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Atherogenic Index of Plasma and Insulin Resistance in Obese Diabetic Patients

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Abstract: ***Background: many indicators show that lipid profiles with insulin resistance were associated with cardiovascular disease. The atherogeninc index now regard as a strong index for cardiac risk application. Aim of study: this study was done to approve the importance of glycated hemoglobin (HbA1c) in predicting dyslipidemia and etherogenecity in obese and non-obese in type 2 diabetes. Subjects and methods: The study consistedof (105) subjects, were dividing into three group, the first contain 50 obese DM, second group contain 35 non obese DM, and 30 as healthy control.Fasting plasma glucose, total cholesterol(TC), high-density lipoprotein (HDL) cholesterol, and triglyceride (TG) levels were measured with an enzymatic colorimetric method, insulin and HbA1c were estimated by sandwich ELISA technique, Low-density lipoprotein (LDL), very low-density lipoprotein (VLDL) homeostasis model assessment (HOMA-IR), Atherogenic Plasma index (AIP) and Atherogenic coefficient (AC) were calculated using special formula. Result: the results of the study revealed a significant increase in BMI, wist/hip, FPG, insulin, HOMA, HbA1c, cholesterol, HDL, LDL, VLDL, TG, TC/HDL, LDL/HDL, AIP and AC, AIP has appositive significant correlation with wist/hip, HOMA, TG, and VLDL, while AC has appositive significant correlation with TC, TC/HDL, LDL/HDL and negative significant correlation with TG, and HDL. Also HbA1 show appositive significant correlation with BMI, FPG, LDL/HDL and negative significant correlation with wist/hip, VLDL in non-obese group Also this study show's appositive significant correlation of AC with BMI, TG, VLDL, TC/HDL and negative significant correlation with insulin. HbA1c was revealed appositive significant correlation with Age, FPG, insulin, HOMA, LDL, LDL/HDL, and negative significant correlation with BMI. AIP appeared appositive significant correlation with TG, LDL, VLDL, TC/HDL, and LDL/HDL in obese group Conclusion: these results concluded that hyperglycemia and high level of HbA1c were associated with increased AIP and AC, these factors leads to increased risk of developing CVD.***

Keywords: Diabetes mellitus, Atherogenicindex AIP, Atherogenic coefficient AC, glycated hemoglobin (HbA1c).

1. Introduction

Diabetes mellitus is a cluster of metabolic diseases appeared byhigh glucose level resulting from decrease in insulin secretion, insulin action, or both, the chronic hyperglycemia of diabetes is associated with long-term damage, dysfunction and failure of various organs, especially the, kidneys, eyes, nerves, heart, and blood vessels that impose a tremendous burden on the individual with diabetes and on the health care system [(1)]. It is well approved that diabetes can cause many complications. Acute complications (hypoglycemia, ketoacidosis, or non-ketosis hyperosmolar coma) may occur if the disease is not enough controlled. Serious long-term complications include cardiovascular disease (double risk), neuropathy (of several kinds), and micro vascular harm, which may cause impotence [(2)], [(3)].It could be implicated in the pathogenesis of type 2 diabetes mellitus (DM) in a process called glucotoxicity[(4)]. This type of harm is the result of damage to small vessels, referred to as micro vascular disease[(5)].Diabetes is also an important factor in accelerating the hardening and narrowing of the arteries (atherosclerosis) leading to coronary heart disease, stroke,, and other large blood vessel diseases[(6).]

Diabetes mellitus is a worldwide health problem which lead to markedly increased cardiovascular mortality and indisposition **[(7)].** Lipid irregularities significantly contribute to the increased risk of cardiovascular disease and other morbidity in diabetics**[(8)].**There is a growing of body proof showing that hyperglycemia and dyslipidemia are linked to increased cardiovascular risk**[(9)]** .It has been demonstrated that high levels of serum TC, triglycerides, LDL, VLDL, glycated hemoglobin (HbA1c),, hypertension, micro albuminuria, low concentration of HDL and increased body mass index (BMI) are significantly associated with coronary heart disease **[(10)]**.

Obesity is a metabolic disease that is casually related to serious medical illness, including T2DM **[(11)]**. The relationship of obesity with T2DM has been recognized for several decades, and a close association between obesity and insulin resistance has been observed in all ethnic groups **[(12)].**It is also found across all ages, both sexes and across the full range of body weights **[(13)]**. The WHO has defined obesity in terms of body mass index (BMI)Kg/m^{2}Weight Status

18.5 and below: Underweight
18.5-24.9 Normal or Healthy Weight
25.0–29.9 Overweight
30.0 and above Obese[(14)]

Serum lipid profile investigation usually consists of total cholesterol TC, Triglyceride TG, Low density lipoprotein LDL-c and High density lipoprotein HDL-c measurements. Lipoproteins enable lipids like cholesterol and triglyceride to be transported within the water-based bloodstream [(15).]

Atherogenic lipoprotein profile of plasma is an important risk factor for CVD. It is characterized by high ratio of LDL-c to HDL-c. Atherogenic index of plasma AIP is the marker

of atherogenicity, AIP is the ratio calculated as log TG/HDL-c. Presence of high concentration of triglyceride will increase the activity of hepatic lipase which leads to the increase of degradation of HDL-c (HDL-c catabolism). Each degradation of 1mg HDL-c will accompanied with 2% increase in the risk coronary heart disease CHD [16, 17].

2. Patients and Methods

From each subjects, (5ml) of blood were obtained after overnight fasting by vein puncture collected and divided into two aliquots, (3ml) in evacuated plastic tubes and (2ml) in EDTA tube .

The study was conducted at National diabetes Center (NDC) /AL-Mustansiryia University between (Oct. - Dec.2015). One hundred and fifteen subjects enrolled in this study dividing into three group, the first group contain obese (26 female and 24male) with age range between of(37 and 73 years), the second contain thirty five non obese (15 female and20 male) with age range between of (40-74 years), finally the thirty as healthy control(10 female and 20 male) with age range between of (41-63 years).

Pregnant and women taking contraceptive pills and insulin treatment were excluded from this study. The routine biochemical parameters, total cholesterol(TC), high-density ipoprotein (HDL) cholesterol, and triglyceride (TG) levels were measured with an enzymatic colorimetric method using a (ARCHITECT c4000, ABBOTT, USA), Low-density lipoprotein (LDL), very low-density lipoprotein (VLDL) were calculated by the Friedewald formula[18]

The Atherogenic Index Plasma (AIP) =logTG/HDL. [19]

Atherogenic coefficient (AC) = TC/HDL [20]
TheHbA1c and fasting blood glucose were estimation by VARIANT Hemoglobin A1c program (Bio-Rad, France). Insulin was estimated by sandwich ELISA technique (DGR); insulin resistance was calculated by means of the homeostasis model assessment (HOMA-IR).

HOMA-IR = [fasting insulin µU/mL) fasting glucose (mg/dl)]/405 high index of insulin resistance a value >2.5.[21]

Statistical analysis
Data presented were the means ± and standard deviations; student-t-test was used to compare the significance of the difference in the mean values of any two groups. (P≤0.05), (P≤0.01)were considered statistically significant. The Statistical Analysis System- SAS (2012) was used to effect of different factors in study parameters. Least significant difference –LSD test was used to significant compare between means in this study.

3. Result

Table (1) showed the baseline characteristics of the study group. BMI and wist/hip scientifically higher in obese diabetic patients, as compared with non-obese diabetic and control, also the routine biochemical analysis: fasting plasma glucose, HOMAIR, HbA1c were significantly higher in obese patients as compared to non-obese diabetic controls and control ($p < 0.01$).
Lipids profile measurement show a significant increase in cholesterol, VLDL, LDL, TG and significant decrease in HDL ($p < 0.01$).

Lipid indices such as AIP and AC and TG/HDL and CHO/HDL were scientifically higher ($p < 0.01$) in obese diabetic patients than non-obese diabetic.

Table (2) show's AIP has appositive significant correlation with wist/hip, HOMA, TG, and VLDL, while AC has appositive significant correlation with TC, TC/HDL, LDL/HDL and negative significant correlation with TG, HDL. Also HbA1 show appositive significant correlation with BMI, FPG, LDL/HDL and negative significant correlation with wist/hip, VLDL in non-obese group.

Table (3) illustrated appositive significant correlation of AC with BMI, TG, VLDL, TC/HDL and negative significant correlation with insulin. HbA1c was revealed appositive significant correlation with Age, FPG, insulin, HOMA, LDL, LDL/HDL, and negative significant correlation with BMI. AIP appeared appositive significant correlation with TG, LDL, VLDL, TC/HDL, and LDL/HDL in obese group

Table 1: Comparison of characteristics study participants and biochemical parameters between diabetic patients and control

Parameters	Mean ± SD			LSD value
	Control Arthegenic	Non-obese diabetic	Obese diabetic	
BMI kg/m2	23.47 ± 0.77	27.24 ± 0.28	34.36 ± 0.51	1.539 **
Waist/HIP	0.737 ± 0.01	0.86 ± 4.74	0.968 ± 0.01	2.210 *
FPG mg/dl	89.56 ± 3.50	213.7 ± 16.7	207.6 ± 10.4	34.178 **
Insulin µU/ml	7.38 ± 2.78	11.80 ± 0.83	20.54 ± 2.07	5.878 **
HOMA	1.008 ± 0.11	5.974 ± 0.70	9.32 ± 1.28	2.974 **
HbA1c	5.25 ± 0.19	7.41 ± 0.39	7.61 ± 0.31	0.933 **
Cholesterolmmol/l	3.95 ± 0.12	4.12 ± 0.22	5.24 ± 0.20	0.561 **
Tri. G.mmol/l	1.303 ± 0.12	3.76 ± 0.26	4.09 ± 0.24	0.674 **
HDLmmol/l	1.50 ± 0.05	1.257 ± 0.06	1.198 ± 0.04	0.138 **
LDLmmol/l	2.056 ± 0.08	2.877 ± 0.19	2.770 ± 0.19	0.516 **
VLDL mmol/l	0.483 ± 0.03	0.906 ± 0.14	1.208 ± 0.10	0.315 **
AIP	0.299 ± 0.08	0.514 ± 0.05	0.476 ± 0.03	0.148 **
A.C	2.906 ± 0.27	2.502 ± 0.22	3.470 ± 0.20	0.642 **
TC/HDL	3.92 ± 0.26	3.508 ± 0.22	4.71 ± 0.27	0.761 **
LDL/HDL	2.246 ± 0.23	2.280 ± 0.22	2.431 ± 0.17	0.589 NS
* (P<0.05), ** (P<0.01), NS: Non-significant				

Table 2: Correlation coefficient between AC, HBA1c and AIP with other parameters ((Non Obese group))

Parameters	Correlation coefficient-r		
	AC	HbA1c	AIP
Age	0.08 NS	-0.09 NS	0.06 NS
BMI kg/m2	-0.08 NS	0.26 *	0.12 NS
Waist/HIP	0.11 NS	-0.46 **	0.28 *
FPG mg/dl	-0.07 NS	0.43 **	0.12 NS
Insulin µU/ml	0.08 NS	-0.12 NS	0.11 NS
HOMA	0.11 NS	-0.05 NS	0.26 *
Cholesterolmmol/l	0.40 **	-0.19 NS	0.12 NS
Tri. G.mmol/l	-0.26 *	0.08 NS	0.42 **
HDLmmol/l	-0.59 **	0.05 NS	0.08 NS
LDLmmol/l	-0.02 NS	0.17 NS	0.001 NS
VLDL mmol/l	0.01 NS	-0.51 **	0.72 **
TC/HDL	0.99 **	-0.17 NS	0.11 NS
LDL/HDL	0.41 **	0.26 *	-0.09 NS
* (P<0.05), ** (P<0.01), NS: Non-significant.			

Table 3: Correlation coefficient between AC, HbA1c and AIP with other parameters ((Obese group))

Parameters	Correlation coefficient-r		
	AC	HbA1c	AIP
Age	-0.14 NS	0.30 *	0.11 NS
BMI	0.27 *	-0.36 **	-0.12 NS
Waist/HIP	0.01 NS	0.03 NS	0.14 NS
FPG	-0.13 NS	0.55 **	-0.06 NS
Insulin	-0.28 *	0.57 **	0.06 NS
HOMA	-0.13 NS	0.27 *	-0.04 NS
Cholesterol	0.07 NS	0.04 NS	0.06 NS
Tri. G.	0.34 **	0.05 NS	0.76 **
HDL	0.04 NS	-0.16 NS	-.018 NS
LDL	-0.05 NS	0.26 *	0.28 *
VLDL	0.26 *	-0.04 NS	0.34 **
TC/HDL	0.70 **	-0.08 NS	0.26 *
LDL/HDL	-0.08 NS	0.26 *	0.31 *
* (P<0.05), ** (P<0.01), NS: Non-significant.			

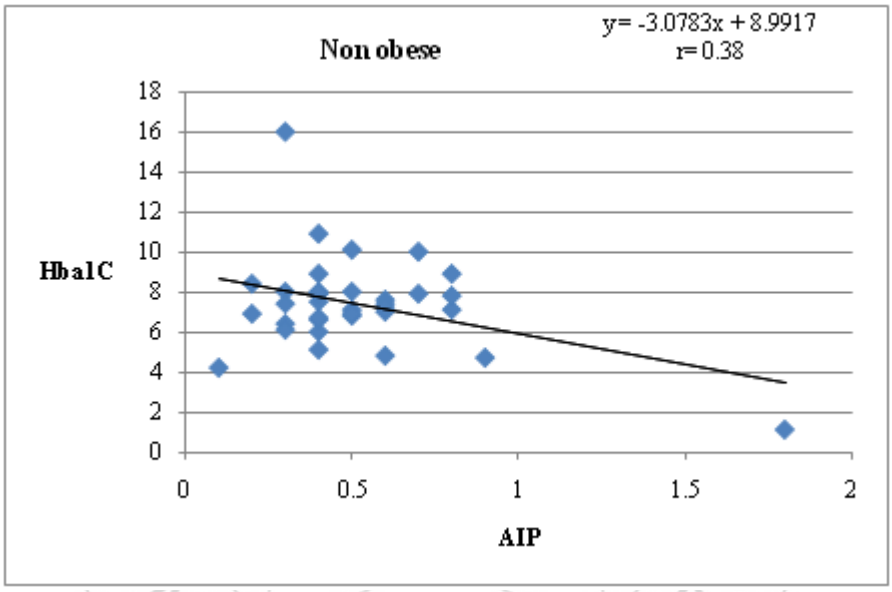

Figure 1: Show the Correlation between HbA1c and AIP in non obese group

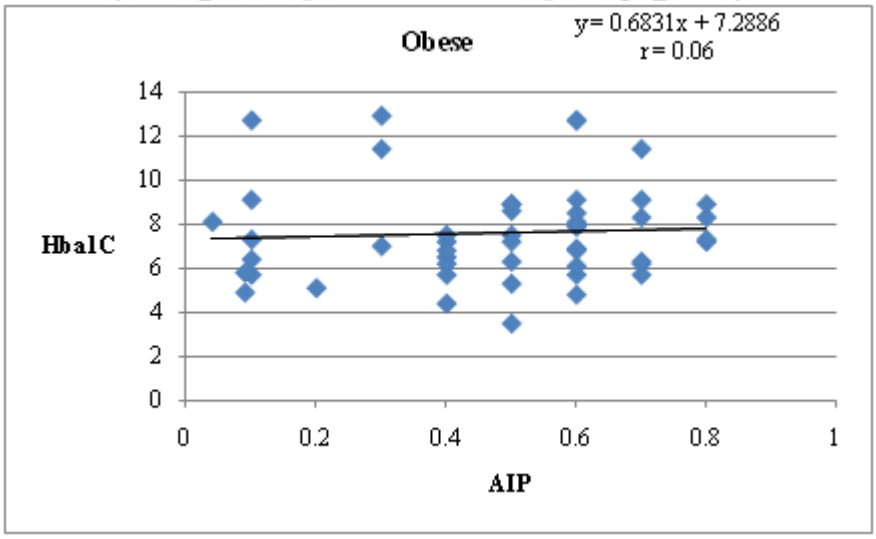

Figure 2: Show the correlation between HbA1c and AIP in obese group

4. Discussion

Obesity in men and women can be causing high AIP, which lead to high blood pressure, diabetes and cardiovascular disease (CVD).The increased risk of CDV has many causes but dyslipidemia plays a major role in it, which commonly associated with an abnormal lipoprotein phenotype characterized by increased TG, decrease HDL-C and an accumulation of small dense LDL-C particles.[22]

A number of other parameters have been succeeding to predicts the risk of coronary artery disease, according to Grover *et. al* either the ratio of LDL-HDL-C/ or TC/HDL-C is the best related predictor of future cardio vascular events.[23]

Later TG/HDL-C was shown to be more accurate predictor of heart disease, the log arithmetically transformed ratio of plasma TG to HDL-C closely correlated with the LDL-C particle size and could serve as an indicator of atherogenic lipoprotein phenotype, high blood pressure, diabetes and vascular events, atherogenic of plasma (log triglyceride /high density lipoprotein-cholesterol).[24]

The value of AIP show a balance between the actual concentration of plasma TG and HDL-C which predetermine the direction of cholesterol transport in the intravascular pool toward atherogenic HDL-C.

In the present study sex, age, BMI, were adjusted, all groups of diabetic patients showed significant dyslipidemia as compared to control and this agree with the result of (Tariq M.2012)

As shown in table (2) direct correlation of HbA1c with FPG, wist /hip, TG, LDL, insulin, LDL/HDL, while inverse correlation was observed between HbA1c and HDL, BMI and AIP. The result show statistically highly significant P value for FPG, insulin, HOMA, HbA1c, TG, HDL, CHO/HDL, cholesterol, VLDL, and non-significant with LDL/HDL-C.

Our result agrees with that obtained by (Chintamani Bodhe *et al*, 2012) and this due to the conditions of sustained, hyperglycemia such as in diabetes mellitus.

Binding of glucose is enzymatic process that occurs continuously during the life of the red blood cell, Made the amount of glycated hemoglobin reflects hemoglobin reflects the glycemic control of a patient during the (6-8) periods before the blood sample was obtained, given the average life span of red blood cells of 120 days. It in turn correlated with fasting blood glucose level.

Hyperglycemia causes increased activity of hepatic lipase that leads to increased clearance of HDL while impaired catabolism of VLDL causes formation of HDL and this explain why HDL decrease in type2diabetes.

Dyslipidemia increase in patients with elevated HbA1c value, diabetic patients with elevated HbA1c and dyslipidemia can be considered as very high risk group for CVD. Triglyceride and HDL cholesterol in AIP reflect the balance between the atherogenic protective lipoproteins.

AIP is an easily available cardiovascular risk marker and useful measure of response to treatment, AIP < 0.11 low risk, AIP< 0.11-0.21 intermediate risk, AIP< 0.2 increased risk [25, 26].

Significant and positive correlation of HbA1cwith AIP indicates HbA1c that can also be used as a potential biomarker for predicting atherogenicty in patients with type 2 diabetes. The correlation of HbA1c with TG/HDL, HOMA, and cholesterol were statistically not significant.

5. Conclusion

Present study showed that hyperglycemia and HbA1c were associated with increased AIP and AC, these factors leads to increased risk of developing CVD.

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