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COMPARATIVE EVALUATION OF TRIGLYCERIDE GLUCOSE INDEX AND HOMA-IR IN DIABETIC AND NON-DIABETIC PATIENTS WITH MYOCARDIAL INFARCTION

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ABSTRACT

Aims and Objective: To evaluate the association between Insulin Resistance & Myocardial Infarction using HOMA IR and TyG Index as a marker of Insulin Resistance. Materials and Method: This study was Baseline Cross sectional Observational study of 165 patients admitted with Myocardial Infarction between November 2022 and February 2024. Brief history was taken and baseline demographic details were noted. Fasting Blood sample was collected & HbA1c, TyG Index and HOMA IR, was estimated. Patients were divided into Diabetics and Non diabetics based on history & HbA1c. Results: The study's participant pool is predominantly male with the mean age of 55.39±11.48 years. Age is distributed equally between Diabetics and Non-Diabetics. Obese and overweight individuals contributed to 74.5% of the study participants with a mean BMI of 27.24±3.76 kg/m². The mean TyG index for Diabetics was 9.47±0.46, whereas for Non Diabetics it was 8.76±0.34 (P<0.0001). The mean HOMA-IR for diabetics was 4.96±4.46, & for non-diabetics it was 3.49±3.75 (P=0.022). We found that TyG Index & HOMA IR were raised in both Diabetics and Non Diabetics indicating underlying Insulin Resistance contributing to its complications. We compared baseline characteristics, clinical findings, and outcomes between these groups. **Conclusion:** We conclude that HOMA IR & TyG index can be used in our Routine health screening as marker of Insulin Resistance to start initial lifestyle changes to prevent complications of long-standing insulin resistance.

KEYWORDS: HOMA IR, Insulin resistance, Myocardial Infarction, TyG Index.

INTRODUCTION

Insulin resistance is associated with an increased risk of cardiovascular events like Myocardial Infarction.[1] Acute myocardial infarction (AMI) is a leading cause of death in developed nations, claiming over a million lives annually in the United States alone, with a prevalence of nearly 3 million cases.[2] Atherosclerotic plaque rupture and thrombosis are the primary causes, while other factors include coronary artery embolism, cocaine-induced vasoconstriction, and vasospasm.[3] Several large-scale cohort studies have documented that insulin resistance and hyperinsulinemia are associated with an increased risk of cardiovascular events like Myocardial Infarction.[1] Obesity, Insulin Resistance (IR), and type 2 diabetes mellitus are increasing and are powerful risk factors for Ischemic Heart Disease.[4] The metabolic syndrome, also known as syndrome X or insulin resistance syndrome, is a collection of metabolic abnormalities that increase the risk of cardiovascular disease (CVD) and diabetes mellitus.[4] Diabetes is a significant risk factor for myocardial infarction (Myocardial Infarction), with diabetic individuals having a higher likelihood of developing cardiovascular complications, including acute ST-segment elevation myocardial infarction (STEMI).[5] Prognosis depends on factors like ejection fraction, age, and comorbidities, with early reperfusion associated with better outcomes. Overall, prompt diagnosis and treatment are crucial for improving outcomes in MI patients.[6] Insulin resistance, a common feature of diabetes, exacerbates myocardial and microvascular dysfunction, contributing to larger infarct sizes and poorer clinical outcomes in diabetic patients experiencing myocardial infarction.[9] Insulin resistance is defined as ‘a condition in which a cell, tissue, or organism requires more insulin to elicit a normal response’.[7] The Homeostatic Model Assessment (HOMA) index is a simple and inexpensive Insulin Resistance marker.[8] In addition, the Triglyceride Glucose (TyG) index is derived from fasting triglyceride (TG) and fasting plasma glucose (FPG) levels, and it has been suggested as a reliable surrogate marker of insulin resistance (IR).[9] Furthermore, growing evidence has indicated that the TyG index is related to morbidity and mortality of cardiovascular disease in the general population and many patient cohorts, including patients with and without diabetes.[10]

The study aims to evaluate the association between Insulin Resistance & Myocardial Infarction using HOMA IR and TyG Index in Diabetics & Non-Diabetics.

MATERIALS AND METHODS

A cross sectional observational study was conducted in a tertiary care hospital in Western India, following the approval by the Institutional Review Board (Ethical committee) of the hospital. The patients included during a study period between November 2022 and February 2024. We included the patients admitted in the hospital under Department of Medicine diagnosed with Myocardial infarction above 20 years of age of either sex was included in our study after obtaining an informed consent. Following data are collected from the patient,

1. Demographic data (Name, age, geographical location)
2. Body mass index (kg/m^2)

The following data are obtained from the fasting blood sample collected,

1) HbA1c *(Reference Range : < 6%)*

2) HOMA IR= Fasting insulin (U/ml) X fasting glucose (mg/dl)/405 [or fasting glucose (mmol/l)/22.5] *(Reference Range : <1.9mU/ml)*

3) TyG Index= Ln fasting Triglyceride(mg/dL) × Fasting plasma glucose(mg/ dL) /2 *(Reference Range : 4-8)*

The primary objective was to estimate and correlate TyG index, HbA1c and HOMA IR in patients admitted with Myocardial infarction. The records of patients were analyzed, and baseline demographic data were extracted. Fasting Blood sample was collected to analyze laboratory parameters such as Triglyceride, fasting glucose, HOMA IR, HbA1c, TyG index. According to literature, the prevalence of IHD from previous study was found to be 10% and with absolute error of 4% the sample size came as 165.

Methods of estimation

Table 1: Method of estimation of Various parameters.

Parameter	Method
Fasting Glucose	Colorimetry(Glucose-hexokinase)
Triglycerides	Colorimetry (Glycerol 3 phosphate oxidase)
Insulin	Electrochemiluminescence Immunoassay
HbA1c	High performance liquid Chromatography (HPLC)

Statistical methods – The distribution of incidence of various qualitative characteristics was shown as n (% of cases), while the distribution of various quantitative characteristics was shown using Mean ± Standard deviation across two study groups. The statistical comparison of continuous variables across two groups was done using independent sample ‘t’ test after

confirming the underlying normality assumption. The significance of difference of categorical variables across two groups was tested using Chi-square test or Fisher's exact probability test. P-values less than 0.05 was considered to be statistically significant. All statistical analysis was done using SPSS 25.

RESULTS

In this study, 165 patients admitted with Myocardial Infarction, were included (2022-2024).

1. Demography

The study's participant pool is predominantly Male (72.7%).

The age distribution revealed that most patients were in the age group of 51-60 years (31.5%). The mean age was 55.39±11.48 years.

Obese and overweight individuals contributed to 74.5% of the study participants with a mean BMI of 27.24±3.76 kg/m².

Table 2: Study Participants Demographic.

Parameter	Details
Gender Distribution	Male: 72.7%
Age Group (Most Common)	51–60 years (31.5%)
Mean Age (± SD)	55.39 ± 11.48 years
BMI Category (Overweight/Obese)	74.5% of participants
Mean BMI (± SD)	27.24 ± 3.76 kg/m²

2. Biochemical parameters

When biochemical parameters were compared between diabetics and non-diabetics, a statistically significant difference was observed in HbA1c, TyG Index, and HOMA-IR (Table 3). Interestingly, both TyG Index and HOMA-IR were elevated even among non-diabetic individuals, despite normal glycaemic levels. This suggests the presence of underlying insulin resistance in the non-diabetic group.

The TyG Index (Triglyceride-Glucose Index) was notably higher in diabetics (mean: 9.47) compared to non-diabetics (mean: 8.76), with a p-value < 0.0001, indicating a highly significant difference. Similarly, the HOMA-IR (Homeostatic Model Assessment of Insulin Resistance) was elevated in diabetics (mean: 4.96) compared to non-diabetics (mean: 3.49), and the difference was statistically significant (p = 0.022), although less robust than the other parameters.

Table 3: Comparison of average TyG, HbA1c & HOMA-IR in DM vs non DM cases.

Parameter	Diabetic (N=88)		Non Diabetic (N=77)		Total		P
	Mean	SD	Mean	SD	Mean	SD	
HbA1C%	8.61	2.04	5.77	0.4	7.09	2.01	<0.0001*
TyG Index	9.47	0.46	8.76	0.34	9.09	0.53	<0.0001*
HOMA IR	4.96	4.46	3.49	3.75	4.17	4.15	0.022*

3. HbA1c correlation with TyG Index and HOMA IR

In a study involving 165 myocardial infarction patients, higher HbA1c levels showed a significant association with increased insulin resistance. A moderate to strong positive correlation was observed between HbA1c% and the TyG index ($r = 0.655$, $p < 0.001$), indicating that as HbA1c levels rise, the TyG index also increases significantly (Table 4). In contrast, the correlation between HbA1c% and HOMA-IR was weaker ($r = 0.203$), though still statistically significant ($p = 0.009$), suggesting a mild but consistent relationship between glycemic control and insulin resistance measured by HOMA-IR (Table 4).

Table 4: Correlation of HbA1c with HOMA IR and TyG index in patients admitted with MI.

		TYG	HOMA IR
HbA1C%	Pearson	.655**	.203**
	P	<0.001	0.009*
	N	165	165
**Correlation is significant at the 0.01 level (2-tailed).			

DISCUSSION

The cross sectional observational study included 165 patients admitted with Myocardial Infarction over a period of 2 years (2022-2024). The study participants were evaluated for Body Mass Index, TyG index, HOMA IR & HbA1c. Based on the literature review, it is well-established that hypertension, dyslipidaemia, obesity, impaired glucose tolerance, coronary artery disease, insulin resistance, and hyperinsulinemia are associated and collectively referred to as the insulin resistance syndrome or 'syndrome X'. Among these disorders, the connection between atherosclerosis and insulin resistance is least established. The HOMA IR model illustrates how glucose and insulin interact in the body to predict the levels of both when insulin resistance and beta-cell function are taken into account. Also, studies have shown that the TyG index not only reflects glycaemic control but also serves as a good predictor of insulin resistance. Keeping that in mind, we measured Insulin Resistance using HOMA IR & TyG Index & compared these parameters in patients admitted with Myocardial Infarction in Diabetic and Non Diabetic Patients.

Demography

Gender: The study's participant pool is predominantly male accounting for 72.7% of the total. This trend is similar to the one Henri Roukoz et al also published.[11]

Also, In a study by Samaneh Mozaffarian et al on short- and long-term survival rates following myocardial infarction and its predictive factors, using national registry data, a high incidence rate of MI was found in men compared to women (72.4% vs. 27.6%).[12]

Age: The age distribution revealed the mean age of 55.39±11.48.

A study on Risk Factors for In-Hospital Mortality from Cardiac Causes After Acute Myocardial Infarction by Gabriel Vasconcelos Oliveira[13] concluded that advanced age, along with systolic Blood pressure and female gender, were significant risk factors for death within 30 days after STEMI.

Body mass index: In the present study the overall mean BMI was 27.24±3.76 kg/m², with 74.5% overweight and obese indicating BMI closely linked to major cardiac events like myocardial infarction.

There was a significant difference in BMI between genders (p=0.001).

Our study is in agreement with Wolk et al.[14] who examined the association between BMI and acute coronary syndromes, including unstable angina pectoris and myocardial infarction, in US adults and reported that BMI and C-reactive protein were independent risk factors for coronary syndromes.

Zeller et al.[15] investigated the relationship between obesity and death after acute myocardial infarction in the French population and argued that neither WC nor BMI independently predicted death after acute myocardial infarction due to the obesity paradox, and it is important to measure both WC and BMI because of the possibility of high WC and low BMI.

Ke et al.[16] studied how a history of Myocardial Infarction, chest pain (angina), and strokes (both ischemic and hemorrhagic) as well as transient ischemic attack were associated with four different measures of obesity in Chinese patients with type 2 diabetes. They concluded that waist-to-height ratio (WHtR) was more strongly associated with these conditions than waist circumference (WC), waist-to-hip ratio (WHR), and body mass index (BMI).

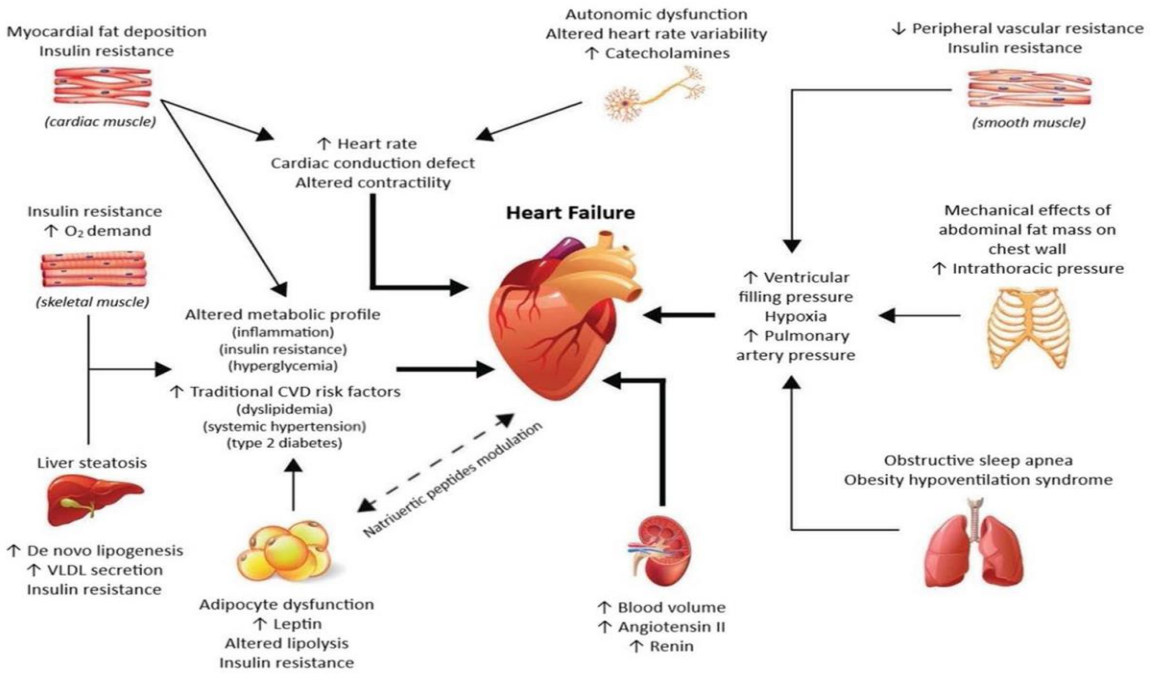

Figure 1: Pathophysiology of heart failure and CVD in obesity. Adapted from Rodriguez Flores et al(28).

Biochemical findings

In our study we enrolled patients admitted with Myocardial Infarction irrespective of their glycaemic status and grouped them as diabetes and non-diabetes based on history and HbA1c levels. There were 88 diabetic and 77 non diabetics in our study. It is a well-known fact that diabetics have an increased risk of cardiovascular disease. However very few studies have shown IR independent of diabetes predisposes to Myocardial Infarction. For the current study, we investigated to determine the correlation between insulin resistance measured by HOMA IR & TyG Index, as well as serum triglycerides, fasting glucose, and myocardial infarction.

Diabetics & Non Diabetics

Fasting Glucose, HbA1c, HOMA IR, & TyG Index were compared in MI. It was observed that Fasting Glucose, HbA1c,HOMA IR, TyG Index was statistically significant in Diabetes as compared to Non-Diabetes.

In our study, we also found that both HOMA IR and TyG Index were elevated in non-diabetic individuals as well, indicating that insulin resistance may be associated with atherosclerosis thus leading to complications like Myocardial Infarction.

A study by Jinyun Jing et al[17] found that elevated Homeostatic Model Assessment for Insulin Resistance (HOMO-IR) score and elevated triglyceride (TG) levels from baseline were associated with an increased risk of prediabetes. Also, in a study by Wanlu Su et al.[18] found that a population with a higher TyG index level was more likely to have an enhanced incidence of Type 2 DM and Hypertension comorbidity. TyG index could be clinically significant in early protection against Type 2 DM with Hypertension. In a study by Ronald M Krauss.[19] found that Insulin resistance plays a key role in the development of diabetic dyslipidemia. Each lipid abnormality (low HDL, small dense LDL, and elevated triglycerides) is associated with an increased risk of CHD.

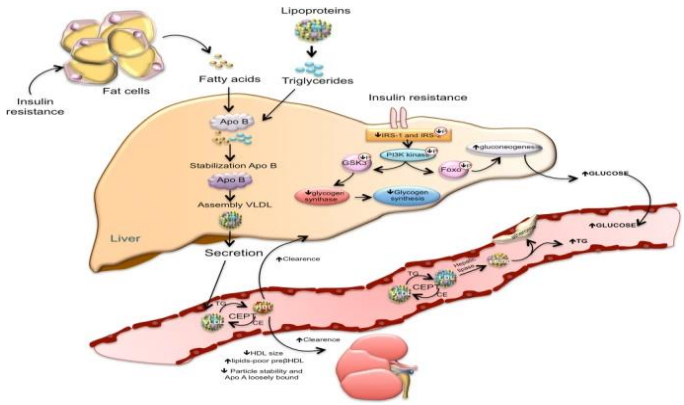

Figure 2 A simplified. Model of insulin resistance. Adapted from Ormazabal, V., Nair, S., Elfeky, O. et al. Association between insulin resistance and the development of cardiovascular disease. Cardiovasc Diabetol 17, 122 (2018 35))

Whatsoever may be the cause of Insulin Resistance, it leads to dyslipidemia. Dyslipidemia in Insulin resistance can be explained due to the loss of insulin's suppressive effects on lipolysis in adipocytes, leading to increased free fatty acids. Increased flux of free fatty acids to the liver stimulates VLDL assembly and secretion, leading to hypertriglyceridemia. Triglycerides (TG) in VLDL get transferred to both HDL and LDL through the action of cholesteryl ester transfer protein (CETP). This process leads to the formation of triglyceride-enriched HDL and LDL particles. Triglyceride-enriched HDL is cleared more rapidly from the circulation by the kidney, leading to fewer HDL particles available to accept cholesterol from the vasculature.[20] This may be the reason why Insulin Resistance is observed in patients of Myocardial infarction in our present study.

Fernando *et al* reported that TyG index was significantly correlated with HOMA-IR and euglycemic-hyper insulinemic clamp test for identifying insulin resistance.[21] Insulin,

independent of its effects on blood pressure, Glucose and plasma lipids, is known to be atherogenic. The hormone insulin enhances cholesterol transport into arteriolar smooth muscle cells and increases the cells' endogenous lipid synthesis. Additionally, insulin promotes the growth of smooth muscle cells in small arteries, enhances the production of collagen in the vessel wall, increases the formation of lipid plaques, and inhibits their regression. It also stimulates the production of various growth factors. However, it is difficult to determine whether hyperinsulinemia or insulin resistance is responsible for the development of CAD.[22] Insulin resistance sets in much before the occurrence of Diabetes and can lead to adverse outcomes like Myocardial infarction. Thus managing insulin resistance in a much earlier stage can prevent not only diabetes but also other thrombosis-related complications.

Correlation of HbA1c with HOMA IR & TyG Index

In our study of 165 patients admitted with Myocardial Infarction, higher HbA1c levels strongly correlates with increased insulin resistance measured by both HOMA IR & TyG Index indicating poor glycaemic control linked to higher insulin resistance in these individuals. This implies TyG index & HOMA IR can be used as effective screening tools in predicting glycemic control in Type 2 DM.

Similarly, Hameed et al. illustrated that the TyG index had the largest AUC of 0.836 in ROC analysis, which correlated with HbA1c and HOMA-IR[23] Also, TyG index is useful in assessing the magnitude of insulin resistance in Type 2 DM.[24]

In this study, finding AUC of TyG Index and HOMA IR can assess the magnitude of Insulin Resistance and also which one is the better indicator of Insulin resistance.

Our findings suggest that measuring the HOMA IR & TyG index, even in non-diabetic individuals, may provide additional value in predicting atherosclerosis in the coming years.

CONCLUSION

Our study revealed that patients with Myocardial Infarction exhibited significantly elevated HOMA IR levels. This confirms the strong association between insulin resistance and cardiovascular diseases.

In our study, we found that levels of serum triglyceride, fasting glucose, and HbA1c, HOMA IR & TyG index were significantly higher in diabetics compared to non-diabetics indicating a strong association with diabetes.

We also found that both HOMA IR and TyG Index were significantly elevated in non-diabetic individuals, and hyperinsulinemia may be associated with atherosclerosis thus implying Insulin, independent of its effects on blood pressure, Glucose and plasma lipids, is known to be atherogenic.

Hence, we conclude that HOMA IR & TyG index can be used in our Routine health screening to start initial lifestyle changes to prevent complications of long-standing insulin resistance.

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TABLES

FIGURES

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