

# Estimation of Proteinuria in Type 2 Diabetes Mellitus: Is Spot Urine Protein-Creatinine Ratio as Efficacious as 24 Hours Urinary Protein?

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## ABSTRACT

**Introduction:** Diabetic nephropathy is a leading cause of morbidity and mortality in patients with diabetes mellitus. This study aims to compare the efficacy of spot urine protein creatinine ratio (PCR) with 24 hours urinary protein and urinary dipstick analysis in detection of proteinuria in patients with type 2 diabetes mellitus.

**Material and methods:** Cross sectional study involving 75 consecutive patients with type 2 diabetes mellitus. The relationship between spot urine PCR and 24 urine protein and the relationship between spot urine PCR and urine protein dipstick analysis was found out using Pearson's correlation analysis. The sensitivity, specificity, positive predictive value, negative predictive value of spot urine PCR for detecting proteinuria at a cut off value of 0.2 was calculated.

**Results:** 75 patients of type 2 Diabetes mellitus were included (56 males and 19 females). The mean spot PCR was 0.38+/-0.57 and the mean 24 hour urinary protein was 84.85+/-43.54 mg/day. Good positive correlation between spot urine PCR and 24 hour urine protein ( $r=0.805$ ) was noted. The sensitivity of spot urine PCR at a cutoff value of 0.2 was 98.25% and specificity was 94.44%. The area under curve for urine PCR was 0.996 (95% Confidence interval:0.986-1,  $p<0.0001$ ).

**Conclusion:** The spot urine PCR is as reliable as 24 hour urine protein and more reliable than spot urine dipstick analysis in detecting proteinuria in patients with type 2 diabetes mellitus. Hence, spot urine PCR can be used as an alternative to 24 hour urine protein for estimating proteinuria.

**Keywords:** Type 2 Diabetes Mellitus, Proteinuria, 24 Hour Urine Protein, Spot Urine Protein Creatinine Ratio

urinary protein, various studies have proposed the calculation of ratios such as protein creatinine index in spot urine samples as an alternative method. The aim of this study was to compare the efficacy of spot urine protein creatinine ratio (PCR) with 24 hours urinary protein and urinary dipstick analysis in detection of proteinuria in patients with type 2 diabetes mellitus.

## MATERIAL AND METHODS

This was a cross sectional study involving 75 consecutive patients with type 2 diabetes mellitus admitted to Vydehi institute of medical sciences and research centre, Bengaluru. Patients with hypertension, urinary tract infection, glomerulonephritis, chronic renal disease were excluded. Demographic details, duration of diabetes, co-morbid conditions, Fasting blood glucose and HbA1C values of patients were obtained. First morning urine sample was collected for protein dipstick analysis and spot urine protein-creatinine ratio and subsequent samples were collected for 24 hours urinary protein estimation including the last void urine at the end of 24 hours.

Statistical methodology:-

The data was collected and analysed by appropriate statistical tests. SPSS version 21 was used for the statistical analysis. The relationship between spot urine PCR and 24 urine protein and the relationship between spot urine PCR and urine protein dipstick analysis was found out using Pearson's correlation analysis. The sensitivity, specificity, PPV (positive predictive value), NPV (negative predictive value) of spot urine PCR for detecting proteinuria at a cut off value of 0.2 was calculated. A ROC (Receiver operating characteristic) curve was determined.

## RESULTS

The study included a total of 75 patients with type 2 Diabetes

## INTRODUCTION

Diabetic nephropathy is a leading cause of morbidity and mortality in patients with type 2 diabetes mellitus.<sup>1</sup> Proteinuria is the hallmark and earliest clinical evidence of deterioration of renal function. Proteinuria is also an independent risk factor for renal diseases. Accurate identification and quantification of proteinuria is important in detection and management of diabetic nephropathy at an early stage.<sup>2</sup> Detection of proteinuria by urine dipstick analysis has been found by many researchers to be too insensitive to evaluate the diabetic patients for microproteinuria.<sup>3</sup> Quantification of proteinuria has diagnostic and prognostic significance in assessing the progression of disease. The gold standard for quantitative evaluation of proteinuria is the measurement of 24 hour urinary protein excretion.<sup>4</sup> This method is very cumbersome, inconvenient and thus leads to discarding of nearly 1/3<sup>rd</sup> of the samples.<sup>5</sup> To obviate these difficulties and to fulfil the need for a reliable and quick assessment of

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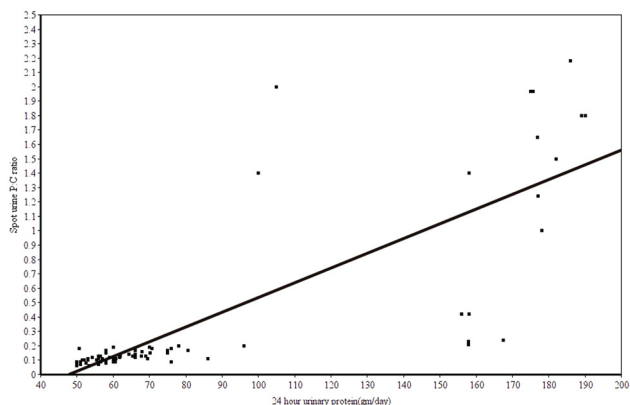
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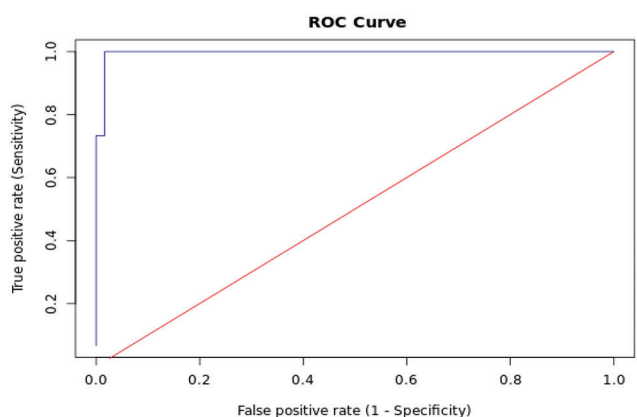
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Statistics	Value
Sensitivity	98.25%
Specificity	94.44%
Positive predictive value	98.25%
Negative predictive value	94.44%
Accuracy	97.33%

**Table-1:** Efficacy of spot urine PCR at a cut off of 0.2



**Figure-1:** Correlation between 24 hour urinary protein and spot urine PCR in patients with type 2 diabetes mellitus



**Figure-2:** ROC curve

mellitus of which 56 were males and 19 were females. The average age was  $66.84 \pm 5.46$  years. The mean duration of diabetes was  $5.37 \pm 4.25$  years. The mean fasting blood glucose was  $167.02 \pm 35.17$  mg/dl and mean HbA1C  $8.94 \pm 1.88\%$ . The mean spot protein-creatinine ratio was  $0.38 \pm 0.57$  and the mean 24 hour urinary protein was  $84.85 \pm 43.54$  mg/day. There was a good positive correlation between spot urine protein-creatinine ratio and 24 hour urine protein ( $r=0.805$ ) (Figure 1).

The sensitivity of spot urine PCR for detection of proteinuria at a cut off value of 0.2 was 98.25% and specificity 94.44%. (Table 1).

The area under the curve for spot urine PCR at various cut off levels was 0.996 (95% CI, 0.986-1;  $p<0.0001$ ) (Figure 2). The assessment of proteinuria by spot urine dipstick showed false negative results in 3 (17.6%) patients and false positive results in 54 (90%).

## DISCUSSION

Considerable evidence accumulated in the past suggests

that even small quantities of proteinuria or albuminuria is an important and early sign of kidney disease.<sup>5</sup> Quantifying the protein excretion accurately is essential for monitoring the disease progression and for timely administration of therapy to prevent irreversible end stage renal damage in patients with diabetes mellitus. Estimation of 24 hour urinary protein remains the gold standard but it has major limitations like time consumption and error in sample collection.<sup>1</sup> Measurement of spot urine PCR is an alternative method for quantitative evaluation of proteinuria which has been substantiated by several studies in patients with pre-eclampsia,<sup>6-8</sup> type 1 diabetes mellitus,<sup>9</sup> renal transplantation<sup>10</sup> and lupus nephritis.<sup>11</sup> In a study done by Biradar SB et al on 42 patients of type 2 diabetes mellitus, a positive correlation was noted between 24 hours urinary protein and spot urine PCR ( $r=0.925$ ,  $p<0.0001$ ). The area under ROC curve for urine PCR at various cut off was 0.947 (95% CI: 0.831-0.992,  $p<0.0001$ ). Sensitivity was 80.65% and specificity 100% at spot urine PCR cut off of 0.3.<sup>2</sup> In their study random urine sample was tested for spot urine PCR and had a higher cut off of 0.3 in comparison to our study where early morning sample and a lower cut off was taken. In our study a good positive correlation was noted between spot urine PCR and 24 hour urine protein ( $r=0.805$ ). The sensitivity of spot urine PCR for detection of proteinuria at a cut off value of 0.2 was 98.25% and specificity 94.44%.

A longitudinal study conducted to validate the clinical usefulness of the spot urine PCR in comparison with 24 hours urinary protein in 41 adult patients with primary glomerulopathies showed a good correlation between the mean values of the two methods at baseline ( $r=0.90$ ,  $P<0.001$ ). There was also a significant correlation between the 2 values throughout the follow up period of 6 months.<sup>12</sup> A similar finding was noted in another study done in 103 patients with type 2 diabetes mellitus patients which showed significant correlation between spot urine PCR and 24 hours urinary protein ( $r=+0.97$ ).<sup>1</sup>

In our study, 3 patients had false negative urine dipstick result. In the same 3 patients spot urine PCR was  $>0.2$ . It was also found that a large number of patients who had 24 hour urine protein excretion  $<150$ mg/day had a false positive urine dipstick test. In almost all these patients spot urine PCR was  $<0.2$ . In a study done by Kumar et al., it was noted that although the samples were found to show elevated levels of urinary protein concentration on quantitative estimation by sulphosalicylic acid test, 5 out of 28 (17.86%) diabetic patients showed negative dipstick test.<sup>3</sup>

In our study spot urine PCR was estimated in first morning sample. A study which compared correlation between spot urine PCR at 2 different times of the day and 24 hour urine protein noted best correlation in early morning sample than evening sample ( $r=0.931$  in 7 AM and  $r=0.872$  in 7PM;  $p<0.001$ ). The same study also found maximum correlation in patients with normal/ mild renal dysfunction and non-nephrotic range proteinuria.<sup>5</sup>

Our study had a good sample size and we assessed the efficacy of both spot urine PCR and spot urine protein dipstick

analysis. The first morning void urine sample was used in our study for estimating proteinuria. So one limitation of this study would be that we should have done comparison with a random urine sample to find its correlation with 24 hour urine protein to reestablish that first morning void sample is the best sample for estimating proteinuria.

## CONCLUSION

The present study shows that spot urine protein-creatinine ratio is as reliable as 24 hour urine protein and more reliable than spot urine dipstick analysis in detection of proteinuria in patients with type 2 diabetes mellitus. Hence, spot urine protein-creatinine ratio can be used as an alternative for 24 hour urinary protein for the estimation of proteinuria.

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