PREDIABETES PATIENTS WITH ACUTE CORONARY SYNDROME AND HOSPITAL CLINICAL OUTCOME

Eman Abdullah Al-Shorbagy [(1)]**, Gehan Abdel –Kader Ibrahim** [(1)]**,**
Mohamed S. S. Saad [(1)] **and Khaled Bashir Salem Harsha**

[(1)] Professor of Internal Medicine, Faculty of Medicine - Zagazig University
[(2)] M.B; B.CH.; Internal Medicine department, Faculty of Medicine, Tripoli University, Libya
Corresponding author : Khaled Bashir Salem Harsha
E-mail: khaledbashir603@yahoo.com

ABSTRACT

Background: Prediabetes is common in patients presenting with ACS who are not previously known to have diabetes. Prediabetic patients had worse in-hospital clinical outcomes compared with patients without diabetes. The aim of the study was to explore the relation prediabetes patients with acute coronary syndromes the in-hospital clinical outcomes.

Patients and Methods: This prospective study was conducted on 60 patients with acute coronary syndrome who 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: Pre-diabetic patients had worse in-hospital clinical outcomes compared with patients without diabetes. Pre-diabetic patients with ACS have greater prevalence of cardiometabolic risk factors (abdominal obesity, and hypertension) as compared to non-diabetic patients.

Keywords: Acute coronary syndrome; Coronary complications; Prediabetes

INTRODUCTION

Diabetes mellitus is a well recognized risk factor for cardiovascular disease and diabetic individuals with acute coronary syndrome (ACS) have a two- to fourfold increased risk of adverse cardiovascular events compared to non-diabetic individuals. It is becoming increasingly clear that impaired glucose metabolism and the pre-diabetic state are also associated with adverse clinical outcomes [1].

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 acute coronary syndrome (ACS) were associated with worse clinical outcomes irrespective of the presence of diabetes mellitus. [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 nondiabetic subjects. The glycemic metabolic status indicated by the blood glucose and glycosylated hemoglobin (A1C) 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 acute coronary syndrome (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 the study was to explore the relation prediabetes patients with acute coronary syndromes the in-hospital clinical outcomes

PATIENTS AND METHODS

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

Written informed consent was obtained from all patients and the study was approved by the research ethical committee of Faculty of Medicine, Zagazig University (International review board ZU-IRB #5270/1-9-2019. The study was done according to The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Inclusion Criteria: (Patients > 18 year with ACS, Patients without known history of diabetes).

Exclusion Criteria: (Patients ≤ 18 y, Patients receiving corticosteroids, Patients with diagnosed diabetes, 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:

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 (m2). Laboratory tests included 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.

ST elevation MI defined as ECG showing ST elevation measured at J point found in two contagious leads and ≥0.25mV in men below the age of 40years, 0.2mV in men over the age of 40years, or ≥0.15mV 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 < 0.05 and high significance 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 (21 – 44.5)	33 (27 – 44)	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 wasn't significant difference between them regarding sex, BMI, smoking, hypertension, family history, and presentation.

Table (2): Comparison of biochemical 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
FBS (mg/dL) Median (Range)	96 (70 – 100)	116 (100 – 126)	**MW** 400	1 (NS)
HbA1c % Median (Range)	5.4 (5.1 – 5.6)	6 (5.8 – 6.4)	**MW** 0.0	**0.0001 (S)**
Creatinine (mg/dL) Median (Range)	0.9 (0.6 – 3)	1.2 (0.9 – 2.3)	**MW** 250	**0.018 (S)**
BUN (mg/dL) Median (Range)	13.5 (8.6 – 69)	17 (13– 60)	**MW** 250	0.051 (NS)
Hemoglobin(g/dL) Mean± SD	13.2 ± 1.88	13 ± 1.6	**t** -0.499	0.61 (NS)
Total cholesterol (mg/dL) Median (Range)	173 (20 – 244)	200 (132 – 246)	**MW** 336	0.31 (NS)
Triglycerides (mg/dL) Median (Range)	106 (72 – 170)	105 (91 – 126)	**MW** 392	0.9 (NS)
LDL cholesterol (mg/dL) Median (Range)	100.5 (50 – 170)	97 (55 – 149)	**MW** 396	0.95 (NS)
HDL cholesterol (mg/dL) Median (Range)	43 (3 – 68)	38 (26.8 – 45)	**MW** 220	**0.0046 (S)**

t = independent student (t) test; MW = Mann-Whitney U test, p value <0.05 was considered statistically significant(S).

Table (2) showed that there was statistically significant difference between studied groups regarding HbA1c, serum creatinine, and HDL cholesterol. There wasn't significant difference between them regarding fasting blood sugar, blood urea nitrogen, hemoglobin level, total cholesterol, triglycerides, and LDL cholesterol.

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 wasn't 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 there was statistically significant difference between the studied patients grouped according to the clinical outcome regarding ACS types.

Table (5): Comparison of biochemical 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
FBS (mg/dL) Median (Range)	108 (80 – 170)	119 (90 – 164)	**MW** 328	0.07 (NS)
HbA1c Median (Range)	5.4(5.1 – 6.4)	5.6 (5.3– 6.3)	**MW** 0.14	**0.0036 (S)**
Creatinine (mg/dL) Median (Range)	1.1 (0.7– 1.8)	0.9 (0.6 – 3)	**MW** 446	0.95 (NS)
BUN (mg/dL) Median (Range)	14.8 (8.6 – 25)	17.8(10 – 69)	**MW** 400	0.45 (NS)
Hemoglobin(g/dL) Mean± SD	13.6 ± 1.57	12.7 ± 1.88	**t** - 1.96	0.054 (NS)
Total cholesterol (mg/dL) Median (Range)	169 (20– 244)	200 (132– 246)	**MW** 262	**0.0054 (S)**
Triglycerides (mg/dL) Median (Range)	114 (89– 170)	104 (72– 120)	**MW** 376	0.273 (NS)
LDL cholesterol (mg/dL) Median (Range)	98 (50 – 170)	103 (55 – 170)	**MW** 366	0.21 (NS)
HDL cholesterol (mg/dL) Median (Range)	42 (3– 67)	41 (30 – 68)	**MW** 430	0.76 (NS)

t = independent student (t) test; MW = Mann-Whitney U test

A p value <0.05 was considered statistically significant(S).

Table (5) showed that there was statistically significant difference between the studied patients grouped according to the clinical outcome regarding HbA1c and total cholesterol. There wasn't significant difference between them regarding fasting blood sugar, serum creatinine, blood urea nitrogen, hemoglobin level, triglycerides, and LDL cholesterol and HDL cholesterol.

DISCUSSION

It is well known that among patients with acute coronary syndrome (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 nondiabetic patients[7].

As regarding our results, the study showed that the mean age of the studied group was 60.2 ± 11.2 for Non diabetic patients versus 67.2 ± 8.6 for Pre-diabetic patients, with a statistical significant difference between the two groups (P = 0.017), which 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 for Pre-diabetic patients, P = 0.04).

In the current study, the median (Range) of BMI was 29.4 (21 – 44.5) for the non diabetic patients versus 33 (27 – 44) for Pre-diabetic patients, with no statistical significant between the two groups (P = 0.06), which in contrast to 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 statistical significant difference (p = 0.465), which in agreement with the study of **Abu Shady et al. [2],** 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), which in agreement with the study of **Abu Shady et al. [2],** 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 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.

Which in agreement with the study of **Cueva-Recalde et al. [10]**, who found the ratio of HbA1c (5.42 ± 0.17 for non diabetic versus 5.81±0.14 for pre-diabetic, 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 grouped according to days of hospital stay, where it was 4 (3– 7) in non diabetic versus 7 (3– 11) in pre-diabetic patients (P < 0.001). which in agreement with the study of **Zhou et al. [11],** 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 wasn't significant difference between them regarding age, sex, BMI, smoking, hypertension, family history, and presentation. Which 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 grouped according to the clinical outcome regarding ACS types, where NSTEMI was 6 (20%) in non diabetic versus 12 (40%) in pre-diabetic patients (P = 0.0183). Which in agreement with the study of **Mirghan et al. [12],** who found NSTEMI was reported in 3 patients (15.8%) of non diabetic versus 7 (33.3%) in pre-diabetic patients (P < 0.05).

In the current study, there was statistically significant difference between the studied patients grouped according to the clinical outcome regarding HbA1c and total cholesterol and there wasn't significant difference between them regarding fasting blood sugar, serum creatinine, blood urea nitrogen, hemoglobin level, triglycerides, and LDL cholesterol and HDL cholesterol. Also, the study of **Abu Shady et al. [2],** showed that there was statistically significant difference between the studied patients grouped according to the clinical outcome regarding HbA1c (p<0.001), but total cholesterol was 6.11 ± 0.39 in patients without diabetes versus 6.16 ± 0.36 in patients with prediabetes (P = 0.50), LDL cholesterol was 4.04 ± 0.36 in patients without diabetes versus 4.09 ± 0.21 in patients with prediabetes (P = 0.29) and HDL cholesterol was 1.06 ± 0.21in patients without diabetes versus 1.04 ± 0.21in patients with prediabetes (P = 0.61)

Conclusion

Pre-diabetic patients had worse in-hospital clinical outcomes compared with patients without diabetes. Pre-diabetic patients with ACS have greater prevalence of cardiometabolic risk factors (abdominal obesity, and hypertension) as compared to non-diabetic patients.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request

Conflicting Interest (If present, give more details): No Conflict of Interest

No financial disclosure

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Not applicable

Declarations

-Ethics approval and consent to participate

Written informed consent was obtained from all patients and the study was approved by the research ethical committee of Faculty of Medicine, Zagazig University (International review board ZU-IRB #5270/1-9-2019). The study was done according to The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

-Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests.

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