Study of Relation between Hyperglycemia and Inflammation in Type 2 Diabetes Mellitus

Dr. Sunil Patani¹, Dr. Maulik Nayak²*, Dr. Reenu Sharma³

¹Associate Professor, ²Assistant Professor, ³Tutor

¹, ², ³Department of Biochemistry, GMERS Medical College, Sola-Ahmedabad.

*(Corresponding author)

Abstract

Background: Inflammatory responses may have either a causal relationship leading to resistance to insulin or may be intensified by the uncontrolled hyperglycemic state which is reflected by the levels of Glycated Hemoglobin-HbA1c. High sensitivity C-reactive protein (hs-CRP) is considered to be a major prognostic marker in response to tissue injury or infection which can be used to assess inflammatory process in Type 2 DM.

Objectives: This study was carried out to examine the association of HbA1c levels with the hs-CRP levels in type 2 DM subjects. Methods: We included 100 (50 males, 50 females) Type 2 DM subjects (with and without complications) and 100 healthy controls. Blood samples were analysed for the Fasting Plasma Glucose, HbA1c and Serum hs-CRP.

Results & Interpretation: The mean Fasting plasma glucose, HbA1c and hs-CRP levels were significantly high (P < 0.001) in type 2 diabetic subjects with complications compared to type 2 diabetic subjects without complications. A significant positive correlation was observed between hs-CRP and HbA1c levels in diabetic subjects with complications (r = + 0.36, P = 0.004). Conclusion: We concluded that poor glycemic control precipitate inflammatory events and complications in Type 2 DM.

Key Words: Type 2 Diabetes mellitus, HbA1c, High Sensitivity C-Reactive Protein.

INTRODUCTION

Type 2 DM, is a combination of resistance to insulin action and an inadequate compensatory insulin secretory response. In the latter category, a degree of hyperglycemia sufficient to cause pathologic and functional changes in various target tissues, but without clinical symptoms, may be present for a long period of time.
before diabetes is detected.\[1\] According to one review of Rolo et al.(2006) four of the most important molecular mechanisms involved in hyperglycemia – induced tissue damage are: activation of protein kinase C isoforms through denovo synthesis of the lipid second messenger diacylglycerol, increased hexosamine pathway flux, increased advanced glycation end products (AGEs) formation and increased polyol pathway flux.\[2,3\] Among the various markers of glycemic control, HbA1c has now been established as most reliable. High sensitivity CRP (hs-CRP) assays have a range of measurement that extends below the measurement range typical of most conventional CRP assays. This lower range of measurement may expand the indications for use to include the evaluation of conditions thought to be associated with inflammation in otherwise healthy individuals.\[4\] The study was planned to evaluate serum inflammatory marker- hs-CRP and glycemic control marker HbA1c in type 2 DM patients.

**Material and Methods**

The present study was conducted in the Department of Biochemistry, GMERS Medical College and Hospital, Sola, Ahmedabad. The subjects included in the study were:

A) **100 Healthy controls –Group 1 (50 males and 50 females)**

B) **50 (25 males, 25 females) Type 2 DM patients without complications having good glycemic control-Group 2 and**

C) **50 (25 males, 25 females) Type 2 DM patients with complications having poor glycemic control-Group 3** attending the outpatient clinics or admitted in wards of Department of Medicine, Hospital, Sola-Ahmedabad.

Fasting blood samples were collected in plain, Flouride and EDTA vacutainers for estimation of hs-CRP measured by Immunoturbidimetric Method- a sensitive method with detection range ≤ 5mg/L,\[5\] Plasma glucose by Glucose Oxidase-Peroxidase method and HbA1c by Cation Exchange Resin method respectively.\[6,7\]

**TABLE 1: MEAN FBS, hs-CRP AND HbA1c VALUES IN VARIOUS GROUPS OF SUBJECTS**

<table>
<thead>
<tr>
<th>S. No</th>
<th>Parameter</th>
<th>Groups Studied</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Group 1</td>
<td>Group 2</td>
</tr>
<tr>
<td>1</td>
<td>FBS mg/dl</td>
<td>82.2 ± 13.4</td>
<td>136.0 ± 29.3</td>
</tr>
</tbody>
</table>
Results: The mean Fasting plasma glucose, HbA1c and hs-CRP levels were significantly high (P < 0.001) in type 2 diabetic subjects with complications compared to type 2 diabetic subjects without complications.

<table>
<thead>
<tr>
<th>Groups Studied</th>
<th>HbA1c</th>
<th>FBS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy Control subject (n=100)</td>
<td>+0.04</td>
<td>0.38</td>
</tr>
<tr>
<td></td>
<td>+0.01</td>
<td>0.12</td>
</tr>
<tr>
<td></td>
<td>+0.04</td>
<td>0.45 (NS)</td>
</tr>
<tr>
<td>GROUP 2 (n=50)</td>
<td>+0.30</td>
<td>2.2</td>
</tr>
<tr>
<td></td>
<td>+0.28</td>
<td>2.04</td>
</tr>
<tr>
<td></td>
<td>+0.02</td>
<td>0.02 (S)</td>
</tr>
<tr>
<td>GROUP 3 (n=50)</td>
<td>+0.36</td>
<td>2.7</td>
</tr>
<tr>
<td></td>
<td>+0.38</td>
<td>2.8</td>
</tr>
<tr>
<td></td>
<td>+0.003</td>
<td>0.003 (HS)</td>
</tr>
</tbody>
</table>

HS: Highly Significant  r : Correlation Coefficient  S:Significant  NS: Non significant  FBS: Fasting Blood Sugar

DISCUSSION

This clinical study shows that chronic subclinical inflammation as indicated by elevated levels of hs-CRP in diabetics with complications is associated with hyperglycemia and poorly controlled glucose levels (as indicated by significant correlation with FBS and HbA1c values in diabetic subjects with complications). Dandona et al. also put forward a working hypothesis linking in a feedback loop of glucose, insulin, and inflammation. According to this paradigm, hyperglycemia has a proinflammatory action that is normally restrained by the anti-inflammatory effect of insulin secreted in response to that stimulus. [8]

Increasing evidence demonstrates that advanced glycation end products (AGEs) play a pivotal role in the development and progression of diabetic vascular damage. AGEs are generated as a result of chronic hyperglycemia. These events leads to enhanced expression of pro inflammatory mediators [8]. The stimulation of monocyte/macrophage by AGEs might therefore be an initial signal of an inflammatory cascade leading to CRP production in the liver. [9]
**Conclusion**

The main indication of the findings of the present study is that inflammatory events precipitate due to poor glycemic control in subjects with Type 2 Diabetes Mellitus. This association of poor glycemic control and higher hs-CRP levels is the harbinger of complications of Type 2 Diabetes Mellitus. Targeting glycemic control is mandatory to reduce chronic complications and prolong life expectancy in diabetic patients. Conflict of Interest: None

**References:**


