GLYCOSYLATED HEMOGLOBIN as a PREDICTOR of MORBIDITY and MORTALITY in PATIENTS with ACUTE CORONARY SYNDROME

Thesis

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List of Abbreviation

ACC	American College of Cardiology
ACS	Acute coronary syndrome
ADA	American Diabetes Association
AF	Atrial Fibrillation
AHA	American Heart Association
AGEs	Advanced glycation end products
AMI	Acute myocardial infarction
AP-1	Activator protein-1
ASK1	Apoptosis signal-regulating kinase 1
AT II	Angiotensin II
CABG	Coronary artery bypass graft.
CAD	Coronary artery disease .
CAMS	Cell adhesion molecules
CHB	Complete heart block
CK	Creatine phosphokinase
Cox-2	Cyclooxygenase-2
CVD	Cardiovascular diseases
DAG	Diacylglycerol
DM	Diabetes mellitus
hsCRP	High sensetivity C reactive protein
eNOS	Endothelial NO synthase
E-selectin	Endothelial selectin
ET-1	Endothelin-1
GM-CSF	Granulocyte-macrophage colony stimulating factor
HDL	High-density lipoprotein
HTN	Hypertension.
HS	Highly significant .

IFG	Impaired fasting glucose
IGT	Impaired glucose tolerance
KLF-2	Krupple-like factor-2
ICAM	Intercellular adhesion molecule
IL	Interleukin
JNC	Joint national comitte
LAO	Left anterior oblique .
LAD	Left anterior descending coronary artery .
LCA	Left coronary artery .
LCX	Left circumflex coronary artery.
LDL	low-density lipoprotein
LMCA	Left main coronary artery.
Lp a	Lipoprotein a
LT	Left.
LV	Left ventricular.
LVEF	Left ventricular ejection fraction.
MACE	Major adverse cardiac events
MI	Myocardial infarction.
MCP-1	Monocyte chemoattractant protein-1
M-CSF	Macrophage-colony stimulating factor
MMPs	Matrix metalloproteinases
NADPH Ox	Nicotinamide adenine dinucleotide phosphate oxidase
NFkB	Nuclear factor kappa B
NO	Nitric oxide
NSTEMI	Non ST elevation myocardial infarction
MTHFR	Methylene tetrahydrofolate reductase
PAI-1	Plasminogen activator inhibitor 1
PCI	Percutaneous coronary intervention
PDA	Posterior descending artery
PKC	Protein kinase C
PTCA	Percutaneous transluminal coronary angioplasty.

P-selectin	Platelet selectin
RAGE	Receptor for advanced glycation end products
RAO	Right anterior oblique.
RBS	Random Blood sugar
RCA	Right coronary artery.
SMCs	Smooth muscle cells
STEMI	ST elevation myocardial infarction
SWMI	Segmental wall motion index
TIMI	Thrombolysis in Myocardial Infarction
t-PA	Tissue plasminogen activator
T1D	Type 1 diabetes
T2D	Type 2 diabetes
TF	Tissue factor
Thr	Thrombin
Txnip	thioredoxin-interacting protein
UA	Unstable angina
VCAM	vascular cell adhesion molecule
VF	Ventricular fibrillation
VLA-4	very late antigen-4
VSMC	Vascular smooth muscle cell
VT	Ventricular tachycardia
VWF	Von Willebrand factor
WHO	World health organization

INTRODUCTION

There are several firmly established risk factors for cardiovascular disease such as family history, increase age, smoking, diabetes, high blood cholesterol, hypertension, overweight and physical inactivity.

Diabetes mellitus is associated with a high risk of CHD. ***(*Kannel WB et al, 2000*)***

Diabetes mellitus is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. The chronic hyperglycemia of diabetes is associated with long-term damage, dysfunction, and failure of various organs, especially the eyes, kidneys, nerves, heart, and blood vessels. Its classified as follow :

- ***Type 1 diabetes*** encompasses diabetes that is primarily a result of pancreatic beta cell destruction and is prone to ketoacidosis. This form includes cases due to an autoimmune process and those for which the etiology of beta cell destruction is unknown.

- ***Type 2 diabetes*** may range from predominant insulin resistance with relative insulin deficiency to a predominant secretory defect with insulin resistance.

- ***Gestational diabetes mellitus*** refers to glucose intolerance with onset or first recognition during pregnancy.

- ***Other specific types*** include a wide variety of relatively uncommon conditions, primarily specific genetically defined forms of diabetes or diabetes associated with other diseases or drug use .***(American Diabetes Association,2012)***

Prediabetes is a practical and convenient term referring to impaired fasting glucose (IFG), impaired glucose tolerance (IGT) or a glycated hemoglobin (HBA1C) of 6.0% to 6.4%, each of which places individuals at high risk of developing diabetes and its complications.***(American Diabetes Association,2012)***

Diabetes is an important chronic disease which incidence is globally increasing and though considered as an epidemic. The World Health Organization (WHO) estimated there were 30 million people who had diabetes worldwide in 1985. This number increased to 135 million by 1995 and reached 217 million in 2005. By the year 2030 WHO predicts this number will increase to at least 366 million. This growth in diabetes prevalence, driven principally by an increased prevalence of type 2 diabetes (T2D), is occurring in both developing and developed countries. ***(Wild S et al, 2004)***

Diabetes is a disease that is strongly associated with both microvascular and macrovascular complications, including retinopathy, nephropathy, and neuropathy (microvascular) and ischemic heart disease, peripheral vascular disease, and cerebrovascular disease (macrovascular), resulting in organ and tissue damage in approximately one third to one half of people with diabetes. ***(UKPDS, 1991)***

Cardiovascular diseases (CVD) are the most prevalent cause of mortality and morbidity among people with T2D and T1D. ***(Orasanu G and Plutzky J, 2009).***

In 2004, in the USA the presence of CVD and stroke was found in 68% and 16% of deaths related to diabetes among people older than 65 years, respectively.

Adult people with diabetes present rates of mortality due to heart disease and stroke from two to four times higher than those without diabetes. ***(Centers for Disease Control and Prevention, 2011).***

It has been stated that patients with T2D without a previous history of myocardial infarction have the same risk of coronary artery disease (CADs) as nondiabetic subjects with a history of myocardial infarction. ***(Haffner SM et al, 1998)***

This has led the National Cholesterol Education Program to consider diabetes as a coronary heart disease risk equivalent. ***(National Cholesterol Education Program, 2002)***

However, there is still some uncertainty as to whether the cardiovascular risk conferred by diabetes is truly equivalent to that of a previous myocardial infarction. ***(Bulugahapitiya U et al, 2009)***

In general, patients with diabetes aggregate other comorbidities such as obesity, hypertension, and dyslipidemia which also contribute to increase the risk for CVD. ***(AlGhatrif M et al, 2011)***