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REVIEW ARTICLE

Possible correlations between Acute coronary syndrome and Diabetes Mellitus: Review Article

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ABSTRACT

Background: Hyperglycemia and glucose intolerance are hallmarks of diabetes mellitus, an illness that can arise from insulin insufficiency, decreased insulin action, or both**.** Coronary artery disease (CHD) account for most health-care costs in diabetic people. T2DM is closely linked to CHD. Several investigations have demonstrated this strong association. The risk of cerebrovascular disease and stroke is increased by having diabetes. There are a number of macrovascular problems associated with type 2 diabetes, including an increased risk of death, ischemic disease, stroke, and other cardiovascular events. Conditions such as unstable angina, ST-elevation myocardial infarction (STEMI), and non-ST elevation myocardial infarction (NSTEMI) are all part of acute coronary syndrome (ACS). It is a subtype of CHD that accounts for one-third of all fatalities in adults over the age of 35. The present evidence regarding the Possible correlations between Acute coronary syndrome and Diabetes is summarized in this review. **Conclusion:** With a high death rate and a growing frequency over the past decade, diabetes is a common comorbidity among patients hospitalized for acute coronary syndromes (ACS). Diabetic individuals make up about 25-30% of ACS admissions. Diabetics are more likely to experience ACS, which happens earlier in the disease and is linked to higher mortality and the likelihood of further ischemic episodes. The worse outcomes seen by diabetic individuals are accompanied by an elevated proinflammatory and prothrombotic condition.

Keywords: Acute coronary syndrome, Diabetes Mellitus, ST-elevation myocardial infarction

INTRODUCTION

Hyperglycemia and glucose intolerance are hallmarks of diabetes mellitus, a syndrome that can develop due to insulin insufficiency, decreased insulin action, or both [1]. Life expectancy is shortened, microvascular complications of diabetes are a major cause of morbidity, macrovascular repercussions (such as ischemic heart disease, stroke, and peripheral vascular disease) are more likely to occur, and quality of life is reduced. The pathogenetic pathways that cause type II diabetes are multifactorial. Both insulin insufficiency and insulin resistance can be caused by various processes, some of which harm pancreatic beta cells [2,3]. Diabetes mellitus can cause symptoms including thirst, polyuria, blurred vision, and weight loss. Symptoms are frequently mild or nonexistent [4].

One of the world's most pressing health concerns, diabetes is on the rise. The International Diabetes Federation predicts that 463 million people will be living with diabetes in 2019, rising to 578 million by 2030 and 700 million by 2045. Three quarters of people with diabetes are of working age, and two-thirds reside in urban areas [5].

The International Diabetes Federation- Middle East and North Africa (IDF MENA) region counts Egypt among its 21 member states. An estimated 108 million people in the MENA region would have diabetes by 2045, up from the current 55 million. According to the IDF's 2019 predictions, Egypt will have 8,850,400 cases and a frequency of 15.2% among adults, putting it seventh globally. By 2045, Egypt is projected to surpass all other countries in terms of size [5].

Organs such as the eyes, nerves, feet, blood arteries, kidneys, and heart are particularly vulnerable to injury, dysfunction, and failure in those with chronic diabetes. Coronary artery disease, cerebrovascular disease, peripheral vascular disease, and microvascular consequences like retinopathy, neuropathy, and nephropathy are all linked to diabetes [6,7].

A few instances of macrovascular problems include coronary heart disease (CHD), heart failure, arrhythmias, and sudden cardiac death. People with type 2 diabetes are at increased risk for cardiovascular diseases, including cerebral vascular disease and peripheral artery disease (T2DM). Both forms of diabetes are characterized by complications, which can lead to serious health problems or even death. The primary killer of type 2 diabetics is cardiovascular disease [8].

Coronary artery disease (CAD), peripheral artery disease (PAD), congenital heart disease (CHD), heart failure (HF), cerebrovascular disease (CVD), and other similar conditions are all part of the cardiovascular disease (CVD) umbrella. Heart failure, cerebrovascular illness, coronary artery disease (CAD), and other major adverse cardiovascular events (MACE) are the primary emphasis of this scientific statement. The clumping of lipoproteins in the artery wall is the first step in atherosclerosis. Vascular alterations occur because of foam cell aggregation in the subendothelial space and oxidation of low-density lipoprotein (LDL) particles [9].

Most healthcare expenditures incurred by diabetics are due to coronary artery disease (CHD). Obesity is associated with type 2 diabetes. This substantial relationship has been shown by multiple investigations. The risk of cerebrovascular disease and stroke is increased by having diabetes. There are a number of macrovascular consequences associated with type 2 diabetes, including an increased risk of death, ischemic illness, and stroke. Heart failure and cardiac dysfunction develop in type 2 diabetics as a consequence of a process that affects the myocardium [8].

If there is no epicardial coronary artery disease, hypertension, or significant valve disease, but there is decreased myocardial function or structure, the cardiac ailment is called "diabetic cardiomyopathy" (DC). DC is characterized by enlarged heart muscles and malfunction during diastole; this condition can cause heart failure while maintaining an adequate ejection fraction (HFpEF) [10].

Many abnormalities of cardiac function, such as arrhythmias and SCD, are caused by chronic hyperglycemia in type 2 diabetes. Cardiac autonomic neuropathy is a common cause of arrhythmias in type 2 diabetes. The various types of arrhythmias were examined in a cross-sectional study involving one hundred types 2 diabetic patients. Sinus tachycardia (32% of cases), total heart block (20%), sinus bradycardia (15%), and atrial fibrillation (AF) were the most common arrhythmias (15 percent). The Atrial premature complex affected 3% of patients, while ventricular premature complex affected 10%. Additionally, 3% had first-degree AV block, 1% had ventricular tachycardia, and 1% had paroxysmal supraventricular tachycardia. The likelihood of arrhythmias was significantly higher in patients with uncontrolled diabetes and other comorbidities [11]. Cardiovascular disease (CVD) in all its forms (CAD, stroke, HF, AF, peripheral artery disorders, etc.) is two- to four-fold more common in those with type 2 diabetes [12].

In addition, many patients with CVD have undiagnosed T2DM. Given that having diabetes and CVD, especially at a younger age, has a major impact on prognosis, it is of utmost importance to screen patients with CVD for diabetes and to assess CV risk in individuals with diabetes, and evaluate them for CV and kidney disease [13].

Ischemia with ST-elevation, non-ST-elevation, unstable angina, and other related disorders are known collectively as acute coronary syndrome (ACS). Among adults over the age of 35, it accounts for one-third of all fatalities due to coronary heart disease (CHD) [14].

Diabetic individuals make up about 25-30% of ACS admissions. Diabetics are more likely to experience

ACS, which happens earlier in the disease and is linked to higher mortality and the likelihood of further ischemic episodes [15].

About 25% of patients who arrive with ST-elevation myocardial infarction (STEMI) have a family history of diabetes, and over 40% have type 2 diabetes or pre-diabetes that was not previously identified [16]. The death rate is higher for diabetic patients with ACS when contrasted with nondiabetic people. Plaque rupture can occur in these patients due to their propensity for a proinflammatory and prothrombotic condition brought on by several pathophysiological abnormalities [17].

Atherosclerosis worsens and the risk of acute coronary syndrome is higher in those with diabetes. Diabetic individuals make up about 25-30% of ACS admissions. The occurrence of ACS is early in diabetics, and it is linked to higher mortality rates and a greater likelihood of repeated ischemia episodes [15].

Diagnosis

Diabetic patients are more likely to have unusual symptoms than non-diabetic patients, which hinders the ability to diagnose and treat the disease quickly. In addition, there is an increased prevalence of atherosclerotic plaques linked to decreased microvasculature vasodilation, a larger percentage of coronary lesions, and multivessel disease in diabetic patients [18].

Management of STEMI in diabetic patient

1)Reperfusion

Urgent mechanical or pharmacological reperfusion should be administered to individuals with myocardial infarction who have persistent ST-elevation or fresh left bundle branch block to limit the extent of myocardial damage [19].

a) Pharmacological reperfusion

Diabetic patients receive thrombolytic treatment less frequently than non-diabetes patients, even though this treatment lowers the mortality rate of patients with acute myocardial infarction (MI). The advantage is just as significant in diabetic patients as it is in non-diabetic patients. Nobody knows why this is happening. Some argue that people with diabetes who get a myocardial infarction do not get the best care possible. [20]. Another theory is that diabetic individuals aren't good candidates for thrombolysis since it takes so long for their symptoms to appear before they're admitted to the hospital [21].

b) Interventional reperfusion

Although fibrinolysis was initially successful in reducing STEMI mortality, it is ineffective in reopening blocked arteries in half of the patients. Since primary PCI is more effective than fibrinolysis in reducing mortality, independent of the period from symptom onset, it has replaced fibrinolysis as the preferred reperfusion method [22].

2)Antithrombotic therapy

Patients with diabetes mellitus (DM) require more effective antithrombotic treatment plans due to their higher atherothrombotic risk and recurrent ischemic event rates. One possible explanation is that this group of patients has anomalies in platelet function, which cause them to be more reactive to platelets. Based on these results, platelet-inhibiting medications are crucial for diabetic individuals [23].

Anti platelets

A) (COX-1) inhibitors (aspirin)

Patients with diabetes mellitus (DM) require more effective antithrombotic treatment plans due to their higher atherothrombotic risk and recurrent ischemic event rates. One possible explanation is that this group of patients has anomalies in platelet function, which cause them to be more reactive to platelets. Based on these results, platelet-inhibiting medications are crucial for diabetic individuals [24]. Previous studies, such as those examining STEMI92–94 and unstable angina/NSTEMI92–94, have consistently shown that aspirin therapy is beneficial in the early management of patients with ACS [25].

B) Glycoprotein IIb/IIIa inhibitors

b) Oral P2Y12 inhibitors

c) anticoagulants

Previous studies, such as those examining STEMI92–94 and unstable angina/NSTEMI92–94, have consistently shown that aspirin therapy is

beneficial in the early management of patients with ACS [26]. When deciding whether to provide oral anticoagulant to patients with atrial fibrillation (AF), the CHA2DS2VASc score takes the presence of diabetes mellitus (DM) into account in order to evaluate stroke risk [27].

D)The significant ischemia risk associated with prolonged combined antithrombotic or antiplatelet therapy: Patients with diabetes should exercise extra caution when selecting antithrombotic medication, and they will reap greater benefits from a longer course of treatment. Current guidelines recommend low dose ticagrelor instead of clopidogrel and prasugrel, and DAPT can be prolonged after 12 months in patients who do not have bleeding problems [28].

Increased platelet reactivity decreased antiplatelet drug response, and an increased risk of thrombotic and ischemic events as well as mortality are all symptoms that diabetic patients experiencing acute coronary syndrome (ACS) and undergoing percutaneous coronary intervention (PCI) should be treated with more effective platelet inhibitors [29].

4) Acute coronary syndrome patients' glucose control: An increased risk of death, a greater infarct size, and more acute pump failure are all consequences of decreased microvascular performance, which is linked to hyperglycemia. Death risk is increased for patients admitted to the hospital with acute coronary syndrome (ACS) and hyperglycemia compared to those with ACS but no hyperglycemia, regardless of diabetes status [30].

The level of glucose in the blood has a stronger correlation with mortality than diabetes itself. 419,420 Hence, it is highly advised that all subjects undergo early blood glucose level evaluation [31].

Hyperglycemia during the acute phase of acute coronary syndromes (ACS) may reflect stress hyperglycemia and is insufficient to establish a diagnosis of diabetes. Once these patients are released, they should undergo additional evaluations. Current recommendations stress the need of selecting an antidiabetic medication class that has been shown to reduce cardiovascular complications and death. Following metformin, the American Diabetes Association and the American College of Cardiology both support SGLT2 inhibitors and GLP-1 RAs as second-line therapy alternatives [32].

Second-line options after metformin include antidiabetic drug classes that have undergone cardiovascular outcome trials to confirm their safety, such as sodium-glucose co-transporter 2 (SGLT2) inhibitors, glucagon-like peptide 1 (GLP-1) receptor agonists, and dipeptidyl peptidase-4 (DPP-4) inhibitors. The greatest overall mortality, renal, and cardiovascular outcomes have been demonstrated with SGLT2 inhibitors. Consistently lower rates of heart failure hospitalization [33].

Assessment of glycemic control:

Glucose management indicator (GMI), time in range (TIR), and continuous glucose monitoring (CGM) plus blood glucose monitoring are the methods used to assess glycemic control (BGM) [34].

Glucose management indicators, time in range, or A1C should be checked at least twice yearly in patients who are achieving treatment objectives (and who have stable glycemic control). Make sure to check a patient's blood sugar levels at least once every three months, or more frequently if their treatment plan has altered or if they aren't reaching their target range [34].

HbA1C:

Hb A1C measures the 3-month glycemic control. With a strong predictive value for diabetic complications, the test is the main tool for assessing glycemic control. This means that A1C testing should be a regular component of diabetes patient treatment, as well as part of the initial evaluation. Patients' glycemic goals are reviewed every three months to ensure they have been achieved and are being maintained [35].

Clinical circumstances, treatment plans, and physician judgement dictate the frequency of A1C measurement. A1C and other glucose tests should only be performed twice yearly for people with type 2 diabetes who have stable glycemia well within objective. Patients who are not responding to treatment or who are experiencing instability may need more frequent testing (every three months, interim evaluations as needed for safety) or may need to be treated more aggressively [36].

Hb A1C limitations:

Due to its indirect nature, the A1C test has limitations when it comes to determining average glycemia. A1C testing, like any other laboratory procedure, might have some degree of error. Healthcare providers should exercise caution when relying solely on A1C to evaluate glycemic control, particularly when the result is near the cutoff for pharmacological therapy adjustments, even though A1C variability is lower than blood glucose fluctuation. Anemias (hemolytic and others), glucose-6-phosphate dehydrogenase deficiencies, recent blood transfusions, erythropoiesis-stimulating medication use, end-stage renal illness, pregnancy, and other circumstances can all impact red blood cell turnover, which in turn affects the Hb A1C result [37].

A1C cannot detect hypoglycemia or glycemic fluctuations. The best way to assess glycemic control in those who are prone to glycemic fluctuations is to combine BGM/CGM and A1C data. This is especially true for people with type 1 diabetes or type 2 diabetes who have a major insulin shortage. It is possible that the aforementioned factors or glycemic variability, with BGM failing to detect the extremes, are to blame for the contradictory results between BGM/CGM and A1C. [34].

2. Glucose assessment by continuous glucose monitoring:

All continuous glucose monitoring (CGM) devices should be regarded as providing standardised, one-page glucose reports with visual indicators like the ambulatory glucose profile. One way to measure glycemic control is by looking at the time in range, which is linked to the risk of microvascular problems. Furthermore, time below aim, and time above target are valuable metrics for assessing the treatment plan [34].

Continuous glucose monitors are rapidly enhancing diabetes care. One useful indication of glycemic control and glucose patterns that correlates well with A1C is time in range (TIR), as suggested in the guidelines [38].

To reach their glycemic goals, many diabetics rely on glucose monitoring. As part of multifactorial therapy, BGM has been utilized in large-scale clinical trials of insulin-treated patients to demonstrate the effectiveness of rigorous glycemic control in preventing diabetic complications. That is why BGM is a must-have for effective insulin therapy. Most people with type 1 diabetes now routinely use CGM to check their glucose levels [39].

Glycemic goals

Many adults who are not pregnant should aim for an A1C level of less than 7% (53 mmol/mol) if they do not experience severe hypoglycemia. To evaluate glycemia, many persons who are not pregnant aim for a time in the range of >70% when utilizing an ambulatory glucose profile or glucose management indicator, with a time below <4% and a time <54 mg/dL <1%. If it is possible to safely reach A1C values lower than 7% without experiencing major hypoglycemia or other treatment-related side effects, it may be tolerable and even useful, depending on provider discretion and patient preference. Patients with a short life expectancy or in cases when the treatment's risks outweigh its advantages might benefit from less strict A1C targets, like <8% [64 mmol/mol]. (**Figure 1)** [34].

Diabetic patients with ACS still have poorer outcomes than non-diabetic patients, despite improvements in percutaneous coronary intervention (PCI) and coronary artery by-pass graft (CABG) techniques and the use of more powerful antiplatelet medications such as ticagrelor and prasugrel in the last decade. The guidelines recommend an early invasive approach for patients with non-ST elevation ACS; however, the revascularization strategy is less clear in the setting of multivessel (MV) or complex coronary artery disease (CAD). Urgent percutaneous coronary intervention (PCI) is the preferred method of revascularization in ST elevation myocardial infarction [15].

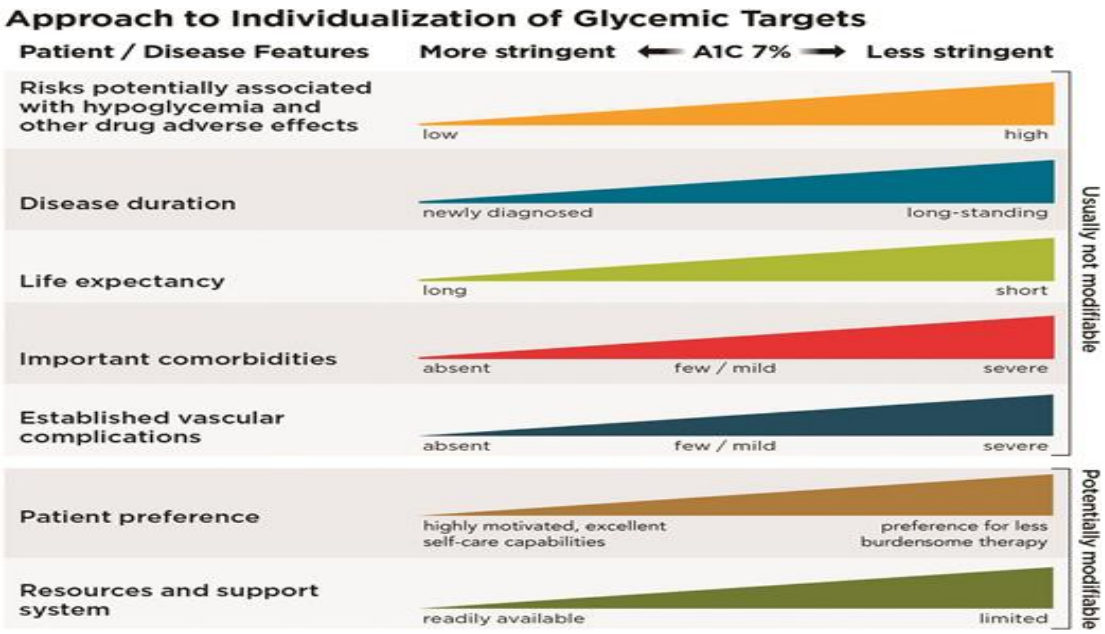

Figure (1): Patient and disease factors used to determine optimal glycemic targets [34].

CONCLUSION

Hospitalized patients with acute coronary syndrome (ACS) often have diabetes as a co-morbidity; this condition has been more common in the past decade and is associated with a high mortality rate. Patients admitted for ACS typically have diabetes, making up about 25-30% of the total. Diabetics have an elevated risk of death and repeated ischemia episodes due to the earlier onset of ACS. Patients with diabetes have worse outcomes due to an elevated proinflammatory and prothrombotic condition.

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