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A STUDY OF URINE PROTEIN CREATININE RATIO AS AN EARLIER PREDICTOR IN DIABETIC NEPHROPATHY

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Introduction

A chronic microvascular consequence of diabetes mellitus (DM), diabetic nephropathy (DN) can affect the kidneys. Micro albuminuria and impaired renal function, as shown by a reduction in glomerular filtration and rise in serum urea and creatinine levels, are hallmarks of Diabetic Nephropathy (DN), which is a subtype of nephropathy caused by Diabetes. One of the initial markers of DN is called microalbuminuria. In order to stop the progression of Diabetic Nephropathy, effective screening procedures are essential for early identification and care.

Aim & Objectives:

The purpose of this research was to investigate the correlation between diabetic and non-diabetic participants' blood levels of urea and creatinine, as well as their blood glucose levels, in order to determine the diagnostic value of these parameters in the context of diabetic nephropathy and to compare these parameters to glycaemic status.

Material and Methods: This is a cross sectional study conducted among 100 patients of type-2 DM admitted in the medical ward GGH Hospital Kurnool, who fulfilled the inclusion and exclusion criteria. RFT, FBS, PPBS, HbA1c. Urine analysis for ACR from random urine sample and 24-hours urine protein from 24-hour urine sample were done.

Results; 100 people who were diagnosed with diabetes mellitus; of them, 67 were males and 33 were females. The mean age was 52.67 ±11.5 years old, and the duration of diabetes mellitus was10.02±3.20 years. .The average glycosylated haemoglobin was 8.78 ±1.54 percent, and the fasting blood glucose was 193.25± 82.23mg/dl. Post prandial blood sugar was 220.56±12.76.Mean eGFR (ml/min/1.73 m^2) was 65.39±4.09. Mean Urinary protein (mg/dl) was 385.23±65.23. Mean Urine creatinine (mg/dl) was 125.23±25.29. Mean Urine protein creatinine ratio was 3.35±1.56. Among 100 patients 14 patients had minimal proteinuria of (<1 g/day), 38 patients had moderate proteinuria (1- 3g/day), 48 patients had heavy proteinuria (>3g/day)

Conclusions: The P C ratio of a random urine sample can give a very helpful, simple, and convenient approach for the quantitative assessment of proteinuria, for judging the level of

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kidney damage, and for avoiding the problems of the 24 - hr urine collections. Hence urine protein creatinine ratio as an earlier predictor in diabetic nephropathy.

Introduction;

The prevalence of Diabetes Mellitus in India range from 5-17%. Diabetes Mellitus cause considerable morbidity and mortality primary due to micro and macro vascular complication which are Preventable, one such micro vascular Complication of Diabetes is Diabetic Nephropathy (DN).[1] Microalbuminuria is the earliest clinical manifestations of Diabetic Nephropathy (DN). Microalbuminuria will be present progress even before the time of diagnosis of Diabetes Mellitus. It will progress to overt proteinuria in 20-40% of cases. [2]

The gold standard for the quantification of proteinuria was once thought to be timed urine collections, which are typically carried out over the course of 24 hours. [3]However, these collections have considerable drawbacks, such as the amount of time they take and the potential for error while collecting samples. The estimation of total protein from a spot urine sample eliminates the need to collect urine continuously for 24 hours, but the results are still heavily impacted by the body's hydration level. It is possible to get rid of this variance by calculating the ratio of the total protein concentration in spot urine to the concentration of creatinine in urine, also known as the urine protein to creatinine ratio (P: C ratio).[4] It would be more acceptable and take less time if urine samples were taken at random to determine the P: C ratio. In the case of a steady GFR, the P: C ratio takes into consideration the fact that the amount of creatinine that is excreted remains relatively unchanged. Additionally, the amount of protein expelled would be quite consistent. Due to the fact that the two stable rates would balance out the time factor, the ratio of the two in a single voided sample would therefore reflect the cumulative protein excretion over the course of the day. There is a strong correlation between the total protein to creatinine ratio (TPCR) measured on a random (spot) urine sample and total protein excretion over a period of 24 hours.[5]

Early detection can help the timely use of renal preventive measure, so that progressive to ESRD can be delayed. Therefore effective screening measures are required for early diagnosis and management to halt the progression to DN. Therefore, the present study was planned to evaluate study of Urine Protein Creatinine Ratio as an earlier predictor in Diabetic Nephropathy.

Aims and Objectives: To study the urine protein creatinine ratio as an earlier predictor in Diabetic Nephropathy.

Materials and Methods:

100 diabetes patients are selected based on the inclusion criteria t from the outpatient department of the Government General Hospital, Kurnool between January and September 2023 The criteria established by the American Diabetes Association were utilised in the diagnostic process of diabetes. This study covered all of the subjects ranging in age from 25 to 80 years old. Patients who had a urinary tract obstruction , congestive heart failure, other chronic kidney disease, myopathy, or muscular dystrophy were excluded to participate in the study .Informed consent was received from the participants, and the study got approved from ethical committee of the Institute.

5 ml of venous blood sample was collected for estimation of Renal function tests (RFT), Fasting blood sugars (FBS) with fasting of 8-10 hours, Post-prandial blood sugars (PPBS) collected 2 hours after food, HbA1c (estimated using HPLC method) were measured in all patients in the study. Urine samples were evaluated for albumin, sugar by dipstick method and by microscopy for deposits. . A urine sample of 2 ml was taken in the morning when the patient first void urine into the container for estimation of protein creatinine ratio.

Spot urine protein concentration was estimated by using dye binding technique with Pyrogallol red .Spot Urine for Creatinine was estimated by using modified Jaffe’s method

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Spot Urine Protein – Creatinine ratio was calculated from the above measured value in the first morning urine sample and in the evening sample by the following formulae.
Protein-Creatinine ratio= urine protein (mg/dl)/ urine creatinine (mg/dl)
Clinical Definitions
1. Diabetes mellitus (as per the American Diabetes Association) [6]
Fasting blood sugar >/=126 mg/dl (fasting is defined as no caloric intake for >=8 hours)
2-hour Post prandial blood sugar >=200 mg/dl during an oral glucose tolerance test. (The test should be performed using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water)
HbA1c >= 6.5%
And all those patients who were diagnosed with type 2 diabetes mellitus already on oral Hypoglycaemic drugs and/or insulin were also included in the study.
2. Proteinuria is defined as urine Albumin Creatinine Ratio (ACR) in a single spot urine sample
Normo-albuminuria = <30 mg/g.
Micro-albuminuria = 30-299 mg/g.
Macro albuminuria = > 300 mg/g.
3. Overt proteinuria is defined as proteinuria of > 150 mg/24 hours urine protein.

Statistical Analysis: Data was collected in a Microsoft Excel database. Statistical analysis was done using nonparametric ANOVA and Fisher test.

Results:

Table 1 shows Demographic Characteristics of study subject. This study included the participation of 100 people who were diagnosed with diabetes mellitus; of them, 67 were males and 33 were females. The mean age was 52.67 ±11.5 years old, and the duration of diabetes mellitus was10.02±3.20 years. The BMI of the patients was in the normal range 23.05±3.02 kg/m^2

Table 1 shows Demographic Characteristics of study subject

Sociodemographic characteristics	Study group
Sex Male /female	**67/33**
Age(Years)	**52.67 ±11.5**
Weight (kg)	**70.12±7.54**
Height (m)	**171.20±4.23**
BMI (Kg/M^2)	**23.05±3.02**
Duration of Diabetes Mellitus (yrs.)	**10.02±3.20**

Table 2 shows Biochemical Parameters of study subject. The average glycosylated haemoglobin was 8.78 ±1.54 percent, and the fasting blood glucose was 193.25± 82.23mg/dl. Post prandial blood sugar was Post prandial blood sugar 220.56±12.76.
Mean HBA1C was 8.78 ±1.54. Mean Serum Urea was 35.15±19.26. Mean Serum Creatinine was 1.53±0.30.Mean eGFR (ml/min/1.73 m^2) was 65.39±4.09. Mean Urinary protein (mg/dl) was 385.23±65.23. Mean Urine creatinine (mg/dl) was 125.23±25.29. Mean Urine protein creatinine ratio was 3.35±1.56

Table 2 shows Biochemical Parameters of study subject

Biochemical Parameters	Study group
Fasting blood sugar	193.25± 82.23mg/dl.
Post prandial blood sugar	220.56±12.76
HBA1C	8.78 ±1.54
Serum Urea	35.15±19.26
Serum Creatinine	1.53±0.30
eGFR(ml/min/1.73 m^2)*	65.39±4.09

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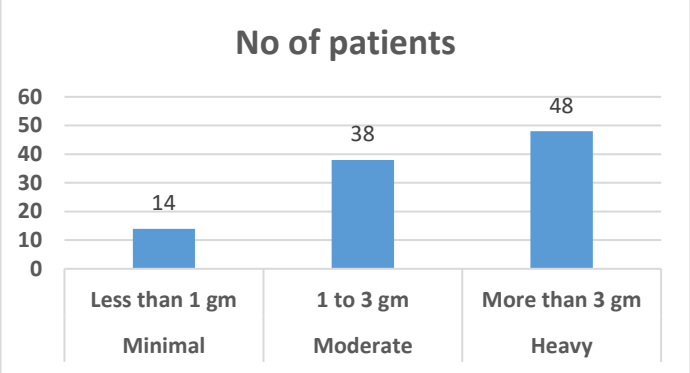
Urinary protein (mg/dl)	385.23±65.23
Urine creatinine (mg/dl)*	125.23±25.29
Urine protein creatinine ratio*	3.35±1.56

Graph no: 1 shows Distribution of patients based on degree of proteinuria.
Among 100 patients 14 patients had minimal proteinuria of (<1 g/day), 38 patients had moderate proteinuria (1- 3g/day), 48 patients had heavy proteinuria (>3g/day)

Graph no: 1 Distribution of patients based on degree of proteinuria



Discussion : Diabetes is a major contributor to end-stage renal disease and is one of the leading causes overall.[7] In diabetic patients with type 1 and type 2 diabetes, an early sign of eventual renal function impairment is the excretion of small amounts of albumin in the urine[8] (a condition known as microalbuminuria, which can range from 30-300 mg/24 hours). Diabetic nephropathy is a condition that can develop after years of having the disease. It is distinguished by glomerular proteinuria, which is brought on by damage to the glomerular membrane. Approximately ten years of having type 1 diabetes, an increase in the amount of albumin that is excreted in the urine is seen. Microalbuminuria is most usually already present at the time a diabetic patient is diagnosed with the condition due to the asymptomatic beginning of type 2 diabetes.[10] the progression of renal function begins with an increase in glomerular filtration rate (GFR), which is the standard measure of kidney function. According to the findings of our study, inadequate management of blood sugar levels can lead to an increase in serum urea levels, which in turn raises the likelihood that the patient will develop diabetic nephropathy. This lends credence to the findings of other research, which found that hyperglycaemia is one of the primary factors contributing to increasing kidney impairment. When there is injury to the kidney, there will be an increase in the amount of urea in the blood. [11]

In the present study the mean age was 52.67 ±11.5 years old, since the average age of diabetes in India is 40 years (39.6 years) and the duration of diabetes mellitus was10.02±3.20 years. The BMI of the patients was in the normal range 23.05±3.02 kg/m^2

The average glycosylated haemoglobin was 8.78 ±1.54 percent, and the fasting blood glucose was 193.25± 82.23mg/dl. Post prandial blood sugar was Post prandial blood sugar 220.56±12.76.Mean HBA1C was 8.78 ±1.54. Mean Serum Urea was 35.15±19.26. Mean Serum Creatinine was 1.53±0.30.Mean eGFR (ml/min/1.73 m^2) was 65.39±4.09. Mean Urinary protein (mg/dl) was 385.23±65.23. Mean Urine creatinine (mg/dl) was 125.23±25.29. Mean Urine protein creatinine ratio was 3.35±1.56. The above results can be compared to study conducted by Ewald and Attia, [12, Sunil] Dhanraj Bhaisare [13]. The result of our study and similar other studies have reported higher sensitivity of ACR in diagnosing micro-albuminuria. [14, 15] It should be used routinely for early diagnosis of DN, since it is easy to conduct and with a very high sensitivity. Majority of the patients had ACR between 30-300 mg/g i.e. microalbuminuria followed by those with >300 mg/g i.e. macro albuminuria. Among those with ACR >300 mg/g

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(macro albuminuria/overt proteinuria) the duration of diabetes and 24hr urinary protein was significantly higher as compared to those with ACR 30-300 mg/g (microalbuminuria). The above results were in line with study conducted by Monika Pathania where the average duration of diabetes was significantly high in patients with macro albuminuria/overt proteinuria as compared to those with microalbuminuria. Similarly, 24 hr urinary protein was also significantly high in patients with macro albuminuria

Conclusions: Maximum participants in our study were aged 50- 60 yrs. and had diabetes for 15 to 20 years. Comparing BUN, S. Creatinine with Urine Protein Creatinine Ratio exhibited early Urine Protein Creatinine Ratio and e-GFR dysregulation. Urine Protein Creatinine Ratio was more abnormal in the Diabetics. Urine Protein Creatinine Ratio and eGFR are early indicators of diabetic nephropathy.

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