

## Relationship between Glycated Haemoglobin and Complexity of Coronary Artery Disease in Diabetic Patients

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### ABSTRACT

**AIM:** The aim of this study is to examine the relation between glycated haemoglobin (HbA1c) and complexity of coronary artery lesion.

**METHODS:** This study enrolled 80 diabetic patients who underwent their first elective coronary angiography and had their HbA1c levels measured at Menoufia University Hospital between September 2015 and September 2016.

The complexity of the coronary artery lesions were evaluated using syntax score. Logistic regression and correlation coefficient were used to analyze the association between the measured HbA1c levels and syntax score.

**RESULTS:** Eighty diabetic patients with a mean age  $60 \pm 8.1$  years underwent elective coronary angiography with pre-procedural mea-

surement of HbA1c were included. Increased and a higher HbA1c levels were significantly associated with a higher syntax score ( $p$  value  $< 0.001$ ). After adjustment of age, gender, smoking, hypertension, dyslipidaemia and duration of diabetes, it was found that a higher HbA1c levels were able to independently predict patients with intermediate or high syntax score ( $\geq 18$ ).

**CONCLUSION:** The complexity of coronary artery lesions was significantly correlated with HbA1c among diabetic patients. A higher HbA1c value is an independent predictor of the complexity of coronary lesions.

**Key words:** Glycated haemoglobin; Coronary artery; Lesion; Diabetes

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### INTRODUCTION

Diabetes mellitus (DM) is an important risk factor for coronary heart disease<sup>[1]</sup>, and it is associated with a high prevalence of coronary artery disease (CAD) and an unfavorable prognosis<sup>[2]</sup>.

Glycated hemoglobin (HbA1c) reflects the average blood glucose concentrations over the preceding 2 to 3 months. Compared with the fasting blood glucose test, HbA1c has several advantages: it has higher repeatability<sup>[3]</sup>, can be assessed in the non-fasting state, and the committee highlighted that HbA1c is a more convenient test, with less biological variability and greater stability<sup>[4]</sup>.

Glycated hemoglobin (HbA1c) has been established as a risk factor for developing microvascular angiopathies in patients with DM. However, the relationship between HbA1c, and severity of coronary artery disease (CAD), and coronary perfusion in DM patients has not yet been clarified<sup>[5]</sup>.

HbA1c level is utilized clinically as an indicator of the adequacy

of glycemic control over several months prior to testing. Thus, it is measured to reflect the effectiveness of long-term glucose control in diabetic patients. The American Diabetes Association has recommended that an HbA1c breakpoint of 7% would realize the greatest cardiovascular benefit<sup>[6]</sup>. HbA1c levels may be of prognostic value regarding future cardiovascular disease. Several previous studies have demonstrated positive correlations of HbA1c with mortality and even subclinical cardiovascular disease in subjects without a history of diabetes<sup>[7]</sup>.

The risk of microvascular complications rises exponentially rather than linearly as HbA1c increases. Conversely, each 1% reduction in HbA1c has been shown to be associated with a 37% decrease in risk for microvascular complications and a 21% decrease in the risk of any end point or death related to diabetes<sup>[8]</sup>. Selvin *et al.*<sup>[9]</sup> demonstrated that the HbA1c was also a strong predictor of future DM, cardiovascular disease and all cause of mortality.

The Syntax score is an angiographic grading system based on the severity and complexity of the characteristics of coronary artery lesions<sup>[10]</sup>. This system is widely accepted as a CAD complexity marker, and its prognostic value has been demonstrated in different clinical situations, and patients with the higher Syntax score have significantly more major adverse cardiovascular events (MACE)<sup>[11]</sup>.

## PATIENTS AND METHODS

### Study population

This is a prospective randomized study that was done in the period from September 2015 to September 2016 at Menoufia University Hospital after taking a written informed consents from all patients.

The study included 80 diabetic patients presented to the cath lab for elective coronary angiography who either had previous documented acute coronary syndrome or patients with symptoms and investigations suggestive of ischemic heart disease (IHD), like ST changes in ECG, wall motion abnormality in echo or positive stress testing. Patients were subjected to elective coronary angiography to assess suspected coronary artery lesion. Patients with history of coronary revascularization, heart failure, moderate to severe valvular heart disease and congenital heart disease were excluded from this study. All patients were subjected to full history taking including personal history and risk factors profile. Thorough clinical examination with local cardiac examination to assess HbA1c, a 5 mL of venous blood was withdrawn from each patient with EDTA purple-topped anticoagulant then sample was paced in biohazard bag and HbA1c level was measured by immunoassay technique.

From the baseline diagnostic angiogram, each coronary lesion producing  $\geq 50\%$  diameter stenosis in vessels  $\geq 1.5$  mm had been scored separately and added together to provide the overall Syntax score, which had been calculated using the Syntax score algorithm<sup>[12]</sup>. Syntax score was used to evaluate the complexity of coronary artery lesions. According to Syntax score patients were divided into three groups. Group I (High Syntax score  $> 27$ ), Group II (moderate Syntax score 18-27), and Group III (low Syntax score  $< 18$ ).

### Statistical analysis

Collected data was presented as mean  $\pm$  SDs, and compared by the students test. The categorical variables were presented as proportions (percentages). Univariate, multivariate regression analysis and correlation coefficient were performed to evaluate the relationship between HbA1c and severity of coronary artery lesion (syntax score). Statistical analysis was performed using SPSS software version 20. *P* value  $< 0.05$  was considered significant.

## RESULTS

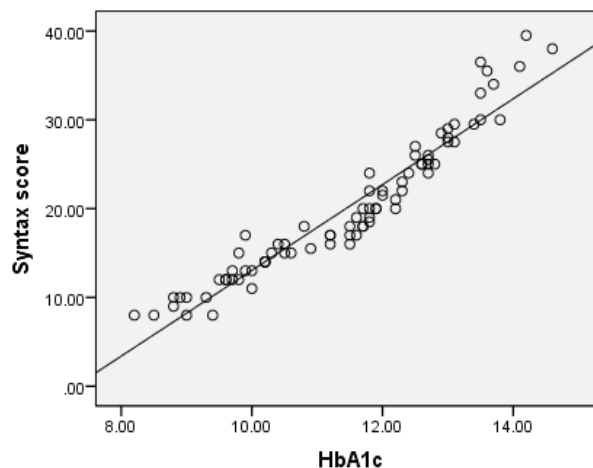
Of the 80 patients included in this study mean age was  $60 \pm 8.1$  years and 28 of them were females, 30 patients were smokers, 26 patients hypertensives, 20 patients had dyslipidaemia and 35 patients were on insulin others were on oral hypoglycaemics as shown in (Tables 1 and 2).

This study revealed that there was a significant positive correlation between HbA1c level and syntax score ( $r = 0.95$ ,  $p < 0.001$ ) as shown in Figure 1.

There was a highly significant difference in HbA1c level ( $p < 0.001$ ) among the three groups where group III patients with high Syntax score ( $> 27$ ) had a higher levels of HbA1c than Group II patients with moderate Syntax score (18-27) and Group III patients with low syntax score ( $< 18$ ). In addition the higher Syntax score category was significantly associated with age, smoking, hypertension, dyslipidemia, duration of diabetes and random blood sugar. (Tables 3 and 4). Using multivariate regression analysis, our study revealed that HbA1c was found to be an independent predictor of complexity of coronary artery lesion in diabetic patients (Table 5).

## DISCUSSION

Diabetes mellitus is a known risk factor of coronary artery disease (CAD). Cardiovascular disease is the leading cause of death in DM patients. Antecedent to and associated with epicardial coronary artery stenosis, DM patients develop abnormal micro vascular function in systemic circulatory beds, including those of the myocardium<sup>[13]</sup>. In light of the severity of coronary artery disease in diabetic patients it is necessary to take measures that prevent or delay it. Tight control of diabetes to decrease the level of HbA1c should be weighed against the disabling hypoglycaemia especially in older patients. The main finding in our study was that HbA1c was associated with coronary lesion complexity in diabetic patients. Previous studies had showed an association between elevated cardiovascular risk and elevated HbA1c level<sup>[14]</sup>, independent of other risk factors. HbA1c level is utilized clinically as an indicator of the adequacy of glycemic control over several months prior to testing. Thus, it is felt to reflect the effectiveness of long-term glucose control in diabetic patients. The American Diabetes Association has recommended that an HbA1c breakpoint of 7% would realize the greatest cardiovascular benefit<sup>[15]</sup>.



Positive correlation HbA1c and syntax score  $r=0.95$   $p=0.0$   
**Figure 1** Correlation between HbA1c & Syntax score.

HbA1c levels may be of prognostic value with regard to future cardiovascular disease. Several previous studies have demonstrated positive correlations of HbA1c with mortality and even subclinical cardiovascular disease in subjects without a history of diabetes.

**Table 1** Descriptive analysis of studied population regarding smoking, hypertension, dyslipidemia and Insulin injection among diabetic patients.

Variables	Characteristics of studied patients	
	No	%
Current smoking status	30	37.5
Hypertension	26	32.5
History of dyslipidaemia	20	25
History of ACS	33	41
Insulin treatment	35	44

ACS: Acute Coronary Syndrome.

**Table 2** Descriptive analysis of studied population (mean, SD, median and range) regarding age, duration of DM, Random Blood Sugar(RBS), HbA1c and Syntax score .

Variables	Mean $\pm$ SD	Median	Range
Age/years	60 $\pm$ 8.1	60	(45-78)
Duration of diabetes/years	14 $\pm$ 7.3	13.5	( 3-30 )
Random blood sugar mg/dL	300.9 $\pm$ 63	271	(220-420)
HbA1c	11.4 $\pm$ 1.55	11.7	(8.2-14.6)
Syntax score	20 $\pm$ 7.8	19	(8-39.5)

HbA1c: glycated haemoglobin.

**Table 3** Mean and standard deviation of HbA1c Regard Syntax score.

Syntax score groups	Group I (high >27)		Group II (Moderate (18-27)		Group III (low <18)		F	P
	No.	Mean $\pm$ SD	No.	Mean $\pm$ SD	No.	Mean $\pm$ SD		
HbA1c	16	13.5 $\pm$ 0.49	30	12 $\pm$ 0.58	34	9.9 $\pm$ 0.89	145	0.001

SD: standard deviation; f: f test; value p: probability value; HbA1c: glycated haemoglobin.

**Table 4** Correlation between Syntax score and HbA1c, lipid profile, age, duration of disease and random blood sugar.

Syntax score	Correlation coefficient (r)	P
HbA1c	0.95	0.000
Total cholesterol	0.78	0.000
LDL	0.86	0.000
Triglycerides	0.36	0.001
Age	0.81	0.001
Duration of DM	0.87	0.022
RBS	0.92	0.01

HbA1c: glycated haemoglobin; RBS: random blood sugar; LDL: Low Density Lipoprotein.

**Table 5** Multi-linear regression illustrates predictor factors for multiple arterial affection of diabetic patients (Syntax score).

	Unstandardized Coefficients		Standardized Coefficients	T	P
	B	SE	Beta		
(Constant)	-28.651	2.858		-10.02	0
HbA1c	2.607	0.389	0.517	6.706	0.000
Age	0.109	0.046	0.113	2.403	0.019
Duration	0.112	0.062	0.104	1.793	0.077
Random blood sugar	0.036	0.008	0.289	4.56	0.01
LDL	0.047	0.012	0.205	4.023	0.000

SE: standard error; t: t test; value p: probability value; HbA1c: glycated haemoglobin; RBS: random blood sugar; LDL: Low Density Lipoprotein.

In our study, we found that HbA1c was an independent predictor of the prevalence of complex coronary artery lesions (Syntax score >18) in diabetic patients. We established that the HbA1c level was significantly associated with complexity of coronary lesions independent of age, gender, smoking and other risk factors such as hypertension and dyslipidaemia. Even after adjustment of other risk factors, HbA1c level was still significantly correlated with Syntax score. The multivariate regression analysis showed that HbA1c was independently associated with Syntax score. So our study demonstrated that HbA1c can be a predictor of severity of coronary lesions in diabetic patients. Also the patients with low HbA1c had lower risk of complexity of coronary lesions, so diabetic patients should pay more attention to their blood glucose levels and should keep their HbA1c near the control levels. Improvement in glycaemic control results in better and favorable prognosis of clinical outcomes, as suggested by this study.

Limitation of this study was that patients with history of PCI or CABG were excluded, so our findings may not apply to these subjects who represent more severe cases. Also we did not consider obesity, glomerular filtration rate and cerebrovascular diseases which were associated with burden of atherosclerosis. This study is a single center study and multicenter studies are needed to support our findings.

In conclusion, HbA1c was significantly correlated with the complexity of coronary artery lesions in diabetic patients. Also HbA1c value was found to be an independent predictor of complexity of coronary artery lesions even after adjusting other risk factors. Good control of HbA1c level is important for improving the clinical outcome in diabetic patients.

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