



## Original Research Article

## Type 2 Diabetes and Inflammation; Correlation of commonly used inflammatory biomarker with marker of glycemic control

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## ABSTRACT

**Background:** India leads the world with the largest number of Diabetic subjects, hence can be called as Diabetic Capital of World. Diabetes is a serious, chronic disease that occurs due to defects in insulin secretion or insulin action or may be both. Optimal glycemic control is fundamental and still is the main therapeutic objective for the managing and prevention micro and macrovascular complications arising from diabetes that can impact on quality of life. The linkage of inflammation and type 2 diabetes mellitus (T2DM) has been extensively investigated for over a decade. The main objective of the study is to identify correlation between glycemic control and inflammation.

**Materials and Methods:** Total 500 subjects were studied which were divided into two groups of 250 of Diabetic cases and Healthy controls after defining proper inclusion and exclusion criteria. Gender wise distribution was also done. HbA1C and CRP were estimated on fully automated analyzers.

**Results:** The result had shown that cases have significantly elevated HbA1C and CRP when compared to age and sex matched healthy controls with  $p < 0.0001$ . We also identified Pearson correlation between CRP and HbA1C found to be correlated, however positive correlation was weak.

**Conclusion:** We can conclude that in developing countries like India estimation of Glycated Hemoglobin and CRP can predict secondary complications of disease.

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### 1. Introduction

India leads the world with largest number of Diabetics subjects hence can be called as Diabetic capital of World. Diabetes Mellitus (DM) is nothing but a disorder of glucose metabolism which has been known to human since immemorial time. About 415 Million people are suffering from Diabetes and this figure is expected to be 640 Million by 2040.<sup>1</sup>

Many research studies have demonstrated importance of monitoring glycemia because there is positive direct relationship between blood sugar level and progression of diabetic complications.<sup>2,3</sup>

In last decade though studies hypothesis has been drawn that pathogenesis of diabetes connects to a state of subclinical chronic inflammation.<sup>4,5</sup>

As such inflammation is protective mechanism of the body, but in chronic condition like diabetes this protective mechanism becomes important mechanism for progression of disease.<sup>6</sup>

C-reactive protein(C-RP) is major acute phase protein which is consider as an indicator of low grade systemic inflammation.<sup>7</sup>

In case of Type 2 Diabetes mellitus, CRP is an independent predictor of T2DM.<sup>8-12</sup>

Over nutrition and physical inactivity leads to excess fat accumulation, acts as a major risk factor for insulin resistance and Type 2 Diabetes.<sup>13</sup> It has been evident that

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hypertrophied adipocytes are involved with inflammatory condition.<sup>14-18</sup> Inflammatory cytokines released from adipose tissues exert an endocrine effect to promote insulin resistance and also leads to elevated CRP.<sup>19-21</sup>

HbA1c which is also called as glycated hemoglobin is considered as best available biochemical parameter to assess glycemic control in diabetic patients. HbA1c is closely associated to response to treatment and risk of developing complications.

It provides overall glycemic control for previous 6-8 weeks.<sup>22</sup>

In past decades the number of people with Type 2 Diabetes has been more than doubled globally, making it one of the most important public health challenges to all nations. Diabetes is recently known to be an inflammatory disease.

The severity of disease and grave complications has been prompted to undertake the following study. Hence our study was planned to correlate glycemic marker with pro inflammatory maker (C - reactive protein) in type 2 diabetes and its comparison with healthy controls. Important objectives of study:

1. To compare efficiency of HbA1C in diagnosis of Type 2 Diabetes.
2. To evaluate CRP for further complications of Type 2 Diabetes
3. To derive correlation b/w CRP and HbA1C

## 2. Material and Methods

This study was conducted in Peoples College of Medical Sciences and Research Centre Bhopal and associated People's Hospital Bhopal. Total 500 subjects included in this study were divided into 2 groups:

1. Group I: included 249 normal healthy individuals, who were in the age group 25- 70 years, of either sex and without any family history of diabetes mellitus.
2. Group II: included 250 diagnosed patients of type 2 DM in the same age group i.e., 25-70 years.
3. Subjects were also classified on the basis of gender, 140 Males and 110 Females were there in Control-Case group.

### 2.1. Inclusion criteria

Type-2 DM diagnosed on the basis of the ADA 2015 guidelines was included in the study.

### 2.2. Exclusion criteria

Type 1 DM, congestive heart failure, tuberculosis, gout, rheumatoid arthritis, renal failure and those who were on hypoglycaemic drugs and on insulin therapy were excluded from the study.

### Criteria for diabetes diagnosis: 4 options

**A1C  $\geq 6.5\%$** \* Perform in lab using NGSP-certified method and standardized to DCCT assay

**FBG  $\geq 126$  mg/dL (7.0 mmol/L)**\* Fasting defined as no caloric intake for  $\geq 8$  hours

**2-hour PG  $\geq 200$  mg/dL (11.1 mmol/L) during OGTT (75-g)**\* Performed as described by the WHO, using glucose load containing the equivalent of 75g anhydrous glucose dissolved in water

**Random PG  $\geq 200$  mg/dL (11.1 mmol/L)** In persons with symptoms of hyperglycemia or hyperglycemic crisis<sup>23</sup>

C - reactive protein and HbA1C, were analysed on Roche Cobas C311

Test	Bulb	Method
Glycosylated hemoglobin (HbA1C)	EDTA	Immunoturbidimetric method
C-Reactive Protein	Plain Vial/Serum Separating Tube	Immunoturbidimetric assay

Statistical analysis of data: All data were expressed as Mean  $\pm$  SD. Statistical analysis was done using unpaired students-t-test. A level of p value  $<0.05$  was used to indicate statistical significance in all analyses. The correlation between the parameters was carried out using Pearson's correlation.

## 3. Result

The comparison of 250 controls with 250 cases has been shown in following tables:

**Table 1:** This table shows comparison of HbA1C and CRP in controls and Cases. The results were statistically significant as p value  $<0.001$ .

S.No	Parameters	Controls	Cases	P value
1.	No of subjects	250	250	-
2.	HbA1c	4.45 $\pm$ 0.64	9.06 $\pm$ 2.79	$<0.0001$
3.	CRP	4.52 $\pm$ 1.09	16.87 $\pm$ 0.97	$<0.0001$

**Table 2:** This table shows comparison of HbA1C and CRP in Healthy Male Controls and Diabetic Male Cases. The results were statistically significant as p value  $<0.001$ .

S.No	Parameters	Controls Male	Cases Male	P value
1.	No of subjects	140	140	-
2.	HbA1c	4.46 $\pm$ 0.37	8.89 $\pm$ 2.76	$<0.0001$
3.	CRP	4.37 $\pm$ 0.34	16.87 $\pm$ 0.97	$<0.0001$

**Table 3:** This table shows comparison of HbA1C and CRP in Healthy Female Controls and Diabetic Female Cases. The results were statistically significant as p value <0.001.

S.No	Parameters	Controls Female	Cases Female	P value
1.	No of subjects	110	110	-
2.	HbA1c	4.43±0.36	9.28±2.82	<0.0001
3.	CRP	4.37±0.35	16.97±1.00	<0.0001

**Table 4:** This table shows Correlation b/w HbA1C and CRP in Diabetic Cases. HbA1C and C - reactive protein showed positive correlation with each other, but correlation was found to be a weak.

S.No	Variable	Correlation Coefficient	p Value
4	C-Reactive Protein	0.08	0.18

p<0.05 was considered as statistically significant

The Pearson correlation b/w CRP and HbA1C was 0.0.08 ( $r^2= 0.007$ ) which means it is a positive correlation but a weak one

#### 4. Discussion

The exponential rise in the prevalence of diabetes and hence its complications has been of great concern to health care provider worldwide. In our study HbA1c was significantly elevated in diabetic cases when compared with healthy controls. (Table 2).

We have also compared HbA1C on the basis of Gender. Control males were compared with cases males (Table No. 2), and female controls were compared to female cases comparison were statistically significant ( $p<0.005$ ).

The study conducted by Prof. K Goswami<sup>24</sup> to estimate HbA1c among 204 subjects showed similar results as our study. They also demonstrated correlation of HbA1c and estimated average glucose and found that on increasing Blood Sugar level, HbA1c % also increases. Miza Asif Baig concluded in his study that HbA1c can be used effectively for diagnosis of Type 2 Diabetes mellitus and also as a predictive marker for complication of diabetes.<sup>25</sup> Pro-inflammatory marker CRP has also been studied and compared among cases and controls. Diabetic cases showed significant elevation of CRP when compared to healthy controls (Table 2). CRP was also compared on the basis of gender within study groups. (Tables 3 and 4) and difference among cases and controls was statistically different. One of the hypotheses suggests that CRP may have indirect effect on insulin sensitivity and insulin production from pancreatic beta cells through alteration of immune response due to elevated systemic inflammation. High levels of CRP is also involved in production of adhesion molecules like E-selectin, ICAM-1, VCAM-1 which play role in vascular endothelial dysfunction insulin

transport and insulin resistance.<sup>26</sup> We have also correlated mean HbA1c in cases with mean CRP level and found weak positive correlation ( p value- 0.008,  $R^2$ -0.007). This correlation could be explained by formation of advanced glycation end products (AGE). AGEs are product of non enzymatic glycation and oxidation of proteins and lipids, which are formed in hypoglycaemia and diabetes.<sup>27,28</sup> AGEs produced from glycation is having toxic properties associated with inflammation and oxidative stress.<sup>29</sup> Tejan wu<sup>30</sup> et al conducted the third national health and nutrition examination survey which investigated associated between CRP and HbA1c among 2466 men and 2876 women and conclusion was drawn that CRP level was associated with higher HbA1c. This study suggests possible role of inflammation in diabetes.

#### 5. Conclusion

Over study revealed that HbA1c is elevated in type 2 Diabetes and is a most reliable marker and screening tool that can predict complication of diabetes.

CRP is an pro-inflammatory marker which is elevated in low grade systemic inflammation disease. HbA1c and CRP when detected together the impact was substantially greater. This HbA1c and CRP in combination can be a potential Predictive marker for Type 2 Diabetes mellitus.

These results support the role of hyperglycemia in development of inflammation and resistance in Type 2 Diabetes Mellitus. Early Detection of hyperglycemia and Blood Glycemic Control can prevent complication and further decrease morbidity and mortality.

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#### 7. Conflict of Interest

The authors declare they have no conflict of interest.

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