

**ESTIMATION OF HIGH SENSITIVITY C-REACTIVE PROTEIN LEVELS AS A EARLY  
MARKER OF DIABETIC NEPHROPATHY****Dr. Likitesh A. B.<sup>1\*</sup>, Dr. Prabhakar K.<sup>2</sup>, Dr. Reddy Prasad K.<sup>3</sup> and Dr. Prasanna Kumar<sup>4</sup>**<sup>1</sup>Junior Resident, Department of Medicine, Sdumc, Kolar.  
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**ABSTRACT**

Diabetic nephropathy (DN) is one of the major long-term complications of diabetes mellitus (DM). Type 2 DM is frequently associated with an inflammatory status, but limited information is available on the relationship between low-grade inflammation and DN. The aim of the study is to determine the serum level of high sensitivity C-reactive protein (hsCRP) patients with diabetes with microalbuminuria and to compare with patients with diabetes without microalbuminuria. Forty diabetic patients in the age group of 50–70 years with more than ten years of duration of diabetes were recruited for this study and 40 age- and sex-matched diabetics without microalbuminuria were included in this study as controls. Serum hsCRP levels were measured by turbidometry method. There was a statistically significant increase in serum hsCRP levels in diabetic patients with microalbuminuria cases as compared to normal controls. These results suggest that estimation of serum hsCRP levels and aiming at good glycemic control help in early intervention and prevention of further complications in diabetic patients.

**KEYWORDS** – Diabetic nephropathy, hs – CRP, Microalbuminuria, Good glycemic control**INTRODUCTION**

Diabetic nephropathy (DN) is a progressive kidney disease caused by angiopathy of capillaries in glomeruli secondary to longstanding diabetes and is the major cause of morbidity and mortality in patients with Type 2 diabetes mellitus (Type 2 DM). This emphasizes the importance of early interventions in patients with Type 2 diabetes which reduce the risk of diabetic nephropathy.<sup>[1]</sup>

Previous studies have proved that Type 2 DM is frequently associated with chronic inflammatory state. Chronic inflammation plays an important role in the development and progression of late complications of diabetes. C-reactive protein (CRP), an acute phase reactant, is a highly sensitive marker of inflammation. Its level rises dramatically during an inflammatory processes.<sup>[2]</sup> CRP has a long half-life, affordability of estimation, and stability of its levels with no circadian variation, and therefore is one of the best markers of vascular inflammation.<sup>[3]</sup> CRP has been found to be associated with disorders like DM, cardiovascular disorders, metabolic syndrome, renal failure, etc.<sup>[4]</sup> Serum high sensitivity CRP (hs-CRP) level is higher in patients with Type 2 diabetes than in normal subjects and plays an important role in the development and progression of Type 2 DM.<sup>[5]</sup>

Quantitative estimation of Urine Albumin-creatinine ratio (ACR) is diagnostic measurement for

microalbuminuria & diabetic nephropathy.<sup>6</sup> Inflammatory parameters in patients with type 2 diabetes at an early stage of nephropathy are independently associated with Urinary albumin excretion.<sup>[7]</sup> The relationships between low-grade inflammation and diabetic nephropathy are still unclear.<sup>[8]</sup>

Hence this study was taken up to see the relationship between hs CRP and diabetic patients leading to diabetic nephropathy.

**MATERIALS AND METHODS**

Forty clinically diagnosed Diabetic patients in the age group of 50–70 years with more than ten years of duration of Type II DM, on conservative management was taken into study. The study was done in the Department of General Medicine at RL Jalappa Hospital, Kolar over a period of 6 months, both inpatients and outpatients was taken into study. Forty age- and sex-matched diabetic without microalbuminuria subjects constituted the control group. Subjects with history of any significant infections, trauma, malignancy, smoking, cancer, rheumatoid arthritis, those on any anti-inflammatory drug or with body mass index (BMI) >30<sup>9</sup> were excluded from the study. Patients on dialysis were also excluded. This study was approved by the institution's ethics committee, and informed consent was obtained from every subject.

After 12 hours of fasting, blood samples were collected under aseptic precautions from median cubital vein using commercially available vacutainers. The level of HbA1c was determined by borate affinity assay. Serum creatinine was estimated by dry chemistry. Serum hsCRP concentration was measured by immunoturbidometric method.

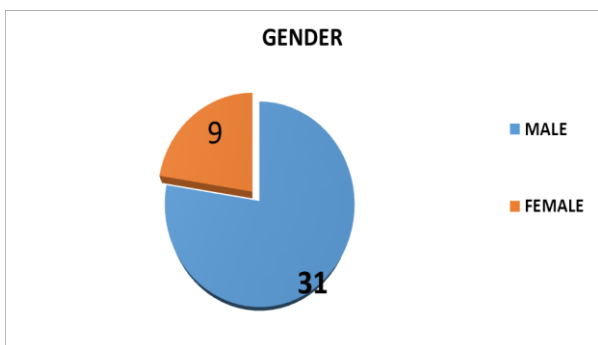
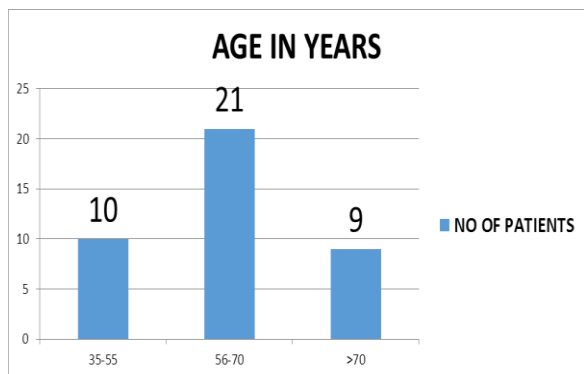
**STATISTICAL ANALYSIS**

The Statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc 9.0.1 ,Systat 12.0 and R environment ver.2.11.1 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc.

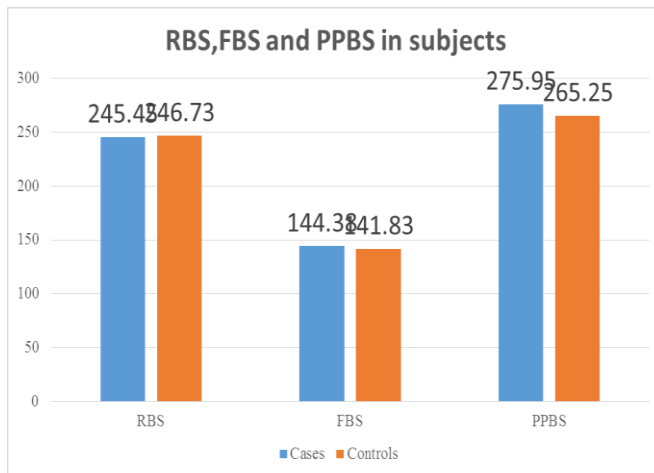
**RESULTS**

A total of 80 patients were enrolled in the study. Based on the albuminuria evaluation, 40 of the patients had microalbuminuria (mean urine albumin, 80.25 ± 60.68 mg/L), and 40 patients did not have this condition (mean urine albumin, 12.42 ± 10.25 mg/d). There was no significant difference in the kidney function, measured by serum creatinine levels, between these two groups .Microalbuminuric patients were significantly older (0.004) and were affected by DM for a longer duration (P = .03) when compared with diabetic patients without microalbuminuria and HS-CRP (P < .034) were higher.

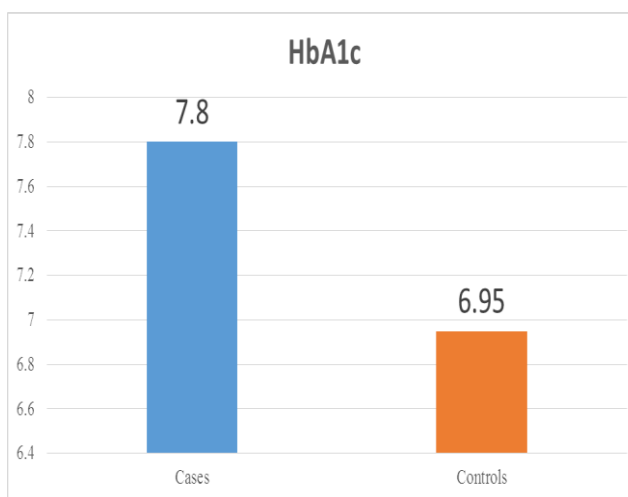
The mean hs CRP level was higher in cases (mean 5.78mg/dl) than the controls (mean 2.22) which was significantly higher.



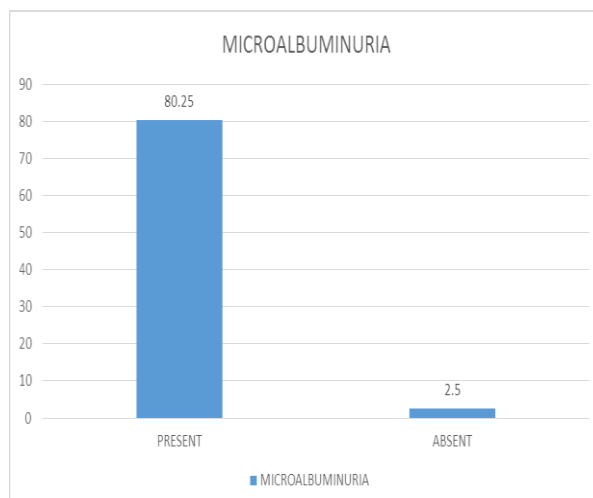
**Graph 1 - Age and gender distribution graphs which showed that most of the patients were in age group of 56-70 years and 31 were males and 9 were females. Both cases and controls matched**



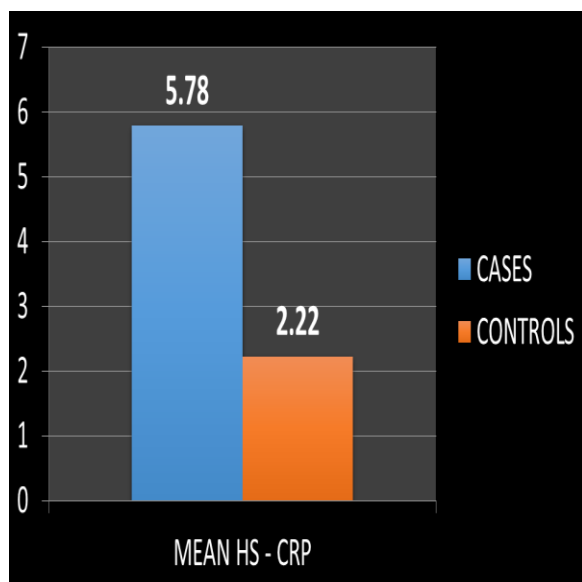
**Graph 2 – Bar graph showing mean RBS,FBS,PPBS in cases and controls.**



**Graph 3 – Bar graph showing mean HbA1C in cases and controls**



**Graph 4 – bar graph showing mean microalbuminuria in cases and controls**



Graph – 5 bar graph showing mean hs CRP levels

## DISCUSSION

In several studies, it has been reported that there is a correlation between serum CRP levels and microalbuminuria in diabetic patients and even in the general population.<sup>[9]</sup> These observations suggest that low-grade inflammation, reflected by high serum HS-CRP levels, may play a role in the induction of microalbuminuria, which can be considered as a risk factor of cardiovascular diseases.<sup>[10]</sup>

Persistent microalbuminuria is a strong predictor of development of clinical diabetic nephropathy, which is reversible, but may lead to kidney failure if neglected.<sup>[11]</sup> Therefore, early diagnosis may help to prevent of progression of kidney disease.

Accordingly, annual screening of microalbuminuria is recommended by experts in DM.<sup>[12]</sup> It is reported that prevalence of microalbuminuria is about 12.6% to 25.3% in patients with type 2 DM. In order to find an easier method for detection of diabetic nephropathy this study was done in which hs crp was thought to be easier and convenient method.<sup>[17,18]</sup> In our study Microalbuminuria patients were significantly older and affected by diabetes mellitus longer than those without microalbuminuria. Their mean HS-CRP was significantly higher ( $5.78 \pm 1.35$  mg/L versus  $2.22 \pm 1.80$  mg/L;  $P < .001$ ). The Pearson correlation test showed a significant correlation between HS-CRP level and urine albumin level ( $r = 0.45$ ;  $P < .001$ ). Navarro et al studied patients with type 2 diabetes and revealed that CRP levels were high in patients with or mild proteinuria (urinary protein, 1 g/day) compared with those with normoalbuminuria. Experimental and clinical studies suggest that CRP is associated with insulin resistance and hyperglycemia.<sup>[16]</sup> Which was similar in our study.

In some studies, it has been shown that there exist a relationship between microalbuminuria and age. We

found this result too. In this study, they also reported there were no differences between men and women in terms of these parameters, that is similar to our findings. A limitation of our study was that since many factors can affect CRP level, we had to limit our inclusion criteria to avoid confounding factors, such as administration of statins and angiotensin converting enzyme inhibitor, which is used by many diabetic patients.<sup>[13,14,15]</sup>

## CONCLUSION

In type 2 diabetic patients, microalbuminuria is accompanied by elevated HS-CRP, suggesting activation of inflammatory pathways in progression of renal disease. As it is a easier and cheaper test for assessment of diabetic nephropathy. So hs – CRP can be used as early marker for detection of diabetic nephropathy.

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