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Value of Glycated Hemoglobin (HbA1c%) as an Indicator of Severity of Acute Coronary Syndrome in Non-Diabetic Adults

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Abstract

Background: Glycated hemoglobin (HbA1c%) is a dependable indicator of glycemic status in both diabetic and non-diabetic patients and a good indicator of Coronary Artery Disease (CAD) presence and its severity.

Aim of Work: Correlating (HbA1c%) level with the severity of acute coronary syndrome presentation, degree of affection of systolic and diastolic function of the cardiac muscle measured by TTE and degree of coronary vasculature affection as shown by diagnostic coronary angiography, in non-diabetic patients.

Methodology: A cross sectional study conducted from May 2016 to April 2017, at Cardiovascular Medicine Department, Tanta University Hospitals in Gharbia Governorate, Egypt. 123 non-diabetic patients presented to our CCU with Acute Coronary Syndrome (ACS), had Trans-Thoracic Echocardiography (TTE), diagnostic coronary angiography and SYNTAX score was calculated based on its results. HbA1c% level was measured and correlated to previous parameters.

Result: Patients was divided into 3 tertiles according to their HbA1c% level, ≤ 5.5, 5.6-5.9 and 6-6.4. Significant relationship was detected between HbA1 c% level and severity of ACS presentation. Moderate positive correlation was found between HbA1c% level and SYNTAX score (r.=0.504, p= 0.001). Also, moderate positive correlation was found between (HbA1c%) level and number of affected coronary vessels as detected by diagnostic coronary angiography (r.=0.397, p= 0.001). Moderate negative correlation was found between (HbA1c%) level and LV systolic function as measured by simpson method through TTE (r.=–0.466, p=0.001).

Conclusion: HbA1c% level is a fundamental marker for chronic glycemia and could be utilized as an independent predictor of CAD presence, severity of acute emergent presentation and degree of cardiac muscle affection due to CAD even in non-diabetic individuals.

Key Words: *(HbA1 c) Glycated Hemoglobin – (ACS) Acute Coronary Syndrome.*

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Introduction

THE relationship between cardiovascular diseases and glucose metabolism has drawn a lot of attention for decades. The central part of this attention was paid towards the relationship between those diseases and Diabetes Mellitus (DM) which is by far the most important systemic metabolic disease we have ever known **[1,2]**.

Although DM is a prominent risk factor for Coronary Artery Disease (CAD) **[3,4]**, new information is now available suggesting the need for a careful consideration not only of DM, but also of other disturbances of glucose metabolism, such as Impaired Glucose Tolerance (IGT), which is now considered an independent risk factor for cardiovascular disease morbidity and mortality **[5]**.

In the last years, many studies have shown that HbA1c% is a better indicator of CAD presence and severity than other glycemic variables **[6,7]**. HbA1c% also reflects the glycemic metabolic state in the preceding months. So, it has been used to assess efficiency of DM control **[8]**. Now, it has become one of the most commonly used measure of chronic hyperglycemia in epidemiological studies and clinical trials **[9]**. In addition, HbA1C% level of 6.5% or more, is considered a diagnostic criterion for presence of DM in a patient **[10]**.

Another strong point for HbA1C% is that its level can reflects post-prandial spikes in the blood glucose level **[11]**. Post-prandial hyperglycemia has been strongly related to DM complications. However, patients with postprandial hyperglycemia do not always present with a high fasting blood glucose value **[12]**. In these patients, fasting blood glucose may underestimate the severity of gluco-metabolic affection. This phenomenon gives

superiority to HbA 1 C% over fasting glucose for long-term macro-vascular risk stratification [13].

Elevated HbA1C% levels in diabetic patients are not only associated with higher cardiovascular events and mortality, but also strongly associated with increased all-cause mortality [14]. It is now well-established that elevated HbA1c% is associated with presence of CAD and severity of its morbidity and mortality even in non-diabetics [15].

Many studies reported the relationship between HbA1c% and stable CAD in non-diabetics, but few studies focused exclusively on the relationship between HbA1c% and Acute Coronary Syndrome (ACS) and severity of its presentation in non-diabetic patients.

Subjects and Methods

A cross-sectional study carried-out in Cardiovascular Medicine Department, Tanta University Hospitals, from May 2016 to April 2017. The study included 123 non-diabetic patients presented to our CCU in Cardiology Department of Tanta University Hospitals with ACS. All patients received proper emergency care. TTE and diagnostic coronary angiography were done as part of their management.

Exclusion criteria were: (1) Known diabetics (on/off medications). (2) Patients with chronic stable CAD.

For all included patients, the following were done:

- Detailed history taking, general and local examinations.
- Urgent Electro-Cardiogram (ECG) with cardiac bio-markers testing (high-sensitivity troponin).
- Categorization of clinical presentations of patients to either unstable angina, Non-ST Elevation Myocardial Infarction (NSTEMI) or ST Elevation Myocardial Infarction (STEMI).
- Laboratory essays included: renal profile, random blood sugar, fasting blood sugar and HbA1c% for all patients.
- TTE was performed by competent echocardiographic performers to evaluate both diastolic and systolic functions. Systolic function (Ejection Fraction=EF) was assessed using simpson method. Resting Segmental Wall Motion Abnormalities (RSWMAs) were assessed in all TTE views.
- Coronary angiography was performed by Judkin's technique. Two experienced cardiologists analyzed the results to figure out the number of coronary artery stenosis.
- The synergy between PCI with TAXUS and cardiac surgery (SYNTAX) score was applied, interpreting the coronary angiographic findings to assess complexity of coronary tree affection. According to the diagnostic angiogram, each coronary lesion creating a stenosis obstructing ≥50% of the diameter in vessels ≥1.5mm was scored separately, and these scores were added together to produce the overall SYNTAX score, which was calculated using SYNTAX algorithm. This algorithm is available on the SYNTAX website [16].

Statistical presentation and analysis of the present study was conducted, using the mean, standard deviation and chi-square tests by SPSS. V. 20. Numerical data was presented as mean and Standard Deviation (SD) and categorical data was presented as number and percentage. Chi-square test was used for statistical analysis. When the chi-squared test was not appropriate, the Fisher likelihood ratio test was applied. The level of significance was adopted at $p<0.05$.

Subjects were informed about the purpose, procedure and benefits of the study. Ethical considerations were carried out according to Helsinki Declaration.

Results

The study population was stratified according HbA1c% into tertiles: (1 st) HbA1c% ≤5.5% (n=47), (2nd) HbA1c%=5.6-5.9% (n=35), (3 rd) HbA1c%= 6.0-6.4% (n=41).

Age of the study participants ranged from 28-81 with a mean of 56.2±11.6 years old. More than two thirds (71.5%) of them were males. Hypertensive patients represented 53.7% of all study patients. As regard smoking, more than half (59.3%) of the patients were smokers. As regard cholesterol level, 30.9% of the patients had cholesterol level ≥200 mg/dl. 19% of the patients had family history of pre-mature coronary heart diseases (Table 1).

Fasting glucose level ranged from 75 to 124 mg/dl with a mean of 105.2±10.6 as the study included only non-diabetic patients. Serum creatinine level among study patients ranged from 0.6 to 9.0 (mg/dl) with a mean of 1.26±0.79. CK-MB ranged from 5 to 313 with a mean of 87.73±64.14. Regarding Troponin, it was positive in 73.2% of the study patients.

When patients were distributed according to ACS presentation, we found that nearly two thirds (65.8%) of them were presented with STEMI, one

sixth (17.1%) of them presented with NSTEMI and one sixth (17.1%) of them presented with Unstable Angina (Table 3).

More than half of the patients (56.1%) of the patients had Ejection fraction <50% by Simpson method. As regard diastolic dysfunction, Grade I diastolic dysfunction represented 71.5%, Grade II represented 25.2%, and Grade III represented 3.3% of study patients (Table 4).

Affection of one coronary epi-cardial vessel only was found in 38.2% of the patients. While 34.1% of the patients had two-vessel disease, 26.0% had three-vessel disease (Table 5).

SYNTAX score among study patients ranged from 5-35 with a mean of 15.13 ±7.01.

Highest percentage of hypercholesterolemia (48.8%) was present in patients with HbA1c% level ranging from 6-6.4% (the 3 rd tertile) and there was statistically significant relationship between HbA1c% level and hypercholesterolemia. The highest serum creatinine level was also present among the patients of the third HbA 1 c% tertile (6-6.4%) (Table 6).

It was found that HbA 1 c% level had a statistically significant relationship with severity of ACS presentation. Unstable angina represented the highest percentage among patients with HbA1c% ≤5.5%. While, patients with STEMI represented the highest percentage among patients with HBA 1 c ranging from 6 to 6.4%. (Table 7).

HbA1c% level had a statistically significant relationship on Ejection Fraction (EF%) estimated by Simpson method. The percentage of systolic dysfunction (EF% <50%) as assessed by Simpson method was as the following; 78.9% in the 3 rd HbA1c% tertile, 62.9% among 2 nd HbA1c% tertile group, and only 31.9% among 1 st HbA1c% tertile group. (Table 8).

The mean value of EF% in the studied was higher in the 1 st tertile (50.92±8.16) and was the lowest in the 3rd tertile(43.56± 11.30). (Table 9).

HbA1c% level had a statistically significant effect on SYNTAX score. the mean of SYNTAX score among 1 st tertile patients was much lower than 2 nd and 3 rd tertiles respectively. (Table 10).

A statistically significant positive moderate correlation was present between HbA1c% and SYNTAX score. A statistically significant positive moderate correlation was present between HbA1c% and no of affected vessels. A statistically significant negative moderate correlation was present between HbA1c% and ejection fraction by Simpson method.

It was observed that significant correlation occurred between severity of acute coronary syndrome presentation and HbA1c% level in non-diabetics continued even after adjustment to other known risk factors of acute coronary syndrome. (Table 12).

Table (1): Basic characteristics of the study population.

Characteristics	n=(123)	(%)
Age:		
Range	28-81	
Mean ± S.D	56.2± 1 1.6	
Gender:		
Male	88	71.5
Female	35	28.5
Hypertension	66	53.7
Smoking	73	59.3
Hyperlipidemia: (Cholesterol level ≥200mg/dl)	38	30.9
Family history	19	15.4

Table (2): Laboratory characteristics of the study population.

Characteristics	Mean ± SD	Range
Fasting glucose level (mg/dl)	105.2± 10.6	75-124
Serum creatinine (mg/dl)	1.26±0.79	0.6-9.0
CK-MB (mg/dl)	87.73±64.14	5-313
Positive Troponin (no.)	90 (73.2%)	

Table (3): Patients distribution according to acute coronary syndrome presentation.

ACS. presentation	No.	(%)
Unstable angina	21	17.1
NSTEMI	21	17.1
STEMI	81	65.8
Total	123	100.0

Table (4): Echocardiographic findings of the study patients.

Echo-cardiographic findings Systolic function		
Ejection fraction (Simpson method):		
<50%	69	56.1%
≥50%	54	43.9%
Diastolic dysfunction:		
Grade I	88	71.5%
Grade II	31	25.2%
Grade III	4	3.3%

Table (5): Number of affected coronary vessels by diagnostic coronary angiography.

Diagnostic coronary angiographic findings Number of vessels affected		
1 vessel	47	3 8.2%
2 vessels	42	34.1%
3 vessels	32	26.0%
4 vessels	2	1.6%

Table (6): HbA1c% tertiles and different laboratory findings of the study patients.

Variables	HBA1c Tertiles 1st Tertile ≤5.5% (n=47)	2nd Tertile 5.6-5.9% (n=35)	3rd Tertile 6.0-6.4% (n=41)	Sig. test	*p*.
• Hypercholesteremia	11 (23.4%)	7 (20.0%)	20 (48.8%)	χ^2 12.478	0.006*
• Serum creatinine Mean ± S.D	1.12± 0.21	1.18± 0.47	1.49± 1.25	F 2.538	0.060

*: Statistically significant.
χ^2 : Chi square test.
F : One way Analysis Of Variance (ANOVA).

Table (7): Glycated Hemoglobin (HbA1c%) and Acute Coronary Syndrome (ACS).

Variables	HbA1c tertiles 1st Tertile ≤5.5% (n=47)	2nd Tertile 5.6-5.9% (n=35)	3rd Tertile 6.0-6.4% (n=41)	χ^2	*p*.
Unstable angina	18 (38.3%)	1 (2.9%)	2 (4.9%)	28.67	0.001*
NSTEMI	10 (21.3%)	6 (17.1%)	5 (12.2%)		
STEMI	19 (40.4%)	28 (80.0%)	34 (82.9%)		

*: Statistically significant.
χ^2 : Chi square.

Table (8): Relationship between HbA1c% tertiles and echocardiographic findings.

Variables	HBA1c Tertiles 1st Tertile ≤5.5% (n=47)	2nd Tertile 5.6-5.9% (n=35)	3rd Tertile 6.0-6.4% (n=41)	χ^2	*p*.
• *EF (Simpson method):*					
<50%	15 (31.9%)	22 (62.9%)	32 (78.9%)	19.831	0.001
≥50%	32 (68.1%)	13 (37.1%)	9 (22.0%)		
• *Diastolic dysfunction:*					
Grade I	36 (76.6%)	25 (71.4%)	27 (65.9%)	3.273	0.513
Grade II	11 (23.4%)	8 (22.9%)	12 (29.3%)		
Grade III	0 (0%)	2 (5.7%)	2 (4.9%)		

*: Statistically significant.
χ^2 : Chi square.

Table (9): Glycated hemoglobin tertiles and mean value of ejection fraction.

Variables	HBA1c Tertiles 1st Tertile ≤5.5% (n=47)	2nd Tertile 5.6-5.9% (n=35)	3rd Tertile 6.0-6.4% (n=41)	Sig. test	*p*.
• EF: (Simpson method) Mean ± S.D	50.92±8.16	45.19±7.05	43.56±11.30	F 8.522	0.001*
• Comparing groups	p_1 0.001*	p_3 0.459	p_3 0.005*		

Table (10): Glycated hemoglobin (HbA1c%) and SYNTAX score.

SYNTAX score	HBA1c Tertiles 1st Tertile ≤5.5% (n=47)	2nd Tertile 5.6-5.9% (n=35)	3rd Tertile 6.0-6.4% (n=41)	F	*p*.
Mean ± S.D	10.55±4.07	17.25±6.88	18.55±7.05	22.228	0.001*

*: Statistically significant.
F: One way Analysis of Variance (ANOVA).

Table (11): Correlation between (HBA1c%) and other variables.

Correlations	*r*. HBA1 c	*p* HBA1 c
Age	0.253	0.005*
SYNTAX score	0.504	0.001 *
No of vessels	*p* 0.397	0.001 *
EF% Simpsons	–0.466	0.001 *

r.: Pearson correlation.
p: Spearman correlation.
*: Statistically significant.

Table (12): HbA1c% as a risk factor for severity of acute coronary syndrome adjusted to other common risk factors.

ACS	Glycated hemoglobin HbA1 c% Adjusted for age, sex, family history, hypertension, and cholesterol level OR (95% CI)	*p*-value
Unstable angina	0.02 (0.04-0.94)	0.001*
NSTEMI	0.285 (0.103-0.790)	0.016*
STEMI	3.506 (1.265-9.718)	0.001*

Discussion

We found that there is significant relationship between on admission glycated hemoglobin level HbA1c%) in non-diabetics and presentation of ACS either unstable angina or NSTEMI or STEMI. (*p*-value=0.001). On one hand, the main bulk of unstable angina cases was found in the first HbA 1 c tertile (non pre-diabetic group). On the otherhand, the majority of STEMI patients fell into the 2 nd and 3 rd tertiles especially the third one. This significant results was similar to findings of Anping et al., [17]. That study also showed that the levels of HbA1c% were gradually and significantly higher in unstable conditions in terms of unstable angina and acute myocardial infarction in comparison with chronic stable angina episodes. So, they suggested that increased HbA1c% level might play a role in atherosclerotic plaque pro-rupture, as it is widely known that biologically, glycated hemoglobin HbA1c% is an advanced glycosylation end-product, and increased HbA1c% level could reflect more generation of advanced glycosylation end-product, which might subsequently abundantly attach to vessel wall causing endothelial dysfunc-

tion, oxidative stress promotion and eventually rupture of plaque and emergence of ACS.

This significant relationship between ACS and HbA1c% level in non-diabetics persisted even after adjustment for other known risk factors of CAD and confounders such as age, sex and family history, hypertension and hyperlipidemia.

Statistically significant relationship and negative moderate correlation were found between on admission HbA1 c% level and severity of LV systolic function affection as estimated by Simpson method (p-value=0.001) through TTE done to ACS patients during their admission in our department. The mean value of EF% in our study population was higher in the 1^{st} tertile (50.92 ± 8.16) and was the lowest in the 3^{rd} tertile (43.56 ± 11.30). Similar results were found by the study conducted by Saeed et al., 2016 **[18]**. In that study, the chosen population was presenting with unstable angina. Data analysis revealed that on-admission HbA1c% level was significantly higher in patients with EF $\leq 50\%$ in comparison with EF >50% group (p-value=0.01).

Statistically significant relationship was found between on admission HbA1c% level and severity of coronary tree affection as shown by diagnostic coronary angiography done to our ACS patients. Our results showed that HbA 1 c% level had a statistically significant relationship (p-value=0.002) with the number of affected vessels as diagnosed by coronary angiography. This is consistent with the results of Anping et al., **[17]** which showed that there is a significant association between HbA 1 c% level and the severity of CAD in non-diabetic population, even after adjustment for traditional risk factors, and this relationship is independent of fasting blood glucose.

Our results concerning coronary angiographic assessment and scoring of our patients are to some extent similar to Rivera et al., **[19]** who studied relation between level of HbA1c% and CAD in 1043 asymptomatic Korean individuals without DM who underwent 64-slice cardiac computed tomography angiography as part of a health screening evaluation and found that increasing levels of HbA 1 c in individuals without DM are associated with the presence of coronary atherosclerosis **[19]**. However, his selected population was different, as they were asympotomatic non-diabetic patients.

Naveen et al., **[20]** also found similar results in non-diabetic Indian patients referred to have diagnostic coronary angiography **[20]** similar results were also obtained by Ashraf et al., **[21]** who enrolled 299 consecutive non-diabetic individuals undergoing coronary angiography for suspected ischemia and studied the association between glycated hemoglobin HbA1c% and angiographically proven coronary artery disease CAD and its severity in nondiabetic individuals. They found that with increasing HbA 1 c% levels, there was a significant increase in the prevalence of CAD and number of vessels involved. In multivariate analysis, HbA1c% emerged as an independent predictor of significant CAD (OR: 2.8, 95% CI: 1.3-6.2, p=0.009) **[21]**.

Verdoia M et al., **[22]**, also evaluated the relationship between HbA1c% and CAD in a group of non-diabetic patients undergoing coronary angiography and found that HbA1c%, not fasting glycemia, was significantly associated with the prevalence of CAD (adjusted OR:1.51, 95% CI:1.15, 1.97, p:0.002). Conflicting results were obtained by Doer et al., **[23]** who compared HbA1c% with OGT for early detection of silent diabetes, presence and progression of angiographically CAD in routine catheterization laboratory patients. They found no correlation between HbA1c% levels and angiographically proven presence or progression of CAD **[23]**.

In our study, we found a statistically significant positive moderate correlation between HbA1c% and SYNTAX score (p-value=0.001) and also statistically significant positive moderate correlation was present between HbA1c% and number of affected vessels. (p-value=0.001).

Considering this correlation between HbA1c% and SYNTAX scoring for CAD angiographic severity, our results were similar to results of Yaron et al., **[24]**. They evaluated 226 non-diabetic patients hospitalized with myocardial infarction or stable angina and underwent coronary angiography. Glucose intolerance was assessed by serum admission glucose, fasting glucose and HbA1c levels. HbA1c% was the only gluco-metabolic factor associated with higher SYNTAX score above 22 (OR=3.03, CI 95% 1.03-8.9, p=0.04). HbA1c% was also significantly associated with CAD presentation and severity in subgroup analysis.

Similar results were obtained by Bornali et al., **[25]** which showed that increasing HbA 1 c% level was strongly correlated with disease severity, number of diseased vessels and higher SYNTAX score, in a graded fashion (p<0.001) in non-diabetics. Also, linear regression analysis showed that HbA 1 c% values were significantly correlated with the SYNTAX score. It showed also that with increasing HbA 1 c% levels, a significant increase was noted in the mean number of diseased vessels

(p-value <0.001). Similarly there was a linear correlation between HbA 1 c% and number of vessels involved (r–0.402 and 0.429; p<0.001) in non-diabetics [25].

In non-diabetic patients in the study, mean SYNTAX score significantly increased with increased HbA1c levels (SYNTAX scores were 6.5, 7.8, 11.5 and 20.22 in patients with HbA1c levels <4.8, 4.8-5.1, 5.1-5.6 and 5.6 to <6.5 respectively). In SYNTAX subgroups (<23, 23-32 and >32), mean HbA1c values were 4.9±0.4, 5.7±0.3 and 6.0±0.92 respectively [25].

Ghaffari et al., [26], studied coronary angiographic findings and multi-vessel involvement based on HbA1c% quartiles in non-diabetics. Non-diabetic patients with HbA1c >5.8% had twice more chance of having triple-vessel diseases [Odds Ratio (OR)=2.21, 95% CI 1.34-3.65; p=0.002] [26].

Sasso et al., [27] also found that HbA1c% levels in patients with normal glucose tolerance are significantly higher in those with more severe CAD disease.

Kowalska et al., [28] observed that those with advanced damage in the coronary arteries experienced a higher prevalence of glycemic disturbances. The authors observed that level of HbA1c% is significantly, but not independently, correlated with the number of involved vessels [28] this significant correlation between glycated hemoglobin HbA1c% and CAD severity were also found when CAD severity was assessed by Gensini score [21]. That study was designed as a prevalence study and hence does not attempt to offer a pathogenic explanation for the relationship between glucose metabolism and CHD in non-diabetic patients. In this regard, some authors suggested that advanced glycation end products could play a pathogenic role by impairing cytokine production, [29] monocyte activation [30] or endothelial function.

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الهيموجلوبين السكرى كمؤشر على شدة متلازمة الشريان التاجى الحادة لدى غير المصابين بداء السكرى

تعتبر آمراض الشرايين التاجية من آهم آسباب الوفاة حول العالم. ومتلازمة الشريان التاجى الحادة هى آخطر مضاعفاتها الطارئة. وتشير الدراسات المتاحة الآن إلى مدى خطورة إضطرابات آيض الجلوكوز فى التسببية المرضية لآمراض الشرايين التاجية. لا يقتصر الآمر على مرض السكرى فقط، إنما آيضا على الحالات التى تسمى بما قبل السكرى، كإختلال عدم تحمل الجلوكوز، وإختلال إرتفاع السكر الصائم. فقد آصبحت هذه الحالات هى آيضا من عوامل الخطر لآمراض الشرايين التاجية ومضاعفاتها والوفيات الناجمة عنها. ومن هنا جاءت آهمية دراسة متغيرات قياس الإختلالات السكرية وفى مقدمتها الهيموجلوبين السكرى.

تم إدراج مائة وثلاثة وعشرين مريضا من غير المصابين بداء السكرى، ممن عانوا من آى من درجات متلازمة الشريان التاجى الحادة وتم حجزهم بعناية القلب بمستشفيات جامعة طنطا فى الفترة بين مايو ٢٠١٦–آبريل ٢٠١٧. تم آخذ التاريخ المرضى كاملا، وإجراء الفحص السريرى المفصل، وعمل رسم قلب كهربائى، والتحاليل الطبية الآساسية كإنزيمات القلب، ووظائف الكلى، والسكر العشوائى، ونسبة الكوليسترول بالدم، ونسبة الهيموجلوبين السكرى بالدم. وكذلك إجراء قسطرة قلبية تشخيصية، وعمل موجات صوتية على عضلة القلب عن طريق الصدر.

ظهر وجود علاقة طردية قيمة إحصائيا بين مستوى الهيموجلوبين السكرى فى دم المرضى غير المصابين بداء السكرى، ودرجة الإصابة بمتلازمة الشريان التاجى الحادة. وقد ثبتت العلاقة بعد تحييد عوامل الخطر التقليدية الآخرى كإرتفاع ضغط الدم، والكوليسترول، والعمر، والتاريخ المرضى العائلى. وكذلك وجدت علاقة طردية قيمة إحصائيا بين مستوى الهيموجلوبين السكرى، ومدى تضرر وظيفة عضلة القلب الإنقباضية نتيجة الإصابة، وآيضا مدى تضرر شرايين القلب التاجية كما ظهر فى القسطرة القلبية التشخيصية، وكما تم تقديره بمعامل سينتاكس.

وجد إرتباط بين مستوى الهيموجلوبين السكرى فى دم غير المصابين بمرض السكرى، ومدى شدة إصابتهم بمتلازمة الشرايين التاجية الحادة، وكذلك مدى تضرر الشرايين التاجية كما يظهر بالقسطرة القلبية التشخيصية. وتحافظ هذه العلاقة على وجودها بعد تحييد عوامل الخطر التقليدية. والسبب قد يرجع إلى آن الهيموجلوبين السكرى يعبر عن الإختلال فى آيض الجلوكوز، ويعبر عن الإرتفاع المزمن فى معدلات الجلوكوز حتى وإن كانت تحت الخط الآحمر اللازم لتشخيص داء السكرى. هذا الإختلال الآيضى المزمن، يؤدى إلى تراكم منتجات سكرية ضارة فى جدران الشرايين التاجية خاصة تلك المصابة بالتصلب الشريانى نتيجة تراكم الدهون الضارة بها. وهذا يزيد من إحتمال حدوث الإلتهاب والإنفجار الحادة فى العقد الدهنية التصلبية، وهذه هى الآلية التى تبدآ المسار المرضى الخطير لتجلط الدم داخل الشرايين المصابة، وحدوث متلازمة الشريان التاجى الحادة بمختلف درجاتها.