RESEARCH ARTICLE

ASSOCIATION OF HBA1C WITH PREVALENCE AND SEVERITY OF CORONARY ARTERY DISEASE IN DIABETIC AND NONDIABETIC PATIENTS IN KASHMIR

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ABSTRACT

Background: Diabetes mellitus is an established risk factor for coronary artery disease (CAD). In diabetic patients measurement of glycosylated hemoglobin is a way of assessing glycemic control. The major form of glycosylated hemoglobin is HbA1c which reflects the state of glycemia over last three months.

Introduction: Studies conducted to assess the correlation of HbA1c with CAD in diabetic patients have shown it to be an important predictor. Association of raised HbA1c with CAD has also been observed in nondiabetic patients. The present study was undertaken to assess the association of HbA1c with CAD and the relationship between HbA1c level with the severity of CAD in diabetic as well as non-diabetic patients.

Materials and Methods: The study population consisted of 240 patients, out of which 103 were diabetic and 137 were non-diabetic. A detailed history was taken from all the patients which included history of angina, hypertension, smoking and diabetes mellitus. After an informed consent, coronary angiography was performed through femoral artery. The method for estimating HbA1c was High Performance Liquid chromatography (HPLC).

Results: Out of 240 patients, 179 had CAD of whom 119 (~ 66 %) had raised HbA1c (>6.07). All the 73 diabetic patients with CAD had raised HbA1c and 46 (~43%) non-diabetic patients with CAD had raised HbA1c. The mean HbA1c in all the patients increased with an increase in the number of coronary vessels involved. The mean HbA1c level in each group of CAD was higher for diabetic patients as compared to HbA1c in the non-diabetic patients.

Conclusions: HbA1c level had a strong relationship with severity of CAD in both diabetic and non-diabetic patients .It was observed that in diabetic patients, there was a significant increasing trend in HbA1c with an increasing number of vessels involved.

INTRODUCTION

Coronary Artery Disease (CAD) has emerged as a leading cause of morbidity and mortality the world over, more so in developing countries like India. Major risk factors for coronary artery disease include Smoking, Hypertension, Diabetes Mellitus, Dyslipidemia, family history of CAD and Obesity (Thomas *et al*., 2008). Diabetes Mellitus is an independent predictor of mortality in CAD (Alvin, 2008). One important way of assessing glycemic control in diabetic patients is by estimating the blood levels of glycated hemoglobin (HbA1c). Since glycohemoglobins circulate within red blood cells whose life span is upto 120 days ,they generally reflect the state of glycemia over the preceding 8 to 12 weeks, thereby providing an improved method of assessing

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diabetic control. Elevated HbA1c level has been shown to be an independent risk factor for coronary heart disease in persons with and without diabetes (Elizabeth Selvin *et al*., 2005). Considering the magnitude of CAD and diabetes

mellitus in our country, the present study was undertaken to assess the association of HbA1c with CAD and the relationship between HbA1c level with the severity of CAD in diabetic as well as non-diabetic patients.

MATERIALS AND METHODS

The study population consisted of 240 patients, out of which 103 were diabetic and 137 were non-diabetic.

Material: Our study group consisted of those patients who were admitted in department of cardiology, SKIMS for undergoing coronary angiography from June 2007 to October 2009. Only those patients who had a normal complete blood

count, blood urea and serum creatinine were taken for this study. In addition known Type 1 diabetic patients were excluded from this study.

Method: A detailed history was taken from all the patients which included history of Angina, Hypertension, Smoking, and Diabetes Mellitus. All the patients who were not known diabetic were screened by oral glucose tolerance test (OGTT). HbA1c was performed in all the patients at one laboratory, so as to standardize the test values and the normal range.

(v. 17.0, Chicago, IL). Quantitative data was analysed by using two sample independent 't test' and multivariate analysis using SPSS-17 software. P values less than 0.05 were considered to be significant. All data are expressed in mean ± standard deviation (SD).

RESULTS

Out of 240 patients, (145 males and 95 females) 103 were diabetic patients, out of which 62 were on oral anti-diabetic drugs and 41 were on Insulin. HbA1c was raised (> 6.07) in

Table 1. HbA1c and CAD in Diabetic and Non Diabetic Patients

		CAD (n=179)				Non-CAD (n=61)			
		Diabetic		Non-Diabetic		Diabetic		Non-Diabetic	
		n	%	n	%	n	%	n	%
HbA1c	Normal	0	0.0	60	56.6	0	0.0	28	90.3
	Raised	73	100.0	46	43.4	30	100.0	3	9.7
	Total	73	40.7	106	59.3	30	49.2	31	50.8
Result		p = 0.000 (Sig)				p = 0.000 (Sig)			
Logistic Regression analysis		R2= 0.637 (Negelkerke), p = 0.000 (Sig)							

* All the diabetic patients irrespective of their coronary artery disease status had a raised HbA1c (>6.07) level.
* Out of 106 non-diabetic patients who had CAD 46 were having a raised HbA1c level.

Table 2. HbA1c and Severity of CAD with Diabetes Mellitus Status

			Normal	Raised	p value
SVD	Diabetic	n	0	26	0.000
		%	0.0	100.0	(Sig)
	Non-Diabetic	n	38	3	
		%	92.7	7.3	
DVD	Diabetic	n	0	24	0.066
		%	0.0	100.0	(NS)
	Non-Diabetic	n	4	26	
		%	13.3	86.7	
TVD	Diabetic	n	0	11	1.000
		%	0.0	100.0	(NS)
	Non-Diabetic	n	0	17	
		%	0.0	100.0	

*   SVD – single vessel disease.
*   DVD- double vessel disease.
*   TVD- triple vessel disease.
*   All those patients who had triple vessel disease had a raised HbA1c level.

Table 3. HbA1c among Diabetic and Non Diabetic Patients

Diabetes Mellitus	Coronary Angiography	Mean	SD	ANOVA
Yes	Non obstructive CAD	7.19	0.64	F= 4.3,
	SVD	7.53	0.53	p=0.008
	DVD	7.80	0.65	(Sig)
	TVD	8.09	0.92	
No	Non obstructive CAD	5.18	0.14	F= 121.3,
	SVD	5.53	0.27	p=0.000
	DVD	6.19	0.29	(Sig)
	TVD	6.88	0.49	

*   Mean HbA1c level was higher in each category of CAD for diabetic patients as compared to non-diabetic patients.

The method for determining HbA1c value was High Performance Liquid chromatography (HPLC) using BIORAD machine. Variant II Turbo testing system was used. The normal laboratory range of HbA1c was between 4.27 and 6.07. HbA1c was not taken as a diagnostic marker as that has been recommended in 2010 i.e after completion of this study. After an informed consent, the coronary angiography was performed through femoral artery. A comparison and contrast analysis of data was done through standard statistical methods. Data were analyzed using Statistical Package for the Social Sciences

152 of 240 patients. Out of 240 patients, 179 had coronary artery disease (CAD) and 61 did not have CAD. 67 had single vessel disease (SVD), 54 had double vessel disease (DVD) and 28 had triple vessel disease (TVD). Non-obstructive coronary artery disease was seen in 30 patients. All of the 103 diabetic patients had a raised hbA1c whereas 49 out of 137 non-diabetic patients (~36 %) had raised HbA1c level. 119 (~ 66 %) out of 179 CAD patients had raised HbA1c level. 73 (~ 40 %) of 179 CAD patients were diabetic and 106 were non-diabetic. All the 73 diabetic patients with CAD had raised HbA1c level and 46 out of 106 (~43%) non-diabetic patients with CAD had raised HbA1c level. The mean HbA1c in all the patients increased with an increase in the number of coronary vessels involved. In the diabetic group of patients, the mean HbA1c level for non-obstructive CAD was 7.19 ± 0.64, for SVD it was 7.53 ± 0.53, for DVD it was 7.80 ± 0.65, and for TVD it was 8.09 ± 0.92. On ANOVA, the p value was 0.008 which is statistically significant. In the non-diabetic group the mean HbA1c for non-obstructive CAD, SVD, DVD and TVD was 5.18 ± 0.14, 5.53 ± 0.27, 6.19 ± 0.29 and 6.88 ± 0.49 respectively. The p value on ANOVA was statistically significant. The mean HbA1c level in each group of CAD is higher for diabetic patients as compared to HbA1c in the non-diabetic patients.

DISCUSSION

HbA1c has been found to be associated with coronary artery disease (CAD) in diabetic as well as non-diabetic patients. In the last two decades, a number of studies have been conducted to correlate the risk and outcome in patients of CAD with levels of HbA1c.One such study and the only one conducted in India so far found that there is a strong association of HbA_{1c} with prevalent cardiovascular risk factors in Indian subjects with normal glucose tolerance (James Dilley *et al.*, 2007). HbA1c levels have been seen to correlate with the extent and severity of coronary artery disease in terms of the number of coronary arteries involved and the degree of obstruction.

In our study , the mean HbA_{1c} levels in diabetic patients for single vessel disease (SVD) was 7.53 ± 0.53, for double vessel disease (DVD) 7.8 ± 0.65, for triple vessel disease (TVD) 8.09 ± 0.92 whereas in another study of similar design it was 8.00 ± 0.84 for SVD, 8.83 ± 1.45 % for DVD and 10.40 ± 2.28% for TVD (22). Multivariate analysis of our study revealed that independent of the diabetic status of the patients, HbA_{1c} and coronary artery disease had statistically significant relationship ($p<0.005$). It proves that HbA_{1c} is a significant risk factor for CAD in both diabetic and non-diabetic persons. On statistical analysis, we found that HbA1c level had a strong relationship with severity of CAD especially for double and triple vessel disease in both diabetic and non-diabetic patients. Some of the other studies testing this hypothesis came to similar conclusions (Kowalska *et al*., 2001; Milo Engoren *et al*., 2008). They have also reported that HbA1c level increased with the progression of atherosclerotic lesions in coronary arteries. In our study as well as the studies conducted by other investigators, a significant correlation was observed between the number of involved vessels and HbA1c level, in both diabetics as well as non-diabetic patients (Kowalska *et al*., 2001).

Conclusion

HbA1c level has a strong relationship with severity of CAD especially for double and triple vessel disease in both diabetic and non-diabetic patients. A significant correlation exists between the number of involved vessels and HbA1c level, in both diabetics as well as non-diabetic patients.

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