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Original Research Article

CORRELATION OF ATHEROGENIC INDEX OF PLASMA AND CASTELLI RISK INDICES WITH HBA1C IN TYPE II DIABETES MELLITUS PATIENTS

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ABSTRACT

Background: Dyslipidemia and poor glycemic control in type 2 Diabetes mellitus (T2DM) pose an increased the risk of cardiovascular disease (CVD). As atherogenic index of plasma (AIP) and castelli risk indices I & II were potential markers of adverse cardiovascular events, we planned a study to evaluate the relationship between these indices with HbA1c among T2DM participants.

Materials and Methods: An observational cross-sectional study was conducted among the type 2 diabetes patients. The study period was between September 2023 and February 2024. HbA1c, fasting blood glucose and lipid profile parameters were analysed and Atherogenic index of plasma (AIP) and castelli risk indices I & II were calculated. **Statistical Analysis:** Data was analyzed using SPSS software. The descriptive variables were expressed as mean and standard deviation. Student t test was used to compare two independent groups. Correlation of Atherogenic index of plasma (AIP) and castelli risk indices I & II with HbA1c was performed by pearson's correlation coefficient. P value of < 0.05 was considered statistically significant.

Results: A total of 173 study subjects were included in the study. The mean HbA1c of the study subjects with good and poor glycemic control were 6.6±0.3% and 10.3± 2.5% respectively. Our study reported a significant higher concentration of Triglycerides, Total cholesterol (TC), Low density lipoprotein (LDL), Very low density lipoprotein (VLDL) and a low concentration of High density lipoprotein (HDL) in individuals with poor glycemic control. Correlation analysis showed a significant moderate positive correlation between HbA1c and castelli risk index I (r= 0.598); strong positive correlation between HbA1c and castelli risk index II (r= 0.616); very strong positive correlation between HbA1c and atherogenic index of plasma (r= 0.964).

Conclusion: High values of atherogenic index of plasma and castelli risk indices proves an increased atherogenic risk in individuals with poor glycemic control.

Keywords: Atherogenic index of plasma, Cardiovascular disease, Castelli risk index, Glycemic control, Type 2 diabetes mellitus.

INTRODUCTION

Diabetes mellitus is a chronic metabolic condition caused due to defects in insulin secretion or its action or both resulting in increased blood glucose level.[1] About 540 million people in the world have been affected by diabetes and India is the second most affected country in the world. About 1.5

million deaths have been directly attributed due to diabetes.[2] Uncontrolled diabetes mellitus characterized by hyperglycemia often leads to long-term complications affecting many organ systems. This risk of chronic complications increases with increase in the duration of hyperglycemia and usually manifests in second decade of diabetic duration.[3]

The microvascular complications include neuropathy, nephropathy and retinopathy whereas the macrovascular complications include cardiovascular disease, stroke and peripheral artery disease.[4] Cardiovascular disease is related to increased morbidity and mortality in people with diabetes mellitus. Since HbA1c shows the amount of glucose which binds to hemoglobin in red blood cells whose life span is 3-4 months, this test estimates the glycemic control in the past 2-3 months so, it has been suggested that a 0.2% decrease in HbA1c could result in a 10% reduction in mortality.[5] Several studies shows that a 1% rise in the absolute glycosylated hemoglobin (HbA1c) value corresponds to an 18% increase in the estimated risk of cardiovascular disease.[7]

Dyslipidemia is disorder of lipoprotein metabolism which is characterized by an elevation of serum total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), or triglycerides (TG) and reduced serum high-density lipoprotein cholesterol (HDL-C) concentration.[8] Glycemic control has an effect on the serum lipid level in people with diabetes due to their poor glycemic control.[9] Apart from hypertriglyceridemia and decreased HDL, there are structural abnormalities in lipoproteins. The predominant form of LDL cholesterol in diabetic patients is small dense form. These small LDL molecules can easily penetrate and bind to arterial wall thereby forming plaque resulting in atheroscelrosis.[10] Dyslipidemia together with increased HbA1C levels among diabetic patients shall be considered as predominant risk factor in development of cardiovascular disease.[9,10] Recently atherogenic index of plasma and castelli risk indices have been used to assess cardiovascular risk in diabetic patients. The aim of this study was to evaluate the relationship of HbA1c levels with atherogenic index of plasma and castelli risk indices I & II T2DM patients.

MATERIALS AND METHODS

It is an observational cross- sectional study which was conducted at Trichy SRM medical college and hospital and research centre. The study period was between September 2023 and February 2024. The sample size was calculated using stata software based on the previous study findings of Prasad PS et al (2018) 11, a sample size of 170 type 2 diabetic patients was considered adequate for 80% power and 5% level of significance.

Inclusion Criteria: Type 2 diabetic patients between the age of 19 and 65 years of both gender.

Exclusion Criteria: Patients with Type 1 diabetes mellitus, familial hypercholesteremic syndromes, chronic renal failure, cardiovascular and liver disease, endocrinopathies, gestational diabetes mellitus and individuals on lipid-lowering therapy were excluded from the study.

Methods

A detailed case history with demographic data was obtained from the patients after a written and informed consent. 5ml of sample was collected after an overnight fast for analysis of parameters like fasting blood sugar (FBS), lipid profile and HbA1c. FBS was estimated by Hexokinase method; HbA1c by high pressure chromatography method in D10 analyser; Total cholesterol by Cholesterol oxidase and peroxidase (CHOD-POD); Triglycerides by Glycerol-3-phosphate oxidase (GPO PAP) enzymatic colorimetric method and Serum HDL & LDL levels by direct enzymatic methods. VLDL-C was calculated by Triglycerides divided by 5. All the lipid parameters and fasting blood glucose was assayed by using fully automated analyzer –Roche cobas-c311. Atherogenic index and Castelli risk index I & II was calculated by:

Atherogenic index of plasma=log10(TG/HDL); Castelli risk index I=TC/HDL; Castelli risk index II = LDL/HDL, Non HDL =TC-HDL

Statistical Analysis

The collected data was entered in MS Excel and statistical analysis was performed using SPSS software. The normality of the test was tested using Kolmogorov-smirnov test in which our data followed a normal distribution. Descriptive data was presented as mean and standard deviation. Student t test was used to compare two independent groups. Correlation of Atherogenic index of plasma (AIP) and castelli risk indices I & II with HbA1c was performed by pearson's correlation coefficient. For all the statistical tests a two-tailed and p value of < 0.05 was considered as statistically significant.

RESULTS

Our study included 173 study subjects with T2DM. The mean age of the study subjects was 52.8 ± 0.83 years. Majority of participants (59 %) were in the age group of more than 60 years (Figure 1) and 54 % of study subjects were females (Figure 2). Mean HbA1c levels of the study participants was 9.67 + 2.68% in males and 9.56 + 2.74 % in females. Males have significantly increased BMI (30.4 + 8.1 kg/m²)kg/m² than females (27.5±5.1 kg/m²).Males had higher total cholesterol ,TGL,LDL,VLDL values than females. Females had a significantly increase HDL value of (49.3±18.2 mg/dl) than male population (43.9±12.2 mg/dl). [Table 1]

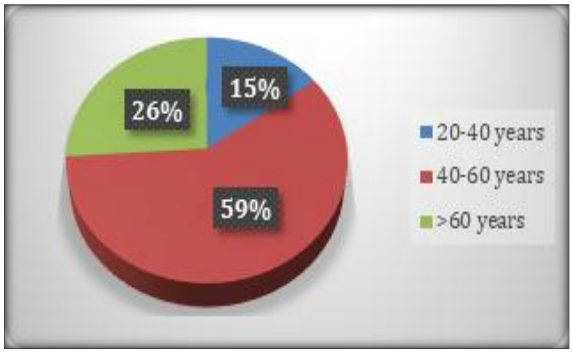

Figure 1: Age distribution of study population

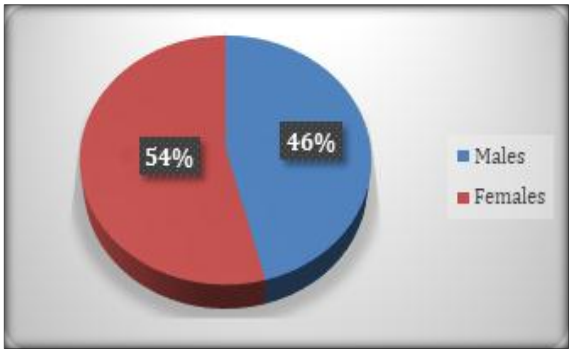

Figure 2: Gender distribution of study population

Table 1: Baseline characteristics of study population

Variable	Males(n=79)	Females (n=94)
Age (years)	54.78 ±11.2	51.13 ±10.52
BMI (kg/m^2)	30.4 ± 8.1	27.5 ± 5.1*
SBP (mm Hg)	122 ± 7.8	108 ± 10.2*
DBP (mm Hg)	82.3 ± 6.9	80 ± 5.4*
FBG (mg/dL)	157.5 ± 66.7	146.7± 61.0
HBA1C (%)	9.67 ±2.68	9.56 ±2.74
TC (mg/dL)	188.96±48.5	175.7±46.4
TGL (mg/dL)	143.6± 50.6	142.1± 50.86
HDL (mg/dL)	43.9± 12.2	49.3± 18.2*
LDL (mg/dL)	107.8± 44.1	102.3± 52.9
VLDL (mg/dL)	29.9±17.3	27.6± 18.2
LDL/HDL ratio	2.06± 1.45	1.96± 1.24
AIP	0.4 ±0.23	0.35±0.24*

**p value- <0.05 statistically significant*

We sub-grouped our population based on the levels of HbA1c. Individuals who had HbA1c of less than or equal to 7% were considered to have good glycemic control, while those who had HbA1c of more than or equal to 7% were considered to have poor glycemic control. The gender distribution of glycemic control is given in figure 3.

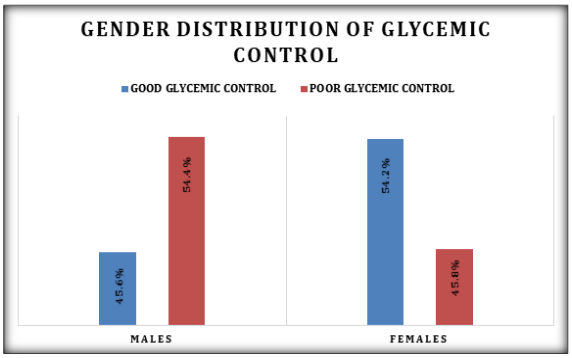

Figure 3: Gender distribution of glycemic control

In our study the population with poor glycemic control (HbA1c >7%) had significant increase in TGL, VLDL, LDL and non significant increase in TC concentration. There is significant increase in HDL (59.88±39.39) in good glycemic control group than the poorly controlled (49.63±25.83) indicating dyslipidemia in these population.

On analysis of atherogenic indices, AIP, CRI I & II are significantly increased in poorly controlled diabetic patients with dyslipidemia.

Table 2: Baseline characteristics of study population with good and poor glycemic control

Variable	Good glycemic control (n= 87)	Poor glycemic control (n= 86)
BMI (kg/m2)	26.3 ± 4.1	28.8 ± 5.7*
SBP (mm Hg)	121.4 ± 6.3	123.1 ± 9.5
DBP (mm Hg)	81.4 ± 4.1	83.3 ± 9.1
FBG (mg/dL)	148.70±64.22	163.85±63.28 *
HbA1c (%)	6.6±0.3	10.3±2.5*
TGL (mg/dL)	94.91±36.15	149.66±51.76 *
TC (mg/dL)	180.66±50.45	192.15±36.77
HDL (mg/dL)	59.88±39.39	49.63±25.83 *
LDL (mg/dL)	112.65±39.98	103.80±47.86 *
VLDL (mg/dL)	24.91±10.99	32.60±16.49 *
AIP (mg/dl)	0.3±1.4	5.1± 1.8*
CRI I	2.35±1.42	4.76±1.56*
CRI II	0.99±1.11	3.05±1.38*

p value- <0.05 statistically significant

Correlation analysis showed a significant moderate positive correlation between HbA1c and castelli risk index I (r= 0.598); strong positive correlation between HbA1c and castelli risk index II (r= 0.616) and very strong positive correlation between HbA1c and atherogenic index of plasma (r= 0.964). [Table 3]

Table 3: Correlation between HbA1c and Castelli risk index I & II among study subjects

Variable	r value
Castelli risk index I Vs HbA1c	0.598*
Castelli risk index II Vs HbA1c	0.616*
Atherogenic index of plasma (AIP) Vs HbA1c	0.964*

**- p value <0.05 – statistically significant*

DISCUSSIONS

Uncontrolled hyperglycemia and Dysregulated lipid profile for a long duration pose a greater risk of developing cardiovascular complications. Hence, we assessed the atherogenic index of plasma and castelli risk indices I & II and compared these indices with glycemic control in diabetic population. The mean age of the current study was 52.8 + 0.83 years, comparable to a study carried out in Karnataka, India by Prasad PS et al,[11] which showed a mean age of 50.88±10.10 years. Since diabetes is a multifactorial illness, the mean age finding above confirms that being older than 45 is a non-modifiable risk factor for diabetes. In our study, majority (54%) were females which is contradictory to a study conducted by Patil M et al,[12] which showed majority (65%) were male. Men are more likely to have diabetes than women in the general population.[13] But, the discrepancy in our study finding may be due to center-based study rather than population-based in above-stated studies. The mean values of HbA1c 9.67 +2.68% in males and 9.19+ 2.25 in females were in line with Kidwai SS et al study with 9.56 + 2.74 and 9.19 + 2.5 in males and females respectively.[14] Males had a greater BMI (30.4 + 8.1 kg/m²) with increased total cholesterol, LDLc and triglycerides with low HDL than females in our center based study. This is similar Mehta RK et al study,[15] and contradictory Bhambhani G et al study.[16] Higher BMI and disordered lipid profile may be attributed to lifestyle modifications with high calorie and low fiber diet in the population.

HbA1c is considered the gold standard for glycemic management, according to the Diabetes Complications and Management Trial.[17] An HbA1c of up to 7.0% may lower the risk of cardiovascular problems, according to several studies.[18,19] Thus, based on the HbA1c % we grouped our study population. Subgroup analysis according to glycemic control showed that majority (54.4%) of males had a poorly controlled glycemic status similar to Kidwai SS et al study.[14] It was found that the levels of FBS, TGL, LDL and VLDLand BMI were higher and lower HDL among the study subjects with good glycaemic control than those with poor glyacemic control. The above findings are supported by several studies conducted among type 2 diabetes patients.[20,21,22] It has been proposed that the development of diabetic dyslipidemia is mostly influenced by insulin resistance. Increased release of free fatty acids from insulin-resistant fat cells is one of the explanations.[23] When free fatty acids are present in sufficient amounts, they stimulate the formation of TG, which in turn increases the levels of Apolipoprotein B (Apo-B) and VLDL. Also higher BMI is suggestive of insulin resistance causing increased HbA1c in poorly controlled group.[24] Thus by enhancing glycemic management could significantly lower the chance of cardiovascular incidents. It has been estimated that a 0.2% drop in HbA1c level could result in a 10% reduction in mortality due to diabetic complications.[5]

In addition to the lipid parameters, the current study looked at the relationship between HbA1c, Castelli risk indices and plasma atherogenic index and found a substantial positive link. The finding of very strong significant positive relation (r=0.964) of atherogenic index of plasma with HbA1c was congruent with a previous study conducted by Bozkur E et al,[25] who found a favorable connection between HbA1c and plasma atherogenic index. Similar to our finding of positive corealtion of castelli risk indices with HbA1c, a study conducted by Ambreen A. et al,[26] also showed that castelli risk indices are significantly lower among subjects with good glycaemic control than those with poor glycaemic control. As previously discussed, the atherogenic index of plasma and the castelli risk indices I & II can be used to predict the cardiovascular risk among patients with poorly controlled diabetes. Among these indices, AIP had a better predictive value in situations where other atherogenic risk parameters like TG and HDLc appear normal. Thus AIP may be the good predictor adverse cardiac events.

CONCLUSION

The atherogenic index of plasma and castelli risk indices I & II increases with increased HbA1c levels. When compared with castelli risk index I & II, AIP calculated with TGL and HDL concentration, provided a strong positive correlation with Hba1c. Hence, we recommend the utility of atherogenic indices in place of individual lipid

profile parameters for screening of cardiovascular risk diabetic patients

Limitations

First limitation is the findings of the current study cannot be generalized since it is conducted a center based setting and also the study subjects were recruited by convenient sampling technique i.e by physician referral. Secondly, the information regarding dietary history, physical activity and genetic factors were not taken into account, that would have influenced our study outcome.

Conflict of interest: Nil

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Authors Contribution

All authors in our study contributed to the data collection of the patients

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