

## Comparison of C-reactive protein among controlled, moderately controlled and uncontrolled diabetic subjects in a Bangladeshi population

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### ABSTRACT

Poor glycemic control is significantly associated with the development of macrovascular complications of diabetes. C-reactive protein (CRP) is considered as a sensitive and independent risk factor for cardiovascular events. The aim of this study was to compare elevated CRP among controlled, moderately controlled and uncontrolled diabetic subjects in a Bangladeshi population. CRP and glycosylated hemoglobin A<sub>1c</sub> (HbA<sub>1c</sub>) were measured in 226 confirmed diabetic subjects purposively and randomly. Elevation of CRP in the moderately controlled (relative risk 1.64, P<0.01) and uncontrolled diabetic subjects (relative risk 1.8, P<0.001) were significantly higher than controlled diabetic subjects. HbA<sub>1c</sub> was significantly associated with the likelihood of elevated CRP in the moderately controlled diabetic subjects (OR:2.87, 95% CI: 1.41 to 5.87, P<0.01) and in the uncontrolled diabetic subjects (OR:3.83, 95% CI: 1.94 to 7.58, P<0.001). This study revealed that the likelihood of elevated CRP is associated with the increase of HbA<sub>1c</sub> in diabetic subjects.

**Key words:** CRP, HbA<sub>1c</sub>, diabetes, cardiovascular disease

### Introduction

C-reactive protein (CRP), an acute phase protein, is considered as a marker of nonspecific systemic inflammation. Most of the healthy individuals have CRP concentration < 6 mg/L. It is a stronger predictor of future cardiovascular events than low-density lipoprotein cholesterol (LDL-C) (1). The co localization of CRP and LDL-C is a fundamental initializing step in cellular migration and plaque development. Once present, CRP upregulates adhesion molecule expression, activates complement, and induces monocyte tissue factor expression (2). CRP also has pro-inflammatory properties that could potentially contribute to the pathogenesis, progression and complications of atheroma (3,4). Elevated CRP is associated with higher level of insulin and HbA<sub>1c</sub> (5,6) and increased risk of later development of diabetes (7,8). The

base-line plasma concentration of CRP predicts the future myocardial infarction and stroke (9). Elevated CRP is also considered as an independent predictor of development of peripheral arterial disease and may provide additive information over the traditional lipid parameters (10).

Diabetes and cardiovascular complications are increasing in our country. As CRP is a predictor of both the development of diabetes and cardiovascular events, we aimed to compare CRP among controlled, moderately controlled and uncontrolled diabetic subjects in a Bangladeshi population.

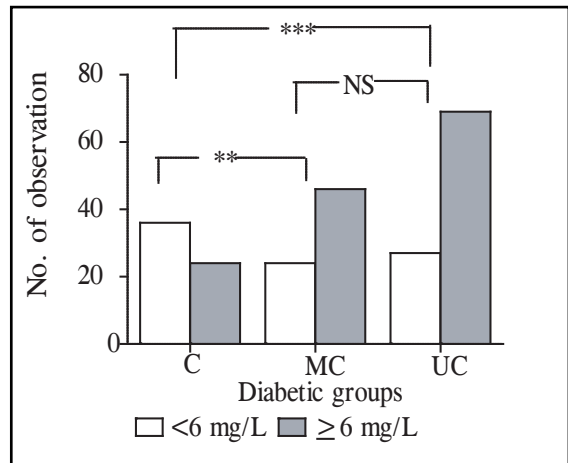
### Methods

This study was conducted in the Department of Biochemistry and Cell Biology and Department of Immunology, Bangladesh Institute of Health Sciences (BIHS) during January to March 2010.

Two hundred twenty six confirmed diabetic subjects were included randomly in this study. Serum CRP was measured by a semi-quantitative method (Omega Diagnostic Ltd., UK). HbA<sub>1c</sub> was measured by HPLC based method using D-10<sup>®</sup> hemoglobin assay system (Bio-Rad, USA) in confirmed diabetic subjects. Subjects were grouped as controlled diabetic subjects (HbA<sub>1c</sub> 7.0%), moderately controlled diabetic subjects (HbA<sub>1c</sub>: 7.1 - 9.0%) and uncontrolled diabetic subjects (HbA<sub>1c</sub> > 9.0%). Results of CRP were expressed as negative (CRP concentration < 6 mg/L) and positive (CRP concentration ≥ 6 mg/L) and compared by Fisher's exact test among different diabetic groups classified according to HbA<sub>1c</sub> values.

## Results

Mean±SD age of the controlled, uncontrolled and moderately controlled diabetic group were 45.6±9.2, 47.74±9.65 and 46.53±8.96 years respectively; the differences of mean ages were not statistically significant compared by unpaired t test ( $p > 0.05$ ). Of the total study subjects, 51% were male and 49% were female. 32% study subjects had CRP < 6 mg/L and 68% had CRP ≥ 6 mg/L. The mean±SD values of HbA<sub>1c</sub> in the controlled, moderately controlled and uncontrolled diabetic subjects were 6.17±0.49%, 8.02±0.6% and 11.7±1.89% respectively ( $P < 0.001$ ). Number of study subjects with positive CRP was significantly higher among the moderately controlled diabetic subjects than controlled diabetic subjects (OR:2.87, 95% CI: 1.41 to 5.87,  $P < 0.01$ , Figure 1) and the relative risk was 1.64 (95% CI: 1.15 to 2.34). The relative risk was not statistically significant in the uncontrolled diabetic subjects than moderately controlled diabetic subjects (relative risk: 1.09, 95% CI: 0.89 to 1.35; OR:1.33, 95% CI:0.69-2.59,  $P > 0.05$ ). The relative risk in the uncontrolled diabetic subjects was 1.8 (95% CI: 1.29 to 2.51) compared to controlled diabetic subjects and it was statistically significant (OR:3.83, 95% CI: 1.94 to 7.58,  $P < 0.001$ ,



**Figure 1.** Comparison of CRP among controlled, moderately controlled and uncontrolled diabetic subjects. NS, not significant; \*\*,  $P < 0.01$ ; \*\*\*,  $P < 0.001$

## Discussion

This study shows that elevated serum CRP level (CRP ≥ 6 mg/L) was associated with higher level of HbA<sub>1c</sub> in moderately controlled and uncontrolled diabetic subjects. Subjects with elevated CRP were also higher (32% for CRP < 6 mg/L and 68% for CRP ≥ 6 mg/L) in the total study group. In a study carried out in a Bangladeshi population showed that CRP level was significantly elevated in newly diagnosed diabetic subjects than apparently healthy individuals (11) and significant positive correlation was found between LDL-C and HbA<sub>1c</sub> in established diabetic subjects (12). As elevated CRP with elevated serum LDL-C have higher mortality and morbidity than elevated LDL-C alone (1), much attention should be paid to the CRP beside the traditional risk factors (lipid profile) of cardiovascular disease in diabetic subjects.

In conclusion, this study demonstrated that a higher HbA<sub>1c</sub> is significantly associated with a greater likelihood of higher CRP in moderately controlled and uncontrolled diabetic subjects.

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