International Journal of Current Advanced Research
ISSN: O: 2319-6475, ISSN: P: 2319-6505, Impact Factor: 6.614
Available Online at www.journalijcar.org
Volume 7; Issue 8(D); August 2018; Page No. 14789-14793
DOI: http://dx.doi.org/10.24327/ijcar.2018.14793.2695

Research Article

CORRELATION BETWEEN HBA1C AND ATHEROGENIC INDEX IN TYPE 2 DIABETIC PATIENTS

Ashish Prakash Anjankar[1]*., Anita b. Kale[2] and Pratibha L. Sharma[3]

[1]Department of Biochemistry, Jawaharlal Nehru Medical College, Sawangi (Meghe), Wardha, Maharashtra
[2]Department of Biochemistry, Seth G.S. Medical College and KEM Hospital, Parel, Mumbai, Maharashtra
[3]Department of Biochemistry, Netaji Subhash Chandra Bose Medical College, Jabalpur, MP

A R T I C L E I N F O

Article History:

Received 04th May, 2018
Received in revised form 16th June, 2018 Accepted 25th July, 2018
Published online 28th August, 2018

Key words:

AIP, Diabetic patients, Fasting blood glucose, Glycated hemoglobin

A B S T R A C T

Introduction: HbA1c is considered the "gold standard" of glycemic control during the 6-8 week period. The atherogenic index of plasma (AIP) is considered as a predictive marker for plasma atherogenicity. This study was aimed to find out association between fasting blood glucose (FBG), HbA1c and atherogenic index in type 2 diabetic patients.

Objectives

1. To find out the correlation between fasting plasma glucose and atherogenic index in type 2 diabetic patients.
2. To find out the correlation between HbA1c and atherogenic index in type 2 diabetic patients.

Methods: It is a prospective analytical study. 100 diagnosed type 2 diabetes mellitus patients were divided into two groups depending on their HbA1c levels;
Group I: Good Glycemic Control group having HbA1c < 7.0% (n= 50) and
Group II: Poor Glycemic Control group having HbA1c ≥ 7.0% (n= 50).
Fasting blood sample was used to measure FBG, HbA1C, TC, TG, LDL-C and HDL-C with standard tests. Atherogenic index was calculated by using formula = log (TG/HDL-C).

Results: In type 2 diabetes mellitus patients; mean FBG, mean HbA1c and mean atherogenic index values were significantly higher in those patients having poor glycemic control than in those patients having good glycemic control. Also, atherogenic index is positively correlated with FBG and HbA1C.

Conclusion: AIP, which can be easily calculated from lipid profile, may be utilized for screening diabetic patients to predict both dyslipidemia and glycemic control. So, diabetic patients should be educated about regular monitoring of lipid profiles. Also, HbA1c can be utilized for screening high risk diabetic patients for early diagnosis of dyslipidemia.

INTRODUCTION

Developing country like India with fast urbanization is facing a serious problem having the largest number of patients with diabetes [1] which is estimated to reach 80 million by the end of 2030.[2,3] Serum lipid and lipoprotein profile abnormality in type 2 diabetes mellitus (DM) may contribute to the risk of coronary artery disease (CAD).[4,5] So, DM is associated with a greater risk of morbidity and mortality from cardiovascular disease (CVD). Fasting blood glucose (FBG) test and 2 hr post prandial glucose test were being used from decades for screening diabetes. Currently, glycosylated hemoglobin (HbA1c) is considered the "gold standard" of glycemic control during the 6-8 week period.

Corresponding author:* **Ashish Prakash Anjankar
Department of Biochemistry, Jawaharlal Nehru Medical College, Sawangi (Meghe), Wardha, Maharashtra

The Diabetes complications and control trial (DCCT) approved HbA1c as the gold standard of glycemic control.The American Diabetes Association (ADA) has indicated HbA1c level of <7% as a goal of optimal blood glucose control.[6] The level of HbA1c value ≤ 7.0% is considered appropriate for reducing the risk of cardiovascular complications.[7,8,9] Estimated risk of CVD has shown to be increased by 18% for each 1% increase in absolute HbA1c value in diabetic.[10] So, HbA1C is an independent risk factor for CHD and stroke.[11]Adult Treatment Panel III has identified the crucial roles of HDL-C and TGs, named this combination an atherogenic dyslipidemia.[12] The atherogenic index of plasma (AIP), defined as logarithm [log] of the ratio of plasma concentration of triglycerides to high-density lipoprotein cholesterol (HDL-C), has recently been considered as a predictive marker for plasma atherogenicity and is positively correlated with CVD risk.[12,13] This study was aimed to find out association between fasting blood glucose (FBG), glycemic

control (HbA1c) and atherogenic index in type 2 diabetic patients.

Objectives

1. To compare fasting plasma glucose, HbA1c and atherogenic index in type 2 diabetic patients.
2. To find out the correlation between fasting plasma glucose and atherogenic index in type 2 diabetic patients.
3. To find out the correlation between HbA1c and atherogenic index in type 2 diabetic patients.

MATERIALS AND METHODS

Study site: Department of Biochemistry of Tertiary care hospital.

Duration of study: 1st July 2015 to 30th Aug 2016.

***Study design*:** This is an observational, cross sectional study. It is a prospective analytical study.

***Selection of study subjects*:**100 diagnosed type 2 diabetes mellitus patients of all age groups and of either sex attending medicine outpatient department (OPD) and/or admitted in ward in the tertiary care hospital and who were willing to participate in the study were selected for the present study. These were divided into two groups depending on their glycated hemoglobin (HbA1c) levels;

Group I: Good Glycemic Control group having HbA1c < 7.0% (n= 50) and
Group II: Poor Glycemic Control group having HbA1c ≥ 7.0% (n= 50).

Inclusion criteria

Diagnosed cases of type 2 diabetes mellitus of all age groups and of either sex.

Exclusion Criteria

Patients with known diagnosis of type 1 DM Hypothyroidism Chronic renal failure, Nephrotic syndrome Familial hypercholesteremic syndromes. Cholestatic jaundice Patients already on lipid lowering drugs.

Hypertensive patients using beta blockers or thiazide Diuretics The study protocol was approved by the Institutional Ethical Committee (IEC). Informed written consent was obtained from all the enrolled study subjects.

Specimen collection

5 ml of fasting blood sample (after at least 10 hours fasting) was withdrawn from the anti-cubital vein of each participant after taking all aseptic precautions using sterile needles and syringes. Hemolysed samples were excluded from the study. The blood was allowed to clot and then centrifuged at 3000 rpm for 15 min at room temperature. History was obtained from each patient followed by physical examination and investigations.

Standard tests were used to analyze various parameters

No.	Parameter	Method
1.	Fasting plasma glucose	GOD / POD (Glucose oxidase peroxidase) method63
2.	HbA1c	Immunoturbidimetric method
3.	Total Cholesterol (TC)	Enzymatic method - Cholesterol esterase, cholesterol oxidase and peroxidase
4.	High-density lipoprotein Cholesterol (HDL-C)	Direct Enzymatic method
5.	Triglycerides (TG)	Enzymatic method- Liquid stable Glycerol phosphate oxidase and peroxidase; End point
6.	Very low-density lipoprotein Cholesterol (VLDL-C) and Low-density lipoprotein Cholesterol (LDL-C)	Indirect method- Friedewald Equation[14] VLDL-C = TG/5 LDL-C = TC - HDL-C – (TG/5).

Atherogenic index was calculated by using formula = log (TG/HDL-C).[15,16]

For serum lipid reference level, National Cholesterol Education Programme (NCEP) Adult Treatment Panel III (ATP III) guideline was referred. According to NCEP-ATP III guideline, hypercholesterolemia is defined as TC levels ≥ 200 mg/dl, high LDL when value ≥ 100 mg/dl, hypertriglyceridemia as TG ≥ 150 mg/dl and low HDL when value < 40 mg/dl. Dyslipidemia was defined by presence of one or more than one abnormal serum lipid concentration.[8]

Statistical Analysis

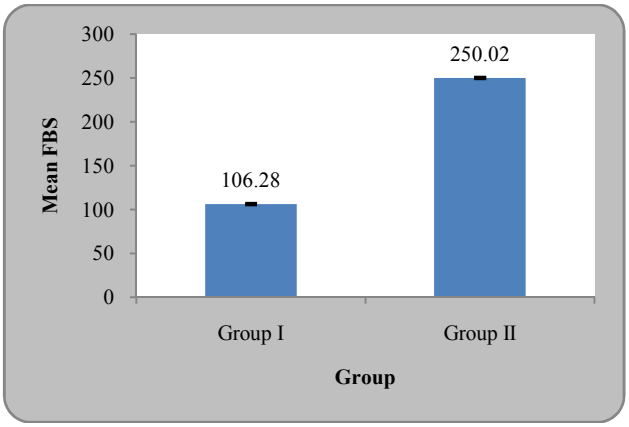
Statistical data was recorded on Microsoft excel programme. All the biochemical parameters were presented as mean ± standard deviation (mean ± SD). Statistical analysis was done by using descriptive and inferential statistics using student's unpaired t test and Pearson's correlation coefficient. The software used in the analysis was SPSS 17.0 version and $p<0.05$ is considered as level of significance.

Observations and Results

Table 1 Comparison of fasting blood sugar in type 2 diabetes mellitus patients having good glycemic control (Group I) and poor glycemic control (Group II)

Group	N	Mean	Std. Deviation	Std. Error Mean	t-value	p-value
Group I	50	106.28	20.13	2.84	13.14	0.0001,S
Group II	50	250.02	74.63	10.55		

S-Significance, $p<0.05$



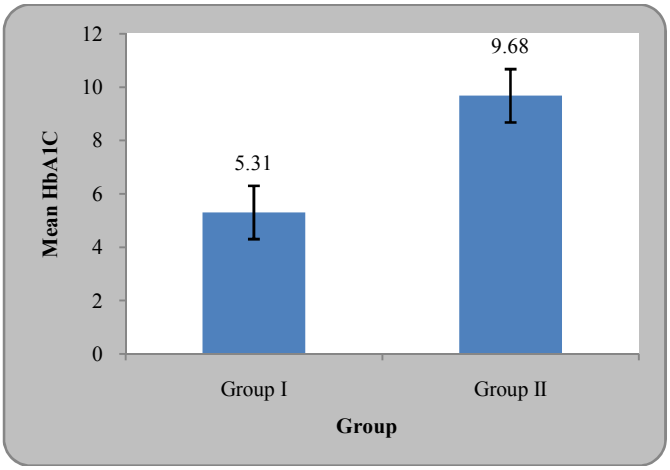
Graph 1 Comparison of fasting blood sugar in both the groups

The mean fasting blood sugar levels in group I and group II patients was found to be 106.28 ± 20.13 and 250.02 ± 74.63 respectively. (Table 1 and graph 1)

Table 2 Comparison of HbA1C in type 2 diabetes mellitus patients having good glycemic control (Group I) and poor glycemic control (Group II).

Group	N	Mean	Std. Deviation	Std. Error Mean	t-value	p-value
Group I	50	5.31	0.79	0.11	14.79	0.0001,S
Group II	50	9.68	1.93	0.27		

S-Significance, p<0.05



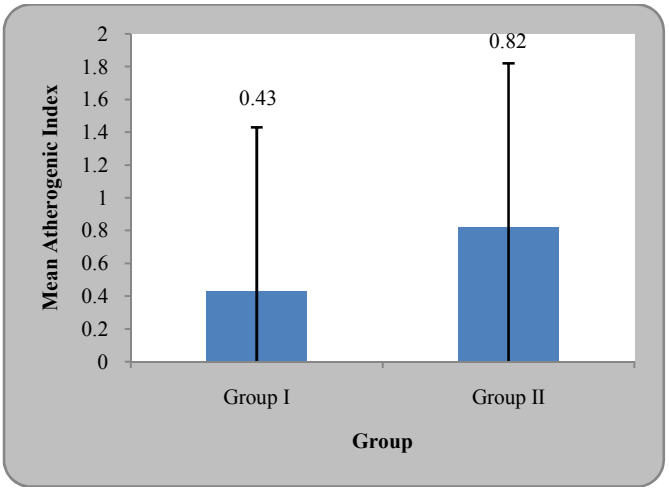
Graph 2 Comparison of HbA1C in both the groups

The mean HbA1c level in group I and group II patients was found to be 5.31 ± 0.79 and 9.68 ± 1.93 respectively. (Table 2 and graph 2)

Table 3 Comparison of Atherogenic Index in type 2 diabetes mellitus patients having good glycemic control (Group I) and poor glycemic control (Group II).

Group	N	Mean	Std. Deviation	Std. Error Mean	t-value	p-value
Group I	50	0.43	0.16	0.02	12.09	0.0001,S
Group II	50	0.82	0.14	0.02		

S-Significance, p<0.05



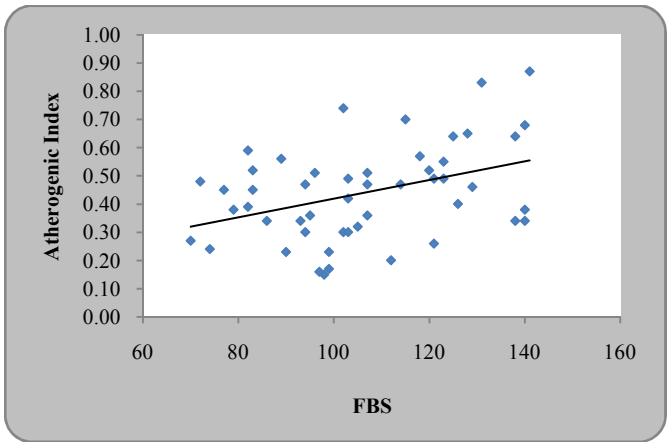
Graph 3 Comparison of Atherogenic Index in both the groups

The mean atherogenic index in group I and group II patients was found to be 0.43 ± 0.16 and 0.82 ± 0.14 respectively. (Table 3 and graph 3)

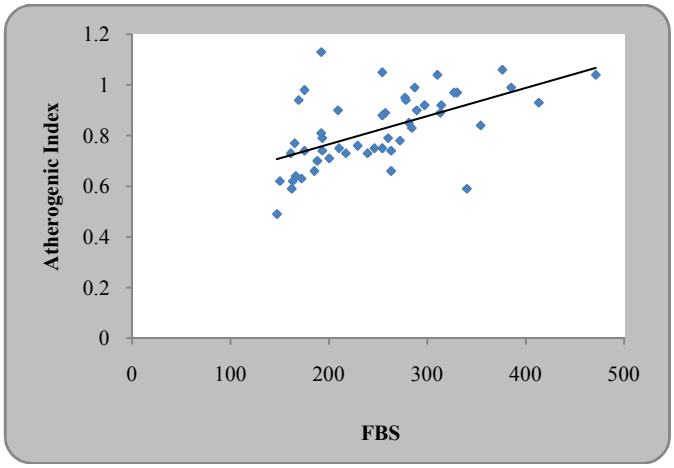
Table 4 Correlation between fasting plasma glucose and atherogenic index in type 2 DM patients having good glycemic control (Group I) and poor glycemic control (Group II)

Group	FBS		Atherogenic Index		Correlation 'r'	p-value
	Mean	SD	Mean	SD		
Group I	106.28	20.13	0.43	0.16	0.393	0.005,S
Group II	250.02	74.63	0.82	0.14	0.568	0.0001,S

S-Significance, p<0.05



Group I



Group II

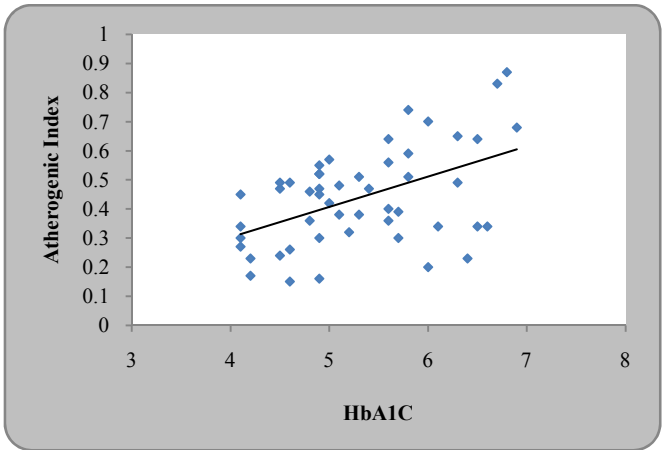
Graph 4 Correlation between fasting plasma glucose and atherogenic index in both the groups

The correlation between fasting plasma glucose and atherogenic index in type 2 diabetes mellitus patients having good glycemic control (Group I) and poor glycemic control (Group II) was found to be 0.393 and 0.568 respectively. (Table 4 and Graph 4)

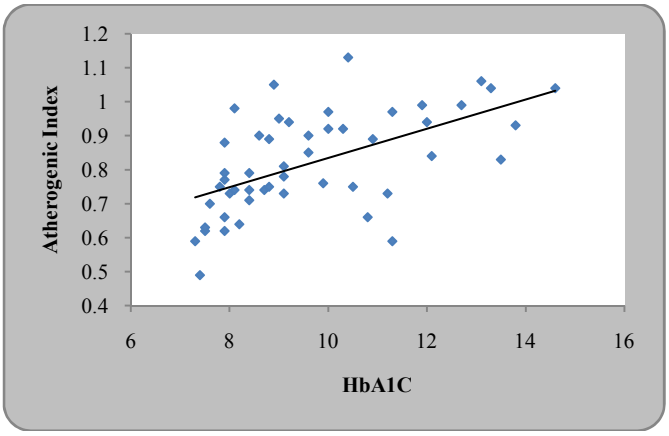
Table 5 Correlation between HbA1C and atherogenic index in type 2 diabetes mellitus patients having good glycemic control (Group I) and poor glycemic control (Group II).

Group	HbA1C		Atherogenic Index		Correlation 'r'	p-value
	Mean	SD	Mean	SD		
Group I	5.31	0.79	0.43	0.16	0.490	0.005,S
Group II	9.68	1.93	0.82	0.14	0.568	0.0001,S

S-Significance, p<0.05



Group I



Group II

Graph 5 Correlation between HbA1C and atherogenic index in both the groups

The correlation between HbA1c and atherogenic index in type 2 diabetes mellitus patients having good glycemic control (Group I) and poor glycemic control (Group II) was found to be 0.490 and 0.568 respectively. (Table 5 and Graph 5)

DISCUSSION

Findings in our study suggested that, in type 2 diabetes mellitus patients; mean fasting blood glucose, mean HbA1c and mean atherogenic index values were significantly higher in those patients having poor glycemic control than in those patients having good glycemic control (p =0.0001), which was in accordance with Dobiasava *et al*.[15]

Another finding suggested that in type 2 diabetes mellitus patients having either poor glycemic control or good glycemic control; atherogenic index is positively correlated with fasting blood glucose and HbA1C.

In our study, type 2 diabetic patients with HbA1c value ≥ 7.0 % (poor glycemic control) showed increased mean values of fasting blood sugar, TC, TG, LDL / HDL-C ratio and atherogenic index. It means in patients with higher HbA1c value the severity of dyslipidemia increases, which was previously shown by Khan *et al*.[16]

Moreover, HbA1c is a user friendly and stable test with very minimal biological variability and which is not affected by factors which otherwise has considerable impact on glucose measurement.[17-19] So, HbA1c is utilized for screening high risk diabetic patients for early diagnosis of dyslipidemia and timely intervention with lipid lowering drugs. Improving glycemic control can reduce the risk of cardiovascular events in diabetes.[20] Khaw *et al* has reported that reducing the HbA1c level by 0.2% could lower the mortality by 10%.[21]

Dobiasova and Frohlich[15] proposed the term Atherogenic Index of Plasma (AIP) and defined as log (TG/HDL-C), with the view that people with high AIP have a higher risk for CAD than those with low AIP. Triglycerides and HDL-C in AIP indicate the balance between the pro-atherogenic and anti-atherogenic lipoproteins. As a marker AIP is significant as it is found increased in patients who were at high risk for CAD. AIP has positively correlation with the fractional esterification rate of HDL-C (FERHDL) and negative correlation with LDL-C particle size.[22] FERHDL reflects particle size in HDL and LDL which shows AIP correlates with the size of pro-atherogenic and protective lipoprotein particles which in turn predicts the risk of CAD.

TG/HDL-C is determined to assess insulin resistance status in type 2 diabetes as it is regarded as reliable as fasting serum insulin levels.[23] Also, insulin resistance is often correlated with raised TG and lowered HDL-C concentrations, which is accompanied by increased CAD risk.

AIP can easily be calculated from lipid profile which makes it an important cardiovascular risk marker which can be a useful measure of response to the treatment. AIP is a sensitive predictor of coronary atherosclerosis and cardiovascular risk[15] and a useful surrogate for insulin resistance.[24]

Significant and positive correlation of atherogenic index with fasting blood glucose and HbA1C shows that atherogenic index can be used to predict glycemic control also. So, AIP which is a very easy to calculate from lipid profile can be used to predict dyslipidemia and glycemic control simultaneously.

CONCLUSION

In type 2 DM patients, positive correlation was found between HbA1c and atherogenic index which indicates that HbA1c, besides its primary role in monitoring glycemic control, can provide information about lipids and atherogenic index. It clearly shows that glycemic control of the patient has got a strong impact on the serum lipid profile levels and atherosclerosis. So, diabetic patients should be educated about regular monitoring of lipid profiles and if found to be abnormal, should control blood glucose and cholesterol very effectively.

Also Atherogenic Index can be effectively used to predict glycemic control as is positively correlated with fasting blood glucose and HbA1C. Thus this study has clearly added value of AIP as a dual biomarker as lipid profile as well as glycemic control. So, AIP, which can be easily calculated from lipid profile, may be utilized for screening diabetic patients to predict both dyslipidemia and glycemic control.

Abbreviations

DM: Diabetes Mellitus
CAD: Coronary artery disease
CHD: Coronary heart disease
FBG: Fasting blood glucose
RBC: Red blood cell
ADA: American Diabetes Association
CVD: Cardio Vascular Diseases
AIP: Atherogenic index of plasma

Log: Logarithm
HDL-C: High-density lipoprotein cholesterol
VLDL-C: Very low-density lipoprotein Cholesterol
LDL-C: Low-density lipoprotein Cholesterol
TC: Total cholesterol
TG: Triglycerides

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How to cite this article:

Ashish Prakash Anjankar *et al* (2018) 'Correlation Between Hba1c and Atherogenic Inde in Type 2 Diabetic Patients', *International Journal of Current Advanced Research,* 07(8), pp. 14789-14793.
DOI: http://dx.doi.org/10.24327/ijcar.2018.14793.2695

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