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A CROSS SECTIONAL STUDY OF URINARY MICROALBUMIN AND HBA1C STATUS AMONG TYPE 2 DIABETES MELLITUS PATIENTS ATTENDING IN A TERTIARY CARE HOSPITAL

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ABSTRACT

Introduction: Diabetes mellitus is one of the most common metabolic disorders characterized by chronic hyperglycemia and disturbances in carbohydrate, fat, and protein metabolism due to absolute or relative deficiency of Insulin secretion or its action.

Aims: To study the urinary micro albumin and HbA1c status among Type 2 diabetes mellitus patients, to estimate the urinary micro albumin & HbA1c in type 2 Diabetes mellitus patients and to find out the correlation between urinary micro albumin & HbA1c in type 2 Diabetes Mellitus patients.

Materials and Methods: The present cross sectional study has been carried out for two years among 290 cases of type 2 diabetes mellitus patients fulfilling the inclusion and exclusion criteria attending the diabetic clinic, in the Department of Medicine, in collaboration with Department of Biochemistry Agartala Government Medical College and GBP hospital, Agartala, West Tripura.

Result: In our study showed a positive Pearson correlation of Albumin creatinine ratio vs urinary microalbumin where albumin creatinine ratio correlated positively with urinary microalbumin ($r=0.8$), which is statistically significant at ($p<0.01$). Where mean albumin creatinine ratio was 88.134±76.4mg/g and mean urinary microalbumin is 90.263±69.3348mg/L.

Conclusion: It is concluded that incidence of microalbuminuria is higher among diabetic patients with poor glycaemic control and it is a significant marker for long term diabetic complications and despite its devastating consequences, microalbuminuria is still a largely

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unrecognized risk factor, and a large proportion of individuals with diabetes are not regularly screened.

Keywords: Diabetes mellitus, Microalbumin, HBA1C Status and hyperglycemia.

INTRODUCTION

Diabetes mellitus is one of the most common metabolic disorders characterized by chronic hyperglycemia and disturbances in carbohydrate, fat, and protein metabolism due to absolute or relative deficiency of Insulin secretion or its action.[1]

Type 1 Diabetes: It is due to decreased insulin production .Onset usually below 30 years of age, most commonly during adolescence. They are more prone to develop ketosis. An autoimmune basis is attributed to most of these cases. Circulating antibodies against insulin is seen in 50% of cases, antibodies against islet cell cytoplasmic protein is seen in 80% of the cases. Autoreactive T cells of the immune system attack insulin secreating pancreatic islets of langerhans. Cytotoxic T cells bearing CD8 protein on their membrane kill islets, leading to lifelong dependence on insulin for affected patients. Poorly controlled blood glucose levels result in early illness and early death.[2]

Type 2 Diabetes: About 95% of the patients belong to this type. This disease is due to decreased biological response to insulin, otherwise called insulin resistance. Patients have high plasma insulin levels. The Maturity Onset Diabetes of the Young (MODY) is due to defective glucokinase via pancreatic β cell. This mutation produces relative insulin deficiency increasing threashold for glucose induced insulin secreation.

Metabolic Syndrome:

It is characterised by:

- Impaired glucose tolerance
- Hyperinsulinemia & insulin resistance
- Obesity
- Hyperlipidemia or dyslipidemia
- Hypertension
- Excess nutrients
- Reduced physical activity

Secondary to Other known causes include:

- Endocrinopathies(cushings disease, thyrotoxicosis, acromegally).
- Drug induced (steroids, beta blockers etc.)
- Pancreatic diseases (chronic pancreatitis, fibrocalculus pancreatitis, hemochromatosis, cystic fibrosis).

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AIM AND OBJECTIVES

AIM

To study the urinary micro albumin and HbA1c status among Type 2 diabetes mellitus patients.

OBJECTIVES

1. To estimate the urinary micro albumin & HbA1c in type 2 Diabetes mellitus patients.

2. To find out the correlation between urinary micro albumin & HbA1c in type 2 Diabetes Mellitus patients.

3. To find the association of micro albuminuria with the duration of Type 2 Diabetes Mellitus patients.

MATERIALS AND METHODS

Study design: Cross sectional study

Study setting: The study is a hospital based study and was carried at the diabetic clinic, Department of Medicine, in collaboration with the Department of Biochemistry.

Study duration: The study was carried out for a period two years. One& half years will be for data collection.

Study population: The study includes type 2 diabetes mellitus patients fulfilling the inclusion and exclusion criteria attending the diabetic clinic, in the department of medicine, Agartala Govt. Medical College and GBP hospital, Agartala, west Tripura. Based on last one year records it is estimated that about 19500 patients attended Diabetic clinic last year.

Inclusion criteria: Individuals whose age is 18 years and above irrespective of sex, caste and creed, diagnosed case of type 2 Diabetes Mellitus as per American Diabetic Association and who are willing to give consent in the study voluntarily were included in this study.

Exclusion criteria:

1. Those who are not willing to participate in the study.

2. Patients with diseases like Ischemic and Valvular heart disease, Congestive cardiac failure and Severe Anemia.

3. Patients with alcohol or drug dependence

4. Overt nephropathy.

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RESULT AND DISCUSSION

Type 2 diabetes mellitus is being increasingly recognized as a disease, which is characterized by dysfunction of the endothelium of various tissues. Endothelial dysfunction occurs in a generalized and widespread manner in diabetic subjects. The severity of the dysfunction is directly proportional to the age of the patient and duration of the diabetes. The clinical markers of the generalized endothelial dysfunction becomes manifest in several forms. Microalbuminuria marks the onset of endothelial dysfunction related to the kidney. Microalbuminuria serves as a warning for imminent nephropathy. But its true value is that it heralds generalized endothelial dysfunction. Thus diabetic subjects with microalbuminuria not only have ongoing progressive nephropathy but are also likely to have retinopathy, nephropathy and cardiovascular problems including coronary artery disease and hypertension. A slight increase in the percentage of microalbuminuria in our study can be attributed to several factors such as, large number of elderly patients, longer duration of diabetes and poor glycemic control.

As, main objective behind our study was to find out correlation between urinary microalbumin & HbA1c and to find out association of microalbuminuria with the duration of diabetes mellitus, but we have seen other parameters also like age, sex and systolic blood pressure, and serum creatinine in relation to microalbuminuria.

In our study we found that microalbuminuria mainly occurs in old age and maximum number of cases was with microalbuminuria is in age group 61-70 years. & the statistical difference in number of cases in age group 51-60 and 61-70 was statistically significant , ($P<0.05$) which is similar to a study by **Ambariyam Av et al**[3] were among 200 study participants who had type II diabetes mellitus. Out of 200 Type 2 diabetes mellitus patients, 59.5% belongs to age group 51-70 years. Mean age of study participants were 57.34±10.37 years. They also found among the study Participants belonging to age group >70 years, 70.8% had microalbuminuria.

It is very well recognized that microalbuminuria occurs more commonly in diabetic subjects who are more than 50 years of age. In our study microalbuminuria tended to more common in the age group of above 50 years as compared to the age group of less than 50 years. There are many reasons for this phenomenon. Firstly deterioration in the β-cell function, which occurs with increasing duration of diabetes, is likely to contribute to worsening glycemic control. Poor values of HbA1c are known to be associated with increasing incidence of microalbuminuria.

In our study we found there were more number of cases of Diabetes of Male(73.8%) than female, (26.2%) and maximum number were male patients. and the difference in number of cases with and without microalbuminuria in male is statistically significant.($p<0.05$) and maximum number of cases with microalbuminuria are in male patients, (n=200 out of total 214 cases, followed by female patients, (n= 45 out of 76 cases, The difference in the number of cases with and without microalbuminuria in male is statistically significant (<0.05) which is similar to a study by **Purkayastha A et al**[4] in their case-control descriptive study at Silchar Medical College,

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conducted a study where. The male female ratio was 64:36. Male preponderance was more in study population.

Our study showed mean urinary microalbumin level with increasing HbA1c in a scatter plot showed positive correlation at p<0.05 (ANOVA),where mean urinary microalbumin was highest(157.8±62.01)mg/L. in HbA1c group >8.5 and lowest (45.17±27.85)mg/Lin HbA1c group <7% Also Pearson's correlation showed that level of urinary microalbumin (r=0.73), where mean urinary microalbumin level is 90.82±69.33 mg/L and mean HbA1c is 8.3±3.0% statistically significant at (p<0.01).

Our study showed in a scatter plot correlation of urinary microalbumin level with increasing duration of diabetes where P<0.05), microalbumin level was highest (212.8±30.4) mg/dl, in duration of diabetes of >10 years and lowest (43.1±28.5)mg/L in duration of diabetes < 5 years which is similar to a study by **D Kundu et al[5]**: In their study, found that urinary microalbumin, HbA1c levels were significantly higher in the cases. Microalbumin levels were linearly correlated to the duration of diabetes & HbA1c. In type 2 diabetes mellitus patients, the duration of diabetes was the strongest predictor as well predicted increased microalbumin excretion rate. So, it may be suggested that determination of microalbumin levels in urine is an easy method of screening diabetes. **Bahman et al[6]** reported that in Type 2 diabetes mellitus patients with duration of diabetes 10-14 years, risk of developing microalbuminuria was higher compared to patients with diabetes duration of 0-4 years. **Gupta M et al[7]** in their observational s tudy with 75 patients having diabetic nephropathy, at JAH hospitals found that Microalbuminuria (r=0.91, p≤0.05), HbA1c (r=0.67, p≤0.05) duration of 0-4 years. And concluded that the Level of microalbuminuria increase with increase in duration of diabetes and worsening of diabetes. Glycosylated hemoglobin (HbA1c) is the gold standard to measure severity of diabetes mellitus.

In our study we also showed mean plot of urinary albumin creatinine ratio with HbA1c groups, Mean albumin creatinine ratio was highest (163.9±69.7)mg/g in HbA1c group > 8.5 and lowest (36.7±26.4)mg/L in HbA1c group <7. The scatter plot showed positive correlation Albumin creatinine ratio level with increasing HbA1c group. Pearson's correlation test also showed HbA1c positively correlated with albumin creatinine ratio (r=0.73) which is statistically significant, p<0.01. Our study showed, that mean albumin creatinine ratio level is highest (189.8 ± 70.3)mg/g in Duration of diabetes group of >10 years and lowest (37.5 ± 32.3)mg/g in Duration of diabetes group <5 years. Scatter plot showed positive correlation of urinary albumin creatinine ratio level with increasing duration of diabetes at P<0.05 (ANOVA) which is similar to a study by **Muhammad Ahsan Sana et al[8]**: found that Urine Albumin creatinine ratio was higher in patients with Type 2 Diabetes Mellitus in terms of higher HbA1c value & with a longer duration of diabetes. It is recommended that UACR (Urinary Albumin Creatinine Ratio) should be inculcated in routine practice, annually for all patients with T2DM (Type 2 Diabetes Mellitus) for causing the development of underlying renal involvement and prompt management.

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In our study it is found that by Pearson's correlation test, Urinary microalbumin and systolic B.P is positively correlated (r=0.84) which is statistically significant at P<0.01. Mean level of urinary microalbumin was 90.263±69.3348mg/L with comparison to mean level of systolic B.P at 135.09±23.035mm Hg.

In our study it is found that by Pearson's correlation of urine microalbumin vs serum creatinine where level of urinary microalbumin positively correlated with serum creatinine (r=0.59), which is statistically significant (p<0.01), where mean of urinary microalbumin is 90.263±69.3348mg/L), and mean of serum creatinine was 1.527±0.7346mg/dl, which is similar to a study by **Francesco Perticone et al**[9]: showed microalbuminuria maintained a significant positive association with serum creatinine, microalbuminuria reflects a (renal) endothelial dysfunction and it may contribute to renal impairment independently of inflammation and hemodynamic endothelial dysfunction.

In our study showed a positive Pearson correlation of Albumin creatinine ratio vs urinary microalbumin where albumin creatinine ratio correlated positively with urinary microalbumin (r=0.8), which is statistically significant at (p<0.01). Where mean albumin creatinine ratio was 88.134±76.4mg/g and mean urinary microalbumin is 90.263±69.3348mg/L.

In the present study, HbA1c levels showed a significant correlation with urinary microalbumin level. Thus it is clear that glycemic control over a long period has a greater influence on the urinary microalbumin level.

Numerous clinical studies in individuals with either type 1 or type 2 diabetes with microalbuminuria demonstrates higher cardiovascular and renal disease mortality. The patho-physiologic basis for elevated urinary albumin excretion is the binding of glucose to proteins resulting in excessive protein glycosylation with the buildup of advanced glycosylated end products (AGE's). This leads to deposition of AGE's on the glomerulus resulting in renal and glomerular hypertrophy, mesangial matrix accumulation and thickening of glomerulus basement membrane. This abnormality permits the leakage of low molecular weight proteins (albumin)12

This is the stage of microalbuminuria (Incipient Nephropathy) which could be reversible with good glycemic control. Increased level of microalbuminuria is associated with increased risk of progressive kidney disease leading towards end stage renal disease (ESRD) and cardiovascular morbidity and mortality in diabetic patients13 as reported in an earlier study.

CONCLUSION

This study shows conclusive evidence that urinary microalbumin excretion was significantly correlated with duration of the diabetes , level of HbA1c Systolic Blood Pressure and serum creatinine. Also microalbuminuria was seen more in male sex and more elderly patients.

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The present study reported that a poor glycaemic control, that is elevated HbA1c level in type 2 diabetes mellitus may lead to development of microalbuminuria which in turn may bring about changes resulting in progressive renal disease and also cardiovascular complications. The study further proposes assessment of the association of microalbuminuria with other cardiovascular risk factors such as blood pressure etc.

Microalbuminuria in diabetic patients was strongly associated with elevated glycosylated haemoglobin (HbA1C), which is an index of glycaemic control. This study shows conclusive evidence that urinary microalbumin excretion was significantly correlated with duration of the diabetes and level of HbA1c. It is concluded that incidence of microalbuminuria is higher among diabetic patients with poor glycaemic control and it is a significant marker for long term diabetic complications.

Since Type 2 diabetes mellitus is slow onset disease and most of the Type 2 patients are unaware of the symptoms of diabetes. Decreasing the levels of albuminuria reduces the risk of adverse renal and cardiovascular complications. Strict control of glycemic status and blood pressure reduces the albuminuria thereby overt proteinuria. Initiation of drug treatment should be considered in these patients and level of microalbuminuria should be followed. The American Diabetics Association recommends that patients with Type 2 diabetes should be tested for albuminuria at the time of initial diabetes diagnosis and yearly thereafter.

Taking all the results into consideration, we can conclude that the present study reported that Microalbuminuria in diabetic patients was strongly associated with elevated glycosylated hemoglobin (HbA1c), which is an index of glycemic control. The study suggests a regular screening of HbA1c, microalbumin in type 2 diabetic patients for identification and timely management of patients at risk. Despite its devastating consequences, microalbuminuria is still a largely unrecognized risk factor, and a large proportion of individuals with diabetes are not regularly screened.

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Table: Shows the analysis of Clinical & Bio Chemical Parameters

Descriptive Statistics					
Variables	No. of cases	Minimum	Maximum	Mean	Std. Deviation
Blood Sugar F(mg/dl)	290	110	375	168.30	52.342
Blood Sugar PP(mg/dl)	290	156	432	276.91	64.371
Urinary Microalbumin (mg/L)	290	7.0	254.0	90.263	69.3348
Albumin/Creatinine Ratio (mg/g)	290	4.1	291.0	88.134	76.4078
HbA1c (%)	290	4.0	14.0	8.300	3.0311
Blood Urea (mg/dl)	290	33	98	59.265	17.166
Serum Creatinine (mg/dl)	290	0.6	4.0	1.527	0.7346
Systolic BP(mm Hg)	290	110	198	135.09	23.035
Diastolic BP(mm Hg)	290	68	110	82.931	8.4199
Total (N)	290				

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Table: Shows comparative analysis of Clinical, Biochemical and other Parameters

Descriptive Statistics					
Variables	No. of cases	Minimum	Maximum	Mean	Std. Deviation
HbA1c (%)	290	4.0	14.0	8.300	3.0311
Duration of disease (Years)	290	2	31	7.12	5.449
Urinary Microalbumin (mg/L)	290	7.0	254.0	90.263	69.3348
Albumin/Creatinine Ratio (mg/g)	290	4.1	291.0	88.134	76.4078
Serum Creatinine (mg/dl)	290	0.6	4.0	1.527	0.7346
Systolic BP(mm Hg)	290	110	198	135.09	23.035
Total (N)	290				

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Table: Shows comparison between urinary microalbumin and HbA1c level groups using ANOVA. Urinary microalbumin level

HbA1c Group(%)	No. of cases	Mean	Std. Deviation	Std. Error	Minimum	Maximum
<7	146	45.179	27.8527	2.3051	7.0	168.0
7-8.5	36	71.677	41.8588	7.5181	7.0	231.0
>8.5	108	157.889	62.0168	5.9676	82.0	254.0
Total	290	90.773	69.6540	4.1259	7.0	254.0