Obesity and lipid profile in type 2 diabetics

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Abstract:

This case-control study includes 356 diabetics and 384 apparently healthy age and sex matched controls who attended Al-Zahrawi Private Hospital Outpatient Department in Mosul during the period from January to December 2004.The aim of the study was to assess the changes in serum lipid profile among type 2 diabetics in relation to body mass index (BMI) and to determine the magnitude and pattern of dyslipidaemia in obese diabetics. Fasting plasma glucose and serum lipid profile were compared in type 2 diabetics and control subjects according to BMI. The collected data were analyzed by chi-square, Z, ANOVA and Duncan tests. Fasting plasma glucose levels were highest in obese diabetics and the frequency of poorly controlled diabetics was increased with increasing BMI. There was a significant and positive association between the BMI and serum triglyceride (TG) (p 0.01), total cholesterol (TC) (p 0.001), LDL-C (P<0.001) and VLDL-C (P<0.01). Serum HDL-C levels were significantly decreased (P<0.01) by increasing BMI. The prevalence of dyslipidaemia was increased with increasing BMI levels in both genders. In conclusion several lipid abnormalities in type 2 diabetics have pointed to the significance of diabetic control, regular lipid profile and control of obesity.

Key Words: Obesity, lipid profile, type 2 diabetes, body mass index, dyslipidaemia .

Introduction:

Obesity is an excessive accumulation of body fat and in its gross manifestation possesses a real threat to health [(1)]. It is well established that obesity is directly or indirectly associated with type 2 diabetes mellitus [(2)]. Furthermore, alterations in body fat distribution are associated with changes in lipids and lipoproteins and with increased coronary heart disease (CHD)[(3)]. Moreover, obesity is considered as part of the metabolic syndrome in the pathogenesis of type 2 diabetes[(3)].

Different methods are used for the measurement of obesity including the determination of (a) body mass index[(4)],(b) skin fold thickness or waist hip ratio[(5)] ,(c) fat cell size and number, and (d) body density[(6)]. Body mass index has gained favor as a better measure for adiposity [(7,8)] that is frequently used as a measure for body fatness in large epidemiological studies[(9)].

The aim of the present study is to determine the changes in serum lipid profile and the frequency of dyslipidaemia among three groups of patients with type 2 diabetes mellitus classified according to their BMI.

Subjects and Methods:

This study was conducted during a period of 12 months from January to December 2004. It was performed on diabetic patients with fasting plasma glucose >7.0 mmol/L [(10)].Patients with diseases other than type 2 diabetes were excluded from this study. Three hundred and fifty six diabetics who were attending Al-Zahrawi Private Hospital Outpatient Department in Mosul were included in this study, they were 184 males and 172 females aged 37-75 years (mean $\pm$ SD, 52.5 $\pm$ 6.4 years). All patients were taking sulfonylureas oral tablet in addition to diet restriction. The control group included 384 apparently healthy subjects (182 males, 202 females) aged 38-72 years (mean $\pm$ SD, 48.4$\pm$ 6.5 years).

A general physical examination involved the measurement of height (to the nearest 0.5 cm, without shoes), weight (to the nearest 0.1

kg, without coats). Body mass index was calculated as the ratio of weight (Kg) divided by height (m^2) square meter. Patients were divided according to their BMI into non-obese (D1, n=43, BMI<25 Kg/m^2), over weight (D2, n=187, BMI 25-29.9 Kg/m^2) and obese (D3, n=126, BMI> 30 Kg/m^2) [11]. The controls were divided similarly into non-obese (C1, n= 276, BMI < 25Kg/m^2), overweight (C2, n=88, BMI 25-29.9 Kg/m^2), and obese (C3, n=20, BMI>30 Kg/m^2). Blood sample (10ml) was taken after an overnight fasting from all subjects and divided into two aliquots. The first aliquot was transferred into flouride-oxalate tube for plasma glucose measurement and the second aliquot was transferred into plain tube for serum lipid profile measurement.

Fasting plasma glucose (FPG) was measured by glucose oxidase peroxidase method [12]. Determination of total cholesterol (TC), high density lipoprotein cholesterol (HDL-C) and triglycerides (TG) were performed using enzymatic methods [12]. Low density lipoprotein cholesterol (LDL-C) was calculated by using Friedewald formula for those with triglycerides <4.5 mmol/L [13].

LDL-C(mmol/L)=TC -HDL-C - TG ×0.455

Classification of hyperlipidaemia and dyslipidaemia was based on the recommendation of the British Hyperlipidaemia Association (1998)[14] using thresholds of TG : 180 mg/dl (2.4 mmol/L), TC : 194 mg/dl (5.0 mmol/L), LDL-C.116 : mg/dl (3.0 mmol/L), HDL-C ≤45 mg/dl (1.15 mmol/L), total cholesterol : HDL-C: 5.0, LDL-C: HDL-C: 2.5 and triglycerides: HDL-C: 3.0.A subject was considered dyslipidaemic when one of the above criteria was abnormally high (or low for HDL-C) [14].

The statistical analyses used included Z test with values quoted as mean ± SD. Analysis of variance (ANOVA) and Duncan test were used to compare the biochemical changes among the groups and within groups. Chi-square test was used for non parametric comparison. The P value at <0.05 was considered as significant.

Results:

The mean ± SD of age of the non-obese, over-weight and obese diabetic patients were 50.4 ± 7.0 , 52.0 ± 6.0 and 53.9 ± 6.4 years respectively while the mean ± SD age of non-obese, overweight and obese control subjects were 47.9 ± 6.4, 48.3 ± 7.1 and 49.5 ± 5.8 years respectively. The mean ± SD of BMI of non-obese, overweight and obese diabetic patients were 23.9 ± 0.9, 27.7±1.4 and 32.1±1.6 Kg/m^2 respectively while the mean ± SD of BMI of non-obese , overweight and obese control subjects were 22.7 ± 1.1, 26.7 ± 1.3 and 32.0 ± 1.6 Kg/m^2 respectively. Table 1.

The gender distribution according to BMI in the non-obese, overweight and obese male diabetics were 26 (14.1 %), 93 (50.6 %) and 65 (35.3 %) respectively versus 17 (9.8 %), 94 (54.7 %) and 61 (35.5 %) in female diabetics. Table 1.

Based on the BMI, changes in (FPG) were noted in patients with respect to the degree of overweight and obesity. The mean ± SD. of FPG were 9.9 ± 2.8, 9.7 ± 3.1 and 12.4 ± 3.7 mmol/L in non-obese, overweight and obese diabetics respectively. Mean fasting plasma glucose level was highest in the obese patients. Table 2.

The total number of uncontrolled diabetics was 287 who were distributed according to their BMI into non obese 33 out of 43 (76.6%), 148 out of 187 (78.7%) over-weight and 106 out of 126 (92%) obese diabetics respectively. This means that the percentage of poorly controlled diabetics was increased with increasing BMI (Data was not shown). No significant sex differences were noted in lipid profile and FPG levels of the diabetics (Data was not shown). There was a significant and positive association between the BMI and serum TG (P<0.01), TC (P<0.001), LDL-C (P<0.001) and VLDL-C (P<0.01). Serum HDL-C levels were significantly decreased (P<0.01) by increasing BMI. The lowest HDL-C was obtained with BMI>30 Kg/m^2 while all other parameters of lipid profile were highest in the obese diabetics comparable to other groups of BMI. These differences were statistically significant. This is also applicable in the control subjects for all parameters except

HDL-C levels which were not significant. Table 2.

A subject was considered dyslipidaemic when the criteria of cutoff value was fulfilled according to the recommendations of the British Hyperlipidaemia Association (1998). The prevalence of dyslipidaemia was increased with increasing BMI levels in both sexes. This also means that the prevalence rate of dyslipidaemia was lower in the non-obese and higher in the overweight and obese diabetics. Table 3.

Discussion:

Accelerated coronary and peripheral vascular atherosclerosis is one of the most common and serious complications of long term diabetes mellitus[15].Along with other risk factors including hypertension, smoking and obesity, increasing importance has been given to secondary hyperlipidaemia in the causation of accelerated atherosclerosis [16].

The findings in table 1 show that BMI was increased with age in diabetics. These findings are consistent with other studies [17-19]. An increase in 1 body mass index unit from 20.0-21.9 onwards was associated with an approximately 10% increase in the rate of coronary events. Diabetes increased progressively with the increase in BMI [18]. In the present study 35.3 % of male diabetics and 35.5 % of female diabetics were obese. This high prevalence of obesity could be attributed to the dietary habits, lack of physical activity and genetic factors [20]. Obesity is significantly higher in the diabetics compared to non-diabetics, and this may be one of the factors in the development of type 2 diabetes mellitus [21]. Studies implicating overweight as a potent factor in the etiology of type 2 diabetes include analysis of Third National Health And Nutrition Examination Survey (HNANES III) data in which the prevalence rate of diabetes increased steeply with increasing BMI, which means 2-18 times higher in obese than normal weight patients, depending on the severity of obesity [22].

In the present study, plasma glucose concentration was increased with increasing BMI and the percentage of poorly controlled diabetics was increased with increasing BMI which means that poorly controlled diabetics were more in obese patients than non-obese patients. This is an important finding which showed that hyperglycaemia was closely related to hypercholesterolaemia, hypertriglyceridaemia and elevation of LDL-C which were all documented as risk factors for CHD [15,23]. It is well documented that the higher levels of fat prevent the action of insulin or down regulate its receptors and so produce insulin resistance state that leads to type 2 diabetes mellitus [24].

The most characteristic lipid abnormality in diabetes is hypertriglyceridaemia with or without increase in plasma cholesterol [17]. In the present study, obese diabetics, when compared to non- obese diabetics, showed significant increase in the levels of serum total cholesterol, triglycerides, LDL-C and VLDL-C while serum HDL-C differs significantly. These results are consistent with other studies [24-28]. Earlier studies have shown that high triglycerides and low HDL-C in type 2 diabetes are independent on the degree of obesity [29,30]. This is inconsistent with this study, while laakso and pyorala (1990) stated that obesity (BMI) effects on serum lipids and lipoproteins were more in diabetics than in non diabetic subjects [31] which is consistent with present study . Garg (1992) stated that the severity of obesity is a determinant of lipoprotein abnormalities in type 2 diabetes besides the degree of glycaemic control [32]. The present study had clearly shown that all lipid fractions (except HDL-C) were abnormally elevated in obese diabetics when compared with obese control subjects. There are studies which seem to suggest that lipoprotein distribution in type 2 diabetes mellitus is not significantly altered by the degree of glycaemia [29,33].

This study showed the magnitude and pattern of dyslipidaemia among group of Iraqi adult diabetic patients. The prevalence of dyslipidaemia was increased with increasing BMI levels in both sexes which is consistent with the study of Brown et al (2000) [19]. The reported prevalence of dyslipidaemia varied from 25 to 60% [34]. This wide variation could be attributed to the studied population

and the degree of glycaemic control as well as to the variation in the definition of the "cut off" values for lipid profile parameters.

In conclusion the study has documented several lipid abnormalities in type 2 diabetic patients and has pointed to the significance of diabetic management in the control of lipid abnormalities where the control of overweight and obesity is of importance.

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Table 1: Age and sex distribution of diabetics and control subjects according to BMI .

	Diabetics (n=356)			Control subjects (n=384)		
BMI	**Non-obese (n=43)**	**Overweight (n=187)**	**Obese (n=126)**	**Obese (n=276)**	**Overweight (n=88)**	**Obese (n=20)**
Age (years), Mean ± SD	50.4 ± 7.0	52.0 ± 6.0	53.9 ± 6.4	47.9 ± 6.4	48.3 ± 7.1	49.5 ± 5.8
BMI (kg/m^2), Mean ± SD	23.9 ± 0.9	27.7 ± 1.4	32.1 ± 1.6	22.7 ± 1.1	26.7 ± 1.3	32.0 ± 1.6
Males (n) %	26(14.1)	93 (50.6)	65 (35.3)	127(69.7)	42(23.3)	13 (7)
Females (n) %	17(9.8)	94 (54.7)	61(35.5)	149(73.7)	46(22.8)	7(3.5)

Table (2) Clinical and laboratory characteristics of diabetics without obesity (D1, n=43), with overweight (D2, n=187) and with obesity (D3, n=126) and in control subjects without obesity (C1, n=276), with overweight (C2, n=88) and with obesity (C3, n=20).

Parameters (mmol/L)	**Diabetics (n=356)**			**ANOVA**	**Control subjects (n=384)**			**ANOVA**
	D1	**D2**	**D3**		**C1**	**C2**	**C3**	
Total cholesterol (TC)	5.2 ± 1.2 a	5.3 ± 0.9 a	5.8 ± 1.3 b	F = 10.77 p<0.001 HS	4.8 ± 0.9 a	5.0 ± 0.8 a	5.4 ± 1.0 b	F = 14.55 p<0.001 HS
Triglycerides (TG)	1.9 ± 0.8 a	2.0 ± 1.2 a	2.4 ± 1.5 b	F = 4.65 p<0.01 S	1.5 ± 0.7 a	1.8 ± 1.0 a	2.3 ± 1.5 b	F = 13.50 p<0.001 HS
HDL-C	1.2 ± 0.3 a	1.1 ± 0.2 ab	1.0 ± 0.2 b	F = 4.42 p<0.01 S	1.2 ± 0.3 a	1.2 ± 0.3 a	1.1 ± 0.3 a	F = 0.77 NS
LDL-C	3.1 ± 1.0 a	3.3 ± 0.9 a	3.9 ± 1.2 b	F = 8.2 p<0.001 HS	2.9 ± 0.9 a	3.0 ± 0.9 a	3.5 ± 1.1 b	F = 6.14 p<0.002 S
VLDL-C	0.38 ± 0.16 a	0.38 ± 0.23 a	0.47 ± 0.3 b	F = 4.65 p<0.01 S	0.28 ± 0.16 a	0.35 ± 0.19 b	0.46 ± 0.28 c	F = 15.4 p<0.001 HS
Fasting plasma glucose (FPG)	9.9 ± 2.8 a	9.7 ± 3.1 a	12.4 ± 3.7 b	F = 25.7 p<0.001 HS	5.0 ± 0.7 a	5.2 ± 1.0 a	5.7 ± 0.8 a	F = 7.4 p<0.001HS

Different letters horizontally mean a significant difference at p<0.05 level according to Duncan test(ab = not significant with either a or b)
HS = Highly significant

NS = Not significant

Table (3) Prevalence of dyslipidaemia in diabetics (in relation to BMI) according to the recommendation of the British Hyperlipidaemia Association (1998). Results are expressed as number (%) of patients.

BMI (Kg/m^2)	**Hypercholestrolaemia TC ≥3 mmol/L**		**Hypertriglyceridaemia TG ≥2.4 mmol/L**		**LDL-C ≥3 mmol/L**		**Low HDL-C ≤1.5 mmol/L**		**TC: HDL ratio ≥5.0**		**LDL-C: HDL-C ratio ≥2.5**		**TG: HDL-C ratio ≥3.0**	
	No.	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**
Non-obese BMI <25 (n=43)	25	7.0	15	4.2	23	6.5	23	6.4	15	4.2	29	8.2	6	1.7
Over weight BMI 25-29.9 (n=187)	125	35.1	55	15.5	125	35.1	115	32.3	88	24.7	138	38.8	23	6.5
Obese BMI>30 (n=126)	98	27.5	59	16.5	97	27.2	90	25.3	89	25.0	106	29.8	32	9.0
Total	248	69.6	129	36.2	245	68.8	228	64	192	53.8	273	76.8	61	17.1
p-value	<0.05 (S)		<0.01 (S)		<0.05 (S)		>0.05 (NS)		<0.001 (S)		<0.05 (S)		<0.01 (S)	