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Study of Microalbuminuria and Uric Acid in Type 2 Diabetes Mellitus

Prajakta Warjukar[1], Pradip Jain[2], Prakash Kute[3], Ashish Anjankar[3], S.S. Ghangale[4]

[1]Assistant Professor, Department of Biochemistry, Datta Meghe Medical College Nagpur-441110; [2]Professor & Head, Department of Biochemistry, Datta Meghe Medical College Nagpur-441110; [3]Assistant Professor, Department of Biochemistry, Jawaharlal Nehru Medical College, Datta Meghe Institute of Medical Sciences, Sawangi, Wardha-442001; [4]Professor and HOD Dept. of Biochemistry GMC Gondia.

ABSTRACT

Introduction: A significant complication of diabetes mellitus is diabetic nephropathy. Microalbuminuria (30-300 mg/24 hour urinary albumin excretion) is an indicator of diabetic nephropathy in type II mellitus diabetes patients. Research has shown that the development of microalbuminuria with therapies to closely regulate blood sugar and blood pressure is reversible. Hyper-uricemia represents an independent threat of renal dysfunction in diabetes mellitus (DM) patients. Hyperuricemia can lead to endothelial dysfunction and nitric oxide inhibition, which can cause insulin resistance and thus diabetes. Uric acid assessment is cost-effective, preventive, and has significant consequences for public health.

Aim: To assess the significance of microalbuminuria and uric acid for early detection of kidney and cardiovascular involvement in type 2 Diabetes mellitus and early prevention its complications.

Method: In this cross-sectional study, 100 diagnosed patients of type-2 Diabetes Mellitus were taken as cases and 100 age and sex-matched normal persons were taken as controls. Fasting plasma glucose (FPG), 2 hours postprandial glucose levels (2hPG), serum uric acid and serum creatinine, urinary microalbumin, urinary creatinine were analyzed in them. Urinary albumin creatinine ratio (ACR) was calculated.

Result: In this study, it was seen that the prevalence of microalbuminuria was 37% in cases and 8% in control. Mean value of age, BMI, fasting glucose, post-meal plasma glucose, serum uric acid, microalbuminuria in patients of diabetes mellitus was found to be highly significant as compared to the control group (p<0.0001)). Males had higher values of microalbuminuria than females whereas serum uric acid was higher in females than males. There is positive and significant correlationship of micro-albuminuria with age, duration of diabetes, BMI, fasting blood sugar (FBS), post meal blood sugar (PMBS), and uric acid (r-value=0.32, p-value=0.0013) in patients of diabetes mellitus. There is positive and significant correlation between serum UA with age and BMI in patients of diabetes mellitus.

Conclusion: Microalbuminuria may be used as a predictor for early kidney involvement in type 2 diabetes. Early diagnosis of renal involvement as predicted by microalbuminuria may be used to avoid diabetic nephropathy in type 2 diabetes. Uric acid may be used to screen diabetic nephropathy in patients with diabetes mellitus. Hyperuricemia can be represented as increased glucose intolerance, and diabetes and diabetic nephropathy.

Key Words: Microalbuminuria, Uric acid, Type 2 Diabetes mellitus, Creatinine, Nephropathy

INTRODUCTION

Diabetes mellitus is a chronic metabolic condition which is characterised by hyperglycemia, and protein and fat metabolism derangement.[1] Globally, the occurrence of diabetes in 2000 was approximately 2.8 %, which is predicted to grow to 4.4 % by 2030. About 40 % of people having type 1 diabetes (T1DM) as well as 5-15 % of people with type 2 diabetes (T2DM) ultimately experience end-stage renal dis-ease (ESRD), even if the occurrence in some ethnic groups is significantly higher.[2,3] Ethnic differences, altered lifestyles, changes in eating preferences, and obesity are the main risk factors for diabetes development. In type II diabetic patients, however, external factors correlated with or non-associated with diabetes serve a significant part in the diagnosis of diabetes nephropathy such as dyslipidemia, hypertension, obesity, and metabolic syndrome.[4]

Diabetic nephropathy is among the most serious health problems of diabetes, which most commonly leads to end-stage renal disease. Advanced diabetic nephropathy is the other main reason of end-stage renal disease and worldwide occurring glomerulosclerosis. In the end, 20-40% of diabetes patients experience nephropathy, although it is uncertain if not all patients with diabetes experience this complication.[5] This is tragic that most diabetics would have hypertension at the time of diagnosis, and studies have shown that 50 % of diabetics and hypertensive patients result in a seven-fold rise in mortality. Accompanying nephropathy leads to a 37-fold rise in mortality among diabetes and hypertension patients[6].

Diabetic nephropathy can be avoided as diabetic nephropathy develops from subclinical condition to the earliest clinically detectable stage of microalbuminuria, i.e. 30 to 300 mg/day urinary albumin to overt nephropathy suggested by macroalbuminuria .[7-9]

Microalbuminuria identification in these patients detects individuals at risk of developing kidney disease[10,11] cardiovascular problems, diabetic retinopathy, and death.[12] Up to 30 % of people with recently diagnosed type 2 diabetes may still have abnormally elevated amounts of urinary albumin, i.e. macroalbuminuria, meaning that at the time of diagnosis most patients will have significant diabetic nephropathy. Microalbuminuria is the initial clinically identifiable stage of diabetic kidney disease at which proper treatments can reverse disease progression. The American Diabetes Association (ADA) has suggested that diabetic patients must do an annual microalbuminuria check and serum creatinine assessment.[13]

Diabetic kidney disease (DKD) corresponds to the diabetes-specific kidney disease.[14] DKD is indicated by elevated urinary albumin excretion which is arbitrarily divided into:

Table I: Urinary protein excretion categories of Type 2 diabetes patients[14]

Category	Spot Collection (mg/g creatinine)	24-Hour Collection (mg/24 hrs)
Normo-albuminuria	<30	<30
Microalbuminuria	30-300	30-300
Macroalbuminuria	>300	>300

Uric acid (UA) is a final product of human purine metabolism, approximately one-third of it is processed in the intestine, while two-thirds is excreted through the kidneys.[15-17] Since uricase is absent, humans have a greater amount of UA in serum as compared to other mammals. UA is predominantly excreted in the urine.

Nearly all serum UA is present in the ionized form, monosodium urate, while only about 5 % of urate is bound to protein at physiological pH. The interpretation of hyperuricemia is typically subjective and ranges from >6 mg/dl (360µmol/l) in women, >7 mg/dl (416µmol/l) in men, and $\geq$ 6.5 mg/dl (387µmol/l) to >8.3 mg/dl (494 µmol/l), irrespective of gender. In human life, concentrations of UA rise physiologically and gradually over time; in females, rates of UA increase after menopause additionally.[18]Although hyperuricemia.[19,20] may associate with decreased function of the kidney depending on some epidemiological studies, in patients with DM, hyperuricemia is a separate risk factor for the dysfunction of the kidney.[17] Elevated UA is related to endothelial dysfunction, insulin resistance, hypertension development and cardiovascular disease.[21]

Different clinical studies have shown that high concentrations of uric acid in the serum are strongly associated with common health conditions such as obesity, insulin resistance, diabetes, metabolic syndrome, essential hypertension, and renal disease. The rise in serum UA appears at the early and middle stages of CKD and exacerbates with renal function deterioration.[22]Chronic renal disease affects 10-13% of the general population. CKD patients have an exceptionally high chance of developing CVD as compared to the general population.

As observed, an elevated level of UA often precedes hyperinsulinemia[21], obesity[23], and diabetes.[24-25]Moreover, uric acid has been associated in developing metabolic syndrome[26] and hypertension.[27]

Measuring uric acid in terms of pre-analytics is fast, can be performed in regular laboratories using simple methods, and is affordable. Therefore a preventive, cost-effective approach is feasible, with potential consequences for public health.

With this overview, this study was undertaken to assess the significance of microalbuminuria and uric acid in the early detection of renal and cardiovascular involvement in type 2 Diabetes mellitus and early prevention of T2DM complications.

MATERIAL AND METHODS

This cross-sectional study was carried out at Datta Meghe Medical College, Nagpur in collaboration with Jawaharlal Nehru Medical College Datta Meghe Institute of Medical Science (Deemed University) Sawangi, Maharashtra, India, between August 2019 to March 2020. 100 diagnosed patients of type 2 Diabetes Mellitus in the age group of 25-75 years, coming in medicine OPD / Diabetic clinic of DMMC Nagpur, JNMC and DMIMS Sawangi Wardha, Maharashtra were taken as cases and 100 age and sex-matched normal persons were taken as controls. Patients with complications like retinopathy, h/o diabetic foot lesion, cardiovascular diseases, overt nephropathy, Type 1 Diabetes Mellitus, hyper-

tension, pregnancy, urinary tract infections, acute febrile illness, patients on ACE inhibitors, on chronic NSAIDS, patients on treatment with uric acid lowering drugs or diuretics, patients having hepatic diseases or renal diseases, patients with gouty arthritis, menstruation or vaginal discharge, leukemia, myeloma, chemotherapy, radiotherapy, congestive cardiac failure or any other chronic illness were excluded from the study. The clearance was obtained from the Ethical Committee of the Institution. The patients obtained informed and written consent, with the clarification of the study protocol.

Following at least 8 hours of fasting, venous blood samples were obtained from all subjects and tested on auto-analyser for fasting plasma glucose (FPG), 2 hours prandial glucose (2hPG), serum uric acid and serum creatinine. The urine sample was collected with all precautions, as random spot urine sample, urinary microalbumin, urinary creatinine was analysed. Urinary albumin creatinine ratio(ACR) was calculated.

Urine Microalbumin estimation was done by Kit based on the immunoturbidimetry method. Glucose estimation was done by kit based on Glucose oxidase-peroxidase method. Serum and urine creatinine estimation was done by kit based on Modified kinetic method of Jaffe. Serum uric acid estimation was done by kit based on Uricase Enzymatic colorimetric method**.** For estimation of urine creatinine, urine samples were diluted in 1: 49 ratio with distilled water and result were multiplied by 50.

Albumin creatinine ratio (ACR) is ratio of urinary albumin to urinary creatinine. It was measured as mg of albumin per gram of creatinine.

Urinary albumin concentration (UAC): It is the concentration of albumin in one litre of urine or albumin excreted per litre of urine. It is expressed as (mg/L).

UAC (mg/L)= Albumin (mg/dl) x10

Creatinine (g/dl) = 1000 x Creatinine (mg/dl)

ACR (mg/g of creatinine) was calculated as albumin (md/dl) divided by creatinine (g/dl).

Fasting plasma glucose (FPG), 2 hours postprandial glucose levels (2hPG), microalbuminuria (MAU), serum Uric acid (UA), and serum creatinine were compared between cases and control.

Microalbuminuria has been described as urinary albumin creatinine ratio (ACR) between 30- 300 mg/g of creatinine. ACR less than 30 mg/g creatinine was considered as normoalbuminuria (NA).

Hyperuricemia was defined as serum uric acid more than 7mg/dl in males and more than 5.7 mg/dl in females.

Stastical Analysis

The demographic and biochemical factors were described as Mean ± SD. Categorical variables were described in percentage and real numbers. The demographic and biochemical parameters were compared in both cases and control by conducting unpaired t-test. Chi-square tests were used to evaluate categorical variables. Chi square test for linear trend was used to correlate the prevalence of microalbuminuria and duration of diabetes.

Wilcoxon Rank sum test was used to compare microalbuminuria and serum Uric acid between males and females in cases and controls as well as to compare microalbuminuria and serum Uric acid between cases and controls.

Statistical software STATA version 13.0 was used for data analysis.

$p < 0.05$ was taken as significant(S)

$p < 0.001$ was taken as highly significant(HS)

$p > 0.05$ was taken as non-significant (NS).

RESULTS

Table 1 shows a comparison of clinical and metabolic characteristics in cases and controls. Out of 100 cases studied, there were 30 males and 70 females whereas there were 22 males and 78 females in controls. The mean value of age (years) in cases and control was found to be   54.2 ± 10.94 and 51.1 ± 11.50 respectively. The mean value of BMI (kg/mt²) in cases and control was found to be 25.40± 2.14 and 23.33 ± 1.78 respectively. The mean value of fasting plasma glucose (FPG) (mg/dl) in cases and control was found to be 194.76± 68.83 and 85.14 ± 10.44, respectively. The mean value of postmeal plasma glucose (2hPG) (mg/dl) in cases and control was found to be 278.49 ± 91.82 and 121.06 ± 20.33, respectively. The mean value of urine microalbumin (MAU) (mg/g creatinine) in cases and control was found to be 74.33 ± 86.59 and 25.87± 9.9, respectively. The mean value of serum uric acid (mg/dl) in cases and control was found to be 5.89 ± 1.64 and 4.6 ± 0.99, respectively. The mean value of serum creatinine (mg/dl) in cases and control was found to be 1.14 ± 0.41 and 0.94 ± 0.96, respectively. The age group, BMI, fasting plasma glucose(FPG), postmeal plasma glucose (2hPG), urine microalbumin (MAU) were higher in cases as compared to control and the difference was statistically highly significant (p<0.0001).

There was higher serum uric acid observed in cases as compared to control and the difference was statistically significant (p=0.0396). There was high serum creatinine observed in cases as compared to control and the difference was statistically non-significant (p=0.0854).

Table 1: Comparison of Clinical and Metabolic Characteristics in Cases and Controls

Variable		Cases	Control	p-value
Age (Yrs)		54.2 ± 10.94	51.1 ± 11.50	<0.0001, HS
Sex (Total No.)	Males	30	22	
	Females	70	78	
BMI (kg/mt²)		25.40± 2.14	23.33 ± 1.78	<0.0001, HS
FPG (mg/dl)		194.76± 68.83	85.14± 10.44	<0.0001, HS
2hPG(mg/dl)		278.49± 91.82	121.06 ± 20.33	<0.0001, HS
MAU (mg/gm creatinine)		74.33± 86.59	25.87± 9.9	<0.0001, HS
Serum Uric Acid (mg/dl)		5.89 ± 1.64	4.6 ± 0.99	0.0396,S
Serum Creatinine (mg/dl)		1.14± 0.41	0.94 ± 0.96	0.0854,NS

HS- highly significant, S- significant ,NS- Non significant

Table 2: Distribution of Cases and Control According to Prevalence of Microalbuminuria

Microalbuminuria (MAU)	Cases	Control
Present	37	8
Absent	63	92
Total	100	100

Table 2 revealed the distribution of cases and control according to prevalence of microalbuminuria. Out of the 100 patients studied, 37 patients had microalbuminuria and 63 patients had normoalbuminuria and out of 100 normal subjects 8 had microalbuminuria and 92 had normoalbuminuria.

Table 3: Gender Wise Disribution of Microalbuminuria (MAU) and Serum Uric Acid (UA) in Cases.

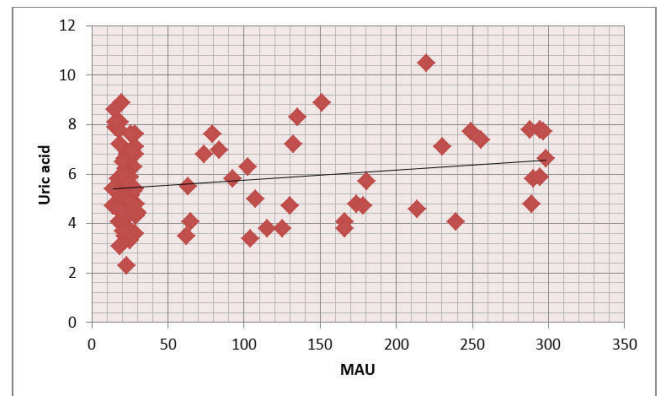|	CASES				p-value
	Male		Female		
	Mean	SD	Mean	SD	
MAU (mg/g creatinine)	119.43	110.92	55.06	65.80	0.0224,S
Sr UA (mg/dl)	5.22	1.43	5.90	1.64	0.0382,S

S- significant

Table 3 shows gender-wise distribution of microalbuminuria (mau) and serum uric acid (UA) in cases. The comparison of MAU AND UA between males and females in cases showed that males had higher values of MAU as compared to females and these values were significant. Serum UA was higher in females as compared to males and these values were significant.

Table 4: Correlation of Microalbuminuria (Mau) with other Parameters in Cases

Parameter	Micro-Albumin (ACR)	
	r-VALUE	p-value
Age in yrs	0.28	0.0074,HS
Duration of DM	0.28	0.0052,HS
BMI	0.29	0.0032,HS
FBS	0.28	0.0049,HS
2hPG	0.23	0.0205,S
Uric Acid	0.32	0.0013,HS
Serum Creatinine	0.14	0.1695,NS

S- significant , HS- highly significant , r-Pearson's Correlation Coefficient

Table 4 shows correlation of MAU with other parameters in cases. There is direct and highly significant correlation of MAU with age (r=0.28,p=0.0074), duration of diabetes (r=0.28,p=0.0052), BMI (r=0.29,p=0.0032) , FBS (r=0.28,p=0.0049) , UA (r=0.32,p=0.0013) (Figure 1).Correlation of MAU with 2hPG is direct and significant (r=0.29,p=0.0205). Correlation of MAU with serum creatinine was non-significant (r=0.14, p=0.1695).

Figure 1: Correlation of MAU with Uric acid (r=0.32)

Table 5: Correlation of Uric Acid with other Parametres in Cases

Parameter	Uric Acid	
	r-value	p - value
Age in Yrs	0.33	0.0008, HS
Duration of DM	0.02	0.8082,NS
BMI	0.33	0.0001,HS
FBS	0.12	0.2196,NS
PMBS	0.10	0.3093,NS
Serum Creatinine	0.10	0.9991,NS

NS-Non significant, HS- highly significant, r-Pearson's Correlation Coefficient

Table 5 shows correlation of UA with other parameters in cases. There is direct and highly significant correlation of UA with age (r=0.33,P=0.0008)and BMI (r=0.33, p=0.0001). Correlation of UA with duration of diabetes(r=0.02,p=0.8082) , FBS(r=0.12,p=0.2196), PMBS(r=0.1,p=0.3093) and serum creatinine (r=0.1,p=0.9991) were found to be non- significant.

DISCUSSION

Diabetic nephropathy is a significant health concern in diabetes patients. The normal course of diabetic nephropathy was generally seen as a downward trajectory from normoalbuminuria to end-stage renal disease (ESRD) via an intermediate stage indicated by microalbuminuria and evident proteinuria.[28] Approximately 30 percent of chronic renal failures in India are due to diabetic nephropathy.[29] The earliest clinical symptom of nephropathy is the existence in the urine of small but increased concentrations of albumin, called microalbuminuria (30-300 mg / day). [30]

Presenting the concept of microalbuminuria, i.e., elevated but clinically undetectable excretion of urinary albumin, has revealed fresh and exciting information with important clinical implications for diabetic patients.[31] The American Diabetes Association (ADA) has indicated that an annual serum creatinine and microalbuminuria analysis is needed for people with diabetes.[13] Primary control of diabetic nephropathy is achievable as it is possible to recognize and treat the conditions that cause the transition from normal urinary excretion to microalbuminuria and from microalbuminuria to diabetic nephropathy.[32]

Serum uric acid is the end product of purine metabolism.[33]

Hyperuricemia is closely related to insulin resistance syndrome, an known risk factor for type 2 diabetes.[34] Hyperuricemia is possibly related to glucose intolerance due to multiple mechanisms, although the most significant is the correlation between insulin and renal resistance to urate absorption.[35] Therefore, research into the role of uric acid in the pathogenesis of the development of type 2 diabetes is important.

In our study, the mean age of diabetics was 54.2 ± 10.94 years, comprising 30 males and 70 females, and the mean age of the control group was 51.1 ± 11.50 years comprising of 22 males and 78 females.

In our study, we found the mean value of fasting plasma glucose in cases (194.76± 68.83mg/dl) was significantly higher (p<0.0001) than fasting plasma glucose in control (85.14± 10.44 mg/dl).

In our study, we found the mean value of post-meal plasma glucose in cases (278.49± 91.82 mg/dl) was significantly higher (p<0.0001) than post-meal plasma glucose in control (121.06 ± 20.33 mg/dl).

In our study, the diabetic patients showed higher levels of fasting and post-prandial glycemia in comparison to the controls, as expected.

Our study agrees with the studies conducted by Khatib N et al.(2008)[36], Ganesh G et al.(2012)[37], Rohitash K et al.(2014).[38] They found the higher levels of fasting and post-prandial blood sugar in diabetes mellitus patients compared to control.

In our study, we found mean value of urine microalbumin in cases (74.33±86.59mg/g creatinine) was significantly higher (p<0.0001) than urine microalbumin in control (25.87± 9.9 mg/g creatinine).

Hyperglycemia leads to kidney dysfunction through many pathways, i.e. non-enzymatic protein glycation, hexosamine activation, and increased intracellular reactive oxygen species. Certain factors that contribute to diabetic kidney disease are increased glomerular capillary pressure, as well as proteinuria. An increase in Microalbuminuria is associated with a fractional mesangial expansion that eventually contributes to diabetic nephropathy.

The findings of our study are similar to those observed by Prasad et al.(2012)[39] who observed higher levels of glycosylated haemoglobin and microalbuminuria in type 2 diabetes patients as compared with controls. In another study done by Naveen et al.(2012)[40] similar results were observed. They found higher microalbuminuria in diabetes mellitus patients than controls.

In our study, we found the mean value of serum uric acid in cases (5.89 ± 1.64 mg/dl) was significantly higher (p<0.0001) than serum uric acid in control (4.6 ± 0.99 mg/dl). Hyperuricemia was found to be related to insulin resistance and thus to type 2 diabetes mellitus.[41]

Our study agrees with the studies conducted by A. Dehghan et al.(2008)[42], Chien KL et al.(2008).[43] They also reported higher uric acid in diabetics as compared to controls.

Similar observations were found in studies done by C. K. Kramer et al.(2009)[44], N. Nakanishi (2003)[45], S. Kodama et al.(2009)[46]. They also observed higher uric acid in diabetics than controls.

In our study, we found that, out of 100 diabetic patients, 37 patients had microalbuminuria (prevalence 37% in cases). The higher prevalence in this study can be due to the low glycemic control in most patients due to irregular treatment and also due to small sample size.

In our study, out of 100 control subjects, 8 had microalbuminuria (prevalence 8% in control). It suggests that microalbuminuria may precede and even predict later onset of NIDDM.[31]

Numerous variations in the prevalence of microalbuminuria

have been identified in various epidemiological and cross-sectional researches. OnyechiModebe et al.(2000)[47] reported prevalence of microalbuminuria to be 25% in diabetics. H-H Parving et al.(2006)[48,] and Iranparvar Alamdari M et al.(2006)[49]both found the prevalence of microalbuminuriain diabetics to be 39% .

In studies done by Janet Joy Kachuchuru Lutale et al.(2007)[50], Unnikrishnan R et al.(2007) [51], Thakkar B et al.(2011)[52], and Dayanidhi S et al.(2013)[53] prevalence of microalbuminuria in diabetics was found to be 10.7%, 26.9%, 54.09%, and 51%, respectively.

The wide variations found in the prevalence of nephropathy in various studies may be due to differences in the nature of the research and the methodologies adopted for the disease description.

In our study, we found that microalbuminuria in diabetic males (119.31±110.92 mg/g creatinine) was significantly higher(p=0.0224) as compared to diabetic females (55.06±65.80 mg/g creatinine). The distinct prevalence of microalbuminuria between males and females can be attributable to the lower excretion of creatinine in females than males and the fact that the albumin to creatinine ratio was used in order to diagnose microalbuminuria .[54]

ThakkarB et al.(2011) [52] also found male dominance in gender-wise correlation of microalbuminuria. Varghese et al.(2001)[55] observed increased microalbuminuria prevalence among Indian men as compared to Indian women. Olivarius *et al*[56] also found that microalbuminuria prevalence was higher in males compared with females. In our study, we found that, uric acid was significantly higher (p=0.0382) in diabetic females (5.90±1.64mg/dl) as compared to diabetic males (5.22±1.43mg/dl) in cases. The basic pathophysiological mechanisms for the strong correlation of hyperuricemia with the explanations for the differences in gender are unclear and should be studied further. However, it has been shown that the genetic basis of uric acid production has major sex-specific impact [57], indicating probably a genetic basis for gender differences even in the metabolism of glucose.

Latest cohort study reported gender differences in the association between uric acid levels and diabetes development.[58-60] Previous studies with a different sample from the MONICA / KORA study have shown a clear association between uric acid levels and incident diabetes in females and not in males.[58]

Yamada et al.[59] reported in another study that increased uric serum acid predicted impaired fasting glucose and type 2 diabetes only in Japanese women but not in men undergoing health checks. Chou *et al*[60] found that levels of insulin resistance and plasma glucose were more associated with levels of serum uric acid in women than in men.   O u r study showed statistically significant linear relationship of microalbuminuria with age (r=0.28,p=0.0074). In a similar study done by Chowta NK et al.(2009)61 it was observed that there was a positive correlation between microalbuminuria and age.

Similar results were found in studies done by Ruilope LM et al.(2006)[62], Metcalf P et al.(1992).[63] They observed a positive correlation between microalbuminuria and age.

Our study showed a statistically significant linear relationship of microalbuminuria with duration of diabetes (r=0.28,p=0.0052). Diabetes duration has significant contribution to microalbuminuria production through accumulations of advanced glycosylation end products caused by hyperglycemia due to long term exposure.

Our study was in accordance with in accordance to study done by H-H Parving et al.(2006)[48], who observed that the duration of diabetes was the independent risk factor for microalbuminuria. In another study, Eghan BA et al.(2007)[64]reported that duration of diabetes is a significant predictor of micro-albumin.

Similar results were observed in studies done by Janet Joy Kachuchuru Lutale et al.(Jan 2007)[50], Unnikrishnan R et al.(AUG 2007) [51], Chowta NK et al.(2009)[61] in which significant positive correlation was observed between microalbuminuria and duration of diabetes.

The present study showed a statistically significant linear relationship of microalbuminuria with BMI (r=0.29, p=0.0032)**.** The American Diabetes Association advocates monitoring for adults up to the age of 45, particularly those with 25kg / m2 of BMI. BMI 19.5-24.9 is regarded as a good weight while 25-29.9 is considered overweight and BMI 30 is considered obese.[65] The significant diabetic nephropathy related weight gain was observed in this study. Weight gain is correlated considerably with the diabetics that we studied in this report. Diabetic patients had a BMI of 25.40± 2.14 kg / mt2 compared to control patients with a BMI of 23.33 ± 1.78 kg / mt2 suggesting overweight patients.

A study on Type 2 diabetic patients by Mokdad et al.(2001)[66] reported a correlation between obesity and microalbumin. They found that patients with higher BMI were strongly associated with microalbuminuria. Dayanidhi S et al.(2013)[53]

Onyechi Modebe et al.(2000)[47]*,* Gall ma et al.(1997)[11], Phillips CA et al.(2002)[67] also performed similar studies. They observed a positive correlation between microalbuminuria and BMI.

In our study we found a direct and significant correlation between urine microalbumin and FBS (r=0.28,p=0.0049) and PMBS (r=0.23,p=0.0205). Chronic hyperglycaemia is a significant factor in diabetic nephropathy progression by polyol pathways, increase in oxidative stress, production of advanced glycosylated end products (AGEs), and protein

kinase activation-C.[68] Hyperglycaemia promotes the production of mesangial cell-matrix and apoptosis of mesangial cell.[69] AGEs are present in different tissues attached to collagen which can lead to the associated renal and microvascular complications.[70] Diabetic nephropathy can impair the renal expression of nephrin.[71]

Our study favoured the studies done by Iranparvar Alamdari M et al.(2006)[49] and Onyechi Modebe et al.(2000).[47] They observed that the mean value of fasting plasma glucose was higher significantly in patients with microalbuminuria than in patients with normoalbuminuria, respectively. Varghese et al.(2001)[55] reported a positive correlation of the prevalence of microalbuminuria with the fasting blood sugar.

Our study showed a statistically significant linear relationship of microalbuminuria with serum uric acid (r=0.32, p=0.0013). An increased concentration of uric acid in serum is a dangerous factor for the kidneys,[16] as it is observed that hyperuricemia-induced endothelial dysfunction, glomerular hypertension, and renal hypertrophy reduce renal perfusion by inducing proliferation of afferent arteriolar vascular smooth muscle cell .[72] As the development of albuminuria is the first indication of kidney damage and diabetic nephropathy in patients with diabetes, it confirmed the association of ACR and hyperuricemia thereby confirming that hyperuricemia plays a role in diabetic nephropathy. Similar result was found in the study done by Shokoofeh Bonakdaran et al.(2011).[73] who reported that hyperuricemia was associated with a greater chance of albuminuria in patients with type 2 diabetes mellitus.

Siu and colleagues observed a decrease in serum uric acid levels in hyperuricemic patients associated with regression in kidney disease.[74]

A direct and significant correlation was seen between UA and age(r=0.33,p=0.0008) and UA and BMI (r=0.33,p=0.0001). Hyperuricemia was found to be linked with obesity and insulin resistance and hence type 2 diabetes mellitus.[41] Similar results were found in study done by Abbas Dehghan et al.(2008)[42], J. A. Robles-Cervantes et al.(2011)[75] who found a positive correlation between UA and BMI.

There were suggestions for a variety of mechanisms through which uric acid would cause changes in the metabolism of glucose. Hyperuricemia was found to be associated with systemic inflammation and oxidative stress which both play a major role in diabetes mellitus development.[17] Uric acid also reduces the production of endothelial nitric oxide and thus causes endothelial dysfunction and insulin resistance.[76]

Lastly, Uric acid is correlated with elevated glomerular pressure and elevated sodium reabsorption of kidney and these renal reactions are significantly impaired by high concentrations of insulin.[77] The cumulative effects of high levels of uric acid and insulin resistance on renal functions may lead to increased glucose intolerance, diabetes progression, and hypertension. Hyperuricemia causes endothelial dysfunction in patients with type 2 DM that results in nephropathy.[37] Study done by Tseng also says even mild hyperuricemia will results in kidney injury.[16]

Anju Gill et al.[2013] [78]found a positive correlationship between UA and serum insulin in newly diagnosed diabetics. They observed that, in newly diagnosed diabetics, the serum uric acid levels increased in accordance with increasing serum insulin levels.

Abbas Dehghan et al.[2008] [42] found that subjects with higher serum uric acid levels are more at risk for type 2 diabetes. C .K. Kramer et al.(2009)[79] showed that serum uric acid values in adults who were intolerant to glucose may be useful as predictors of DM2.

The progression of diabetic nephropathy once initiated is one of the gradual and persistent declines in renal function, and once developed, treatment is ultimately ineffective and refractory. In addition, the emergence of diabetic nephropathy leaves the diabetic patient characteristically susceptible to atherosclerotic disease, an affliction that tends to deny diabetic patients the possibility of a healthier, longer existence even after renal replacement therapy has been implemented. Therefore, it is clear that the safest and most successful approach for preventing diabetic nephropathy should be aimed at identifying and treating the disease at an early phase of development, i.e. at a time when it is considered to be more treatable, in order to minimize the morbidity and mortality associated with the disease.

CONCLUSION

Diabetic nephropathy is amongst the most serious diabetes complications and the major cause of end-stage renal disease**.** For patients with type 2 diabetes, microalbuminuria is the most significant early symptom that heralds the initiation of chronic vasculopathy and is associated with damage to the target organ. The effect of high levels of uric acid on kidney functions can lead to increased glucose intolerance, hypertension, and diabetes development.

Early identification of the risk of diabetic nephropathy will help to decrease morbidity and mortality in type 2 diabetes and its related complications. Strict glycemic control, microalbuminuria monitoring, and serum uric acid monitoring with better management may delay diabetic nephropathy.

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