

Correlation of Clinical and Biochemical Parameters with the Stages of Chronic Kidney Disease in Type 2 DM Patients in a Tertiary Care Hospital in Chittagong

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Abstract

Background : Microalbuminuria is a term to describe a moderate increase in the level of urine albumin. It occurs when the kidney leaks small amounts of albumin into the urine. The main objective of this study is to determine the correlation between microalbuminuria and diabetic kidney disease at a tertiary care hospital in Chittagong.

Materials and methods : Institutional based cross-sectional study design was conducted on randomly selected diabetic population from Chittagong Diabetic and General Hospital by using systematic random sampling method from 1st June to 30th November 2019.

Results : Out of a total of 160 participants, the prevalence of microalbuminuria was in 59(36.9%) patients. Ten (6.3%) patients had cardiovascular disease, 18(11.3%) had neuropathy, 7(4.4%) had retinopathy, 117(73.1%) had hypertension and 47(29.4%) had duration of diabetes of 6-10 years. Majority 132(82.5%) patients had stage 1-2 followed by 22(13.8%) had stage 3, 4(2.5%) had stage 4 and 2(1.3%) had stage 5. Gender, age, cardiovascular, retinopathy, hypertension, BMI, albumin to creatinine ratio, fasting sugar, creatinine level and LDL were not statistically significant ($p>0.05$) when compared to different stages of CKD. Stage 1-2 was significantly higher in no microalbuminuria group than microalbuminuria group (92.1% vs 66.1%). Stage 3 was significantly higher in microalbuminuria group than no microalbuminuria group (23.7% vs 7.9%). Stage 4 was significantly higher in microalbuminuria group 4(6.8%) and Stage 5 was higher in the microalbuminuria group 2(3.4%).

Conclusion: Neuropathy, mean diabetes duration, mean HbA1c, and mean Triglyceride were significantly greater in CKD stage 5 than in other stages of illness in the current research. When comparing different stages of CKD, mean HDL was considerably lower in stage 5. In the microalbuminuria group, CKD Stages 3, 4, and 5 were considerably higher than in the non-microalbuminuria group.

Key words: Diabetic kidney disease; Diabetes mellitus; Microalbuminuria.

Introduction

Microalbuminuria is an early indicator of diabetic nephropathy, which accounts for a considerable reduction in diabetic patients' life expectancy. Microalbuminuria diagnosis in a timely manner allows for suitable preventive and treatment methods to reduce hazards.¹ The prevalence of diabetic kidney disease has remained steady, with a wide range of variability. Normoalbuminuric diabetes with renal insufficiency has been identified as an albuminuria-independent phenotype of diabetic kidney disease. Epidemiological statistics show that the normoalbuminuric phenotype is common. When compared to the albuminuric phenotype, the normoalbuminuric phenotype exhibits different clinical characteristics as well as a wide range of pathological abnormalities.² Diabetic nephropathy is distinguished by chronic albuminuria, a steady reduction in glomerular filtration rate, and an elevated arterial blood pressure.³ Microalbuminuria is defined as the presence of 30-300 mg of albumin in a 24-hour urine sample or 30-300 mcg of albumin/mg creatinine in a spot sample. It affects 20 to 40% of individuals after 10 to 15 years after diabetes onset.⁴ Diabetes microvascular problems involve kidney damage known as Diabetic Nephropathy (DN) which is the most prevalent consequence of type 2 diabetes mellitus and the major cause of end-stage renal disease globally, with substantial morbidity and death.^{5,6} It arises in around 40% of diabetic patients after 10 years of type 2 diabetes mellitus

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diagnosis.^{7,8} DN is defined by persistent albuminuria (or albuminuria excretion rate of >300 mg/d or 200 µg/min) measured at least twice within three to six months interval, progressive decrease in Glomerular Filtration Rate (GFR) which frequently occurs in conjunction with an increase in blood pressure, eventually leading to end-stage renal disease.^{9,10} Early detection enhances the likelihood of preventing the progression of incipient to overt nephropathy. The purpose of this study is to assess the prevalence of microalbuminuria and its relationship to the clinical profile and consequences of diabetic kidney disease.

Materials and methods

This is a cross sectional study conducted among 160 patients of type-2 DM admitted in the Medicine ward of a tertiary care hospital from 1st June to 30th November 2019, who fulfilled the inclusion and exclusion criteria. Ethical clearance and approval of the study was obtained from Institutional Review Board of Chittagong Diabetic General Hospital (CDGH) and the formal letter of cooperation was given to CDGH medical director. Verbal informed consent was obtained from each respondent, and they will be told that they have the right not to participate in the study. The information from the clients were kept confidential.

Relevant history including duration of DM, and other comorbidities were taken from the patients. Vital parameters such as heart rate, systolic and diastolic blood pressure were recorded. CBC, RFT, FPG, PPPG, HbA1c, Fundoscopy were done in all patients. Urine analysis for ACR from random urine sample and 24-hours urine protein from 24-hour urine sample were done. Patients who have been diagnosed with type 2 diabetes mellitus according to the American Diabetes Association (ADA) and patients who were already taking treatment either OHA or insulin for type 2 DM were included in the study. Patients suffering from type-1 DM, fever, urinary tract infections were excluded. Patients with pre-existing nephropathy, pre-existing hypertension before the diagnosis of DM, bed ridden patients and pregnant women were also excluded in the study. History was taken in the form of questionnaire: Information regarding age, gender, duration of

DM, other comorbidities like hypertension, stroke, and complaints of sensory motor neuropathy were recorded. Examination was done in the form of Heart rate; systolic and diastolic blood pressure were measured. Presence of pallor, pedal oedema, crepitations were also recorded. Fundoscopy were done in all patients. Complete Blood Counts (CBC) Renal function tests (RFT) Fasting Plasma Glucose (FPG) with fasting of 8-10 hours, Post-Prandial Plasma Glucose (PPPG) collected 2 hours after food, HbA1c (Estimated using HPLC method) were measured in all patients in the study. For Urine analysis, two samples of urine were collected from the patients, one included random urine sample in a sterile container with a capacity of 10 ml and a urine sterile container of capacity of 5 liter for 24-hours urine sample collection. 24-hour urine sample were used for measurement of 24-hour urine protein. Urine ACR was measured from random urine sample. Urinary albumin was measured by 'Immuno Turbidometry method' while urinary creatinine was measured by 'Jaffe's spectrophotometric method'. Diabetes mellitus (As per the American Diabetes Association) Fasting plasma glucose \geq 126 mg/dl (fasting is defined as no caloric intake for \geq 8 hours) 2-hour Post prandial plasma glucose \geq 200 mg/dl during an oral glucose tolerance test. (the test should be performed using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water). HbA1c \geq 6.5%. And all those patients who were diagnosed with type 2 diabetes mellitus already on oral hypoglycaemic drugs and/or insulin were also included in the study. Proteinuria is defined as urine Albumin Creatinine Ratio (ACR) in a single spot urine sample Normo-albuminuria = <30 mg/g. Micro-albuminuria = 30-299 mg/g. Macroalbuminuria = > 300 mg/g. Overt proteinuria is defined as proteinuria of > 150 mg/24 hours urine protein. Data was collected in a SPSS ver-23. Statistical analysis was done using nonparametric ANOVA, Chi square test and Fisher test and Pearson correlation.

Results

Out of 160 patients, the prevalence of microalbuminuria was in 59(36.9%). More than half (52.5%) patients were male and 76(47.5%) were female. Majority 95(59.4%) patients

belonged to age group of 35-54 years; the mean age was 50.4±10.7 years. Ten (6.3%) patients had cardiovascular disease, 18(11.3%) had neuropathy, 7(4.4%) had retinopathy, 117(73.1%) had hypertension, 47(29.4%) had duration of diabetes of 6-10 years and the mean duration of diabetes was 11.4±5.7 years. Majority 77(48.1%) of the patients were obese and mean BMI was 29.5±5.3 kg/m² (Table I). Albumin to creatinine ratio <30 was 98(61.25%), mean albumin to creatinine ratio was 37.6±49.5. HbA1c >7 was found 127(79.4%), mean HbA1c was 8.4±2.1%. Abnormal fasting plasma glucose was 129(80.6%), mean fasting plasma glucose was 8.9±2.5 mg/dL. Abnormal creatinine was found in 35(21.9%), mean creatinine was 1.35±1.1 mg/dL. Abnormal LDL was found in 89(55.6%), mean LDL was 3.2±1.2 mmol/L. Abnormal HDL was found in 145(90.6%), mean HDL was 1.27±0.88 mmol/L. Abnormal triglyceride was found in 63(39.4%), mean triglyceride was 1.59±0.8 mmol/L (Table II). Majority 132(82.5%) patients had stage 1-2 followed by 22(13.8%) had stage 3, 4(2.5%) had stage 4 and 2(1.3%) had stage 5 (Table III). Neuropathy was significant higher in stage 5, (100%) than other stages of disease. Mean duration of diabetes was significantly higher in stage 5 (14.9±4.2 years) than other stage of disease. Mean HbA1c (%) was significantly higher in stage 5, (11.5±1.9 %) than other stage of disease. Mean HDL was significantly lower in stage 5, (1.12±0.2 mmol/L). Mean Triglyceride was significantly higher in stage 5, (1.85±0.6 mmol/L). Gender, age, cardiovascular, retinopathy, hypertension, BMI, albumin to creatinine ratio, fasting sugar, creatinine level and LDL were not statistically significant (p>0.05) when compared to different stages of CKD (Table IV). Stage 1-2 was significantly higher in no microalbuminuria group than microalbuminuria group (92.1% vs 66.1%). Stage 3 was significantly higher in microalbuminuria group than no microalbuminuria group (23.7% vs 7.9%). Stage 4 was significantly higher in microalbuminuria group 4(6.8%). Stage 5 was higher in microalbuminuria group 2(3.4%) (Table V).

Table I Diabetics' socio-demographic features and disease-related variable characteristics

Variable	Frequency (n)	Percentage (%)
Gender		
Male	84	52.5
Female	76	47.5
Age group (Years)		
20-34	10	6.3
35-54	95	59.4
≥55	55	34.4
Mean±SD	50.4±10.7	
Cardiovascular disease		
Present	10	6.3
Absent	150	93.8
Neuropathy		
Present	18	11.3
Absent	142	88.8
Retinopathy		
Present	7	4.4
Absent	153	95.6
Hypertension		
Yes	117	73.1
No	43	26.9
Duration of diabetes (Years)		
1-5	43	26.9
6-10	47	29.4
11-15	25	15.6
>15	45	28.1
Mean±SD	11.4±5.7	
BMI (kg/m ²)		
≤24.9	24	15.0
25.0-29.9	59	36.9
30.0-39.9	77	48.1
Mean±SD	29.5±5.3	

Table II Frequency of biochemical variables

Variable	Frequency (n)	Percentage (%)
Albumin to creatinine ratio		
<30	98	61.25
30-300	62	38.75
Mean±SD	37.6±49.5	
HbA1c (%)		
≤7	33	20.6
>7	127	79.4
Mean±SD	8.4±2.1	
Fasting plasma glucose (mg/dL)		
Normal (What is normal value) (<130)	31	19.4
Abnormal (what is abnormal value) (>130)	129	80.6
Mean±SD	8.9±2.5	
Creatinine level		
Normal (<1.3)	125	78.1
Abnormal (>1.3)	35	21.9
Mean±SD	1.35±1.1	

Variable	Frequency (n)	Percentage (%)
LDL (mmol/L)		
Normal (<100)	71	44.4
Abnormal (>100)	89	55.6
Mean±SD	3.2±1.2	
HDL (mmol/L)		
Normal (>40)	15	9.4
Abnormal (<40)	145	90.6
Mean±SD	1.27±0.88	
Triglyceride(mmol/L)		
Normal (<150)	97	60.6
Abnormal (>150)	63	39.4
Mean±SD	1.59±0.8	

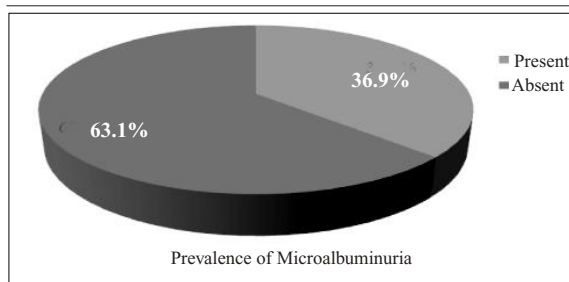


Figure 1 Prevalence of microalbuminuria

Table III Diabetic patients according to the stages of kidney disease

Stage of kidney disease	Frequency	Percentage
Stage 1-2	132	82.5
Stage 3	22	13.8
Stage 4	4	2.5
Stage 5	2	1.3

Table IV Clinical characteristics of diabetic patients according to the stage of kidney disease

Variable	Stage 1-2 (n=132)	Stage 3 (n=22)	Stage 4 (n=4)	Stage 5 (n=2)	p value
Gender					
Male (%)	84(50.8)	13(59.1)	3(75.0)	1(50.0)	0.779 ^{ns}
Female (%)	76 (49.2)	9(40.9)	1(25.0)	1(50.0)	
Age (Years)	52.4±9.2	50.7±8.2	53.8±9.5	49.6±10.1	0.813 ^{ns}
Cardiovascular disease (%)	6(4.5)	3(13.6)	1(25.0)	0(0.0)	0.153 ^{ns}
Neuropathy (%)	8(6.1)	6(27.3)	2(50.0)	2(100)	0.001 ^s
Retinopathy (%)	5(3.8)	1(4.5)	1(25.0)	0(0.0)	0.231 ^{ns}
Hypertension (%)	97(73.5)	15(68.2)	3(75.0)	2(100)	0.793 ^{ns}
Duration of diabetes (Years)	7.5±4.5	8.1±5.3	12.1±4.7	14.9±4.2	0.034 ^s
BMI (kg/m ²)	28.5±4.7	27.5±5.6	26.5±6.1	25.6±5.7	0.578 ^{ns}
Albumin to creatinine ratio	35.5±44.3	39.5±47.2	36.7±41.5	38.5±45.9	0.984 ^{ns}
HbA1c (%)	7.6±2.5	8.1±2.1	9.7±2.3	11.5±1.9	0.045 ^s
Fasting plasma glucose (mg/dL)	8.7±1.8	8.3±2.4	8.6±3.1	8.3±2.3	0.831 ^{ns}
Creatinine level (mg/dL)	1.18±0.8	1.21±0.9	1.32±1.1	1.37±1.1	0.999 ^{ns}
LDL (mmol/L)	3.2±1.2	3.1±1.3	3.3±1.1	3.4±1.2	0.973 ^{ns}
HDL (mmol/L)	1.43±0.3	1.22±0.6	1.17±0.5	1.12±0.2	0.029 ^s
Triglyceride (mmol/L)	1.21±0.7	1.59±0.5	1.68±0.7	1.85±0.6	0.034 ^s

s=significant, ns=not significant.

p value reached from Chi square test and ANOVA test.

Table V Relation between stages of kidney disease and microalbuminuria

Variable	Microalbuminuria		p value		
	Absent (n=101)	Present (n=59)			
Stage 1-2	93	92.1	39	66.1	0.001 ^s
Stage 3	8	7.9	14	23.7	0.005 ^s
Stage 4	0	0.0	4	6.8	0.008 ^s
Stage 5	0	0.0	2	3.4	0.062 ^{ns}

s=significant, ns=not significant.

p value reached from Chi square test.

Discussion

The current study showed that more than half (52.5%) of the patients were male and 76(47.5%) were females. Majority 95(59.4%) of the patients belonged to age group 35-54 years; the mean age was 50.4±10.7 years. Ten (6.3%) patients had cardiovascular disease, 18(11.3%) had neuropathy, 7(4.4%) had retinopathy, 117(73.1%) had hypertension, 47(29.4%) had duration of diabetes of 6-10 years; mean duration of diabetes was 11.4±5.7 years. Majority 77(48.1%) patients were obese and mean BMI was 29.5±5.3 kg/m². Al Fehaid, study revealed male patients constituted 50.2% while females were 49.8%.¹¹ The mean age of the patients was 52.01 years with standard deviation of 11.43, majority were between 35-54 (59.5%) followed by 55 years or older (34.4). Other complications such as cardiovascular, neuropathy and retinopathy were absent in 94.9%, 90.7% and 97%, respectively. The majority of the patients (70.4%) had hypertension. The analysis of collected data showed that 25% had diabetes for 1-4.9 years, 28.5% had it for 5-9.9 years, 18% for 10-14.9 years, and 27.5% for more than 15 years. The mean duration of diabetes was 9.83 ± 6.59 years. Nearly 31.8% of the patients were obese and 27.9% were morbidly obese. The mean BMI was 31.89 ± 6.88 kg/m².

Present study observed that albumin to creatinine ratio <30 was 98(61.25%), mean albumin to creatinine ratio was 37.6±49.5. HbA1c >7 was found 127(79.4%), mean HbA1c was 8.4±2.1%. Abnormal fasting glucose was 129(80.6%), mean fasting glucose was 8.9±2.5 mg/dL. Abnormal creatinine was found in 35(21.9%) mean creatinine was 1.35±1.1 mg/dL. Abnormal LDL was found in 89(55.6%), mean LDL was 3.2±1.2 mmol/L. Abnormal HDL was found in 145(90.6%), mean HDL was 1.27±0.88 mmol/L. Abnormal triglyceride

was found in 63(39.4%), mean triglyceride was 1.59 ± 0.8 mmol/L. Okada et al reported the mean HbA1c was $7.2 \pm 1.3\%$, mean creatinine 67.2 ± 16.8 $\mu\text{mol/L}$, mean serum triglyceride 1.6 ± 1.0 mmol/L.¹² Al Fehaid, study showed the overall prevalence of MA was 37.4%.¹¹ Most patients had high glycated hemoglobin (80.4%) and high fasting sugar (83%). The percentage of abnormal laboratory value in patients with diabetes was as follows: creatinine 23.7%, Low-Density Lipoprotein (LDL) 53%, High-Density Lipoprotein (HDL) 91.1%, and triglyceride 40.9%. The mean FBS, HbA1c, and creatinine levels were 8.82 ± 2.93 mg/dL, 8.28 ± 1.94 , and 1.33 ± 1.14 , respectively. The mean serum triglyceride, LDL, and HDL levels were 1.56 ± 0.85 , 3.1 ± 1.104 , and 1.06 ± 0.95 mg/dL, respectively. Al-Maskari et al reported Dyslipidemia, assessed by elevated total cholesterol, was present in 34% and elevated triglycerides was present in 24% of the sample population.¹³

Current study revealed that microalbuminuria was present in 59(36.9%) and absent in 101(63.1%). In the Al Fehaid, study, 494 patients with type II diabetes were studied and the overall prevalence of MA found was 37.4%.¹¹ Chowta et al. reported overall prevalence of microalbuminuria in the present study was 37%.¹⁴ Al-Maskari et al observed MA was found in 61%.¹³

Present study showed that majority 132(82.5%) patients had stage 1-2 followed by 22(13.8%) had stage 3, 4(2.5%) had stage 4 and 2(1.3%) had stage 5. Dwyer et al reported Stage 1 was found in 13.0%, stage 2 was 24.0%, stage 3 was 10%, stage 4 was 0.6%, stage 5 was 0.07% and unknown 58.0%.¹⁵

Our study showed that neuropathy was significant higher in stage 5, (100%) than other stage of disease. Mean duration of diabetes was significantly higher in stage 5 (14.9 ± 4.2 years) than other stage of disease. Mean HbA1c (%) was significantly higher in stage 5, (11.5 ± 1.9 %) than other stage of disease. Mean HDL was significantly lower in stage 5, (1.12 ± 0.2 mmol/L). Mean Triglyceride was significantly higher in stage 5, (1.85 ± 0.6 mmol/L). Gender, age, cardiovascular, retinopathy, hypertension, BMI, albumin to creatinine ratio, fasting sugar, creatinine level and LDL were not statistically

significant ($p > 0.05$) when compared to different stages of CKD. Yokoyama et al reported that the parameters that commonly aggravated albuminuria stages and CKD stages were age, duration of diabetes, levels of systemic BP and PP, serum concentrations of HDL and TG, use of insulin and proportion of hypertension, hyperlipidemia, retinopathy, neuropathy and CVD.¹⁶ Proportions of men and smokers and A1C increased according to albuminuria stage, but decreased according to CKD stage. These findings indicate that low eGFR could be due to age-associated senescence and interstitial fibrosis, and renal ischemia due to intrarenal arteriosclerosis and cholesterol emboli involvements.^{17,18} Lipid abnormalities by high TG and low HDL were indicated in association with progression of renal dysfunction.¹⁹

The present study showed that stage 1-2 was significantly higher in no microalbuminuria group than microalbuminuria group (92.1% vs 66.1%). Stage 3 was significantly higher in micro albuminuria group than no microalbuminuria group (23.7% vs 7.9%). Stage 4 was significantly higher in microalbuminuria group 4(6.8%). Stage 5 was higher in the microalbuminuria group 2(3.4%).

Limitation

Small sample size & single centre study.

Conclusion

Neuropathy, mean diabetes duration, mean HbA1c, and mean Triglyceride were significantly greater in CKD stage 5 than in other stages of illness in the current research. When comparing different stages of CKD, mean HDL was considerably lower in stage 5. In the microalbuminuria group, CKD Stages 3, 4, and 5 were considerably higher than in the non-microalbuminuria group.

Recommendation

Similar study with large sample size with multicentre and long duration can be done for proper picture.

Acknowledgment

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Contribution of authors

SA-Conception, design, data analysis, manuscript writing & final approval.

SRC-Design, critical revision & final approval.

RB-Data collection, data analysis, critical revision & final approval.

AZS-Interpretation of data, critical revision & final approval.

Disclosure

All the authors declared no competing interest.

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