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Correlation between Serum Fructosamine Level and Severity of Coronary Artery Disease in Diabetic Patients with Symptomatic Chronic Coronary Syndrome

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Abstract

Background: In patients with diabetes mellitus (DM), compared with those without DM, (CAD) tends to be more diffuse, complex, and associated with increased morbidity and mortality from cardiovascular disease. The SYNTAX score (SS) uses coronary anatomy to objectively guide decisions regarding mode of revascularization. It characterizes the extent of coronary disease in terms of the number of lesions, their functional importance, and their complexity, while GENSINI Score accounts for the degree of artery disease in diabetic patients.

Aim of Study: The aim of this study was to assess the correlation between fructosamine level and the severity of CAD by calculating SYNTAX and GENSINI scores in diabetic patients presenting to Ain Shams University Hospital with symptomatic chronic coronary syndrome undergoing elective coronary angiography.

Patient and Methods: This study was conducted on 200 diabetic patients with chronic coronary syndrome undergoing elective coronary angiography, with mean age 54.36±5.86 years ranging from 32 years to 65 years. The majority of them were males (64%).

Results: Atotal of 200 diabetic patients were included in the study. Mean ± SD age was 54.36±5.86 years. Of the total 64% (128) were males, 74% (149) were hypertensive and 57% (113) were smokers.We found that higher fructosamine level was strongly correlated with disease severity and higher SYNTAXas well as GENSINI score as fructosamine and SYNTAX score (r=0.668) and with GENSINI (r=0.734) (p-values <0.001 and <0.001 respectively). A significant increase in fructosamine level was notedin higher tertiles of SYNTAX and GENSINI scores (p-values <0.001 and <0.001 respectively). There was also a positive correlation between both HbA1c and SYNTAX score (r=0.636) and with GENSINI score (r=0.716).

Conclusion: There was a significant correlation between serum fructosamine level and severity of CAD assessed by the angiographically derived SYNTAX and GENSINI scores and fructosamine may have a value as a predictor of severity of CAD and risk stratification of diabetic patients as patients with a higher level of fructosamine had significant severe lesions where higher SYNTAX (third tertile >32) and Gensini (third tertile >38). In addition to that a strong positive correlation was found between markers of glycemic variability fructosamine and HbA1c.

Key Words: *Coronary artery disease – Diabetes mellitus – Fructosamine.*

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Introduction

IN patients with diabetes mellitus (DM), compared with those without DM, coronary artery disease (CAD) tends to be more diffuse, complex, and associated with increased morbidity and mortality from cardiovascular disease **[1,2]**.

Cardiac disease that develops as a direct consequence of DM in patients with type 1 DM (T1DM) or type 2 DM (T2DM) is known as diabetic heart disease. Diabetic heart disease is a conglomeration of CAD, cardiac autonomic neuropathy (CAN), and diabetic cardiomyopathy (DCM), and these diseases are characterized by molecular, structural, and functional changes in the myocardium **[3]**.

The SYNTAX score (SS) uses coronary anatomy to objectively guide decisions regarding mode of revascularization **[4,5]**. Studies have confirmed the clinical validity of the SS for identifying higher-risk subjects and aiding decision making between CABG and PCI in a broad range of patient types **[6,7]**. It characterizes the extent of CAD in terms of the number of lesions, their functional importance, and their complexity. Previous studies have categorized the SYNTAX score to identify patients at low (22), medium (2332), and high (33) risk and demonstrated superior outcomes for patients

receiving CABG over PCI, primarily in those patients with high SYNTAX scores.

The number of diseased coronary vessels is not the only marker for CAD severity. The location of the lesions and their impact on blood flow, the degree of vessel stenosis, lesion classifications, and the diameter and calcification of the vessel are also important factors that affect the technical feasibility of performing PCI, and the prognosis. Considering these factors, there are different degrees of multivessel disease and the preferred revascularisation strategy may be different for specific lesion complexities. To assess this hypothesis both the angiographic SYNTAX score and GENSINI score were introduced **[8,9]**.

The INTERHEART study supported the association between diabetes and MI on a global platform. With the implementation of appropriate primary prevention strategies, the risk for first-time cardiovascular complications has come down significantly. Similarly, with effective revascularisation techniques and secondary prevention strategies, the risk for recurrent cardiovascular events has significantly reduced **[10]**.

Interestingly, the ADA has acknowledged that in patients in whom HbA1c and blood glucose are unreliable (especially those with hemoglobinopathies, altered red cell turnover or impaired renal function), the assessment of other indices of chronic glycemia may be advisable, although their relation with average glucose and prognosis remains uncertain. These alternative measures essentially include fructosamine and glycated albumin (GA) **[11]**.

Aim of the work:

To assess the correlation between fructosamine level and the severity of CAD by calculating SYNTAX score and GENSINI score in diabetic patients presenting to Ain Shams University Hospitals with symptomatic chronic coronary syndrome undergoing elective coronary angiography.

Patients and Methods

Patients: This study included 200 diabetic patients with symptomatic chronic coronary syndrome who presented to Ain Shams University hospital for elective coronary angiography.

Inclusion criteria: Diabetic patients with symptomatic chronic coronary syndrome presented to Ain Shams University Hospital to undergo elective coronary angiography. Age group from 18-60 years old.

Exclusion criteria: Patients with normal coronary angiography. Patients with renal failure (eGFR <40%). Patients with hypoalbuminemia (serum albumin <3.5).

Methods:

Study design: It is a single-center observational cross-sectional study performed at Ain Shams University Hospital during the period from November 2021 to January 2022. Our study included patients with documented CAD by invasive coronary angiogram. A total of 200 diabetic patients who were admitted with symptomatic chronic coronary syndrome had undergone non-emergent coronary angiogram were included.

Prior to elective coronary angiography, the patients were subjected to the following:

History taking: All the patients were subjected to the following: Personal, present, past and family history and the major coronary artery disease documented risk factors (HTN, DM, dyslipidemia, smoking, family history of CAD)

CAD documented risk factors:

- *Diabetes:* Classification and duration of diabetes, use of antidiabetics (oral hypoglycemic meds vs. Insulin) (controlled vs. uncontrolled), fasting blood glucose, hemoglobin A1c (HbA1c), presence of diabetic complications (diabetic retinopathy, diabetic neuropathy, diabetic nephropathy). DM was diagnosed in patients with fasting serum glucose level of 126mg/dl by multiple determinations or under active treatment with insulin or oral hypoglycemic agents **[12]**.
- Hypertension: Duration and antihypertensive medications used (controlled vs. uncontrolled). Hypertension was defined as repeated (at least two times in different peaceful circumstances) blood pressure measurements 140/90mmHg or currently taking antihypertensive drugs **[13]**.
- *Dyslipidemia:* Lipid profile and presence or absence of familial dyslipidemia.
- *Smoking:* (Active or passive) and calculating smoking index.

Personal History: Including demographic data.

Present History (symptomatology): Chest pain, its relation to physical activity, and radiation of the pain into the jaw, neck, left arm, or into the back. Dyspnea at rest and also on activity. Syncope, palpitations, tachypnea, lower extremity edema, orthopnea, and exercise capacity.

Past History of previously documented ASCVD: CAD was defined as the presence of significant obstructive stenosis, at least 50% of the vessel lumen diameters, in any of the main coronary arteries by at least two independent senior interventional cardiologists based on quantity coronary angiography. History of acute coronary syndrome, elective CA±PCI, Cerebrovascular disease (stroke-hemorrhage) or Peripheral vascular disease.

Family History of premature CVD: Premature CAD was defined as the presence of a primary relative who had been diagnosed with CAD prior to the age of 55 years in a male relative or 65 years in a female relative).

Surgical history and Drug history:

Thorough clinical examination: General and local examination and excluding other chronic illnesses as follow: Body mass index was calculated (the weight in kilograms divided by the square of height in meters). Blood pressure and heart rate were recorded. Cardiac examination (auscultation and palpation for thrill and heave). Chest auscultation for excluding any chest infection or signs of congestion. Lower limb examination (The extent of peripheral edema if present was evaluated).

Electrocardiogram: Initial ECG was recorded and considered baseline ECG.

Conventional 2D echocardiography: Full echocardiographic study was done by an expert to assess LV systolic and diastolic function, LV internal dimensions, resting segmental wall motion abnormalities, cardiac valves morphology and function and RV function.

Routine Laboratory investigations: cbc. fasting plasma glucose.serum cholesterol, serum triglycerides, HDL, LDL.renal function tests.liver function tests.virology markers.coagulation profile / HbA1C. Glycated hemoglobin A1c (HbA1c) was estimated by high pressure liquid chromatography (Bio-Rad, Hercules, CA). The intra and inter assay coefficient of variation of HbA1c was less than 5%.

Fructosamine level using (HUMAN FRUCTOSAMINE ELISA KITS): By adding fructosamine (FRA) to monoclonal antibody enzyme well which was pre-coated with Human fructosamine (FRA) monoclonal antibody, incubated; then, fructosamine (FRA) antibodies were added labeled with biotin, and combined with Streptavidin-HRP to form immune complex; then incubation was carried out with washing again to remove the uncombined enzyme. Then Chromogen Solution A, B, the color of the liquid changes into the blue, and at the effect of acid, the color finally became yellow. The chroma of color and the concentration of the Human Substance fructosamine (FRA) of sample were positively correlated. Sensitivity: 0.042mmol/L: The sensitivity of this assay was defined as the lowest protein concentration that could be differentiated from zero. Assay range: 0.05mmol/L→15mmol/L CV(%) = SD/meanX100. Intra-Assay: CV <10%. Inter-Assay: CV <12%.

Coronary angiography (CA): All patients were informed about the exam and written consent was obtained. CA was performed using standard diagnostic catheters (JR3.5 and JL3.5), Seldinger's technique through femoral approach. The maximum contrast dose was calculated, according to the formula (5 x body weight [kg])/serum creatinine). Reno-protection in the form of adequate hydration, 0.9% saline 500mls at least 2h before and 2h after the procedure, and oral N- Acetylcysteine 600mg twice daily at day –1, 0, and +1 was administered in all cases. All potentially nephrotoxic drugs were withheld 24h before the angiogram, and recommenced 48h later, if not contraindicated. In the cath lab room ECG and invasive hemodynamic monitoring were done, then sterilizations precautions were followed an arterial line was done by the percutaneous modified Seldinger's technique.

SYNTAX and GENSINI scores were calculated as follow:

Syntax score: An angiographic grading tool to quantify the complexity of left main (LM) or three-vessel disease, it was developed through expert consultation and integrated previous angiographic scores that assessed lesion complexity. Score is classified into 3 tertiles Mild<22, moderate 22-32 and severe >32 (Table 1) **[14]**.

GENSINI score:

Calculation of the Gensini score was initiated by giving a severity score to each coronary stenosis as follows: **[15]**

- 1 point for 25% narrowing.
- 2 points for 26 to 50% narrowing.
- 4 points for 51 to 75% narrowing.
- 8 points for 76 to 90% narrowing.
- 16 points for 91 to 99% narrowing.
- 32 points for total occlusion.

Thereafter, each lesion score is multiplied by a factor that takes into account the importance of the lesion's position in the coronary circulation.

- 5 for the left main coronary artery.
- 2.5 for the proximal segment of the left anterior descending.

- Coronary artery.
- 2.5 for the proximal segment of the circumflex artery.
- 1.5 for the mid-segment of the left anterior descending coronary artery.
- 1.0 for the right coronary artery, the distal segment of the left anterior descending coronary artery, the posterolateral artery, and the obtuse marginal artery.
- 0.5 for other segments.

Finally, the Gensini score was calculated by summation of the individual coronary segment scores. The patients were classified into 3 groups according to the tertile of Gensini score.

- Mild <11, moderate 11-38 and severe >38.

Statistical analysis:

All data were collected, tabulated and statistically analyzed using SPSS 26.0 for windows (SPSS Inc., Chicago, IL, USA). Qualitative data were described using number and percent. Quantitative data were described using range (minimum and maximum), mean, standard deviation and median. All statistical comparisons were two tailed with significance Level of p-value 0.05 indicates significant, $p<0.001$ indicates highly significant difference while, $p>0.05$ indicates non-significant difference. Correlation between continuous variables was determined by Pearson correlation coefficients. Linear regression analysis was performed to show association between severity of CADand markers of glycemic control (fructosamine and HbA 1 c).

Table (1): Guide for calculating online Syntax score **[14]**.

Step 1	Dominance	The weight of individual coronary segments varies according to coronary artery dominance (right or left). Co-dominance does not exist as an option in the SYNTAX score.
Step 2	Coronary segment	The diseased coronary segment directly affects the score as each coronary segment is assigned a weight depending on its location, ranging from 0.5 (i.e. the posterolateral branch) to 6 (i.e. left main in case of left dominance).
Step 3	Diameter stenosis	The score of each diseased coronary segment is multiplied by two in case of a stenosis 50-99% and by five in case of total occlusion. *In case of total occlusion, additional points will be added as follows:* - Age >3 months or unknown +1 - Blunt stump +1 - Bridging +1 - First segment visible distally +1 per non-visible segment - Side branch at the occlusion +1 if <1.5 mm diameter +1 if both <1.5 mm and 1.5 mm diameter +0 if 1.5 mm diameter (ie. bifurcation lesion)
Step 4	Trifurcation lesion	*The presence of a trifurcation lesion adds additional points based on the number of diseased segments:* - 1 segment +3 • 2 segments +4 -3 segments +5 • 4 segments +6
Step 5	Bifurcation lesion	The presence of a bifurcation lesion adds additional points based on the type of bifurcation according to the Medina classification: 126 Medina 1,0,0-0,1,0-1,1,0 +1 Medina 1,1,1-0,0,1-1,0,1-0,1,1 +2 Moreover, the presence of a bifurcation angle <70° adds one additional point.
Step 6	Aorto-ostial lesion	The presence of aorto-ostial lesion segments adds one additional point.
Step 7	Severe tortuosity	The presence of severe tortuosity proximal of the diseased segment adds two additional points.
Step 8	Lesion length	Lesion length >20 mm adds one additional point.
Step 9	Calcification	The presence of heavy calcification adds two additional points.
Step 10	Thrombus	The presence of thrombus adds one additional point.
Step 11	Diffuse disease/ small vessels	The presence of diffusely diseased and narrowed segments distal to the lesion (i.e. when at least 75% of the length of the segment distal to the lesion has a vessel diameter <2 mm) adds one point per segment number.

Results

The study population was 200 diabetic patients who were recruited in a prospective fashion from the Cardiology Department at Ain Shams University Hospital 2021. The aim of the study was to assess the correlation between serum fructosamine level and severity of CAD by calculating SYNTAX and GENSINI scores in patients with chronic coronary syndrome undergoing elective coronary angiography.

Demographic data and risk factor distribution among the study population:

The study was conducted with a total of 200 diabeticcases,199 (99.50%) were type 2 vs. 1 (0.50%) were type 1 and 64% (n=128) were males. The ages of the patients ranged from 32 to 65 years with a mean age of 54.36±5.86 years. Of the total 74.50% (n=149) were HTN while 113 (57%) were smokers. Diabetic complications were shown in 7% of the study population only in peripheral vascular disease 14 patients (7%). Hyperlipidemia among the study population was shown in 130 cases (65%) andpast history of CAD among the study population was shown in 43% of patients. Family history of CAD was found in 45 patients (22.50%) (Table 2).

Table (2): Demographic data and risk factors' distribution among the study population.

	Study population (n = 200)	
	Number	Percentage %
Gender:		
Male	128	64
Female	72	36
Age (years):		
Mean ± SD.	54.36±5.86	
Median (IQR)	56 (50-60)	
Range (Min-Max)	33 (32-65)	
Risk factors:		
1- Smoking	113	57
2- Hypertension	149	75
3- Diabetes mellitus	200	100
NIDDM	199	99.5
IDDM	1	1
4- Diabetic complications	14	7
5- Hyperlipidemia	130	65
6- Past History of CAD	83	43
7- Family history of CAD	45	22.5

Markers of glycemic control:

HbA1c in the study population ranged from 6.5 to 14.3, with mean ± SD of 9.61±2.01 while fructosamine level in the study population ranged from 201 to 653, with mean ± SD of 392.31±123.28 umol/L (Table 3).

Table (3): Measurements of HbA1c and Fructosamine among the study population.

	Study population (n = 200)	
	HbA1c	Fructosamine
Mean ± SD.	9.61±2.01	392.31±123.28
Median (IQR)	9.1 (8-11)	378.5 (292.9-477)
Range (Min-Max)	7.8 (6.5-14.3)	452 (201-653)

Coronary artery disease severity assessment scores:

SYNTAX score in the study population ranged from 4 to 58, with mean ± SD of 25.4±11.09 while GENSINI score ranged from 4 to 160, with mean ± SD of 58.86±37.92 (Table 4).

Table (4): Measurements of SYNTAX score and GENSINI score among the study population.

	Study population (n = 200)	
	SYNTAX score	GENSINI score
Mean ± SD.	25.4±11.09	58.86±37.92
Median (IQR)	25 (16.75-33)	48 (27.5-88)
Range (Min-Max)	54 (4-58)	156 (4-160)

There is a correlation between fructosamine and HbA1c was found as Pearson's correlation coefficient (*r*) between fructosamine and HbA1c was 0.855 (Table 5).

Table (5): Pearson's correlation coefficients (*r*) between Fructosamine and HbA1C.

	Fructosamine	
	Pearson's correlation coefficients (*r*)	*p*
HbA1C	0.855	<0.001

Markers of glycemic control and severity assessment scores:

A strong positive correlation was found between markers of glycemic control (Fructosamine and HBA1c) and severity of coronary artery disease assessed by SYNTAX score and GENSINI score as Pearson's correlation coefficient (*r*) between fructosamine and SYNTAX score was 0.668, with GENSINI score was 0.734, compared with HbA1c and SYNTAX score Pearson's correlation coefficient (*r*) was 0.636, andHbA1c and GENSINI score was 0.716 (Table 6) and (Figs. 1-4).

Table (6): Pearson's correlation coefficients (*r*) between fructosamine and HBA1c with SYNTAX score and GENSINI score.

	Fructosamine		HBA1C	
	Pearson's correlation coefficients (*r*)	*p*	Pearson's correlation coefficients (*r*)	*p*
SYNTAX score	0.668	<0.001	0.636	<0.001
GENSINI score	0.734	<0.001	0.716	<0.001

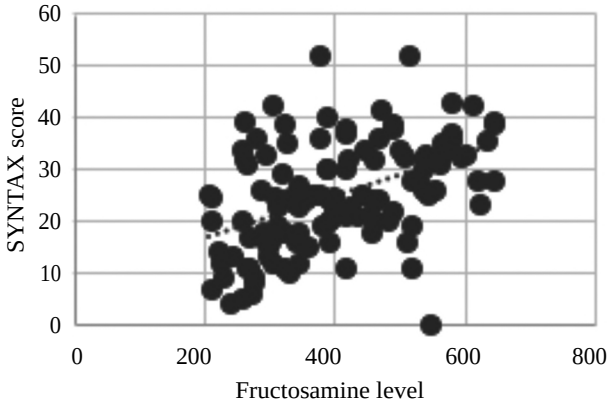

Fig. (1): Scatter plot graph showing correlation between Fructosamine and SYNTAX score.

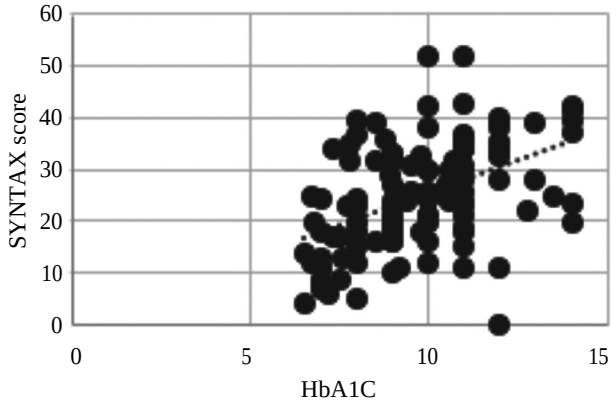

Fig. (2): Scatter plot graph showing correlation between HbA1C and SYNTAX score.

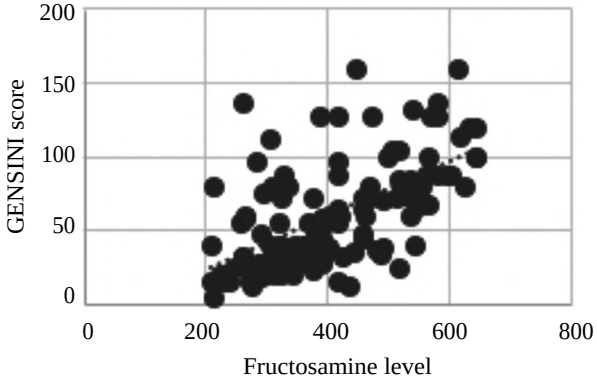

Fig. (3): Scatter plot graph showing correlation between Fructosamine and GENSINI score.

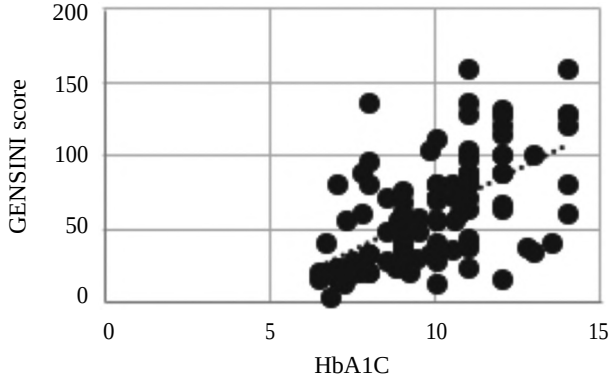

Fig. (4): Scatter plot graph showing correlation between Fructosamine and GENSINI score.

The correlation between fructosamine and SYNTAX was found to be significantly higher in cases with higher SYNTAX score (>32) than those with lower ones (<22). Higher fructosamine levels increases the risk of risk of severity of CAD (Table 7).

Table (7): Pearson's correlation coefficients (*r*) between fructosamine and SYNTAX score tertiles.

	Fructosamine	
	Pearson's correlation coefficients (*r*)	*p*
Syntax score first tertile (<22)	–0.586	<0.001
Syntax score second tertile (22-32)	0.108	0.129
Syntax score third tertile (>32)	0.526	<0.001

The correlation between fructosamine and GENSINI was found to be significantly higher in cases with higher GENSINI score (>38) than those with lower ones (<11). Higher fructosamine levels increases the risk of risk of severity of CAD (Table 8).

Table (8): Pearson's correlation coefficients (*r*) between fructosamine and GENSINI score tertiles.

	Fructosamine	
	Pearson's correlation coefficients (*r*)	*p*
Gensini score first tertile (<11)	–0.276	<0.001
Gensini score second tertile (11-38)	–0.492	<0.001
Gensini score third tertile (>38)	0.588	<0.001

Discussion

DM poses as a major risk factor for the development of cardiovascular disease (CVD), which ultimately results as the most common cause of death in those with DM **[16]**.

Cardiac disease that develops as a direct consequence of DM in patients with type 1 DM (T1DM) or type 2 DM (T2DM) is known as diabetic heart disease. Diabetic heart disease is a conglomeration of CAD, cardiac autonomic neuropathy (CAN), and diabetic cardiomyopathy (DCM), and these diseases are characterized by molecular, structural, and functional changes in the myocardium **[17]**.

The SYNTAX score is an angiographic tool and even if the SYNTAX score is not among the newest angiographic tools which have been used in clinical practice, it was the most common one to be used to stratify patients who would benefit from either PCI or CABG. A low SYNTAX score was associated with significantly better cardiovascular outcomes in comparison with a higher SYNTAX score **[18]**.

The SYNTAX score characterizes the extent of coronary disease in terms of the number of lesions, their functional importance, and their complexity. Previous studies have categorized the SYNTAX score to identify patients at low (22), medium (23-32), and high (33) risk and demonstrated superior outcomes for patients receiving CABG over PCI, primarily in those patients with high SYNTAX scores **[19]**.

The number of diseased coronary vessels is not the only marker for CAD severity. The location of the lesions and their impact on blood flow, the degree of vessel stenosis, lesion classifications, and the diameter and calcification of the vessel are also important factors that affect the technical feasibility of performing PCI, and the prognosis. Considering these factors, there are different degrees of multivessel disease and the preferred revascularization strategy may be different for specific lesion complexities. To assess this hypothesis the angiographic SYNTAX score and GENSINI score were introduced **[9]**.

The aim of this study was to assess the correlation between Fructosamine Level and the severity of coronary artery disease by calculating SYNTAX score and GENSINI score in diabetic patients presenting to Ain Shams University Hospital with symptomatic chronic coronary syndrome undergoing elective coronary angiography.

This study was conducted on 200 diabetic patients with chronic coronary syndrome undergoing elective coronary angiography, with mean age 54.36±5.86 years ranging from 32 years to 65 years. The majority of them were males (64%). 57% were smokers. The majority of the patients in this study were hypertensive (74.50%). While 7% of them have diabetic complications in the form of peripheral vascular disease.

HbA1c in the study population ranged from 6.5 to 14.3 with mean 9.61±2.01, while fructosamine level in the study population ranged from 201 to 653 with mean 392.31±123.28.

SYNTAX score in the study population ranged from 4 to 58 with mean 25.4±11.09, while GENSINI score ranged from 4 to 160 with mean 58.86±37.92.

The acceptance of new measures of hyperglycemia is partly dependent on establishing their association with long-term outcomes. Furthermore, the comparison of risk factor associations for elevations in nontraditional versus traditional biomarkers of hyperglycemia is important for the interpretation of these biomarkers in the general population and the clinic. Previous studies have demonstrated strong associations between fructosamine and glycated albumin with microvascular conditions, with associations of similar magnitude to those observed for HbA1c. Data on risk associations using modern assays of fructosamine with cardiovascular disease are sparse, and previous studies have been limited by cross-sectional designs or prospective studies with small numbers of cardiovascular events **[20-22]**.

In the present study, we found that both fructosamine and glycated albumin were associated with coronary heart disease with patterns of association similar to those observed for HbA1c. As there was a strong positive relationship between Fructosamine and HbA1C.

Supporting to the present study, a previously conducted study aimed to clarify the performance of fructosamine and glycated albumin measurements for identifying people at risk of incident diabetes or diabetic complications they measured glycated albumin and fructosamine in blood samples from 11348 adults without diabetes and 958 adults diagnosed with diabetes mellitus in the total population. It was detected that HbA1c was highly correlated with fructosamine (r=082) and glycated albumin (r=086) **[23]**.

In the present study, we found that there was a strong positive correlation between fructosamine and both of SYNTAX score and GENSINI score, pointing out to the associations of higher fructosamine level with the risk of CAD. This comes in concordance with a previous study that aimed to characterize the associations of fructosamine and glycated albumin with risk of CAD, ischemic stroke, heart failure, and total mortality in the community. It was found that fructosamine was associated with CAD, ischemic stroke, heart failure, and death **[24]**.

In concordance with the present study, Tanabe et al., aimed to examine the usefulness of hyperfructosaminemia as an index of risk state of abnormal glucose metabolism for coronary atherosclerotic disease. Serum fructosamine concentration was compared between 130 male cases with coronary stenosis, aged 60 years or younger, and 260 age-matched male controls. Hyperfructosaminemics was significantly higher in the cases (36.2%) than in the controls (15.0%, $p<0.01$) **[25]**.

Other studies on different population was consistent with the present study; Higher fructosamine levels have also been linked to an increased risk of CVD (and all-cause) mortality in a case-cohort study of elderly women at risk of osteoporotic fractures. Similarly, in a prospective study including hemodialysis patients, serum fructosamine predicted CVD morbidity and mortality **[26]**.

Observational studies have confirmed the continuous and positive association between glycemic control and the risk of cardiovascular disease among diabetic patients **[27]**. According to this study findings both syntax score and GENSINI score had a strong positive correlation with HbA1c.

Chen et al., conducted a study to investigate whether glycemic control affects the relation between endothelial dysfunction and coronary artery disease in patients with type 2 diabetes mellitus (T2DM). In type 2 diabetic patients with stable angina the degree of coronary atherosclerosis (Gensini score and SYNTAX score) were determined. Agreeing with the current study, It was found that the prevalence of significant CAD was higher (67.9% vs. 37.0%, $p=0.002$), and the severity of coronary atherosclerosis was more prominent (Gensini score: 48.99±48.88 vs. 15.07±21.03, $p<0.001$; SYNTAX score: 15.88±16.36 vs. 7.28± 10.54, $p=0.003$) in patients with poor glycemic control (HbA1c 7.0%) than those with good glycemic control **[28]**.

Similarly, Eeg-Olofsson and coworkers assessed the association between HbA1C and (CVDs) in an observational study of 7,454 patients with type 1 diabetes followed for 5 years. A strong association was demonstrated between HbA1C and both CAD and CVD. Each 1% unit increase in baseline HbA1C or updated mean HbA1C was associated with risk increases of 31-34% for CAD and 26-32% for CVD **[29]**.

In another study that aimed to investigate the relationship between (HbA1c), fasting blood glucose (FBG), postprandial glucose (PPG), and SYNTAX Score (SS) and SS II in patients with type 2 diabetes mellitus and CAD, Karakoyun et al., reported that higher HbA1c was significantly associated with elevated SYNTAX score tertile in patients with DM and CAD **[30]**.

Ayhan and colleagues conducted a study to investigate the relationship between (HbA1c) levels and the severity of CAD in <40 years old patients. It was reported that HbA1c levels significantly positively correlated with the GENSINI score ($r=0.662$, $p<0.001$) **[31]**.

Another work tested the hypothesis that glycemic control (HbA1c) is positively associated with incident CHD independent of other known risk factors in persons with and without diabetes in a community-based cohort of middle-aged adults. In persons with diabetes, a graded relationship was observed for increasing CHD risk with increasing HbA1c level in a linear fashion after adjustment for other CHD risk factors. The relationship between HbA1c level and CHD risk increased throughout the range of HbA1c values **[32]**.

Khaw et al., have also reported on the association between HbA1c levels and major cardiovascular events and mortality. They reported that increasing levels of HbA1c are associated with all-cause and cardiovascular mortality. An increase of 1% in HbA1c was associated with a 28% increase in the risk of death, independent of traditional cardiovascular risk factors. Interestingly, the association between increasing HbA1c levels and death persisted (hazard ratio 1.46) after individuals with DM and those with a HbA1c level above 7% were excluded from the analysis, suggesting a role of HbA1c assessment in risk stratification and prediction among individuals without DM **[33]**.

Supporting to the current study, Berry et al., found that fasting blood glucose, HbA1c, and presence of diabetes were associated with the severity and progression of coronary atherosclerosis. They concluded that better glycaemic control

favourably influences CAD in patients with abnormal glucose tolerance or diabetes **[34]**.

Ravipati et al., underwent a study to assess the association of HA1c level with the severity of CAD in patients with diabetes mellitus. It showed that the HbA1c level increased significantly with the number of arteries with CAD in diabetics **[35]**.

In another study, Mi et al., evaluated glycaemic variability and HbA1c as risk factors for CAD in newly diagnosed diabetics. They found that HbA1c and glycaemic variability were associated with the presence and severity of CAD in patients with newly-diagnosed DM. They also evaluated CAD severity using the Gensini score **[36]**.

In another study by Sahal et al., who enrolled 905 patients with CAD, their results exhibited a positive relationship between raised HbA1c levels in people with diabetes and a higher syntax score (23) than non-diabetics **[37]**

Supporting to this study among diabetic patients admitted to the coronary care unit included in Saleem et al study that was performed to find the association between (HbA1c) level and the severity of CAD. There was a positive significant correlation between GENSINI score and HbA1C **[38]**.

In Su and colleagues study, that assessed the relationship between glycemic variability determined by a continuous glucose monitoring (CGM) system and the presence and severity of (CAD) in patients with T2DM. Pearson correlation analysis showed that Gensini score correlated positively with HbA1c **[39]**.

Conclusion:

The study shows that there isa significant correlation between serum fructosamine Level and severity of CAD assessed by the angiographically derived SYNTAX and GENSINI scores. Fructosamine level may have a value as a predictor of severity of CADand risk stratification of diabetic patientsespecially patients with a higher level of fructosamine who had significant severe lesions with higher SYNTAX (third tertile >32) and Gensini (third tertile >38). In addition to that a strong positive correlation was found between markers of glycemic variability fructosamine and HbA1c.

Study limitations:

- The sample size was relatively small, which limited our ability to determine significance. Therefore, more in-depth prospective, multi-center studies are required to further verify the current findings.
- Secondly, factors such as age, obesity, inflammation, etc. may impact cardiovascular risk in this work.
- Another limitation of this study was that evaluation was based on a single HbA1c measurement.

Conflicts of interest:

No Conflicts of interest were found in the study.

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العلاقة بين مستوى الفركتوزامين فى الدم وشدة مرض الشريان التاجى من خلال حساب c و GENSINI المشتقة من تصوير الشرايين التاجية فى مرضى السكرى الذين يعانون من مرض الشريان التاجى المستقر

يميل مرض الشريان التاجى إلى أن يكون أكثر انتشاراً وتعقيداً لدى مرضى السكرى، مقارنة مع غير المصابين بداء السكرى، ويرتبط بزيادة معدلات الاعتلال والوفيات الناجمة عن أمراض القلب والأوعية الدموية.

الهدف من هذه الدراسة : هو تقييم العلاقة بين مستوى الفركتوزامين وشدة مرض الشريان التاجى من خلال حساب درجة SYNTAX ودرجة GENSINI فى مرضى السكرى الذين يتقدمون إلى مستشفى جامعة عين شمس ويعانون من أعراض متلازمة الشريان التاجى المزمنة ويخضعون لتصوير الأوعية التاجية الاختيارى.

أجريت هذه الدراسة على ٢٠٠ مريض بالسكرى مصابين بمتلازمة الشريان التاجى المزمنة يخضعون لتصوير الأوعية التاجية الاختيارى بمتوسط ٥٤.٣٦±٥.٨٦ عمر سنة تتراوح من ٣٢ سنة إلى ٦٥ سنة. وكانت هناك علاقة إيجابية قوية بين الفركتوزامين ودرجة SYNTAX، مع معامل الارتباط ٠.٦٦٨. هناك ارتباط كبير بين الفركتوزامين وشدة مرض الشريان التاجى حيث وجد ارتفاع شديد بمستوى الفراكتوزامين مع الفئة الثالثة لمقياس SYNTAX (>٣٢). إضافة إلى أن معامل ارتباط بيرسون بين الفركتوزامين وGENSINI يساوى ٠.٧٣٤، مما يعنى أن هناك علاقة إيجابية قوية بين درجة الفركتوزامين و GENSINI. هناك ارتباط كبير بين ارتفاع مستوى الفركتوزامين و GENSINI الفئة الثالثة (>٣٨).

معامل الارتباط بيرسونبين الهيموجلوبين السكرى ومقياس SYNTAX كانت النتيجة النحوية ٠.٦٣٦، مما يعنى أن هناك علاقة إيجابية قوية الهيموجلوبين السكرى و SYNTAX. إضافة إلى أن نتيجة معامل ارتباط بيرسون بين الهيموجلوبين السكرى و GENSINI كانت ٠.٧١٦، مما يعنى وجود علاقة إيجابية قوية بين الهيموجلوبين السكرى ومقياس GENSINI .

فى الختام: تم الكشف عن ارتباط كبير بين مستوى الفركتوزامين فى الدم وشدة مرض الشريان التاجى التى تم تقييمها من خلال درجات SYNTAX و GENSINI المشتقة من التصوير الوعائى فى مرضى السكرى الذين يعانون من أعراض متلازمة الشريان التاجى المزمنة.