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Research Paper

Assessment of Hs-Crp with Serum Uric Acid in Type-2 Diabetic Patients in Western Region of Nepal

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ABSTRACT:- *High- sensitivitye C- reactive protein (hs-CRP) is an α globulin produced by liver as a marker of inflammation.[14] It may play a role as predictor of inflammation in diabetic nephropathic patients. The aim of present study was to estimate hs-CRP levels and blood uric acid and to determine association between them.*
The relationship between inflammation and blood uric acid level in type- 2 diabetes has not yet been reported in Nepalese population. So a quantitative, analytical study were done by enrolling 89 type 2 diabetic patients conducted at Tertiary care Hospital. We analyzed serum concentrations of hs-CRP, serum uric acid, blood glucose and family history of the patients. In our study, we found the significant association between serum hs-CRP and Serum uric acid level (P values=0.001).We also found the significant association between serum hs-CRP and Blood Glucose level (P values<0.01). Furthermore, serum hs-CRP was not correlated with family history of patients (P >0.599) and sex(P>0.08).

This study concludes that the increase in serum hs-CRP value in type 2 diabetic patients increase the risk of diabetic nephropathy and thus increase the value of serum uric acid level. And there is no correlation of both serum hs-CRP and uric acid level with the risk factors especially sex and family history of type 2 diabetes.
The significance of these findings emphasizes to choose these association for early screening of diabetic nephropathy in type 2 diabetic patients to prevent from further complication.

Keywords:- *serum Uric acid, High sensitivity- C- reactive protein, Blood glucose, Type 2 diabetes, Diabetic Nephropathy.*

I INTRODUCTION

Diabetes mellitus (DM) is the most prevalent metabolic, non communicable disorder characterized by hyperglycemia.[1] Diabetic nephropathy is one of the dreaded complications of diabetes.[4] It has been predicted as one of the leading cause of end-stage renal disease (ESRD) worldwide. Nearly 30% of chronic renal failures in South Asia are due to diabetic nephropathy[3].The earliest clinical evidence of nephropathy is the appearance of low but abnormal levels of albumin in the urine. Apart from this, there are a number of several metabolic defects like dyslipidemia, hyperuremia, hyperuricamia which have been shown to predict the abnormal functioning of kidney in type 2 diabetes.[26] Increased blood Uric acid indicate the abnormality of nephron.[2] Factors such as age, sex and genetic factor influence serum uric level in diabetic patients. Certain aspects of the lifestyle, including the diet, physical activity, diabetes control level, alcohol consumption, smoking status also affect the serum uric acid level in diabetic patients. [4,14,19 ,31]Abnormal blood uric acid is the symptom of kidney disease.[2]

High sensitive C-reactive protein (hs-CRP), is a acute phase protein produced by hepatocyte cell, which is considered earlier as the inflammatory biomarker and has been reported to be associated with both diabetes and CAD.[8] CRP test helps to determine heart disease risk, tissue injury, inflammatory disorder etc. Elevated hs-CRP is related to increased risk for heart attack, coronary arteries after angioplasty, stroke and peripheral vascular disease (PVD).[9,10,11,12,26]

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Therefore to prevent the early incidence of kidney diseases and other drastic consequences, an advance technique is needed, that will help the people to know their health condition, monitor and control. Hence present study aims at studying the association of serum uric acid level with the level of serum hs-CRP which will be beneficial for staging of kidney damage.

II. MATERIALS AND METHODS

Study Design

This study was conducted on subjects attending the diabetes ward in the Department of Medicine, as well as the general OPD and the patients admitted in the wards of Department of Medicine, Manipal Medical College, Pokhara, Nepal, from November 2013 to April 2014.

A total of 89 type- 2 diabetic patients have been screened for serum Uric acid and hs-CRP after obtaining informed consent. The criteria for diagnosing diabetes were the same as laid down by WHO. Detailed interview by using a structured questionnaire was also documented. The study was approved by the Institutional ethical committee on human research. Patients with Type I Diabetic Patients, Patients < 30 years, Gestational Diabetes, Muscular Dystrophy, Dehydration, Pyelonephritis, Urinary tract obstruction, the diseases due to other than diabetes were excluded from the study.

Blood Collection & Biochemical Assay

Blood samples were withdrawn by using sterile syringe from the 12 to 14 hours of overnight fasting diabetic patients in the morning. Blood Samples were collected in sterile tubes, centrifuged at 3000 rpm for 10 minutes and serum was stored at 4°C. Fasting (FBG) and Postprandial (PPBG) blood glucose level were measured by an enzymatic GOD-POD method.[23] serum Uric acid level was estimated by standard enzymatic uricase method[29]. All chemicals and reagents of excellent quality obtained from Tulip company Ltd, India. And marker of inflammation high-sensitivity C-reactive protein (hs-CRP) was measured by Sandwich Enzyme Linked Immunosorbent Assay Method. [7]

The data collected was entered in Microsoft Excel and checked for any inconsistency. The Pearson correlation coefficient was used to find out the correlation between Serum uric acid with hs-CRP. The value of $p<0.05$ was taken as significant. All the analysis was carried out by using SPSS 15.1 version.

III. RESULTS

The study was conducted on 89 type 2 diabetic patients. Among them 51 were male and 38 were female patients of the age ranging from greater than 30 to 72 years. Based on serum uric acid estimation, 86.51% diabetic patients had normal serum uric acid level while 11.23% patients had high and 2.24% had low value for the same. Similarly, serum hs- CRP was significantly higher in all diabetic patients but nearly 50% diabetic patients were found to be low risk when classified the patients on the basis of serum hs- CRP level as Low risk=<2mg/L, Moderate risk 2-6mg/L, High risk=>6 mg/L (This classification is on the basis of American Diabetic association)

Table 1. Serum Uric acid , Blood Glucose and Serum Hs-CRP level in diabetic patients

Parameters	Patients having low value	Patients having normal Values	Patients having high Values	Total Patients	Normal Range
Serum Uric Acid	2(2.24%)	77(86.51%)	10(11.23%)	89	2-6 mg/dl
Fasting Plasma Glucose	0(0%)	29(32.58%)	60(67.41%)	89	70-110mg/dl
Serum hs-CRP	44(49.43% (Low risk)	23(25.84%) (Moderate risk)	22(24.71%) (High risk)	89	Low risk=<2mg/L Moderate risk 2-6mg/L High risk=>6 mg/L

Table1 shows that 77(86.51%) patients out of 89 have normal uric acid level and 10(11.23%) patients have high serum uric acid values. Similarly, 29(32.58%) have normal fasting plasma glucose level. On the other hand, 60(67.41%) samples have high fasting plasma glucose level, 22(24.71%) patients are at the high risk of diabetic nephropathy(hs-CRP value above 6mg/L), 44 (49.43%) patients at low risk(hs-CRP value less than 2mg/L) and 23(25.84%) patients at moderate risk(serum hs-CRP value between 2mg/L-6mg/L).

Table 2. Correlations of serum hs-CRP level with serum Uric acid and Fasting plasma Glucose level of Diabetic patients

Parameters	Value of serum Uric acid level	Value of Fasting plasma glucose level
Serum hs-CRP of the patients (γ) Spearman's correlation coefficient	0.349	0.258
2 tailed P value	0.001**	0.014**
Number	89	89

***2-tailed P value is significant at the 0.01 level.**

Table 2 shows the significant correlation of serum hs-CRP level with the value of fasting plasma glucose of the patients. p value between serum hs-CRP and serum uric acid was found to be significantly correlated(γ=0.349, p< 0.01). Similarly hs-CRP and fasting plasma glucose were also significantly correlated (γ= 0.258 , p=0.01).

Table-3. Correlation of Serum Uric acid (UA) level with risk factors of Diabetic nephropathy

Variables	Concentration, of serum Uric Acid level			Chi square values	P value
	High	**Low**	**Normal**		
Family history					
Yes	7(14.3%)	1(2.0%)	41(83.7%)	1.025[a]	0.599
No	3(7.5%)	1(2.5%)	36(90.0%)		
Sex					
Male	8(15.7%)	0(0.0%)	43(84.3%)	4.857[a]	0.08
Female	2(53%)	2(53%)	34(89.5%)		

Table 3 shows that there is no significant association of serum uric acid with the other risk factors like sex, family history of diabetic nephropathy.

Table-4.Correlation of Serum hs-CRP level with risk factors of Diabetic nephropathy

Variables	Serum hs-RP level (High)	Serum hs CRP level (Low)	Serum hs CRP Normal	Chi Square test value	P values
Family History				3.254[a]	0.197
Yes	14(28.6%)	20(40.8%)	15(30.6%)		
No	8(20%)	24(60%)	8(20.0%)		
Sex				2.656[a]	0.265
Male	11(21.6%)	29(56.9%)	11(21.6%)		
Female	11(28.9%)	15(39.5%)	12(31.6%)		

Table 4. Shows that there is no association of serum hs- CRP with the other risk factors like family history and sex of Diabetic nephropathy.

IV. DISCUSSION

Hyperuricemia is a metabolic abnormality that are closely associated with obesity and type 2 diabetes.[30] Its biological effects is related to endothelial dysfunction by inducing anti-proliferative effects on endothelium and impairing nitric oxide production and inflammation, through increased C- reactive protein expression[28]. The present study has clearly shown that serum uric acid has significant association with serum hs-CRP level in diabetic patients. The risk factors such as family history and sex were insignificantly related with serum hs-CRP level in the development of diabetic nephropathy.

In several studies, it has been reported that there is a clear association of serum uric acid level with acute-phase marker C-reactive protein (CRP) in diabetic patients[22,29]. CRP may play an important role in induction of serum uric acid level which is the indicative of diabetic nephropathy. So Serum uric acid estimation along with CRP is a strong predictor for development of clinical diabetic nephropathy and their early diagnosis may help to prevent the further progression of kidney disease.

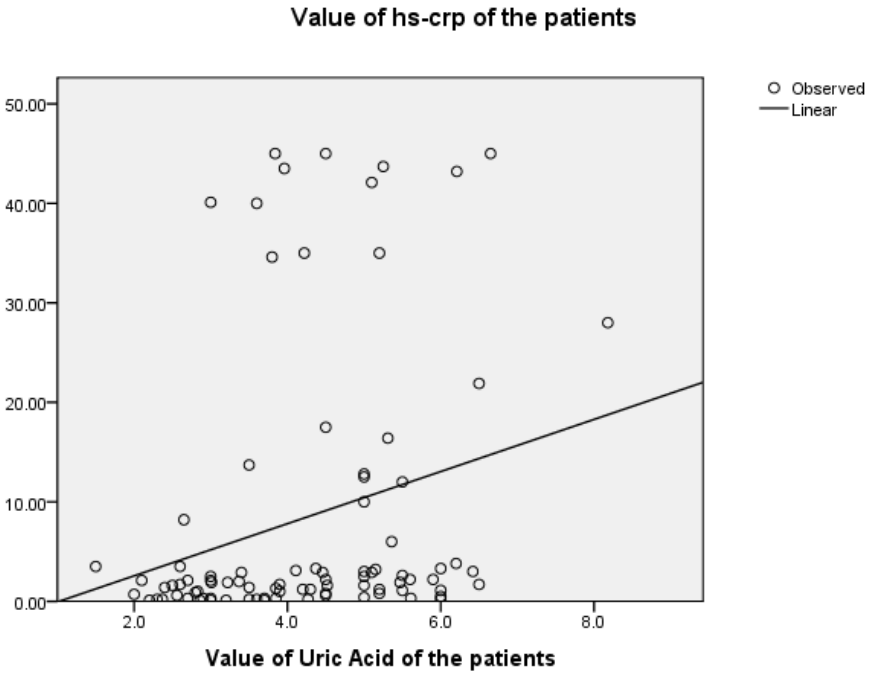

Figure 1. Correlation between hs-CRP and serum uric acid in type II diabetic patients (P=0.001, □= 0349).

Therefore, in order to support for the detection of diabetic nephropathy, we tried to find a relation between hs-CRP and serum uric acid level.

Lee JE et al.(2006) have been reported that there is a clear association of serum uric acid with high levels of C-reactive protein (CRP) in diabetic patients[29]. And similar type of finding was also found by Lyngdoh TM et al. (2011)[27]. These findings suggest that CRP along with Uric acid are not only a biomarker, but also a mediator involved in the pathogenesis of diabetic nephropathy. A potential explanation for the mechanism of the interrelationship between CRP and uric acid is that CRP and uric acid affect diabetic nephropathy through distinct pathways, but they are closely interrelated with each other at the same time[2,28]. It has been shown that elevated serum uric acid is associated with high circulating CRP, and uric acid when entering the vascular smooth muscle cell can stimulate the release of CRP, thus potentially creating a vicious cycle of inflammatory activity and endothelial dysfunction[2].

V. CONCLUSION

This present investigation demonstrates that serum hs-CRP level is significantly correlated with serum uric acid level in type 2 diabetes. It indicates that the elevation in serum hs-CRP value increase the risk of diabetic nephropathy and thus increase the value of serum uric acid level. This study has also shown that hs-CRP and blood uric acid are not significantly correlated with risk factors like sex and family history of type 2 diabetes.

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