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Evaluation Of Serum Uric Acid, Serum CRP With Microalbuminuria In Type 2DM.

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ABSTRACT

Diabetes mellitus is a major emerging clinical health problem in the 21st centuary. Diabetic nephropathy is one of the most common consequences of diabetes mellitus. Evidence shows that subclinical chronic inflammation is involved in the pathogenesis of diabetic nephropathy. To determine the significant association between serum CRP, serum uric acid and microalbuminuria in type 2 diabetic patients. This is cross sectional study carried out in 100 diagnosed type 2 diabetic patients. Blood sample collected for the analysis of serum CRP, serum uric acid, HbA1c, and early morning mid-stream urine sample for the estimation of the microalbuminuria. Data was statistically analysed. Serum uric acid and serum CRP shows significant association with microalbuminuria in type 2 diabetic patients. Elevated serum CRP and serum uricacid level were associated with microalbuminuria in type 2 diabetic patients suggesting the risk factors for the development of incipient diabetic nephropathy. Thus regular screening of serum CRP and serum uric acid along with microalbuminuria helpful in risk prediction of diabetic nephropathy and early intervention to prevent complications.

Keywords: Serum uricacid, Serum CRP; Microalbuminuria, Type2 Diabetes Mellitus.

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INTRODUCTION

Diabetes mellitus is one of the commonest endocrine disorder seen in clinical practice. It is characterized by hyperglycemia due to absolute or relative deficiency of insulin. Non-insulin dependent diabetes mellitus (NIDDM) occurs at any age but is more common between 40-80 years of age and also has strong genetic component. Diabetic nephropathy is a long standing common complication of type 2 DM which is leading cause of end stage renal disease and cause of DM related morbidity and mortality [1].There are evidences that subclinical chronic inflammation is involved in the pathogenesis of diabetic nephropathy [2-4]. Inflammation may also underlie the association between obesity and insulin resistance with diabetic nephropathy [5,6]. C-reactive protein (CRP), which is produced by the macrophages in the liver and adipocytes and is integrated in the acute-phase response pathways, is a very sensitive and well-characterized marker of subclinical low-grade inflammation [7]. Recent clinical studies found that CRP is associated with diabetic nephropathy in both type 1 and type 2 diabetes [8,9]. Circulating CRP levels may predict the development of albuminuria in cohort studies of patients with type 2 diabetes [4].

Many evidences supported that elevated serum uric acid is associated with high circulating inflammatory cytokines, including CRP, interleukin 6 and tumor necrosis factor α [11-14]. A high level of serum uric acid was found to predict the development of hypertension [15,16], obesity [17], type 2 diabetes [18,19] , metabolic syndrome [20,21] . On the other hand, uric acid plays an important role in the development and progression of chronic kidney diseases (CKD) [22] .Some studies have demonstrated that hyperuricemia is significantly associated with diabetic nephropathy [23,24] and serum uric acid level is positively correlated to urinary albumin excretion in diabetic patients [25,26]. It also has been shown that hyperuricemia is an independent risk factor for the development of incident CKD in type 2 diabetic patients with preserved kidney function [27] . Based on this our study aimed to determine the significant association between serum CRP, serum uric acid and microalbuminuria in type 2 diabetic patients.

MATERIAL AND METHODS

The present cross sectional study was conducted from December 2012 to November 2013 in teaching health center located at Raichur, Karnataka. One hundred known type 2 diabetic patients (Male-56 and Female-44) with age range 30-80 years were included. In the study purposive random sampling technique was used for data collection. Ethical committee approval was taken. The study population was categorized into two groups based on level of albuminuria, Group A-Type 2 diabetic patient with normoalbuminuria (<30mg/dl). Group B- Type two diabetic patients with microalbuminuria (30-300mg/dl). Informed consent was obtained. A Structured questionnaire regarding the demographic data such as age, sex, duration of diabetes, complete clinical details with general physical and systemic examination were recorded for each patient. Exclusion criteria were diabetes other than type 2 diabetes, known non-diabetic kidney disease, obstructive uropathy, urinary tract infection, fever, acute illness, congestive heart failure, malignancy and pregnancy. Patients using uric acid lowering agents or diuretics were also excluded. Venous blood was drawn with no anticoagulant for the estimation of serum uric acid, serum CRP and EDTA for the estimation of HbA1c. Early morning mid stream urine sample in a sterile container without preservative for the estimation of albuminuria is taken. Serum uric acid was estimated by enzymatic method. Serum CRP was estimated by Immunoturbidimetric method. HbA1c was estimated by Immunoassay. Albuminuria was estimated by Immunoturbidimeteric assay .All parameters were estimated in fully automated Randox auto analyzer.

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 tables etc**.** $P < 0.05$ was considered statistical significance.

RESULTS

From the (Table no. 1) Group B- type 2 diabetic patient with microalbuminuria shows statistically highly significant association with serum uric acid ($p<0.001$) and serum CRP ($P<0.001$) as compared to Group A- type 2 diabetic patient with Normoalbuminuria. However Group A and Group B shows no statistical significant association with HbA1c.

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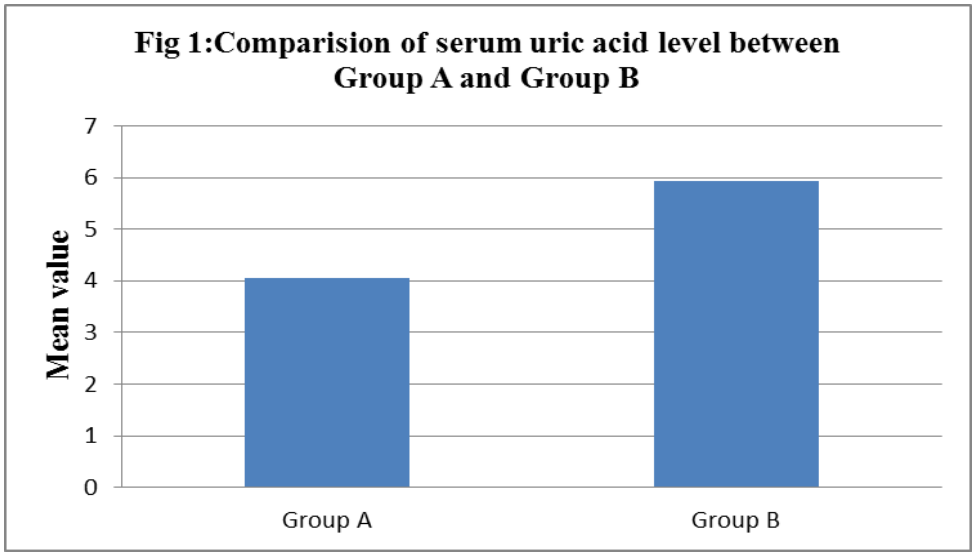
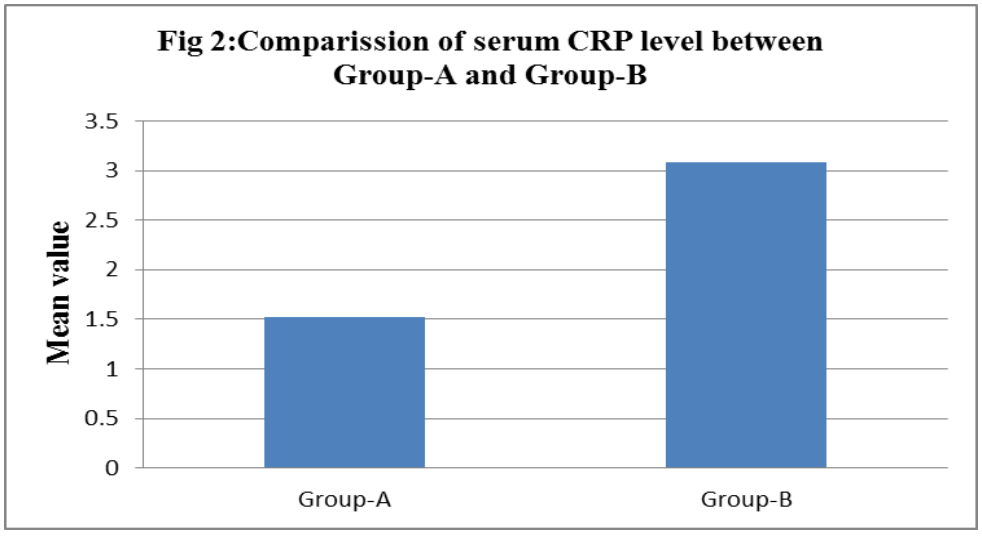
Table 1: Baseline characteristics of study subjects

Variables	Type 2 Diabetes Mellitus		P value
	Group-A n=70 (Mean±SD)	Group-B n=30 (Mean±SD)	
Age (years)	55.91±7.73	62.96±6.84	<0.001*
HbA1c(%)	6.92±1.09	7.02±0.9	0.35
Serum uric acid (mg/dl)	4.05±1.21	5.93±1.3	<0.001*
Serum CRP(mg/L)	1.52±0.83	3.08±1.9	<0.001*

* highly significant





DISCUSSION

In this cross sectional study we found serum CRP and serum uric acid levels were significantly associated with microalbuminuria, independent of glycemic control which is similar to previous studies [8-10, 23-26]. Group B patients show serum CRP with mean value (3.08±1.9) and serum uric acid (5.93±1.3) compared to Group A patients with mean value for serum CRP (1.52±0.83) and serum uric acid (4.05±1.21). Thus elevated serum CRP and serum uric acid suggests that the presence of subclinical inflammation and may amplify the effect on albuminuria in type2 diabetes and vice versa. Evidence supporting the pathogenic importance of serum CRP in diabetic nephropathy from the previous study Liu et al [28] found that *CRP* transgenic diabetic mice developed much more severe kidney injury than wild-type diabetic mice, as indicated by a significant increase in urinary albumin excretion and kidney injury molecule-1 abundance, enhanced

infiltration of macrophages and T cells, and up regulation of pro-inflammatory cytokines and extracellular matrix. They also demonstrated that enhanced activation of TGF-β/SMAD and nuclear factor κB signalling pathways may be the mechanisms by which CRP promotes renal inflammation and fibrosis under diabetic conditions [28] . These findings suggest that CRP is not only a biomarker, but also a mediator involved in the pathogenesis of diabetic nephropathy.

There are evidences that uric acid may play a pathological role in endothelial dysfunction and kidney disease. Mild hyperuricemia induces endothelial dysfunction and hypertension in animal models, both of which are reversed by lowering uric acid levels [29, 30]. Furthermore, elevated uric acid can lead to a primary renal arteriolopathy in rats, which is not dependent on blood pressure and instead is a consequence of activation of the renin-angiotensin system [31]. Recently, Kosugi et al [32] found that allopurinol treatment of diabetic (*db/db*) mice significantly lowered uric acid levels, reduced albuminuria and ameliorated tubulointerstitial injury, suggesting a pathogenic role of uric acid in diabetic nephropathy.

It has been shown that elevated serum uric acid is associated with high circulating CRP [14] and uric acid when entering the vascular smooth muscle cell can stimulate the release of CRP [33] thus potentially creating a vicious cycle of inflammatory activity and endothelial dysfunction. Thus our finding suggests that serum CRP and serum uric acid are associated with risk of albuminuria in type 2 diabetic patients and progression to diabetic nephropathy.

CONCLUSION

Elevated serum CRP and serum uricacid level were associated with microalbuminuria in type 2 diabetic patients suggesting the risk factors for the development of incipient diabetic nepropathy. Thus regular screening of serum CRP and serum uric acid along with microalbuminuria helpful in risk prediction of diabetic nephropathy and early intervention to prevent complications.

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