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Association Of Glycosylated Haemoglobin Level And Microalbuminuria With The Severity Of Coronary Artery Disease

Thesis Submitted by

Mohamed Mahmoud Elhattab, MBBCh

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Supervisors

Ahmed Elsherif, MD.

Professor of Critical Care Medicine

Critical Care Department

Cairo University

Mohamed Khaled, MD

Lecturer of Critical Care Medicine

Critical Care Department

Cairo University

Ahmed Ibrahim, MD

Lecturer of Critical Care Medicine

Critical Care Department

Cairo University

Department of Critical Care Medicine
Faculty of Medicine
Cairo University

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Mohamed Elhattab

Contents

List of abbreviations

A1c	**:**	glycosylated hemoglobin
ACC	**:**	American Collage of Cardiology
ACE	**:**	Angiotensin Converting Enzyme
ACEIs	**:**	Angiotensin-Converting Enzyme Inhibitors
ACS	**:**	Acute Coronary Syndrome
ADA	**:**	American Diabetes Association
AGEs	**:**	Advanced Glycation End products
AHA	**:**	American Heart Association
ANCA	**:**	Antineutrophil Cytoplasmic Antibodies
ARBs	**:**	Angiotensin II Receptor Blockers
ARTS	**:**	Arterial Revascularization Therapies Study
BMI	**:**	Body Mass Index
cAMP	**:**	cyclic Adenosine MonoPhosphate
CAC		Coronary Artery Calcification
CAD		Coronary Artery Disease
CCU	**:**	Coronary Care Unit
CHD	**:**	Coronary Heart Disease
CKD	**:**	Chronic Kidney Disease
CRP	**:**	C-Reactive Protein
CST	**:**	Crush Stent Technique
CV	**:**	Cardio-Vascular
CVA	**:**	Cerebro-Vascular Accident
CVD	**:**	CardioVascular Disease
CX	**:**	Circumflex Artery

DM	**:**	Diabetes Mellitus
eNOS	**:**	endothelial Nitric Oxide Synthase
FH		Family History
FSGS	**:**	Focal Segmental Glomerulosclerosis
GBM	**:**	Glomerular Basement Membrane
GCW	**:**	Glomerular Capillary Wall
GFR	**:**	Glomerular Filtration Rate
GIK	**:**	Glucose-Insulin-Potassium
GP	**:**	Glyco-Protein
GPIIb/IIIa	**:**	Platelet Glyco-Protein IIb/IIIa Receptors
HDL	**:**	High-Density Lipoprotein
HF	**:**	Heart Failure
IABP	**:**	Intra-Aortic Balloon Pump
ICAM	**:**	Inter-Cellular Adhesion Molecule
ICPS	**:**	Institut Cardiovasculaire Paris Sud
IHD		Ischemic Heart Disease
IκB	**:**	Inhibitor of nuclear factor κB
IL	**:**	Inter-Leukin
K_{ATP}		Adenosine triphosphate dependent potassium channels
KST	**:**	Kissing Stent Technique
LAD	**:**	Left Anterior Descending artery
LCA	**:**	Left Coronary Artery
LCX	**:**	Left Circumflex Artery
LDL	**:**	low-density lipoprotein
LMS	**:**	Left Main Stem
LV	**:**	Left Ventricle
MA		Microalbuminuria
MACE	**:**	Major Adverse Cardiac Events

MCP	**:**	Monocyte Chemoattractant Protein
MI	**:**	Myocardial Infarction
NCDR	**:**	National Cardiovascular Device Registry
NF	**:**	Nuclear Factor
NFκB	**:**	Nuclear Factor κB
NNE	**:**	Northern New England
NO	**:**	Nitric Oxide
NYHA	**:**	New York Heart Association
PAI-1	**:**	Plasminogen Activator Inhibitor 1
PCI	**:**	Percutaneous Coronary Intervention
PCT	**:**	Proximal Convoluted Tubule
PPAR	**:**	Peroxisome Proliferator–Activated Receptor
PVD	**:**	Peripheral Vascular Disease
RAAS	**:**	Renin Angiotensin Aldosterone System
RAGE	**:**	Receptor for Advanced Glycation End products
RCA	**:**	Right Coronary Artery
ROS	**:**	Reactive Oxygen Species
SB	**:**	Side Branch
SCAI	**:**	Society for Cardiac Angiography and Intervention
Syntax	**:**	**Syn**ergy Between Percutaneous Coronary Intervention With **TAX**US and Cardiac Surgery
TF	**:**	Tissue Factor
TO	**:**	Total Occlusion
UACRs	**:**	Urinary Albumin-to-Creatinine Ratios
UAER	**:**	Urine Albumin Excretion Rate
VCAMs	**:**	Vascular Cell Adhesion Molecules

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Association Of Glycosylated HaemoglobinLevel And MicroalbuminuriaWith The Severity Of Coronary Artery Disease

Abstract

Diabetes mellitus (DM) is known to cause microvascular and possibly macrovascular complications

Aim: This study was designed to evaluate the association between glycosylated hemoglobin (HbA1C) level and the severity of coronary artery disease and to uncover the scope of the relation between albuminuria and the severity of coronary artery disease in diabetic patients

Methods: 100 diabetic Patients and were scheduled for cardiac catheterization were enrolled in our study. The severity of CAD was assessed using the Gensini score.

Results: In our study hypertension was present in 70 patients, dyslipidemia in 48, obesity in 32, family history of IHD was present in 36 and 36 patients were smokers, microalbuminuria in 22 patients. The mean Gensini score was 50±39.4 and the mean HbA1C was 10.3±3.9 %,. There was a significant positive correlation between Gensini score and HbA1C ($p < 0.001$),also between Gensini score and both of duration of DM ($p=0.011$) and age ($p=0.017$). There was significant difference between patients with microalbuminuria versus those without microalbumnuria regarding their Gensini scores (73.1±40 versus 43.6±30.6, *P* value <0.001).

Conclusion: There was a positive correlation between severity of CAD and glycosylated hemoglobin, microalbuminuria, age and duration of diabetes

Key Words: diabetes mellitus, Gensini score, HbA1C, microalbuminuria, severity of coronary artery disease.

Introduction

Atherosclerotic disease accounts for most of the excess mortality in patients with diabetes mellitus (DM).[1]

Whereas much attention historically has focused on the prevention and treatment of microvascular disease complications of diabetes (i.e., retinopathy, nephropathy, and neuropathy), cardiovascular disease (CVD) remains the principal morbidity and driver of mortality in the setting of diabetes, most commonly in the form of coronary heart disease (CHD), but also in the incremental risk associated with diabetes for cerebrovascular disease, peripheral vascular disease, and heart failure. For these reasons, continual efforts toward mitigating the risk of CVD in diabetes remain a global public health imperative.

Whereas older studies have suggested a diabetes-associated CVD risk similar to that observed among non diabetic patients with a prior myocardial infarction (MI) that is, a “coronary disease equivalent”.

More recent observations from clinical trials showed that diabetic patients have a higher prevalence of coronary heart disease (CAD) with an increased number of fatal coronary events due to a higher incidence of plaque rupture and superimposed thrombosis in diffusely diseased coronary arteries. Additionally Diabetic patients develop complications more frequently after myocardial infarction (MI) and have double the in-hospital and six-month mortality compared to non-diabetic patients.[1]

In the United Kingdom Prospective Diabetic Study (UKPDS), deaths from cardiovascular events were 70 times more common than deaths from microvascular complications. The UKPDS3 demonstrated that intensive glucose control, by keeping the HbA1c < 7%, helped to reduce microvascular complications; the reduction in risk of MI was of borderline significance. Other studies suggest that coronary artery disease and HbA1c are predictors of cardiovascular mortality.[2, 4]

The American Diabetes Association in its recent position statement stated that lowering HbA1c may be associated with reduction of microvascular, neuropathic and possibly macrovascular complications of diabetes mellitus. They suggested that more studies should be done to establish the relationship between HbA1c and macrovascular complications.[5]

Cardiovascular disease (CVD) is the major cause of morbidity and mortality in people with impaired renal function and ESRD.[6-7]

Individuals with diabetes-associated nephropathy typically have long periods of excessive albuminuria with gradual reductions in creatinine clearance as they approach end stage. There is a graded increase in risk for cardiovascular and total mortality with incremental increases in urine albumin:creatinine ratio (ACR) among high-risk individuals with hypertension and diabetes .[8]

There seems to be no threshold level at which this increase in risk starts, as even minor increases in ACR are associated with higher mortality rates.

Cross-sectional studies of both diabetic and non-diabetic patients have shown microalbuminuria to be associated with coronary heart disease and peripheral vascular disease.[9-11] In addition, it is also a sensitive index of generalized microvascular disease and a marker for multiorgan damage.[12] Albumin excretion rate between 30 and 300 mg/day or 20 and 200 μg/min is known as microalbuminuria, which is below the detection threshold of conventional methods for measuring urinary protein (e.g. dipstick). Above 300 mg/day is overt albuminuria. In prior studies, there has been consistent evidence that microalbuminuria was an independent factor of excess mortality regardless of the collection procedure used.[13]

Aim of the work

The aim of our study was:

1) To examine the correlation between the control of diabetes mellitus as assessed by HbA1c and the severity of coronary artery disease as assessed by coronary angiogram, using the Gensini score.

2) To uncover the scope of the relation between albuminuria and the severity of coronary artery disease in diabetic patients.

Diabetes and coronary artery disease

Diabetes mellitus affects approximately 180 million people worldwide, and the number is expected to double by 2030,[14] of those with diabetes, 90% have type 2 diabetes, approximately 80% of whom live in low- and middle-income countries. Future growth will be highest in developing regions such as Asia, Latin America and the Caribbean, and sub-Saharan Africa, where growth rates of diabetes are expected to be between 105% and 162%, compared with about 72% in the United States and 32% in Europe.[15-16] In addition, most cases are and will remain within the 45- to 64-year-old age group in developing countries, whereas those older than 65 years are most affected in developed countries, Figure (1).

Rising rates of obesity, as well as an aging and urbanized population, likely link to the diabetes epidemic. Almost 90% of type 2 diabetes cases are related to obesity, and diabetes and its related complications are the costliest consequences of obesity. Mortality from diabetes is also increasing. About 1.1 million people died of diabetes in 2005, and that number is estimated to increase by 50% in 10 years.[14]

Interestingly, Asian countries face a relatively larger burden of diabetes compared with the Europe and Central Asia or Latin America and Caribbean regions. For example, India and China have the largest numbers of diabetics—32 million and 21 million, respectively—in the world.[16]Indonesia, Pakistan, and Bangladesh are in the top 10 in terms of high absolute number of diabetics. Asian populations may have a higher risk for developing diabetes, even at a lower body mass index (BMI),

because of a greater tendency toward visceral obesity. In addition, this population may experience both under-nutrition (during the peri-natal period) and rapid weight gain (during childhood), a combination that increases the risk for insulin resistance.[15]

In Egypt, it is estimated that;by the year 2025, the number of urban residents with diabetes will increase 3.2 times from approximately 2.28 million to 7.21 million and 13.3% of the population above 20 years of age will have diabetes.[15]

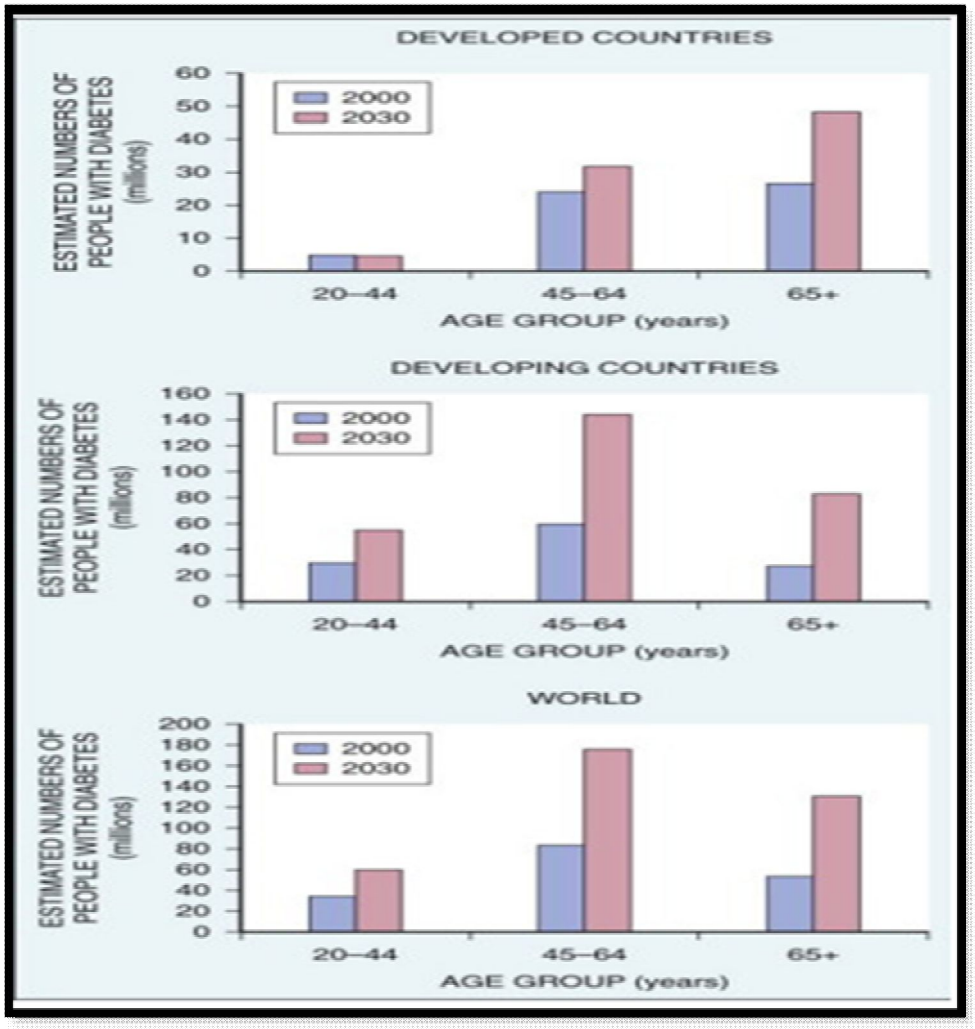

FIGURE 1 : Estimated number of adults with diabetes in 2000 and projected for 2030 stratified by age group, with projections for the overall global population and by developed and developing country categories.[15]