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OBESITY AND HYPERTENSION; NON-INSULIN-DEPENDENT DIABETES MELLITUS PATIENTS

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ABSTRACT... Objectives: To assess the associations of obesity and hypertension in diabetics and non-diabetics. **Patients and Methods:** A total of 430 Saudi patients suffering from non-insulin-dependent (type 2) diabetes mellitus comprising of 205(48 %) males and 225(52 %) females were studied. Height and weight were measured for calculating body mass index (BMI). The type 2 diabetics and non-diabetic individuals were investigated separately to determine the prevalence of obesity and overweight. Systolic and diastolic blood pressure was recorded using the standard method in a sitting position. The patients were diagnosed as diabetics and hypertensive on the criteria of the World Health Organization. **Results:** The prevalence of obesity was 16.7% and 22.9%, and overweight was 27.1% and 22.9% in the total men and women studied in healthy non-diabetics; while the prevalence of obesity was 26.8% and 42.7%, and overweight was 45.8 and 38.2% in the total men and women, in the diabetics respectively. In diabetic subjects, glycemic status (HbA_{1c}) and BMI had coefficient of correlation between 26 matched pairs as r= 0.36, but not impressive. In over-all population, irrespective of gender, the diabetic subjects had higher obesit/overweight (ob/ow) ratio value (0.84) than non-diabetics (0.79). The prevalence of HT in non-diabetic group was 4.42% in males compared to 2.1% in females, while in the diabetic group the prevalence of HT was 24.39% in males and 41.33% in females, respectively. Prevalence of HT in diabetics was higher in females than males, in contrast to non-diabetics. **Conclusion:** Our study shows that obesity and hypertension are both contributing factors in the development of type 2 diabetes mellitus; and the measures should be adopted for control of obesity and hypertension to reduce the cause of diabetes mellitus.

Key words: Glycosylated hemoglobin, hypertension, obesity, type 2 diabetes mellitus.

INTRODUCTION

Overweight is defined as relative weight up to 20% above normal, and obesity relative weight over 20% above ideal body weight^{1,2}. Obesity often precedes the development of non-insulin dependent diabetes mellitus (NIDDM) which accounts for 80 to 90% of the diabetes,

and that the obese patients are usually hyperinsulinemic³. Obesity is implicated for several important diseases, especially hypertension, coronary heart diseases, dyslipidemia, diabetes mellitus, breast cancer, and osteoarthritis⁴⁻⁷. Like-wise, the important risk factors for type 2 diabetes mellitus include obesity,

ethnicity, age, sex, sedentary lifestyle, family history, and perinatal influences⁸. Obesity is a major epidemic in United States⁹ and in a trial for hypertension, weight loss produced slightly greater reductions in blood pressure than did sodium restriction¹⁰.

Diabetes mellitus (DM) and hypertension (HT) are both multi-factorial disorders which occur at a higher prevalence in elderly and result from both genetic and environmental etiological factor^{11,12} and occur frequently in obese individuals. Like DM, HT is also one of the most common causes of morbidity and mortality in humans¹³. Several studies have shown that a close association between HT and DM exists even in different ethnic groups where the prevalence of HT is significantly higher in the patients with non-insulin dependent diabetes mellitus¹⁴⁻¹⁶. It has been reported that the link between diabetes and essential HT is hyperinsulinemia^{17,18}. Diabetes mellitus and HT are interrelated diseases that strongly predispose people to atherosclerotic cardiovascular disease, and hence have been referred to as "the bad companions"¹⁶.

Though association between development of non-insulin dependent diabetes mellitus and obesity has been shown, yet several aspects of this association are not yet clear¹⁹. Significant ethnic differences have been reported in the nature and also the complications and prevalence of HT, and obesity in patients with NIDDM^{18,20,21}. In a continued study on the diabetic patients of unique ethnic community of Makkah, Saudi Arabia, where-in the dyslipidemic pattern and lipid peroxides level were determined²², the associations of obesity and hypertension in diabetics and non-diabetics are evaluated, here.

MATERIALS AND METHODS

A total of 430 Saudi patients of Makkah area suffering from non-insulin-dependent (type 2) diabetes mellitus comprising of 205(48 %) males and 225(52 %) females

were the subjects of our study. The patients were diagnosed as diabetics on the basis of WHO criteria^{23,24}; fasting whole blood venous > 6.7 mM (120 mg/dl) and / or the value 2 hours after the glucose load > 10.0 mM (180 mg/dl). Subjects with an age of onset > 30 year and dependent on dietary control or use of oral hypoglycemic drugs were classified as type 2 diabetics and included in our study. 96 normoglycemic subjects of whom 48(50 %) were males and 48(50 %) females without having any classical diabetic symptoms and signs, from the same population, served as control.

The fasting blood sample from the patients and control were collected by venipuncture in heparinized tubes (or K oxalate/Na fluoride), and / or in standard plain tubes for sera. Glycosylated hemoglobin (HbA_{1c}), which is a reliable index and invaluable tool of average glycemic control²⁵, was determined using BM/Hitachi system, based on the turbidometric immunological inhibition assay for hemolyzed whole blood (Kit No. 1822039). Triglycerides (TG), total cholesterol, high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C) were determined as described earlier²². Lipid peroxides level was determined by the reaction with thiobarbituric acid²⁶.

Height and weight were measured by using standard techniques according to WHO report²⁷. The body mass index (BMI) is well correlated with measures of body fat and is defined as weight (kg) divided by height² (m²). Using this index, BMI was calculated²⁸. The type 2 diabetics and non-diabetic individuals were investigated separately to determine the prevalence of obesity and overweight. A BMI value of 18.5-24.9 was considered normal-weight persons as reference group, while a BMI value between 25.0 - 29.9 overweight, and 30 and over was considered obese²⁹.

Systolic and diastolic blood pressure was recorded using the standard method in a sitting position. Diagnosis of

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HT was based on WHO criteria³⁰. Values of systolic pressure \geq 140 mm Hg and/or diastolic pressure \geq 90 mm Hg and individuals on antihypertensive drugs were considered as hypertensive³¹.

The data was analyzed by z-statistic, student's t-test and chi square test where appropriate. Relationship between two variables was determined by Pearson's Product Moment Correlation Coefficient (r).

RESULTS

Physical characteristics, BMI value and the levels of glycated hemoglobin for each individual in diabetic (430) and non-diabetic (96) subjects are presented in Table I.

Table-I. Certain characteristics of study population (Mean ± SEM).							
	DM type 2	2 patients	Control group				
	Male	Female	Male	Female			
Age (yr)	49.5±1.13	48.5±1.11	48.5±0.86	46.5±0.92			
Height (m)	163.05±1.08	154.9±1.04	165.3±0.73	155.8±0.58			
Weight (kg)	74.32±1.49	73.26±1.73	66.5±0.89	62.5±0.92			
Body mass index (kg/m²)	27.84±0.70	29.63±0.80	26.88±0.36	28.58±0.50			
HbA _{lc} (%)	11.47±0.23*	10.71±0.20*	6.06±0.17	5.65±0.14			
*p<0.001 statistically significant compared to the control group of the same gender							

The results of blood glucose levels were published elsewhere²². The prevalence and association of obesity and overweight in the total diabetic and non-diabetic population and segregated as men and women are shown in Table II.

The prevalence of obesity was 16.7% and 22.9%, and overweight was 27.1% and 22.9% in the total men and women studied in healthy non-diabetics; while the prevalence of obesity was 26.8% and 42.7%, and overweight was 45.8 and 38.2% in the total men and women, in the diabetics respectively. Prevalence of obesity was higher significantly (42.7%) among diabetic women compared to 22.9% among non-diabetic women (p< 0.001).

The prevalence of obesity was lower while overweight was higher among men compared to the women in diabetic group; a pattern similar to non-diabetics but aggravated significantly. On the other hand, overweight men were more prevalent (45.8%) than the women (38.2%) in the diabetic group and also in the non-diabetic group, 27.1% compared to 22.9%, respectively. If obese and overweight populations are grouped together, then almost 3/4th of the diabetic individuals were either obese or overweight. Both in men and women, the prevalence of obesity and overweight are significantly higher in the diabetic individuals compared to the non-diabetic individuals (p<0.001). In diabetic subjects, glycemic status (HbA1c) and BMI had coefficient of correlation between 26 matched pairs as r= 0.36, which was not impressive.

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Table-II. Prevalence of obesity and overweight in diabetic and non-diabetic males and females								
Population	Diabetic			Non-diabetic				
	No. investigated	Overweight No. (%)	Obese No. (%)	No. investigated	Overweight No. (%)	Obese No. (%)		
Male ^(a)	205	94 (45.85)	55 (26.83)	48	13 (27.08)	8 (16.67)		
Female ^(b)	225	86 (38.22)	96 (42.67)	48	11 (22.92)	11 (22.92)		
Total ^(c)	430	180 (41.86)	151 (35.12)	96	24 (25.0)	19 (19.79)		
Statistical significant of the difference in the results of obesity in diabetic and non-diabetic population (a) $x^2 = 14.79$; DF = 2; p<0.001 (b) $x^2 = 26.88$; DF = 2; p<0.001 (c) $x^2 = 39.61$; DF = 2; p<0.001								

Prevalence of HT in the total number of type 2 DM and non-diabetic males and females screened are shown in

Table III.

Table-III. Prevalence of hypertension (HT) in non-diabetic and diabetic males and females							
Diabetic				Non-diabetic			
Population	No. Investigated	Total No. HT	Prevalence of HT (%)	Total No. Investigated	Prevalence of HT (%)	X2*	p-value
Male	205	50	(24.39)	48	2 (4.2)	8.5	<0.005
Female	225	93	(41.33)	48	1 (2.1)	25.3	<0.001
Total	430	143	(3.33)	96	3 (3.13)	34.0	<0.001
*Significance of the difference in prevalence of HT in diabetic and non-diabetic subjects.							

The prevalence HT in non-diabetic group was 4.42% in males compared to 2.1% in females, while in the diabetic group the prevalence of HT was 24.39% in males and 41.33% in females, respectively. Similar to obesity, the prevalence of HT is highest in diabetic females. The difference in the prevalence of HT in the two groups was statistically significant in both males (p<0.05) and females (p<0.001). The increase in prevalence of HT in diabetic was significantly higher in the females compared to males. Among the non-diabetics, males showed a higher prevalence of HT as compared to the females.

Over all, the prevalence of HT was significantly higher in the diabetic group compared to the non-diabetic group (p<0.001).

DISCUSSION

The high prevalence of obesity and overweight in the diabetic individuals points to the fact that obesity is one of the major etiological factors in the development of diabetes. The role of obesity in the etiology of diabetes mellitus is well documented and according to World Health Organization "Expert Committee on diabetes mellitus", obesity is considered as the most powerful known risk factor for the development of type 2 DM^{32} . It was reported that persons having genetic susceptibility, the presence of obesity may act more as a potentiator of type 2 DM^{33} . It has been suggested that obesity and the other risk factors associated with life style modernization may interact and result in increased prevalence of type 2 DM^{34} .

Obesity always causes some degree of insulin resistance, a poorly understood phenomenon, where-in the number or affinity of insulin receptors is reduced in some patients: other have normal insulin binding but abnormal post-receptor responses and hence predisposition to hyperglycemia. The high obesity/overweight (ob/ow) ratio value is indicative of a relatively higher prevalence of obesity³⁵. In our study we found higher ob/ow ratio value for female (1.12) than male subjects (0.59) in diabetics as well as in nondiabetics (1.00 and 0.62 in females and males respectively). This ratio was highest in diabetic females (Table II). In over-all population, irrespective of gender, the diabetic subjects had higher ob/ow ratio value (0.84) than non-diabetics (0.79). The higher BMI can be seen in females in both diabetic and diabetic subjects (Table I). The results of our study suggest that obesity may be considered as a major etiological factor in the development of type 2 diabetes mellitus in this community.

Environmental as well as genetic factors contribute to the development of obesity³³. Longini et al³⁶ have estimated that the heritability for BMI is over 30% and the rest is accounted for by other factors, these include demographic factors, familial factors and personal factors. Obesity and leanness though run in families, yet do not follow a Mendelian pattern of inheritance. BMI, even within the non-obese level, is a dose-dependent risk factor for diabetes mellitus in middle-aged Japanese. Increase in BMI of 1 kg/m² (=body-weight gain of 2.4-2.9

kg) may raise the risk by about $25\%^{37}$.

The higher prevalence and association of obesity and hypertension; correlated with DM shows a significant epidemiological transformation in this community. The coherent sedentary way of life has eventually resulted in precipitation of several multi-factorial traits both in males and females. Females are particularly more prone to sedentary life, and have thus showing higher ob/ow ratio. This study on diabetic and non-diabetic Makkans has revealed that the prevalence of HT is significantly higher in both male and female diabetics in comparison to nondiabetics. In males: the prevalence of HT is increased almost 5.81 times in the diabetic group, while in the female diabetics; the prevalence of HT is increased almost 19.68 times. Several studies showed close association between HT and DM14-16; even the prevalence of HT was reported to be almost 50% in the NIDDM patients³⁸.Relationship between weight reduction and reduction in blood pressure³⁹ reveals that reduction in weight is a promising step to control blood pressure or risk of hypertension.

Hypertension is a common problem among diabetic patients accelerating progression of vascular diabetic complications. It is significantly associated with old age, obesity, prolonged diabetic duration and poor glycemic control⁴⁰. The age-adjusted relative risk (RR) for new hypertension was highly associated with overweight status; men: RR, 1.46; women: RR, 1.75²⁹; while Aucott et al⁴¹ found 10 kg weight loss with decrease of 4.6 mm Hg and 6.0 mm Hg in diastolic and systolic blood pressure respectively, in a study of long-term effects of weight loss on hypertension showing the complexity of weight/hypertension relationship.

We also found statistically significant higher frequency of dyslipidemia in combined overweight-obese diabetic group of females than males; while in poor glycemic control (HbA_{1c} > 10%) subjects, it was higher in females

than male but statistically not significant (results not shown here). There were 69% of the total diabetic patients who had elevated HbA_{1c}; showing poor glycemic control. There appeared to be no significant difference between males and females in the values of HbA_{1c} (Table I). The serum concentrations of triglycerides, cholesterol and LDL-C were significantly higher in diabetic patients as compared to control, and their correlation with HbA_{1c} were also statistically significant (r=0.23; P < 0.02, r=0.16; P < 0.05, r=0.14; P < 0.05, respectively); but we could not find statistical difference of HDL-C level between diabetics and non-diabetics, rather no significant reduction in HDL-C which is a predictor of stroke in patients with NIDDM⁴², in our population.

Diabetes mellitus which apart from a disorder of glucose homeostasis also accompanies various degenerative manifestations such as accelerated aging, the events related to elevated levels of lipid peroxidation products in plasma of patients with diabetes mellitus⁴³. Our results support the production of lipid peroxides in diabetes mellitus and that related significantly with glycosylated hemoglobin as we found that the plasma levels of TBARS (2.69 μ M±0.15 SEM) is significantly higher in the diabetic patients as compared to those in control (1.97 μ M±0.12 SEM).

Ethnic variation, overall physique, and genetic disorders all contribute to these disorders. Since the type 2 diabetic affects elderly of >35 year, a pathogenic mechanism initiated by insulin excess and resistance is suggestive. The strong association of obesity, type 2 diabetes and hypertension, has led to a new term "diabesity" for the association. The main link between obesity and type 2 diabetes is insulin resistance leading to excessive secretion of insulin to compensate, and maintain normoglycemia. Thus the resulting hyperinsulinemia, through some pathogenic mechanism, causes hypertension. It is of significance that BP is controlled in diabetic patients. In Saudi Arabia, the prevalence of DM is high⁴⁴, and with the increase in the prevalence of HT in diabetics, as shown in this study, the associated morbidity and complications are expected to increase. Hence, control of DM and HT by appropriate methods, particularly dietary restriction of calories and sodium, and regular physical exercise to decrease both the prevalence of HT and NIDDM are recommended. By losing weight, insulin receptors will increase in number, and also the post receptor abnormalities will improve by increasing both tissues sensitivity to insulin and glucose tolerance.

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