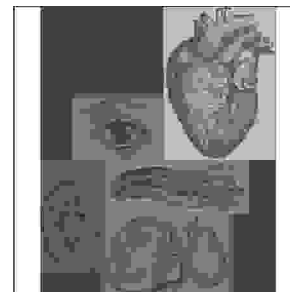


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PROF-1154

## TYPE 2 DIABETICS COMPONENTS OF THE METABOLIC SYNDROME

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**ABSTRACT...** mohsin\_rana64@yahoo.com. **Introduction:** The combination of hypertension, dyslipidemia, central obesity with insulin resistance or hyperinsulinemia or glucose intolerance has been termed the "Metabolic Syndrome." This syndrome is a powerful determinant for cardiovascular disease. Presence of one risk factor mandates search for other factors. Hypertension and obesity and smoking are assessed clinically while Hyperglycemia and dyslipidemia are detected by lab screening. **Objective:** To detect the other component of metabolic syndrome in type 2 diabetics. **Design of study:** Observational study. **Setting:** At Al-Shifa Metabolic Center, Faisalabad. **Study Period:** From January 2005 to June 2006 **Materials And Methods:** All patients with type2 diabetes mellitus were assessed for hypertension, central obesity and fasting serum cholesterol to define the different components of the Metabolic Syndrome. on diabetics presenting for routine consultancy. **Results.** A total of 8300 labeled type2 diabetics were enrolled. Random blood sugar, blood pressure and central obesity by waist hip ratio were assessed and appointment was given for complimentary screening of fasting serum cholesterol and triglyceroid level. Only 2656 presented for screening of lipids and only this group was evaluated further. 92% of patients were between 30-70 years of age. 8% were above the age of 70. There were 39% males and 61% females, 39% of diabetics had hypertension, 60% were centrally obese, 69% had fasting serum cholesterol level above 150 mg/dL and 49% had fasting serum triglyceride level above 150mg/dl. **Conclusion.** Diabetes Mellitus, obesity, especially the central type, hypertension and dyslipidemia are metabolically linked together. All of these are clustered together quiet frequently. These are well-established risk factors for coronary heart disease, the major cause of mortality. Treating hyperglycemia alone in diabetics does not protect coronaries. All of the risk factors shall be defined and treated together in every patient at risk of CHD. Treating obesity is beneficial in glycemc, lipemic and hypertension control.

**Key words:** Diabetes, Obesity, Dyslipidemia, Metabolic Syndrome

## INTRODUCTION

Diabetes Mellitus (DM), Hypertension (HTN), Obesity, Smoking, Hypercholesteremia, Hypertriglyceridemia and hyperurecemia are all recognized and modifiable risk factors for Coronary Heart Disease (CHD). They often occur in combination. This is especially true with diabetes, obesity, hypertension and dyslipidemia. The combination of hypertension, dyslipidemia and central obesity with insulin resistance or hyperinsulinemia or glucose intolerance has been termed the "metabolic syndrome." This syndrome is a powerful determinant of cardiovascular disease<sup>1</sup>. According to the (American) Third National Health and Nutrition Examination Survey (NHANES III) and the (National Cholesterol Education Program (NCEP) the incidence of the metabolic syndrome is around 44% in the U.S. population over 50 years of age<sup>2-4</sup>. It is inferred that presence of one CHD risk mandates search for others.

Diabetes mellitus is a life long disease known to cause complications in almost each and every system of the body. Of these complications coronary heart disease is the leading cause of morbidity and mortality so much so that type2 diabetes is considered to be a CHD equivalent state right at the diagnosis. Presence of more than one coronary heart disease risk factors not only increases the mortality individually but also multiplies to increase the risk. It is responsibility of the treating physician to define these commonly co-existing CHD risk factors in each diabetic. It is only then possible to recommend the necessary behavioral change, dietary modification and the appropriate medicine. The following study was carried out to fulfill the responsibility and to share the experience with fellow colleagues.

## MATERIALS AND METHODS

This study was carried out at Al-Shifa Metabolic Center, Faisalabad, Pakistan, from January 2005 to June 2006, on diabetics presenting for routine consultancy.

On the first visit diagnosis of type2 diabetes was confirmed through available record and random blood sugar was checked by glucometer. Blood Pressure was recorded in lying, sitting and standing position. We

selected sitting Blood Pressure as the reference for this study because this is closer to the actual clinical scenario. Basic biodata, weight in Kilograms with ordinary clothes and height in Centimeters without shoes was recorded. Waist circumference was measured at the level of umbilicus in lying position and hip circumference was measured as the widest level of the buttocks<sup>5</sup>.

Diabetes was defined as a fasting glucose level of  $\geq 126$  mg/dl or a 2-hour post-prandial plasma glucose level of  $>200$  mg/dl. Sitting blood pressure above 140/90 in the absence of antihypertensive medicines or a lower blood pressure reading with present use of relevant drugs with documented previous higher readings was accepted as Hypertension. Body Mass Index (BMI) was calculated as weight/height in (meters<sup>2</sup>) (kg/m<sup>2</sup>). Waist Hip Ratio (WHR) was calculated as waist circumference (cm) divided by hip circumference (cm) in accordance with Retzlaff et al<sup>6</sup>. Obesity is decided on the basis of standard weight- height scales, and on calculated BMI index or by WHR. BMI of more than 28 was considered as medically significant. Abnormal Waist: Hip ratio (WHR) is decided on the basis of Sex as per standard i.e.  $>0.85$  in females and  $>0.9$  in males. Waist circumference  $>102$  cm ( $>40$  in) for men and  $>88$  cm ( $>35$  in) for women was accepted to label central obesity. Serum level above 150mg/dl was considered to be dyslipidemia for both fasting cholesterol and triglyceroid<sup>6</sup>.

Patients were given appointment for complimentary screening of overnight fasting blood Sugar, total serum Cholesterol and fasting Triglyceroid level in specially arranged camp through courtesy of Pharmaceuticals. All three tests were carried out on Accutrend GCT meter manufactured by Roche that uses ELISA technique on capillary blood. This data was added to their Performa. If patient had already been investigated recently for lipid profile i.e. within last six months, this data was accepted for recording.

Only those diabetics who presented for lipids screening or presented with results were entered for final evaluation.

**INCLUSION CRITERIA**

Any patient presenting with valid diagnosis of type2 Diabetes Mellitus.

**EXCLUSION CRITERIA**

Patients <30 and >80 Years of age, patients not able to stand erect for any reason, patient with ascites of any cause, seriously sick patient, patients with history suggestive of Myocardial Infarction in last 4 months, patients on lipid lowering agents without a prior testing for serum lipids.

**RESULTS**

A total of 8300 type2 diabetic patients were invited in the study. All were given appointment for complimentary screening for fasting Cholesterol and Triglyceroid.

A total number of 2656 patients presented for testing Fasting blood sugar, Fasting Total Cholesterol and Fasting Triglyceride. These were evaluated for different parameters. There were 1030(38.78%) Males and 1626 (61.22%) Females. Majority (92%) of patients were between 30 to 70 years of age.

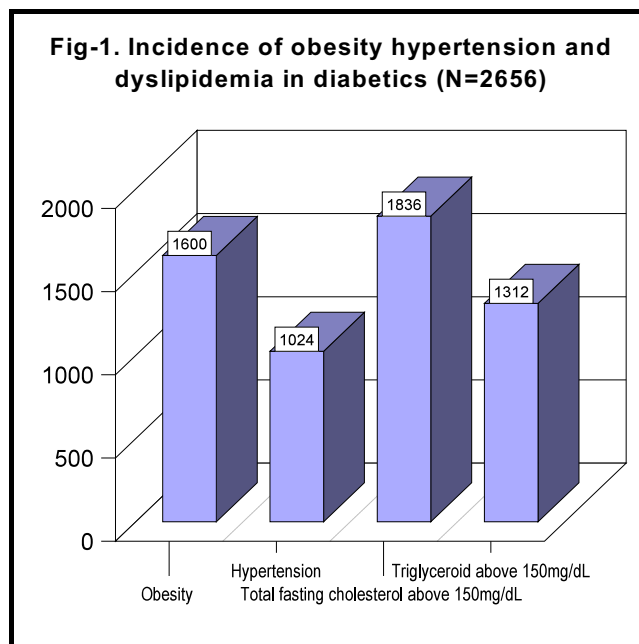
Among diabetics 60% were obese by standard weight: height scale or had BMI>30 or had abnormal WHR, 39% were Hypertensive, 69% had fasting serum Cholesterol level above 150mg/dl and 49% had serum fasting Triglyceride level above 150 mg/dl. Table, I.

Count (%)	Diabetics	Condition
1600 (60.24%)	Diabetics	were obese
1024 (38.55%)	Diabetics	had HTN
1836 (69.12)	Diabetics	had total fasting cholesterol above 150 mg/dl
1312 (49.4%)	Diabetics	had triglyceroid above 150 mg/dl

**DISCUSSION**

Metabolic syndrome and its implications are now well established. From clinical point of view the most

important observation from this study is the remarkably low turnout for lipids screening i.e. only a third of patients bothered to make a special visit even if it was complimentary. It points to the behavioral problem at both patients and clinicians part.



Age (yrs)	No of pts	%age
30-40	212	8%
41-50	372	14%
51-60	1116	42%
61-70	744	28%
71-80	212	8%

This could be attributed to my team and me, which could not stress upon the patients about the importance of this screening. Or it reflected the general non-caring attitude of the patients. Logically speaking we were trying to conduct a study specially designed to the screening program; we should have been able to convince many more patients for the screening of lipids. If only one fourth of the patients could be convinced with special effort, the actual ground situation in clinical practice shall

be much worse. The similar situation was reflected in the report by Gleeson et al.<sup>7</sup>, where even in a managed care setting only 69% diabetics were screened for cholesterol. Goal attainment for HbA1c, High Density Lipoprotein Cholesterol (HDL-C) and Triglyceride was 37%, 37%, and 34%, respectively, while even fewer patients (23%) attained the Low-Density Lipoprotein cholesterol (LDL-C) goal. The proportion of diabetic patients on insulin, oral agents, or combination therapy (insulin and oral agents) was 72%, while the overall medication rate for lipid control was only 28%. Of those with LDL-C < 100 mg/dL, 53% were on lipid lowering medication, compared to 33% of those with borderline (100-130 mg/dL) and 35% of those with high-risk LDL-C (>130 mg/dL), respectively. This clearly points towards inadequacy in the management of lipemic axis. Another study by Inzucchi et al.<sup>8</sup> reported the inadequacy of coronary heart disease risk factors control in diabetes.

They have strongly suggested that control of hyperglycemia, the cardinal manifestation of Type 2 DM, has not been unequivocally demonstrated to reduce the incidence of coronary artery disease (CAD). Control of other features of the metabolic syndrome such as hypertension, dyslipidemia, body weight, and hypercoagulability, appear to be more important. These studies and our results very strongly point to the need for a much more concrete and directed effort on the part of clinicians to stress upon the screening of other CHD risk factors in susceptible patients.

The NCEP ATP III panel (1) defined metabolic syndrome as the presence of three or more of the following risk determinants:

1. Increased waist circumference (>102 cm [>40 in] for men, >88 cm [>35 in] for women);
2. Elevated Triglyceride ( $\geq 150$  mg/dl);
3. Low High Density Lipoprotein (HDL) cholesterol (<40 mg/dl in men, <50 mg/dl in women);
4. Hypertension ( $\geq 130/\geq 85$  mmHg);
5. Impaired fasting glucose (IGT) ( $\geq 110$  mg/dl).

We did not go for IGT testing and HDL testing due to

logistic reasons and only included the labeled diabetic patients as the initial point. As serum cholesterol screening is an accepted approach, we decided to include total cholesterol and triglyceride as our parameter for dyslipidemia.

Majority (92%) of patients in our study were between 30 to 70 years of age. A progressive increase in visceral adiposity is a common feature of aging, and epidemiological evidence supports its role as a prominent risk factor for insulin resistance, impaired glucose tolerance, overt diabetes, and mortality from atherosclerotic cardiovascular disease. This does contribute toward increasingly higher incidence of metabolic syndrome with advancing age. Patients over 50 years of age shall be the special focus of screening for metabolic syndrome<sup>9-12</sup>.

DM, obesity, especially the central type, and dyslipidemia are so strongly interlinked that they deserve a special discussion in the background of Metabolic Syndrome. There is a large amount of research and clinical data that even in individuals at risk for type 2 DM, insulin resistance and hyperinsulinemia are the earliest common abnormalities at the stage of even impaired glucose tolerance (IGT)<sup>13</sup> or in the first-degree relatives of individuals with type 2 diabetes<sup>14-15</sup>. Effect of abdominal obesity and a low metabolic rate are so strong that they seem to precede the development of insulin resistance in offspring of type 2 diabetic patients<sup>16</sup>.

Looking at it from another angle, prevention treatment strategies have been successfully applied to type 2 diabetes. Lifestyle modifications largely designed to alter fat mass and distribution have been shown to delay the onset of hyperglycemia in individuals at high risk for the disease. Importantly, reduction in visceral adiposity is a common feature of all these interventions. Adipose tissue from different anatomical sites has markedly different effects on metabolic outcomes. Selective removal of visceral but not subcutaneous fats in animal models has an overall dramatic improvement in peripheral and hepatic insulin action<sup>17</sup>. Caloric restriction,

which results in weight loss and decreased intra-abdominal fat (IAF), results in an improvement in an atherogenic lipid profile. However, the changes that follow caloric restriction are compounded somewhat by the fact that insulin sensitivity also improves with weight loss<sup>18-19</sup>.

Similarly, exercise training, which improves the lipoprotein profile, is also associated with reductions in body weight and IAF as well as an increase in insulin sensitivity<sup>20</sup>. Both increased IAF and insulin resistance have been associated with increased hepatic lipase activity, leading to small dense LDL and decreased HDL cholesterol levels<sup>21-22</sup>.

Central adiposity, like hyperinsulinemia and insulin resistance, not only accompanies but also antedates type 2 diabetes<sup>23-25</sup>. There is a strong correlation between free fatty acid (FFA) levels and hepatic glucose output<sup>13-15</sup>. Omental fat contributes to liver insulin resistance by increasing portal delivery of FFAs. This could lead to inappropriately elevated hepatic glucose production, hyperinsulinemia, and eventual beta-cell failure<sup>27</sup>.

BMI cannot be used as a simple means of determining whether an individual is or is not likely to have a lipoprotein profile associated with an increased risk of atherosclerosis. Apparently "lean" individuals can be insulin resistant and have increased amounts of IAF, with this characterization being associated with an adverse lipoprotein profile. Subcutaneous Fat (SCF) is increased in lean subjects who are insulin resistant compared with those who are insulin sensitive, and is further increased in individuals who are obese and insulin resistant. IAF is more strongly associated with an adverse lipoprotein profile than is SCF, the latter more likely reflecting total body fat<sup>28-33</sup>.

Proper management of Hypertension in diabetics is important not only for coronary disease prevention, it is considered to be even more important than the control of hyperglycemia in the prevention of diabetic nephropathy<sup>34</sup>. Its importance cannot be over stressed.

As it is now well established that the desirable value for cholesterol and triglyceride is dependant on the presence or absence of other coronary risk factors. According to latest recommendations of American Heart Association, presence of each coronary risk factor means some more reduction in cholesterol. Accordingly each diabetic or hypertensive or obese or dyslipidemia or smoker or a person with family history of premature coronary related death in near family members shall have less than 150% mg/dl of serum fasting cholesterol. Control of HTN has been considered to be more important than glycemic control in the prevention from an adverse coronary event by famous DCCT trial<sup>35</sup>. Importance of lipemic control over glycemic control has already been discussed.

## CONCLUSION

Diabetes Mellitus, obesity, especially the central type, hypertension and dyslipidemia are metabolically linked together. All of these are clustered together quiet frequently. These are well-established risk factors for coronary heart disease. All of the risk factors shall be defined and treated together in every patient at risk from CHD. Treating hyperglycemia alone in diabetics does not prevent CHD. Treating obesity is beneficial in glycemic and lipemic control and hypertension. Lipids screening in all these patients shall be given more importance.

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