CENTRAL ADIPOSITY AND ATHEROGENIC LIPIDS IN SAUDI DIABETICS

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A high caloric intake from fat sources and prevailing obesity in the Saudi population prompted this study. Waist to hip circumference ratio (WHR), fasting cholesterol, triglycerides and insulin were measured in 76 non-insulin dependent adult Saudi diabetics. Serum LDL, HDL and VLDL were measured in 45 of these diabetics. WHR of Saudi diabetics was higher (0.98 in males, 0.91 in females) than reported for diabetics from the West. Serum cholesterol levels (5.52 mmol/L in males, 5.98 mmol/L in females) were higher than reported in the past for normal Saudi subjects. Lipid profile was strikingly different in the two sexes. Male diabetics (n=28) had significantly higher WHR associated with elevated triglycerides and VLDL but a lower HDL/cholesterol ratio. Female diabetics (n=48) were obese and had healthier HDL levels. Interestingly, LDL cholesterol changed reciprocally with WHR in female diabetics. This preliminary study reveals the presence of significant central adiposity and an atherogenic lipid profile in Saudi diabetics. The sex differences in lipids indicates the need for studies involving lipoprotein metabolism in Saudis. Further, an increase in atherosclerosis-related disorders should be expected in Saudi diabetics. *Ann Saudi Med 1994;14(4):329-332.*

Central adiposity is known to be associated with abnormal carbohydrate and fat metabolism and increased incidence of coronary artery disease (CAD).[1] Similarly, diabetes has well known association with hyperlipidemia and increased atherosclerosis-related complications; namely, coronary artery disease, cerebrovascular events and peripheral arterial disease.

Saudi non-insulin dependent diabetes mellitus (NIDDM) patients have been reported to have a lower prevalence of CAD. This has been explained by lower levels of serum cholesterol and blood pressure in Saudi NIDDM.[2] However, an increase in admission for acute myocardial infarction to hospitals has been observed lately.[3] This is expected, considering the high prevalence of obesity and diabetes in the Saudi population.[4] Further, caloric consumption from oil and fat has increased fourfold from 1975 to 1985.[5] This is expected to increase the body weight and abdominal obesity and worsen the lipid profile of Saudis, especially of diabetics. An increased waist to hip circumference ratio (WHR) as a measure of central adiposity is known to be associated with hyperinsulinemia and hyperlipidemia.[1]

We present a preliminary report on the WHR, lipids and insulin in Saudi NIDDM subjects.

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Material and Methods

Maturity onset NIDDM subjects from the diabetic clinic of King Fahd Specialist Hospital, Buraidah, were screened for cardiac, renal, and hepatic disease or thyroid disorder, drug exposure, current pregnancy or postpartum state of less than six months. Diabetics of these categories were excluded. Seventy-six NIDDM subjects of both sexes (28 males and 48 females) with a mean age of 49 were selected for the study. They were not known to be smokers or alcoholics and none of the female diabetics were on oral contraceptive pills for the previous three months. There has been no recent change in the dose of oral antidiabetic drugs. A majority of these patients were only partly compliant with diet restriction and were sedentary.

The waist was used as the minimum circumference between the costal margin and umbilicus and the hips as the maximum circumference between the iliac crest and thighs.[6] Blood pressure in the right arm was taken in the sitting position with diastolic level at muffling of the sound. Body mass index (BMI) was calculated as weight in kilogram/height in meter^2 and waist to hip ratio (WHR) was waist divided by hip circumference. The mean blood pressure (MBP) was calculated as the sum of one-third of pulse pressure and diastolic pressure.

Instruction in Arabic was given to all patients regarding fasting blood sampling and the compliance was confirmed on their next clinic visit by a questionnaire. After an overnight fast of 12 hours, venous blood was collected. Plasma glucose and lipids were measured on the same day, but plasma was stored at -70°C for insulin assay. Glucose

levels were determined by an enzymatic method using commercial kits. Cholesterol and triglycerides were determined by an enzymatic method.[7,8] Lipoprotein was measured according to the method described by Delong et al.[9] Insulin level was measured by standard radio-immunoassay using commercial kits from Amersham, United Kingdom. Serum total cholesterol (TC) and triglycerides (TG) were measured in all 76 subjects but low density lipoprotein cholesterol (LDL), high density lipoprotein cholesterol (HDL) and very low density lipoprotein cholesterol (VLDL) were measured in only 45 patients (20 males, 25 females) due to noncooperation of the patients. HDL/TC and insulin glucose ratio (IGR) were computed.

Results

Seventy-six NIDDM subjects comprised of 28 males and 48 females participated in the study (Table 1). Both males and females were more or less in the similar age range (30 to 60 years). Female diabetics were obese (mean BMI >29) while males were overweight (BMI >25). Adiposity distribution in both sexes was predominantly central but more marked in males, "mean WHR + SE = 0.98 + 0.07" as compared to females "0.91 + 0.07". Mild hypertension (BP >140/90 mm/Hg) was noted in five out of 28 males (17.8%) and eight out of 48 females (16.6%). No difference in mean blood pressure was noted between the two sexes.

Lipid profile was found to be distinctly different in the two sexes, so also the blood glucose levels (Table 2). Males had significantly higher glucose ($P<0.05$), TG ($P<0.05$), VLDL ($P<0.05$) and lower HDL ($P<0.01$) levels, while no significant differences were observed in the levels of TC, LDL and HDL/TC in the two groups.

The pattern of lipoproteins also was different in the two groups (Table 3). The most common abnormality observed in males was type IV hyperlipoproteinemia in 10 cases (35.7%) and among the females, polygenic hypercholesterolemia was more common in 27 cases (56.7%); six males also had polygenic hypercholesterolemia (21.4%); 10 males (35.7%) and nine females (18.7%) had type IV pattern commonly associated with uncontrolled diabetes.

Correlation of metabolic parameters with age and anthropometry was different in the two sexes. TG (r=0.53, $P<0.05$) and VLDL (r=0.45, $P<0.05$) increased significantly with age while HDL decreased significantly (r=0.42, $P<0.05$) in males. No age related changes were observed in females (data not shown). However, females had higher levels of insulin which increased significantly with BMI (r=0.48, $P<0.05$) and WHR (r=0.39, $P<0.05$) and interestingly showed a significant negative correlation with TC (r=-0.23, $P<0.05$) and LDL (r=-0.43, $P<0.05$). A reciprocal relation of LDL with WHR (r=-0.43, $P<0.05$) was also observed, which was unexpected and surprising.

Data were computed for all 76 Saudi diabetics to study the relationship of metabolic parameters with lipids. WHR was negatively correlated with TG (r= -0.19, $P<0.05$) and with LDL (r= -0.34, $P<0.05$) and HDL (r= -0.29, $P<0.05$) while with BMI it did not show any particular trend in either sex. Correlation matrix for all the subjects showed an elevated TG with age (r=0.35, $P<0.05$) and insulin with BMI (r=0.48, $P<0.05$). A positive correlation of WHR with VLDL (r=0.4, $P<0.05$) was observed.

Some similarities were observed between the two sexes, such as: 1. no correlation of BMI with WHR; and 2. reciprocal correlation of HDL/TC "r= -0.53, $P<0.05$" in males and "r= -0.82, $P<0.01$" in females and of TG with HDL/TC "r= -0.72 in males and r= -0.51" in females.

Apart from this, comparable lipids and insulin levels were found between age groups >5 and <50 years and BMI

TABLE 1. *Anthropometry and blood pressure of Saudi non-insulin dependent diabetes.*

Subjects	Age	BMI	WHR	Blood Pressure (mm/Hg)
Males	49.6±1.5	28.1±0.07	0.98±0.07	95.01±1.99
n=28	(27-60)	(21-36.4)	(0.89-1.0)	(80-115)
Females	47.1±1.1	31.5±0.6	0.91±0.07	95.5±1.2
n=48	(28-65)	(21-43)	(0.77-1.3)	(80-113)
P value	NS	<0.001	<0.001	NS

BMI=body mass index; WHR=waist to hip ratio; Values are expressed as ± S.E.; The numbers in parentheses indicate the range; NS=not significant.

TABLE 2. *Carbohydrate and lipid profile in Saudi non-insulin diabetes.*

Subjects	Males (n=28)	Females (n=48)	*P* value
Insulin (pmol/L) Mean ± SE	185.8±22.2	210.2±21.5	NS
Blood Glucose	10.2±0.68	9.61±0.52	<0.05
Insulin/Glucose	0.16±0.02	0.18±0.02	NS
Lipid Profile			
Cholesterol	5.52±0.22	5.97±0.12	NS
Triglycerides	2.41±0.21	1.96±0.11	<0.05
LDL	3.46±0.27	3.98±0.14	NS
HDL	0.91±0.05	1.11±0.03	<0.01
VLDL	1.15±0.11	0.86±0.07	<0.05
HDL/Cholesterol	0.17±0.01	0.19±0.01	NS

LDL=low density lipoprotein; HDL=high density lipoprotein; VLDL=very low density lipoprotein; NS=not significant; The values are expressed as ± SE of mmol/L.

TABLE 3. *Lipoprotein pattern in Saudi non-insulin dependent diabetes mellitus subjects.*

	Males		Females	
	%	n	%	n
Normal	35.7	10	12.5	6
Type IIb	7.1	2	12.5	6
Type IV	35.7	10	18.7	9
Polygenic Hypercholesterolemia	21.4	6	56.7	27
Total		28		48

groups <29 and >29, except for LDL, which was higher in the obese group ($P<0.05$) (data not shown).

Discussion

The present study evaluated the relationship between the central adiposity and atherogenic lipids in a homogeneous group of the Saudi population, who had uncomplicated NIDDM. WHR as the measure of central obesity has been used in different populations and shows sex difference in its metabolic associations.[10]

As expected, male diabetics had higher WHR ($P<0.001$) while females had higher BMI ($P<0.001$). WHR, being a physiologic parameter, changes with time and body weight. A healthy level of WHR has not been clearly defined, although attempts have been made. Studies on European subjects suggested WHR of 1.0 and 0.8 as risk levels for CAD in males and females respectively.[11] WHR levels in our group are higher than reported in British diabetics[18] and that of females was higher than reported earlier in Arab diabetic females.[19]

Total cholesterol levels of >200 mg/dL in both groups and TG >175 mg/dL in males indicates risk of CAD in diabetics as per consensus of LRC-CPPT trial[10] and the National Cholesterol Education Program of the USA.[12] However, opinions differ and also our group was well within the healthy range (<250 mg/dL) as recommended by the National Institute of Health sponsored consensus conference.[13]

The level of cholesterol was screened by some workers in healthy and NIDDM Saudi subjects in different years; in 1982, Bacchus et al.[15] reported the level of cholesterol as 4.27 mmol/L in males and 4.23 mmol/L in females. In 1985, Kingston and Scooge reported lower levels of cholesterol (mean 209 mg/dL equivalent to 5.2 mmol/L), blood pressure and CAD prevalence in Saudi NIDDM subjects, as compared to the West.[2] In an extensive cholesterol screening in 1991 by Inam et al., a mean cholesterol of 5.25 mmol/L in males and 5.49 mmol/L in healthy Saudi female adults was reported. This rise in atherogenic lipids is expected, considering the rise in per capita caloric supply and increased saturated fat-derived calories as established by dietary interviews.[3]

Triglycerides and VLDL increased while HDL decreased significantly with age in males but not in females. Because of multifactorial influences on lipids, differences in population studies are expected. Confirming this, HDL levels have been reported to undergo a minor change with age in males but may increase up to menopause and decrease during the postmenopausal state in women.[16] Females, however, have a higher HDL level throughout adult life as was seen in our study (<0.91 mmol/L) which correlated reciprocally with TG ($P<0.01$). HDL/TC ratio has been found to be a discriminatory parameter for CAD and reciprocally correlates with angiography proven coronary atheroma.[17] HDL/TC in our group was considerably lower (males -0.17 +0.01, females 0.19 +0.01) as compared to age-matched healthy Finnish subjects (males 0.19 to 0.21, females 0.2 to 0.26).[16] Thus, the metabolic parameters seem to fall into a pattern. Male Saudi diabetics with predominantly central obesity had a lower HDL/cholesterol ratio and elevated TG and VLDL while female Saudi diabetics were obese and had healthier LDL levels but elevated HDL levels.

Elevated TC, LDL and low HDL are known to increase the risk of CAD.[14,18] These alone are not responsible, as only a majority of patients with CAD have LDL cholesterol levels above the 95th percentile.[19] Further, low HDL levels are often associated with fasting hypertriglyceridemia.[20] Indeed, some studies have attributed better discriminatory power to TG and VLDL levels to differentiate myocardial infarction survivors from controls.[21]

Fasting total insulin levels, plasma glucose and IGR were comparable in both sexes. The insulin levels were higher in females (males 185.8 $\pm$ 22.2 pmol/L, females 210.2 $\pm$ 21.5 pmol/L). Hyperinsulinemia in the presence of hyperglycemia suggests a state of insulin resistance. Female diabetics also showed a stronger correlation of insulin with BMI (r=0.48) than with WHR (r=0.39). This confirms the view that a high WHR predisposes to diabetes, especially when associated with high BMI.[1] The complex relationship between the central obesity, insulin sensitivity and lipoprotein metabolism may be different among population and sex. A role of abdominal obesity in insulin resistance has been proposed.[22] This results in a reduced VLDL clearance which is the basis of hypertriglyceridemia in diabetics. A high VLDL/HDL ratio expected in such a state has been shown to increase the activity of enzyme cholesterol ester transfer protein (CCETP) in *in vitro* experiments.[23] This enzyme is responsible for the lipoprotein remodeling which goes on in circulation and involves transfer of cholesterol from LDL and HDL to VLDL, thus reducing LDL cholesterol levels.[24] Whether these mechanisms have a protective role and control the rise in LDL levels in Saudi females with high WHR needs further evaluation.

In conclusion, this preliminary study points to the presence of significant central obesity, hyperinsulinemia and an atherogenic lipid profile in Saudi diabetics. Metabolic correlation of WHR was seen in female diabetics alone. Lipoprotein handling metabolism may be different in the Saudi population and further genetic and environmental factors need to be studied.

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