Original Article

Screening of Risk Phenotypes Among Metabolic Syndrome Subjects in Adult Pakistani Population

Muhammad Fiaz[1,2], Ghazala Kaukab Raja[2], Muhammad Saqlain[2], Muhammad Shafiq[1], Ahmareen Khalid[1], Ayesha Siddiqa[1]

[1]Department of Pathology, Pakistan Institute of Medical Sciences, Islamabad, Pakistan
[2]Department of Biochemistry, PMAS Arid Agriculture University Rawalpindi, Pakistan

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*Correspondence:
ch.mohd.fiaz@gmail.com

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ABSTRACT

Background: Metabolic Syndrome is a clustering of multiple risk factors including central obesity, hypertension, dyslipidemia and hyperglycemia. These risk phenotypes of metabolic syndrome (MetS) prevalent world-wide, Therefore, we aimed to identify the frequency of risk phenotypes among metabolic syndrome subjects in local adult Pakistani population.

Methodology: Screening of subjects visiting out-patient department of medicine, Pakistan Institute of Medical Sciences, Islamabad was performed to assess the occurrence of risk phenotypes among MetS subjects in Pakistani population. The Metabolic Syndrome was defined based on International Diabetes Federation (IDF) criteria. Anthropometric and biochemical assay results were recorded. Data was analyzed using SPSS software (16.0).

Results: Our results showed that dyslipidemia (31.50%) and hyperglycemia (30.50%) was most population specific risk phenotypes of MetS. The results showed the order of association of metabolic risk phenotypes to MetS as follows hyperglycemia>dyslipidemia>obesity >hypertension.

Conclusion: The hyperglycemia and dyslipidemia were found be the major risk phenotypes among the MetS subjects and have greater chances of developing MetS among Pakistani Population.

Key Words: Metabolic syndrome**,** Hypertention, Dyslipidemia, Obesity, MetS

Introduction

Metabolic syndrome (MetS) is a combination of complex risk factors such as central obesity, hypertension, dysglycemia, and dyslipidemia. These risk factors if untreated could lead to the development of CVDs and T2D. Since awareness of the health risks of MetS has become global, surveys of the prevalence of MetS have been conducted in different regions of the world and data are also available through scientific databases. The prevalence of MetS in US was more than 25% of the total adult population and 23% in populations of seven European countries. In South India, the prevalence was 20-23%,[1] while it was 18–46% in Pakistan.[2,3] The overall MetS prevalence in the East India urban community is 33.8%, 24.9% in males and 42.3% in females.[4]

MetS is main promoter of risk of developing atherosclerotic cardiovascular disease (ASCVD). In ASCVD, atherogenic plaque is developed by the increase of apoB containing lipoproteins and is accelerated by raised blood glucose, low level of high-density lipoprotein (HDL) and release of certain cytokines which are major risk factors of MetS.[5] The main clinical feature of the MetS is obesity especially the central obesity; measured by weight or waist circumference (WC).[6] Central obesity is outcome of the deposition of adipose tissue that contributes the major role in the occurrence of MetS. The adipose tissue is considered as the endocrine organ that secretes adipocytokine which influence the development of MetS. In addition to free fatty acids (FFA), central obesity is actively involved in much pronounced production of adipokines such as leptin (LEP), tumor necrosis factor alpha (TNF α), interleukin-6 (IL-6), resistin and less production of adiponectin (ADIPOQ). All the adipokines thought to affect different organs like liver, pancreas, gall bladder, skeletal muscles and brain. The disturbance in secretion of adipokines causes the proinflammatory state that may lead to the development of MetS.[7]

Insulin resistance (IR) is among the major causes of the MetS that may be referred to improper response of organs to insulin which normally lowers the glucose levels in blood by stimulating the uptake of glucose into the cells. There is no unifying cause of

IR as it is found to rises with increase in body fat content and insulin sensitivities variation found at different levels of obesity. So, obesity and insulin resistance are interlinked in MetS disease process. When muscle are already overloaded with FFA, Free Fatty Acids in plasma are diverted to liver causing fatty liver and dyslipidemia as a result the output of very low density lipoprotein (VLDL) becomes low and thus TG increased in the blood. Insulin resistance may also influence the glucose intolerance which may be pronounced due to the gluconeogenesis in insulin resistant liver.[8]

Because the etiology of the MetS is unclear so MetS is considered to be the interplay of the life style changes, environmental and genetic factors. There are also different determinants of MetS such as age, diet alcohol, smoking and ethnicity,[9] but excessive weight gain and sedentary life style are major determinants of the MetS.[10]

Methodology

The questionnaire based anthropometric data and blood sampling of subjects was collected by visiting outpatient departments of medicine of Pakistan Institute of Medical Sciences (PIMS), Islamabad, Pakistan. The personals were interviewed and physician's diagnosis based medical records were screened to get the relevant information. The study was approved by the Ethics Committees of PIMS, Islamabad All study subjects gave their written informed consent for participation in study. The MetS subjects were diagnosed using IDF based criterion of diagnosis of Mets.[11]

The measurements for anthropometric data like height, body weight, WC, SBP and DBP were recorded. For the recording of body weight measurement (using an electronic balance), subjects removed heavy clothes and shoes, whereas the wall mounted measuring tape was used for the measurement of height of subjects in standing position and feet together.[1] The WC was measured in the standing position using non-elastic measuring tape. A ratio of body weight in Kg to the height in meter^2 (kg/m^2) was computed to estimate BMI. Twice Blood pressure readings of subjects were taken using a mercury sphygmomanometer in a sitting position and average values were recorded.

After an overnight fast of 12 to 14 hours, a venous blood sample was collected from each subject using disposable sterile syringes in evacuated gel tubes.[1] To obtain serum for biochemical analysis, blood sample was centrifuged at 3500 rpm for 30 minutes within 2 hours of sampling. The biochemical assays for FBG, TG, TC, LDL and HDL were performed on automated chemistry analyzer (Roche Hitachi 912 Chemistry Analyzer, Roche Diagnostics, USA) using commercial kits (Roche Diagnostics, USA).

The results for continuous variables were expressed as mean ± standard deviation (SD). The prevalence of risk phenotypes of MetS were estimated in total study population using proportions difference test. The association of risk phenotypes to MetS was found using Age and gender adjusted model. A nominal two-sided p-value of <0.05 was considered significant. All statistical tests were computed using SPSS v21 software.

Ethical approval was granted by the ethical committee of PIMS on 31-07-2011.

Results

The descriptive statistics based on anthropometric and biochemical data are presented in Table 1. The mean age of subjects was 42.82±8.07 with target age group 25-70 years of adult population for present study. The total body weight and waist circumference in anthropometric parameters were within normal limits, however, a mean BMI of 26.05Kg/m^2 shows over-weight trend of average study population. The mean values of SBP (128.01mmHg) and DBP (87.08mmHg) clearly indicate pre-hypertensive state of sampled population. As for the metabolic profile, only mean fasting TC levels were within optimal ranges (<200mg/dL), but TG, LDL, and FBG levels were raised above the optimal ranges whereas HDL levels were lower than the normal limits. The raised biochemical profiles of TG (172.35mg/dl), LDL (114.06mg/dl) and below optimal levels of HDL (40.98mg/dl) indicate hyperlipidemic condition while raised FBG levels (116mg/dl) indicate hyperglycemic/pre-diabetic state. The frequency analysis of risk phenotypes in MetS subjects is presented in Figure1. The frequency of risk phenotypes in our study was found to be dyslipidemia (31.5 %) hyperglycemia (30.5 %), obesity was (20.5 %), whereas the frequency of hypertension was (17.5 %)

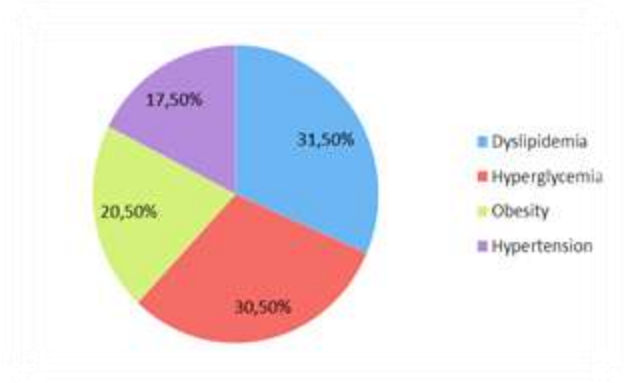

Figure.1 Frequency of metabolic risk phenotypes in total study population

Table I. General Characteristics of Study Population			
Variables	Minimum	Maximum	Means±SD
Age (Years)	23.00	71.00	42.82±8.07
SBP (mmHg)	95.00	210.00	128.04±15.62
DBP (mmHg	60.00	130.00	87.80±11.63
Weight (Kg)	35.00	135.00	70.67±11.94
Height (Meters)	4.00	6.20	5.45±0.29
WC (Cm)	73.66	116.84	86.23±9.04
BMI (Kg/m2)	16.00	42.00	26.05±4.80
TC (mg/dl)	56.00	419.00	189.95±48.34
TG mg/dl)	65.00	630.00	172.35±87.58
HDL (mg/dl)	10.00	98.00	40.98±10.40
LDL (mg/dl)	130.00	411.00	114.06±39.88
FBG (mg/dl)	42.00	647.00	116.00±58.95

Table II. Association of Risk Phenotypes with MetS		
Risk Phenotypes	Odds Ratio (CI at 95 %)	p-value
Sex (Male/Female)	1.11 (0.90-1.14)	0.3
Age (Years)	1.45 (1.18-1.8)	≤0.0001
Hyperglycemia (mg/dL)	6.13 (3.6-10.45)	≤0.0001
Dyslipidemia (mg/dL)	4.17 (3.05-5.7)	≤0.0001
Obesity (BMI > 28.9Kg/m^2)	3.04 (1.88-4.9)	≤0.0001
Hypertension (mmHg)	2.64 (1.9-3.52)	≤0.0001

The association analysis of risk phenotypes to MetS is presented in Table II. The results showed the significant association of all metabolic risk phenotypes with MetS (p≤0.0001) in an age and sex adjusted model. The table showed the order of association of metabolic risk phenotypes to MetS as follows;
hyperglycemia>dyslipidemia>obesity>hypertension. The association analysis showed the strong association of hyperglycemia (OR=6.13, CI=3.6-10.45), dyslipidemia (OR=4.17, CI=3.05-5.70), obesity (OR=3.04, CI=1.88-4.90) and hypertension (OR=2.64, CI=1.90-3.52) with MetS.

Discussion

The metabolic syndrome is combination of risk phenotypes such as central obesity, hypertension, hyperglycemia and dyslipidemia. These risk phenotypes contributes to the development of MetS over the world. In our study, the contribution of these risk phenotypes to MetS population was explored. The association analysis results showed highly strong correlation (p≤0.0001) of hyperglycemia with MetS. Thus, hyperglycemia proved to be one of the major disease risk factors increasing susceptibility towards MetS as compared to the other risk factors. Besides, high prevalence of hyperglycemia in our study population clearly indicates that it is an alarming health burden for Pakistani population. The major causes for hyperglycemia explored were high consumption of saturated fats high salt diets, carbonated drinks and high fructose containing pre-packed juices.[12]

The second highly associated metabolic risk phenotype with MetS in our study population was dyslipidemia (Table 2). Dyslipidemia is characterized by raised level of TG and low levels of HDL. This derangement of lipid parameter has been reported for significant association with MetS and development of CVD. [13]

According to association analysis results, dyslipidemia is the second main predictor of MetS in our Pakistani study population cohort. The subjects diagnosed with MetS carry 4.17 times higher risk of being dyslipidemic (OR = 4.17, CI = 3.05-5.7, p≤0.0001) as compared to control non-MetS subjects. Thus, dyslipidemia does seem to be a strong predictor of MetS, after hyperglycemia in our study cohort. In present study an overall dyslipidemia frequency of 31.50% was found among MetS patients along with 88.2% with low HDL levels, High prevalence of low HDL cholesterol has been reported in 4% of Asian Indian men while 5% Asian Indian women had optimal HDL levels.[14] With advanced age, the incidence of dyslipidemia which could increase the risk of MetS development. Dyslipidemia has been linked with high intake of saturated fats, high sucrose diets and sedentary lifestyle which also increases the risk of hypertension, weight gain, and central obesity.[12]

Our risk phenotypes result clearly indicate obesity being the third most common health issue in

the study population. Obesity is declared as an endemic in different world populations.[15] Increased body weight is reported as a key risk factor of hypertension as well as insulin resistance which could ultimately lead to the development of MetS. Obesity associated insulin resistance is shown to result from the increased production of cytokines and a decrease in adiponectin levels which is the main cause of MetS. If left un-checked, these health complications could lead to the development of CVDs and T2D, the major causes of death worldwide.[16]

Our analysis clearly demonstrates hypertension as an important predictor of MetS in our study in Pakistani population. Hypertension increases the risk of developing MetS which have an increased CHD risk and risk of developing T2D.[17] The studies as Framingham study and Prospective Cardiovascular Munster (PROCAM) study which were conducted in United States and Germany respectively have been predicted the risk of CVD in originally asymptomatic individuals.[18,19] These studies have identified the major risk factors of CVD such as diabetes, hypertension and HDL cholesterol concentrations. Overall, the results of present study indicate a very high dyslipidemia and hyperglycemia ratios of MetS diagnosed patients screened from the total studied population which is an alarming health risk if not taken care of seriously, could put one at an increased risk of developing CVD and T2D.

Conclusion

The Hyperglycemia and dyslipdemia are proved to be the major disease risk factors increasing susceptibility towards MetS as compared to the other risk factors of MetS in Pakistani adult population. Besides, high prevalence of hyperglycemia and dyslipidema are alarming conditions for development of MetS. Therefore, there is need of awareness study regarding sedentary life style and dietary pattern to prevent occurrence of state of hyperglycemia and dyslipidemia which may increase the chances of developing MetS in Pakistani adult population.

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