



## A COMPARATIVE STUDY OF LEVELS OF HIGH SENSITIVITY C-REACTIVE PROTEIN (hs-CRP) IN DIABETIC AND NON- DIABETIC POPULATION OF CENTRAL INDIA

**Dr. Parag Gupta**

Assistant Professor, Department of Pathology, Amaltes Institute of Medical Sciences, Dewas, Madhya Pradesh.

**Dr. Lal Pranay Singh\***

Assistant Professor, Department of Pathology, Atal Bihari Vajpayee Government Medical College, Vidisha, Madhya Pradesh. \*Corresponding Author

**ABSTRACT** **Background:** Diabetes mellitus is the most common metabolic disorder characterized by metabolic abnormalities and long term complications. It is characterized by hyperglycemia resulting from defect in insulin secretion and in its action. It has become a leading cause of morbidity and mortality world over. hs- CRP is a marker of low-grade inflammation and it is raised in patients with type 2 DM. The present study was undertaken with the objective of studying the relation of High Sensitivity CRP (hs-CRP) in patients of type 2 Diabetes Mellitus and in non-diseased population. **Methods:** This was a comparative observational study, conducted at Diabetic clinic, Index Medical College, Indore during August 2014 to July 2015. Cases and control were selected as per the inclusion criteria. Statistical analysis was done using SPSS v20. **Results:** Mean age of the group was 48years. The mean hs CRP in the diabetic group was 0.45 compared with 0.35, in the control group. **Conclusion:** hs CRP levels are directly related to insulin resistance and is highly associated with diabetic population.

**KEYWORDS :** hs Crp, diabetes mellitus, chronic inflammation.

### INTRODUCTION:

Diabetes mellitus comprises a group of common metabolic disorders that share the phenotype of hyperglycemia. The worldwide prevalence of diabetes mellitus has risen dramatically over the past two decades and it is projected that it will continue to increase in near future. The relation between chronic subclinical low-grade inflammation and insulin resistance (IR) has long been known [1, 2]. IR is the major contributor and mediating factor in the development of type 2 DM (T2DM) along with concomitant hypertension (HT) and cardiovascular disease (CVD) [3, 4]. The relationship between the development of DM and some markers of inflammation such as C-reactive protein (CRP), IL-6, fibrinogen, and PAI-1 has been described previously. Serum concentration of CRP increases in both impaired glucose tolerance (IGT) and overt T2DM [3, 5–10]. On the other hand, some studies reported that elevation of CRP is an indicator of development of T2DM [11]. In view of the above concepts and due to paucity of similar studies in the Indian patients, this study has been undertaken to know the significance of hs-CRP in the diabetic population.

### MATERIALS AND METHODS:

This was a comparative observational study, conducted at Diabetic clinic, Index Medical College, Indore during August 2014 to July 2015. Age and sex matched population were chosen for study groups after obtaining written informed consent. For diabetic group, persons with confirmed reports for diagnosis, either newly detected or older cases, who visited the out-patient care/ Diabetic clinic at Index hospital were included in the study. For the other group, non-diabetic healthy subjects accompanying the patients and healthy people from the nearby areas at Indore were included. Those who were not consenting, less than 18 years of age, pregnant females, those with other comorbidities were excluded from the study. An appropriate case report form was designed, which was used to gather baseline data and other relevant information. Statistical analysis was done using SPSS.v20. Continuous data are expressed as means with standard deviations, and categorical data are expressed as numbers and percentages. Cases were classified on their relative risk of future cardiovascular events as: Low risk: hs-CRP < 1.0 mg/L• Intermediate risk: hs-CRP 1.0-3.0 mg/L• High risk: hs-CRP > 3.0 mg/L

**RESULTS: Age Distribution:** In the present study, a sum total of 91 cases were included in which 6 subjects were in the age group of 36-45 years, 18 subjects in the age group of 46-55 years and 67 subjects in the age group of >56 years ie. Most of our cases are in this age group.

**Gender distribution:** In our study of 91 subjects, 58 subjects were males and 33 subjects were females

**Table 1: Age distribution of Diabetic Subjects**

Age in years	Subjects, n=91
36-45	6
46-55	18
>56	67

**Table 2: Student's t test comparing hs-CRP levels between the diabetic subset and control group.**

Group	No.	Mean	SD	"t"	p-Value
Group 1 (diabetic)	91	0.45	0.37	11.64	0.001
Group 2 (non-diabetic)	96	0.35	0.29	11.64	

### DISCUSSION:

It has been suggested that low grade inflammation may play a role in the development and complications of type 2 Diabetes mellitus. The mechanisms by which chronic inflammation can evoke type 2 diabetes are not clear. However it is known that adipose tissue can synthesize and release the main pro inflammatory cytokines -tumor necrosis factor-alpha (TNF- $\alpha$ ), interleukin-1 (IL-1) and interleukin-6 (IL-6) and that inflammatory markers are associated with body fat mass. Pro-inflammatory cytokines and acute phase reactants are involved in multiple metabolic pathways relevant to insulin resistance, including regulation, reactive oxygen species, lipoprotein lipase action and adipocyte function. C-reactive protein (CRP) is an acute-phase protein, which is an inflammatory marker produced and released by the liver under the stimulation of cytokines. It is a strong biomarker of inflammation in the progression of various diseases like coronary heart disease, cancer, diabetes, and others. It has emerged as the 'golden marker for inflammation. The hs-CRP test is a highly sensitive quantification of CRP. C-reactive protein (CRP) is a liver-derived pattern recognition molecule that is increased in inflammatory states. It rapidly increases within hours after tissue injury, and it is suggested that it is part of the innate immune system and contributes to host defense. Since cardiovascular disease is at least in part an inflammatory process, CRP has been investigated in the context of arteriosclerosis and subsequent vascular disorders. Based on multiple epidemiological and intervention studies, minor CRP elevation [high-sensitivity CRP (hsCRP)] has been shown to be associated with future major cardiovascular risk (hsCRP:<1 mg/L=low risk; 1-3 mg/L=intermediate risk; 3-10 mg/L=high risk; >10 mg/L=unspecific elevation). It is recommended by the American Heart Association that patients at intermediate or high risk of coronary heart disease may benefit from measurement of hsCRP with regard to their individual risk prediction. Elevation of hsCRP is associated with increased risk of type 2 diabetes development in patients with all levels of metabolic syndrome. In type 1 and type 2 diabetes mellitus, hemoglobin A1c significantly correlates with hsCRP levels and future cardiovascular risk. Also, hsCRP levels increase with the stage of beta-cell dysfunction and insulin resistance. [11] In our study, there is a positive co-relation between the high levels for hs CRP in diabetic population. Similar results were shown by multiple studies. Laaksonan et al, in their prospective study suggested that an elevated level of CRP is associated with an increased risk of developing type 2 diabetes. [12] Festa et al. demonstrated that elevated levels of CRP are associated with obesity, insulin resistance and glucose intolerance, suggesting that inflammation is also involved in the etiology of type 2 diabetes. [13] Sangappa Virupaxappa Kashinakunti et al. in a study on serum high sensitivity - C reactive protein levels in Type 2 Diabetes Mellitus

observed among statistically significant increase in all the biochemical parameters viz FBS, PPBS, HbA1c and hs-CRP levels in cases as compared to controls. [14] The P value was 0.0001 for all the parameters, which is highly significant, but in our study hs-CRP was not significant with FBS and PPBS suggesting that these parameters are not indicators for monitoring and prognostication as HbA1c. Study done by Yildiz Tutuncu et al on comparison of hs-CRP levels in new Diabetes groups observed a positive correlation between hs-CRP levels and age, BMI, waist, hip, SBP, DBP, pulse, FPG, HbA1c, TG, non-HDL cholesterol; and there was a negative correlation with HDL-cholesterol and eGFR. [15] Soinio M et al in their study shows that CRP is an independent risk factor for CHD mortality in patients with type 2 diabetes. This suggests that inflammation plays an important role in fatal CHD events also among this high-risk population. This might partly explain why statins and aspirin, in addition to their LDL-lowering and antiplatelet effects, have had favorable effects in studies on the prevention of CHD events in patients with type 2 diabetes. [16] Hence, from the above discussion, it is conclusive that high levels of hsCRP are associated diabetic population compared with the non-diabetic ones.

### CONCLUSIONS:

High levels of hs-CRP is associated increased inflammatory response. Positive co-relation with hsCRP and other markers of inflammation is associated with increased risk of morbidity in diabetic population as compared to the non-diabetic population.

### REFERENCES:

1. J. C. Pickup and M. A. Crook, "Is type II diabetes mellitus a disease of the innate immune system?" *Diabetologia*, vol. 41, no. 10, pp. 1241–1248, 1998.
2. M. Y. Donath and S. E. Shoelson, "Type 2 diabetes as an inflammatory disease," *Nature Reviews Immunology*, vol. 11, no. 2, pp. 98–107, 2011.
3. A. Festa, R. D'Agostino Jr., G. Howard, L. Mykkanen, R. P. Tracy, and S. M. Haffner, "Chronic subclinical inflammation as part of the insulin resistance syndrome: the insulin resistance atherosclerosis study (IRAS)," *Circulation*, vol. 102, no. 1, pp. 42–47, 2000.
4. P. M. Ridker, J. E. Buring, N. R. Cook, and N. Rifai, "C-reactive protein, the metabolic syndrome, and risk of incident cardiovascular events: an 8-year follow-up of 14 719 initially healthy American women," *Circulation*, vol. 107, no. 3, pp. 391–397, 2003.
5. The Expert Committee on the Diagnosis and Classification of Diabetes Mellitus, "Follow-up report on the diagnosis of diabetes mellitus," *Diabetes Care*, vol. 26, no. 11, pp. 3160–3167, 2003.
6. G. S. Hotamisligil, P. Peraldi, A. Budavari, R. Ellis, M. F. White, and B. M. Spiegelman, "IRS-1-mediated inhibition of insulin receptor tyrosine kinase activity in TNF- $\alpha$ - and obesity-induced insulin resistance," *Science*, vol. 271, no. 5249, pp. 665–668, 1996.
7. A. D. Pradhan, J. E. Manson, N. Rifai, J. E. Buring, and P. M. Ridker, "C-reactive protein, interleukin 6, and risk of developing type 2 diabetes mellitus," *The Journal of the American Medical Association*, vol. 286, no. 3, pp. 327–334, 2001.
8. N. de Rekenseire, R. Peila, J. Ding et al., "Diabetes, hyperglycemia, and inflammation in older individuals: the health, aging and body composition study," *Diabetes Care*, vol. 29, no. 8, pp. 1902–1908, 2006.
9. J. I. Barzilay, L. Abraham, S. R. Heckbert et al., "The relation of markers of inflammation to the development of glucose disorders in the elderly: the Cardiovascular Health study," *Diabetes*, vol. 50, no. 10, pp. 2384–2389, 2001.
10. D. J. Freeman, J. Norrie, M. J. Caslake et al., "C-reactive protein is an independent predictor of risk for the development of diabetes in the west of Scotland Coronary Prevention Study," *Diabetes*, vol. 51, no. 5, pp. 1596–1600, 2002.
11. Pfitzner A, Forst T. High-sensitivity C-reactive protein as cardiovascular risk marker in patients with diabetes mellitus. *Diabetes Technol Ther*. 2006 Feb;8(1):28-36. doi: 10.1089/dia.2006.8.28.
12. Laaksonen DE, Niskanen L, Nyyssonen K et al. C-reactive protein and the development of the metabolic syndrome and diabetes in middle-aged men. *Diabetologia* 2004; 47(1): 1403-10.
13. Festa A, D'Agostino R Jr, Tracy RP, Haffner SM: Elevated levels of acute phase proteins and plasminogen activator inhibitor-1 predict the development of type 2 diabetes: the Insulin Resistance Atherosclerosis Study. *Diabetes* 2002;51(3):1131–1137.
14. Sangappa Virupaxappa Kashinakunti, Manjula Rangappa Gurupadappa Shantappa Kallaganada. Serum High Sensitive - C Reactive Protein Levels in Type 2 Diabetes Mellitus -A Case Control Study. *International Journal of Biochemistry Research & Review* 2016;11(4): 1-8.
15. Yildiz Tutuncu, Ilhan Satman Selda Celik, Nevin Dincceg, Kubilay Karsidag, Aysegul Telci, Sema Genc, Halim Issever. A Comparison of hs-CRP Levels in New Diabetes Groups Diagnosed Based on FPG, 2-hPG, or HbA1c Criteria. *Journal of Diabetes Research*. 2016, Article ID 5827041, 1-9.
16. Minna Soinio, Jukka Marniemi, Markku Laakso, Seppo Lehto, Tapani Ronnema. High-Sensitivity C-Reactive Protein and Coronary Heart Disease Mortality in Patients With Type 2 Diabetes. *Diabetes Care* Feb 2006, 29(2) 329-333.