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The significance of ratio between serum triglycerides and HDL cholesterol as a common man's bio marker of insulin resistance in type 2 diabetes mellitus: A cross sectional comparative study

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Abstract

Introduction: Insulin resistance is the most common abnormality associated with obesity, as a major pathophysiological factor in the development and progression of cardiovascular diseases and diabetes mellitus. This study is undertaken to know the significance of ratio of triglycerides (TG) to high-density lipoprotein (HDL) cholesterol as a serum biomarker in assessing the insulin resistance compared to homeostatic model assessment of insulin resistance (HOMA-IR) in type 2 diabetes mellitus (DM) subjects.

Materials and methods: This was a cross sectional comparative study done at Mysore Medical College and Research Institute, Mysuru on 180 subjects of type 2 DM from April 2022 to October 2022. The blood sample was subjected for laboratory tests, such as complete blood count (CBC), fasting blood sugar (FBS), post prandial blood sugar (PPBS), HbA1c, lipid profile, ECG, serum insulin level and HOMA-IR, renal function tests (RFT), liver function tests (LFT). The results were tabulated and compared between the HOMA-IR value and triglycerides/HDL cholesterol ratio of type 2 DM subjects. The cut off value of HOMA-IR to assess insulin resistance was 2.50 and triglycerides to HDL ratio was 3.0.

Results: The majority of patients i.e. 112(62.22%) had TG/HDL ratio of >3.0 and 116(64.44%) patients had HOMA-IR of >2.5.The patients with uncontrolled type 2 DM had significantly higher TG/HDL ratio [p value 0.01] and HOMA-IR (p value- 0.01).

Conclusion: This study concludes that, the ratio of serum triglycerides /HDL cholesterol is a cost effective blood biomarker and it's correlating significantly with the HOMA-IR and serum fasting insulin levels, while assessing the insulin resistance in type 2 DM subjects.

Keywords: bio marker; HOMA-IR; triglycerides; HDL ratio; type 2 diabetes mellitus

Introduction

According to International Diabetic Federation, the current (2019) prevalence of diabetes mellitus (DM) is 463 million, depending on the current trends it can go up to 642 million by 2040 [1, 2]. Although extensive research work has been done throughout the globe to understand the details of type 2 DM, still so many aspects of this disease are not yet explored [3]. With the major improvement in public health the prevalence of infectious disease has gone down, yet paradoxically a marked raise in prevalence of non- communicable diseases such as type 2 DM, hypertension, stroke and cancer are seen and they have become the major

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attributors of morbidity and mortality [4]. When insulin resistance is associated with dysfunction of pancreatic islet β-cells, it leads to failure in control of blood glucose levels and dyslipidaemia. The β-cell dysfunction is critical in defining the risk and development of type 2 DM and its complications [5]. In obese individuals, adipose tissue releases increased amounts of non-esterified fatty acids, glycerol, hormones, pro-inflammatory cytokines and other factors, that are associated with the development of insulin resistance [6].

Dyslipidemia is one of the major risk factors of cardiovascular diseases in DM. The salient features of diabetic dyslipidemia are a high plasma triglyceride concentration, low high-density lipoprotein (HDL) cholesterol and elevated concentration of small dense low-density lipoprotein (LDL) cholesterol particles [7]. The dyslipidaemia associated with diabetes mellitus is attributed to increased free fatty acid levels secondary to insulin resistance. Although drug therapy for dyslipidemia is individualized, most people with diabetes mellitus needs statin therapy and often requires multiple agents to achieve therapeutic goals amid high insulin resistance [8].

Insulin resistance is the most common abnormality associated with obesity, as a major pathophysiological factor in the development and progression cardiovascular diseases and diabetes mellitus [9]. There are currently a number of direct and indirect procedures available for determining insulin resistance, such as hyperinsulinemic euglycemic clamp test (HEC test) and homeostastis model assessment of insulin resistance [HOMA-IR]. HEC test is serving as the gold standard test at present. But this test is intrusive, time-consuming and costly. As a result, the HOMA-IR test has been used to assess the insulin resistance in most of the centres, which uses fasting plasma glucose and fasting plasma insulin levels to calculate Insulin resistance [10, 11].

What ever the available methods used to assess the insulin resistance needs insulin level also. Some patients may not afford to get it done, because of financial and feasibility constraints [12]. So this study is undertaken to know the significance of triglycerides to HDL cholesterol ratio in comparison with HOMA-IR as a serum bio marker in assessing the insulin resistance in type 2 DM subjects.

Materials and methods

This was a cross sectional comparative study done at KR Hospital, Mysore Medical College and Research Institute, Mysuru on 180 subjects of type 2 DM from April 2022 to October 2022. This study was started after obtaining ethical clearance from the ethics committee of Mysore Medical College and Research Institute.

The sample size was calculated with formula of $Z^2PQ/d2$. Z2 is the standard normal deviate, p- prevalence of Diabetes mellitus.q= 1-p, d2 is degree of accuracy.

Z=1.96,P=8.9%[13], d2=0.05. The actual required sample size was 125.

Inclusion criteria was the subjects with the type 2 DM fulfilling the ADA [13] criteria with age more than 18 years. Exclusion criteria were patients with type 1 diabetes mellitus, on steroids, CKD, liver dysfunction, connective tissue diseases, autoimmine diseases, malignancy,on anti metabolites, immunocompromised status.

The sample was collected from subjects with type 2 daibetes mellitus attending the OPD of General Medicine Department, after obtaining informed consent. The criteria for selecting the subjects was FBS of >130mg/dl, PPBS of >180 mg/dl, HbA1c of >7% and mean fasting insulin level of >12.94μU/ml of blood inspite of being on highest tolerated dose of three OHAs and/or insulin requirement of >200 units/day [13]. The cut off value for assessing insulin resistance by using HOMA-IR was >2.50 [14] and triglycerides to HDL cholesterol ratio was >3.0 [15]. After getting detailed history and clinical examination, the blood sample was collected from all the patients and subjected for laboratory tests, such as CBC, FBS, PPBS, HbA1c, lipid profile, ECG, serum insulin level and HOMA-IR, RFT, LFT. The results were tabulated and compared with the HOMA-IR value and triglycerides/HDL cholesterol ratio of type 2 DM subjects. The triglycerides to HDL ratio and HOMA-IR values were correlated with the diabetes complications like retinopathy, nephropathy, neuropathy and cardiovascular complications. The retinopathy was detected with fundocopic examination by looking for changes like microaneurysms, flame shaped hemorrhages, cotton wool spots and maculopathy [16]. The early nephropathy was detected by microalbuminuria [17], neuropathy was detected by biosthesiometry with vibration perception threshold of 25 and above was considered to have significant damage to nerves [18]. Cardiovascular changes was detected with electrocardiogram and 2D-echocardiogram by looking for ischemic changes with wall motion abnormalities and LV dysfunction [19].

Diagnosis of insulin resistance

The insulin resistance was calculated using HOMA-IR method. HOMA-IR was calculated by fasting glucose

levels (mg/dl) and fasting plasma insulin levels (microU/L) [20].

Statistical analysis

Data obtained from the study was entered into Microsoft Excel sheets and analysed using IBM SPSS software version 20.0 (Trial version). The descriptive statistics was applied to calculate mean ± SD for all the individual variables. Anova and multivariate regression analysis was used for testing the significance between the blood glucose control status, dyslipidaemia, diabetes complications with HOMA-IR and triglycerides to HDL ratio. Pearson's correlation coefficient formula was used to know the significance between Homa-IR and triglycerides to HDL ratio. The p value of <0.05 is considered statistically significant.

Results

The majority of patients were male sex [98(54.44%)] with the age more than 60 years [102(56.66%)] with type 2 diabetes mellitus. In majority of patients TG/HDL ratio and Homa-IR were towards the higher side than the normal level (Table 1).

Table 1: Distribution of demographic and other study parameters.

Parameters		*Numbers (%)*
Age (Years)	>60	102(56.66)
	45-60	52(28.88)
	18 -45	26(14.44)
Sex	Male	98(54.44)
	Female	82(45.55)
FBS-Mean ±SD(mg/dl)	155.12±35.04	180
PPBS-Mean ±SD(mg/dl)	224.21±48.05	180
HbA1C- Mean ±SD	>8.4±1.6	102(56.66)
	<8.4±1.6	78(43.33)
Mean HDL±SD(mg/dl)	35.15±5.6	180
Mean trigycerides±SD	220.24±62.15	180
SERUM insulin level-Mean±SD(µU/ml)	12.94±2.56	180
TG/HDL ratio	>3.0	112(62.22)
	<3.0	68(37.77)
HOMA-IR	>2.5	116(64.44)
	<2.5	64(35.55)
Number of patients on >3 oral hypoglycemic agents		102(56.66)
Number of patients on insulin		78(43.33)

Table 2: Comparison between dyslipidaemia and HOMA-IR with control status of type 2 DM subjects.

Parameters		*Diabetes mellitus subjects in numbers-N(%)*					
		FBS- Mean±SD 155.12±35.04mg/dl	*P value*	*PPBS-Mean±SD 224.21±48.05mg/dl*	*P value*	*Mean±SD HbA1c 8.4±1.6*	*p value*
Triglycerides- Mean±SD 220.24±62.15mg/dl		108(60)	0.05	112(62.22)	0.05	104(57.77)	0.05
HDL level- Mean±SD 35.15±5.6mg/dl		98(54.44)	0.05	102(56.66)	0.05	104(57.77)	0.05
Triglycerides / HDL ratio	>3.0	106(58.88)	0.001	112(62.22)	0.04	104(57.77)	0.001
	<3.0	74(41.11)	0.14	68(37.77)	0.2	76(42.22)	0.16
HOMA-IR	>2.5	108(60)	0.01	102(56.66)	0.05	108(60)	0.01
	<2.5	72(40)	0.14	78(43.33)	0.2	72(40)	0.10

Table 3: Correlation between dyslipidaemia and HOMA-IR level with insulin level of type 2 DM subjects.

Parameters of dyslipidaemia	*Subjects with insulin resistance, in numbers-N(%)*		*p value*
	Homa-IR,Mean value- 3.89	*Insulin level of 12.94±2.56 µunits/ml (Mean±SD)*	
Triglycerides level (mg/dl)- mean± SD 220.24±62.15	104(57.77)	105(58.33)	0.05
HDL level (mg/dl)-mean± SD 35.15±5.6	102(56.66)	104(57.77)	0.05
TG/HDL ratio- >6.26	108(60)	102(56.66)	0.01

Notes: TG/HDL ratio cut off values =/>3.0, HOMA-IR cut off value = />2.5

The patients with uncontrolled type 2 DM had significantly higher triglycerides/HDL cholesterol ratio (TG/HDL) (P value 0.001) and HOMA-IR values (P value-0.01) (Table 2).

The TG/HDL ratio and other dyslipidemic parameters were significantly (p value 0.01) elevated than normal values and they were positively correlating with high HOMA-IR and elevated insulin levels (Table 3).

The significant number of patients with higher TG/HDL ratio (p value-0.01) and HOMA-IR (p value -0.01) had early diabetic complications like neuropathy, retinopathy, nephropathy and cardiac abnormalities (Table 4).

Table 4: Comparison between Homa-IR and TG/HDL ratio with complications of type 2 diabetes mellitus.

Parameters		*Diabetes complications in numbers (%)*				
		Early nephropathy	*Neuropathy*	*Retinopathy*	*Cardiac abnormality*	*p-value*
TG/HDL ratio	>3.0	104(57.77)	112(62.22)	103(57.22)	116(64.44)	0.01
	<3.0	76(42.22)	68(37.77)	77(42.77)	64(35.55)	0.06
Homa- IR	>2.5	112(62.22)	101(56.11)	98(54.44)	106(58.88)	0.01
	<2.5	68(37.77)	79(43.88)	82(45.55)	74(41.11)	0.06

Discussion

The current study tried to find the importance of triglycerides/HDL cholesterol ratio as a marker of insulin resistance in type 2 DM subjects as compared to HOMA-IR. This study finds that,there was no significant difference in sensitivity between HOMA-IR and triglycerides/HDL cholesterol ratio in assessing the insulin resistance among type 2 DM subjects. In this study the mean age of study population was 60 years and the number of subjects above 60 years were 102(56.66%). As per study by Chunyan et al. the prevalence of type 2 DM was common in the age group of more than 54.60±9.48 years. It shows that the type 2 DM is still a disease of middle age to elderly population [21]. In this study the male [98(54.44%)] patients were got affected more with the type 2 DM than female [82(45.55%)]. According to study by Pradeepa et al., the prevalence of type 2 DM was 9.6% in male and 9% in female [22].

In this study the mean HbA1C of >8.4±1.6gm/dl was found in 102(56.66%) patients, which in comparison to study by Azhar Saud, the mean HbA1C was 8 to 9% in uncontrolled type 2 DM with high cardiac risk patients [23]. In this study triglycerides/HDL cholesterol ratio of >3.0 was found in 112(62.22%) patients. The dyslipidaemia was a well known modifiable complication and a risk factor of type 2 DM [23]. As per study by Ajay et al., the mean triglycerides/HDL cholesterol ratio of > 2.50 ± 2.2 increases the risk of metabolic syndrome with insulin resistance in type 2 DM subjects [24]. The mean HOMA-IR of more than 2.5 was found in 98(54.44%) patients of this study,which was compared with the study by Ajay et al., where the mean HOMA-IR was 3.12 (2.73-3.595) in majority of cases of Uncontrolled type 2 DM patients. [24]. This study shows that, there was a positive correlation between the high HbA1C (8.4±1.6%) level and the triglycerides/HDL cholesterol ratio with HOMA-IR . Which in comparison with the study by Valeska et al. states that, there was a significant and demonstrable positive correlation found between uncontrolled type 2 DM subjects and the high triglycerides/HDL cholesterol ratio with high HOMA-IR [25]. The high triglycerides/HDL cholesterol ratio had high cardiovascular morbidity and mortality in the form of high incidence of sudden death,total occlusion of multiple coronary vessels, refractory cardiac failure,recurrent coronary artery occlusion inspite of being on appropriate medicatioins [25, 26].

As per the study of Trevor et al., there was a high degree insulin resistance found with the elevated levels of triglycerides with low HDL cholesterol level in uncontrolled type 2 DM individuals [26]. The well controlled type 2 DM plays an important role in bringing down the insulin resistance and management of dyslipidaemia [25, 26]. The Yohannes study says that, there was a significant inflammation with high triglycerides found in patients of uncontrolled type 2 DM with insulin resistance [27]. The statins and physical exercise could bring down chronic inflammation with significant drop in triglycerides level and insulin resistance [20, 26]. In this study, the majority of patients,who had high triglycerides/HDL cholesterol ratio and HOMA-IR found with significant complications of DM, such as early nephropathy, neuropathy, retinopathy and cardiao vascular changes. As per the study of Mitrofanova et al., the modification of risk factors like dyslipidaemia with high triglycerides and low HDL cholesterol, would reduce the rates of DM related cardio renal complications [17, 19]. Several studies had shown that, there was a significant and direct correlation between diabetic hypertriglyceridaemia with microvascular complications like renal,retinal and cardio neural complications [16, 17, 19, 28]. There was a high level of positive association found between

high triglycerides/HDL cholesterol ratio with all microvascular and macrovascualr complications of type 2 DM [16-19, 29].

The limitations associated with this study were the methods to calculate the insulin resistance like hyperinsulinemic euglycemic clamp test (HEC test) and QUICKI test were not used because of feasibility limitations. The sample size needs to be increased to draw further conclusions of triglycerides/ HDL ratio as a credible marker in assessing insulin resistance. The study was restricted to single ethnic group, therefore it requires further studies in other ethnic groups in order to evaluate the relationship between triglycerides/ HDL ratio and insulin resistance.

Conclusion

This study concludes that, the ratio of triglycerides / HDL cholesterol is a cost effective blood bio marker and it's correlating significantly with the HOMA-IR and serum fasting insulin level, while assessing the insulin resistance in type 2 DM subjects. The serum triglycerides to HDL ratio can be the investigation of choice in place of HOMA-IR for assessing the insulin resistance in type 2 DM subjects in financially poor, non feasible and remote hospital settings.

Conflicts of interest

Authors declare no conflicts of interest.

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