



## ORIGINAL ARTICLE

### Association of hsCRP with Serum Creatinine in Type 2 Diabetic Patients at Tertiary Care Hospital

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[Received on: 1 April 2022; Accepted on: 20 May 2022; Published on: 1 July 2022]

#### Abstract

**Background:** High-sensitive C-reactive protein (hs-CRP) is a marker of inflammation. CRP may play a significant role as a predictor of inflammation in nephropathy and chronic kidney disease. **Objective:** The aim of the present study was to estimate hs-CRP levels and serum creatinine levels among type 2 diabetes mellitus patients and to determine association between them. **Methodology:** This was an analytical, quantitative, hospital-based study performed on type 2 diabetic patients and was conducted at the Department of Biochemistry of BIRDEM General Hospital, Dhaka, Bangladesh. It was analyzed serum concentrations of hs-CRP, serum creatinine, serum glucose and family history of the patients. **Results:** This observational study showed that a greater number of diabetics had high serum creatinine level (41% vs 59%). 67.6% of study population had moderate to high level of hsCRP. hs-CRP was found significantly higher in diabetics with renal impairment ( $1.66 \pm 0.86$  vs.  $7.01 \pm 3.44$ ,  $p < 0.001$ ). Serum creatinine had positive ( $r = 0.88$ ,  $p < 0.001$ ) correlation with hs-CRP. Glycated hemoglobin and serum creatinine were linearly related with inflammatory marker. When creatinine increased by 1 unit, hs-CRP increased by 0.84 units ( $\beta = 0.84$ ,  $p < 0.001$ ). **Conclusion:** This study concludes that the increase in serum hs-CRP value type 2 diabetic patients increase the risk of diabetic nephropathy and thus increase the value of serum creatinine level. [*Journal of Current and Advance Medical Research*, July 2022;9(2):59-62]

**Keywords:** Serum creatinine; high sensitivity; C-reactive protein; diabetic nephropathy

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**Cite this article as:** Aziz M, Ayub T, Islam F, Ahmed F, Nusrat J, Nadia F. Association of hsCRP with Serum Creatinine in Type 2 Diabetic Patients at Tertiary Care Hospital. *J Curr Adv Med Res* 2022;9(2):59-62

**Funding:** This study has been performed without any funding from outside else.

**Conflict of Interest:** There was no conflict of interest to any of the authors.

**Contributions to authors:** All authors involved from protocol preparation up to manuscript writing & revision.

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## Introduction

Diabetes is a metabolic disorder with inappropriate hyperglycemia<sup>1-2</sup> either due to an absolute or relative deficiency of insulin or reduction in the biologic effectiveness of insulin or both<sup>3</sup>. The decreased uptake of glucose into muscle and adipose tissue leads to chronic extracellular hyperglycemia which results in both type 1 and 2 Diabetes Mellitus<sup>4-5</sup>. There are currently 382 million diabetic people in the world and more than 72.1 million people in the South East Asia<sup>6</sup>. IDF estimates in 2014 that 387 million people had diabetes, 8.3% of adult world population. 80.0% of the global cases of DM live in low and middle income countries<sup>7</sup>. In Bangladesh there were 5.9 million cases of diabetes with a comparative prevalence of 6.3% in adults aged 20-79 years which costs 42.6 USD per diabetic person<sup>8</sup>. So there is no doubt to conclude that diabetes has emerged one of the most challenging problem in 21<sup>st</sup> century. Currently, diabetic people have threatened from long-term life-threatening kidney complications. Nearly 180,000 people in the United States are living with kidney failure as a result of diabetes<sup>9</sup>.

Diabetic nephropathy is a serious complication that has emerged as one of the most common long-term sequel of Diabetes mellitus and it is the single largest cause of end-stage renal disease worldwide and accounting for 20.0% to 40.0% new cases<sup>10</sup>. Diabetic nephropathy, a multistage disorder, is a leading cause of End Stage Renal Disease (ESRD)<sup>3</sup>. It affects 20.0% to 40.0% of diabetic patients, and is associated with enormous morbidity and mortality with greater health care cost<sup>4</sup>. Among several markers of inflammation, hs-CRP is found to be significant in people with diabetes. Insulin resistance and inadequate insulin secretion are the two main factors leading to type 2 diabetes mellitus. Basic research studies are in tune with the hypothesis that chronic subclinical inflammation is the main cause of insulin resistance leading to development of type 2 diabetes mellitus<sup>12-14</sup>. CRP is a pentameric protein produced by the liver and it has emerged as the golden marker for inflammation. It is a non-immunoglobulin protein having five identical sub units. It is an acute phase response protein markedly increased in both inflammatory and infectious diseases. It plays an important role in innate immunity<sup>11</sup>.

CRP may play a significant role as predictor of inflammation in nephropathy and chronic kidney disease [1]. Metabolic diseases are affecting human health all over the world. These chronic disease states are associated with high sensitive CRP<sup>2</sup>.

There to prevent the early incidence of kidney diseases and other drastic consequences, an advance technique is needed, that will help people to know their health condition, monitor and control. The aim of the present study was to estimate hs-CRP levels and serum creatinine levels among type 2 diabetes mellitus patients and to determine association between them.

## Methodology

**Study Settings and Population:** This was an analytical, quantitative, hospital-based study done on type 2 diabetic patients conducted at the Department of Biochemistry of BIRDEM General Hospital to predict the association of hsCRP with serum creatinine. Patients aging more than 30 years who were suffering from type 2 diabetes and visited the outpatient department of BIRDEM for their routine medical checkups were included as the study subjects. Age and gender-matched healthy persons were included as control.

**Questionnaire and Data Collection:** The study data were collected by personal interview using a pretested questionnaire containing demographic condition, past medical history, family history, duration of diabetes, history of treatment of DM and hypertension, smoking, alcohol behavior and dietary habit. The subjects are also asked for the presence of any other complication of DM.

**Sample Collection:** Overnight fasting diabetic patients were selected for blood collection and about 3ml venous blood was collected from each patient, of which 2ml of whole blood from each was added in fluoride vial for glucose measurement and remaining blood was added in plain test tube for serum hs-CRP measurement. The blood collected in the tubes was allowed to clot at room temperature and then centrifuged at 3000 rpm for 10 min. Blood glucose was analyzed in the same day. The remaining serum was preserved in eppendorf tube at -20°C for hs-CRP estimation.

**Biochemical analysis:** Plasma glucose level was measured by enzymatic end point glucose oxidase peroxidase method<sup>15</sup>. And serum hs-CRP was measured by sandwich ELISA method<sup>16</sup>.

**Statistical Analysis:** The collected data were entered in SPSS and checked for any inconsistency. The Pearson correlation coefficient was used to find out the correlation between serum creatinine with hs-CRP. The value of  $p < 0.05$  was taken as

significant. All the analyses were carried out by using SPSS 15.1 version.

**Results**

The study was conducted on 136 subjects including 45 apparently healthy volunteers. Among them 89 were female and 47 were male aged 30 to 65 years. A greater number of diabetics had high serum creatinine level (41.0% vs 59.0%). About 67.6% of study population had moderate to high level of hsCRP. hsCRP and serum Creatinine were significantly higher in diabetic population. The clinical and biochemical characteristics of the study population are shown in table-1. Total study population was classified into 3 groups on the basis of hs-CRP level.

**Table 1: Clinical and Biochemical Characteristics of Study Population (Mean±SD)**

Variable	Group		P value
	DM	Control	
Age (Years)	50.80±9.21	44.73±8.70	0.001
FBS*	8.42±2.25	5.34±0.99	0.001
2hABF*	12.16±3.89	9.08±1.84	0.001
HbA <sub>1c</sub>	6.86±1.51	5.48±0.55	0.001
hsCRP**	4.83±3.77	2.35±1.00	0.001
S.creatinine**	1.94±0.98	1.11±0.41	0.001

p-value calculated by independent student's t-test; \*mmol/L; \*\*mg/L

Table 2 revealed that high risk group of hs-CRP had significant hyperglycemia in fasting, blood glucose 2hABF and HbA<sub>1c</sub> and also had significant renal impairment compared to low and moderate risk group of hs-CRP.

**Table 2: Association of Biochemical Parameters with hs-CRP levels (Mean±SD)**

Variable	Low risk of hs-CRP (<1 mg/L)	Moderate risk of hs-CRP (1-3mg/L)	High risk of hs-CRP (>3 mg/L)	P value
Serum Creatinine	0.97±0.26	1.51±0.63	3.03±0.55	<0.001
FBS	6.35±1.55	6.98±1.93	9.80±2.77	0.022
ABF	9.52±2.42	10.82±2.87	14.20±4.68	0.013
HbA <sub>1c</sub>	5.77±0.99	6.13±1.14	7.87±1.52	0.008

One way ANOVA test was done.

The hs-CRP was found significantly higher in diabetics with renal impairment (1.66±0.86 vs. 7.01±3.44, p<0.001) (Table 3).

**Table 3: Glycemic and Inflammatory Parameters in DM Population with Normal and High Creatinine Level (Mean±SD)**

Variables	Serum creatinine Level		P value
	Normal	High	
FBS	7.54±1.41	9.02±2.52	0.001
ABF	10.33±2.48	13.41±4.19	<0.001
HbA <sub>1c</sub>	6.16±1.35	7.33±1.43	<0.001
hsCRP	1.66±0.86	7.01±3.44	<0.001

Independent t-test was done.

Serum creatinine had positive (r=0.88, p<0.001) correlation with hs-CRP (table-4) . Table-5 revealed positive association of HbA<sub>1c</sub> and serum creatinine with hs-CRP, however FBS and ABF were inversely associated.

**Table 4: Correlation of Serum Creatinine and Glycemic Variables with hs-CRP Level (n=136)**

Variables	r-value	P-value
FBS	0.5	<0.001
ABF	0.41	<0.001
HbA <sub>1c</sub>	0.55	<0.001
S. Creatinine	0.88	<0.001

Pearson's correlation was done.

Glycated hemoglobin and serum creatinine were linearly related with inflammatory marker. When creatinine increased by 1 unit, hs-CRP increased by 0.84 units (β=0.84, p=<0.001) (Table 5).

**Table 5: Regression analysis of hs-CRP with Creatinine and Glycemic Parameters**

Variables	β	P value
HbA <sub>1c</sub>	0.16	0.006
S. Creatinine	0.84	<0.001

Linear regression was done.

## Discussion

This present study showed that serum creatinine had significant association with serum hs-CRP level in DM population. Acute phase marker hs-CRP may play an important role in induction of serum creatinine level which determines diabetic nephropathy. That is why creatinine estimation in blood along with hs-CRP is a strong predictor for developing clinical diabetic nephropathy and their early diagnosis may help to resist further progression of kidney disease. Therefore, in the aim for early prediction of diabetic nephropathy we observed the association between hs-CRP and serum creatinine in DM.

Deebukkum et al<sup>17</sup> also found a clear significant association of serum creatinine with high levels of C-reactive protein (CRP) in diabetic patients. Similar type of finding was also shown by Arik et al<sup>18</sup>. Therefore these findings suggest that high hs-CRP along with raised creatinine are involved in the pathogenesis of diabetic nephropathy. It has been shown that elevated circulating hs-CRP is due to inflammation of kidney that ultimately hinders glomerular filtration. Thus serum creatinine level is increased due to its decreased excretion<sup>17-18</sup>.

Interpretation may be limited due to the small sample size. Though high-sensitivity CRP could be measured, an oral glucose tolerance test was not done due to technical issues. However, DM and prediabetic volunteers were excluded from the control group.

## Conclusion

This study concludes that the increase in serum hs-CRP value type 2 diabetic patients increase the risk of diabetic nephropathy and thus increase the value of serum creatinine level. Based on this study, we recommend the measurement of serum hs-CRP along with creatinine as a screening method to be considered in the future studies that will help us diagnosing the early stages of diabetic nephropathy easier

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