Syndrome X (Metabolic Syndrome) and Diabetic Retinopathy: A Comparative Study in Type 2 Diabetes Mellitus Patients

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ABSTRACT

Objective: To determine the frequency of retinopathy in patients of type 2 diabetes with and without metabolic syndrome.

Study design: Non-interventional: comparative cross sectional study.

Place and duration of study: This study was conducted in West Medical Ward, Mayo Hospital, Lahore, from 15th January 2009 to 15th July 2010.

Patients & methods: Two hundred patients fulfilling the inclusion criteria were selected for this study and divided into two groups. Demographic data of each patient including age, sex, height and weight were collected. Each patient was interviewed about the duration, treatment and complications of diabetes.

Results: In group I, the mean height was 1.60±0.08 meters, mean weight was 68.82±7.36 kilograms and mean BMI was 26.38±1.10 kg/m^2 and In group II, the mean height was 1.56±0.12 meters, mean weight was 81.58±9.85 kilograms and mean BMI was 33.80±3.61 kg/m^2. In group I microaneurysims, dot hemorrhages, blot hemorrhages and hard exudates were found in 12.22% patients. In group II, microaneurysims, dot hemorrhages, blot hemorrhages and hard exudates were found in 25% patients. In group I, there were 10.56% patients in which cotton wool spots was found and in group II there were 11.67% patients in which cotton wool spots was found. In group I, there were 2.78% patients in which new blood vessel formation was found and in group II there were 4.44% patients in which new blood vessel formation was found.

Conclusion: It is concluded from this study that frequency of retinopathy is high in patients with metabolic syndrome as compared to patients without metabolic syndrome.

Key words: Type 2 diabetes mellitus, metabolic syndrome, retinopathy.

INTRODUCTION

The metabolic syndrome is a cluster of metabolic abnormalities including abdominal obesity, glucose intolerance, hypertension and dyslipidemia[1]. It has been postulated that hyperinsulinemia and insulin resistance play a direct role in metabolic syndrome, but supportive evidence is inconclusive[2]. Since increased insulin resistance is usually associated with type 2 diabetes mellitus, most subjects with this disease can be defined as having metabolic syndrome as well[3,4]. Using the NCEP-III or World Health Organization criteria, 70-80% of diabetic subjects are diagnosed with metabolic syndrome[3,4].

Diabetic retinopathy is common sequel of diabetes[5]. Poor glycemic control, disease duration, hypertension and dyslipidemia are considered to be important risk factors for microvascular complications[6]. Persons with metabolic syndrome are more likely to have retinopathy, arteriovenous nicking, focal arteriolar narrowing, generalized retinal

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arteriolar narrowing and generalized retinal venular dilatation than persons without metabolic syndrome[7]. Diabetes mellitus is a syndrome with disordered metabolism and inappropriate hyperglycaemia due to either deficiency of insulin secretion or to a combination of insulin resistance and inadequate insulin secretion to compensate. The prevalence of diabetes mellitus in adults worldwide was estimated to be 4.0% in 1995 and is expected to rise to 5.4% by the year 2025[8,9.]

An international committee of experts in the field has recommended the use of the terms Type-1 and Type-2 diabetes mellitus with Arabic numerals being used rather than roman numerals. Type-2 diabetes mellitus the more common form, accounting for 90% of patients with diabetes[10]. Patients are typically obese, older adults (older than 40 years at diagnosis) with such mild symptoms that diagnosis may occur late in the disease often from complications such as retinopathy or cardiovascular disease. In type-2 diabetes mellitus insensitivity of the tissues to insulin (insulin resistance) and inadequate beta-cell response to blood glucose are characteristic, leading

to overproduction of glucose by the liver and under–utilization by the tissues[11]. Ketosis is unusual as patients have sufficient insulin to prevent lipolysis. Although initially controlled with diet and oral hypoglycemic, many patients eventually need supplemental insulin, making them insulin requiring type-2 diabetics.

The UK prospective study (UKPS) has shown that after ten years of type -2 diabetes mellitus, patients have a twofold greater mortality than the general population and one third of patients have a macro or micro vascular complications that requires clinical attention[12]. Vascular complications account for 75% of deaths. The incidence of coronary artery occlusion at post-mortem is five times higher in diabetics than non-diabetics, regardless of age and sex. There is two to three time increased risk of myocardial infarction. Women with diabetes loose their premenopausal protection from coronary artery disease. Peripheral artery occlusion in legs is 40 times more common in diabetics, leading to claudication, rest pain, ulcer formation and gangrene. Stroke is twice as likely. Patients with diabetes, without a prior myocardial infarction, are at a similar risk of coronary heart disease events as non-diabetic subjects with a prior myocardial infarction. Furthermore, prognosis after the first myocardial infarction is worse in diabetics as compared to non-diabetics.

Hyperglycaemia itself is a risk factor for cardiovascular disease[13]. In absolute terms, a 50 years old individual with diabetes and without clinical evidence of macrovascular disease has a 20% risk of mortality due to cardiovascular disease and a 15% risk of a non-fatal myocardial infarction within next 10 years. This risk is even higher if there are additional associated risk factors (hypertension, dyslipidaemia, obesity) for cardiovascular disease. Type-2 diabetes tends to cluster with other cardiovascular risk factors such as hypertension, central obesity and lipid abnormalities[14,15.] Cardiovascular risk factors occurring together tend to have a multiplicative effect on the overall level of cardiovascular risk.[16] For this reason it is vital to tackle all cardiovascular risk factors together in diabetes mellitus and not just to focus on glucose level. Hypertension occurs more often in patients with diabetes than in individuals without diabetes. The prevalence of hypertension in type-2 diabetes mellitus has been reported to be 30% to 80%[17]. Hypertension is important in diabetes because it accelerate both macrovascular (ischaemic heart disease, stroke, peripheral vascular disease, heart failure) and microvascular complications[18]. Most diabetic complications occur in association with hypertension. Cardiovascular complications account for upto 75% of mortality in patients with type-2 diabetes. Elevated blood pressure is known to contribute micro and macro vascular complications. Fortunately reduction in blood pressure can decrease the risk of these complications.[19] In general only 25% of patients with hypertension have adequate control of blood pressure. Blood pressure goals are lower and thus more difficult to achieve in patients who have diabetes also. Regardless of the type of antihypertensive agents used in reduction of blood pressure, it helps to prevent diabetic complications.

Obesity is associated with increase risk for hypertension, diabetes mellitus and dyslipedemia. Insulin resistance has been proposed as a common link among these risk factors. Obese patients are at risk of early death, mainly from diabetes and coronary heart disease. The greater the obesity the higher the morbidity and mortality rates e.g., men who are 10% overweight have a 13% increased risk of death, while increase in mortality for those 20% overweight is 25%. Reduction in weight reduces these risks.[20] Hypertriglycerdemia often associated with low HDL-cholesterol is common in type-2 diabetes mellitus. The simultaneous presence of high fasting glucose with low HDL-cholesterol or higher total triglyceride further increases the risk for coronary artery disease even upto three fold. Dyslipedemia with poor glycemic control predict coronary artery disease, morbidity and mortality in-patients with type-2 diabetes[21].

MATERIAL & METODS

This Non-interventional: comparative cross sectional study was conducted in West Medical Ward, Mayo Hospital, Lahore, from 15th January 2009 to 15th July 2010. All the patients with diagnosed type 2 diabetes mellitus with and without metabolic syndrome were included in the study. While Type 2 diabetic subjects with advanced renal disease, cardiac disease or liver disease were excluded.

Two hundred patients fulfilling the inclusion criteria were selected and divided into two groups, in group I, 100 patients without metabolic syndrome and in group II, 100 patients with metabolic syndrome. Each patient was explained the purpose of the study and an informed consent was taken. Demographic data of each patient including age, sex, height and weight were collected. Each patient was interviewed about the duration, treatment and complications of diabetes. Blood pressure was recorded of each patient on three visits. Laboratory tests for fasting blood sugar level and fasting lipid profile were collected. The patients were examined by a trained experienced physician with the help of an ophthalmoscope and findings were recorded.

The data was entered in SPSS version 17.0

computer program. Descriptive statistics were calculated. The study variables like age, height, weight, BMI, duration of diabetes, blood pressure, blood sugar level and cholesterol levels were presented as mean and standard deviation. Sex, frequency and type of retinopathy in each group were presented as percentages. Chi square test was used to calculate the significance of difference in the prevalence between two groups. P $\leq$0.05 was taken as significant.

RESULTS

Two hundred patients with type 2 diabetes fulfilled the inclusion criteria were selected for this study. They were divided into two groups, in group I, 100 patients without metabolic syndrome and in group II, 100 patients with metabolic syndrome. The mean age of the patients in group I was 53.30±4.57 years and majority of the patients 95 (95%) were in the age group of 41-60 years. The mean age of the patients in group II was 48.79±2.90 years and majority of the patients 99 (99.44%) were in the age range of 41-60 years of age. In group I, there were 63 (63.33%) patients were male and 36 (36.67%) patients were female and in group II there were 50 (50%) patients were male and 50 (50%) patients were female. The mean duration of diabetes mellitus in group I was 8.86±2.80 years and the majority of patients 73 (73.89%) were in the duration of diabetes mellitus of 7 to 11 years. The mean duration of diabetes mellitus in group II was 6.91±1.94 years and the majority of patients 90 (90.55%) were in the duration of diabetes mellitus of 4 to 9 years. In group I, there were 42 (42.78%) patients who were on insulin and 57 (57.22%) patients who were on oral hypoglycemic drugs. In group II, there were 30 (29.44%) patients who were on insulin and 71 (70.56%) patients who were on oral hypoglycemic drugs.

In group I, there were 70 (70.22%) patients of control diabetes mellitus and 27 (27.78%) patients of uncontrolled diabetes mellitus. In group II, there were 49 (48.89%) patients of control diabetes mellitus and 51 (51.11%) patients of uncontrolled diabetes mellitus. In group I, the mean fasting blood sugar level was 110.18±19.88 mg/dl on first visit and 108.64±20.41mg/dl on second visit. In group II, the mean fasting blood sugar level was 120.56±20.40 mg/dl on first visit and 118.75±22.20 mg/dl on second visit. In group I, the mean systolic blood pressure was 131.44±6.94 mmHg on first visit, 130.28±6.55 mmHg on second visit and 130.17±6.30 mmHg on third visit. In group II, the mean systolic blood pressure was 146.36±9.72 mmHg on first visit, 144.22±8.11 mmHg on second visit and 143.35±7.92 mmHg on third visit. In group I, the mean diastolic blood pressure was

83.33±7.17 mmHg on first visit, 81.50±7.21 mmHg on second visit and 81.50±7.20 mmHg on third visit. In group II, the mean diastolic blood pressure was 96.78±6.98 mmHg on first visit, 95.28±6.15 mmHg on second visit and 94.35±6.02 mmHg on third visit.

In group I, the mean triglyceride was 140.91±9.23 mg/dl, mean LDL cholesterol was 112.49±13.49 mg/dl and mean HDL cholesterol was 47.58±3.20 mg/dl. In group II, the mean triglycerides was 251.21±24.76 mg/dl, mean LDL cholesterol was 192.56±18.56 mg/dl and mean HDL cholesterol was 43.0±3.06 mg/dl. In group I, the mean height was 1.60±0.08 meters, mean weight was 68.82±7.36 kilograms and mean BMI was 26.38±1.10. In group II, the mean height was 1.56±0.12 meters, mean weight was 81.58±9.85 kilograms and mean BMI was 33.80±3.61. In group I, there were 12 (12.22%) patients in which microaneurysims, dot hemorrhages, blot hemorrhages and hard exudates were found. In group II, there were 25 (25.0%) patients in which microaneurysims, dot hemorrhages, blot hemorrhages and hard exudates were found (p 0.018). In group I, there were 10 (10.56%) patients in which cotton wool spots was found and in group II there were 11 (11.67%) patients in which cotton wool spots was found (p 0.358). In group I, there were 3 (2.78%) patients in which new blood vessel formation was found and in group II there were 5 (4.44%) patients in which new blood vessel formation was found (p 0.625)

DISCUSSION

In this study it was aimed to find out the frequency of retinopathy in patients with type-2 diabetes mellitus, with and without metabolic syndrome like hypertension, dyslipidaemia and obesity. In our study the mean duration of diabetes mellitus in group I was 8.86±2.80 years. The mean duration of diabetes mellitus in group II was 6.91±1.94 years. While in the study of Rotimi et al [22] the mean duration of diabetes mellitus was 7 years and in the study of Ashraf et al [23] the mean duration of diabetes mellitus was 13 years. So our results are comparable with the results of Rotimi et al. [24] The associated factors in type-2 diabetes mellitus like, hypertension, dyslipidaemia and obesity are also part of metabolic syndrome. The frequency of metabolic syndrome, defined as association of obesity, NIDDM, hypertension, raised LDL and raised triglyceride, was noted in 2.6% patients above the age of 40 years. In a study conducted at a tertiary health care hospital in a mega city of a developing country. The significant frequency of metabolic syndrome is alarming and we need to strengthen our existing clinical strategies for prevention of obesity, better management of

hypertension and diabetes and increased physical activity to prevent macrovascular complication in type-2 diabetes mellitus. The frequency of hypertension and diabetes mellitus also increases with age. It is seen that these two are then associated with higher incidence of obesity, hypertriglyceredemia and decrease HDL cholesterol. In type 2 diabetes mellitus increased triglyceride and reduced HDL-cholesterol levels are the key characteristic of dyslipedemia. A retrospective study was carried out to find out the percentage of dyslipedemia in type-2 diabetes. It was observed that patient with low HDL-cholesterol and predominance of LDL-cholesterol carry an increased risk of developing coronary artery disease.

In our study, In group I, the mean triglyceride was 140.91±9.23 mg/dl, LDL cholesterol was 112.49±13.49 mg/dl and HDL cholesterol was 47.58±3.20 mg/dl. In group II, the mean triglycerides was 251.21±24.76 mg/dl, LDL cholesterol was 192.56±18.56 mg/dl and HDL cholesterol was 43.0±3.06 mg/dl. The associated factors in type-2 diabetes mellitus like, hypertension, dyslipidaemia and obesity are also part of metabolic syndrome. The frequency of metabolic syndrome, defined as association of obesity, NIDDM, hypertension, raised LDL and raised triglyceride, was noted in 2.6% patients above the age of 40 years. In a study conducted at a tertiary health care hospital in a mega city of a developing country. The significant frequency of metabolic syndrome is alarming and we need to strengthen our existing clinical strategies for prevention of obesity, better management of hypertension and diabetes and increased physical activity to prevent macrovascular complication in type-2 diabetes mellitus. The frequency of hypertension and diabetes mellitus also increases with age. It is seen that these two are then associated with higher incidence of obesity, hypertriglyceredemia and decrease HDL cholesterol. The presence of hypertension and diabetes together with other risk factors like obesity, hyperlipedemia, smoking and atherosclerosis make the prognosis worse.

In our study, in group I, the mean systolic blood pressure was 131.44±6.94 mmHg on first visit, 130.28±6.55 mmHg on second visit and 130.17±6.30 mmHg on third visit. In group II, the mean systolic blood pressure was 146.36±9.72 mmHg on first visit, 144.22±8.11 mmHg on second visit and 143.35±7.92 mmHg on third visit. While comparing with the study of Fawwad et al [25] the mean systolic blood pressure was 129.7±19.7mmHg. In group I, the mean diastolic blood pressure was 83.33±7.17 mmHg on first visit, 81.50±7.21 mmHg on second visit and 81.50±7.20 mmHg on third visit. In group II, the mean diastolic

blood pressure was 96.78±6.98 mmHg on first visit, 95.28±6.15 mmHg on second visit and 94.35±6.02 mmHg on third visit. While comparing with the study of Fawwad et al [25] the mean diastolic blood pressure was 80.9±10.8mmHg.

In our study in group I, the mean height was 1.60±0.08 meters, mean weight was 68.82±7.36 kilograms and mean BMI was 26.38±1.10. In group II, the mean the mean height was 1.56±0.12 meters, mean weight was 81.58±9.85 kilograms and mean BMI was 33.80±3.61. While comparing with the study of Fawwad et al [25-26] the mean BMI was 27.8±4.9kg/m^2. In our study in group I, there were 12.22% patients in which microaneurysims, dot hemorrhages, blot hemorrhages and hard exudates were found. In group II, there were 25% patients in which microaneurysims, dot hemorrhages, blot hemorrhages and hard exudates were found (p 0.018). In our study in group I, there were 10.56% patients in which cotton wool spots was found and in group II there were 11.67% patients in which cotton wool spots was found (p 0.358). In our study in group I, there were 2.78% patients in which new blood vessel formation was found and in group II there were 4.44% patients in which new blood vessel formation was found (p 0.625). While comparing with the study of Rotimi et al [27-28] prevalence of diabetic retinopathy was 17.9%.

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