



Correlation between Spot Urine Protein-Creatinine Ratio and 24-Hour Urine Protein Estimation in Type 2 Diabetes Mellitus Patients Attending A Tertiary Care Centre in Alappuzha

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Abstract

About 20% of cases of chronic renal failure is due to diabetic nephropathy and is the most common cause of end stage renal disease (ESRD) in many countries. Proteinuria is an independent risk factor for renal diseases and a predictor of ESRD. For the diagnosis and management of chronic renal disease, accurate identification and quantification of proteinuria is very important. An increased proteinuria has both diagnostic and prognostic values in detection and confirmation of renal diseases and to assess response to therapy. Increased proteinuria is associated with an increased risk of progressive renal failure. The gold standard for the quantitative evaluation of proteinuria is the measurement of protein excretion in a 24hr urine sample. 24hr urine sample collection is an inconvenient method especially in outpatient setting. An alternate convenient method for evaluation of proteinuria is measurement of protein to creatinine ratio in a spot urine sample. There are a number of studies that show urine spot protein to creatinine ratio (urinary PCR) can replace 24hr urine protein estimation in the screening and evaluation of diabetic nephropathy.

Objectives

- 1) To determine the correlation of spot urine protein creatinine ratio (PCR) with 24 hr urine protein estimation in patients with type 2 diabetes mellitus.
- 2) To study the association of biochemical and clinical parameters like serum creatinine, eGFR, glycated hemoglobin, duration of diabetes, presence of diabetic retinopathy with urine PCR in patients with type 2 diabetes mellitus.

Methodology: The design of study is cross sectional study and the study population included Type II Diabetes Mellitus patients attending Medicine OPD, of either sex, in Govt. TDMC, Alappuzha for a period of 12 months from December 2015 to December 2016. The sample size is 73. 24hour urine protein and urine protein creatinine ratio was done in the study population. The patients were also evaluated for associated clinical and biochemical parameters. The data collected was analyzed using a standard statistical package-SPSS version 16.

Results: Seventy three patients with type 2 diabetes mellitus and proteinuria were studied. Maximum number of patients were noted in the age group 41-50 years. Males were more than females in the ratio of 2.04:1. The mean duration of diabetes was 9.24 +/- 6.1 yrs. Majority of patients had a duration of diabetes between 5 -10 yrs (52.05%). Ten patients (13.7%) did not have diabetic retinopathy. Twenty five patients (34.25%) had nephrotic range proteinuria. There was good correlation between urine PCR and 24 hr urine protein at different levels of GFR. The correlation in different levels of GFR were: (0-15) group: $r = 0.784$, $p < 0.001$, (15-30) group: $r = 0.756$, $p < 0.001$, (30-60) group: $r = 0.725$, $p < 0.001$, >60 group: $r = 0.99$, $p < 0.001$. Maximum correlation between urine PCR and 24 hr urine protein was seen in the GFR >60 group. There was good correlation between urine PCR and 24 hr urine protein at different ranges of proteinuria. The correlation in different levels of proteinuria were: <300 mg ($r = 0.93$, $P < 0.001$), 300-3500 mg ($r = 0.632$, $P < 0.001$) and ≥ 3500 mg ($r = 0.783$, $P < 0.001$). Maximum correlation between urine PCR and 24 hr urine was seen in the proteinuria group <300 mg. No statistically significant

correlation was found between HBA1C levels and degree of proteinuria. There was good correlation between degree of diabetic retinopathy and proteinuria. No significant correlation was found between duration of diabetes and urine PCR.

Conclusion: Spot urine protein creatinine ratio can replace 24 hr urine protein estimation in the screening and evaluation of diabetic nephropathy.

Introduction

In the modern world the burden of diabetes mellitus (DM) is rapidly rising. The main problem with this disease entity is its propensity to incur macro- and microvascular complications over time, crippling both the individual and our resource restricted healthcare system. Diabetic nephropathy (DN) is estimated to affect one-third of individuals with DM and is associated with considerable cardiovascular morbidity and mortality. It is the leading cause of end-stage renal disease (ESRD) worldwide. Unfortunately, the magnitude of this clinical entity continues to grow in association with an expanding diabetic population and remarkably the excess mortality risk of DM is associated almost entirely with the presence of DN^{1,2}. Proteinuria is an independent risk factor for renal diseases and a predictor of end stage renal disease (ESRD)³. Accurate identification and quantification of proteinuria is of prime importance in the diagnosis and management of chronic renal disease. An increased proteinuria is associated with an increased risk of progressive renal failure and is used as both diagnostic and prognostic values in detection and confirmation of renal diseases, or response to therapy⁴.

Early identification of patients at high risk for diabetic nephropathy (DN) is important to intensify the treatment and modify associated risk factors. Measurement of protein excretion in a 24hr urine collection is the gold standard for the quantitative evaluation of proteinuria. This method carries significant inconvenience for the patient especially in the outpatient setting. So an alternate simpler method was proposed. It is the quantitative evaluation of proteinuria by measurement of protein to creatinine ratio in a spot urine sample which provides a convenient method to assess protein excretion.⁵ The spot

urine protein creatinine ratio can be used as a surrogate and may replace 24 hr urine protein estimation in the screening and evaluation of diabetic nephropathy.

Objectives

Primary Objective

1. To determine the correlation of spot urine protein creatinine ratio (PCR) with 24 hr urine protein estimation in patients with diabetic nephropathy.

Secondary Objective

2. To study the association of biochemical and clinical parameters like serum creatinine, eGFR, glycated hemoglobin, duration of diabetes, presence of diabetic retinopathy with urine PCR in patients with diabetic nephropathy.

Materials and Methods

Study Design: Cross sectional Study

Study Duration: For a period of 1 year after ethical committee clearance (December 2015-December 2016)

Study Setting: This study is carried out in patients attending General Medicine OPD in Govt TDMC Alappuzha for a period of 12 months after getting permission from research and ethical committee.

Sample Size: 73

Study Population

Type II Diabetes Mellitus patients attending Medicine OPD, of either sex, in Govt. TDMC, Alappuzha

Inclusion Criteria

- Type 2 Diabetes Mellitus patients with proteinuria.

Exclusion Criteria

Patients with

- Acute febrile illness

- Urinary tract infection
- Taking ACEI/ARB
- Glomerulonephritis due to systemic conditions
- Malignancies ,collagen vascular disorders or any other systemic condition causing proteinuria
- Age < 18 yrs
- Pregnant women

Method of data Collection

A random sample of male and female patients with type 2 diabetes mellitus satisfying the inclusion and exclusion criteria was selected. Data was collected with the aid of a proforma, which included patient history, clinical parameters like duration of diabetes, prevalence of diabetic retinopathy and biochemical parameters like serum creatinine, eGFR, glycated hemoglobin ,urine protein creatinine ratio and 24 hr urine protein. On the test day, in the morning at the start of collection period (6.00 a.m.) patients were asked to void urine and discard this sample (as it contains the overnight urine present in the bladder). Subsequently urine was collected for next 24 hrs. The last sample was to be collected on next day at 6.00 a.m. A random sample was also collected on the day of deposition of 24 hr sample (the test day). Urine protein was estimated using Pyrogallol red molybdate method and urine creatinine by modified Jaffe's method .Creatinine

clearance was calculated using the MDRD (Modified Diet in Renal Disease) equation : $GFR (mL/min/1.73 m^2) = 175 \times (S_{cr})^{-1.154} \times (Age)^{-0.203} \times (0.742 \text{ if female}) \times (1.212 \text{ if African American})$.

Statistical Analysis

- The data collected was analyzed using a standard statistical package-SPSS version 16. Spearman's correlation coefficient was used for correlation of numerical variables. Kruskal Wallis test was used for the association between retinopathy and urine PCR.

Results

This study included 73 patients with type 2 diabetes mellitus who got admitted to the medicine ward of Govt TD Medical College, Alappuzha. Findings in the patients studied were evaluated and tabulated using Microsoft Excel and has been given as Annexure. Statistical analyses were conducted using SPSS 16.0 for Windows (SPSS Inc, Chicago, USA).

Patient Characteristics

Age wise distribution

The age of the patients studied ranged from 30 years to 80 years. Mean age of the patients was 51.9 +/-10.4 yrs. Mean age of female and male patients were 51.2 +/- 10.4 yrs and 52.37 +/- 10.5 respectively.

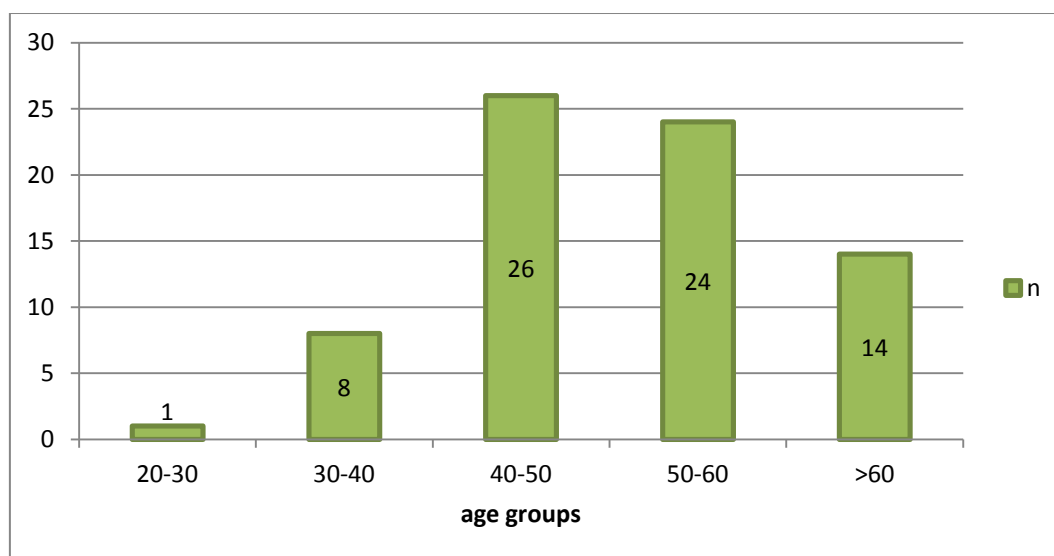


Chart 1: Age wise Distribution of Cases

Maximum number of patients were noted in the age group 41-50 years i.e., 26 (35.1%) and least in the age group 20-30 years i.e., 1 (1.35%).

Gender wise distribution

Of the 73 patients studied, 49 (67.1%) patients were males and 24 (32.9%) patients were females

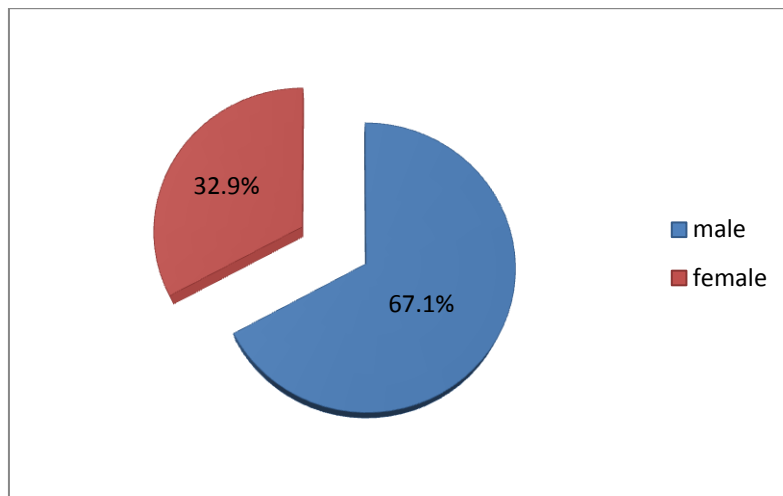


Chart 2: Gender wise distribution of cases

Diabetic Retinopathy

Of the 73 patients studied, 10 (13.7%) did not have diabetic retinopathy, 9(12.33%) had

proliferative diabetic retinopathy (PDR) and the rest non proliferative diabetic retinopathy (NPDR).

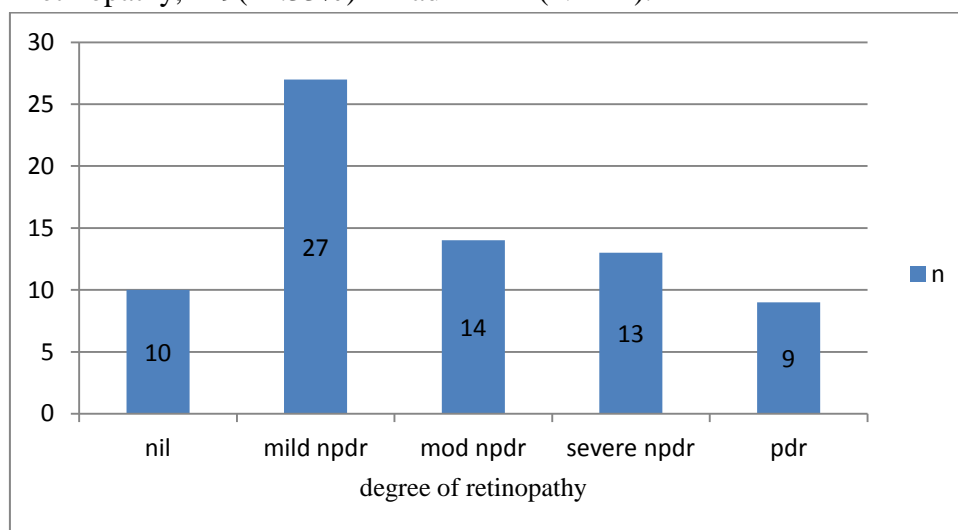


Chart 3 : Frequency distribution based on degree of diabetic retinopathy

Table 1: Percentage of patients based on the degree of retinopathy

Degree of retinopathy	Percentage	No. of patients
Mild NPDR	36.99%	27
Moderate NPDR	19.18%	14
Severe NPDR	17.80%	13
PDR	12.33%	9
No retinopathy	13.70%	10

Degree of Proteinuria

Out of the 73 patients with proteinuria, 25 patients (34.25%) had proteinuria of more than 3.5 gms/24

hours and 48 patients (65.75%) had proteinuria of less than 3.5 gms/24 hours.

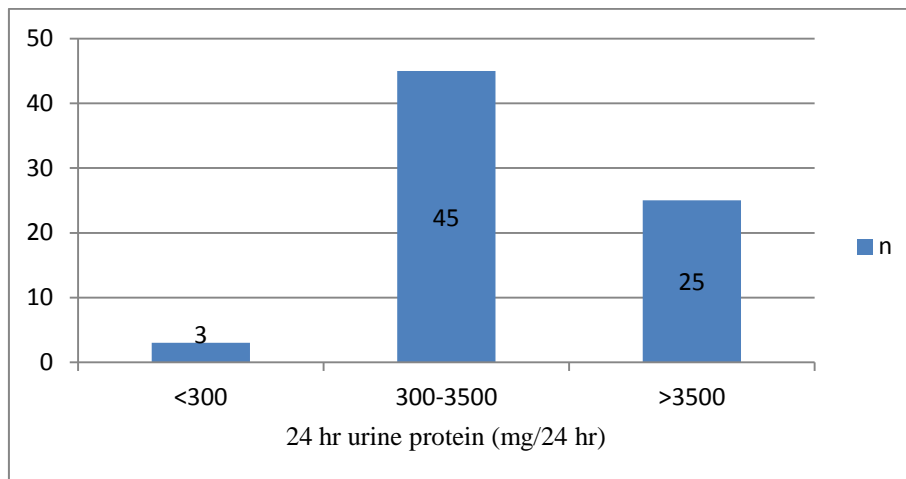


Chart 4 : Frequency distribution based on degree of proteinuria

Table 2: Percentage of patients based on the degree of proteinuria

Degree of proteinuria (mg/24hr)	Percentage	No. of patients
<300	4.11%	3
300-3500	61.64%	45
>3500	34.25%	25

Creatinine Clearance

In our study, majority of patients had creatinine clearance (calculated by MDRD equation)

between 30-60 ml/min¹/ 1.73m⁻² - 25 patients (34.24%).

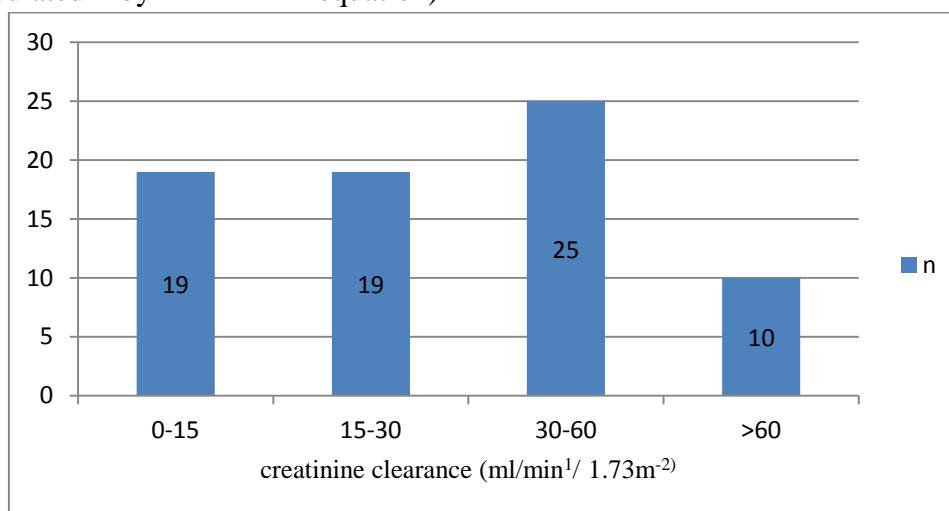


Chart 5 : Frequency distribution based on creatinine clearance

Table 3 : Percentage of patients based on creatinine clearance

Creatinine clearance(ml/min ¹ / 1.73m ⁻²)	Percentage	No. of patients
0-15	26.03%	19
15-30	27.03%	19
30-60	34.24%	25
>60	13.70%	10

Duration of Diabetes

In our study, majority of patients had duration of diabetes between 5 to 10 yrs - 38 patients

(52.05%). The mean duration of diabetes was 9.24 +/- 6.1 yrs.

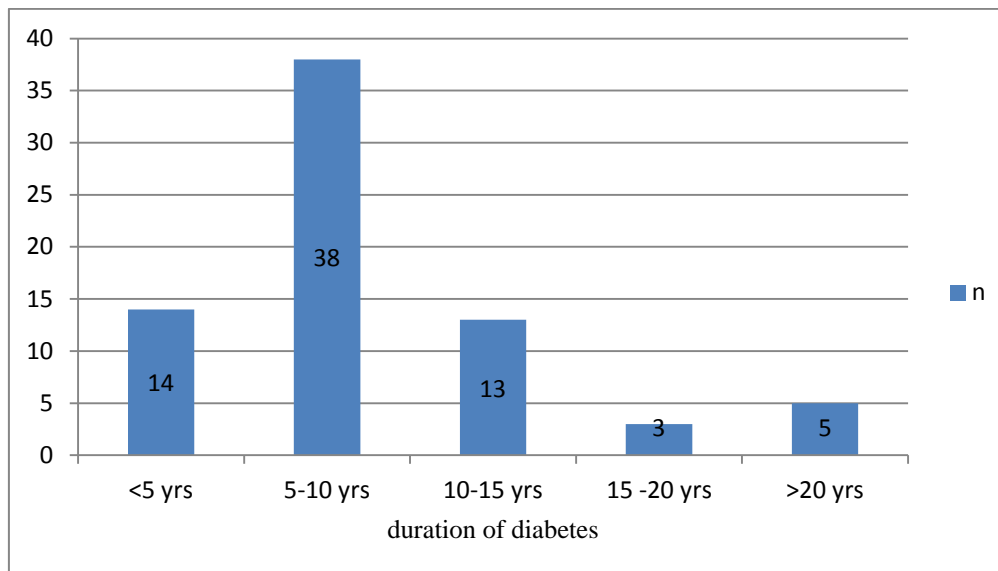


Chart 6: Frequency distribution based on duration of diabetes

Table 4 : Percentage of patients based on duration of diabetes

Duration of diabetes (yrs)	Percentage	No. of patients
<5	19.18%	14
5-10	52.05%	38
10-15	17.81%	13
15-20	4.11%	3
>20	6.85%	5

Correlation between Urine PCR and 24 Hr Urine Protein

There was a significant positive correlation between urine PCR and 24 hr urine protein in our study ($r = 0.87$ $p < 0.001$).

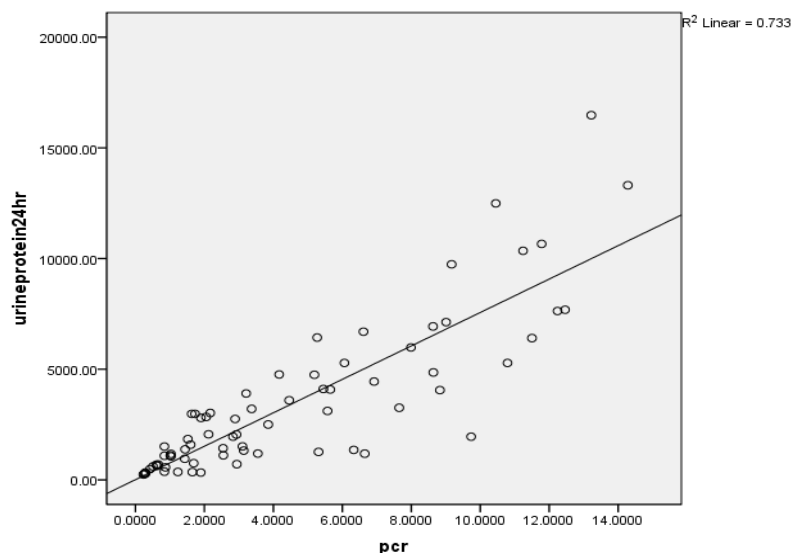


Chart 7 : Correlation between urine PCR and 24 hr urine protein

Correlation coefficient (r) : 0.87
 P value : <0.001

Correlation between Urine PCR and Serum Creatinine

A significant positive correlation was found between urine PCR and serum creatinine in our study ($r = 0.774$, P value <0.001).

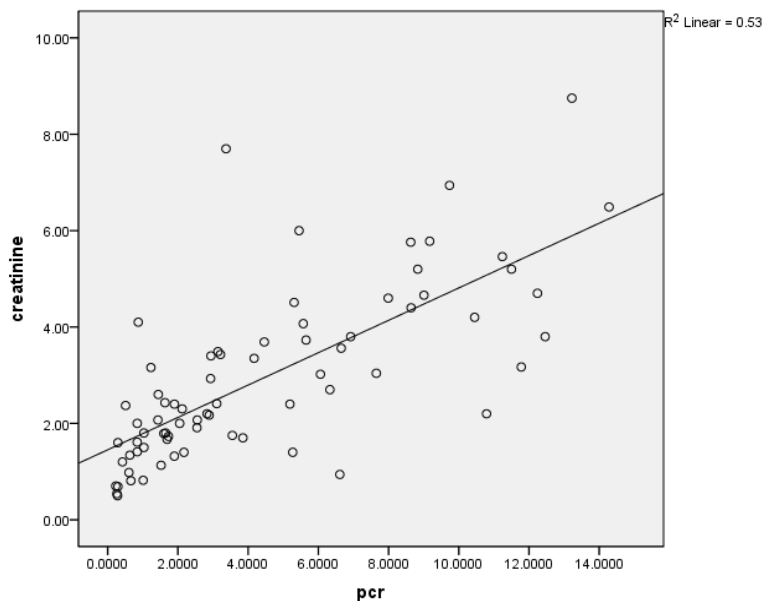


Chart 15 : correlation between urine PCR and creatinine (mg/dL)

Correlation coefficient (r) : 0.774
 P value : <0.001

Correlation between 24 Hr Urine Protein and Serum Creatinine

There was significant positive correlation between serum creatinine and 24 hr urine protein in our study population ($r = 0.656$, p value <0.001).

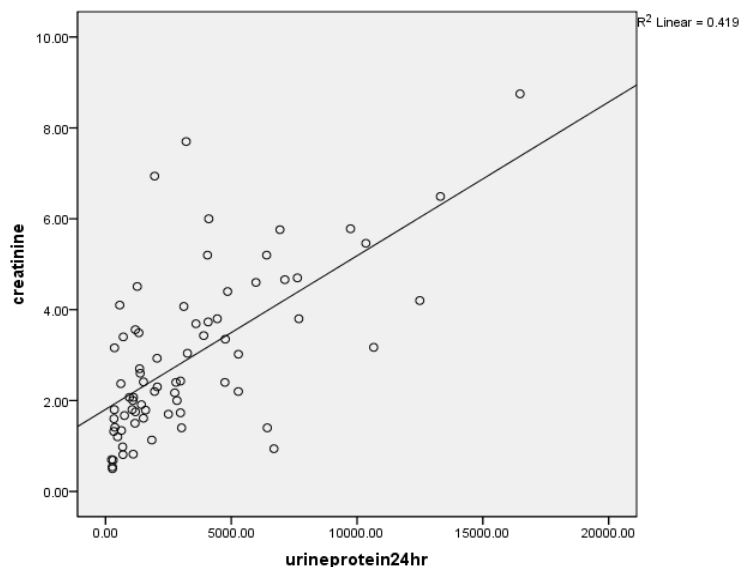


Chart 16 : correlation between 24 hr urine protein and creatinine

Correlation coefficient (r): 0.656
 P value : <0.001

Correlation between Urine PCR and HBA1C

There was no significant correlation between urine PCR and HBA1C levels ($r = 0.076$, p value 0.956)

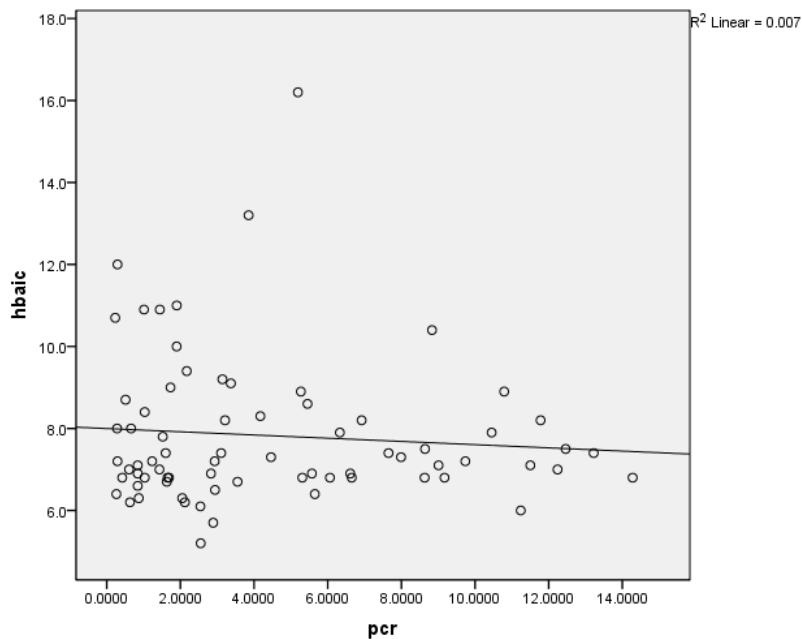


Chart 17 : Correlation between urine PCR and HBA1C

Correlation coefficient (r) : 0.007
 P value : 0.956

Correlation between 24 Hr Urine Protein and HBA1C

There was no significant correlation between urine PCR and HBA1C levels ($r = 0.076$, p value 0.52)

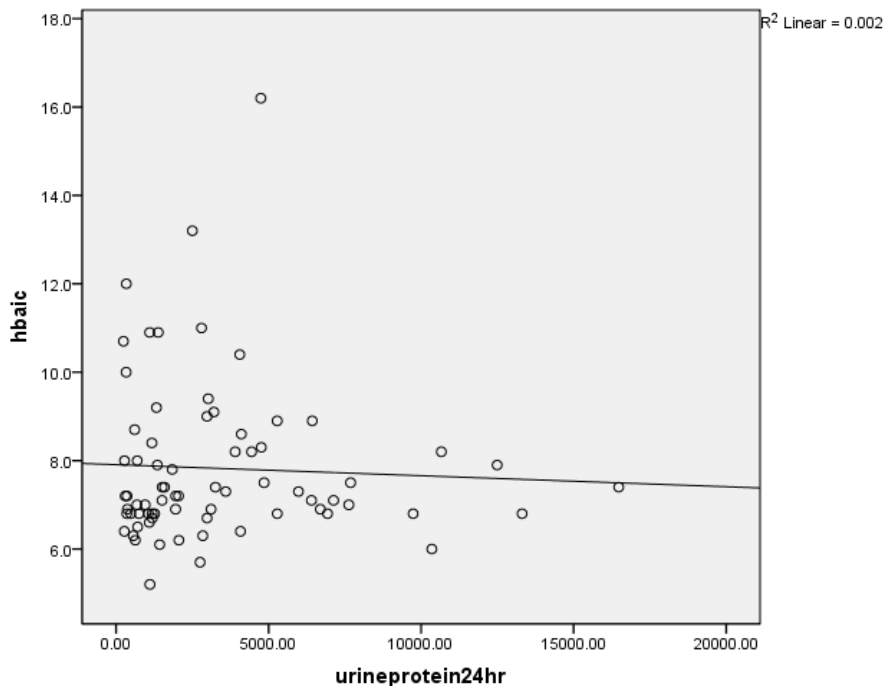


Chart 18 : correlation between 24 hr urine protein and HBA1C

Correlation coefficient (r) : 0.076
 P value : 0.52

Correlation between Urine PCR and Retinopathy

There was a good correlation between degree of diabetic retinopathy and urine PCR in our study.

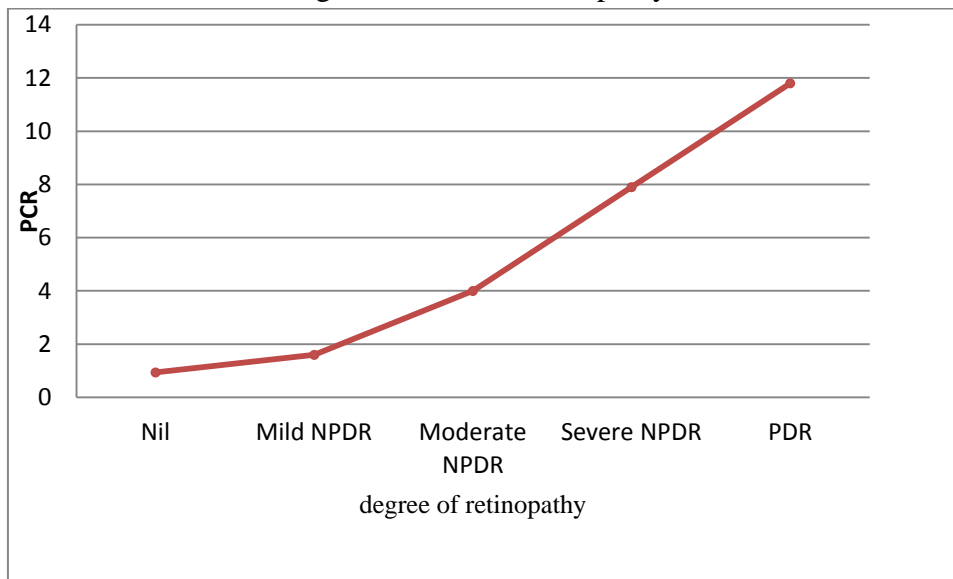


Chart 19 : correlation between urine PCR and degree of retinopathy

Degree of retinopathy	Median pcr	Quartiles		P value
		Q1	Q3	
Nil	0.94	0.38	1.33	<0.001
Mild NPDR	1.60	0.84	2.17	
Moderate NPDR	4.01	3.19	5.34	
Severe NPDR	7.9	6.63	8.91	
PDR	11.7	11.01	12.84	

Association between urine PCR and retinopathy

Conclusion

In this study of 73 patients with type 2 diabetes mellitus and proteinuria, it was found that:

- Maximum number of patients were noted in the age group 41-50 years.
- Males were more than females in the ratio of 2.04:1
- Majority of patients had a duration of diabetes between 5 -10 yrs (52.05%).
- The mean duration of diabetes was 9.24+/- 6.1 yrs.
- Ten patients (13.7%) did not have diabetic retinopathy.
- Twenty five patients (34.25%) had nephrotic range proteinuria.

- There was good correlation between urine PCR and 24 hr urine protein at different levels of GFR.
- Maximum correlation between urine PCR and 24 hr urine protein was seen in the GFR >60 group.
- There was good correlation between urine PCR and 24 hr urine protein at different ranges of proteinuria.
- Maximum correlation between urine PCR and 24 hr urine was seen in the proteinuria group <300.
- There was good correlation between urine PCR and serum creatinine.

- No statistically significant correlation was found between HBA1C levels and degree of proteinuria.
- There was no significant correlation between urine PCR and duration of diabetes.
- There was good correlation between degree of diabetic retinopathy and proteinuria.
- So urine protein creatinine ratio can replace 24 hr urine protein estimation in the screening and evaluation of diabetic nephropathy.

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