

## CORRELATION OF MEAN HBA1C LEVELS WITH SEVERITY OF CORONARY ARTERIES DISEASE IN DIABETICS

Riaz Muhammad<sup>1</sup>, Arslan Masood<sup>2</sup>, Junaid Zaffar<sup>3</sup>, Usman Butt<sup>4</sup>

<sup>1</sup> Department of Cardiology, Punjab Institute of Cardiology, Lahore, Pakistan

<sup>2-4</sup> Department of Cardiology, Jinnah Hospital, Lahore, Pakistan

### **Address for Correspondence:**

**Dr. Riaz Muhammad,**

Department of Cardiology, Punjab Institute of Cardiology, Lahore, Pakistan

E-Mail:

doctorriazmuhammad@gmail.com

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### **Contribution**

All the authors contributed significantly to the research that resulted in the submitted manuscript.

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### **ABSTRACT**

**Objective:** The aim of this study was to know the correlation of mean HbA1c levels with severity of coronary arteries disease (CAD) in diabetics.

**Methodology:** This descriptive cross sectional study was conducted at Punjab Institute of Cardiology, Lahore from May 2011 to November 2011 including 228 patients, 30 to 70 years of age with the diagnosis of ACS or stable angina and no contraindication to coronary angiography. HbA1c levels were measured in all patients. Severity of CAD was determined on the basis of number of coronary arteries involved and patients were divided into three groups i.e. mild, moderate and severe CAD. Mean HbA1c values were then compared in all three groups to determine the correlation HbA1c levels with severity of CAD.

**Results:** The mean age of study population was  $51.5 \pm 9.5$  years. Males were 151 (65.7%). Mild CAD patients were 89 (38.7%), 71 (30.9%) were moderate disease while 70 (30.4%) had severe CAD. Hypertensive patients were 128 (55.7%), 52 (22.6%) were smokers, 82 (35.7%) were dyslipidemic and 26 (11.3%) patients had positive family history of premature CAD. Mean HbA1c of the study population was  $9.1 \pm 1.02$  ( $8.1 \pm 0.37$  in mild CAD group,  $9.1 \pm 0.50$  in moderate and  $10.3 \pm 0.53$  in severe CAD group. Severity of coronary artery disease increases with increase in Hemoglobin A1c level ( $p < 0.0001$ ). Patients with high HbA1c levels have more number of coronaries diseased as compared to those who have lower levels.

**Conclusion:** HbA1c is directly related to severity of coronary artery disease; the more the HbA1c level the more severe is the coronary artery disease.

**Key Words:** Hemoglobin A1c, Coronary Artery Disease, Diabetes Mellitus

## INTRODUCTION

The worldwide prevalence of diabetes mellitus (DM) has dramatically increased over the past two decades from 30 million cases in 1985 to 177 million in 2000.<sup>1</sup> Based on these trends, nearly 360 million individuals will have diabetes by the year 2030.<sup>1</sup> DM is associated with microvascular and macrovascular complications in the long-term, which cause significant morbidity and mortality in diabetics.<sup>2</sup> Atherosclerotic coronary artery disease (CAD) is responsible for most of the excess mortality in diabetics and different studies have recognized cardiovascular complications to be mostly or partially dependent on long standing constant hyperglycemia. HbA1c is now a days a well-known measure of long-term glycemic control in diabetic patients, and several studies have demonstrated that elevated HbA1c level is considered to be related with increased future risk of cardiovascular disease (CVD).<sup>3</sup> Baqiyyah Conway et al, observed the Pittsburgh Epidemiology of Diabetes Complications study cohort of DM for 18 years for cardiovascular events including fatal and non fatal CAD. Baseline HbA1c was found to be an independent risk factor for fatal CAD, along with duration of diabetes and albuminuria.<sup>4</sup>

HbA1c is a better marker for determining risks of CAD and mortality than fasting blood glucose and even non-diabetic patients with elevated HbA1c levels are also at increased risk for CVD and mortality.<sup>5</sup> In diabetics there is an increased frequency of fatal or non fatal coronary events due to unstable atherosclerotic plaque which may lead to vaso-occlusive thrombus formation in case of fissuring. Several studies have demonstrated a close relation between chronic sustained hyperglycemia and development of atherosclerosis. The American Diabetes Association in its 2007 position statement on glycaemic control stated that lowering HbA1c may be associated with reduction of microvascular and neuropathic complications of diabetes mellitus and possibly macrovascular complications.<sup>6</sup> According to EDIC (Epidemiology of Diabetes Interventions and Complications) study the patients who had previously been kept on aggressive glucose control during the Diabetes Control and Complications Trial (DCCT) had a significantly reduced risk of CVD than patients receiving standard treatment.<sup>7</sup>

This study was aimed to correlate the mean HbA1c levels with severity of coronary arteries disease as evaluated by coronary angiogram in diabetic patients, so that preventive measures may be taken to achieve intensive glucose control in order to reduce the severity of CAD.

## METHODOLOGY

This descriptive cross sectional study was conducted at Punjab Institute of Cardiology, Lahore from May 2011 to

November 2011 including 228 patients, 30 to 70 years of age with the diagnosis of ACS or stable angina and no contraindication to coronary angiography. Patients who refused to give consent for participation in study and those with chronic renal failure (already diagnosed/serum creatinine >1.5mg/dl), chronic liver disease or having INR >1.4, women having gestational diabetes (on available antenatal record) were excluded from study. Informed consent was taken. Duration of diabetes, history of hypertension, smoking, dyslipidemia and family history of coronary artery disease was also inquired. Baseline investigations including serum glucose level and HbA1c level were sent to central lab of the hospital. Coronary angiographic data was analysed by a single experienced operator. Number of coronary arteries involved with >50% stenosis were noted. Patients were divided into three groups according to number of coronary arteries involved:

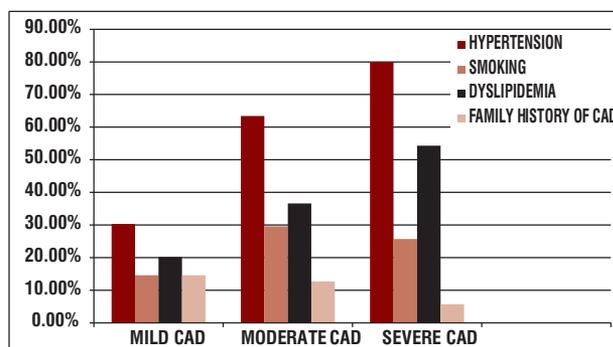
1. Mild coronary artery disease i.e >50% stenosis in one artery
2. Moderate coronary artery disease i.e >50% stenosis in 2 arteries
3. Severe coronary artery disease. i.e >50% stenosis in >2 arteries

All the collected information was entered and analysed in SPSS (Statistical Package for The mean HbA1c level was compared between the three groups of patients by using ANOVA keeping a p-value  $\leq 0.05$  as significant.

## RESULTS

The mean age of study population was  $51.5 \pm 9.5$  years including 151 (65.7%) males and 79 (34.3%) females. 89 (38.7%) patients had mild CAD, 71 (30.9%) moderate disease while 70 (30.4%) had severe disease. 128 (55.7%) patients were hypertensive, 52 (22.6%) were smokers, 82 (35.7%) were dyslipidemic and 26 (11.3%) patients had positive family history of premature CAD (Figure 1). Mean HbA1c of the study population was  $9.1 \pm 1.02$  ( $8.1 \pm 0.37$  in mild CAD group,  $9.1 \pm 0.50$  in

**Figure 1: Frequency of Coronary Risk Factors in CAD Severity Groups**



**Table 1: Mean HbA1c Levels in the Cad Severity Groups**

Mild CAD n=89	Moderate CAD n=71	Severe CAD n=70	Total n=230	P-value
8.134±.3763	9.141±.5058	10.354±.5263	9.120±1.02	<0.001

moderate and 10.3±0.53 in severe CAD group) (Table 1). HbA1c levels thus showed a progressively worsening pattern among the three CAD severity groups ( $p < 0.001$ ).

## DISCUSSION

Waden et al, reported the variability in HbA1c levels predictive for cardiovascular diseases as well as renal involvement in diabetics.<sup>8</sup> They concluded that in patients with type 1 diabetes, HbA1c variability was indicative of development and worsening of diabetic nephropathy as well as CVD events. Su et al, had a similar observation in their study that HbA1c levels was independent determinant of higher Gensini Score which in turn points towards increasing severity of coronary artery disease.<sup>9</sup> Gensini score closely correlated with age, MAGE (mean amplitude of glycemic excursions), PPGE (post prandial glycemic excursion), hemoglobin A1c (HbA1c), hs-CRP and total cholesterol (TC).

Eeg-Olofsson et al, studied a total of 7,454 patients from the Swedish National Diabetes Register over a period of 5 years (aged 20–65 years, diabetes duration 1–35 years) and found a progressively increasing risk of coronary heart disease and cardiovascular diseases with higher HbA1c levels, independent of traditional risk factors.<sup>10</sup> Khaw and colleagues conducted prospective population Study in the UK and showed a relative risk for death from any cause of 1.24 in males and 1.28 in females with every 1% increase in HbA1c levels ( $p < 0.001$ ).<sup>11,12</sup> Similar results have been reported by the UKPDS and by Selvin's meta-analysis which included 1,688 patients with type 1 diabetes in three studies and 7,435 patients with type 2 diabetes in 10 studies.<sup>13,14</sup> The Diabetes Control and Complications Trial (DCCT) had revealed an improved glycemic control in type 1 DM linked to a steady decline in complications related to vascular and nervous system.<sup>15</sup>

Saleem et al, conducted a similar prospective study in Saudi Arabia to find the association between HbA1c levels and the severity of coronary artery disease in diabetics who presented with acute myocardial infarction.<sup>16</sup> They found significant association of Diabetes mellitus and Hypertension with higher Gensini score, suggesting an increase in severity of coronary artery disease in the presence of either of the factors. They further demonstrated a positive correlation between Gensini score and HbA1c ( $p < 0.001$ ). Ravipati et al, studied the severity of coronary artery disease in diabetic patients who had complaint of

chest pain.<sup>17</sup> There was a significant increasing trend of hemoglobin A1c levels over the increasing number of vessels with CAD ( $p < 0.0001$ ). In our study we also measured the severity of coronary artery disease according to the number of coronary arteries involved and the results of our study are comparable to Ravipati et al.

Our study clearly showed that HbA1c is an independent factor influencing the severity of coronary artery disease as demonstrated by coronary angiography. Poor glycemic control in diabetics leads to development and progression of atherosclerotic vascular diseases and a good glycemic control can effectively halt this process. As glycosylated hemoglobin is a marker of glycemic control therefore achievement of an adequate target HbA1c level can be helpful in prevention of atherosclerosis in this population.

## CONCLUSION

HbA1C is directly related to severity of coronary artery disease; the more the HbA1c level the more severe is the coronary artery disease.

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