Correlation between Prediabetes and Coronary Artery Disease Severity in Patients Undergoing Elective Coronary Angiography

Thesis

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بسم الله الرحمن الرحيم
وَأَنْزَلَ اللهُ عَلَيْكَ
الْكِتَابَ وَالْحِكْمَةَ
وَعَلَّمَكَ مَا لَمْ
تَكُنْ تَعْلَمُ وَكَانَ
فَضْلُ اللهِ عَلَيْكَ
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Ahmed Mostafa Ahmed Muhammed

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List of Abbreviations

Abb.	Full term
A1C	*Glycated hemoglobin*
ACS	*Acute coronary syndrome*
ADA	*American diabetes association*
AGE	*Advanced glycation end products*
CA	*Coronary angiography*
CABG	*Coronary artery Bypass grafting*
CAC	*Coronary artery calcification*
CAD	*Coronary artery disease*
CKD	*Chronic kidney disease*
CVD	*Cardiovascular disease*
DCCT	*Diabetes Control and Complications Trial*
DM	*Diabetes mellitus*
eGFR	*Estimated glomerular filtration rate*
eNOS	*Endothelial nitric oxide synthase*
FFA	*Free fatty acids*
FPG	*Fasting plasma glusoce*
GDM	*Gestational diabetes mellitus*
GLP-1	*Glucagon like peptide-1*
GSH	*Glutathione*
hs-CRP	*High sensitivity C-reactive protein*
HTN	*Hypertension*
IFG	*Impaired fasting glucose*
IGT	*Impaired glucose tolerance*
IHD	*Ischemic heart disease*

List of Abbreviations cont...

Abb.	Full term
IQR	*Interquartile range*
LDL	*Low density lipoproteins*
MAU	*Microalbuminuria*
MDA	*Malondialdehyde*
MDRD	*Modification of direct in renal disease*
MODY	*Maturity-onset diabetes of the young*
NGSP	*National Glycohemoglobin Standardization Program*
OCT	*Optical coherence tomography*
PCI	*Percutaneous coronary intervention*
PTCA	*Percutaneous trans luminal coronary angioplasty*
SCAD	*Stable Coronary artery disease*
TLR	*Toll like receptors*

INTRODUCTION

Diabetes is a chronic disease that is responsible for a high rate of morbidity & mortality which can be attributed to atherosclerosis & cardiovascular disease ***(Kramer et al., 2003)***. It is estimated that type II diabetes doubles the risk of cardiovascular disease even after adjustment of other cardiovascular risk factors ***(DECODE Study Group, 2003)***.

Despite the increase in the rate of treatment of diabetic patients with statins and glucose lowering drugs achieving target glycated hemoglobin (HBA1C) levels and low density lipoprotein(LDL) levels ***(American Diabetes Association, 2016)***, another strategy of effective management of diabetes lies in management of the disease process at earlier stage (prediabetes) ***(Kramer et al., 2003)***.

"Prediabetes" is a collective term that encloses individuals with glucose levels lower than cut off levels for diabetes but too high to be considered normal." It is the term used for individuals with impaired fasting glucose (IFG) and/or impaired glucose tolerance (IGT) and/or HbA1C levels ranging from 5.7 to 6.4%" ***(American Diabetes Association, 2017)***.

Prediabetes is not an uncommon condition with an estimated worldwide prevalence of 343 million expected to rise to 471 million by 2035 ***(International Diabetes Federation, 2015)***.

Prediabetes is a serious clinical condition that not only increases the risk of developing diabetes but also increases the burden of cardiovascular disease risk. Compared to normoglycemic individuals, patients with prediabetes show 20% higher risk of developing cardiovascular disease (CVD) ***(Færch et al., 2014)***.

Prediabetes is a toxic state in which both micro & macro vascular complications of diabetes can manifest ***(Brannick et al., 2016)***.

Prediabetes is associated with low grade inflammation with high level of inflammatory cytokines ***(Sabanayagam et al., 2011)*** as well as adipose tissue inflammation & dysfunction ***(Lopategi et al., 2016)*** thus accelerating atherosclerosis. Compared to normal subjects, prediabetics showed a higher atherosclerotic burden that was comparable to patients with overt diabetes ***(Kurihara et al., 2013)***. Such atherosclerotic process involved coronary & cerebral vascular beds and caused significant morbidity & mortality ***(Barr et al., 2007)***. It was demonstrated that among patients with acute coronary syndrome (ACS) prediabetes prolonged the patients' hospital stay and increased the incidence of major adverse cardiac events (MACE) during in-hospital stay ***(AbuShady et al., 2015)***.

Aim of the Work

Observing the effect of prediabetes on the severity of coronary artery disease in patients undergoing elective coronary angiography.

Chapter 1

DIAGNOSIS OF DIABETES AND PRE DIABETES

Diabetes is a chronic disease that is responsible for high rate of morbidity & mortality which can be attributed to atherosclerosis & cardiovascular disease ***(Kramer et al., 2003).*** Diabetes is a worldwide health problem that affects around 415 million people ***(World Health Organization, 2016)*** expected to rise to 522 million by 2030 ***(International Diabetes Federation, 2011).*** A large burden of morbidity and mortality can be attributed to diabetes being the most common cause for blindness, amputation, doubling the risk of cardiovascular disease specifically myocardial infarction and stroke ***(Brannick et al., 2016) (Centers for Disease Control and Prevention, 2014)*** as well as being the leading cause of chronic kidney disease ***(USRDS, 2018).***

The major causes of death in patients with diabetes are cardiovascular diseases ***(Martín-Timón et al., 2014).***

It is estimated that the risk of cerebrovascular stroke and coronary artery disease (CAD) is increased two to four times in patients with DM as well as the risk of heart failure ***(Huo et al., 2016).***

The cardiovascular risk in DM has a gradient that is affected by many factors; the most important among them are

modifiable risk factors of CVD as obesity, hypertension and dyslipidemia which are highly prevalent in patients with DM ***(Echouffo-Tcheugui & Kengne, 2013).***

The management of diabetes is not limited to appropriate control of hyperglycemia but it extends to management of existing comorbidities and risk factors including dyslipidemia and hypertension and screening for complications including cardiovascular diseases, retinal disease and chronic kidney disease ***(World Health Organization, 2016).*** Proper management of those factors substantially reduces the risk of CVD in patients with DM ***(del Cañizo Gómez FJ & Moreira Andrés, 2008).***

There are variable lab tests to diagnose diabetes including fasting plasma glucose (FPG) and 2-hour plasma glucose (2-h PG) and A1C test ***(International Expert Committee, 2009; American Diabetes Association, 2014).***

DM can be diagnosed by one of the following criteria:

"1-FPG ≥126 mg/dL (7.0 mmol/L). Fasting is defined as no caloric intake for at least 8 h.

OR

2-2h PG ≥ 200 mg/dL (11.1 mmol/L) during an OGTT. The test should be performed as described by the WHO, using a

glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water.

OR

3-A1C ≥ 6.5% (48 mmol/mol). The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay.

OR

In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥ 200 mg/dL (11.1 mmol/L)." ***(American Diabetes Association, 2017).***

The correlation between those tests is not complete with the 2-h PG being the most sensitive test among them ***(American Diabetes Association, 2017)***. Although A1C test showed lower sensitivity at the given cut points (A cut off of 6.5% identifies only two thirds of cases diagnosed by an FPG cut point of 126mg/dl) ***(Cowie et al., 2010)*** yet it has many advantages over plasma glucose tests including the need for a single sample without the necessity of fasting ***(American Diabetes Association, 2017).***

"Diabetes can be classified into the following general categories:

1. Type 1 diabetes (due to autoimmune β -cell destruction, usually leading to absolute insulin deficiency).

2. Type 2 diabetes (due to a progressive loss of β -cell insulin secretion frequently on the background of insulin resistance).

3. Gestational diabetes mellitus (GDM) (diabetes diagnosed in the second or third Trimester of pregnancy that was not clearly overt diabetes prior to gestation).

4. Specific types of diabetes due to other causes, e.g. monogenic diabetes syndromes (Such as neonatal diabetes and maturity-onset diabetes of the young [MODY]), diseases of the exocrine pancreas (such as cystic fibrosis), and drug- or chemical-induced diabetes (such as with glucocorticoid use, in the treatment of HIV/AIDS, or after organ transplantation)" ***(American Diabetes Association, 2017).***

Type 2 diabetes is the most common type accounting for over 90% of cases ***(World Health Organization, 2016).***

The development of Type 2 diabetes is heralded by a stage called prediabetes ***(Brannick et al., 2016).*** It is a grey zone in which glucose level are too high to be considered normal yet they are lower than cut off for definite diagnosis of diabetes ***(Bansal, 2015).***

Prediabetes is a spectrum that includes patients with impaired fasting glucose (IFG) with FPG ranging from 100 to 125 mg/dl and/or impaired glucose tolerance (IGT) with 2-h PG