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Correlation between Glycated Hemoglobin and Serum Lipids in Type 2 Diabetics in Eastern Libya

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Authors' contributions

This work was carried out in collaboration between all authors. Author JRP designed the study, author SN performed the statistical analysis, authors NMN and KSG wrote the protocol, and wrote the first draft of the manuscript and managed literature searches. Authors LTP, VLK and AA helped in writing and formatting. Authors SS, SJD, SDK, ARS and RNY managed the analyses of the study and literature searches. Author AR helped reviewing process. All authors read and approved the final manuscript.

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ABSTRACT

Introduction: Type 2 diabetes is an increasingly common metabolic disorder characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. Diabetes mellitus is frequently associated with dyslipidemia and an increased percentage of glycated hemoglobin. Patients with type 2 diabetes mellitus are at increased risk for cardiovascular complications.
Objective: To assess the relationship between glycemic control (as reflected by glycated hemoglobin; HbA1c) and serum lipid profile in type 2 diabetic patients.
Materials and Methods: A total of 60 patients were selected from those attending Diabetes Mellitus Clinic, Seventeenth of February Teaching Hospital, Al- Baida as outpatients. The subjects were divided into 3 groups such as group I as the control group, group II as the diabetic group with all related complications excluded and group III as those with type 2 DM with atleast cardiovascular event in the last two years considered as cardiovascular complication of DM. Blood samples were collected from all the subjects and tested for glucose level, glycated hemoglobin, total cholesterol, triglycerides and HDL cholesterol using authenticated reagents kits on an auto analyzer. LDL cholesterol was calculated using Friedwald's formula.
Results: The levels of glycated hemoglobin ($p<0.0001$), fasting glucose level ($p<0.0001$) and triglycerides ($p<0.0001$), were significantly raised and HDL cholesterol ($p<0.0001$) is found to have significantly decreased in diabetic patients with or without cardiovascular complications. In those patients with diabetic complications, total cholesterol and low density lipoprotein cholesterol were significantly raised and high density lipoprotein cholesterol significantly decreased when compared to control subjects.
Conclusion: The findings of the study showed significant positive correlation between glycated hemoglobin with the levels of total cholesterol, triacylglycerol, and low density lipoprotein cholesterol in both control and diabetic groups with or without complications. Glycated hemoglobin level was significant and positively correlated with total cholesterol and triglycerides in type 2 DM.

Keywords: Glycated hemoglobin; type 2 DM; serum lipids.

1. INTRODUCTION

Diabetes mellitus is a metabolic disorder characterized by chronic hyperglycemia with disturbances of carbohydrate, fat and protein metabolism resulting from a defect in insulin secretion, insulin action or both [1,2]. Glycated hemoglobin is an objective measure of glycemic control, which reflects average plasma glucose over the previous eight to twelve weeks. Type 2 DM was previously referred to as non–insulin dependent diabetes or adult-onset diabetes. It consists of an array of dysfunctions characterized by hyperglycemia resulting from the combination of resistance to insulin action, inadequate insulin secretion, and excessive or inappropriate glucagon secretion [3-5]. Dyslipidemia is another more prominent in biochemical finding in type-2 diabetes and in poorly controlled diabetes there is impaired low density lipoprotein (LDL) catabolism which leads to its elevated concentration in blood [6].

Prevalence of diabetes mellitus is a global problem and Libya is no exception to this problem mainly due to the raised incidence of metabolic syndrome, genetic predisposition and dietary habits. Complications of diabetes includes neuropathy, nephropathy, retinopathy and other vascular complications particularly atherosclerosis.

The aim of the current prospective study was to evaluate correlation between glycated hemoglobin and serum lipids in type 2 diabetics in eastern Libya.

2. MATERIALS AND METHODS

In the present study, 60 subjects of either sex in the age group between 30 to 75 years were selected. The details of the age, body weight and body mass index (BMI) were given in Table 1. The study was carried out on outpatients from the department of Diabetes Mellitus Clinic,

Seventeenth of February Teaching Hospital, Al- Baida. This study was approved by ethics committee of Al Mukthar University, Al Baida, Libya in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki. The subjects were grouped based on cardiovascular complications such as coronary heart disease as follows:

Study groups	
Group I	Control group with twenty subjects from similar age group and physical characteristics. . 18 males and 2 females
Group II	Consists of twenty patients with diabetes with no other diabetes associated complications. 11 males and 9 females
Group III	Consists of twenty patients with diabetes with known history of coronary heart disease in the last two years. 11 males and 9 females.

Blood samples from all the subjects were collected and analyzed for Glycated Hemoglobin, Fasting plasma glucose and lipid profile. All laboratory work was carried out at the labs of Biochemistry Department, Omar Al-Mukhtar Faculty of Medicine and Clinical Laboratory at Seventeenth of February Teaching Hospital, Al-Baida. The blood samples were collected into EDTA tubes for determination of HbA1c; in fluoride oxalate tubes for fasting glucose (FG) and serum separator tube for lipid profile measurement.

Table 1. Mean age, body weight and BMI

Groups	**Age**	**Body weight**	**BMI**
Group I	46.05±11.408	65±4.576	21.7±2.5
Group II	57.65±7.915	66±7.765	22.7±2.8
Group III	61.5±6.030	69±6.435	23.8±2.0

Blood glucose was estimated by enzymatic colorimetric method [7]. Glycated hemoglobin was estimated by chromatographic spectrometric Ion exchange method [8]. Cholesterol was measured by enzymatic method [9-12].

LDL cholesterol was calculated using Friedwald's formula (LDL = TC-HDL-TGS/5) [13] Lipid risk ratio was calculated by the ratio between total cholesterol and HDL cholesterol. Correlation test was done by pearson method using microsoft excel sheet.

Statistical analysis was done by using SPSS software and calculated post hoc sample size. We used Mann Whitney U test for calculating p-values. Correlation was done by pearson method in Microsoft excel sheet.

3. RESULTS

The fasting glucose and glycated hemoglobin levels of the study groups are presented in Tables 2 and 3, respectively. The p-value showed a significant difference in fasting plasma glucose ($p<0.001$), and in hemoglobin A1c ($p<0.001$) in control (group I) compared with other two study groups II and III. There was no significant difference ($p>0.05$) between group II and group III.

The results of lipid profile are presented in Table 4. It is revealed that serum total cholesterol, serum LDL-C, serum triacylglycerides and lipid risk ratio were found to be in the higher range in patients with diabetic complication (group III) in comparison to control subjects (group I). Serum total cholesterol, serum LDL, serum triacylglycerides, lipid risk ratio were raised in patients with diabetic (group II) in comparison to control subjects (group I).

The p-value for all the parameters showed that there was significant difference in the serum total cholesterol ($p<0.001$), serum LDL cholesterol ($p<0.05$), serum triacylglyceride levels ($p<0.001$) and serum lipids risk ratio ($p<0.001$) between group I and group III. There was significant difference in the serum LDL cholesterol ($p<0.05$), serum lipids risk ratio ($p<0.001$) between group II and group III. However, there was no significant difference in the serum total cholesterol ($p>0.05$), serum triacylglycerides ($p>0.05$) and serum lipids risk ratio ($p<0.001$) between group (II) and group (III).

There is a positive correlation between Glycated hemoglobin and Total Cholesterol, LDL cholesterol, Triglycerides and negative correlation to HDL cholesterol but not significant may be due to small sample size in each category. The results of correlation between glycated hemoglobin and other lipids were mentioned in Table 5.

4. DISCUSSION

The characteristic features of diabetic dyslipidemia are a high plasma triglyceride

Table 2. Fasting plasma glucose (mg/dl) in control and two other studied groups (Number = 20 each)

Groups	Control (group I)	Group II (group I Vs. Group II)	Group III (group I Vs. Group III)
Range	64 – 110	86 – 224	124 - 377
Mean	90.7	158.95**	191.85**
S.D.	± 13.85	± 39.99	± 56.053

*** p<0.001*

Table 3. HbA1c% in control and two other study groups

Groups	Control (group I)	Group II (group I Vs. Group II)	Group III (group I Vs. Group III)
Range	4.2 – 6.0%	6.3 – 15.8%	6.6 – 13%
Mean	5.64	9.23**	8.86**
S.D.	± 1.66	± 2.265	± 1.62

*** p<0.001*

Table 4. Serum cholesterol, triglycerides, LDL cholesterol, and HDL cholesterol levels in control and two other studied groups

Parameters	Control (group I)	Group II (group I vs. group II)	Group III (group I vs. group III)
	mean±S.D	mean±S.D	mean±S.D
Total cholesterol(mg/dL)	124.65±29.16	150.20±52.62**	171.2±47.246**
LDL cholesterol(mg/dL)	54.82±28.80	107.97±46.17*	109.55±46.40*
Triglycerides (mg/dL)	136.40±39.83	163.60±82.25**	162.70±59.54**
HDL cholesterol (mg/dL)	46.15±18.58	35.65±8.66*	28.10±5.37**
Lipids risk ratio	2.70±1.611	4.5±2.275**	6.255±2.072**

** P<0/05 ** p< 0.001*

Table 5. Correlation between glycated haemoglobin and lipid parameters and glucose

Groups		TG	HDL	LDL	TC	Glucose
Group I	r	0.20908	0.360826	0.133325	0.07368	0.152485
	p value	0.3765	0.1124	0.5760	0.7521	0.5220
Group II	r	-0.11597	-0.16323	0.2865	0.2284	0.337888
	p value	0.6265	0-4920	0.2207	0.3333	0.1452
Group III	r	0.031536	-0.3585	0.2468	0.275519	0.415772
	p value	0.8952	0.1206	0.2941	0.2390	0.0680

concentration, low HDL cholesterol concentration and increased concentration of LDL-cholesterol. The lipid changes associated with diabetes mellitus are attributed to increased free fatty acid flux secondary to insulin resistance [14].

The relationship between the typical lipid profile exhibited by patients with type 2 diabetes and risk of cardiovascular disease are also proved [15]. Hemoglobin A1c provides a tool for blood sugar monitoring in persons with diabetes; chronic hyperglycemia is related to the development of micro vascular disease, and also represents correlation between glycated hemoglobin and serum lipids in diabetic patients.[16]

In the present study, the pattern of lipid profile in type 2 diabetic patients and its correlation with HbA1c is studied. Earlier studies have shown that high level of cholesterol, triglyceride, LDL and low HDL in type 2 diabetics are well known risk factors for cardiovascular disease. Insulin resistance and hyperglycemia promote atherosclerosis at the arterial wall with the help of macrophages and endothelial cells results in plaque formation. At the same time hyperglycemia acts synergistically with other

cardio vascular risk factors [17]. The cause of dyslipidemia in type 2 diabetes mellitus may be due to the resistance of the insulin action which in turn influences the liver apo-lipoprotein production. The direct correlation between FBS and HbA1c with total cholesterol (TC), triglycerides (TG) and LDL and inverse correlation with HDL are also well postulated [18].

Inflammatory markers such as IL-1, IL-6, IL-15, and TNF- α were found to be low in type 2 diabetes patients, but the levels of IL-10, IFN- ɣ, and caspase-1 were high, compared to normal controls. Type 2 diabetes patients with hypertension show significantly decreased levels of IL-1 and caspase-1 compared to patients without hypertension [19].

There is risk of colorectal cancer is more in diabetes because of their sharing environmental factors such as obesity, sedentary life style and high fat diet. Excess insulin levels were shown in animals to stimulate IGF-1 which is also a risk factor for colorectal cancer [20].

In the current study, the levels of glycated hemoglobin in diabetic groups (II and III) were found to be highly significant in comparison to control group. The study also revealed that there is an increase in the cholesterol levels in group III diabetic patients with cardiovascular complications when compared to the control group. Such significance was not found between the control group and the uncomplicated diabetic group II. Group III showed significant increase in LDL-cholesterol in comparison to the control group (group I) and uncomplicated diabetic group (group II).

The HDL-cholesterol values were significantly lower in both uncomplicated and complicated groups (II and III) when compared to the control group. There was also significant decrease in HDL-cholesterol in complicated group when compared to uncomplicated diabetic group. Lipoprotein lipase is the key enzyme in the metabolism of triglyceride rich lipoproteins. LPL in the pre heparin serum mass reflects the insulin sensitivity of diabetic patients receiving neither insulin nor hypoglycemic agents. [21], low pre heparin LPL mass may be deeply involved in the progression of coronary atherosclerosis [22]. Significant high concentration of triglycerides was found in uncomplicated and complicated groups (II and III). There was significant rise in all the lipid profiles in diabetic patients with cardiovascular complication as compared to the controls and also diabetics with no recognized complications. Thus, this study suggests association of serum lipids and glycated hemoglobin with complications in type 2 diabetes. In another study, significant correlations between HbA1c with TC, LDL and LDL/HDL ratio were observed [23]. In a study, HbA1c demonstrated significant positive relationship with TC, TG, HDL and LDL [24]. A significantly higher cardiovascular disease (CVD) in persons with high levels of HbA1c is also reported [25]. HbA1c can predict serum lipid levels in both male and female diabetic patients and is a marker routinely used for long-term glycemic control and they observed a direct and significant correlation between HbA1c with TC, TG and LDL, and reverse correlation with HDL [26,27].

5. CONCLUSION

Type 2 diabetes mellitus continues to be a serious health concern in the growing world. Cardiovascular events in type 2 diabetes mellitus patients is an important complication that requires immediate attention. Studies have shown that an increase in glycated hemoglobin and abnormal lipid profile is prevalent in diabetic patients. The current study concluded that there is a definite positive correlation of glycated hemoglobin with the levels of total cholesterol, triglyceride, and low density lipoprotein cholesterol. This strongly suggests dyslipidemia in diabetic patients when not under optimal control.

CONSENT

Not applicable since this is an observational study.

DISCLAIMER

This manuscript was presented in the conference "American Association of Clinical Chemistry, Annual Meeting 2014 and Clinical Lab Expo, at Chicago, USA" available link is "http://www.researchgate.net/publication/262840903_CORRELATION_BETWEEN_GLYCATED_HEMOGLOBIN_AND_SERUM_LIPIDS_IN_TYPE_2_DIABETICS_IN_EASTERN_LIBYA".

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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