Abstract: Background: many indicators show that lipid profiles with insulin resistance were associated with cardiovascular disease. The atherogenic 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 atherosgenicity in obese and non-obese in type 2 diabetes. Subjects and methods: The study consisted of (105) subjects, were dividing into three group, the first contain 50 obese DM, second group contain 35 non obse 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, waist, FPG, insulin, HOMA, HbA1c, cholesterol, HDL, LDL, VLDL, TC, TCHDL, LDL/HDL, AIP and AC. AIP has appositive significant correlation with wist/hip, HOMA, TG, and VLDL, while AC has negative significant correlation with BMI, FPG, LDL, VLDL and negative significant correlation with wist/hip. Also HbA1c was revealed appositive significant correlation with Age, FPG, insulin, HOMA, LDL, LDL/HDL, and HOMA-IR correlation with BMI. AIP appeared appositive significant correlation with TC, TG, VLDL, TCHDL and negative significant correlation with insulin. HbA1c was revealed appositive significant correlation with Age, FPG, insulin, HOMA, LDL, LDL/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 index AIP, Atherogenic coefficient AC, glycated hemoglobin (HbA1c).

1. Introduction

Diabetes mellitus is a cluster of metabolic diseases appeared by high 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. 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). It could be implicated in the pathogenesis of type 2 diabetes mellitus (DM) in a process called glucotoxicity (3). This type of harm is the result of damage to small vessels, referred to as micro vascular disease. 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. There is a growing of body proof showing that hyperglycemia and dyslipidemia are linked to increased cardiovascular risk (8). 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 (9).

Obesity is a metabolic disease that is casually related to serious medical illness, including T2DM. 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 (10). It is also found across all ages, both sexes and across the full range of body weights (11). The WHO has defined obesity in terms of body mass index (BMI)kg/m²

<table>
<thead>
<tr>
<th>Status</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Underweight</td>
<td>18.5-24.9</td>
</tr>
<tr>
<td>Normal or Healthy Weight</td>
<td>25.0-29.9</td>
</tr>
<tr>
<td>Overweight</td>
<td>30.0 and above</td>
</tr>
</tbody>
</table>

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 (12).

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)
One hundred and fifteen subjects enrolled in this study
divided 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
and 20 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
lipoprotein (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\(^{(20)}\).
The HbA1c 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 ± 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 showed 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

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Mean ± SD</th>
<th>Control</th>
<th>Non-obese diabetic</th>
<th>Obese diabetic</th>
<th>LSD value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI kg/m2</td>
<td>23.47 ± 0.77</td>
<td>27.24 ± 0.28</td>
<td>34.36 ± 0.51</td>
<td>1.539</td>
<td>**</td>
</tr>
<tr>
<td>Waist/HIP</td>
<td>0.737 ± 0.01</td>
<td>0.86 ± 0.47</td>
<td>0.968 ± 0.01</td>
<td>2.210</td>
<td>**</td>
</tr>
<tr>
<td>FPG mg/dl</td>
<td>89.56 ± 3.50</td>
<td>213.7 ± 16.7</td>
<td>207.6 ± 10.4</td>
<td>34.178</td>
<td>**</td>
</tr>
<tr>
<td>Insulin μU/ml</td>
<td>7.38 ± 2.78</td>
<td>11.80 ± 0.83</td>
<td>20.54 ± 2.07</td>
<td>5.878</td>
<td>**</td>
</tr>
<tr>
<td>HOMA</td>
<td>1.008 ± 0.11</td>
<td>5.974 ± 0.70</td>
<td>9.32 ± 1.28</td>
<td>2.974</td>
<td>**</td>
</tr>
<tr>
<td>HbA1c</td>
<td>5.25 ± 0.19</td>
<td>7.41 ± 0.39</td>
<td>7.61 ± 0.31</td>
<td>0.933</td>
<td>**</td>
</tr>
<tr>
<td>Cholesterol mmol/l</td>
<td>3.95 ± 0.12</td>
<td>4.12 ± 0.22</td>
<td>5.24 ± 0.20</td>
<td>0.561</td>
<td>**</td>
</tr>
<tr>
<td>Tri. G mmol/l</td>
<td>1.303 ± 0.12</td>
<td>3.76 ± 0.26</td>
<td>4.09 ± 0.24</td>
<td>0.674</td>
<td>**</td>
</tr>
<tr>
<td>HDL mmol/l</td>
<td>1.50 ± 0.05</td>
<td>1.257 ± 0.06</td>
<td>1.198 ± 0.04</td>
<td>0.138</td>
<td>**</td>
</tr>
<tr>
<td>LDL mmol/l</td>
<td>2.056 ± 0.08</td>
<td>2.877 ± 0.19</td>
<td>2.770 ± 0.19</td>
<td>0.516</td>
<td>**</td>
</tr>
<tr>
<td>VLDL mmol/l</td>
<td>0.483 ± 0.03</td>
<td>0.906 ± 0.14</td>
<td>1.208 ± 0.10</td>
<td>0.315</td>
<td>**</td>
</tr>
<tr>
<td>AIP</td>
<td>0.299 ± 0.08</td>
<td>0.514 ± 0.05</td>
<td>0.476 ± 0.03</td>
<td>0.148</td>
<td>**</td>
</tr>
<tr>
<td>A.C</td>
<td>2.906 ± 0.27</td>
<td>2.502 ± 0.22</td>
<td>3.470 ± 0.20</td>
<td>0.642</td>
<td>**</td>
</tr>
<tr>
<td>TC/HDL</td>
<td>3.92 ± 0.26</td>
<td>3.508 ± 0.22</td>
<td>4.71 ± 0.27</td>
<td>0.761</td>
<td>**</td>
</tr>
<tr>
<td>LDL/HDL</td>
<td>2.246 ± 0.23</td>
<td>2.280 ± 0.22</td>
<td>2.431 ± 0.17</td>
<td>0.589</td>
<td>NS</td>
</tr>
</tbody>
</table>

* (P<0.05), ** (P<0.01), NS: Non-significant
Table 2: Correlation coefficient between AC, HbA1c and AIP with other parameters ((Non Obese group))

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Correlation coefficient-ρ</th>
<th>AC</th>
<th>HbA1c</th>
<th>AIP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.08 NS</td>
<td>-0.09 NS</td>
<td>0.06 NS</td>
<td></td>
</tr>
<tr>
<td>BMI kg/m2</td>
<td>-0.08 NS</td>
<td>0.26 *</td>
<td>0.12 NS</td>
<td></td>
</tr>
<tr>
<td>Waist/HP</td>
<td>0.11 NS</td>
<td>-0.46 **</td>
<td>0.28 *</td>
<td></td>
</tr>
<tr>
<td>FPG mg/dl</td>
<td>-0.07 NS</td>
<td>0.43 **</td>
<td>0.12 NS</td>
<td></td>
</tr>
<tr>
<td>Insulin µU/ml</td>
<td>0.08 NS</td>
<td>-0.12 NS</td>
<td>0.11 NS</td>
<td></td>
</tr>
<tr>
<td>HOMA</td>
<td>0.11 NS</td>
<td>-0.05 NS</td>
<td>0.26 *</td>
<td></td>
</tr>
<tr>
<td>Cholesterol mmol/l</td>
<td>0.40 **</td>
<td>-0.19 NS</td>
<td>0.12 NS</td>
<td></td>
</tr>
<tr>
<td>Tri. G. mmol/l</td>
<td>-0.26 *</td>
<td>0.08 NS</td>
<td>0.42 **</td>
<td></td>
</tr>
<tr>
<td>HDL mmol/l</td>
<td>-0.59 **</td>
<td>0.05 NS</td>
<td>0.08 NS</td>
<td></td>
</tr>
<tr>
<td>VLDL mmol/l</td>
<td>-0.02 NS</td>
<td>0.17 NS</td>
<td>0.001 NS</td>
<td></td>
</tr>
<tr>
<td>TC/HDL</td>
<td>0.01 NS</td>
<td>-0.51 **</td>
<td>0.72 **</td>
<td></td>
</tr>
<tr>
<td>LDL/HDL</td>
<td>0.99 **</td>
<td>-0.17 NS</td>
<td>0.11 NS</td>
<td></td>
</tr>
<tr>
<td>VLDL</td>
<td>0.41 **</td>
<td>0.26 *</td>
<td>-0.09 NS</td>
<td></td>
</tr>
</tbody>
</table>

* (P<0.05), ** (P<0.01), NS: Non-significant.

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

\[ y = -3.0783x + 8.9917 \]
\[ r = 0.38 \]

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

\[ y = 0.8331x + 7.2896 \]
\[ r = 0.96 \]

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

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Correlation coefficient-ρ</th>
<th>AC</th>
<th>HbA1c</th>
<th>AIP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>-0.14 NS</td>
<td>0.30 *</td>
<td>0.11 NS</td>
<td></td>
</tr>
<tr>
<td>BMI</td>
<td>0.27 *</td>
<td>-0.36 **</td>
<td>-0.12 NS</td>
<td></td>
</tr>
<tr>
<td>Waist/HP</td>
<td>0.01 NS</td>
<td>0.03 NS</td>
<td>0.14 NS</td>
<td></td>
</tr>
<tr>
<td>FPG</td>
<td>-0.13 NS</td>
<td>0.55 **</td>
<td>-0.06 NS</td>
<td></td>
</tr>
<tr>
<td>Insulin</td>
<td>-0.28 *</td>
<td>0.57 **</td>
<td>0.06 NS</td>
<td></td>
</tr>
<tr>
<td>HOMA</td>
<td>-0.13 NS</td>
<td>0.27 *</td>
<td>-0.04 NS</td>
<td></td>
</tr>
<tr>
<td>Cholesterol</td>
<td>0.07 NS</td>
<td>0.04 NS</td>
<td>0.06 NS</td>
<td></td>
</tr>
<tr>
<td>Tri. G.</td>
<td>0.34 **</td>
<td>0.05 NS</td>
<td>0.76 **</td>
<td></td>
</tr>
<tr>
<td>HDL</td>
<td>0.04 NS</td>
<td>-0.16 NS</td>
<td>-0.18 NS</td>
<td></td>
</tr>
<tr>
<td>LDL</td>
<td>-0.05 NS</td>
<td>0.26 *</td>
<td>0.28 *</td>
<td></td>
</tr>
<tr>
<td>VLDL</td>
<td>0.26 *</td>
<td>-0.04 NS</td>
<td>0.34 **</td>
<td></td>
</tr>
<tr>
<td>TC/HDL</td>
<td>0.70 **</td>
<td>-0.08 NS</td>
<td>0.26 *</td>
<td></td>
</tr>
<tr>
<td>LDL/HDL</td>
<td>-0.08 NS</td>
<td>0.26 *</td>
<td>0.31 *</td>
<td></td>
</tr>
</tbody>
</table>

* (P<0.05), ** (P<0.01), NS: Non-significant.
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 CVD 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.(23)

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 type 2 diabetes.

Dyslipidemia 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 HbA1c with AIP indicates HbA1c that can also be used as a potential biomarker for predicting atherogenicy 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.

References


[7] Zimet, P. Z. ; Mccarty, D. J. and De Coute, M. P; The global epidemiology of non-insulin dependent diabetes mellitus and the metabolic syndrome; J Diabetes Complications; (1997); (11):60–68.


