Impact of Admission Glycated Hemoglobin on Angiographic Characteristics and Short Term Clinical Outcomes of Non-diabetic patients with Acute ST Elevation Myocardial Infarction

Thesis

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Dedication

To:

My Mother

for her endless love, support,

and continuous care

Soul of My Father

whom presence is missed a lot

My Fiancée

for her support

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Rami Adel Youssef Bassily

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List of Abbreviations

Abb.	Full term
ACC	American College of Cardiology
ACS	Acute Coronary Syndrome
ADA	American Diabetes Association
AF	Atrial Fibrillation
AGE	Advanced Glycation End-Products
AMI	Acute Myocardial Infarction
BMI	Body Mass Index
BMS	Bare-Metal Stent
BP	Blood Pressure
CAD	Coronary Artery Disease
CCU	Coronary Care Unit
CIN	Contrast Induced Nephropathy
cTn	Cardiac Troponin
CVD	Cardiovascular Diseases
DAPT	Dual Anti Platelet Therapy
DES	Drug-Eluting Stents
DM	Diabetes Mellitus
ECG	Electrocardiogram
ESC	European Society of Cardiology
FFA	Free Fatty Acids
FH	Family History
Hb_{A1c}	Glycosylated hemoglobin
HDL	High-Density Lipoprotein
HGO	Hepatic Glucose Output
HS	Highly Significant
IFG	Impaired Fasting Glucose
IGT	Impaired Glucose Tolerance
IR	Insulin Resistance
IRA	Infarct Related Artery

List of Abbreviations (Cont...)

Abb.	Full term
LDL	*Low-Density Lipoprotein*
LGE	*Late Gadolinium Enhancement*
MACE	*Major Adverse Cardiac Events*
MI	*Myocardial Infarction*
MINOCA	*Myocardial Infarction with Non-Obstructive Coronary Arteries*
MVO	*Micro-Vascular Obstruction*
NS	*Non Significant*
PAI-1	*Plasminogen Activator Inhibitor*
PAMI-II	*Primary Angioplasty in Myocardial Infarction*
PET	*Positron Emission Tomography*
PPAR	*Peroxisome Proliferator-Activated Receptor*
PVD	*Peripheral Vascular Diseases*
ROS	*Reactive Oxygen Species*
ROS/RNS	*Reactive Oxygen Species/Reactive Nitrogen Species*
S	*Significant*
SPECT	*Single-Photon Emission Computed Tomography*
SYNTAX	*Synergy between Percutaneous Coronary Intervention with TAXUS and Cardiac Surgery*
TG	*Triglycerides*
VLDL	*Very-Low-Density Lipoprotein*
VSMC	*Vascular Smooth Muscle Cells*
WHO	*World Health Organization*

ABSTRACT

Background: Coronary artery disease is the most important cause of death in industrialized countries. Diabetes mellitus is one of the most important modifiable risk factors of coronary artery disease. It increases the risk of coronary artery disease by 2 to 4-fold. Interestingly, this increased risk is not confined to patients with DM, but non-diabetic patients with impaired glucose tolerance (IGT) also may have an increased incidence of cardiovascular complications. Moreover, increased admission glucose levels may be related to a higher mortality rates in patients with acute myocardial infarction (AMI), regardless of diabetic status.

Objective: To assess the prognostic impact of admission HbA1c in patients without known diabetes mellitus who were admitted with acute ST elevation myocardial infarction, on outcome of 1ry PCI and short-term outcome of adverse cardiac events.

Material and Methods: This is an observational, this study was conducted at Coronary care unit & coronary catheterization lab unit of cardiology department in Ain Shams University & specialized hospitals. The study period was 6 months (From 1-9-2018 till 1-3-2019).

Results: 100 patients without prior diagnosis of DM were included in our study population Three categories of patients were created according to HbA1c level: Group 1 (< 5.7%): 46 patients (46%); Group 2 (5.5 to 6.4%): 38patients (38%); Group 3 (>6.5%): 16 patients (16%).

Baseline characteristics of the study population are shown in Table 1.

The mean age of our sample was 55.06 ± 11.73 years and 96% were males.

There was highly statistically significant difference found between DM groups regarding SYNTAX score with P-value (0.002) & another highly significant difference in EF between the 3 groups.

Conclusion: The present study showed that admission higher HbA1c level in non-diabetic patients presented by acute STEMI is associated with more severe CAD, lower rate of complete revascularization TIMI 3, and higher incidence of adverse cardiac events and mortality. Introducing measurement of HbA1c in the CCU seems to be a simple method to obtain important information on mortality risk.

Keywords: *Admission Glycated Hemoglobin - Angiographic Characteristics - Myocardial Infarction*

INTRODUCTION

Coronary artery disease is the most important cause of death in industrialized countries.[1] Diabetes mellitus is one of the most important modifiable risk factors of coronary artery disease. It increases the risk of coronary artery disease by 2 to 4-fold.[2] Patients of myocardial infarction having diabetes mellitus have poorer prognosis than patients without diabetes mellitus.[3, 4]

Interestingly, this increased risk is not confined to patients with DM, but non-diabetic patients with impaired glucose tolerance (IGT) also may have an increased incidence of cardiovascular complications.[5] Moreover, increased admission glucose levels may be related to a higher mortality rates in patients with acute myocardial infarction (AMI), regardless of diabetic status.[6, 7] These elevated glucose levels are thought to reflect preexistent IGT or increased physical stress.

There are available reports indicating the lack of a threshold glycemic level for developing cardiovascular complications.[8, 9, 10]

In acute myocardial infarction (AMI), stress hyperglycemia commonly occurs secondary to increased catecholamine levels, so looking only at plasma glucose levels at the time of an AMI cannot predict the prognosis.[11]

Glycosylated hemoglobin (Hb_{A1c}) is a measure of the average blood glucose levels over 2 months [12] and is minimally affected by acute hyperglycemia often observed in myocardial infarction (MI).

Elevated Hb_{A1c} levels are associated with an increased risk for future micro-vascular and macro-vascular disease.[13] Hb_{A1c} can be assessed in the non-fasted state and has higher reproducibility than fasting glucose.[14] There is consistent evidence that optimal glycemic control (defined as $Hb_{A1c} \leq 7\%$) results in a lower incidence of micro-vascular complications in both type 1 and type 2 DM.[15] Moreover, a report found that elevated Hb_{A1c} levels are also predictive for cardiovascular disease and mortality in patients without DM, independent of the fasting glucose value.[16]

Some data demonstrated a significant positive correlation between Hb_{A1c} and coronary angiographic scores, indicating it as a marker of extensive coronary arterial disease.[17]

There are some other studies supporting the association between admission serum Hb_{A1c} level and increased long-term mortality of non-diabetic patients admitted with STEMI and a higher rate of coronary artery disease (CAD) in these patients.[18, 19]

There have been few studies which have shown Hb_{A1c} to be predictive of CAD in non-diabetes, but only in limited studies Hb_{A1c} has been correlated with angiographically proven CAD using Syntax score.[20]

The SYNTAX (Synergy between Percutaneous Coronary Intervention with TAXUS and Cardiac Surgery) score has been developed as a comprehensive angiographic scoring tool for quantification of coronary lesions with respect to their number, location, and complexity.[21]

Aim of the Work

The aim of the present study was to assess the prognostic impact of admission Hb_{A1c} in patients without known diabetes mellitus who were admitted with acute ST elevation myocardial infarction, on outcome of 1ry PCI and short-term outcome of adverse cardiac events.

Chapter 1

ACUTE MYOCARDIAL INFARCTION

In the late 19th century, post-mortem examinations demonstrated a possible relationship between thrombotic occlusion of a coronary artery and myocardial infarction (MI).[22] However; it was not until the beginning of the 20th century that the first clinical descriptions appeared describing a connection between the formation of a thrombus in a coronary artery and its associated clinical features.[23]

The clinical entity was referred to as coronary thrombosis, although use of the term 'MI' ultimately prevailed. Over the years, several different definitions of MI have been used, leading to controversy and confusion. Hence, a general and worldwide definition for MI was needed. This occurred for the first time in the 1950–70s, when working groups from the World Health Organization (WHO) established a primarily electrocardiographic (ECG)-based definition of MI intended for epidemiological use.[24]

With the introduction of more sensitive cardiac biomarkers, the European Society of Cardiology (ESC) and the American College of Cardiology (ACC) collaborated to redefine MI using a biochemical and clinical approach, and reported that myocardial injury detected by abnormal biomarkers in the setting of acute myocardial ischemia should be labeled as MI.[25]

Onset of myocardial ischemia is the initial step in the development of MI and results from an imbalance between oxygen supply and demand. Myocardial ischemia in a clinical setting can most often be identified from the patient's history and from the ECG. Possible ischemic symptoms include various combinations of chest, upper extremity, mandibular, or epigastric discomfort during exertion or at rest, or an ischemic equivalent such as dyspnea or fatigue. Often, the discomfort is diffuse; not localized, nor positional, nor affected by movement of the region. However, these symptoms are not specific for myocardial ischemia and can be observed in other conditions such as gastrointestinal, neurological, pulmonary, or musculoskeletal complaints. MI may occur with atypical symptoms such as palpitations or cardiac arrest, or even without symptoms.[26] Very brief episodes of ischaemia too short to cause necrosis can also cause cTn release and elevations. The involved myocytes can subsequently die due to apoptosis.[27]

If myocardial ischemia is present clinically or detected by ECG changes together with myocardial injury, manifested by a rising and/ or falling pattern of cardiac troponin (cTn) values, a diagnosis of acute MI is appropriate.

Despite the fact that the majority of STEMI patients are classified as a type 1 MI (with evidence of a coronary thrombus), some STEMIs fall into other MI types.[26] MI, even presenting as STEMI, also occurs in the absence of obstructive