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Original Research Paper

Pathology

A tertiary care center study from Southern India on evaluating relationship of microalbuminuria with glycosylated hemoglobin and disease duration in type 2 diabetes mellitus

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ABSTRACT

Objective: *Diabetes Mellitus is a major cause of morbidity and mortality as a result of its complications. Long-term complications have been linked to poor glycaemic control. Microalbuminuria has been identified as predictors of diabetic nephropathy which is the leading cause of end stage renal disease. This study was conducted to correlate and statistically analyse the relation between microalbuminuria with glycosylated hemoglobin (HbA1c) and disease duration.*

Material and Method: *The present prospective study was conducted in Basaveshwar Teaching and General Hospital, Kalaburagi for 06 months.Laboratory tests as HbA1c, urine microalbumin and urine creatinine were measured in semiautomated biochemistry analyser. Ratio of microalbumin to creatinine was considered as a measure of microalbuminuria.*

Results: *Out of 330 cases, 117 cases (35.45%) were of microalbuminuria. The mean age was 51.7±10.5 years. There was male preponderance (65.8%) and duration of diabetes was 6.6±3.4 years. HbA1c level was 7.3±1.4%. There was significant positive correlation between microalbuminuria and HbA1c and between microalbuminuria and duration of diabetes.*

Conclusion: *The present study suggests using microalbuminuria as a method to understand glycemic control in individuals with type 2 Diabetes and emphasizes the importance of regular evaluation of microalbuminuria in all type 2 diabetic patients for timely therapeutic intervention and prevention of renal complications.*

KEYWORDS : Glycosylated hemoglobin, microalbuminuria, duration of diabetes, type 2 diabetes mellitus.

Introduction

Diabetes mellitus (DM) is the most common non-communicable disease worldwide. Its prevalence has now become a serious global health burden and is reaching epidemic proportions (1). India has been called 'the diabetes capital of the world', 'every fifth diabetic in the world is an Indian' (2). In India, 61.3 million people aged 20-79 years live with diabetes (2011 estimates). This number is expected to increase to 101.2 million by 2030 (3). During the period of April2009 to March2010, prevalence of diabetes was 19.8% with an additional 12% with impaired glucose tolerance in Kalaburagi (also known as Gulbarga) which is a northern district in the State of Karnataka, India (4).

Nephropathy is one of the complications of type 2 diabetes mellitus that could lead to end-stage renal disease. Persistent microalbuminuria is the best predictor of diabetic nephropathy and hence, screening for microalbuminuria has become standard of care worldwide (5).

Studies in western literature show linear relationship between degree of microalbuminuria, glycosylated hemoglobin and disease duration. There is neither general consensus on possible factors associated with microalbuminuria in diabetic patients nor any reported study in this region. Hence, this study was planned to determine the correlation of microalbuminuria with glycosylated hemoglobin (HbA1c) and disease duration in order to provide a basis for future development of comprehensive intervention approaches to prevent and manage kidney diseases in patients with type 2 diabetes mellitus.

Material and Methods

2.1 Study Design

This prospective study was conducted in Basaveshwar Teaching and General Hospital attached to Mahadevappa Rampure Medical College, Kalaburagi, Karnataka, India. This study was conducted for a period of one year from 01st Jan 2016 to 30th June 2016.

A total of 117 out of 330 patients of Type 2 DM without complications were included in the study. The study protocol and assessments were conducted in accordance with the Declaration of Helsinki (2013) and approved by institutional ethics committee. Written Informed consent was taken from all the studypatients before any study specific procedures.

2.2 Study Population

Consecutive patients with clinical diagnosis of Type 2 DM without complication who visited Basaveshwar Teaching and General Hospital attached to Mahadevappa Rampure Medical College, Kalaburagi, India for regular follow up were included in this study. Type 1 diabetic patients and patients with Type 2 DM who presented with microalbuminuria other than diabetic nephropathy such as: haematuria, hypertension, dyslipidemia, infections, connective tissue disorders, prostate diseases, renal diseases, recent exercise, medications as chronic NSAIDs, ACE inhibitors, etc. and women with menstruation at the time of sample collection were excluded from the study.

2.3 Laboratory investigations

HbA1c was measured in semiautomated biochemistry analyser, ERBA Chem 7 with Erba HemoglobinA1c kits using immunoturbidimetric method.

Urinary microalbumin was measured in semiautomated biochemistry analyser, ERBA Chem 7.Test was assessed by

Immunoturbidimetric method.

Urinary creatinine was measured in semiautomated biochemistry analyser, ERBA Chem 7.Test was assessed by modified Jaffe's reaction.

Urinary albumin: creatinine ratio was calculated as a measure of microalbuminuria. Normal level of urinary albumin: creatinine ratio was<30mg/g of creatinine and microalbuminuria was defined as 30-300 mg/g of creatinine (6).

2.4 Statistical Analyses

Statistical analysis was done using SPSS software windows 16.0 version. For continuous (quantitative) data, 'Z' test was used. Categorical (qualitative) data was analyzed by using chi-square test. Paired and unpaired t-testswere used for comparable data. Correlation coefficient was used for analyzing relationship between two variables.

Results

3.1 Patient Characteristics

Total 330 cases of Type 2 DM were studied for a period of 06 months from 1st Jan 2016 to 30th June 2016. Out of 330 cases, 117 cases (35.5%) were of microalbuminuria. Detailed analysis of 117 cases was done.Baseline characteristics are given in Table I.

The age of the patients ranged from 32 to 76 years with mean ± SD being 51.7±10.5 years. The maximum number of total cases (32.5%) was seen in the age group of 41- 50 years. Only 6% of the total cases were in the age group of 71-80 years. Majority of the cases (65.8%) were males with male to female ratio 1.9:1.

Majority (42.8% in males and 47.5% in females) of cases were having duration of diabetes for 1-5 years (Figure 1).HbA1c levels ranged from 5.7-11.0% (Figure 2).Range of microalbuminuria was 30 – 297 mg/g in males and 30 – 100 mg/g in females.

3.2 Correlation of microalbuminuria with HbA1c and disease duration

3.2.1 HbA1c

When microalbuminuria was correlated with HbA1c for all the cases, it was observed that there was significant positive correlation between the two variables. The Pearson's co-efficient of correlation (r) was found to be +0.875 and the p value of <0.001, which was highly statistically significant (Figure 3).

The positive correlation of microalbuminuria with HbA1c was further pronounced in males with Pearson's co-efficient of correlation (r) was found to be +0.893and the p value of <0.00001, which was highly statistically significant. The positive correlation of microalbuminuria with HbA1c was also seen in females (Pearson's co-efficient of correlation (r) +0.792, p<0.00001, highly statistically significant).

3.2.2 Disease duration

When microalbuminuria was correlated with duration of diabetes for all the cases, it was observed that there was significant positive correlation between the two variables. The Pearson's co-efficient of correlation (r) was found to be +0.625 and the p value of <0.0001, which was highly statistically significant(Figure 4).

The positive correlation of microalbuminuria with duration of diabetes was also seen in males (Pearson's co-efficient of correlation (r) +0.734, p<0.0001, highly statistically significant). However, the correlation was not seen in females (Pearson's co-efficient of correlation (r) +0.063, p>0.7, not statistically significant).

Discussion

The present study includes 117 cases of Type 2 DM without complications, who were found to have microalbuminuria from the screened pool of 330 cases during the 06-month study period. The objective of the study was to evaluate the relationship between microalbuminuria with HbA1c and disease duration.

In the present study, 35.5% of cases had microalbuminuria (117 out of 330). Varghese A et al (2001) reported determine the prevalence for microalbuminuria among south Indiantype 2 diabetic patients in a single center setting and found 36.3% of the patients had microalbuminuria (7). Similarly, Chowta et al (2009) also determined the correlation of microalbuminuria with age, sex, duration of diabetes, Body mass index and creatinine clearance in patients with type 2 diabetes mellitus in Indian population and found the overall prevalence of microalbuminuria was 37% (8).

In the present study, the duration of diabetes was 6.6 ± 3.4 years which was similar to Chowta NK et al (2009) (8). Other studies have reported slightly longer duration of diabetes (Afkhami-Ardekani M et al (2008) (6), Varghese A et al (2001) (7) and Neupane S et al (2016) (9).This variation of duration of diabetes in different studies may be contributed to difference in health awareness in study population and time of diagnosis of the disease. (Table II)

In the present study, HbA1c was 7.3± 1.4% which was similar to Kundu D et al (5) and Neupane S et al (9). Other studies have reported slightly higher HbA1c at baseline (Varghese A et al (2001) (7), Afkhami-Ardekani M et al (2008) (6) and Debbarma B et al (10) than the present study.

In the present study, there was highly statistically significant positive correlation of microalbuminuria and HbA1c. This is consistent with other studies Varghese A et al (2001) (7), Sheikh S et al (2009) (11), Kundu et al (2013) (5). The increased microalbumin levels in diabetic subjects may be due to an altered glomerular filtration barrier, at the podocyte level. Damage to the podocyte may be explained by the fact that there is an increase in the extracellular release of reactive oxygen species.

Similarly, in the present study, there was highly statistically significant positive correlation of microalbuminuria and duration of diabetes. This is consistent with other studies Varghese A et al (2001) (7), Chowta NK et al (2009) (8), Sheikh S et al (2009) (11), and Kundu et al (2013) (5). Several studies on regression analysis and diabetes duration were identified as a strong predictor for the development of abnormal albuminuria in type 2 diabetes mellitus. Present study also showed that duration of diabetes is a strong predictor of increased microalbumin excretion. This signifies that as the duration of diabetes increases, the Glomerular Filtration Rate decreases.

The study was conducted in a tertiary care center with small sample size of 300 screened individuals of type 2 DM without complications. Usually, individuals with DM are also associated with other co-morbidities like hypertension, obesity, cardiovascular disease, etc and hence, the diabetic complications may also set in these individuals by the time the diagnosis is made. Hence, microalbuminuria testing can be a good screening tool for managing diabetes mellitus for individuals especially in rural areas and smaller towns of Indian states. Also, small sample size and short duration of the study are limitations of the present study.

Conclusions

Prevalence of microalbuminuria is high in individuals with Type 2 Diabetes.However, microalbuminuria is still a largely unrecognized risk factor and a large proportion of patients are not regularly screened. The present study showed glycaemic control and microalbuminuria are correlated and also, microalbuminuria and duration of disease are correlated. Hence, this study suggests using relatively simple and cheap test as estimation of microalbuminuria in comparison to HbA1c as good alternative method to understand glycaemic control in individuals with Type 2 diabetes. Also, this study emphasizes the importance of regular evaluation of microalbuminuria in all Type 2 Diabetes Mellitus patients for timely therapeutic intervention and prevention of renal complications.

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All authors had input into the data interpretation and preparation of the final manuscript for publication, and met the ICMJE criteria for authorship. The lead author affirms that this manuscript is an honest, accurate and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

Declaration of Interests
Authors declare no conflict of interests.

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Tables and Figures:

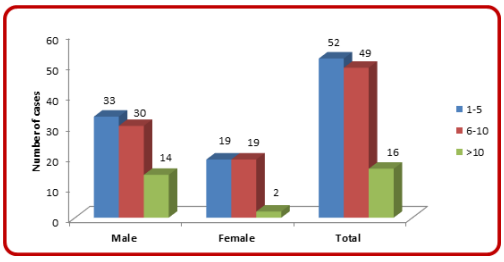

Figure 1. Distribution based on duration of disease (years)

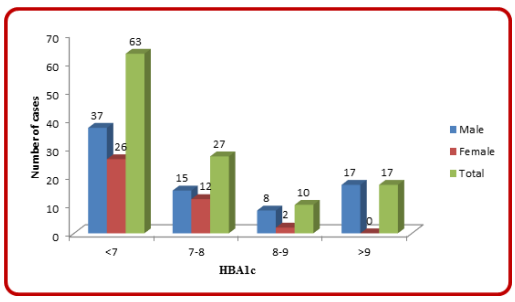

Figure 2.Distribution based on HbA1c (%)

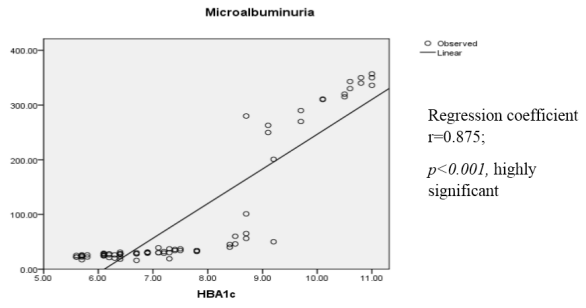

Figure 3. Correlation of microalbuminuria with HbA1c (N=117)

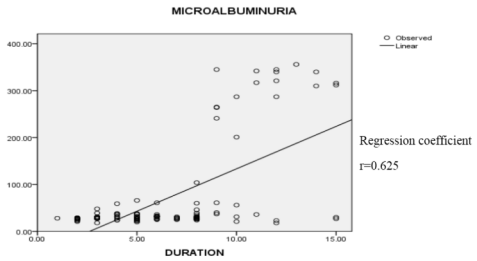

Figure 4. Correlation of microalbuminuria with duration of diabetes (N=117)

Table I. Baseline characteristics

	Total Cases (N=117) Mean ± SD	Male (N=77) Mean ± SD	Female (N=40) Mean ± SD
Age, years	51.7 ±10.5	51.4 ± 10.8	52.3 ± 9.9
Diabetes duration, years	6.6 ± 3.4	6.9 ± 3.5	6.0 ± 3.1
HbA1c %	7.3± 1.4	7.5 ± 1.6	6.7± 0.7*
Microalbuminuria, mg/g of creatinine	72.6 ± 90.5	92.2 ± 116.1	34.8 ± 7.81*

*Statistically highly significant comparing males vs females.
SD, standard deviation; HbA1c, hemoglobin A1c.

Table II: Comparative analysis for the clinical parameters: Duration of diabetes and HbA1c

	Study details	Total number of cases	DoD, Range, years	DoD, years (Mean ± SD)	HbA1c, %, Range, years	HbA1c, %, (Mean ± SD)
Varghese A et al (2001)[7]	Prevalence and risk factorsfor microalbuminuria among South Indiantype 2 diabetic patients	518	-	8 ± 7	-	9.7 ± 2.3
Afkhami-Ardekani M et al (2008)[6]	Prevalence of microalbuminuria and its risk factors in type 2 diabetic patients (Iran)	288	1-36	9.3 ± 6.3	4.2-16.5	9.1 ± 2.15
Chowta NK et al (2009)[8]	Correlation of microalbuminuria with various factors in type 2 diabetes mellitus (Indian population)	100	1-20	5.97 ± 4.98	-	7.87 ± 1.72
Kundu D et al (2013)[5]	Correlation of microalbuminuria with glycosylated hemoglobin level and duration of diabetes	50	-	-	-	7.87 ± 1.72
Debbarma B et al (2015)[10]	Incidence of microalbuminuria in newly diagnosed type 2 diabetes and to identify the risk factors for nephropathy	104	-	2.78±1.6	-	8.89±2.38
Neupane S et al (2016)[9]	Association between serum uric acid, urinary albumin excretion and glycated hemoglobin in type 2 diabetic patient	50	-	9.26±6.48	-	8.12±2.14
Present study (Jain V et al) (2016)	Correlation of microalbuminuria with glycosylated hemoglobin and duration of diabetes	117	1-15	6.6 ± 3.4	5.6–11.4	7.3± 1.4

DoD, Duration of diabetes; HbA1c, hemoglobin A1c.

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