A STUDY ON RELATIONSHIP OF GLYCATED HAEMOGLOBIN WITH SEVERITY OF CORONARY ARTERY DISEASE IN TYPE 2 DIABETES USING SYNTAX SCORE

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ABSTRACT

BACKGROUND

Glycosylated Haemoglobin (HbA1c) is an established marker of long-term glycaemic control in patients with diabetes mellitus (DM) and elevated HbA1c levels are associated with an increased risk for further microvascular and macrovascular disease. There have been few studies, which have shown HbA1c to be predictive of coronary artery disease and only in limited studies HbA1c has been correlated with angiographically proven CAD (coronary artery disease) using Syntax score. To aim the study to evaluate the relationship between increasing HbA1c level and severity of coronary artery disease in type 2 diabetic patients using syntax score in a cohort of proven Coronary Artery Disease (CAD) on angiography at Gauhati Medical College.

MATERIALS AND METHODS

We prospectively collected data of diabetic patients with proven CAD on angiography from June 2014 to June 2015. Patients were divided into four groups (interquartiles) according to HbA1c levels, less than 6.7%, 6.7% to 7.1%, 7.1% to 7.6% and >7.6%. Severity of coronary artery disease was assessed using syntax score and the number of coronary vessels diseased. We compared different quartiles of HbA1c with regard to syntax score and number of diseased vessels.

RESULTS

A total of 133 patients were included in the study. Mean age was 58.1±10.4 years. 87.2% (116) were males, 54.1% (72) were hypertensives, 21.1% (28) were smokers and 39.1% (52) were dyslipidaemic. Among diabetics, mean HbA1c was 7.1%. On analysis, we found that Coronary Artery Disease (CAD) severity by syntax score as well as number of vessels involved was significantly different among quartiles (p values <0.001 and <0.001 respectively). Mean syntax scores significantly increased with increasing HbA1c levels (syntax scores were 7, 8, 10.5, 16.58 and 25.9 in patients with HbA1c levels <6.7, 6.7-7.1, 7.1-7.6 and >7.6, respectively). In syntax subgroups (<23, 23-32 and >32), mean HbA1c values were 6.8±0.2, 7.4±0.5 and 8.0±0.4, respectively. In subgroup analysis where only chronic stable angina patients were considered, there was significant linear correlation between HbA1c and severity of CAD by syntax score (R-0.820; p<0.001) and number of vessels involved (R-0.35; p<0.001). Multivariate logistic regression analysis in diabetic population showed that HbA1c >7% was an independent predictor of syntax score >22 (OR=2.832, 95% CI 1.866-4.299; p<0.001).

CONCLUSION

From this clinical study, we can conclude that a significant correlation exists between level of HbA1c and severity of CAD by syntax score as well as number of vessels involved in 1 diabetes.

KEYWORDS

Syntax Score, Glycated Haemoglobin, Type 2 Diabetes.

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BACKGROUND

Glycosylated Haemoglobin (HbA1c) is an established marker of long-term glycaemic control in patients with Diabetes Mellitus (DM) and elevated HbA1c levels are associated with an increased risk for further microvascular and macrovascular disease.[1] HbA1c levels can be assessed in the non-fasted state and has higher reproducibility than fasting glucose.[2]

Atherosclerosis is defined as a chronic inflammatory disease caused by sustained injury to the vessel wall. Atherosclerotic disease accounts for most of the excess mortality in patients with Diabetes Mellitus (DM).[3]

There is consistent evidence that optimal glycaemic control (defined by as HbA1c ≤7%) results in a lower incidence of microvascular complications in both type 1 and type 2 diabetes mellitus.[4]

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There have been few studies, which have shown HbA1c to be predictive of coronary artery disease and only in limited studies HbA1c has been correlated with angiographically proven CAD (coronary artery disease) using SYNTAX score.

An estimate of coronary artery disease burden can be obtained by analysing each lesion with help of syntax score found at angiography. The SYNTAX (Synergy between PCI with Taxus and Cardiac Surgery) Score (SS) was developed as part of the SYNTAX trial with the object to characterise and objectively quantify the severity and extent of coronary artery disease.[5] This scoring system was used in this study for assessing severity of coronary artery disease.

So, in this study, we aimed to evaluate the relationship between HbA1c level and severity of coronary artery disease in diabetic patients using SYNTAX score in a cohort of proven Coronary Artery Disease (CAD) on angiography at Gauhati Medical College.

MATERIALS AND METHODS

The patients admitted to Cardiology Department, Gauhati Medical College from June 2014 to June 2015 were included in the study. Patients with probable coronary artery disease underwent Coronary Angiography (CAG). Diabetic patients (previous history of diabetes and HbA1c level more than 6.5%) with proven CAD fulfilling inclusion and exclusion criteria were included for the study. It is a single centre cross-sectional study.

Prior ethical clearance from the appropriate authorities was taken. A proforma was predesigned and validated by institutional ethics committee. Written informed consent was taken from the study participants. Study consisted of history, study of angiographic report and relevant biochemical investigations.

It consisted of patient details like hospital number, name, age, gender, history of diabetes, smoking, dyslipidaemia, hypertension and other comorbidities.

Patients were considered as hypertensive according to JNC 8 (The Eight Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure) criteria, diabetic as per ADA (American Diabetes Association) criteria and dyslipidaemia according to NCEP (National Cholesterol Education Program) criteria.

In addition, use of antihypertensive, antidiabetic or lipid lowering medications were used as criteria for hypertension, diabetes and dyslipidaemia, respectively. Either current or past history of tobacco smoking for 6 months was considered as smoking positive.

Details of the angiography were obtained and weighed using Syntax score. The Syntax scores were calculated with the help of professional website tool: http://www.syntaxscore.com/. Serum concentration of Haemoglobin A1c (HbA1c) was determined by immunoturbidimetric method. Patients were divided into four groups (interquartiles) according to HbA1c levels, less than 6.7%, 6.7% to 7.1%, 7.1% to 7.6% and >7.6%. Severity of coronary artery disease was assessed using SYNTAX score and the number of coronary vessels diseased.

We compared different quartiles of HbA1c with regard to SYNTAX score and number of diseased vessel.

Inclusion Criteria

All diabetes patients (previous history of diabetes and HbA1c level more than 6.5%) with proven Coronary Artery Disease (CAD) on angiography were included in the study and CAD is defined as 50% reduction in luminal diameter by visual assessment of epicardial coronary arteries (≥50% obstruction in ≥1 coronary artery).

Exclusion Criteria

1. Patients with <50% reduction in luminal diameter of epicardial coronary arteries on angiography were excluded from the study.
2. Patients with history of prior revascularisation PCI or CABG and known patients with haemoglobinopathies, anaemia or history of recent blood transfusion were excluded from the study.

Statistical Analysis

Severity of coronary artery disease was assessed using SYNTAX score and the number of coronary vessels diseased. Diabetic patients were divided into four quartiles of HbA1c. Data are presented as frequencies and percentages for categorical variables and mean±standard deviation (SD) for continuous variables, unless otherwise indicated. Differences between groups were assessed using the chi-square and ANOVA. Correlation between continuous variables was determined by Pearson correlation coefficients. Linear regression analysis was performed to show association between severity of CAD and HbA1C levels. Multivariate logistic regression was used to show HbA1c level as independent predictor of severity of CAD. $P<0.05$ was considered as statistically significant. The analysis was carried out using SPSS Version 16.

RESULTS

A total of 133 patients were included in the study. Mean age was 58.1±10.4 years. 87.2% (116) were males, 54.1% (72) were hypertensives, 21.1% (28) were smokers and 39.1% (52) were dyslipidaemic.

Patients were divided into four groups (interquartiles) according to HbA1c levels less than 6.7 %, >6.7% to 7.1%, >7.1% to 7.6% and >7.6%. These groups had 24.8% (33), 29.3 (39), 21.0% (28), 24.8% (33) patients, respectively (Table 1). Among diabetics mean HbA1c was 7.1%.

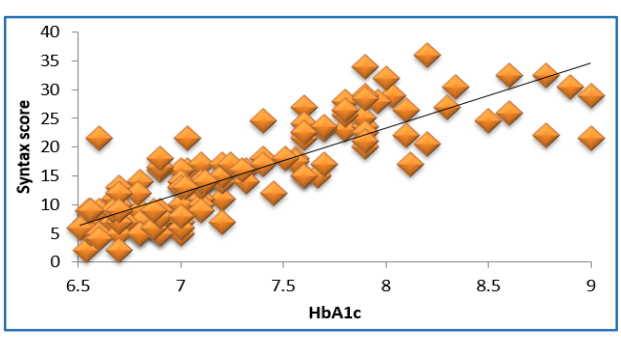
We compared different quartiles of HbA1c among diabetics with regard to SYNTAX score and number of diseased vessels. On analysis, we found that Coronary Artery Disease (CAD) severity by SYNTAX score as well as number of vessels involved was significantly different among quartiles (p values <0.001 and <0.001, respectively) (Figure 2 and Figure 3). Mean syntax scores significantly increased with increasing HbA1c levels (SYNTAX scores were 7.8, 10.5, 16.58 and 25.9 in patients with HbA1c levels 6.5-6.7, 6.7-7.1, 7.1-7.6 and >7.6, respectively). In syntax subgroups (<23, 23-32 and >32), mean HbA1c values were 6.8±0.2,

7.4±0.5 and 8.0±0.4, respectively (Figure 4). Age, gender, smoking, hypertension and dyslipidaemia did not show significant difference among quartiles. For smoking, though there was a trend for positive correlation it was not statistically significant (p >0.05) (Table 1). In subgroup analysis where only chronic stable angina patients were considered, there was significant linear correlation between HbA1c and severity of CAD by SYNTAX score (Figure 7) (R-0.820; p<0.001) and number of vessels involved (R-0.35; p<0.001). Multivariate logistic regression analysis, in diabetic population showed that HbA1c >7.1% was an independent predictor of syntax score >22 (OR=2.832, 95% CI1.866-4.299; p<0.001) (Table 5, 6).

HbA1C Quartiles		6.5-6.7	6.7-7.1	7.1-7.6	>7.6	Total	P Value
Gender	Female	4	5	5	3	17	.786
		3.0%	3.8%	3.8%	2.3%	12.8%	
	Male	29	34	23	30	116	
		21.8%	25.6%	17.3%	22.6%	87.2%	
Total		33	39	28	33	133	
		24.8%	29.3%	21.1%	24.8%	100.0%	
HTN		15	21	15	21	72	.531
		11.3%	15.8%	11.3%	15.8%	54.1%	
Smoking		8	6	6	8	28	.763
		6.0%	4.5%	4.5%	6.0%	21.1%	
CAD	SVD	19	20	8	7	54	.000
		14.3%	15.0%	6.0%	5.3%	40.6%	
	DVD	12	12	6	6	36	
		9.0%	9.0%	4.5%	4.5%	27.1%	
	TVD	2	7	14	20	43	
		1.5%	5.3%	10.5%	15.0%	32.3%	
Diagnosis	CSA	14	14	16	15	59	.419
		10.5%	10.5%	12.0%	11.3%	44.4%	
	UA/NSTEMI	8	9	2	4	23	
		6.0%	6.8%	1.5%	3.0%	17.3%	
	STEMI	11	16	10	14	51	
		8.3%	12.0%	7.5%	10.5%	38.3%	
Dyslipidaemia		12	18	9	13	52	.685
		9.0%	13.5%	6.8%	9.8%	39.1%	
SYNTAX Score	<23	32	32	7	0	71	.000
		24.1%	24.1%	5.3%	.0%	53.4%	
	23-32	1	7	16	8	32	
		.8%	5.3%	12.0%	6.0%	24.1%	
	>32	0	0	5	25	30	
		.0%	.0%	3.8%	18.8%	22.6%	

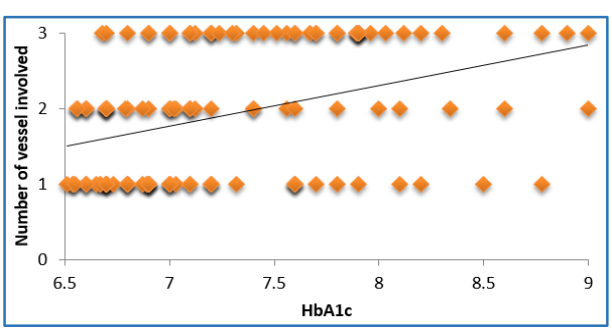
Table 1. Comparison of HbA1c Quartiles Among Diabetic Patients

N=133 (100%)



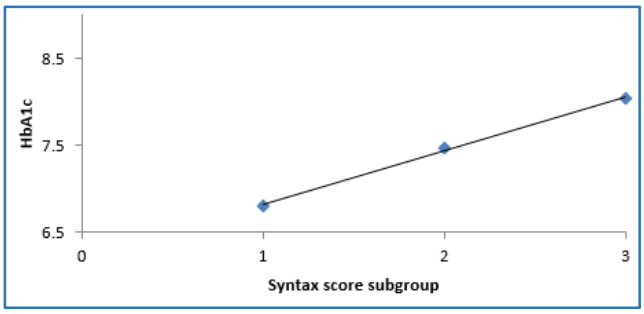
Table/Figure 2. Linear Regression Analysis between HbA1c and SYNTAX Score in Diabetic Patient

R-0.818 respectively, p<0.001



Table/Figure 3. Linear Regression Analysis between HbA1c and CAD (No. of Vessels) in Diabetic Patients

R-0.429; p<0.001



Table/Figure 4. Mean HbA1c in Syntax Score Subgroups in Diabetics

P<0.001

There was Linear Correlation between Mean HbA1c in Three Syntax Score Subgroups

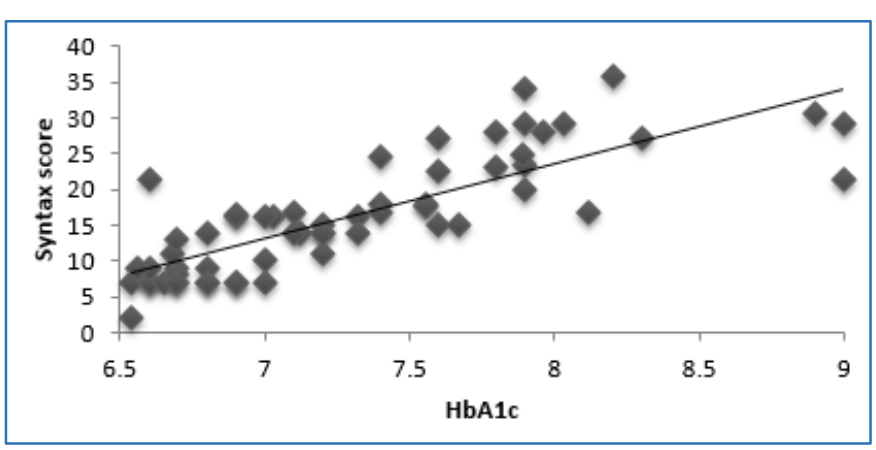
Syntax Score >22		B	Std. Error	Sig.	Exp (B)	95% Confidence Interval for Exp (B)	
						Lower Bound	Upper Bound
	Intercept	15.465	1.001	.000			
	HTN	.736	.641	.251	2.088	.594	7.336
	Smoking	-1.150	.777	.139	.317	.069	1.451
	Dyslipidaemia	.383	.615	.534	1.467	.439	4.900
	Male	-.513	.837	.540	.598	.116	3.088
	Age >60	1.178	.645	.068	3.248	.917	11.506
	HbA1c >7.1	4.665	.678	.000	106.203	28.095	401.456

Table/Figure 5. Multivariate Analysis in Diabetes

We found that, in multivariate analysis only HbA1c >7.1% was independent predictor of severity of disease by involving 3 vessels.

CAD 3 Vessels Involvement (TVD)		B	Std. Error	Sig.	Exp (B)	95% Confidence Interval for Exp (B)	
						Lower Bound	Upper Bound
	Intercept	-2.392	.649	.000			
	Dyslipidaemia	.301	.198	.298	1.301	.801	2.276
	Smoking	.209	.188	.547	1.168	.679	1.904
	Male	.138	.482	.758	1.164	.474	3.680
	Hypertension	.084	.173	.886	1.277	.731	1.939
	Age >60 yrs.	.222	.268	.474	1.249	.732	2.137
	HbA1c >7.1	1.587	.302	.000	5.218	2.648	8.530

Table/Figure 6.



Table/Figure 7. Linear Regression Analysis between HbA1c and SYNTAX Score in Diabetic Patients with Chronic Stable Angina Subgroup

R-0.820; p<0.001

DISCUSSION

In this study, we have established the relationship between HbA1c level and severity of coronary artery disease in type 2 diabetic patients using SYNTAX score. In our study, in diabetics, increasing HbA1c level was strongly correlated with disease severity, number of diseased vessels and higher SYNTAX score in graded fashion ($p<0.001$). In our study, linear regression analysis showed that HbA1c values significantly correlated with the SYNTAX score (p values <0.001). With increasing HbA1c levels, a significant increase was noted in the mean number of diseased vessels (p value <0.001).

Many other studies has shown correlation of HbA1c with severity of CAD. However, only limited studies has utilised SYNTAX score to show relationship between increasing HbA1c and severity of CAD. In a study by Ayhan et al 2012,[6] only HbA1c was found to be an independent risk factor for the presence of severe CAD using Gensini score. Mi Shu-Hua et al[7] has also observed HbA1c to be an independent determinant of CAD with Gensini score. Ghaffari et al[8] utilised multivariate logistic regression analysis to show HbA1c >5.8% as an independent predictor of Califf scores >6 (OR = 3.17, 95% CI 1.79-5.69; p = 0.001). Ikeda et al[9] showed that HbA1c is significantly associated with the complexity of coronary lesions. Ravipati et al[10] 2006 showed increasing mean HbA1c with increasing severity of CAD in diabetics. In study by Kaya et al,[11] cutoff value of 6.0% for HbA1c predicted severe atherosclerosis with a sensitivity and specificity of 54% and 74%, respectively. Similar to our study, Karakoyun S.[12] et al has utilised SYNTAX score to show relationship between increasing HbA1c and severity of CAD.

In our study, on subgroup analysis where only chronic stable angina patients were considered, there was significant linear correlation between HbA1c and severity of CAD by SYNTAX score (R-0.820; $p<0.001$) and number of vessels involved (R-0.35; $p<0.001$). Similar to our study, Hong and colleagues[13] reported a direct correlation between HbA1c levels and the severity of CAD based on the number of involved vessels in patients with stable angina.

STUDY LIMITATIONS

Our study has certain limitations. Firstly, the patients enrolled in our study were candidates with proven CAD, so our findings are relevant to high-risk group. Secondly, we used a single baseline measurement of HbA1c. Hence, we cannot evaluate the effects of changes in this parameter over long-term. So, a prospective long-term study would be ideal for analysing prognostic importance and outcomes.

CONCLUSION

From this clinical study, we can conclude that a significant relationship exists between level of HbA1c and severity of CAD by syntax score as well as number of vessels involved in type 2 diabetes.

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