



Research Article

**A STUDY OF PARAMETERS OF METABOLIC SYNDROME AS BIOCHEMICAL MARKERS IN OBESE
AND NON-OBESE INDIVIDUALS**

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Abstract: Metabolic syndrome is wide spread among adult population in world and increases with age. It consists of a cluster of risk factors that are predictive of the progression to Type 2 Diabetes Mellitus and coronary heart disease. It can be detected with the help of measurement of parameters HDL-cholesterol, triglycerides, blood pressure, fasting plasma glucose, and waist circumference. The present study is undertaken in young persons between ages of 18-35 years to identify the risk factors of Metabolic Syndrome in persons of obesity and compared with the persons of non-obesity using the above parameters of Metabolic Syndrome to know the risk of obesity and overweight. CVD remains the most widespread health care problem of the world. Recently, the Metabolic Syndrome (MetS) has received an increasing amount of attention because of the growing prevalence of obesity and its association with heart disease. Longitudinal observational studies have confirmed that the MetS is a risk factor for the subsequent development of CVD and mortality. Although the scientific basis for the MetS is still debated, its clinical value in identifying individuals who have risk factors are at an increased risk for CVD is undisputed. Lifestyle intervention is fundamental and should be introduced, maintained, and reinforced in all individuals. Pharmacotherapy, targeting individual risk factors, should be guided by global risk assessment and accepted treatment guidelines.

Key words: CVD, diabetes, Metabolic syndrome, Obesity, parameters, risk factors

INTRODUCTION

The metabolic syndrome (MetS) consists of a cluster of risk factors that are predictive of the progression to Type 2 Diabetes Mellitus (T2DM) and coronary heart disease (CHD). Defining the MetS has not been an attempt to declare the existence of a new disease produced by a single pathogenesis, but rather to put together risk factors that as a group have a greater predictive ability for disease than is the case if they are considered separately. It can be a signal to health care physicians that patients who present with such a cluster are at much greater danger of morbidity and mortality from T2DM and Coronary Heart Disease (CHD) than are patients who do not. Insulin resistance is an underlying central component of the MetS. This was the main thrust of the first description of the syndrome by Reaven in 1988¹

Detection of Metabolic Syndrome

The two most widely used definitions in the past have been those proposed by the National Cholesterol Education Program (NCEP)² (Box 1) and by the World Health Organization (WHO)³ (Box 2), but varying versions have been put forward by other organizations⁴. Also, a modification of the NCEP⁵ has been published, and most recently the International Diabetes Federation (IDF) (Box 3) has modified the WHO definition further⁶ Having any three of the five risk factors is considered diagnostic for MetS.

The IDF definition is more recent and it will likely replace the WHO definition. The NCEP-MetS was developed as a tool to identify individuals at high cardiovascular risk,

taking into account the evidence of increased obesity and decreased physical activity around world, whereas the WHO-MetS and the IDF-MetS were developed more as efforts to emphasize insulin resistance as a clinical risk paradigm.

Box 1. NCEP Adult Treatment Panel III (ATPIII) Definition of the metabolic syndrome—any three or more of the following:

Waist circumference >102 cm (40 in) in men and >88 cm (35 in) in women
Serum triglycerides >150 mg/dL (1.7 mmol/L)
HDL cholesterol <40 mg/dL (1.0 mmol/L) in men and <35 mg/dL (1.3 mmol/L) in women
Blood pressure >130/85 mm Hg
Serum glucose >100 mg/dL (5.6 mmol/L)—changed in 2004 from 110 mg/dl (6.1 mmol/L)

Box 2. WHO definition of the metabolic syndrome

Glucose intolerance, impaired fasting glucose, diabetes, or insulin resistance (assessed by clamp studies), plus at least two of the following criteria:
Waist-to-hip ratio of >0.90 in men and >0.85 in women
Serum triglycerides >150 mg/dL (1.7 mmol/L), or HDL cholesterol <35 mg/dL (0.9 mmol/L) in men and <39 mg/dL (1.0 mmol/L) in women
Blood pressure >140/90
Urinary albumin excretion rate >20 ug/min or albumin:creatinine ratio >30 mg/g

OBESITY AND ITS PREVELANCE

The current epidemic of obesity has arisen from a gradual weight gain that appears to have affected all segments of the population over the past several decades⁷. As a result of this consistent, gradual weight gain, the

prevalence of excessive weight gain and obesity continues to increase. It is estimated that childhood obesity has tripled in the last 40 years⁸. Unfortunately, we can now say the majority of world population is currently at an unhealthy body weight that needs some type of management from health care providers.

Box 3. IDF consensus worldwide definition of the metabolic syndrome

Central obesity (defined as waist circumference >94 cm for European men and >80 cm for European women, with ethnicity-specific values for other groups), plus any two of the following four factors:

- Raised triglyceride level >150 mg/dL (1.7 mmol/L), or specific treatment for this lipid abnormality
- Reduced HDL cholesterol <40 mg/dL (0.9 mmol/L) in males and <50 mg/dL (1.1 mmol/L) in females, or specific treatment for this lipid abnormality.
- Raised blood pressure: systolic BP>130 or diastolic BP >85 mm Hg, or treatment of previously diagnosed hypertension
- Raised fasting plasma glucose (FPG) >100 mg/dL (5.6 mmol/L), or previously diagnosed type 2 diabetes. If above 5.6 mmol/L or 100 mg/dL, oral glucose tolerance test (OGTT) strongly recommended but is not necessary to define presence of the syndrome.

This increase in the prevalence of overweight and obesity is concerning primarily because excessive body fat is linked with a long and growing list of comorbidities and adverse health complications. Increasing rates of overweight and obesity translate directly into increased incidence of type 2 diabetes, heart disease, high blood pressure, sleep apnea and certain cancers⁹. Increasing body fat, especially visceral fat, is also associated with increase in the prevalence of the metabolic syndrome¹⁰. Because of these associations, the increase in overweight and obesity are a major public health crisis for the population of the world¹¹.

PREVENTION OF OBESITY

There is general agreement about the urgent need to address the epidemic of obesity, but, there is no general agreement about how best to do this. Past efforts to produce and maintain weight loss have not been over all success, either in obese adults or children¹². One of the reasons for the lack of long term success may be related to the fact that substantial weight loss requires substantial lifestyle changes. Big lifestyle behavioral changes require big efforts. Many experts believe we may have more success in preventing obesity than in reversing it once it is established. Preventing excessive weight gain in children and adults may be our best chance of stopping the obesity epidemic and should be a major public health goal. Furthermore, this goal can be accomplished by promoting small, achievable changes in diet and physical activity¹³.

REVIEW OF LITERATURE

1. **The insulin resistance syndrome** by Jennifer B. Marks, M.D. University of Miami A PROCAM (Prospective Cardiovascular Munster) study in which the relation between cardiac risk factors and incidence of heart attack over a four year period examined 2,754 men aged 40-65 years results showed that

- Presence of diabetes or high blood pressure alone increased the risk of heart attack by 2.5 times.
- Both diabetes and high blood pressure were present; the risk was increased 8 times.

- Abnormal lipid profile increased the risk 16 times.
- Abnormal lipid profile levels were present with high blood pressure and /or diabetes the risk was 20 times higher.

2. Syndrome 'x' and Insulin resistance by

Pat Kendall, Ph.D., Food science and Nutrition specialist. Colorado state university, Co-operative Extension. This syndrome 'x' was coined by group of researchers at Stanford university to describe cluster of symptoms including high blood pressure, high triglycerides, decreased HDL and Obesity which tend to appear together in some individuals with increased risk for diabetes and heart disease. The term syndrome 'x' also linked with insulin resistance. Persons with insulin resistant cells respond sluggishly to the action of insulin. Following meal there will be elevated glucose circulating in the blood signaling more insulin to be released from pancreas, until glucose is taken up by cells. About 10-25% of adult population may be resistant to insulin.

3. Syndrome 'x' Overcoming the silent killer that can give you a heart attack

--Gerald M. Reaven, et .al, Professor of Medicine at StandFord University. This metabolic dysfunction leads to a cluster of abnormalities with serious clinical consequences like cardiovascular disease and or T2DM.

4. Insulin resistance, metabolic diseases and diabetic complications by

Gaetano Crepaldi et.al .Insulin resistance was recognized as a feature and a pathogenic mechanism in pathological states such as T2DM and obesity. More recently it has become apparent that impairment in insulin action is shared by a variety of conditions not necessarily associated with diabetes or obesity

5. **Dr James B. Meigs, M.D, MPH**, Assistant professor of Medicine, General Medicine Division, Harvard Medical School and Massachusetts General Hospital, Boston. According to him large waist circumference (WC) and low HDL, high triglyceride dyslipidemia increase the specificity of diagnosis of Metabolic Syndrome.

MATERIALS AND METHODS

The present study was done on 65 individuals between the ages of 18 and 35yrs of age randomized to 2 groups as follows. Written voluntary informed consent was taken from the participants and the study was approved by the Institutional Ethics Committee.

Control Group (Without Central Obesity): Men and women who were selected of age between 18 to 35 years, with normal waist circumference (Men below 90cm women below 80cm), without hypertension, diabetes and no other clinical abnormality.

Test Group (With Central Obesity):

Men and women who were selected of age between 18 to 35 years, with increased waist circumference (Men \geq 90 cm; women \geq 80 cm)

Blood sample was taken from each individual for the measurements of following parameters:

Fasting Plasma Glucose (FPG){Colorimetric method, normal range -60 – 100 mg/dl}

Lipid profile(Colorimetric method):

Total Triglycerides, (TTG) {normal range- 50 - 150mg / dl }
 Total Cholesterol, (TCH) {normal range <200mg/dl}
 Total HDL Cholesterol (HDL) {normal range males <40 mg%, females<50 mg% }

Physical Parameters: a) Blood Pressure - Systolic(SBP)&Diastolic (DBP)

The parameters are analysed for the prevalence of metabolic syndrome in both test and control groups.

RESULTS

Measurement of Waist Circumference (WC), Blood Pressure (BP), Fasting Plasma Glucose (FPG), Total Triglycerides (TTG), and High Density Lipoprotein

Cholesterol (HDL) are helpful in identifying cases of Metabolic Syndrome. Male individuals with waist circumference above 90 cm, female individuals with waist circumference above 80 cm were considered as having central obesity, as per IDF criteria.

In our present study controls were selected with normal waist circumference between ages of 18 - 35. The cases of central obesity were selected with increased waist circumference. The mean Waist Circumference (WC) control group (men) 83.06±5.87, and that of the obese group (men) is 102.2±9.2. Whereas the mean WC in women control group is 76.71±4.91 of the women obese group is 90.84 ±7.78.

The various parameters of metabolic syndrome in control and obese(male) groups is presented in table-1 and controls with obese (female)group in table-2. The mean systolic and diastolic blood pressure, fasting blood glucose, triglycerides are higher and HDL cholesterol is lower in male and female obese groups compared to the control group. This indicates the risk of developing metabolic syndrome is higher in the obese group compared to the non obese.

TABLE -1: Comparison of metabolic syndrome parameters in controls and obese males

PARAMETER	CONTROL GROUP mean±SD	OBESE GROUP mean±SD	p VALUE
WC (cm)	83.06±5.87	102.2±9.19	<0.001**
SBP (mmHg)	112.66 ±8.83	120.66±8.83	<0.05*
DBP(mmHg)	76.66±6.17	82.67±4.57	<0.01*
FPG (mg%)	81.33 ±7.01	86.26±11.76	<0.5
TTG(mg%)	79.86±19.52	105.8±41.16	<0.05*
HDL(mg%)	50±4.25	41.73±9.69	<0.01*

** highly significant, *significant

The overall risk analysis for Metabolic Syndrome in the 15 (Fifteen) Obese male group shows 3 (Three) are with >3 risk factors which represents 20% male obese having Metabolic Syndrome. But risk analysis for Metabolic Syndrome in the 15 (Fifteen) Control male group, no single case with >3 risk factors was detected.

Whereas out of 19 (Nineteen) Obese female group, 3 (Three) are with >3 risk factors which represents 15.79% female obese having Metabolic Syndrome but no single case with >3 risk factors was detected in 14(Fourteen) Control female group.

Table -2: Comparison of metabolic syndrome parameters in controls and obese females

PARAMETER	CONTROL GROUP mean±SD	OBESE GROUP mean±SD	p VALUE
WC (cm)	76.71±4.91	90.84±7.78	<0.001**
SBP (mmHg)	112.14 ±8.02	114.74±6.97	<0.5
DBP(mmHg)	77.86±4.26	81.05±4.58	<0.05*
FPG (mg%)	88.43 ±7.65	92.11±12.11	<0.5
TTG(mg%)	81.29±25.99	92.42±55.27	<0.5
HDL(mg%)	51±8.14	44.95±7.28	<0.05*

** highly significant, *significant

Table 3 . Showing Incidence of MetS in Male & Female Obese Groups

	<u>No of Obese</u>	<u>Pre MetS</u>	<u>MetS</u>	<u>% MetS</u>
		R* < 3	R* ≥ 3	
Male	15	12	3	20%
Female	19	16	3	15.79%

* Number of Risk Factors

DISCUSSION

Cardiovascular disease (CVD), particularly coronary heart disease (CHD), remains a major health concern worldwide. Despite the advances in both reperfusion therapy and post myocardial infarction (MI) management, approximately 38% of the people who experience a coronary event in a given year will die from it. Primary prevention is obligatory; it is the most affordable and feasible strategy currently available to us worldwide.

The metabolic syndrome (MetS) comprises multiple features, including visceral obesity, hypertension, dyslipidemia, and impaired glucose tolerance. This constellation of conditions has also become synonymous with insulin resistance syndrome, which may be a more appropriate term, as insulin resistance is likely a primary link between the components of the metabolic syndrome¹⁴.

PATHOGENESIS OF METABOLIC SYNDROME

The relationship of abnormal insulin signaling and secretion, impaired glucose disposal, lipotoxicity, and pro-inflammatory cytokines exacerbate insulin resistance and result in the perturbations of the metabolic syndrome is shown in the following figure(Fig.1).



Fig. 1. The metabolic syndrome. The metabolic syndrome is characterized by visceral obesity, dyslipidemia, elevated triglycerides (TG), low high-density lipoprotein (HDL), hypertension, and impaired glucose tolerance. The perturbations of the metabolic syndrome are the result of abnormal insulin signaling and secretion, impaired glucose disposal, lipotoxicity, and pro-inflammatory cytokines which contribute to and exacerbate the insulin resistant state, where IR is the insulin receptor.

The Global Epidemic Of Obesity

The current epidemic of obesity has arisen from a gradual weight gain that appears to have affected all segments of the population over the past several decades

Central Obesity

The International Diabetes Federation (IDF) by describing ethnic-specific central obesity as increase in waist circumference (WC), emphasizes that the risk of an expanded waist circumference (WC) varies, so that in many parts of the world a lower cut-off than the NCEP cut-off of 40 inches (103 cm) for men and 35 inches (88 cm) for women is too high. Whether such criteria will be widely adopted is unclear at this time, but a consensus conference held in Asia in 2000 strongly recommended it¹⁵, citing adequate evidence.

Hyperglycemia

Hyperglycemia is a continuously ascending independent risk factor for CHD, with no apparent threshold¹⁶.

High Blood Pressure

High blood pressure is associated with an increased risk of CHD¹⁷. Thomas and colleagues¹⁸ reported in a 14-year study that hypertension was the most important risk factor associated with increased cardiovascular mortality among overweight and obese persons who have the metabolic syndrome. A Japanese study also reported that hypertension was the strongest risk factor for the development of carotid plaque¹⁹.

Lipids

The MetS is characterized by the development of a highly atherogenic lipid profile known as atherogenic dyslipidemia²⁰. This is characterized by hypertriglyceridemia, low HDL-cholesterol, increased numbers of small, dense, triglyceride-enriched low-density lipoprotein (LDL) particles, increased remnant lipoproteins, and elevated apolipoprotein B concentrations²¹. As the LDL particles are rather low in cholesterol, LDL-C levels are often normal²². The liver is central to the dyslipidemia of insulin resistance, because it remains more insulin sensitive and increases synthesis of triglyceride-rich very-low density lipoprotein (VLDL) particles²³. This results in fasting hypertriglyceridemia, greater postprandial hyperlipemia, and elevations in triglyceride-rich remnant lipoproteins. All of these are associated with increased CVD risk.

Combination Of Risk Factors

A combination of hypertension and obesity on a background of atherosclerotic dyslipidemia and impaired fasting glucose contributes greatly to future CHD risk. Numerous studies have documented a relationship of the MetS defined by one of the MetS clusters and CHD²⁴. The MetS has been shown to be associated with an increasing risk of both all-cause mortality and CVD mortality²⁵. Some components are more important than others for CVD risk assessment. Hyperglycemia, low HDL, and high blood pressure have been found to present greater risk in two studies²⁶, whereas other study suggested that blood pressure and low HDL were most important²⁷.

CONCLUSION

Measurement of Waist Circumference, Blood Pressure, Fasting Plasma Glucose, Triglycerides and HDL cholesterol are useful as screening tools for assessing level of risk of complications like T2DM and Cardiovascular Disease (CVD) and for detection of metabolic syndrome.

In our present study depending upon waist circumference individuals classified into obese and non obese, the study

shows that young obese men and women are more prone to metabolic syndrome compared to those of non obese.

The important concept for physicians to understand from the Metabolic Syndrome paradigm is that they are subclinical patients at risk for T2DM and CVD who can be identified much earlier than they are presently, and in whom preventive treatment is likely to be effective in delaying the onset of disease.

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