



IMPACT OF DURATION OF DIABETES AND AGE ON LIPID PROFILE AND GLYCEMIC CONTROL IN TYPE 2 DIABETICS

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ABSTRACT

Diabetes mellitus (DM) prevalence is increasing in Arabian Gulf countries and Saudi Arabia is ranked as the 7th country worldwide estimated to have the highest number of people with diabetes in 2000 and 2030. In type 2 diabetes mellitus (T2 DM) lipid abnormalities are almost the rule. Abnormal lipid levels contribute to cardiovascular disease (CVD) risk and are of serious concern and can be influenced by age and duration of ailment. This study was conducted on 125 male T2 DM patients attending King Abdulaziz University health clinic, Jeddah (Saudi Arabia). The age limits was 40 to 65 years. Patients were categorized into three group according to duration of illness, Group 1 (5 year), Group 2(6 to 10 year), Group 3(10 year). Subjects were also categorized into 3 group according to age, Group 1 (40 to 45 year), Group 2 (46 to 50 year), Group 3 (50 year). Fasting venous blood samples were analyzed for serum HbA1c, TC, TG, HDL-c, LDL-c and VLDL-c. The results of this study show that duration of type 2 diabetes mellitus have significant effect on TC, TG, LDL, HDL, VLDL and HbA1c. Increasing duration of diabetes is associated with higher incidence of dyslipidemia. There was sharp and definite increase in the percentage of patients having 200mg/dl total cholesterol after five years of diabetes mellitus from 25.5% to 32.1% and then to 52% after 10 years of duration. The percentage of patients having 150mg/dl of low density lipoproteins (LDL) after 10 years of diabetes mellitus was much high (68%) as compared to group 1 (21.3%) and group 2 (47.2%). There was also an increase in the percentage of patients having 160mg/dl of triglycerides after five years of diabetes mellitus from 21.3% to 47.2% of diabetes and then to 56% after 10 years. The results also revealed that age group of subject have significant effect on the HbA1c but no significant effect on lipid profile. The chronicity of T2 DM can disturb the normal levels of HbA1c and lipid profile which can lead to dyslipidemia. The advanced dyslipidemia can progress the atherosclerosis and ultimately cardiovascular disease (CVD), commonest cause of death in type 2 diabetics. Therefore there is an urgent need for screening and therapeutic intervention for dyslipidemia in the diabetics which may help to decrease the morbidity and mortality from CAD.

KEYWORDS: Type 2 diabetes mellitus, diabetic duration, dyslipidemia, glycemic control.

INTRODUCTION

Diabetes mellitus (DM) is an iceberg disease. The metabolic dysregulation associated with DM causes secondary pathological changes in multiple organ systems that impose a tremendous burden on the individual with diabetes and on health care system. Saudi Arabia ranks seventh worldwide and the first in the Gulf in terms of diabetes rates ^[1]. Over 25% of the adult population is suffering from DM and that figure is expected to be more than double by 2030 ^[2]. Half of the people over 30 years of age are prone to diabetes. Compared with individuals without diabetes, patients with type 2 diabetes mellitus (T2 DM) have a considerably higher risk of cardiovascular morbidity and mortality, and are disproportionately affected by cardiovascular disease. Most of this excess risk is associated with an augmented prevalence of well-known risk factors such as hypertension, dyslipidemia and obesity in these patients. In T2 DM lipid abnormalities are almost the rule ^[3,4]. 70% to 97% of adults with T2 DM have one or more lipid abnormalities ^[5,6]. The pattern of lipid profile in T2 DM is called diabetic dyslipidemia or atherogenic dyslipidemia. The term diabetic dyslipidemia comprises a triad of raised triglycerides (TG), reduced HDL-C and excess of small, dense LDL particles ^[7]. Besides, abnormality in the level of each of the major lipids has

been independently related with increased risk of cardiovascular disease (CVD) ^[8].

The previous study has been documented that, for every 1% reduction in low-density lipoprotein cholesterol (LDL-C) levels there is an equivalent reduction in cardiovascular events ^[9]. It is well documented that a high HDL-C level is cardioprotective ^[10] and low HDL-C levels are widespread in type 2 diabetes patients, and this appears to be associated to the increased mortality and morbidity in coronary heart disease (CHD) ^[11]. Additionally, low HDL-C levels are commonly escorted by elevated TG levels ^[12], and the combination appears to be the most severe combination for hastening vascular damage. The main step in the direction of reducing the risk of CVD related with diabetes is detection and treatment of dyslipidemia ^[13]. According to the American Diabetes Association (ADA), LDL-C lowering is the first priority, lowering triglyceride level is the second priority and raising levels of HDL-C is the third priority ^[14]. It is well known that diabetic dyslipidemia patients have an excess risk of cardiovascular morbidity and mortality because the lipid particles in these patients are more atherogenic than in general population ^[15]. Atherosclerosis accounts for up to 80% of deaths in diabetic patients due to coronary heart disease (CHD) and cerebrovascular or peripheral vascular

disease. Again, the lipid abnormality associated with type 2 diabetes increases with increase in duration of diabetes [16-21]. The ministry of Health in Saudi Arabia has warned that there is a rising incidence of heart disease in the country and urged residents and citizens to protect themselves with proper diet and exercise. Although there is considerable evidence that abnormalities in serum lipids and lipid metabolism are important risk factors for this increased incidence of CAD in type 2 diabetes, controversy exists regarding the association of dyslipidemia with the gender, age and duration of diabetes and reports of prevalence and distribution of dyslipidemia are varied. For that reason, there is an urgent need for screening and management of dyslipidemia in diabetics in order to reduce morbidity and mortality from coronary artery disease (CAD) [17]. This study was conducted to know the impact of duration of illness and age on the lipid profile and glycemic control in type 2 diabetic patients.

MATERIALS & METHODS

This study was conducted on 125 type 2 diabetic patients attending King Abdulaziz University health clinic, Jeddah (Saudi Arabia). All our subjects were males of 40 to 65 years age groups. They were all non-smokers, normotensives, with moderate built and moderate active life style. Subjects with history of alcoholism, familial dyslipidemia, any cardiovascular, renal or thyroid disorders, those on lipid lowering drugs, and beta blockers were excluded from the study. Informed consent was sought and obtained from individuals before enrolment into the study. The study protocol was approved by institutional ethical committee. After eliciting history, detailed physical and systemic examination anthropometric measurements were done. Venous blood samples were collected from each patients after at least 10 hours fasting into centrifuge tubes. The blood sample was allowed to clot and then centrifuged at 3000 rpm for 15 minutes at room temperature. The sera were analyzed for glycated hemoglobin (HbA1c), fasting serum glucose (FSG), total cholesterol (TC), triglycerides (TG), and high density lipoprotein cholesterol (HDL-c) using an

autoanalyzer (Roche Modular P-800, Germany). Serum low density lipoprotein cholesterol (LDL-c) was calculated by Friedewald's formula $[TC - (HDL-c + TG/5)]$. The VLDL cholesterol concentration was calculated from the values of TG by Friedewald's formula [22]. Participants of the study were divided into 3 groups according to the duration of detection of diabetes mellitus. In the first group (Group 1) patients with history of type 2 diabetes mellitus below 5 years were included; second group (Group 2) included 6 to 10 years and third group (Group 3) included above 10 years duration of type 2 diabetes mellitus. Subjects were also categorized into 3 groups according to age, group 1 (40 to 45 year), Group 2 (46 to 50 year), Group 3 (50 year). Value of HbA1c was given as percentage of total hemoglobin and values of all other parameters were given in mg/dl. All the results were expressed as mean \pm SD. Student's t-test was applied for comparison of data and $p < 0.05$ considered as the level of significance.

RESULTS

Subjects were categorized into 3 groups according to duration, Group 1 (< 5 year), Group 2 (6 to 10 year), Group 3 (\geq 10 year), lipid profile and Glycemic control were compared in this group. Subjects were also categorized into 3 groups according to age, Group 1 (40 to 45 year), Group 2 (46 to 50 year), Group 3 (\geq 50 year), lipid profile and glycemic control were compared in this group. Table 1 shows the lipid profile of different groups according to duration of illness. The chronicity of type 2 diabetes mellitus can disturb the normal levels of lipid profile which can lead to dyslipidemia.

Table 2 shows the results of HbA1c and lipid profile of diabetics on the basis of duration of type 2 diabetes while Table 3 shows the results of HbA1c and lipid profile of diabetics on the basis of age of diabetic patients. Table 2 shows that duration of diabetics have significant effect on TC, TG, LDL, HDL, VLDL and HbA1c. Table 3 shows that age group of subjects have significant effect on the HbA1c but no significant effect on lipid profile.

TABLE 1: Duration of type 2 diabetes mellitus and lipid profile of different groups

Group	Group 1, (below 5 years)		Group 2, (6 to 10 years)		Group 3,(above 10 years)	
<u>TC (mg/dl)</u>						
150	13(27.7%)	143±48.18	14(26.4%)	145±51.60	4(16%)	148±50.51
150 – 200	22(46.8%)	186±52.72	22(41.5%)	195±59.90	8(32%)	198±60.22
200	12(25.5%)	207±67.41	17(32.1%)	226±65.08	13(52%)	262±58.26
<u>HDL (mg/dl)</u>						
40	11(23.4%)	38±3.51	19(35.8%)	36±3.81	16(64%)	32±2.70
40	36(76.6%)	42±5.01	34(64.2%)	41±4.29	9(36%)	40±4.10
<u>LDL (mg/dl)</u>						
150	37(78.7%)	104±18.51	28(52.8%)	127±39.82	8(32%)	143±43.34
150	10(21.3)	154±27.8	25(47.2%)	157±47.82	17(68%)	168±48.01
<u>TG (mg/dl)</u>						
40 – 160	37(78.7%)	153±61.25	28(52.85)	166±65.28	11(44%)	198±75.23
160	10(21.3%)	176±68.27	25(47.2%)	189±70.50	14(56%)	221±74.53

Among 125 patients with diabetes below 5 years of onset, 13 (27.7%) had total cholesterol levels 150 mg/dl while 22 (46.8%) had total cholesterol levels 150 -200 mg/dl and 12 (25.5%) had 200 mg/dl. Among those with diabetes

for 6 -10 years, 14 (26.4%) had total cholesterol 150 mg/dl while 22(41.5%) had 150 -200 mg/dl and 17 (32.1%) had levels 200 mg/dl. Among those with diabetes for above 10 years, 4 (16%) had total cholesterol

levels 150 mg/dl while 8 (32%) had 150-200 mg/dl and 13 (52%) had 200mg/dl. Among 125 patients with diabetes below 5 years of onset, 11(23.4%) had HDL cholesterol levels 40 mg/dl while 36(76.6%) had 40 mg/dl. Among those with diabetes for 6-10 years, 19(35.8%) had HDL cholesterol 40 mg/dl while 34(64.2%) had 40 mg/dl. Among those with diabetes for above 10 years, 16(64.0%) had HDL cholesterol 40 mg/dl while 9(36.0%) had 40mg/dl. Among 125 patients with diabetes below 5 years of onset, 37(78.8%) had LDL cholesterol levels 150 mg/dl while 10(21.3%) had 150 mg/dl. Among those with diabetes for

6-10 years, 28(52.8%) had LDL cholesterol level 150 mg/dl and 25 (47.2%) had LDL cholesterol 150 mg/dl. Among those with diabetes for above 10 years, 8(32.0%) had LDL cholesterol 150 mg/dl while 17(68.0%) had LDL cholesterol levels 150 mg/dl.

Among 125 patients with diabetes below 5 years of onset, 37(78.7%) had triglycerides levels from 40-160 mg/dl while 10(21.3%) had 160 mg/dl. Among those with diabetes 6-10 years, 28(52.8%) had TG level from 40-160 mg/dl while 25(47.2%) had 160 mg/dl. Among those with diabetes for above 10 years, 11(44%) had TG from 40-160 mg/dl while 14(56%) had 160 mg/dl.

TABLE 2: HbA1c and lipid profile of diabetics on the basis of duration of diabetes

Investigation	Duration			p-value
	5 year	6 to 10 year	10 year	
HbA1c%	6.76 ± 1.01	8.41 ± 1.15	9.22 ± 1.20	0.000
TC (mg/dl)	186.91± 57.94	208.90± 65.98	231.93± 66.80	0.024
TG (mg/dl)	178.98± 80.01	200.96± 76.60	235.81± 91.38	0.027
LDL (mg/dl)	109.76±29.18	125.99±40.75	146.81±47.25	0.007
HDL (mg/dl)	42.72±5.92	41.37±4.80	38.45±4.86	0.006
VLDL (mg/dl)	35.79±16.01	40.19±15.22	47.16±18.17	0.026

TABLE 3: HbA1c and lipid profile diabetic patients on the basis of Age

Investigation	Age Group			p-value
	40 – 45 year	46 – 50 year	50 year	
HbA1c%	7.76 ± 1.03	7.45 ± 1.29	8.20 ± 1.29	0.024
TC (mg/dl)	182.01 ± 38.42	181.10 ± 51.21	215.08 ± 69.12	0.016
HDL (mg/dl)	39.52 ± 2.67	40.48 ± 3.16	38.39 ± 2.96	0.014
LDL (mg/dl)	109.28 ±32.31	119.54 ±41.79	129.09 ± 52.21	0.141
TG (mg/dl)	171.83 ± 90.99	169.86 ± 70.98	212.72 ± 86.92	0.078

DISCUSSION

Diabetes is metabolically heterogeneous and dyslipidemia is commonly seen in diabetic patients. Lipid abnormalities in patients with diabetes play an important role in the development of atherogenesis. Type 2 diabetic patients have several lipid abnormalities including elevated plasma triglycerides, elevated oxidized LDL and decreased HDL cholesterol. Oxidized LDL is taken up by non-specific endocytosis further leading to atherosclerosis [23]. Diabetes in adults is associated with a high risk of vascular disease, two to six times greater in people with type 2 diabetes than those without diabetes and is the leading cause of morbidity and mortality in type 2 diabetes. The life expectancy of people with diabetes is reduced by nearly eight years due to increased mortality. More recent data have confirmed the significant correlation between coronary artery disease (CAD) mortality and increasing plasma triglyceride concentration. Hypertriglyceridemia can lead to the development of atherosclerosis by a number of mechanisms. One of these involving a change in HDL metabolism [24]. Framingham study [25] reported that persons with LDL-c : HDL-c ratio greater than 5 are at high risk of developing coronary heart disease (CHD) and ratio between 2-5 are at intermediate risk of developing CHD. So, in comparison with Framingham study, Group 3 cases who were having T2 DM for more than 10 years are at intermediate to high risk of developing CHD than in Group 2 cases who were having DM for less than 10 years. From our results, it is obvious that the lipid

profile becomes more abnormal with increase in duration of DM. The distribution of all the types of lipid abnormalities increased with an increase in the duration of diabetes in our study was also observed by other studies [3,7,16,19,20,21,26]. Talat N., et al [26] found that duration of diabetes was associated with higher incidence of dyslipidemia. They found elevated TC, LDL and TG but normal HDL. Sultana, R [16] also found similar impact of duration of type 2 DM on lipid profile. There was a sharp and definite increase in the percentage of patients having 200mg/dl total cholesterol after 4 years of diabetes mellitus from (28-34%) to 41%. There was a sharp increase in the percentage of patients having 150mg/dl of low density lipoproteins after 6 years of diabetes mellitus from (8-9%) to 14.2%. There was also an increase in the percentage of patients having 160mg/dl of triglycerides after 4 years of diabetes mellitus from 53% to 61% of diabetes. In an analysis of diabetes duration and risk of major cardiovascular disease events and total mortality by Wannamethee et al [27], only those with diabetes for more than 8 years had an increased risk of cardiovascular disease death compared with those who had diabetes for less than 2 years. CAD risk in patients with diabetes escalates significantly with disease duration and approaches CAD risk equivalence only when disease duration is beyond 8 years. In Canadian patients with type 2 diabetes a Chart audit study revealed that 55% of patients with a diagnosis of 2 years had dyslipidemia. This population rose to 16% in patients with diabetes for 15

years^[28]. The United Kingdom Prospective Study (UKPDS) calculated risk score for CVD, which indicates both the duration and the degree of glycemic control^[29]. The results of present study revealed that age group of subject did not have significant effect on the lipid profile. The distribution of the all types of lipid abnormalities by age showed no particular pattern of predominance. Our study is consistent with the results obtained by different investigators^[20,21,30]. H.O. Otamere^[30] studied on 100 type 2 diabetics and divide age groups comprises of young adult 40 years, middle aged 40-60 years, and elderly, 65 years and duration comprises of 10 years, 10-20 years and 20 years. It was observed that the age group of subject did not have significant effect on the lipid profile. It was also observed that the duration of diabetics did not have any significant effect on lipid profile. Ochei and Kolhatkar^[31] observed that neither the age of the subjects nor the duration of the diabetes significantly affected the level of lipids. Age has also been said to contribute to elevated lipid parameters^[32] but Nakhjavani et al.^[33] reported that there is no correlation between diabetes mellitus and the alteration in the pattern of lipid profile. It is equally important to note that the diabetic subjects were on medications (oral hypoglycemics). Such treatment reduces the blood glucose level and most probably alters the overall pathophysiology, including the lipidemia of the condition. Ali et al.^[34] reported that dyslipidemia in both genders increases with age. On the other hand, Nadeem et al.^[35] reported that no significant correlation existed between age and dyslipidemia. The present study revealed that both duration of diabetics and age group of subject had significant effect on the HbA1c. In literature, there are some contradictory findings regarding the relationship between HbA1c with duration of illness and age group of the patients. The results of different authors^[36-39] revealed that the age of diabetic patients did not show any significant correlation with HbA1c while a close relation between HbA1c and age was observed in diabetic patients by other investigators^[20,40,41]. The results obtained by different authors^[20, 42] indicated that the HbA1c levels showed a significant increase with the duration of diabetes while no correlation was observed between duration and HbA1c by other authors^[17,43]. It was seen by Siddiqui et al.^[44] that there is a gradual rise in HbA1c in relation to duration of diabetes but Pearson correlation gives no significant result in relation to duration of diabetes. Studies conducted by other authors^[45,46] in diabetic patients have shown a significant positive correlation between HbA1c and age as well as duration of diabetes. In contrast Kabadi et al.^[47] found no significant relation between age, duration of diabetes and fasting blood glucose (FBG) & glycated hemoglobin (HbA1c). Our previous results^[48] revealed that TC and LDL correlate positively with FBS and HbA1c, suggesting that poor glycemic control showed to be directly associated with hypercholesterolemia and elevated LDL level. Therefore good glycemic control can prevent progression of lipid abnormalities in diabetic patients. Our results have shown that the majority of the T2 DM patients (70%) did not sustain a good glycemic control; where the mean level of HbA1c was 8.01% . These findings are consistent with previous studies^[49,50]. This result suggests that more

attention be paid by healthcare providers in following the optimal guidelines to achieve the desired glycemic control. Also there is critical need to ensure patients compliance to medication and healthy lifestyle to avoid poor glycemic control. Consequently, identification and treatment of dyslipidemia together with tight glycemic control should be maintained in order to minimize the CVD risk among T2 DM patients. The lipid profile analysis must be made an integral part of Type 2 DM patients' clinical reviews and treatment. Type 2 DM and other diabetics must be educated on the risks they face as a result of their condition and the necessary steps they need to manage it.

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