A Retrospective Comparative Study of Urine Albumin Creatinine Ratio over 24 Hour Urine Albumin in Early Detection of complications in Subjects with Type 2 Diabetes Mellitus

Dr. Radhika Ratanlal Bajaj[1], Dr. S. T. Thorat[2], Dr. Sagar Ramesh Bhutada[3]

[1]Junior Resident, Department of Medicine, Krishna Institute of Medical Sciences Deemed to be University, Karad, Satara, Maharashtra, India
[2]Professor, Department of Medicine, Krishna Institute of Medical Sciences Deemed to be University, Karad, Satara, Maharashtra, India
[3]Senior Resident, Department of Surgery, Punjabrao Deshmukh Medical College, Amravati, Maharashtra, India

Corresponding Author: Dr. S. T. Thorat

ABSTRACT

Background: Measurement of urinary protein is one of the important markers used for assessing the degree of renal impairment. Early detection of renal impairment is important to give appropriate treatment before it progresses to irreversible stage.

Material and Methods: Study design**:** This was retrospective, comparative study done on 70 patients with type 2 diabetes mellitus in a tertiary care hospital over period of 18 months from October 2019 to March 2021**.** Enrolled patients underwent fasting blood sugar, postprandial blood sugar, glycosylated HbA1c, Albumin Creatinine ratio in a spot urine sample, 24 hour urinary albumin.

Results: The mean age of the subjects was 68.75 ±10.22 years The majority of subjects were males (60%) and females were 40%. The majority of subjects were with Diabetes duration of 6-10 years (44.29%) and the mean duration of diabetes was 8.63 ±3.45 years. The fundoscopy findings of diabetic retinopathy among subjects showed that majority of subjects presented with moderate DR (32.86%) followed by mild DR (28.57%) The proliferative DR was seen in 5 (7.14%) subjects. The mean blood urea of the subjects was 44.43 mg/dl while mean serum creatinine among subjects was 1.44 mg/dl. Mean HbA1c was 7.95% among subjects. The mean 24 hour urine albumin and UACR of the subjects were 252.83mg and 232.71 mg/dl respectively. We observed that majority of subjects presented with value between 30-300 mg (35.71%) with 24 hour urine albumin method. The 24 hour urine albumin value>300 mg was seen in 21 (30%) subjects. Majority of subjects showing Urine albumin to creatinine ratio between 30-300 mg (60%), while value>300 mg was seen in 20 (28.57%) subjects. We observed that 24 hour urine albumin and duration of diabetes mellitus showed statistically significant correlation (p<0.001). With respect to the correlation of Urine albumin to creatinine ratio, various study parameters observed that Urine albumin to creatinine ratio showed significant correlation with HbA1c, FBS, PPBS, diabetes duration and Fundoscopy with statistical significance. (p<0.05). It was observed that 24 Hr Urine Albumin showed significant correlation with HbA1c, FBS, PPBS and diabetes duration with statistical significance ('p'<0.05).

Conclusion: The present study was conducted to find out early diagnosis of renal complications of type 2 diabetes mellitus in the form of diabetic nephropathy. The study was predominated by male gender with a ratio of 3:2 and included 2/3rd subjects in age group 61-80 years.

It was found that Urine albumin to creatinine ratio (UACR) was better parameter than 24 hour

urine albumin to detect proteinuria in subjects with type 2 diabetes mellitus.

There was a positive correlation of Urine albumin to creatinine ratio with duration of diabetes, HbA1c levels, and diabetic retinopathy; indicating the role of early detection of proteinuria and strict glycemic control, to halt the disease progression in subjects with type 2 diabetes mellitus.

Keywords: Urine albumin to creatinine ratio (UACR), HbA1c, 24 hour urine albumin.

INTRODUCTION

According to the WHO, diabetes affects more than 170 million people throughout the world, and this figure will rise to 370 million by the year 2030.[1] About one third of these patients affected will eventually have progressive deterioration of renal function. Hyperglycemia promotes the reaction of glucose with components of arterial wall to form advanced glycation products, these products crosslink with collagen which increases the arterial stiffness.[2] The hallmark of diabetic microangiopathy at the level of ultra-structural pathology is the thickening of the capillary basement membrane, associated with this is the increased vascular permeability throughout the body which causes the development of micro vascular complications like diabetic retinopathy, neuropathy and nephropathy.[3] Diabetic nephropathy is a dreaded disease with progressive and continuous deterioration in glomerular function resulting in irreversible renal failure. It is an important cause for morbidity and mortality and is also now among the most common cause of end stage renal disease.[4] However there is an early reversible stage of diabetic renal disease called incipient diabetic nephropathy. In this stage there is rise in urinary excretion of albumin, this may mediate the physiological changes which lead to excretion of albumin in the urine known as albuminuria. Levels of albumin can be expressed as a concentration or as a ratio of albumin to creatinine. But the rise is detectable only by use of sensitive assay for urinary albumin.[5] Microalbuminuria is an established marker of diabetic nephropathy. For quantification of albuminuria, 24 hours urinary albumin concentration (24 hours UAC) in 24 hours urine sample (timed collection) is considered as gold standard.[6,7] But it has major limitations of time consumption, sample collection errors, poor patient compliance and costly. Patient compliance is better with random urine sample collection than spot urinary albumin excretion to spot urinary creatinine excretion; hence if there is any change in glomerular filtration rate secondary to hydration status and other factors or any underlying pathology, the ratio remains unaffected. Thus, UACR in random urine sample correlates well with 24-hour urinary albumin concentration in 24 hours urine sample. Early detection of renal impairment is important to give appropriate treatment before it progresses to irreversible stage. In patients with glomerulopathies with or without nephrotic syndromes repeated measures of proteinuria are needed to evaluate the effects of therapeutic interventions and to determine the outcome of the glomerular disease; in order to achieve an appropriate clinical management.[8,9] In these patients it is necessary to determine the level of proteinuria to identify a total or partial response, or resistance to treatment.

Aim: To study urine albumin: creatinine ratio in subjects with type 2 diabetes mellitus and to find its relation with 24 hour urine albumin.

MATERIAL AND METHODS

This was retrospective, comparative, observational, descriptive study done on patients with type 2 diabetes mellitus. This study was conducted in KIMS Hospital, Medicine department over period of 18 months. We studied 70 patients with type 2 diabetes mellitus in a tertiary care hospital over period of 18 months from October 2019 to March 2021. The Institutional Ethical committee approval was taken (IEC protocol number: 216/2019-2020).

Inclusion criteria: A total sample size of 70 patients who has been diagnosed as type 2 diabetes mellitus were considered for enrollment in to the study.

Exclusion criteria: Patients diagnosed as type 1 diabetes mellitus, pregnant women, recently diagnosed with urinary tract infection, history of long term consumption of drugs like NSAIDS, ACE inhibitors/ARBs, aminoglycosides, lithium or any other nephrotoxic drugs, primary and secondary renal diseases, diagnosed cases of overt nephropathy of any etiology, malignancy and history of exposure to radiation.

Statistical analysis:

Data Collected was analysed for mean, percentage, standard deviation and chi square test for quantitative data by using Microsoft excel spread sheet. Appropriate statistical tests were applied using SPSS software version 21 (trial version) for analysis and 'p' value <0.05 was considered as statistically significant.

RESULTS

Seventy subjects with type 2 diabetes mellitus were selected consecutively during the study period. 46 (65.71%) subjects were in age group 61 to 80 years followed by 22 (31.43%) subjects in 41-60 years and 2(2.86%) subjects in >80 years of age group. The mean age of the subjects was 68.75 ±10.22 years. There were 42 males (60%) and 28 females (40%) in the present study. Male:female ratio was 3:2. Majority of subjects were with diabetes duration 6-10 years (44.29%) followed by duration of 11-15 years (30%). The mean duration of diabetes was 8.63 ±3.45 years. Majority of subjects presented with moderate non proliferative diabetic retinopathy (32.86%) followed by mild non

proliferative diabetic retinopathy (28.57%). The proliferative diabetic retinopathy was seen in 5 (7.14%) subjects whereas diabetic retinopathy was absent in 7 (10%) subjects.

The mean fasting blood sugar of the subjects was 191.29mg/dl while mean post prandial sugar among subjects was 272.89mg/dl. The mean HbA1c was 7.95% among subjects. It was observed that majority of subjects presented with 24 hour urine albumin 30-300 mg (35.71%). The 24 hour urine albumin >300 mg was seen in 21 (30%) subjects and <30 mg in 24 (34.29%) subjects. Majority of subjects presented with Urine albumin to creatinine ratio 30-300 mg/g (60%). The Urine albumin to creatinine ratio >300 mg/g was seen in 20 (28.57%) subjects whereas <30 mg/g in 8 (11.43%) subjects. The mean 24 hour urine albumin was 252.83 mg with maximum value of 840 mg whereas mean UACR of the subjects was 232.71mg/g with maximum value of 580mg/g (Table 1)

Table 1: Study Parameters distribution in the participants

Parameter	Mean	SD
BSL (F)	191.29	85.98
BSL(PP)	272.89	101.71
HbA1c	7.95	1.25
24hour urine albumin (mg)	252.83	239.62
UACR (mg/g)	232.71	152.15

62 subjects (88.57%) had proteinuria present by urine albumin creatine ratio as compared to 46 subjects (65.71%) who had proteinuria by 24 hour urine albumin. Hence we found that urine albumin creatine ratio was better parameter to detect proteinuria in subjects with type 2 diabetes mellitus and was statistically significant. ('p' <0.001).

42 subjects (60%) had microalbuminuria and 20 subjects (28.57%) had macroalbuminuria by urine albumin creatinine ratio whereas 25 subjects (35.71%) had microalbuminuria and 21 subjects (30%) had macroalbuminuria by 24 hour urine albumin method. (Table 2)

Table 2: Comparison of proteinuria values from 24-hour urine albumin and UACR

Proteinuria	A <30	B 30 - 300	C > 300	Total
24 hour urine albumin (mg)	24(34.28%)	25(35.71%)	21(30%)	70
UACR (mg/g)	8(11.4%)	42(60%)	20(28.57%)	70

Correlation of urine albumin to creatinine ratio and Fundoscopy

7 subjects (10%) had no diabetic retinopathy,58 subjects (82.86%) had non proliferative diabetic retinopathy and 5 subjects (7.14%) had proliferative diabetic retinopathy. Urine albumin to creatinine ratio and Fundoscopy showed statistically significant correlation ('p'<0.001) (Table3).

Table 3: Correlation of Fundoscopy & UACR

UACR	No DR	Mild	Moderate	Severe	Proliferative	Total
A <30	7 (10%)	1 (1.42%)	0	0	0	8 (11.42%)
B 30 - 300	0	19 (27.14%)	22 (31.42%)	1 (1.42%)	0	42 (60%)
C > 300	0	0	1 (1.42%)	14 (20%)	5 (7.14%)	20 (28.5%)
Total	7 (10%)	20 (28.57%)	23 (32.86%)	15 (21.43%)	5 (7.14%)	70 (100%)

Correlation of urine albumin to creatinine ratio and duration of diabetes

Among 7 subjects with duration of diabetes <5 years, 3 (4.28%) subjects had UACR value between 30-300 mg/g. Also 25 subjects (35.71%) among total 31 subjects (44.29%) with duration of diabetes 6-10 years had UACR values 30-300 mg/g. However, with increased duration of 15-20 years,9 subjects(12.85%) among 11 subjects (15.71%) had UACR value >300mg/g. Urine albumin to creatinine ratio and duration of diabetes mellitus showed statistically significant correlation ('p'<0.001) (Table 4)

Table 4: Correlation of Duration of Diabetes & UACR

UACR	A <5	B 6 - 10	C 11-15	D 15 - 20	Total
A <30	4 (5.71%)	4 (5.71%)	0	0	8 (11.42%)
B 30 - 300	3(4.28%)	25(35.71%)	12 (17.14%)	2(2.85%)	42 (60%)
C > 300	0	2 (2.85%)	9(12.85%)	9(12.85%)	20 (28.5%)
Total	7 (10%)	31 (44.29%)	21 (30%)	11(15.71%)	70(100%)

Correlation of urine albumin to creatinine ratio and HbA1c

Among 27 subjects (38.57%) with HbA1c value 6.5 to 7.4, 19 subjects (27.14%) had microalbuminuria whereas among 24 subjects (34.28%) with HbA1c >8.5, 14 subjects (20%) had macroalbuminuria. It was observed that Urine albumin to creatinine ratio and HbA1c showed statistically value significant correlation ('p'<0.001) (Table5)

Table 5: Correlation of HbA1c & UACR

UACR	A 6.5 to 7.4	B 7.5 to 8.4	C >8.5	Total
A <30	6(8.57%)	1(1.42%)	1(1.42%)	8(11.42%)
B 30 - 300	19(27.14%)	14(20%)	9(12.85%)	42(60%)
C > 300	2(2.85%)	4(5.71%)	14(20%)	20((28.5%)
Total	27(38.57%)	19(27.14%)	24(34.28%)	70(100%)

Correlation of Duration of diabetes with 24 hour urine albumin

24 hour urine albumin and duration of diabetes mellitus showed statistically significant correlation ('p'<0.001)

Correlations of different study parameters with UACR

Urine albumin to creatinine ratio showed significant correlation with HbA1c, FBS, PPBS and diabetes duration with statistical significance ('p'< 0.05) (Table6)

Table 6: Correlations of different study parameters with UACR

UACR and Different Parameters	UACR<30	UACR 30 - 300	UACR> 300	P Value
Duration of diabetes (Years)	5.75 ± 2.54	10.14 ± 4.55	16.05 ± 5.03	0.011*
FBS (mg/dl)	115.75 ± 15.17	173.52 ± 71.38	255.30 ± 76.94	<0.001*
PPBS(mg/dl)	191.24 ± 42.87	247.95 ± 91.09	351.08 ± 87.41	<0.001*
HbA1c (%)	7.31 ± 0.57	7.83 ± 1.13	9.41 ± 0.76	<0.001*

*Significant, 'p'<0.05, Non parametric ANOVA

Correlations of different study parameters with 24 hour urine albumin

It was observed that 24 hour urine albumin showed significant correlation with HbA1c, FBS, PPBS and diabetes duration with statistical significance ('p'<0.05) (Table7)

Table 7: Correlations of different study parameters with 24 hour urine albumin

24 hr Urine Albumin and Different Parameters	24 hr Urine albumin<30	24 hr Urine albumin 30 - 300	24 hr Urine albumin> 300	P Value
Duration of diabetes (Years)	7.47 ± 4.41	11.42 ± 5.58	15.51 ± 6.38	0.021*
FBS (mg/dl)	108.53 ± 25.79	168.26 ± 61.83	225.92 ± 86.39	<0.001*
PPBS (mg/dl)	183.25 ± 62.75	236.45 ± 83.04	321.83 ± 95.13	<0.001*
HbA1c (%)	6.91 ± 1.07	7.33 ± 1.32	8.91 ± 1.65	<0.001*

DISCUSSION

A total sample size of 70 patients who has been diagnosed as type 2 diabetes mellitus were included in the study. Patients diagnosed as type 1 diabetes mellitus, pregnant women, patients diagnosed recently with urinary tract infection, history of long term consumption of drugs like NSAIDS, ACE inhibitors/ARBs, aminoglycosides, lithium or any other nephrotoxic drugs, primary and secondary renal diseases, diagnosed cases of overt nephropathy of any etiology, malignancy and history of exposure to radiation were excluded.

In the present study, it was observed that majority of patients were in age group 61 to 80 years (65.71%) followed by 41-60 years (31.43%) The mean age of the patients was 68.75 ±10.22 years.

Tarig Karar et al [10] in a study on assessment of microalbuminuria and albumin creatinine ratio in patients with type 2 diabetes mellitus observed among 100 patients in study, 9 patients between 30 and 50 years, 52 patients between 51 and 70 years and 39 patients above 70 years.

Oshin Mantro et al[11] in a study on clinical profile and complications in patients with type 2 diabetes mellitus observed mean age in this study population was 55.36 years with a standard deviation of 11.362..

It was observed in our study that majority of patients were in male (60%) and females were 40%. Similar results are obtained done by Purty A et al[12] in Puducherry institute with 58% male population as diabetes mellitus. Tarig Karar et al[10] in a study on assessment of microalbuminuria and albumin creatinine

ratio in patients with type 2 diabetes mellitus included 46% males (n = 46) and 54% females (n = 54) patients. Oshin Mantro et al[11] in a study on clinical profile and complications in patients with type 2 diabetes mellitus observed out of 66 patients, 23(34.8%) were males whereas 43 (65.2%) were females.

In the present study, it was observed that majority of patients were with duration 6-10 years (44.29%) The mean duration of diabetes was 8.63 ±3.45 years.

Similar results are obtained done by Purty A et al[12], in Puducherry institute. In this population mean duration of diabetes was found to be 9.06 years±4.121 i.e. maximum population were having diabetes of duration 5-10 years.

The distribution of patients according to co-morbidities showed that majority of patients were having hypertension (58.57%) followed by IHD (21.43%) The stroke was observed among 8 (11.43%) patients.

The Fundoscopy findings of diabetic retinopathy among patients showed that majority of patients presented with moderate DR (32.86%) followed by mild DR (28.57%) The proliferative DR was seen in 5 (7.14%) patients.

Oshin Mantro et al[11] in a study observed complication seen in the study group was retinopathy in 46.96% patients.

Birajdar SV et al,[13] retinopathy in 56% patients with diabetes mellitus. This finding was in accordance to present study.

It was observed that female patients had more anemia (64.29%) compared to males (19.05%) with statistical significance. (P<0.001)

The mean blood urea of the patients was 44.43 mg/dl while mean serum creatinine among patients was 1.44 mg/dl. The mean fasting blood sugar of the patients was 191.29 mg/dl while mean post prandial sugar among patients was 272.89 mg/dl. HbA1c was 7.95% among patients. The above table shows distribution of patients according to lipid levels. The mean total cholesterol of the patients was 168.09 mg/dl while mean TG among patients was 153.14 mg/dl. Serum HDL was 37 among patients.

Oshin Mantro et al[11] in a study observed the mean fasting blood sugar level was 196.12±77.180, mean postprandial blood sugar level was 303.26±115.385 and the mean HbA1C levels was 10.95±2.369.

In the present study, the mean 24 hour urine albumin and UACR of the patients was 252.83mg and 232.71 mg/dl respectively. It was observed that majority of patients presented with 24 hour urine albumin 30-300 mg (35.71%) The 24 hour urine albumin >300 mg was seen in 21 (30%) patients. It was observed that majority of patients presented with urine albumin to creatinine ratio 30-300 (60%) The urine albumin to creatinine ratio >300 mg was seen in 20 (28.57%) patients.

In the present study, it was observed that urine albumin to creatinine ratio and Urine Proteinuria among patients showed statistically significant correlation ('p'<0.001) The sensitivity of urine albumin to creatinine ratio was 100% with specificity of 33%.

In the present study, it was observed that urine albumin to creatinine ratio showed positive correlation with 24 hour urine albumin, HbA1c, diabetic retinopathy and diabetes duration with statistical significance. (p<0.001)

Similar findings were seen in Sanjay Shrestha et al[14] study where urine albumin to creatinine ratio showed positive correlation with 24 hour urine albumin and HbA1c.

Tarig Karar et al[10] in a study on assessment of microalbuminuria and urine albumin to creatinine ratio in patients with type 2 diabetes mellitus observed urine albumin to creatinine ratio showed positive correlation with 24 hour urine albumin and HbA1c.

Allon Friedman et al[15] in a study on value of urine albumin to creatinine ratio as a predictor of type 2 diabetes observed positive correlation with 24 hour urine albumin and HbA1c.

It was observed that urine albumin to creatinine ratio and fundoscopy showed statistically significant correlation (p<0.001) Similarly, urine albumin to creatinine ratio and duration of diabetes mellitus showed statistically significant correlation (p<0.001), urine albumin to creatinine ratio and HBA1c showed statistically significant correlation (p<0.001)

It was observed that 24 hour urine albumin and duration of diabetes mellitus showed statistically significant correlation (p<0.001)

The correlation of urine albumin to creatinine ratio and various parameters among patients was observed and it shows that urine albumin to creatinine ratio showed significant correlation with 24 hour urine albumin, HbA1c, FBS, PPBS and diabetes duration with statistical significance. (p<0.05). It was also observed that 24 Hr Urine Albumin showed significant correlation with 24 UACR, HbA1c, FBS, PPBS and diabetes duration with statistical significance ('p'<0.05).

Sanjay Shrestha et al[14] in a study also observed urine albumin to creatinine ratio showed significant correlation with 24 hour urine albumin, HbA1c, FBS, PPBS and diabetes duration with statistical significance(p<0.001) this finding was similar to present study.

Tarig Karar et al[10] in a study on assessment of microalbuminuria and urine albumin to creatinine ratio in patients with type 2 diabetes mellitus observed urine albumin to creatinine ratio showed significant correlation with 24 hour urine albumin and HbA1c.

Allon Friedman et al[15] in a study on value of urine albumin to creatinine ratio as

a predictor of type 2 diabetes observed urine albumin to creatinine ratio showed significant correlation with 24 hour urine albumin and HbA1c.

CONCLUSION

The present study was conducted to compare Urine albumin creatinine ratio (UACR) with twenty four hour urine albumin in subjects with type 2 diabetes mellitus, to anticipate early diagnosis of renal complications of type 2 diabetes mellitus in the form of diabetic nephropathy. The study was predominated by male gender with a ratio of 3:2 and included 2/3rd subjects in age group 61-80 years.

It was found that Urine albumin to creatinine ratio (UACR) was better parameter than twenty four hour urine albumin to detect proteinuria in subjects with type 2 diabetes mellitus and was significant.

There was a positive correlation of Urine albumin to creatinine ratio with duration of diabetes, HbA1c levels, and diabetic retinopathy; indicating the role of early detection of proteinuria and strict glycemic control, to halt the disease progression in subjects with type 2 diabetes mellitus.

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