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IMPACT OF GLYCEMIC CONTROL ON TRIGLYCERIDE-GLUCOSE INDEX AND ATHEROGENIC INDICES : ASSESSING ATHEROGENIC RISK IN TYPE 2 DIABETES MELLITUS

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ABSTRACT

INTRODUCTION : Type 2 Diabetes Mellitus (T2DM) is a prevalent chronic metabolic disorder that is associated with a variety of complications, particularly cardiovascular disease. T2DM is characterized by insulin resistance, beta-cell dysfunction and abnormal lipid metabolism, all of which contribute to the increased risk of cardiovascular morbidity and mortality in affected individuals.While glycemic control, typically evaluated through markers like HbA1c, is essential in managing T2DM, it may not fully capture the overall cardiovascular risk. Alternative biomarkers, such as the Triglyceride-Glucose (TyG) index and the Atherogenic Index of Plasma (AIP) have been suggested as valuable tools for assessing cardiovascular risk in diabetic patients, particularly in relation to insulin resistance and lipid metabolism.

AIMS AND OBJECTIVES :

1. To estimate FBS, HbA1c, Total cholesterol(TC), Triglyceride(TG), HDL-Cholesterol(HDL-C), TyG index and AIP in Type 2 DM with good and poor glycemic control.
2. To compare and evaluate TyG index and AIP in T2DM patients with good and poor glycemic control.

METHODS: 80 patients (male and female) aged between 30-70 years diagnosed with T2DM based on ADA criteria were included and their FBS,lipid profile, TyG and AIP were estimated.

RESULTS: People with poor control have higher blood sugar (8.75% for HbA1c and 182.23 mg/dL for fasting blood sugar), worse cholesterol numbers (286.43 mg/dL for total cholesterol and 254.37 mg/dL for triglycerides), and lower "good" cholesterol (32.90 mg/dL for HDL) as comapred to their good control counterpart. TyG and AIP were elevated in poor glycemic control group with a strong positive correlation between them.

CONCLUSION : TyG and AIP should be assesed in T2DM patients routinely to assess cardiovascular risk in patients with varied glycemic control.

Keywords : Insulin resitance, Glycemic control, Atherogenic index.

INTRODUCTION

Type 2 Diabetes mellitus (T2DM) is a common albeit potentially devastating medical condition that has increased in prevalence over time leading to major public health challenge of the twenty-first century.[1] According to ICMR-INIDAB 2023 report prevalence of T2DM in india is 11.4 %.[2]and global prevalence of 10.5 %.[3]T2DM is characterized by insulin resistance and impaired insulin secretion. Reaven et al., suggested that insulin resistance (IR) manifesting as hyperinsulinemia is the driving factor for the development of dyslipidemia and altered glucose metabolism which also predisposes individuals to a range of comorbidities especially cardiovascular diseases (CVD).[4]

Luis et al., stated that Triglyceride glucose Index (TyG Index) is a reliable and simple surrogate marker of insulin resistance having high sensitivity and specificity.[5] The core link and initiator of various metabolic diseases including diabetes, metabolic syndrome and cardiovascular disease is insulin resistance.[6] It is a metabolic condition in which cells are insensitive to insulin which causes hyperinsulinemia.

Most in vitro studies have demonstrated normal antilipolytic effect of insulin in fat cells of subjects with T2DM.[7] However, in insulin resistant state lipolysis occurs releasing free fatty acid due to inefficiency of insulin in inhibiting lipolysis.

Austin and colleagues first explained Atherogenic Dyslipidemia (AD) as a clinical condition in 1990 [8] . It is characterised by elevated levels of serum triglyceride (TG) levels and small-dense low-density lipoprotein (sdLDL) particles with low levels of high-density lipoprotein cholesterol (HDL-C), highlighting its atherogenic lipoprotein phenotype. [9] The Atherogenic Index of Plasma (AIP) is more closely related to cardiovascular risk than individual lipoprotein cholesterol fractions.[10]

Glycemic control is an essential component in the management of T2DM, as it directly leading to long-term complications, including cardiovascular diseases. The traditional marker of glycemic control is HbA1c which reflects the average blood glucose levels over the past 2-3 months.

METHODOLOGY :

A cross sectional study was conducted at Karwar Institute Of Medical Sciences in which 80 patients (male and female) aged between 30-70 years diagnosed with T2DM based on ADA criteria were included. Fasting blood sugar was measured by GOD-POD method on XL 640. HbA1c was measured by immunoturbidimetry in EM 200. Total cholesterol, Triglycerides and HDL-Cholesterol and LDL-Cholesterol were measured in XL 640. TyG Index and AIP was calculated using formula given below -

TyG index = Ln [{fasting TG (mg/dL)X fasting plasma glucose (mg/dL)/2}]

AIP = log [TG (mg/dL) / HDL-C (mg/dL)]

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Patients unwilling to give consent, alcoholics, smokers, using sedatives or drugs, using medication that alter serum glucose levels, critically ill patients, pregnant females, liver cirrhosis and HIV positive patients were excluded from the study.

RESULTS :

Table 1.1

ANALYTE	GOOD GLYCEMIC CONTROL	POOR GLYCEMIC CONTROL
HbA1c	6.25± 0.39	8.75±1.19
FBS(mg/dL)	108.2± 9.47	182.23±26.75
Total Cholesterol (mg/dl)	185± 10.69	286.43± 72.63
Triglycerides(mg/dL)	149.8± 15.72	254.37± 69.73
HDL- C (mg/dl)	48.7± 8.98	32.90± 7.63
TyG Index	4.84±0.066	5.349± 0.19
AIP	0.493±0.119	0.673± 0.25

In our study people with good control have healthier numbers, like lower average blood sugar (6.25% for HbA1c and 108.2 mg/dL for fasting blood sugar) and better cholesterol levels (185 mg/dL for total cholesterol and 149.8 mg/dL for triglycerides).

They also have more "good" cholesterol (48.7 mg/dL for HDL) and better insulin sensitivity.

On the other hand, people with poor control have higher blood sugar (8.75% for HbA1c and 182.23 mg/dL for fasting blood sugar), worse cholesterol numbers (286.43 mg/dL for total cholesterol and 254.37 mg/dL for triglycerides) and lower "good" cholesterol (32.90 mg/dL for HDL). Their higher triglycerides and insulin resistance also suggest a higher risk of heart problems. Overall, better blood sugar control leads to healthier blood sugar, cholesterol, and heart health markers.

Table 1.2

POOR GLYCEMIC CONTROL

	r value	p value (<0.05)
HbA1c vs TyG	0.908	<0.001

HbA1c vs AIP	0.62	<0.001
TyG vs AIP	**0.727**	**<0.001**

The **r value** measures the strength and direction of the correlation between two variables. In the above table, **r-value of 0.908** suggests a **strong positive correlation**, meaning as **HbA1c** increases, **TyG** also tends to increase, and vice versa.
The **r-value** of **0.62** indicates a **moderate positive correlation** between **HbA1c** and **AIP.**
Whereas the correlation is not as strong as the previous one between **HbA1c** and **TyG**, it still suggests that poor glucose control is related to worse lipid profiles and cardiovascular risk. The **r-value** of **0.727** represents a **strong positive correlation** between **TyG** and **AIP.** If someone has high **HbA1c** (suggesting poor blood sugar control), they might also have higher insulin resistance (**TyG**) and higher cardiovascular risk (**AIP**). These factors should be monitored together for a more comprehensive understanding of a patient's metabolic and cardiovascular health.

Table 1.3
GOOD GLYCEMIC CONTROL

	r value	**p value (<0.05)**
TyG vs AIP	0.023	0.04
AIP vs HDL-C	**-0.952**	**<0.001**

The **r-value** of **-0.952** indicates a **very strong negative correlation** between **AIP** and **HDL-C. Good glycemic control** appears to weaken the relationship between insulin resistance and cardiovascular risk, as reflected by the near-zero correlation between **TyG** and **AIP**.

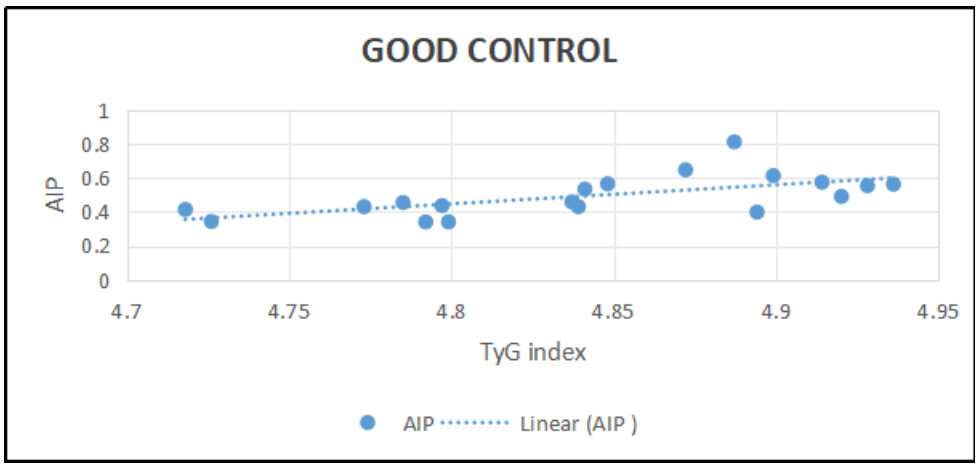


Fig 1

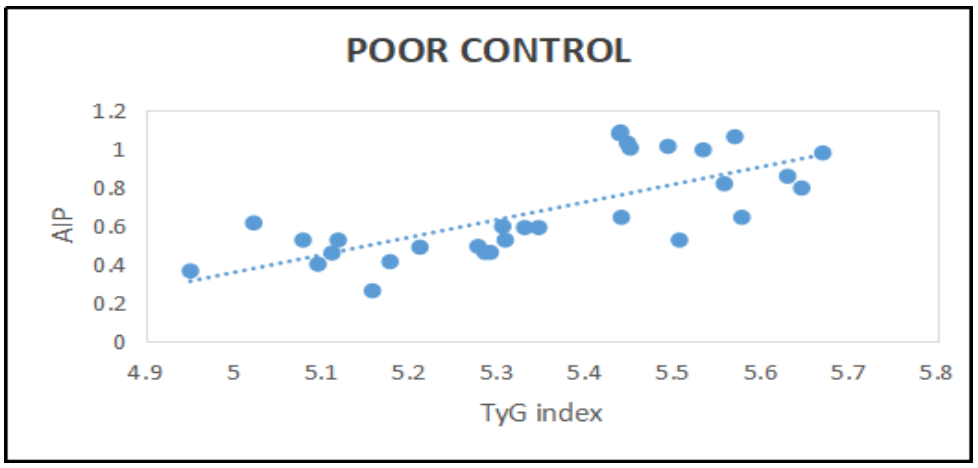


Fig 2

DISCUSSION

In our study patients with good glycemic control (defined as HbA1c <7%) generally show better metabolic parameters, including lower TyG values and more encouraging AIP scores. This is because stable and well-controlled blood glucose levels tend to reduce the degree of insulin resistance, which in turn helps to normalize lipid metabolism. As a result, these patients may have a lower risk of atherosclerosis and cardiovascular events.

On the other hand, patients with poor glycemic control (defined as HbA1c ≥7%) often experience exacerbated insulin resistance, leading to higher TyG indices.[11] This finding is consistent with the study conducted by Nandhini et al.,. Additionally, poor glycemic control is frequently associated with dyslipidemia, characterized by elevated triglycerides and reduced HDL-C levels, which can increase AIP.[12] These patients are at a higher risk for the development of cardiovascular disease due to the combined effects of insulin resistance and dyslipidemia. This finiding is consistent with findings of study done by Carkirka et al.,

Both the TyG index and AIP have been shown to be independent predictors of cardiovascular disease outcomes in patients with T2DM. High TyG values have been associated with an increased incidence of coronary artery disease[13] while elevated AIP scores have been linked to a greater risk of myocardial infarction and stroke.[14]

Elevated TyG and AIP indices combined with poor glycemic control can provide an early warning for clinicians, allowing them to intervene before cardiovascular events occur. While blood glucose control is the key focus in managing T2DM, addressing insulin resistance and lipid disorders is just as important in lowering cardiovascular risk.[15]

Integrating the measurement of TyG and AIP into routine clinical practice could be a cost-effective and efficient way to identify patients at high risk for cardiovascular diseases. These indices can complement the assessment of HbA1c and provide additional insights into the underlying metabolic dysfunction that may not be captured by standard blood glucose monitoring alone.

For patients with good glycemic control, maintaining a normal TyG and AIP could

further reduce their risk of cardiovascular events. For those with poor glycemic control, early intervention aimed at improving insulin sensitivity and managing dyslipidemia could help to mitigate the cardiovascular risks associated with T2DM.

Lifestyle modifications such as weight management, regular physical activity and a balanced diet along with pharmacological treatments targeting insulin resistance and dyslipidemia, should be part of the comprehensive approach to managing T2DM. In some cases, the use of medications like statins, fibrates, or newer drugs like SGLT2 inhibitors and GLP-1 agonists may be necessary to manage lipid profile and improve cardiovascular outcomes.

CONCLUSION :

The TyG index and AIP are emerging biomarkers that provide valuable insight into the cardiovascular risks of T2DM patients, particularly in relation to insulin resistance and dyslipidemia. While glycemic control remains the cornerstone of managing T2DM. These biomarkers (TyG, AIP) help to identify patients at higher risk of cardiovascular events, even in those with well-controlled blood glucose levels. In patients with poor glycemic control, elevated TyG and AIP indices indicate significant metabolic dysfunction, which requires more intensive interventions to mitigate cardiovascular risk.

By incorporating the TyG index and AIP into clinical practice, healthcare providers can achieve a more comprehensive assessment of cardiovascular risk in T2DM patients, leading to better-targeted therapeutic strategies. Future research is needed to further explore the clinical utility of these markers and to investigate potential interventions that could reduce the cardiovascular burden in T2DM patients.

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