To Determine the Frequency of Silent Myocardial Ischemia in Type-II Diabetic Patients with Proteinuria

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ABSTRACT

Objective: To determine the frequency of silent myocardial ischemia in type-II diabetic patients with proteinuria.

Study Design: Cross sectional study.

Place and Duration of Study: This study was performed at Department of Medicine in collaboration with department of Cardiology CMC, Hospital larkana from 15-Nov-2011 to 14-May-2012.

Materials and Methods: There was a **n**on probability purposive sampling. All patients who were type-II diabetics and having proteinuria were included in this study. The age of these patients were > 35 years. They were selected for determination of silent myocardial Ischemia. The electrocardiography of all those patients having FBG>126 mg/dl and proteinuria > 150mg/dl was performed. The ETT of all patients was done in cardiology department. Those patients who have normal ETT were labeled negative for silent myocardial ischemia, while ETT positive patients were labeled as having silent myocardial ischemia.

Results: The total no: of 323 patients were included in this study with mean age of 49.9+10.3 years, 270 (83.6%) were male and 53 (16.4%) were female. The ETT was positive in 69 (21.36%) patients.

Conclusion: The frequency of SMI in our study was 21.36%.

Key Words: Silent myocardial ischemia, Diabetes mellitus, proteinuria.

INTRODUCTION

Diabetes mellitus is a disorder that affects the body's ability to make or use insulin. Diabetes results in raised levels of glucose in the blood stream. This can cause severe short-term and long term consequences[1].

Type 2 Diabetes Mellitus accounts for 90% to 95% of all diabetes mellitus cases, caused by combination of complex metabolic disorders that result from coexisting defects of multiple organ sites such as insulin resistance in muscle and adipose tissue, a progressive decline in pancreatic insulin secretion, unrestrained hepatic glucose production, and other hormonal deficiencies. Most affected individuals are obese and, therefore, have variable degrees of insulin resistance. Other risk factor includes increasing age, sedentary lifestyle and is associated with a strong genetic predisposition[2].

Generally, the injurious effects of diabetes mellitus are separated into macrovascular complications (coronary artery disease, peripheral arterial disease, and stroke) and microvascular complications (diabetic nephropathy, neuropathy, and retinopathy)[3].

Diabetic nephropathy is defined as persistently raised urinary albumin excretion rate (UAER) already above arbitrary established normal range, so-called microalbuminuria (UAER >30 mg/24 hours or 20 µg/min, and less than or equal to 300 mg/24 hours or 200 µg/min). Persistently elevated UAER values >300 mg/24 hours or >200 µg/min, should be named macroalbuminuria[4]. Proteinuria is defined as excessive protein excretion in the urine, generally greater than 150 mg/24 h[5]. Angina pectoris has long been considered the cardinal symptom of myocardial ischemia. However it is now known that angina pectoris may be a poor indicator for myocardial ischemia, particularly in patients with diabetes. Coronary artery disease (CAD) in diabetic patients poses diagnostic and therapeutic challenges for clinicians, especially when patients are asymptomatic during episodes of myocardial ischemia. Silent myocardial ischemia (SMI) refers to the presence of objective findings suggestive of myocardial ischemia that is not associated with angina or angina equivalent symptoms. Such objective evidence includes exercise testing or ambulatory monitoring demonstrating electrocardiographic changes, nuclear Imaging studies demonstrating myocardial perfusion defects, or regional wall motion abnormalities illustrated by echocardiography[6]. It is found that the excess of cardiovascular events and mortality occurs in diabetic patients with persistent microalbuminuria, but is particularly evident in macroalbuminuric diabetic patients and results not only from end-stage renal failure (ESRF) but rather from cardiovascular disease (CVD), the latter mainly in type 2 diabetic patients. Microalbuminuria is currently regarded as a marker of generalized endothelial damage; it reflects transvascular albumin leakage, now recognized as an early event in atherogenesis[4]. The prevalence of silent myocardial ischemia (SMI) in asymptomatic microalbuminuric and normalbuminuric type 2 diabetic patients is 30% and 6.6% respectively[7].

The aim of my study is to use proteinuria in type 2 diabetics as useful marker for identifying people with silent myocardial ischemia. Prompt and timely intervention in people found to have silent myocardial ischemia in this way would help in reducing significant morbidity and mortality from cardiovascular events in our country.

MATERIALS AND METHODS

Study design: Cross sectional study.

Setting: This study was performed at department of medicine, in collaboration with department of cardiology CMC hospital Larkana.

Duration of study: This was a six months study from 15-Nov-2011 to 14-May-2012.

Sampling technique: Non probability purposive sampling.

Sample selection:

Inclusion criteria: All patient of age 35 years and above of either sex with type 2 diabetes having proteinuria with duration of type 2 diabetes being more than 5 years.

Exclusion criteria: Following patients were excluded:

1. Patients with known type 1 diabetes.
2. Patients with known ischemic heart disease or any other heart disease.
3. Patients with known renal or urinary tract disease.
4. Patients with fever, pregnancy, regular prolonged standing, regular severe exercise.
5. Patient with hypertension.
6. Patient with hyperlipidemia.

Data collection procedure: The study was conducted after informed written consent, patients were enrolled from Diabetic clinic of Department of Medicine, C.M.C Teaching Hospital, Larkana. Detailed history was taken from all patients aged above 35 years of either sex. Fasting blood samples were taken and sent to CMC hospital laboratory for determination of fasting blood sugar. Patients diagnosed with type 2 diabetes under went 24 hour urinary protein quantification. Those having 24 hour urinary protein greater than 150 mg/dl and fulfilling the selection criteria were selected for determination of silent myocardial ischemia (SMI). Electrocardiography (ECG) of all patients having FBG $\geq$ 126 mg/dl and proteinuria $>$ 150 mg/dl was performed. Protocols of Exercise tolerance test (ETT) were explained to selected subjects and sent to Department of Cardiology for determination of silent myocardial ischemi.ETT of all selected patients was done after thorough explanation of procedure in department of cardiology and interpreted by consultant cardiologist with experience of at least 5 years. Those patients who have normal ETT were labeled negative for SMI, while those patients whose ETT is positive for ischemia were labeled as having silent myocardial ischemia.

Data analysis procedure: Data was entered and analyzed on SPSS version17.0. The frequency and percentages were calculated for qualitative variables like gender, proteinuria and silent myocardial ischemia status. Mean±SD was computed for quantitative variables like age and duration of diabetes. Stratification was done with regard to age, gender and duration of diabetes to see the effects on these outcomes variables through chi-square test. P-value≤0.05 was taken as significant.

RESULTS

A total of 323 patients were enrolled in this study. Of 323 patients,112 (34.7%) were 35-45 years of age with mean age of 49.9±10.3 years (Graph 1) and 270 (83.6%) were male with male to female ratio 5.1:1 (Graph 2).

Of 323 patients, 117 (36.2%) had duration of diabetes between 5-10 years with mean duration of 7.6±2.9 years (Graph 3). The frequency of SMI was 69 (21.36%) (Graph 4).

Stratified analysis based on age, sex, duration of diabetes is summarized in table 1-3.

Stratified analysis showed that frequency of SMI increases as age increases. Silent Myocardial ischemia is more common in patients within age group 66-75 years that is33.3% and is statistically significant (P-<0.001).

Stratified analysis based on sex showed that SMI in male patients is 23.3%compared to female 11.3%, it is statistically significant (P-0.03).

Stratification based on duration of diabetes shows SMI in group of >15 years duration is30.6% and is statistically significant (P-0.01).

Table No.1: Stratification of age in Participants having Silent Myocardail Ischemia.

Ischemic changes in ECG	Age group				Total
	35-45 years	46-55 years	56-65 years	66-75 years	
Yes	15 (13.4%)	12 (17.9%)	15 (23.8%)	27 (33.3%)	69
No	97 (86.6%)	55 (82.1%)	48 (76.2%)	54 (66.7%)	254
Total	112	67	63	81	323

P-value: <0.001

Table No.2: Stratification of sex in participants having silent myocardial ischemia.

Ischemic changes in ECG	Sex		Total
	Male	Female	
Yes	63 (23.3%)	6 (11.3%)	69
No	207 (76.7%)	47 (88.6%)	254
Total	270	53	323

P-value: 0.03

Table No.3: Stratification of duration of diabetes in participants having silent MI

Ischemic changes in ECG	Duration of DM			Total
	5-10 years	11-15 years	>15 years	
Yes	18 (15.3%)	20 (19%)	31 (30.6%)	69
No	99 (84.6%)	85 (81%)	70 (69.3%)	254
Total	117	105	101	323

P-value: 0.01

DISCUSSION

Coronary heart disease (CHD) is the leading cause of death in patients with type 2 diabetes is often asymptomatic[8] and may present without warning as acute myocardial infarction, heart failure, arrhythmia or sudden death. In acute myocardial infarction and heart failure, mortality is increased in the presence of type 2 diabetes, thus emphasizing the potential value of identifying high-risk asymptomatic individuals with diabetes[9].

Microalbuminuria is present in approximately 25% of patients with type 2 diabetes and is associated with a doubling of the risk of early death, mainly from CHD[10].Microalbuminuria has been defined by consensus, as a urinary albumin excretion rate between 20 and 200 µg/min, though rates of 10.6 µg/min have been linked to increased macrovascular events in type 2 diabetes[11]. Silent myocardial ischemia (SMI) can be detected by various methods[12]. Using treadmill exercise testing, SMI has been defined as exercise-induced ST-segment depression in the absence of CHD symptoms, and, in men free from known CHD, this finding has been associated with increased mortality[13-14]. There is very little data on the prognostic value of SMI, detected by any method, in asymptomatic patients with type 2 diabetes[15-17].

The aim of this study was to determine frequency of SMI in patient with type II diabetes and proteinuria. We found that frequency of SMI was 21.36% in our study. The study conducted by Hussein AZF and Strak SK reveals the prevalence of silent myocardial ischemia (SMI) in asymptomatic microalbuminuric and normalbuminuric type 2 diabetic patients is 30% and 6.6% respectively[7].

The reported frequency of silent myocardial ischaemia in diabetics is variable[18-20]. This study results are in line with findings of Caraccilo[21],Chipkinet[al22] and Airaksinen et al[23], with no significant difference in which silent myocardial ischaemia in diabetics was 19%. Burgess et al reported incidence of SMI was 16%[6].Impaired symptom perception contributes to the lack of recognition of painful stimuli. For angina, this may occur at different levels. Potential reasons may include a higher pain threshold, an excess of endogenous endorphins, and a generalized defective perception of painful stimuli. Episodes of silent myocardial ischemia may represent less severe or shorter events than those associated with angina pectoris. In diabetic patients, it is suspected that partial or complete autonomic denervation may contribute to the prevalence of silent myocardial ischemia[6].

In this study as age increases the frequency of SMI increases. Similar to Burgess et al reported frequency of SMI which was higher in old age group[22]

In this study SMI was more common in patients with duration of diabetes >15 years. Similarly other studies also reported that as duration of diabetes increased the frequency of SMI is also increased.

The strength of this study is that we have included patients with diabetes and proteinuria. Most of above mentioned studies only represented association of type II diabetes with SMI.

This study has few limitations. First, it was a cross sectional study with no comparative group. Cohort study is appropriate design to conduct this study but cohort studies take a lot of time and resources and it's not possible to complete this within limited time frame. However this study will serve as hypothesis generating study. Second, we did not ask about control of diabetes. It is possible that long standing uncontrollable diabetes is more prone to develop SMI compared to well controlled diabetics. Third, we did not asked about socio-economic status (SES) history so patients with low SES may be more prone to develop SMI. Fourth, since this was a hospital based study it was not representative of population.

CONCLUSION

It is concluded from this study that
- The frequency of SMI in diabetic with proteinuria is 21.36%.
- Frequency of SMI in diabetic patients with proteinuria within age group 66-75 years is 33.3%.
- Frequency of SMI in male diabetics patients with proteinuria is 23.3% compared to female 11.3%.
- Frequency of SMI in diabetic patients with proteinuria with duration of diabetes of >15 years is 30.6%.

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