL-C ratio is the best lipid indicator for correlating with IR and identifying metabolic diseases such as NAFLD. (Lu , et al.2022, Fan, et al 2019).

The cut-off point for the TG/HDL-C ratio varies by population, race, gender, and type of metabolic disease. In African Americans, a TG/HDL-C ratio of 1.2 or greater was shown to predict insulin resistance; when gender is considered, ratios of 0.9 and 1.4 are used to predict NAFLD in women and men, respectively (Fan et al., 2019). However, a study conducted by Catanzaro et al. reported that the optimal TG/HDL-C cut-off in the NAFLD population was 1.64, whereas it was 2.48 in patients with metabolic syndrome (Catanzaro et al., 2022).

While the TG/HDL-C ratio has been widely studied as a predictor of insulin resistance and cardiovascular disease in global populations (McLaughlin et al., 2005; da Silva et al., 2019), little is known about its relationship with liver enzymes like AST, ALT, and ALP in African or Sudanese populations. This gap highlights the significance of our study in contributing new insights.

Given the rising incidence of non-alcoholic fatty liver disease in patients with diabetes, understanding how serum triglycerides and HDL cholesterol ratios relate to liver enzymes such as AST, ALT, and ALP may help in early detection and management in resource-limited settings like Sudan. This study aimed to analyze these parameters and their association in Sudanese patients diagnosed with type 2 DM.

2. MATERIALS AND METHODS

2.1 Study protocol

This descriptive cross-sectional study was conducted in Khartoum State from during two months, involving 122 Sudanese patients with type 2 diabetes mellitus admitted for routine follow-up at a military hospital. All participants were randomly selected, and those with a history

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or signs of liver disease were excluded to ensure data quality.

2.2 Sample collection

Fasting blood samples were collected in a heparin container, separated into Eppendorf tubes, and stored in a refrigerator until analysis of triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, and hemoglobin A1c levels using Cobas Integra 400 plus.

2.3 Ethical approval

The institutional ethics and research committee approved the study, demonstrating its adherence to national and international ethical standards. Informed consent, whether written or verbal, was obtained from all participants, ensuring respect for their rights and well-being.

2.4. Statistical analysis

All data were analyzed using the Statistical Package for the Social Sciences (SPSS) version 21, reflecting a comprehensive approach. Descriptive statistics were performed, and the results were presented clearly in graphs and tables, underscoring the study's meticulousness.

3. RESULTS

Type 2 diabetes mellitus is commonly associated with insulin resistance and dyslipidemia, which contribute to metabolic and hepatic complications. The triglycerides are too high-

density

The lipoprotein cholesterol (TG/HDL-C) ratio has emerged as a simple marker of insulin resistance and atherogenic dyslipidemia. Increasing evidence suggests that metabolic disturbances reflected by an elevated TG/HDL-C ratio are closely linked to liver dysfunction, particularly non-alcoholic fatty liver disease. Liver enzymes, such as aminotransferases and alkaline phosphatase, are frequently elevated in patients with type 2 diabetes, indicating hepatocellular injury and impaired hepatic metabolism. Evaluating the relationship between the TG/HDL-C ratio and liver enzymes may provide insight into early hepatic involvement and metabolic risk in patients with type 2 diabetes mellitus. Figure 1: Shows categorized (high& normal) levels of AST, ALT, ALP, TG/HDL Ratio, and HbA1C for the participant. Table 2 shows the range (minimum and maximum levels), mean, and standard deviation (SD) of AST, ALT, ALP, TG/HDL Ratio, and HbA1C for the male group. Table 3 shows the range (minimum and maximum levels), mean, and standard deviation (SD) of AST, ALT, ALP, TG/HDL Ratio, and HbA1C for the female group. Table 4 shows the relationships between AST, ALT, and ALP levels and TG/HDL Ratio and HbA1C. Table 5 shows the correlation between AST, ALT, ALP, TG/HDL Ratio, and HbA1C levels in the male subgroup. Table 6 shows the correlation between AST, ALT, ALP, TG/HDL Ratio, and HbA1C levels in the female subgroup.

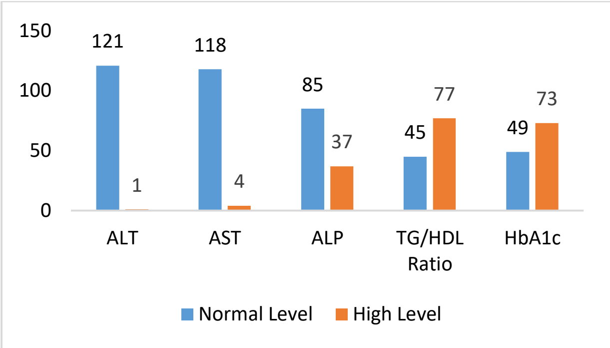

Figure 1. Figure 1: Shows categorized (high& normal) levels of AST, ALT, ALP, TG/HDL Ratio, and HbA1C for the participants

Table (1) shows the range (minimum and maximum levels), mean and standard deviation of AST, ALT, ALP, TG/HDL Ratio, and HbA1C for the participants

Variable N = 122	Range	Mean ± SD
AST (U/L)	4 – 97	17.6 ± 13.8
ALT (U/L)	4 – 94	13.6 ± 9.6
ALP (U/L)	16 – 359	92.4 ± 48.5
TG/HDL Ratio	0.5 – 14.7	3.2 ± 2.4
HbA1C (%)	5.0 – 16.4	8.5 ± 2.6

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Table (2) shows the range (minimum and maximum levels), mean, and standard deviation (SD) of AST, ALT, ALP, TG/HDL Ratio, and HbA1C for the male group:

Descriptive Statistics (Males N = 67)		
Variable	Range	Mean ± SD
AST (U/L)	4 – 97	19.6 – 17.1
ALT (U/L)	4 – 94	14.7 – 11.9
ALP (U/L)	16 – 359	98.7 – 54.8
TG/HDL Ratio	0.5 – 14.7	3.5 – 2.7
HbA1C (%)	5.1 – 16.4	8.5 – 2.6

Table (3) shows the range (minimum and maximum levels), mean, and standard deviation (SD) of AST, ALT, ALP, TG/HDL Ratio, and HbA1C for the female group

Descriptive Statistics (Females N = 55)		
Variable	Range	Mean ± SD
AST (U/L)	4 – 45	15.2 ± 7.8
ALT (U/L)	4 – 29	12.3 ± 5.2
ALP (U/L)	32 – 190	84.7 ± 38.6
TG/HDL Ratio	1.1 – 12.0	2.9 ± 1.9
HbA1C (%)	5.0 – 14.3	8.5 ± 2.7

Table (4) shows the relationship between the levels of AST, ALT, ALP with TG/HDL Ratio, and HbA1C

Correlation		AST	ALT	ALP	TG/HDL Ratio
TG/HDL Ratio	R value	-.143	.163	.312**	.187*
	P value	.116	.073	.000	
HbA1C (%)	R value	-.326**	-0.075	0.385**	
P value	0.000	.412	0.000	0.039	

P- value ≤ 0.05 is considered significant

Table 5 shows the correlation between the levels of AST, ALT, ALP, TG/HDL Ratio, and HbA1C for the male subgroup.

		AST	ALT	ALP	HbA1C
TG/HDL Ratio	Correlation Coefficient	-.191	.160	.245*	.059
	Sig. (2-tailed)	.121	.196	.046	.637
HbA1C (%)	Correlation Coefficient	-.364**	-.149	.325**	1.000
	Sig. (2-tailed)	.002	.229	.007	.
	N	67	67	67	67

Table (6) shows the correlation between the levels of AST, ALT, ALP, TG/HDL Ratio, and HbA1C for the female subgroup.

		AST	ALT	ALP	HbA1C
TG/HDL Ratio	Correlation Coefficient	-.153	.140	.376**	.367**
	Sig. (2-tailed)	.263	.306	.005	.006
HbA1C (%)	Correlation Coefficient	-.293*	.026	.442**	1.000
	Sig. (2-tailed)	.030	.849	.001	.
	N	55	55	55	55

*. Correlation is significant at the 0.05 level (2-tailed).

**. Correlation is significant at the 0.01 level (2-tailed).

4. DISCUSSION

Our study specifically examined the correlation between the TG/HDL-C ratio and liver enzymes, revealing no significant association with AST or ALT levels in participants (P-values> 0.05), suggesting that the TG/HDL-C ratio may not be an accurate indicator of changes in these enzymes in this population. The TG/HDL-C ratio showed weak correlations with ALP and HbA1c levels (r = 0.312, 0.187; P-values = 0.00, 0.039, respectively), suggesting that as the TG/HDL-C ratio increases, ALP and HbA1c levels may also increase. The finding disagrees with those of Shibabaw et al. and Ghimire et al., which may be due to differences in study populations and the use of individuals without diabetes mellitus as a control group (Shibabaw et al., 2019; Ghimire et al., 2018). This study also observed a weak correlation between HbA1c and the level of AST (r = - 0.326) negatively, while positive with ALP level (r = 0.385) (P-value = 0.00) for both variables; when considering the above results it is now precise ALP enzyme is the only variable that affected by markers and indicators of insulin resistance, this finding agrees with several studies such as Mandal et al., S Nagaraj, et al.. Sulafa et al. and the use of HbA1c confirm the TG/HDL ratio results, as both are indicators of insulin resistance. (Mandal et al 2018, Nagaraj et al 2016, Sulafa et al 2020)

In this study, the male subgroup showed a weak positive correlation between the TG/HDL-C ratio and the level of ALP (r = 0.245) (P-value = 0.046). Recognizing gender differences is important to make the audience feel acknowledged and that their specific factors are considered. Nevertheless,

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it revealed a weak correlation between the HbA1c level and the level of AST in a negative pattern (r = - 0.364) (P-value = 0.002) and positive with ALP level (r = 0.325) (P-value = 0.007). On the other hand, the female subgroup demonstrated a weak positive correlation between the TG/HDL-C ratio and ALP and HbA1c levels (r = 0.376, r = 0.367; P-value = 0.005, P-value = 0.006, respectively). However, the correlation between the HbA1c level and the level of AST is weakly negative (r = - 0.293) (P-value = 0.030), and moderately positive with the level of ALP (r = 0.442) (P-value = 0.001).
The outcomes for gender subgroups confirm the hypothesis, supported by some studies, that insulin resistance markers, particularly the TG/HDL ratio, should be adjusted for variation by ethnicity and sex. (Ren et al 2016, Quispe et al 2016, Baneu et al 2024)
Patients were classified into two groups based on the TG/HDL-C ratio: 45 of 122 patients had a ratio ≤ 2 (Normal Ratio Group), and 77 patients had a ratio > 2 (High Ratio Group).
The study also revealed no statistically significant difference in AST and ALT levels between the standard and high TG/HDL groups (P-values> 0.05). However, an important difference was observed in ALP levels; the mean rank for the high ratio group (68.79) was significantly higher than for the normal ratio group (49), indicating higher ALP levels in the high ratio group (p = 0.003). These findings are meaningful and support the relevance of the research, suggesting that, while the TG/HDL-C ratio may not be associated with AST and ALT levels, it is linked to ALP levels in patients with type 2 diabetes mellitus. The moderate correlation underscores the importance of considering this relationship in clinical assessments. These results align with the Sudanese study by Sulafa et al., reinforcing the validity of the findings, though differences with other studies highlight the need for further research (Sulafa et al., 2020; Sunitha et al., 2016).

1. CONCLUSION:

This study found that the TG/HDL-C ratio in patients with type 2 diabetes mellitus was weakly correlated with ALP levels. This nuanced result reflects the complex relationship between insulin resistance markers and liver function. Since the TG/HDL-C ratio is a marker of insulin resistance, atherogenic dyslipidaemia, and cardiometabolic risk-conditions more closely linked with liver fat accumulation and NAFLD—it's important to recognize that ALP, related to biliary tract function and bone metabolism, is less responsive to lipid disturbances. Acknowledging this complexity helps the audience appreciate the detailed nature of the findings and their implications for clinical practice.

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All authors contributed equally to this work.

CONFLICTS OF INTEREST:

The authors declare no conflicts of interest.

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