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Prevalence of Prediabetes in Patients with Acute Coronary Syndrome and Its Relation to In-Hospital Clinical Outcome

Eman Abdullah Al-Shorbagy, Gehan Abdel –Kader Ibrahim, Mohamed S.S. Saad, Khaled Bashir Salem Harsha*

Internal Medicine Department, Faculty of Medicine – Zagazig University, Egypt

***Corresponding author:** Khaled Bashir Salem Harsha, **Mobile:** (+20)01147023222, **E-mail:** khaledbashir603@gmail.com

ABSTRACT

Background: Diabetes mellitus is one of the leading causes of vascular disease. The caseload is expected to reach 350 million by the year 2030, and it is estimated that up to 30% of patients are undiagnosed.

Objective: The aim of the study was to explore the prevalence of prediabetes in patients admitted with acute coronary syndromes (ACS) who were not known to have diabetes and to determine the impact of prediabetes on in-hospital clinical outcomes versus non-diabetic patients.

Patients and methods: This prospective study was conducted on 60 patients with acute coronary syndrome who were admitted to the intensive care unit (ICU), Internal Medicine Department, Faculty of Medicine, Zagazig University during the period from September 2019 to March 2020. All studied subjects were subjected to full history taking complete clinical examination, complete blood count, glycosylated haemoglobin (HbA1c), lipid profile, serum creatinine and oral glucose tolerance test (OGTT), ECG and ECHO.

Results: There was a statistical significant difference between the studied groups regarding acute coronary syndrome types, glycated haemoglobin (HbA1c), serum creatinine, and high-density lipoproteins cholesterol. There was statistically significant difference between the studied patients grouped according to the clinical outcome regarding ACS types.

Conclusion: Prediabetes is common in patients presenting with acute coronary syndrome who are not previously known to have diabetes. Pre-diabetic patients had worse in-hospital clinical outcomes compared with patients without diabetes. Pre-diabetic patients with ACS have greater prevalence of cardio-metabolic risk factors (abdominal obesity, and hypertension) as compared to non-diabetic patients.

Keywords: Acute coronary syndrome, Coronary complications, Prediabetes.

INTRODUCTION

Prediabetes is a serious condition that is associated with an increase in cardiovascular morbidity and mortality, and necessitates early and adequate intervention to prevent the development of complications and progression to overt diabetes. Higher fasting glucose levels in patients with ACS were associated with worse clinical outcomes irrespective of the presence of diabetes mellitus. Similarly, in patients without diabetes presenting with acute ST-segment elevation myocardial infarction (STEMI), higher fasting glucose was a marker of adverse outcome [(1)].

Individuals with diabetes are at higher risk of myocardial infarction than non-diabetics. However, much less is known about the incidence of development of diabetes and impaired fasting glucose in patients who had myocardial infarction [(2)]. Diabetes is a major risk factor for coronary heart diseases. Impaired glucose metabolism is also frequently observed subsequent to an acute coronary event in non-diabetic subjects. The glycemic metabolic status indicated by the blood glucose and glycosylated hemoglobin (HbA1c) concentrations [(3)]. At the time of acute myocardial infarction in diabetic subjects, and even in the case of non-diabetic subjects, are determinants of future cardiovascular events and the increased risk of death [(4)].

Although it is well established that Asian Indians have a higher risk for type 2 diabetes and coronary heart disease, there are only sparse data on the occurrence of hyperglycemia at ACS and its association with the outcome in ACS [(5)]. The association of insulin resistance and elevated proinsulin-to-insulin ratio with cardiovascular diseases has also been demonstrated in both the white population and the Asian-Indian populations [(6)].

The aim of this study was to explore the prevalence of prediabetes in patients admitted with acute coronary syndromes who were not known to have diabetes and to determine the impact of prediabetes on in-hospital clinical outcomes versus non-diabetic patients.

PATIENTS AND METHODS

This prospective study was conducted on 60 patients with (ACS) who were admitted to the ICU, Internal Medicine Department, Faculty of Medicine, Zagazig University during the period from September 2019 to March 2020.

Ethical approval:

Written informed consents were obtained from all participants. The study was approved by The Research Ethical Committee of Faculty of

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Medicine, Zagazig University. The work has been carried out in accordance with The Ethical Code of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Inclusion Criteria: Patients > 18 years with ACS and patients without known history of diabetes.
Exclusion Criteria: Patients ≤ 18 years, patients receiving corticosteroids, patients with diagnosed diabetes and patients with cardiogenic shock.
According to Glycosylated haemoglobin (HbA1c), Patients were divided into two groups:
Group (I): Non-diabetic patients with ACS.
Group (II): Pre-diabetic patients with ACS.
According to outcome results, patients were divided into two groups:
Group (I): Patients with ACS with good clinical outcome.
Group (II): Patients with ACS with poor clinical outcome.

All studied subjects were subjected to the following: Full history taking including age, sex, smoking, hypertension and medications. Complete clinical examination for all patients. Anthropometric measurements: Weight (kilograms), height (meters) and Body Mass Index (BMI). BMI = weight (kg) / height (m^2). Laboratory tests including fasting plasma glucose, complete blood count, glycosylated haemoglobin (HbA1c), Lipid profile, Serum creatinine and Oral glucose tolerance test (OGTT). ECG and ECHO.

A fasting venous blood sample was taken on day 1 of admission after an 8-hour overnight fast. Fasting and 2-hour post-load plasma glucose was measured using an automated glucose oxidase method using Behring Diagnostics Reagents (SVR Glucose Test; Behring, La Jolla, CA). HbA1c was assayed by Stanbio Procedure No. 0350 "Quantitative colorimetric determination of Glycohemoglobin in blood**".** Serum lipid concentrations were assayed by quantitative enzymatic colorimetric determination for total cholesterol, high-density lipoprotein cholesterol and triglycerides in plasma (Stanbio Cholesterol Liquicolor, Procedure NO. 1010). Low-density lipoprotein cholesterol was calculated using the Friedewald equation.

ACS included unstable angina, non-STEMI and STEMI. All patients had persistent ischaemic-type chest pain or other acute symptoms consistent with myocardial ischaemia, at rest or with minimal exercise, lasting for more than 10 minutes. STEMI was defined by persistent ST segment elevation (at least 2 mm in two contiguous precordial leads, or at least 1 mm in two limb leads), new left bundle branch block, or new Q waves in two contiguous leads; with rise of biochemical markers of myocardial necrosis (creatine kinase-MB and/or troponin) at least twice the upper limit of normal. Non-ST-elevation ACS was defined by the presence of new/dynamic electrocardiographic changes compatible with ischaemia such as ST segment depression of at least 1 mm, transient ST segment elevation or ST segment elevation less than 1 mm, or T wave inversion more than 2 mm, in at least two contiguous leads. Non-STEMI was distinguished by rise of biochemical markers at least twice the upper limit of normal.

ST elevation in MI was defined as ECG showing ST elevation measured at J point found in two contagious leads and ≥ 0.25 mV in men below the age of 40 years, 0.2 mV in men over the age of 40 years. While, it was ≥ 0.15 mV in women in leads V2-V3 and/or ≥ 0.1 mV in other leads in absence of left ventricular hypertrophy or left bundle branch block (LBBB).

Prediabetes was defined according to the recommendations of the American Diabetes Association as having impaired fasting glucose and/or impaired glucose tolerance. Impaired fasting glucose was defined as fasting plasma glucose (FPG) level of ≥ 100 mg/dl to < 126 mg/dl. A1c level of ≥ 5.7% to < 6.5%. OGTT ≥ 140 mg/dl to < 200 mg/dl.

In-hospital clinical follow-up:

The primary composite endpoint was in-hospital MACE. MACE was defined as the first occurrence of any of the following during hospital stay: cardiac death, non-fatal re-infarction, or urgent vessel revascularization. Cardiac death was defined as death from cardiovascular causes or any death without another known cause. Re-infarction was diagnosed by a new rise of biochemical markers (creatine kinase-MB and troponin) at least 50% above the lowest level measured previously. Urgent vessel revascularization was defined as any unplanned intervention (percutaneous or surgical) to the infarct-related (or culprit) vessel during hospital stay. Secondary endpoints included the individual components of MACE, ventricular fibrillation, ventricular tachycardia, and heart failure. Ventricular tachycardia was defined as a 3 or more successive ventricular premature beats.

Statistical Analysis

SPSS version 20 was used for statistical analysis, a description was given of the demographic variables in the overall sample, with measures of central tendency (mean) and standard deviation for the quantitative variables, and percentages for the categorical variables. A search was subsequently made for differences in variable distribution between the two study groups. A Student's t test was used for the quantitative variables, and a Chi-square test was used for the categorical variables. Measurement of the incidence of the outcome variables was then continued, after which the relative risk of prediabetes as a function of the outcome variables and the corresponding confidence interval were estimated. Level of significance was considered for $P \leq 0.05$ and high significance was $P < 0.001$.

RESULTS

Table (1): Comparison of demographic and clinical data between studied groups (n=60)

	Group (I) Non-diabetic patients with ACS (n= 40)	**Group (II) Pre-diabetic patients with ACS (n= 20)**	**Test**	**P**
Age (Years) Mean ± SD	60.2 ± 11.2	67.2 ± 8.6	**t** 2.45	**0.017 (S)**
Sex Male Female	26 (65%) 14 (35%)	12 (60%) 8 (40%)	χ^2 0.14	0.7 (NS)
BMI Median (Range**)**	29.4	33	**MW** 284	0.06 (NS)
Smoking No Yes	24 (60%) 16 (40%)	10 (50%) 10 (50%)	χ^2 0.53	0.465 (NS)
HTN No Yes	22 (55%) 18 (45%)	6 (30%) 14 (70%)	χ^2 3.29	0.069 (NS)
Family history Positive Negative	14 (35%) 26 (65%)	6 (30%) 14 (70%)	χ^2 0.148	0.70 (NS**)**
Presentation Typical chest pain Atypical Presentation[#]	30 (75%) 10 (25%)	14 (70%) 6 (30%)	χ^2 0.682	0.68 (NS**)**
Hospital stay(days) Median (Range)	4.5 (3– 10)	6.5 (3– 11)	**MW** 234	**0.008 (S)**
Outcome No complications Serious complications Atrial fibrillation Heart block Pump failure (ejection fraction > 40%).	24 (60%) 16 (40%) 4 (25%) 2 (12.5%) 10 (62.5%)	6 (30%) 14 (70%) 6 (42.8%) 2 (14.4%) 6 (42.8%)	χ^2 4.72	**0.029 (S)**

t = independent student (t) test; MW = Mann-Whitney U test; χ^2 Chi-squared test. P value <0.05 was considered statistically significant(S). [#] Dyspnea, epigastria pain, vomiting, drowsiness

Table (1) showed that there was statistically significant difference between the studied groups regarding age, days of hospitalization and the clinical outcome. There was no significant difference between them regarding sex, BMI, smoking, hypertension, family history, and presentation.

Table (2): Comparison of ACS types between studied groups (n=60)

	Group (I) Non-diabetic patients with ACS, (n= 40)	**Group (II) Pre-diabetic patients with ACS, (n= 20)**	**Test**	**P**
Unstable angina	6 (15%)	0 (0%)	χ^2 14	**0.0009 (S)**
STEMI	28 (70%)	8 (40%)		
NSTEMI	6 (15%)	12 (60%)		

χ^2 Chi-squared test.

Table (2) showed that there was statistically significant difference between the studied groups regarding ACS types.

Table (3): Comparison of demographic and clinical data between studied patients grouped according to clinical outcomes (n=60)

	Group (I) Patients with ACS with good/fair clinical outcome (n= 30)	**Group (II) Patients with ACS with poor clinical outcome (n= 30)**	**Test**	**P**
Age (Years) Mean± SD	61.6 ± 8.38	63.46 ± 12.9	**t** - 0.66	0.50 (NS)
Sex Male Female	18(60%) 12(40%)	20(66.7%) 10(33.3%)	χ^2 0.28	0.59 (NS)
BMI Median (Range**)**	31 (21– 44.5)	29.8 (27 – 41)	**MW** 436	0.83 (NS)
Smoking No Yes	14(46.7%) 16(53.3%)	12(40%) 18 (60%)	χ^2 0.267	0.6 (NS)
HTN No Yes	12(40%) 18(60%)	16 (53.3%) 14(46.7%)	χ^2 1.054	0.131 (NS)
Family history Positive Negative	18(60%) 12(40%)	22 (73.3%) 8 (26.7%)	χ^2 1.18	0.277 (NS**)**
Presentation Typical chest pain Atypical Presentation[#]	22 (73.3%) 8 (26.7%)	22 (73.3%) 8 (26.7%)	χ^2 0.00	1 (NS**)**
Hospital stay(days) Median (Range)	4 (3– 7)	7 (3– 11)	**MW** 138	**<0.0001 (S)**

t = independent student (t) test; MW = Mann-Whitney U test; χ^2 Chi-squared test. p value <0.05 was considered statistically significant(S). Dyspnea, epigastria pain, vomiting, drowsiness

Table (3) showed that there was statistically significant difference between the studied patients grouped according to the clinical outcome regarding days of hospital stay. There was no significant difference between them regarding age, sex, BMI, smoking, hypertension, family history, and presentation.

Table (4): Comparison of ACS types between studied patients grouped according to clinical outcomes (n=60)

	Group (I) Patients with ACS with good/fair clinical outcome (n= 30)	**Group (II) Patients with ACS with poor clinical outcome (n= 30)**	**Test**	**P**
Unstable angina	6 (20%)	0 (0%)	χ^2 8	**0.0183 (S)**
STEMI	18 (60%)	18 (60%)		
NSTEMI	6 (20%)	12 (40%)		

χ^2 Chi-squared test.

Table (4) showed that **t**here was statistically significant difference between the studied patients' groups according to the clinical outcome regarding ACS types.

Table (5): Correlation between hospital stay and different study parameters

	Total population (n=60)		
	R	***P***	
Age	0.205	0.116	(NS)
BMI	0.199	0.126	(NS)
HbA1c	0.356	0.0053	**(S)**
FBs	0.112	0.392	(NS)
Hemoglobin	-0.379	0.0028	**(S)**
Creatinine	0.248	0.055	(NS)
Triglycerides	-0.0508	0.7	(NS)
LDL cholesterol	0.005	0.967	(NS)
HDL cholesterol	0.069	0599	(NS)

r = Spearman's rank correlation coefficient A *p* value <0.05 was considered statistically significant(S).

Table (5) showed that **t**here was significant correlation between days of hospital stay and both HbA1c and hemoglobin.

DISCUSSION

It is well known that among patients with ACS, diabetes mellitus (DM) is associated with worse outcomes and higher mortality rates. Hyperglycemia in patients admitted for ACS is associated with increased in-hospital and long-term mortality in both patients with and without DM. Furthermore, hyperglycemia at admission in ACS patients is a stronger predictor for in-hospital and long-term mortality in non-diabetic patients [(7)].

Regarding our results, the study showed that the mean age was 60.2 ± 11.2 for non-diabetic patients versus 67.2 ± 8.6 years for Pre-diabetic patients, with a statistical significant difference between the two groups (P = 0.017). This is in agreement with the study of **Sousa *et al.*** [(8)] who found a statistical significant difference between the studied groups regarding age, where the mean age was 65.9 ± 13.5 for non-diabetic patients versus 61.2 ± 13.8 years for pre-diabetic patients (P = 0.04). Our result is in contrast to the study of **Abu Shady *et al.*** [(1)] who reported that the mean age of non-diabetic diabetic patients was 51 ± 6.8, and in pre-diabetic was 49.6 ± 6.9 (p= 0.27) with no statistical significant difference.

In the current study, the median (Range) of BMI was 29.4 (21 – 44.5) for the non-diabetic patients versus 33 (27 – 44) kg/m^2 for Pre-diabetic patients, with no statistical significant difference between the two groups (P = 0.06). This is in contrast to the study of **Abu Shady *et al.*** [(1)] who reported that the mean BMI was 27.8 ± 2.4 for the non-diabetic patients versus 29.2 ± 2.2 kg/m^2 for Pre-diabetic patients group with a statistical significant difference between the studied groups (p = 0.002). Besides, the study of **Açar *et al.*** [(9)] who reported that the mean BMI was 26.8 ± 3.4 for the non-diabetic patients versus 27.6 ± 3.7 for pre-diabetic patients group (p = 0.042). This difference may be due to different genetic, lifestyle and quality of life between different populations.

In the current study, regarding current smoking, it was 24 (60%) in non-diabetic patients and 10 (50%) in pre-diabetic patients with no statistically significant difference (p = 0.465). This is in agreement with the study of **Abu Shady *et al.*** [(1)] who reported that current smoking was 62 (55.9) in non diabetic patients and 25 (62.5) in pre-diabetic patients with no statistical significant difference (p = 0.47).

In the current study, regarding hypertension, it was reported in 18 (45%) of non-diabetic patients and 14 (70%) in pre-diabetic patients with no statistical significant difference (p = 0.069). This is in agreement with the study of **Abu Shady *et al.*** [(1)] who reported that in non-diabetic patients, it was 64 (57.7%) and 25 (62.5) in Pre-diabetic patients with no statistical significant difference (p = 0.59).

In the current study, there was statistically significant difference between the studied groups regarding ACS types, where STEMI was reported in 28 (70%) of non-diabetic group versus 8 (40%) in pre-diabetic group and NSTEMI was reported in 6 (15%) of non-diabetic group versus 12 (60%) in pre-diabetic group (P = 0.0009). This is in agreement with the study of **Zhou *et al.*** [(10)] who reported that there was highly statistical significant difference between non-diabetic and pre-diabetic groups regarding ACS types (P < 0.001). While, the study of **Abu Shady *et al.*** [(1)] showed no statistical significant difference between non-diabetic and pre-diabetic groups regarding ACS types, where STEMI was reported in 32 (28.8) of non-diabetic group versus 13 (32.5) in pre-diabetic group and NSTEMI was reported in 20 (18) of non-diabetic group versus 5 (12.5) in pre-diabetic group (P = 0.71).

In the current study, there was a statistical significant difference between studied groups regarding HbA1c, serum creatinine, and HDL cholesterol, but there was no significant difference between them regarding fasting blood sugar, blood urea nitrogen, hemoglobin level, total cholesterol, triglycerides, and LDL cholesterol. This is in agreement with the study of **Cueva-Recalde *et al.*** [(11)] who found that the ratio of HbA1c was 5.42 ± 0.17 for non-diabetic versus 5.81± 0.14 for pre-diabetic with significant difference (P < 0.01), and no significant difference for total cholesterol (p = 0.07) and triglycerides (p = 0.06).

In the current study, there was statistically significant difference between the studied patients groups concerning days of hospital stay, where it was 4 (3– 7) in non-diabetic versus 7 (3– 11) in pre-diabetic patients (P < 0.001). This is in agreement with the study of **Zhou *et al.*** [(10)] who reported 9.0 (7.0–12.0) in non-diabetic versus 10.0 (7.0–13.0) in pre-diabetic patients (P < 0.001). There was no significant difference between them regarding age, sex, BMI, smoking, hypertension, family history, and presentation. This is in agreement with the study of **Mirghan *et al.*** [(12)] who concluded also significant difference between non-diabetic and pre-diabetic patients regarding age, sex, BMI, smoking, hypertension, family history, and presentation.

There was a statistical significant difference between the studied patients concerning the clinical outcome of ACS types, where NSTEMI was 6 (20%) in non-diabetic versus 12 (40%) in pre-diabetic patients (P = 0.0183). This is in agreement with the study of **Mirghan *et al.*** [(12)], who found that NSTEMI was reported in 3 patients (15.8%) of non-diabetic versus 7 (33.3%) in pre-diabetic patients (P < 0.05).

The current study showed that there was significant correlation between days of hospital stay and HbA1c (r= 0.356, P = 0.0053) and hemoglobin (r= -0.379, P = 0.0028), which is in agreement with the study of **Abu Shady *et al.*** [(1)], who reported for HbA1c (r=0.19, p=0.019).

CONCLUSION

Prediabetes is common in patients presenting with acute coronary syndrome who are not previously known to have diabetes. Pre-diabetic patients had worse in-hospital clinical outcomes compared to patients without diabetes. Pre-diabetic patients with ACS have greater prevalence of cardio-metabolic risk factors (abdominal obesity, and hypertension) as compared to non-diabetic patients.

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