

ORIGINAL ARTICLE

EVALUATION OF SERUM HIGH SENSITIVITY C -REACTIVE PROTEIN (hs-CRP) IN TYPE-2 DIABETIC PATIENT

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ABSTRACT:

Background: Type 2 diabetes mellitus (DM2) is an important public health problem worldwide because of its high prevalence and complications. C-reactive protein (CRP), an acute phase reactant, is currently considered an independent risk factor for atherosclerosis and hypertension. The present study was planned to evaluate the concentration of Serum High Sensitivity C-Reactive protein (hs-CRP) in type-2 diabetic patients. **Materials and methods:** 25 type-2 diabetic patients (12 male and 13 female). These selected patients were less than 2 years duration from diagnosis of diabetes, had no complications of type-2 diabetes, no other co-morbid diseases. The mean age of the patients was 49.54 ± 5.2 years (range 40-60 years) in male and 45.23 ± 5.9 years (range 40-60 years) in female. The age and all other criteria matched 15 (9 male and 6 female) healthy control group who were chosen to compare with the diabetic patients. Blood samples were taken from each patient for hs-CRP, RBS and HbA1c. **Results:** The fasting plasma glucose of type-2 patients was $9.28 + 1.82$ (Mean \pm standard deviation) mmol/L, whereas the fasting plasma glucose level of normal healthy people was 6.34 ± 0.43 (Mean \pm standard deviation). HbA1c (Mean \pm standard deviation) of normal healthy people was 6.23 ± 1.23 and type-2 diabetic patients was 10.27 ± 4.05 hs-CRP (mg/L) level of normal healthy people and diabetic patients were $0.412 (\pm 0.26)$ and $1.48 (\pm 1.03)$ respectively. The difference in the plasma hs-CRP level between normal people and type-2 diabetic patients are significant ($P < 0.01$). **Conclusion:** This higher level of mean hs-CRP in diabetic patients is statistically significant ($P < 0.01$) compared with that of the normal healthy subjects mean hs-CRP. This mean level of hs-CRP in normal healthy subjects was below the lower level of cardiovascular risk. Thus, it can be concluded that diabetic patients having higher level of mean hs-CRP level are more prone to the cardiovascular disorders as compared to normal healthy patients.

Keywords: C-reactive protein, Diabetes

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INTRODUCTION:

TYPE 2 DIABETES MELLITUS (DM2) is an important public health problem worldwide because of its high prevalence and complications.¹ The disease is characterized by metabolic alterations that correlate hyperglycaemia to other risk factors that contribute to complications in the circulatory system, such as high blood pressure (HBP).² The number of deaths related to DM2 represents 9% of the world total, with four million cases each year. Cardiovascular diseases (CVD) are the most prevalent cause of death in DM2 patients, including myocardial infarction, ischaemic stroke, peripheral arterial obstructive disease and several other related diseases.^{3, 4} Currently, atherosclerosis is indicated as the main cause for CVD development.⁵

It is now clear that insulin resistance is the primary event and it is followed by increasing degree of β -cell dysfunction, in type-2 diabetes.⁶ Insulin resistance often accompany excess visceral adiposity, dyslipidemia, hypertension, impaired fibrinolysis, increased platelet aggregation, vascular inflammation, endothelial dysfunction and premature atherosclerosis.⁷ All these events may herald the thrombo-embolic manifestations in the body. Certain protein known collectively as the acute

phase response are produced early in inflammation mainly by the liver. The best known of these are C-reactive protein and mannose binding protein. C-reactive protein (CRP) is a non-specific indicator of inflammation and the medical importance of CRP is that an elevated CRP appears to be better predictor of heart attack risk than an elevated cholesterol level.⁸ The highest correlation between CRP and body mass index (BMI) was found, followed by the index of insulin resistance, fasting insulin and insulin sensitivity.⁹ It was established that in persons with higher levels of CRP the possibility of diabetes to develop for the period of 3-4 years is greater than those with the normal values for CRP.¹⁰

C-reactive protein (CRP), an acute phase reactant, is currently considered an independent risk factor for atherosclerosis and hypertension. The CRP level rises in patients with hypertension and this predicts the development of cardiovascular disease. CRP has many functions as it marks antigens for phagocytosis, stimulates cytokine release from leukocytes, binds C1, leading to activation of the classical complement pathway and causing the release of the intracellular adhesion molecule-1 and vascular adhesion molecule-1 from endothelial cells, that are associated with the development of atherosclerosis and coronary heart disease. Currently, CRP is not only

considered a passive marker of inflammation but it affects the vascular system as well has been suggested that CRP is one of the novel risk factors of cardiovascular disease in diabetic patients.

So, the present study was planned to evaluate the concentration of Serum High Sensitivity C-Reactive protein (hs-CRP) in type-2 diabetic patients.

MATERIALS AND METHODS:

This study was conducted in the medicine department of the institution. 25 type-2 diabetic patients (12 male and 13 female). These selected patients were less than 2 years duration from diagnosis of diabetes, had no complications of type-2 diabetes, no other co-morbid diseases. They were non-alcoholics, non-smokers, non-hypertensive and had no evidence of kidney and liver disease, their BMI was <30 Kg/M2 and waist-to-hip ratio was also <1 in man & <0.9 in female. The mean age of the patients was 49.54±5.2 years (range 40-60 years) in male and 45.23±5.9 years (range 40-60 years) in female. The age and all other criteria matched 15 (9 male and 6 female) healthy control group who were chosen to compare with the diabetic patients. Prior to inclusion into the study, written informed consent was taken from each subject. Purposive method was followed. The sample was collected by the investigator himself. Blood samples were taken from each patient for hs-CRP, RBS and HbA1c. With all aseptic precaution 10 cc of blood were collected from the antecubital vein using a disposable plastic syringe. Serum was separated by centrifugations (10 minutes) at the rate of 2000 rpm at a

room temperature immediately after the blood was allowed to clot for 30 minutes. Separated serum was allocated in different appended for subsequent analysis. Data analysis included some clinical and epidemiological data to identify the clinical characteristics of the patients and the data of the patients was compared with the normal healthy people. The data was analyzed with the help of SPSS soft ware programme expressed as Mean ± SD (Standard deviation). Z-test, was done to see the significance of difference of different parameters of diabetic people and normal healthy people. A P-value of <0.05 was considered as significant.

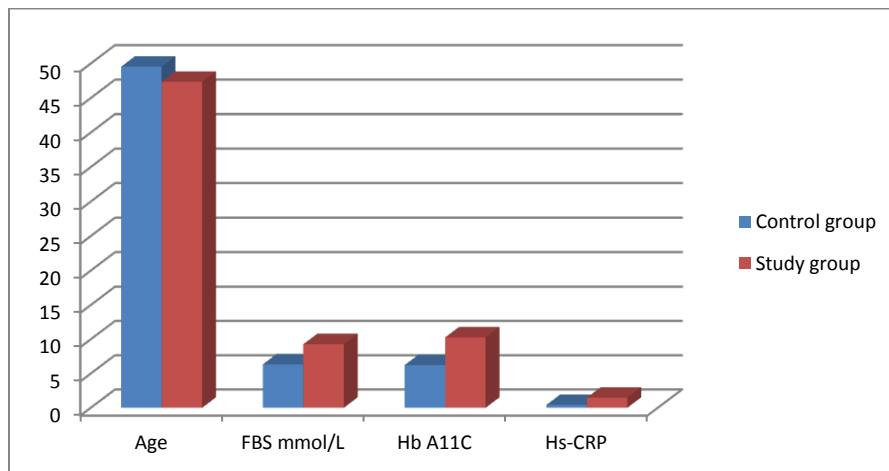
RESULTS:

The present study was intended to asses the difference of hs-CRP level between type-2 diabetic patients and normal healthy people (Table I). The mean age of the type-2 diabetic patients and normal healthy people was 47.34 yearS (standard deviation ± 4.8) and 49.54 (standard deviation ± 5.2) year respectively i.e. the two groups were well matched regarding age. The fasting plasma glucose of type-2 patients was 9.28 + 1.82 (Mean ± standard deviation) mmol/L, whereas the fasting plasma glucose level of normal healthy people was 6.34 ± 0.43 (Mean ± standard deviation). HbA1c (Mean ± standard deviation) of normal healthy people was 6.23 ± 1.23 and type-2 diabetic patients was 10.27 ± 4.05 hs-CRP (mg/L) level of normal healthy people and diabetic patients were 0.412 (± 0.26) and 1.48 (± 1.03) respectively. The difference in the plasma hs-CRP level between normal people and type-2 diabetic patients are significant (P<0.01).

Table 1: Comparison of different parameters between study group and control group

Characteristics	Control group (n=15)	Study group (n=25)	P-value
Age (mean + SD)	49.54 ± 5.2	47.34 + 4.78	>0.05
FBS mmol/L (mean + SD)	6.34 ± 0.43	9.28 ± 1.82	<0.05
Hb A1c (mean + SD)	6.23 ± 1.23	10.27 + 4.05	<0.05
Hs-CRP(mean + SD)	0.412 ± 0.26	1.48 ± 1.03	<0.01

Figure 1: Depiction of comparison of control group and study group



DISCUSSION:

The purpose of this study was to assess the plasma hs-CRP level of type-2 diabetic patients and normal healthy people of similar age distribution. The people of both group were non-smoker, non-alcoholic and non-hypertensive and the diabetic patients had no complications of diabetes.

Similar study was conducted by Lachine NA, Elnekiedy AA et al. to study both serum chemerin and hs-CRP as markers of subclinical atherosclerosis in Egyptian patients with type 2 diabetes, who are angiographically free of coronary artery disease (CAD). This cross-sectional study was conducted on 180 subjects divided into two groups: Group A included 90 type 2 diabetic patients without CAD and group B including 90 nondiabetic control subjects. All study subjects were having normal coronary angiography. Serum chemerin, homeostasis model assessment for insulin resistance (HOMA-IR), glycated haemoglobin (HbA1c), lipid profile, hs-CRP as well as C-IMT were assessed in all study subjects. There was a statistically significant difference between the 2 groups regarding serum chemerin level, HOMA-IR, hs-CRP and C-IMT; being higher in the diabetic patients than in the control group ($p = 0.006$, 0.024 , 0.040 and <0.001 , respectively). There was positive correlation between serum chemerin level and waist-to-hip ratio (WHR), HOMA-IR, hs-CRP and C-IMT. Carotid intima-media thickness was positively correlated with patients' WHR, blood pressure, HbA1c, diabetes duration as well as hs-CRP, and negatively correlated with ankle-brachial index (ABI). Linear regression analysis showed that HbA1c, serum chemerin and hs-CRP were independently affecting C-IMT. Serum hs-CRP was positively correlated with HbA1c and HOMA-IR ($p = 0.006$ and 0.032 , respectively), and negatively correlated with HDL-cholesterol level ($p = 0.018$). It was concluded by the authors that both serum chemerin and hs-CRP could be considered as markers of subclinical atherosclerosis, and hence, may be utilized for the early detection of macrovascular disease, in Egyptian patients with type 2 diabetes.¹³

Owen KR et al performed a research to assess high-sensitivity c-reactive protein levels as diagnostic discriminator of maturity-onset diabetes of the young due to HNF1A mutations. Serum hs-CRP was measured in subjects with HNF1A-MODY ($n = 31$), autoimmune diabetes ($n = 316$), type 2 diabetes ($n = 240$), and glucokinase (GCK) MODY ($n = 24$) and in nondiabetic individuals ($n = 198$). The discriminative accuracy of hs-CRP was evaluated through receiver operating characteristic (ROC) curve analysis, and performance was compared with standard diagnostic criteria. Our primary analyses excluded ~11% of subjects in whom the single available hs-CRP measurement was >10 mg/l. Geometric mean (SD range) hs-CRP levels were significantly lower ($P \leq 0.009$) for HNF1A-MODY individuals, 0.20 (0.03 – 1.14) mg/l, than for any other group: autoimmune diabetes 0.58 (0.10 – 2.75) mg/l, type 2 diabetes 1.33 (0.28 – 6.14)

mg/l, GCK-MODY 1.01 (0.19 – 5.33) mg/l, and nondiabetic 0.48 (0.10 – 2.42) mg/l. The ROC-derived C-statistic for discriminating HNF1A-MODY and type 2 diabetes was 0.8 . Measurement of hs-CRP, either alone or in combination with current diagnostic criteria, was superior to current diagnostic criteria alone. Sensitivity and specificity for the combined criteria approached 80%. It was concluded that Serum hs-CRP levels are markedly lower in HNF1A-MODY than in other forms of diabetes. hs-CRP has potential as a widely available, cost-effective screening test to support more precise targeting of MODY diagnostic testing.¹³

Lima LM et al performed a study for the measurement of plasma levels of high-sensitivity C-reactive protein (hs-CRP) in subjects with DM2 and/or HBP and compared to those of normal subjects. Eighty-nine subjects were analyzed for hs-CRP, including 13 normotensive patients with DM2, 17 patients with HBP, 34 hypertensive patients with DM2 (DM2+HBP) and 25 normal subjects. The plasma hs-CRP levels were significantly lower in the controls than in the HBP+DM2 group ($p < 0.05$). DM2 associated with HBP was also correlated with increased plasma hs-CRP levels ($n = 89$, $r = 0.25$, $p = 0.0162$). Only hypertensive patients with DM2 had higher levels of hs-CRP, a circulating inflammatory marker, than normal subjects. This finding suggests that patients with two associated diseases have a more active inflammatory state.¹⁴

Joshi MD et al. performed a research to describe the distribution of serum high-sensitivity C-reactive protein (hsCRP) in type 2 diabetes mellitus outpatients, and relate it to cardiovascular disease risk. One hundred and ninety seven type 2 diabetic outpatients and fifty age- and sex-matched non-diabetic hypertensive outpatients. The distribution of hsCRP in the diabetic population was skewed, with a mean of 4.33 mg/L and a median of 2.53 mg/L. The majority (42%) of diabetics had hsCRP levels in the high-risk category (hsCRP > 3 mg/L). The median hsCRP was non-significantly higher in the diabetic patients with metabolic syndrome compared to those without (2.68 vs 2.30 mg/L, $p = 0.433$). The median hsCRP was non-significantly higher in the hypertensive group compared to that in matched diabetic non-metabolic syndrome group (2.30 vs 2.23 mg/L, $p = 0.297$). HsCRP increased with number of metabolic syndrome components, patients with four components having higher hsCRP levels than those with one, though the difference was not statistically significant (3.59 vs 1.57 mg/L, $p = 0.095$). This study, though cross-sectional in nature, supports the existence of a correlation between hsCRP levels and cardiovascular disease risk.¹⁵

In our study mean hs-CRP level of healthy people were found 0.412 mg/L which was within normal range and below the level of mild risk for cardiovascular disease (<1 mg/L).¹¹ Besides these in our study we have found that mean hs-CRP of type- 2 diabetic patients was

1.5 mg/L which was significantly higher than that of the normal healthy people (0.412 mg/h) [$P < 0.01$]. Plasma hs-CRP level in type-2 diabetic patients was about 3 times higher than normal people.

CONCLUSION:

This higher level of mean hs-CRP in diabetic patients is statistically significant ($P < 0.01$) compared with that of the normal healthy subjects mean hs-CRP. This mean level of hs-CRP in normal healthy subjects was below the lower level of cardiovascular risk. Thus, it can be concluded that diabetic patients having higher level of mean hs-CRP level are more prone to the cardiovascular disorders as compared to normal healthy patients.

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