A Study of Correlation between High Normal Glycosylated Hemoglobin as Risk Factor for Coronary Heart Disease with Framingham 10 Year Risk Factor in Non-Diabetic Patients

Krishnakant Bhatt¹, Dharmesh Nama², Gauravkumar Divani³

Original Article

Abstract

Background and Purpose: Framingham 10 year risk score traditionally used to diagnose future risk. There is need to find simple and powerful marker for future risks of coronary artery disease. Framingham 10 year risk score take many variables together. Recently, abnormal glucose metabolism is a major determinant of CHD. Although the relationship between cardiovascular disease (CHD) and glycaemia is believed to represent a continuum without a threshold effect, as it is a more stable, accurate parameter of glucose homeostasis. Therefore, the aim of the current study was to establish association between high normal HbA1c and Framingham 10 year risk score for coronary artery diseases in non-diabetics.

Methods: A total 100 patients of coronary artery disease, aged 18-80 years were enrolled. Complete physical and systemic examination including vitals was performed. Framingham’s 10 year risk score, Height, Weight, Hip Circumference, Waist Circumference, and Waist-Hip Ratio and BMI are calculated. Investigated for HbA1c, HsCRP and other routine investigations needed to diagnose coronary artery disease. Chi square test was applied to detect association between HsCRP and High HbA1c and Correlation Coefficient(r) was calculated to study linear relationship.

Results: The Chi square Test significant meaning that higher value of HsCRP associated with high level of HbA1c (p=0.04). The Correlation Coefficient(r) is -0.02 so there were no linear relationship between HbA1c and Framingham risk score. In our study average Framingham risk score was 9.72 while average age of patient was 53.7 years. There were linear relationship between patient’s age and Framingham 10 year risk score (r = 0.60).

Conclusions: Coronary artery disease patients had high prevalence of High HsCRP. there was significant association between glycosylated haemoglobin and High HsCRP (P=0.04). We find association between high normal HbA1c and Framingham risk score in non-diabetic patient. But, There is no any linear correlation between high normal HbA1c and Framingham 10 risk score (r=0.02). We find out that Framingham 10 year risk score has linear relationship with patient’s age and sex. It implies that coronary artery disease calculated by using Framingham 10 year risk score increases with increase in age. But Glycosylated Haemoglobin predicts coronary artery disease risk independence of patient’s age. It predicts low risk in young female patients compare to young male patient in our study. Glycosylated haemoglobin is independent of age and sex of patient. So Glycosylated haemoglobin is good marker for coronary artery disease.

Introduction

Coronary Heart disease (CHD) is the leading cause of mortality in developed countries, especially among diabetic subjects. The rising trade of coronary artery diseases in developing countries like India due to changes in lifestyle.¹

There are approximately 46.9 million patients with CHD in India. Around 2 million people die due to coronary artery disease annually.²

Recently, much attention has been paid to CHD prevention by the identification of new risk factors, and, indeed, abnormal glucose metabolism is a major determinant of CHD. Although the relationship between cardiovascular disease (CHD) and glycemia is believed to represent a continuum without a threshold effect, glycosylated hemoglobin (HbA1c) might offer more advantages in terms of prognostic information, as it is a more stable and accurate parameter of glucose homeostasis.

Several large scale studies have shown the relationship between HbA1c and the rate of long-term microvascular complications in diabetic patients. However, the association between HbA1c and CHD is less clear, with few data reported in patients without diabetes mellitus.

Therefore, the aim of the current study was to evaluate the relationship between HbA1c and CHD among patients without diabetes mellitus.

Aim and Objectives

1. To Study Relation between High Normal HbA1c Level and Coronary Heart Disease.
2. To Determine Early Clinical Markers of CHD and its role in Preventive Measures.
3. Calculation of Framingham 10 Year Risk for Developing CHD And Its Correlation with HbA1c

Review of literature

Coronary Heart Diseases is a condition in which there is an inadequate supply of blood and oxygen to a
portions of the myocardium; it typically occurs when there is an imbalance between myocardial oxygen supply and demand. The most common cause of myocardial ischemia is atherosclerotic disease of an epicardial coronary artery (or arteries) sufficient to cause a regional reduction in myocardial blood flow and inadequate perfusion of the myocardium supplied by the involved coronary artery.

Central to an understanding of the Pathophysiology of coronary heart disease is the concept of myocardial supply and demand. In normal conditions, for any given level of a demand for oxygen, the myocardium will control the supply of oxygen-rich blood to prevent under perfusion of myocytes and the subsequent development of ischemia and infarction.  

Major Risk Factors for CHD

- High LDL cholesterol
- Cigarette smoking
- Hypertension (BP ≥140/90 mmHg or on antihypertensive medication)
- Low HDL cholesterol (<1.0 mmol/L or 40 mg/dl)
- Diabetes mellitus
- Family history of premature CHD
- Age (men ≥45 years; women ≥55 years)
- Lifestyle risk factors
- Obesity (BMI ≥30 kg/m2)
- Physical inactivity
- Atherogenic diet

Emerging risk factors
- Lipoprotein (a)
- Pro-thrombotic factors
- Pro-inflammatory factors
- Impaired fasting glucose
- Subclinical atherosclerosis

HDL cholesterol ≥1.6 mmol/L (≥60 mg/dl) has been viewed as a “negative” risk factor.

The cholesterol guideline defined four statin benefit groups:

1. All individuals who have clinical atherosclerotic cardiovascular disease (CHD), therefore considered “secondary prevention”
2. Those with LDL cholesterol ≥190 mg/dL without a secondary cause such as a high intake of saturated or transfats, various drugs, or certain diseases;
3. Individuals with diabetes without established cardiovascular disease who are 40–75 years old and have LDL cholesterol of 70–189 mg/dL; and
4. Those without established CHD without diabetes who are 40–75 years old and who have LDL cholesterol of 70–189 mg/dl and a calculated CHD risk ≥7.5%.

Framingham Risk Score

The Framingham Risk Score is a gender-specific algorithm used to estimate the 10-year cardiovascular risk of an individual. The Framingham Risk Score was first developed based on data obtained from the Framingham Heart Study, to estimate the 10-year risk of developing coronary heart disease. In order to assess the 10-year cardiovascular disease risk, cerebrovascular events, peripheral artery disease and heart failure were subsequently added as disease outcomes for the 2008 Framingham Risk Score, on top of coronary heart disease.  

HbA1c and Coronary Heart Disease

Currently, owing to advantages of HbA1c over fasting blood glucose such as low intra-individual variability and being capable of evaluating the long-term blood glucose control, a parameter of average blood glucose levels over 12 weeks, has also been suggested using in clinical practice currently. Evidence from epidemiological studies also showed that as compared to fasting blood glucose, HbA1c was more strongly associated with the risks of CHD and mortality from any causes, which further supported the notion that HbA1c was superior to fasting blood glucose in predicting CHD outcomes.

One large-scale study has been done investigating the relationships among HbA1c, C-IMT, and the prevalence of CHD in non-diabetic patients. They found that HbA1c, but not fasting glycemia, was independently associated with CHD and C-IMT.

Recently, HbA1c has become a major parameter of interest that might offer more advantages in terms of prognostic impact, as it is a more stable and accurate parameter of glycemic control. In addition, HbA1c is a good marker of glycosylated proteins, which play a contributory role in atherosclerosis in both diabetic and non-diabetic individuals. However, there is uncertainty as to the nature of this relationship, as some studies report no significant associations between HbA1c and CHD in non-diabetic males whereas others do McNeely et al analyzed patients enrolled in the Multi-Ethnic Study of Atherosclerosis (MESA).

However, the association between HbA1c and prevalence of detectable CHD varied by gender; in fact, higher HbA1c was associated with higher prevalence of CHD in women but not in men.

In light of previous findings, our current study was designed to evaluate whether HbA1c level was associated with the severity of coronary heart diseases (CHD) in populations without diagnostic diabetes, and we believed that the clinical implication of our study would add, if any, valuable information to address whether HbA1c level could be used to predict the CHD risk in non-diabetic population.

Material and Methods

A cross-sectional study is done in medicine department, new civil hospital and government medical College, Surat from April 2015 to November 2015. All diagnosed cases of coronary artery disease are selected for this study. Informed valid consent from all participants have been taken in appropriate “participant information...
Inclusion Criteria
1. Age between 18 To 80 Years.
2. Sex: Both.
3. Patient must give Written Consent to Take Part in Study.
4. Diagnosis Of Coronary Artery Disease (Modified Rose Questionnaire). Symptoms plus Either Diagnostic Electrocardiographic Changes or Elevated Levels of Cardiac Enzymes, those patient having Ischaemic changes in 2D-echo and positive TMT study.

Exclusion Criteria
1. Known case of diabetes mellitus.
2. Patients who refuse take part in study.
3. Patient having Hba1c level >6.5

Table 1: Total cholesterol

<table>
<thead>
<tr>
<th>Total cholesterol</th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;200</td>
<td>48</td>
<td>30</td>
<td>78</td>
</tr>
<tr>
<td>&lt;200</td>
<td>15</td>
<td>7</td>
<td>22</td>
</tr>
<tr>
<td>Total</td>
<td>63</td>
<td>37</td>
<td>100</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Waist-hip ratio</th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>50</td>
<td>36</td>
<td>86</td>
</tr>
<tr>
<td>&gt;1 (male) &gt;0.85 (female)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>13</td>
<td>1</td>
<td>14</td>
</tr>
<tr>
<td>&lt;1 (male) &lt;0.85 (female)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>63</td>
<td>37</td>
<td>100</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Risk of 10 year</th>
<th>HbA1c &gt;=5.5</th>
<th>HbA1c&lt;5.5</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>42</td>
<td>10</td>
<td>52</td>
</tr>
<tr>
<td>Intermediate</td>
<td>10</td>
<td>1</td>
<td>11</td>
</tr>
<tr>
<td>High</td>
<td>26</td>
<td>11</td>
<td>37</td>
</tr>
<tr>
<td>Total</td>
<td>78</td>
<td>22</td>
<td>100</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Framingham Score</th>
<th>Age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average</td>
<td>9.72</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Relationship between Framingham risk score and age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average Framingham Score and age(r=0.6)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Relationship between age and Framingham Score(r=0.6)</th>
</tr>
</thead>
</table>

In our study, 63 out of 73 patients had high HsCRP. 54 out of 63 had high HbA1c (>5.5) while 9 out of 63 patients had Normal HbA1c (<5) in patients with high HsCRP. In previous study Atsushi et al and Daniel et al, most patients had high HsCRP. Chi square test was applied to detect association between HsCRP and High HbA1c. The Test significant meaning that higher value of HsCRP associated with high level of HbA1c (p=0.04).

In our study we have tried to find out association between Framingham 10 year risk score with high normal HbA1c. As given in Table 4 we find out that 42 out 52 patients had high normal HbA1c in low risk score group. 10 out of 11 patients had high normal HbA1c in intermediate risk score group. While 26 out of 37 patients had high normal HbA1c in high risk score group.

<table>
<thead>
<tr>
<th>Framingham 10 year risk score and HbA1c</th>
</tr>
</thead>
</table>

- In our study, 63 out of 73 patients had high HsCRP. 54 out of 63 had high HbA1c (>5.5) while 9 out of 63 patients had Normal HbA1c (<5) in patients with high HsCRP. In previous study Atsushi et al and Daniel et al, most patients had high HsCRP. Chi square test was applied to detect association between HsCRP and High HbA1c. The Test significant meaning that higher value of HsCRP associated with high level of HbA1c (p=0.04).

- In our study we have tried to find out association between Framingham 10 year risk score with high normal HbA1c. As given in Table 4 we find out that 42 out 52 patients had high normal HbA1c in low risk score group. 10 out of 11 patients had high normal HbA1c in intermediate risk score group. While 26 out of 37 patients had high normal HbA1c in high risk score group.

- There were no linear relationship between HbA1c and Framingham risk score. The Correlation Coefficient(r) is -0.02.

- In our study average Framingham risk score was 9.72 while average age of patient was 53.7 years. There were linear relationship between patient’s age and Framingham 10 year risk score. (r= 0.60)

- In our study as shown in Table 3 average Framingham risk score was 9.72 while average age of patient was 53.7 years. When we plotted Framingham risk score against patient’s age, there were linear relationship between patient’s age and Framingham 10 year risk score. (r= 0.60). So in our study Framingham risk score had linear relationship with patient’s age.

- It is known that Framingham risk score is dependent on many factors like age of the patient, sex of patient, smoking habits, lipid profile and presence of hypertension. When only one factor age was plotted using scatter diagram a reasonable correlation was observed between age of patient and Framingham risk score.
score. It also means that if other variables are kept constant, with advancement of age, Framingham risk score also increases.

**Conclusion**

In our study, we find association between high normal HbA1c and Framingham risk score in non-diabetic patient. But, There is no any linear correlation between high normal HbA1c and Framingham 10 risk score (r=0.02).

We also find out that Framingham 10 year risk score has linear relationship with patient’s age. It implies that coronary artery disease calculated by using Framingham 10 year risk score increases with increase in age. But Glycosylated Hemoglobin predicts coronary artery disease risk independence of patient’s age.

**References**

2. Park K. Epidemiology of Coronary Artery Disease, Park’s textbook of Preventive and Social Medicine, Page No.366-367
4. Coronary artery atherosclerosis image, Mayo Foundation for Medical Education Research