Original Article

Microalbuminuria, Other Markers of Nephropathy and Biochemical Derangements in Type 2 Diabetes Mellitus: Relationships and Determinants

Ademola A. Idowu[1,2], Abiodun O. Ajose[3,4], Adeoye T. Adedeji[3,4], Adegbola O. Adegoke[3,4] and Kayode A. Jimoh[5]

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[1]Department of Chemical Pathology, Ekiti State University, Ado Ekiti, Ekiti State, Nigeria [2]Department of Chemical Pathology, Ekiti State University Teaching Hospital, Ado Ekiti, Ekiti State, Nigeria [3]Department of Chemical Pathology, Obafemi Awolowo University Teaching Hospitals Complex, Ile-Ife, Osun State, Nigeria [4]Department of Chemical Pathology, Obafemi Awolowo University, Ile-Ife, Osun State, Nigeria [5]Department of Chemical Pathology, Federal Teaching Hospital Ido-Ekiti, Ekiti State, Nigeria.

Corresponding Author: Dr Ademola A. Idowu **E-mail:** idemola2003@yahoo.com

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SUMMARY

Background: Microalbuminuria is an early indicator of Diabetic nephropathy and cerebrovascular disease.
Objective: To evaluate relationships between microalbuminuria and other predictors of morbidity and mortality in type 2 DM.
Methods: Fifty type 2 diabetic subjects were recruited each for three groups separated by disease durations. Thirty non-diabetic subjects were recruited to control each group. Urine albumin-to-creatinine ratio (ACR) was estimated. Fasting plasma glucose (FPG), serum creatinine, urea, total cholesterol (TC), triglycerides (TG), high- and low density lipoprotein (HDL, LDL) were measured.
Results: The diabetics with longest disease duration of >10 years were the oldest (65.86±1.71), had highest systolic BP (147.12±3.39mmHg) and least BMI (27.20±0.71Kg/m^2); they had poorest lipid control (TC:5.54±0.26mmol/L), though with the least TG (0.97±0.09mmol/L); they also had the most severe microalbuminuria (33.63±8.03g/L) and ACR (65.85±10.38mg/gm). Patients with diabetes of 5-10 years had the poorest glycaemic control:FPG-7.82±0.47mmol/L; HbA1c-13.09±0.74%). Significant negative correlations exist between microalbuminuria, HBA1c(r=-2.28, p=0.028) and serum creatinine(r=-2.11,p=0.042) in patients with 5-10 years disease; a positive correlation between the ACR and TC(r=1.00,p<0.01) in those with >10 years disease. In multivariate analysis, independent predictors of microalbuminuria were disease duration (OR 2.2, p< 0.001); HBA1c (OR 7.3, p=0.02); LDL/HDL ratio (OR 13.4, p< 0.001).
Conclusion: The severity and progression of albuminuria are associated with longer duration of diabetes and poor glycaemic control. Significant relationships exist between ACR and HBA1c, TC, HDL-C, TG, creatinine. Disease duration, ethnicity, HBA1c, TC, TG, HDL-C and LDL/HDL ratio are independent predictors of albuminuria.

Keywords: diabetes, microalbuminuria, albumin-to-creatinine ratio, dyslipidaemia, nephropathy, cardiovascular disease

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INTRODUCTION

The chronic hyperglycaemia of diabetes is associated with long-term damage, dysfunction and failure of various organs, especially the eyes, kidneys, nerves, heart, and blood vessels. Diabetic nephropathy (DN) is an important and life-threatening microvascular complication of diabetes mellitus (DM). It is usually first manifested as an increase in urinary albumin excretion (which could be microalbuminuria, defined as the urinary excretion of albumin of 20-200 µg/min or 30-299 mg/g of creatinine or macroalbuminuria, defined as urinary albumin to creatinine ratio greater than 200 µg/min or ≥300 mg/gm of creatinine and <30mg/gm is normal.[1,2] Macroalbuminuria is an overt clinical manifestation of renal dysfunction which could progress to renal failure.[3] Microalbuminuria has been associated with an increased risk of Cardiovascular diseases (CVD) in patients with and without DM.[4,7]

Therefore, in patients with DN, the increased cardiovascular risk associated with diabetes and with Chronic

Kidney Disease (CKD) are additive and increase as DN progresses.[8] Without specific intervention, 20%-40% of patients with type 2 diabetes and microalbuminuria will progress to overt nephropathy and ultimately End Stage Renal Disease (ESRD).[8]

Microalbuminuria is an indicator of the incipient phase of diabetic nephropathy in diabetes mellitus, and progressive albuminuria is a generally recognized criterion for determining the degree of diabetic nephropathy.[5,8] If present, microalbuminuria identifies patients at risk for early cardiovascular death and progressive renal disease.

Microalbuminuria also identifies patients who need more rigorous cardiovascular risk management, especially more intensive blood pressure control, (preferably below 130/80 mm Hg), and strict attention to glycaemic control and lipid levels.[6,8] Consequently, identification of such patients for early commencement of appropriate therapeutic measures should be an important consideration.[7] Therapeutic approaches to enhance better blood pressure control and reduce microalbuminuria will likely prove to be the most effective way to retard the progression of both renal and cardiovascular diseases or complications in patients with type 2 DM.[7]

Despite the increased attention in various parts of the world on the role of the biochemical parameters in the disease progression and management of diabetes mellitus, there is still paucity of information on the interrelationship among these markers to one another and to presence of microvascular complications in Nigeria especially in relation to disease duration. The study was designed to determine the relationship between these biochemical parameters and disease duration (number of years with DM). Additionally we explored the association between these parameters and microvascular complications of DM.

METHODS

Study design and study population

This study was designed as a cross sectional study. It was conducted over a period of 6 months at the Obafemi Awolowo University Teaching Hospitals Complex (OAUTHC) in Ile-Ife, South Western Nigeria.

A total of 150 type 2 diabetics attending outpatient department of the diabetic clinics at OAUTHC were recruited for this study. Fifty subjects were recruited for each of the three categories based on disease duration thus: 50 newly diagnosed; 50 who have been on therapy for 5-10 years; and 50 who have been on therapy for more than 10 years. Subjects were selected by simple random sampling method for each group.

Those with history suggestive of a haemolytic disorder (like sickle cell anaemia) with shortened red blood cell survival, and subjects with non-diabetes-related conditions that might increase microalbuminuria such as urinary tract infection, haematuria, heart failure, febrile illness, severe hypertension, and vigorous exercise were excluded. All other subjects that satisfied the inclusion criteria consented and were thus consecutively recruited till sample size was achieved.

Thirty (30) age- and sex- matched non-diabetic subjects (members of staff of the hospital, relatives of patients and other volunteers), were recruited as control. Age, sex, disease duration, social status, economic and education status, medical history and type of treatment, were obtained from patients' records. All data were collected by Principal Investigator. Ethics and Research Committee of OAUTHC, Ile-Ife gave its approval (Protocol number ERC/2013/01/02) for the study to be conducted.

Confidentiality: All information gathered in this study was stored in a personal computer, kept confidential and accessed only by authorized personnel.

The sample size per group was statistically derived from the formula:

$\mathbf{n = Z^2pq/d}$ by applying the index prevalence of 2.2% of DM in the population at the time of study. The minimum required for each group was 33.

Sample collection, laboratory methods and analysis

12ml of fasting venous blood was collected from all patients. The collected blood was divided into:

(i) EDTA bottles (2ml) and appropriately stored in a refrigerator at a temperature of 4-8°C until assayed for HBA1c levels within 7 days according to HBA1c assay reagents manufacturers specifications;

(ii) Fluoride oxalate bottles (2ml) for fasting plama glucose estimation and the assay was done same day;

(iii) 8ml into plain serum bottles and allowed for clotting and retraction. Sample was immediately centrifuged, separated and serum collected was stored and analysed the same day; or stored at -70°C until estimated for serum lipids, urea and creatinine, but all within the limit of sample storage and stability for all the analytes.

Overnight urine sample for albumin and creatinine was collected into universal bottle. Urine albumin was estimated in fresh urine while the creatinine sample was stored at -20°C for a maximum of 24hours.

Fasting plasma glucose (FPG) was determined by the glucose oxidase method[9], serum creatinine by Jaffe kinetic method[10], serum urea by urease enzyme method[11], total cholesterol by the oxidase/peroxidase (CHOD-POD) method[12], triglycerides by the enzymatic GPO-POD method[13], high density lipoprotein by phosphotungstate precipitation and (CHOD-POD) method[14], HbA1c by the cation exchange resin method[15,16] and agglutination method[17] was used to determine microalbumin levels in the urine sample.

Fasting plasma glucose of 3-5mmol/L was defined as good glycaemic control, 5-8mmol/L as fair control and >8.0mmol/L as poor control. HBA1c of ≤6.5% defined good glycaemic control. HDL, Normal total cholesterol is taken as <5.2 mmol/L, low density lipoprotein <3.5 mmol/L, triglyceride <1.7 mmol/L and high density lipoprotein >0.9 mmol/L for males and >1.0 mmol/L for females.[18]

Statistical analysis

The data collected was analysed using descriptive and inferential statistics. Continuous variables are given as mean (standard deviation, SD) and categorical variables as percentages. Analysis of Variance was used to compare the means among groups. Paired Students T-tests were used to compare means of pairs of groups. Pearson moment correlation was done to determine the relationship between the variables.

Multiple linear regressions were then used to determine the predictors of different markers of nephropathy and other complications of DM. The level of significance was set at $p \leq 0.05$. Statistical analyses were performed using the SPSS version 17 software package (SPSS Inc., Chicago, Illinois, USA).

RESULTS

Table 1 shows the age and anthropometric characteristics of the three diabetic groups in comparison with the controls. Patients, who were diabetic for 10 years and above were the oldest, had highest systolic BP, but the least BMI than the rest of the groups.

Table 1 Age and anthropometric characteristics: comparison of the diabetic groups with control group

Measured Variables	Control (n=30)	Newly Diagnosed (n=50)	5-10 years DM (n=50)	>10 years DM (n=50)
	Mean±SEM	Mean±SEM	Mean±SEM	Mean±SEM
Age (years)	**53.77±2.02**	**57.96±1.24**	**62.64±1.22**	**65.86±1.71**
p value (Control vs Group)		p=0.07	p<0.01	p<0.01
Weight(kg)	**71.37±2.31**	**73.44±1.67**	**73.1±1.82**	**70.52±1.73**
p value (Control vs Group)		p=0.46	p=0.55	p=0.768
Height(m)	**1.58±0.02**	**1.61±0.01**	**1.63±0.01**	**1.61±0.01**
p value (Control vs Group)		p=0.17	p<0.01	p=0.151
BMI(kg/m^2)	**28.58±0.97**	**28.44±0.70**	**27.55±0.63**	**27.20±0.71**
p value (Control vs Group)		p=0.9	p=0.3	p=0.251
Systolic BP(mmHg)	**125.63±4.01**	**127.36±2.30**	**137.50±2.85**	**147.12±3.39**
p value (Control vs Group)		p=0.69	p=0.016	p<0.01
Diastolic BP(mmHg)	**79.80±2.54**	**77.20±1.03**	**79.82±1.93**	**78.64±1.94**
p value (Control vs Group)		p=0.28	p=0.99	p=0.717
Waist Circumference(cm)	**93.23±2.84**	**94.62±1.88**	**94.82±1.98**	**98.10±1.58**
p value (Control vs Group)		p=0.67	p=0.64	p=0.11
Abdominal Circumference	**94.00±2.33**	**97.48±1.88**	**99.34±1.92**	**97.03±1.39**
p value (Control vs Group)		p=0.25	p=0.086	p=0.23

Table 2 shows the biochemical characteristic of the various diabetic groups and the controls. Patients with diabetes duration of 5-10 years had the poorest glycaemic control as reflected in their highest FPG and HbA1c. Patients with disease duration of more than 10 years had the poorest lipid control, the highest level of microalbuminuria and the albumin-to-creatinine ratio.

Table 2 Biochemical characteristics: comparisons of the diabetic groups with the control group

Measured Variables	Control (n=30)	Newly Diagnosed (n=50)	5-10 years DM (n=50)	>10 years DM (n=50)
	Mean±SEM	Mean±SEM	Mean±SEM	Mean±SEM
FPG (mmol/l)	**4.16±0.10**	**6.53±0.47**	**7.82±0.47**	**7.37±0.40**
p value (Control vs Group)		p<0.001	p<0.01	p<0.01
HBA1C (%)	**5.56±0.17**	**11.48±0.67**	**13.09±0.74**	**10.48±0.71**
p value (Control vs Group)		p<0.001	p<0.01	p<0.01
Total Cholesterol (mmol/l)	**4.92±0.25**	**5.10±0.19**	**5.36±0.22**	**5.54±0.26**
p value (Control vs Group)		p=0.56	p=0.21	p=0.12
HDL-C (mmo/l)	**1.59±0.07**	**2.46±0.13**	**1.96±0.09**	**1.45±0.06**
p value (Control vs Group)		p<0.001	p<0.01	p=0.17
LDL-C (mmol/l)	**3.14±0.22**	**1.86±0.15**	**2.92±0.21**	**3.65±0.24**
p value (Control vs Group)		p<0.001	p=0.49	p=0.15
Triglyceride (mmol/l)	**0.41±0.05**	**1.71±0.18**	**1.05±0.05**	**0.97±0.09**
p value (Control vs Group)		p<0.001	p<0.01	p<0.01
HDL-C/TC	**0.34±0.02**	**0.48±0.02**	**0.38±0.02**	**0.28±0.01**
p value (Control vs Group)		p<0.001	p=0.15	p<005
LDL-C/HDL-C	**2.03±0.14**	**0.97±0.13**	**1.65±0.14**	**2.77±0.23**
p value (Control vs Group)		p<0.001	p=0.084	p<0.05
MICROALBUMINURIA (mg/l)	**14.07±0.90**	**14.03±1.83**	**18.03±2.01**	**33.63±8.03**
p value (Control vs Group)		p<0.001	p=0.146	p=0.06
SERUM UREA (mmol/l)	**4.01±0.24**	**4.41±0.04**	**4,83±0.36**	**7.02±0.64**
p value (Control vs Group)		p<0.001	p=0.11	p<0.01
SERUM CREATININE (umol/l)	**99.77±5.44**	**97.27±5.09**	**214.61±10.36**	**122.32±13.30**
p value (Control vs Group)		p=0.75	p<0.01	p=0.21
URINE CREATININE (g/l)	**0.94±0.03**	**0.65±0.05**	**0.84±0.06**	**0.51±0.03**
p value (Control vs Group)		p<0.01	p=0.167	p<0.01
ALBUMIN:CREATININE	**15.49±1.27**	**23.61±2.12**	**30.56±5.59**	**65.85±10.38**
p value (Control vs Group)		p<0.01	p=0.042	p<0.01

Tables 3 compared the biochemical characteristics among the diabetic subjects. The mean FPG showed an increasing trend from the newly diagnosed and to those on therapy for 5-10 years but a decrease value among those on therapy for over 10 years those on therapy for 5-10 years had the poorest glycaemic control.

The HBA1c showed a slightly different pattern with the group on therapy for over 10 years having the lowest mean followed by the newly diagnosed and finally those on therapy for 5-10 years. The microalbuminuria (measured as microalbumin (mg/L) and albumin in mg/g creatinine) showed increasing values from the newly diagnosed, to those on therapy for 5-10 years and over 10 years.

In addition, the percentage of subjects who had microalbuminuria also increased with increase in disease duration. Microalbuminuria as defined by albumin-to-creatinine ratio suggested 32% microalbuminuria in the newly diagnosed group while mere measurement of urinary albumin without comparison with creatinine excretion resulted in only 8% microalbuminuria. In group C, 60% of the diabetic patients had microalbuminuria by albumin-to-creatinine ratio; but only 32% of the same group had microalbuminuria by urine albumin alone meaning assessment of microalbuminuria by albumin-to-creatinine ratio is more sensitive.

In Table 4, the correlations between microalbumin and ACR and other variables is shown. The control group

microalbumin, shows significant positive correlation with urine creatinine and albumin-to-creatinine ratio (r= 5.91, p<0.01 and r=14.51, p<0.01respectively). It also shows significant negative correlation with triglyceride (r=-2.92, p<0.01). In the newly diagnosed diabetics (group A), microalbumin has significant positive correlation with serum urea, urine creatinine and albumin-to-creatinine ratio(r=2.29, p<0.05; r=6.89, p<0.01 and r=5.68, <0.01) respectively.

Table 3 Biochemical characteristics: comparisons among the diabetic groups

Measured Variables	Newly Diagnosed (n=50)	5-10 years DM (n=50)	p value	5-10 years DM (n=50)	>10 years DM (n=50)	p value	Newly Diagnosed (n=50)	>10 years DM (n=50)	p value
	Mean±SEM	Mean±SEM		Mean±SEM	Mean±SEM		Mean±SEM	Mean±SEM	
FPG (mmol/l)	6.53±0.47	7.82±0.47	0.016	7.82±0.47	7.37±0.40	0.480	6.53±0.47	7.37±0.40	0.18
HBA1C (%)	11.48±0.67	13.09±0.74	0.11	13.09±0.74	10.48±0.71	<0.05	11.48±0.67	10.48±0.71	0.31
Total Cholesterol (mmol/l)	5.10±0.19	5.36±0.22	0.34	5.36±0.22	5.54±0.26	0.61	5.10±0.19	5.54±0.26	0.18
HDL-C (mmo/l)	2.46±0.13	1.96±0.09	<0.01	1.96±0.09	1.45±0.06	<0.01	2.46±0.13	1.45±0.06	<0.01
LDL-C (mmol/l)	1.86±0.15	2.92±0.21	<0.01	2.92±0.21	3.65±0.24	<0.05	1.86±0.15	3.65±0.24	<0.01
Triglyceride (mmol/l)	1.71±0.18	1.05±0.05	0.01	1.05±0.05	0.97±0.09	0.46	1.71±0.18	0.97±0.09	<0.01
HDL-C/TC	0.48±0.02	0.38±0.02	0.001	0.38±0.02	0.28±0.01	<0.01	0.48±0.02	0.28±0.01	<0.01
LDL-/HDL-C	0.97±0.13	1.65±0.14	<0.01	1.65±0.14	2.77±0.23	<0.01	0.97±0.13	2.77±0.23	<0.01
MICROALBUMINURIA (mg/l)	14.03±1.83	18.03±2.01	0.15	18.03±2.01	33.63±8.03	0.06	14.03±1.83	33.63±8.03	<0.05
SERUM UREA (mmol/l)	4.41±0.04	4.83±0.36	0.44	4.83±0.36	7.02±0.64	<0.01	4.41±0.04	7.02±0.64	<0.01
SERUM CREATININE (umol/l)	97.27±5.09	214.61±10.4	<0.01	214.61±10.4	122.32±13.3	<0.01	97.27±5.09	122.32±13.3	0.082
URINE CREATININE (g/l)	0.65±0.05	0.84±0.06	<0.05	0.84±0.06	0.51±0.03	<0.01	0.65±0.05	0.51±0.03	<0.01
ALBUMIN:CREATININE	23.61±2.12	30.56±5.59	0.25	30.56±5.59	65.85±10.38	<0.01	23.61±2.12	65.85±10.38	<0.01

In group B microalbumin showed significant positive correlation with urine creatinine and albumin-to-creatinine ratio (r=5.12, p<0.01 and r=14.44, p<0.01) respectively and significant negative correlation with HBA1c and serum creatinine (r=-2.28, p<0.05 and r= -2.11, p<0.05) respectively.

Albumin-to-creatinine ratio only had significant positive correlation with LDL-C/HDL-C ratio and significant negative correlation with serum creatinine (r =2.03, p=0.05; r = -2.46, p<0.05 and r = -2.72, p<0.01) respectively in addition to urine creatinine and microalbumin in group A; however, in group B, albumin-to-creatinine ratio showed significant positive correlations with HBA1C and LDL-C/HDL-C ratio while it showed significant negative correlations with TG and LDL-C(r=2.74, p<0.01; r=4.83, p<0.01; r= -1.99, p<0.05 and r= -2.27, p<0.05) respectively. In group C subjects, albumin-to-creatinine ratio had significant positive correlations with HBA1C, total cholesterol and serum urea (r=14.76, p<0.001; r=10.13, p<0.001 and r= 10.69, p<0.001) while it had significant negative correlations with FBG, HDL-C,TG, LDL-C/HDL-C, and serum creatinine (r=-2.04, p=0.05; r= -10.88, p<0.001; r=-21.06, p<0.001; r=-6.73, p<0.001; r=-7.47, p<0.001 and r=-3.12, p<0.001) respectively.

Using multivariate analysis, the most significant independent predictor of ACR among the tested variables was disease duration (Odds ratio 2.2, 95% Confidence interval CI 1.7-2.8, p< 0.001); then, ethnicity (OR 0.0001, 95% CI 0.00001-0.001, p=0.002), and level of education (OR 0.001. 95% CI 0.0001-0.004, p= 0.005);

Table 4 The correlations between albumin: creatinine ratio (ACR) with other measured variables

Measured Variables	Control Group (N=30)		Newly Diagnosed (N=50)		5-10 Years Dm (N=50)		>10 Years Dm (N=50)	
	R	P Value	R	P Value	R	P Value	R	P Value
Microalbuminuria								
Urine Creatinine (G/L)	5.91	<0.01	6.883	<0.001	5.118	<0.01	4.289	<0.01
Hba1c (%)	-0.753	0.462	11.96	0.058	-2.28	0.028	1.301	0.201
Triglyceride (Mmol/L)	-2.924	<0.01	0.018	0.985	1.986	0.055	-1.64	0.109
Serum Urea (Mmol/L)	0.37	0.716	2.285	0.028	1.324	0.194	0.917	0.365
Serum Creatinine (Umol/L)	1.442	0.167	1.373	0.178	-2.11	0.042	-0.41	0.683
Albumin:Creatinine Ratio (Acr)								
Ldl-C/Hdl-C	-1.636	0.14	2.034	0.053	4.828	<0.01	-6.73	<0.01
Serum Creatinine (Umol/L)	-0.874	0.408	-2.72	0.012	1.694	0.092	-3.12	<0.01
Hba1c (%)	0.678	0.517	-0.73	0.47	2.737	<0.01	14.76	<0.01
Triglyceride (Mmol/L)	0.989	0.352	-1.63	0.116	-1.993	0.048	-21.1	<0.01
Ldl-C (Mmo/L)	1.343	0.216	-0.87	0.392	-2.271	0.025		
Tc			1.329	0.196	-0.266	0.791	10.13	<0.01
Serum Urea (Mmol/L)	0.001	0.999	-1.91	0.068	-1.808	0.073	10.69	<0.01
Fbg	2.064	0.073	1.302	0.205	-1.361	0.176	-2.04	0.052
Hdl-C (Mmo/L)	-1.289	0.234	-1.15	0.261	1.007	0.316	-10.9	<0.01

Table 5 shows the correlation adjusting for treatment modality, comorbidities, gender, age, weight, height, BMI, waist circumference, abdominal circumference, systolic BP, diastolic BP, occupation, level of education, religion, and ethnicity.

Table 5 Predictors of ACR in the whole cohort of diabetes patients (n=150)

Regression analyses: ACR and its predictors				
Variables	**Univariate OR**	**(95% CI)**	**p***	**Multivariate OR (95% CI) p****
Age (years)	14.1	(3.6-57)	<0.001	
Body weight (Kg)	0.7	(0.2-2.4)	0.564	
Height (m)	0.0001	(0.00001-0.2)	0.048	
BMI (Kg/m^2)				
Waist Circ.	2.2	(0.7- 6.5)	0.153	
Abdominal Circ.	1.4	(0.4- 4.7)	0.552	
Gender				
Systolic BP	1.5	(0.8- 3.0)	0.199	
Diastolic BP	0.5	(0.2- 1.8)	0.314	
Comorbidities	10	(1.9-19)	0.018	
Disease duration	1.9	(1.3- 2.3)	<0.001	2.2 (1.7-2.8) <0.001
Treatment Mode	15.7	(7.2- 24.3)	<0.001	
Occupation	5.5	(1.7- 9.3)	0.005	
Education Level				0.001 (0.0001-0.004) 0.005
Ethnicity				0.0001(0.00001-0.001) 0.002

Significance set at ≤0.05; r= correlation coefficient; p = significance of correlation; OR= Odds ratio; 95% CI= 95% Confidence interval; p*= significance of association; p**= significance of independent association.

DISCUSSION

Microalbuminuria, which is highly prevalent in our study, is commonly associated with cardiovascular risk clustering phenomena.[19] This phenomenon also known as the metabolic cardiovascular syndrome expresses the association between microalbuminuria, dyslipidaemia, glucose intolerance, central obesity, high blood pres-

sure, left ventricular hypertrophy, and loss of nocturnal dip of blood pressure.[19]

Since these risk factors develop on a chronic pattern, disease duration would be a common denominator among the components. Diabetic nephropathy usually develops approximately ten years after the diagnosis of type I diabetes and three to five years after the diagnosis of type 2 diabetes.[20]

The interaction of these risk factors as a cause of injury to blood vessel may be reliably determined by early appearance of microalbumin in the urine, as found in our study. This is consistent with the reports of Tabaei and Associates.[20]

Our finding of the mean FPG showing an increasing trend from the control subjects to the newly diagnosed, those on therapy for 5-10 years but a decrease value among those on therapy for over 10 years, implies that those on therapy for 5-10 years had the poorest glycaemic control. This is corroborated by the glycated haemoglobin showing a pattern with the group on therapy for over 10 years having the lowest mean followed by the newly diagnosed and finally those on therapy for 5-10 years.

This finding may result from differential compliance emanating from relativity of complications, i.e those with longest disease duration (>10 years) might have better compliance due to experience of more complications than those with shorter duration (5-10 years). Thus our finding is similar to the reports of Samatha P et al[21] that the severity of microvascular complications was related to the longer duration of diabetes and the high levels of glycosylated haemoglobin.

Similar findings have been observed by Varghese et al,[22] who reported that the duration of diabetes and retinopathy were the major predictors of microalbuminuria. A linear graded relationship has also been observed between urine albumin-to-creatinine ratio and cardiovascular morbidity and mortality.[23] Przegl Lek et al[23] observed that the most important predictor for all forms of neuropathy was the duration of diabetes.

In our study, patients with disease duration of more than 10 years having highest level of microalbuminuria, albumin-to-creatinine ratio and the poorest lipid control corroborates the reports that diabetes duration is associated with onset and progression of nephropathy, dyslipidemia and cardiovascular disease risk.[20,21]

The microalbuminuria (measured as microalbumin (mg/L) and albumin-to-creatinine showed increasing values from the control group to the newly diagnosed, to those on therapy for 5-10 years and over 10 years.

In addition, the percentage of subjects who had microalbuminuria also increased with increase in disease duration. Thus, nephropathy progresses with diabetes duration.

This study also showed that albumin-to-creatinine ratio reported higher incidence of microalbuminuria in all the studied groups than just measuring the urinary microalbumin. This is why the ratio of urinary concentrations of albumin and creatinine is often used to avoid the requirement (and errors) of collecting a timed urine specimen to calculate the urinary excretion rate of the albumin.[23,24]

The concept underlying this approach is that the rate of excretion of creatinine is relatively constant and thus the amount excreted reflects the time period of the urine collection.[23,24] Intra-individual variability for albumin excretion rate (AER) is much greater than ACR.[24] Therefore, assessment of microalbuminuria by albumin-to-creatinine ratio is more sensitive than urine albumin alone.

Moreover, the mean systolic BP, LDL-C, LDL-C: HDL-C ratio, serum urea and albumin-to-creatinine ratio being significantly higher in patients with DM for over 10years (with HDL-C, HDL-C: Total cholesterol being significantly lower) than those with duration of 5-10 years establishes the fact that disease duration is a predictor of renal and cardiovascular complications and thus, of the marker of nephropathy i.e. microalbuminuria.

This is further buttressed by the microalbumin (albumin-to-creatinine ratio) showing significant positive correlation with FPG, total cholesterol, HBA1C and LDL-C/HDL-C ratio, serum urea, urine creatinine and systolic blood pressure in the groups on treatment for 5-10 years and more than 10 years, unlike in the newly diagnosed patients in which albumin-to-creatinine ratio only had significant positive correlation with LDL-C: HDL-C ratio. In summary, albumin-to-creatinine ratio exhibited significant correlations with virtually all the biochemical variables except HDL-C: Total cholesterol with which it had no relationship in all the groups including the control group.

CONCLUSION

In conclusion, the magnitude, progression and severity of microalbuminuria were associated with the longer

duration of diabetes and a poor glycemic control in our study. Significant relationships exist between ACR and other biochemical parameters- HBA1c, TC, HDL-C, TG, serum urea and creatinine.

Disease duration, education level, ethnicity, AER, HBA1c, TC, TG, HDL-C and LDL/HDL ratio are independent predictors of albuminuria.

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