METABOLIC SYNDROME: A CONSEQUENCE OF OBESITY

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ABSTRACT

The contribution of obesity towards the development of metabolic syndrome, a complex multifactorial disorder is investigated using NCEP-ATP III and AHA criteria. Forty subjects were included in this study form the selected areas of Karachi (Pakistan). Brief description about this syndrome and purpose of study was given to all individuals. Data were collected through a pre-designed questionnaire including inquiries about medical and family history, lifestyle, dietary habits etc. Body weight, height, waist circumference, BMI, systolic and diastolic blood pressure were measured for every individual. Fasting blood samples were collected for the determination of fasting blood sugar (i.e. glucose), triglycerides and high lipoprotein. Prevalence of metabolic syndrome was found to be 80% and 70.58% in obese men and women, respectively, showing a strong association between obesity and metabolic syndrome.

Key-words: Metabolic Syndrome, Obesity, Blood Pressure, Cardiovascular Disease. Insulin Resistance, Triglyceride, Waist Circumference.

INTRODUCTION

Metabolic Syndrome (MetS), also known as "Deadly Quartet" (Kaplan,1988); a clustering of cardiovascular risk factors includes central obesity, elevated blood pressure, raised serum triglycerides (TGs), reduced serum high-density lipoprotein (HDL) and insulin resistance (Gianella-Neto and Gomes Mde , 2009); was first reported by Kylin in 1923 and a clear description was provided in 1988 by Dr. Reaven. It is also called "Syndrome X" (Reaven, 1988).

The prevalence of the MetS is increasing alarmingly throughout the world (Grundy, 2008), particularly in the developing countries. Not surprisingly, the overall prevalence of the MetS increases in parallel with increase in obesity (Hillier *et al*., 2006) (Hollman and Kristenson, 2007). Obesity considered as sixth major risk factor comprising the global burden of disease (Haslam and James, 2005). MetS is recognized as a risk factor for cardiovascular disease (Isommaa et al., 2001) almost doubling its risk (Grundy, 2005). MetS includes clustering of atleast 3 of the 5 traits (Table 1).

Table 1. ATP III‡ and †AHA Clinical Criteria for Metabolic Syndrome.

Risk Factor		Levels
Blood pressure*		≥130/ ≥85 mmHg
Waist circumference	Men	≥40 in.(≥102 cm)
	Women	≥35 in.(≥88 cm)
Triglycerides*		≥150 mg/dl
HDL-cholesterol*	Men	<40 mg/dl
	Women	<50 mg/dl
Fasting blood sugar(i.e. glucose)*		≥100 mg/dl

*Or receiving specific medication; ‡(Grundy, 2005) †(Website no:1).

Central Obesity, a key player of MetS:

Central obesity is a strong predictor of the MetS (Maison *et al*., 2001) (Bergman, 2007) and waist circumference (WC) is proved to a better indicator of obesity as compare to others such as BMI, WHR etc (Brenner *et al*., 2010) (Chan *et al*., 1994). Subsequent findings have strongly related central obesity to various metabolic disturbances such as glucose intolerance, hyperinsulinemia, hypertension etc (Vague, 1956) and also have a

characteristic dyslipidemia (Reaven, 2001). According to another study, Individuals with central obesity are more vulnerable to the disturbance in carbohydrates and lipid metabolism. (Krotkiewski *et al*., 1983), central obesity is not only an established risk of diabetes (Ford *et al*., 1997) but also a significant and independent cardiovascular risk factor (Zavaroni *et al*., 1989), still the exact mechanism of its relation as a cause is not fully understood (Despres et al., 2008), but according to Boden and Chen, there are reasons to believe that plasma free fatty acids (FFAs) are the cause for the connection between fat and insulin resistance (Boden and Chen, 1995) because increased fatty acids inhibit the uptake of glucose that is stimulated by insulin reflects the interference of fatty acid with insulin action (involving glucose transport) (Roden *et al*., 1996) (Boden *et al*., 1994), moreover, reduces hepatic clearance of insulin (Björntop, 1991) and induce insulin resistance by increasing the level of TGs, but exact association is still dubious (Shulman, 2000).

The primary clinical outcome of MetS is CVD defined by ATP III. MetS is associated with an approximately 2-fold increase in CVD risk (Galassi and Reynolds, 2006).

MATERIALS AND METHODS

A research was conducted in different laboratories of Karachi (Pakistan) from March 2010 till June 2010. Two groups were designed (control and obese), and definition proposed by AHA and ATP III was used to determine the prevalence of MetS and to study the contributions of MetS variables. A brief questionnaire was prepared to gather information on variables of interest followed by anthropometric measurements and collection of fasting blood samples for evaluation of serum triglycerides, HDL and blood glucose.

Results were presented as mean±SEM and *t* test (for unequal variance) is used to determine the difference between control and experimental group. A value of $p<0.005$ was chosen as the criteria of statistical significance.

RESULTS AND DISCUSSION

Two groups were designed for obese and diabetic patients. Individuals from both sexes, age unmatched, were included in these groups. Total number of obese males participated were 15 and number of obese females were 17 while the total numbers of diabetic male and female participated were 13 and 11 respectively. Prevalence was determined according to criteria defined by NCEP-ATP III and AHA.

In Table 2, obese individuals (male), 40% showed blood pressure ≥130/≥85mmHg or using antihypertensive agents, 73.33% represented low levels of HDL "good" cholesterol (<40mg/dl) and 66.66% showed elevated TGs levels ≥150mg/dl or receiving lipid lowering agents; moreover, 73.33% represented levels of FBS equal to or greater than 100mg/dl and all of them were classified as obese on the basis of waist circumference that's why 100% of them showed waist circumference ≥40in. or ≥102cm, and On the other hand, 64.70% of obese female participants were having elevated blood pressure ≥130mmHg SBP/ ≥85mmHg DBP or using antihypertensive agents, 76.47% and 58.82% represented reduced HDL levels (<50mg/dl) and increased TGs levels ≥150mg/dl respectively or taking lipid lowering medicine and 41.17% showed elevated FBS (≥100mg/dl). All of them (100%) showed waist circumference ≥35in. or ≥88 cm. As a result of these findings, ratio of obese male and female identified with metabolic syndrome was 80% and 70.58% respectively, imparting high prevalence of metabolic syndrome in obese men as compare to obese women.

In Table 4, the ratio of obese male and female observed to be comparable for 3 factors of metabolic syndrome (HDL, TGs and waist circumference) 91.66%, 83.33% and 100% respectively. More females (75%) were found with BP ≥130/85 mmHg or receiving antihypertensive medications as compare to males (50%). Another prominent difference was noted for FBS i.e. percentage of male obese subjects (83.33%) was higher than female obese subjects. (58.33%)

In Table 3, group of control males, mean age was 45±3.62 year, for obese and diabetics this ratio was 50.66±4.02 year and 56.8±2.38 year respectively. Mean BMI was 23.60±1.78 kg/m² in control, 28.07±0.92 kg/m² in obese and 25.88±0.94 kg/m² in diabetic whereas calculated mean waist circumference in control group was 34.73±1.10 inches and in case of obese and diabetic groups this ratio was high i.e. 41.25±0.49 inches ($p<0.05$) and 37.05±0.48 inches ($p>0.05$) respectively. Mean systolic blood pressure of control, obese and diabetics was 120.25±2.54mmHg, 124.5±2.13 mmHg and 123.6±3.98 mmHg respectively. And mean diastolic blood pressure was noted as 79±1.30mmHg for control, 82.83±2.15 mmHg for obese and 83.2±2.68 mmHg for diabetics. Changes observed in BP among groups were non-significant ($p>0.05$). In addition to this, mean for plasma HDL concentration was 35.87±2.03 mg/dl in control group, 35.78±2.39 mg/dl in obese and 37.83±1.55 mg/dl in diabetic group; moreover, mean value of triglyceride concentration of male subjects was higher in diabetic group i.e. 188.85±36.11 mg/dl as compare to control i.e. 145±21.39 mg/dl, and obese showed highest mean value among all

groups i.e. 214.27±33.66 mg/dl but this increase was non-significant ($p>0.05$). Similarly, in case of fasting blood sugar the mean was higher in obese i.e. 111.08±3.51 mmHg as compared to control i.e. 98.12±5.20 mmHg ($p>0.05$) while diabetics represented highest mean value i.e.132.77±14.54 mmHg ($p<0.05$).

Table 2. Prevalence of Metabolic Syndrome in Obese subjects According to criteria defined by ATP III and AHA.

Parameters	***Obese Participants***	
	Men (n=15)	***Women (n=17)***
BP* **≥130mmHg SBP/ ≥85mmHg DBP**	6(40)	11(64.70)
HDL* **male<40mg/dl** **female<50mg/dl**	11(73.33)	13(76.47)
TGs* **≥150mg/dl**	10(66.66)	10(58.82)
FBS* **≥100 mg/dl**	11(73.33)	7(41.17)
WC **male≥102cm or 40 in.** **female≥88cm or 35in.**	15(100)	17(100)
Individuals with MetS	12(80)	12 (70.58)

WC=Waist Circumference; **TGs**= Triglyceride; **FBS**= Fasting Blood Sugar;
HDL=High Density Lipoprotein; **SBP**=Systolic Blood Pressure;
DBP=Diastolic Blood Pressure; **BMI**=Body Mass Index.
Numerical values are Mean±SEM.

In Table 5, Control female were normal healthy adults whereas obese and diabetic were having metabolic syndrome. Mean age accounted for control as 48.12±3.73 year, for obese as 55.41±3.33 year and for diabetics as 48.8±1.63 year. For experimental group of control, mean BMI was 24.58±0.78 kg/m² however for obese and diabetic groups this ratio was 30.24±2.08 kg/m² and 25.94±0.57 kg/m² respectively. Mean value of waist circumference was 32.87±0.52 inches in control, 38.64±0.76 inches in obese ($p<0.05$), and 33.5±0.29 inches in case of diabetic group i.e. non-significant $p>0.05$. Systolic blood pressure was noticed high in obese (130.16±3.80 mmHg) ($p>0.05$) and diabetics (134.6±2.82 mmHg) ($p<0.05$) as compare to control (122.5±3.26 mmHg) while there was no significant increase in mean diastolic blood pressure among groups and values were 80.25±0.59 mmHg for control, 82.83±1.38 mmHg for obese and 83.4±3.4 mmHg. In addition to this, mean values for HDL in experimental groups of control, obese and diabetics were 46.12±2.91 mg/dl, 46.5±2.98 mg/dl and 41.3±1.67 mg/dl respectively indicating non-significant decrease ($p<0.05$). TGs levels were 128.75±14.88 in control group, and for obese (164.91±19.67 mg/dl) and diabetics (199.6±24.17 mg/dl) this mean value was higher, significantly increase in diabetics ($p<0.05$) but non significant in obese ($p>0.05$). In case of fasting blood sugar, diabetics showed highest mean among all groups i.e. 142.2±19.17 mg/dl, as compare to control (92.25±3.42 mg/dl) obese were also having high mean value of fasting blood sugar i.e. 107.25±3.90 mg/dl and increase noted as significant both for diabetics and obese. ($p<0.05$).

Table 3. Comparison of the Parameters of MetS between Obese male and female.

Parameters	***Obese Subjects***	
	Male (n=12)	***Female (n=12)***
BP* **>130mmHg SBP/ >85mmHg DBP**	6(50)	9(75)
HDL* **male <40mg/dl**	11(91.66)	
female <50mg/dl		11(91.66)
TGs* **>150mg/dl**	10(83.33)	10(83.33)
FBS **>100 mg/dl**	10(83.33)	7(58.33)
WC **male>102cm or 40 in.**	12(100)	
female>88cm or 35in.		12(100)

WC=Waist Circumference; **TGs**= Triglyceride; **FBS**= Fasting Blood Sugar;
HDL=High Density Lipoprotein; **SBP**=Systolic Blood Pressure;
DBP=Diastolic Blood Pressure; **BMI**=Body Mass Index.
Numerical values are Mean±SEM.

Table 4. Principal Characteristics of the Male Subjects (n=20).

Characteristic	***Control*** **(n=8)**	***Obese*** **(n=12)**
Age (yrs)	45±3.62	50.66±4.02
Height (m)	1.70±0.01	1.74±0.01
Weight (kg)	68.25±4.64	85.58±4.19
BMI (kg/m²)	23.60±1.78	28.07±0.92
WC (in.)	34.73±1.10	41.25±0.49
SBP (mmHg)	120.25±2.54	124.5±2.13
DBP (mmHg)	79±1.30	82.83±2.15
HDL (mg/dl)	35.87±2.03	35.78±2.39
TGs (mg/dl)	145±21.39	214.27±33.66
FBS (mg/dl)	98.12±5.20	111.08±3.51

WC=Waist Circumference; **TGs**= Triglyceride; **FBS**= Fasting Blood Sugar;
HDL=High Density Lipoprotein; **SBP**=Systolic Blood Pressure;
DBP=Diastolic Blood Pressure; **BMI**=Body Mass Index.
Numerical values are Mean±SEM.

In table 2, ratio of obese male and female identified with metabolic syndrome was 80 and 70.58%, respectively, imparting high prevalence of metabolic syndrome in obese men as compare to obese women.

In the study of principal characteristics, the ratio of WC was high in obese male and female whereas changes observed in the values of other variables were non-significant ($p>0.05$) in case of obese male. And in obese female, SBP and FBS were higher as compare to control ($p<0.05$).

Table 5. Principal Characteristics of the Female Subjects (n=20).

Characteristic	***Control*** **(n=8)**	***Obese*** **(n=12)**
Age (yrs)	48.12±3.73	55.41±3.33
Height (m)	1.59±0.02	1.55±0.02
Weight (kg)	62.87±2.43	71.95±3.76
BMI (kg/m²)	24.58±0.78	30.24±2.08
WC (in.)	32.87±0.52	38.64±0.76
SBP (mmHg)	122.5±3.26	130.16±3.80
DBP (mmHg)	80.25±0.59	82.83±1.38
HDL (mg/dl)	46.12±2.91	46.5±2.98
TGs (mg/dl)	128.75±14.88	164.91±19.67
FBS (mg/dl)	92.25±3.42	107.25±3.90

WC=Waist Circumference; **TGs**= Triglyceride; **FBS**= Fasting Blood Sugar;
HDL=High Density Lipoprotein; **SBP**=Systolic Blood Pressure;
DBP=Diastolic Blood Pressure; **BMI**=Body Mass Index.
Numerical values are Mean±SEM.

MetS has received increased attention in the past few years. According to this, obesity is accepted as major player of metabolic syndrome. Prevalence data for the MetS clearly represents that it is a large growing problem all around the world and number of people affected continues to increase (Alberti, 2005). Abdominal adiposity represents a major health hazard, measured by WC, better indicator of the obesity (Meisinger *et al*., 2006). During comparative study of mean values, non-significant results were reported due to following reasons:

1) Some of the subjects were receiving specific medications (i.e. lipid lowering, antihypertensive and antiglycemic).
2) Defined levels are not very high values and can't be considered as abnormal if exist alone, only if present three or more together termed as syndrome.

Available data suggest that it is truly a syndrome, found specially in those having unbalanced nutritional status, lack of physical activity and strong family history. Most of the obese people were having FBS≥100 increasing the risk of diabetes because higher the plasma glucose in non-diabetic persons, the more likely that the person are insulin resistant (Reaven *et al*., 1993). In addition to this, hypertension and disturbed lipoprotein levels may contribute to cardiovascular disease risk (Despres et al., 1988). But the exact underlying mechanism is still unknown.

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