INTRODUCTION

Worldwide diabetes mellitus is a major public health issue, its prevalence ranges from 6.9% to 10.4% in developed countries and approximately 7% in developing countries. It is due to the defect in insulin secretion and action or both and is characterized by Hyperglycemia, which is associated with long term damage and failure of various organs like kidneys, nerves, heart, eyes and blood vessels. Globally 463 million people have diabetes. China still has the dubious distinction of diabetic capital of the world with a diabetic population of 111 million and India ranks second with a population of 77 million diabetic patients (IDF Atlas 2019). The morbidity from diabetes is a consequence of macrovascular disease, [cerebrovascular Disease (CVD), Coronary Artery Disease (CAD), and Peripheral Arterial Disease (PAD)] and microvascular disease (Retinopathy, Neuropathy and Neupathy). One of the long-term complications of DM is diabetic nephropathy (DN) and it is leading cause of End Stage Renal Disease (ESRD). Type 2 Diabetic patients may be hypertensive for years prior to the onset of overt diabetes. At the time of diagnosis of type 2 diabetes, hypertension is found in approximately 70-80% of patients and blood pressure rises further in those patients who subsequently develop diabetic nephropathy. Microalbuminuria is the first clinical detectable sign of diabetic nephropathy and is considered as an independent predictor of CKD. The prevalence of MA in patients with type II diabetes has been reported from 20%-61%. The natural history of diabetic nephropathy has generally been viewed as descending path from
normoalbuminuria to ESRD through an intermediate stage marked by microalbuminuria and overt proteinuria.  

Approximately one third of T2DM patients have microalbuminuria and macroalbuminuria, with a greater risk of CKD and progression to ESRD and enhanced cardiovascular disease. Microalbuminuria has been defined using different units of measurements. According to Gento -Mentecatini Convention, MA is present when the urinary albumin excretion rate (UAER) in 24 hr urine or short time collected urine during day time is in the range of 30-300mg /24hr. If not treated and addressed medically nephropathy progresses to chronic kidney disease (CKD) and ESRD. The prevalence of CKD in patients with T2DM is estimated to be approximately 50% worldwide. CKD in such patients decrease the efficacy of oral antibiotic drugs. DM patients with CKD amplify the risk of development of several other complications ranging from heart failure, cardiovascular disease, infections, adverse drug reactions to impaired quality of life and premature death. The mortality rate in T2DM is high because of associated cardiovascular disease. These patients when diagnosed with Microalbuminuria have concomitant hypertension. Beside cardiovascular disease and hypertension in DM patients, microalbuminuria is also an important tool for predicting the morbidity and mortality in patients with peripheral vascular disease. In diabetic patients peripheral artery disease causes significant long term disability because of amputation of lower limb or a part of lower limb. Dyslipidemia is well recognized manifestation in poorly controlled diabetic patients. Metabolic syndrome and insulin resistance syndrome are associated with dyslipidemia which increases the risk of premature coronary artery disease. It was also reported that at onset of DM the detection of dyslipidemia with a corresponding microalbuminuria, therapeutic intervention could control the resulting cardiovascular or renal complications. In individuals with type 2 diabetes microalbuminuria and macroalbuminuria may be associated with diabetic retinopathy than patients with normoalbuminuria.

MATERIALS AND METHODS

This was a cross sectional study and was conducted in Department of Biochemistry and Department of Medicine, Acharya Shri Chander college Of Medical Sciences (ASCOMS) and Hospital Sidhra, Jammu, in collaboration with Department of Biochemistry, Government Medical College Amritsar. Two hundred known type 2 diabetics with and without complications were recruited for the study. The study was approved by ethics committee of ASCOMS and hospital. Informed consent for the inclusion of the patient in study was taken and the purpose of the study was indicated clearly to the participating individuals in vernacular language. Patients with history of urinary tract infection, haematuria, severe anaemia, infection, and hemoglobinopathies were excluded from the study. The detailed history about duration of diabetes, hypertension, their dietary habits, life style, smoking habits and presence of any complications of diabetes were noted, from medical records of patients, as per the Performa designed. All the patients were advised to observe an overnight fast and to comply with the instructions. Blood and urine samples were collected early in the morning. About six ml of blood was collected by venepuncture of the antecubital vein. The blood sample was divided into three vials, one containing anticoagulant (sodium fluoride and potassium oxalate) for estimation of blood glucose, in plain vials for serum separation and a vial containing EDTA for Glycated haemoglobin (HbA1c). Fasting blood glucose was estimated by enzymatic GOD/POD Method. Blood Urea was estimated by GLDH-Urease method. Serum creatinine was estimated by Jaffes Alkaline Picate Method. Glycated haemoglobin was estimated by ion exchange chromatography. Microalbumin in urine was estimated by Pyrogallol Red method. Serum total cholesterol was estimated by enzymatic, CHOD-PAP method of AllainCc. Serum HDL was estimated by the autoenzyme precipitation reagent method in conjunction with autoenzyme cholesterol reagent—for enzymatic determination of HDL cholesterol in the supernatant. Serum LDL-C was calculated by Friedwald’s formula. Serum triglyceride was estimated by enzymatic method of Trinder. Serum electrolytes sodium and potassium were analysed with ion selective electrodes. Serum calcium was estimated by Ortho-cresolphthalein method. Analysis of variance (ANOVA) was applied for comparison between groups. The Chi-square test or Fisher’s Exact test as appropriate, were used to compare all the clinical characteristics of the patients with Microalbuminuria versus those not having microalbuminuria, p<0.05 was considered statistically significant.

RESULTS

In the present study 200 type 2 diabetic individuals were included, out of them 119 (59.9%) were male and their age ranged from 31 to 70 years with mean age of 58 ±11 years, whereas 81 (40.1 %) were females with age range of 37 to 70 years and mean age of 57 ± 9 years. Mean age of all subjects was 57± 6 years. Albumin to creatinine ratio (ACR) in a single urinary specimen is an accepted surrogate of 24 hours urinary albumin excretion. Depending on value of ACR patients were divided in three groups normoalbuminuria (≤30 mg/g creatinine), microalbuminuria (>30-300 mg/g creatinine) and macroalbuminuria (>300 mg/g creatinine). The number of individuals with normoalbuminuria was 57 (28.5%), individuals with microalbuminuria were 84 (42%) and diabetics with overt proteinuria were 59 (29.5%). Mean±SD of all clinical, demographic and various biochemical parameters are mentioned in table 1.

The mean of systolic blood pressure, diastolic blood pressure, creatinine concentration was significantly higher (p <0.05) in people with macroalbuminuria as compared to those with normoalbuminuria and microalbuminuria groups. Levels of blood glucose also increased but no statistically significant difference was observed in different groups. Globulin, Potassium and triglyceride levels increased as microalbumin levels increased from normoalbuminuria to macroalbuminuria, but the values were not significantly associated. However, the values of cholesterol HDL, serum total protein and serum albumin decreased as level changed from normoalbuminuria to macroalbuminuria, the change was not significant except in serum albumin (Table 1).
Patients were divided in 3 groups depending on duration of diabetes. A significant relation was found between HbA1c and duration of diabetes in microalbuminuria, whereas prevalence of microalbuminuria and duration of diabetes were not significantly associated (Table 3).

Patients were divided in 3 groups according to the concentration of glycated hemoglobin (HbA1c). As the degree of Hyperglycemia increased there was an increase in prevalence of CAD and PAD, Neuropathy, Nephropathy whereas in case of CVD and retinopathy prevalence decreased when HbA1c increased (Table 4).

Patients were divided in 3 groups according to duration of diabetes. With increasing duration of diabetes there was an increase in prevalence of complications like CAD, CVD, retinopathy, neuropathy, nephropathy except in PAD (Table 5).

In our study we found no significant association between the prevalence of microalbuminuria and presence of diabetic neuropathy, CVD and PAD, however significant association was observed between microalbuminuria and nephropathy, CAD and retinopathy (p<0.05) (Table 6).

**DISCUSSION**

Prevalence of diabetes is increasing globally and so are its complications. Diabetic nephropathy is a leading cause of CKD and ESRD. Approximately 35% type 2 diabetics develop diabetic nephropathy. Onset of diabetic nephropathy can be prevented if detected early and interventions are incorporated.
before the development of this dreadful complication. Microalbuminuria is a maker of endothelial damage caused by persistent Hyperglycemia and helps in earlier identification of diabetic nephropathy. In present study depending on value of ACR, patients were divided in three groups normoalbuminuria \((\leq 30 \text{ mg/g creatinine})\), microalbuminuria \((>30-300 \text{ mg/g creatinine})\) and macroalbuminuria \((>300 \text{ mg/g creatinine})\). The number of individuals with normoalbuminuria was 57 (28.5%), individuals with microalbuminuria were 84 (42%) and diabetics with overt proteinuria were 59 (29.5%). Prevalence of microalbuminuria in our study was higher than the previous studies. The differences in different studies may be due to the method used for the measurement of albumin, method of urine collection, age distribution, duration of diabetes and patient selection methods. To describe an adequate global picture of development microalbuminuria and diabetic nephropathy, it is necessary to examine data from various continents and with different ethnicity. In our study the values of SBP and DBP increased from normoalbuminuria to microalbuminuria suggesting that hypertension is associated with microalbuminuria, particularly systolic blood pressure, damages the glomerular filtration membrane due to induction of systemic arteriole dysfunction in the kidney (Table 1). Similar findings were also reported earlier by some by Tabassum R et al. Adequate control of BP decreases microalbumin excretion and slow disease progression to overt nephropathy. This suggests emphasizing the use of renin angiotensin aldosterone system (RAAS) inhibitors. The present study showed no significant relation between value of Total Cholesterol (TC) and Triglyceride (TG) in normoalbuminuria and microalbuminuria. These results are consistent to a study done by Tabassum R et al in which they have suggested that MA is independent of plasma TC and TG values to predict renal as well as cardiovascular disease risk. We observed that mean blood glucose levels increased from normoalbuminuria to microalbuminuria suggesting the fact that poor control increases endothelial damage. As the duration of diabetes increased with age, nephropathy was associated with both variables. However, it is difficult to record the duration of the disease in T2DM as it is well known that Hyperglycemia usually begins 4-7 years before diabetes is detected clinically, sometimes well-established complications were present in newly diagnosed patients with diabetes (Table 1).

We observed a strong association between glycemic control (HbA1c) and albuminuria (Table 4). Prevalence of nephropathy was highest 21(24.70%) followed by retinopathy 20(23.52%), CAD 15(17.64%) (Table 2), which is different from other studies. In our study we found no significant association between the prevalence of MA and the presence of neuropathy, not consistent to other studies. Significant association was observed between the prevalence of MA and presence of coronary artery disease which is supported by some authors. Prior studies have reported that the prevalence of albuminuria was significantly associated with PAD; we didn’t observe any association between MA and PAD in our study. This may be due to the small number of PAD cases in the microalbuminuria group. The microvascular complications nephropathy and retinopathy are significantly associated with microalbuminuria (Table 6).

**CONCLUSION**

It was observed that maximum number of complications was present in T2DM patients belonging to microalbuminuria group, suggesting that the early therapeutic intervention in diabetic patients can delay onset of complications and improve outcomes. Assessment of MA therefore is helpful in early identification of patients at risk of developing various microvascular and macrovascular complications and to reduce the burden of diabetic kidney disease in the future. The control of modifiable risk factors, specially hyperglycemia, obesity and hypertension, as well as timely detection can decrease the prevalence of microalbuminuria in diabetic patients as well as development of various complications of diabetes so that burden of diabetic complications can be reduced.

**References**

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