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DIABETES MELLITUS AND CARDIOVASCULAR DISEASES

Medicine

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ABSTRACT

The incidence of Diabetes Mellitus is increasing substantially worldwide & has come into the category of one of the most prevalent and expensive chronic diseases . One of the most predominant cause of morbidity and mortality in a diabetic patient is cardiovascular disease. Cardiovascular (CV) risk factors such as obesity, hypertension and dyslipidemia are common in patients with DM, placing them at increased risk for cardiac events. There has been found and proved associations between diabetes and cardiovascular diseases. Therefore, it necessitates the early treatment of cardiovascular risk factors in patients with diabetes to minimize the long term complications of this dreadful disease. This paper throws light upon the relationship between diabetes and cardiovascular diseases.

KEYWORDS

INTRODUCTION

Overall Numbers, Diabetes and Prediabetes The incidence of diabetes continues to rise rapidly . The Prevalence of diabetes In 2015 was estimated to be 30.3 million Americans, or 9.4% of the population. Approximately 1.25 million American children and adults have type 1 diabetes. Of the 30.3 million adults with diabetes, 23.1 million were diagnosed, and 7.2 million were undiagnosed. The percentage of Americans aged 65 and older remains high, at 25.2%, or 12.0 million seniors (diagnosed and undiagnosed). 1.5 million Americans are diagnosed with diabetes every year. In 2015, 84.1 million Americans age 18 and older had prediabetes. Diabetes remains the 7th leading cause of death in the United States in 2015, with 79,535 death certificates listing it as the underlying cause of death, and a total of 252,806 death certificates listing diabetes as an underlying or contributing cause of death. The latest estimates by the international diabetes federation project that 592 million (1 in 10 persons) worldwide will have DM by 2035. While the rates of both type 1 DM (T1DM) and T2DM are growing, T2DM has a disproportionately greater contribution to the rising prevalence of DM globally compared to T1DM. One consequence of the growing rates of DM is a considerable economic burden both for the patient and the healthcare system. Macrovascular and Microvascular complications such as coronary artery disease, myocardial infarction, hypertension, peripheral vascular disease, retinopathy, end-stage renal disease and neuropathy are catastrophically high priced and are posing an economic burden on the people and the government.

Cardiovascular diseases and Diabetes mellitus are closely linked to each other. The most prevalent cause of morbidity and mortality in diabetic population is cardiovascular diseases. CVD death rates in the United States are 1.7 times higher among adults (> 18 years) with DM than those without diagnosed DM, largely due to an increased risk of stroke and myocardial infarction (MI) which is seen both in men and women.

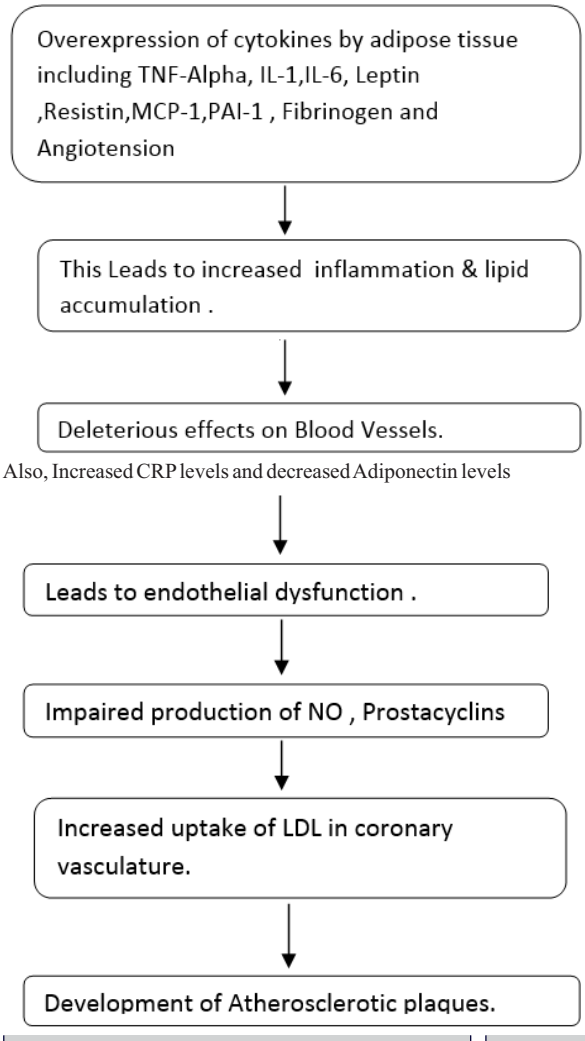
As both the prevalence and economic burden of the disease continue to rise, proper control and treatment of Diabetes Mellitus is critical. The primary goal of diabetes treatment is should be to improve the cardiovascular risk of diabetic patients. However, the multifaceted nature of the relationship between DM & CVD is one major challenge associated with its treatment. CV risk factors including obesity, hypertension and dyslipidemia are common in patients with DM, particularly those with T2DM. In addition, studies have reported that several factors including increased oxidative stress, increased coagulability, endothelial dysfunction and autonomic neuropathy are often present in patients with DM and may directly contribute to the development of CVD. The increased prevalence of MI, revascularization, stroke and CHF is contributed by the high rates of CV risk factors and direct biological effects of diabetes on the CV system. Due to the complexity and numerous mechanisms linking DM to CVD, it is crucial to focus treatment to what will have the greatest clinical impact on improving CV outcomes.

CV RISK FACTORS AND CVD

Obesity

Diabetic patients particularly type 2 DM , are commonly obese , which is associated with increased risk of cardiovascular diseases. Low-grade inflammation is one of the possible mechanism linking DM and Obesity with subsequent CVD.

Pathogenesis



This increase in atherosclerotic plaque can place diabetic patients at a heightened risk of MI.

Insulin resistance is also associated with an elevation of plasma free fatty acids, leading to increases in muscular triglycerides stores, hepatic glucose production, and increased insulin production in patients with T2DM[1]. Insulin resistance has also been linked to CMP in diabetics *via* cardiomyocyte hypertrophy and contractile dysfunction[1,2].

HYPERTENSION

Hypertension is twice as frequent in patients with diabetes compared with those who do not have diabetes. Moreover, patients with hypertension often exhibit insulin resistance and are at greater risk of diabetes developing than are normotensive individuals. The major cause of morbidity and mortality in diabetes is cardiovascular disease, which is exacerbated by hypertension. Accordingly, diabetes and hypertension are closely interlinked because of similar risk factors, such as

- endothelial dysfunction,
- vascular inflammation,
- arterial remodelling,
- atherosclerosis,
- dyslipidemia
- obesity.

There is also substantial overlap in the cardiovascular complications of diabetes and hypertension related primarily to microvascular and macrovascular disease.

Common mechanisms, such as upregulation of the renin-angiotensin-aldosterone system, oxidative stress, inflammation, and activation of the immune system likely contribute to the close relationship between diabetes and hypertension.

DYSLIPIDEMIA

Diabetic patients are at increased risk of developing dyslipidemia[3]. One mechanism underlying this connection is increased free fatty-acid release present in insulin-resistant fat cells.

- High levels of free-fatty acids promote triglyceride production, which in turn stimulates the secretion of apolipoprotein B (ApoB) and very LDL (VLDL) cholesterol.
- High levels of ApoB and VLDL have both been linked to increased risk of CVD[4-5].
- In addition to high ApoB and VLDL, hyperinsulinemia is associated with low high-density lipoprotein (HDL) cholesterol levels[6].
- Hyperglycemia may also negatively impact lipoproteins (particularly LDL and VLDL) through increased glycosylation and oxidation, decreasing vascular compliance and facilitating the development of aggressive atherosclerosis[7].
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High circulating FFA's and triglycerides, increased stimulation of ApoB and VLDL cholesterol, decreased HDL levels and lipoprotein modification have all been appreciated in patients with DM and likely contributes to the high prevalence of CVD in diabetic patients.

Diabetic cardiomyopathy

DM appears to contribute directly to the development of CMP, rather than solely *via* coronary atherosclerosis and hypertension[8].
Diabetics tend to have :

- Greater LV cardiac mass than those without DM[9,10]. This may be related to an increased adipocyte release of cytokines such as leptin and resistin which have hypertrophic effects on cardiomyocytes[11,12]
- Diminished diastolic function compared to nondiabetics[13,14]. One possible mechanism could be that increased triglyceride synthesis in patients with DM leads to increased myocardial triglyceride content[15].Increased cardiac triglyceride accumulation is associated with lipotoxicity and altered calcium hemostasis in myocardium, both of which negatively impact diastolic function[16,17].
- Subtle abnormalities in systolic function have also been observed in patients with DM. This systolic dysfunction may be related to impaired myocardial sympathetic innervation and impaired contractile reserve[18].
- In addition, interstitial fibrosis with increased collagen deposition has been observed in patients with DM and may negatively contribute to the diminished cardiac function seen in diabetics[19].
- The prevalence of HF, particularly heart failure and preserved ejection fraction, is higher in diabetic patients (16%-31%) than the general population (4%-6%)[20]. While some of the difference may be accounted for by traditional CV risk factors, DM may independently alter cardiac structure and function by promoting hypertrophy and fibrosis[21].

Cardiovascular autonomic neuropathy

Cardiovascular autonomic neuropathy (CAN) is common among patients with DM and is associated with an increased 5-year mortality rate from CVD[22]. Resting tachycardia, postural hypotension, exercise intolerance, abnormal coronary vasomotor regulation, increased QT interval, and perioperative instability are the important clinical manifestations. All together , the clinical manifestations of CAN are related to an increased risk of Kidney disease, stroke, CVD and sudden death[23]. The development and progression of CAN is likely related to dysregulation of the autonomic nervous system (ANS) with increased sympathetic activity and elevated inflammatory markers. As the ANS is responsible for maintaining the activity of the sinus node, end diastolic volume, end systolic volume and systemic vascular resistance, ANS dysfunction can lead to arterial stiffness, left ventricular hypertrophy and ventricular diastolic dysfunction[24]. Incidence of CAN increases with age and inadequate glycemic control, which places patients with DM at higher risk of developing both CAN and CVD[25].

Myocardial infarction and DM

Diabetes is a major risk factor for the development of CAD with a higher incidence of MI in patients with DM than those without[26,27]. In addition, following a MI, diabetic patients have higher rates of morbidity, mortality and re-infarction than non-diabetics, with one-year mortality rates of nearly 50%[28]. Although the exact pathophysiology of CAD progression in patients with DM has not yet been determined, the most recent studies postulate that the underlying atherosclerotic process is similar between those with and without DM. It is thought that the higher incidence of myocardial infarction in patients with DM is attributable to increased coagulability[29].
Factors responsible for increased coagulability are :

- Increased expression of glycoprotein IIB/IIIA receptors and vWF, which are responsible for platelet activation[30,31].
- Increased plasminogen activator inhibitor type 1 which could decrease fibrinolysis, increase thrombus formation and accelerate plaque formation .
- Decreased circulating anti-coagulants such as protein c and antithrombin III due in a large part to the proteinuria present with DN[32].

Collectively, these factors place patients with DM in a prothrombotic and procoagulant state, which may account for the higher rates of MI seen in diabetics.

TREATMENT

As CVD is the most prevalent cause of mortality and morbidity in patients with DM, effective treatment is critical to lower the subsequent risk of CV events, particularly MI, CAD, stroke and CHF in diabetics. Suboptimal glycemic control, obesity, hypertension, dyslipidemia and autonomic dysfunction are common CV risk factors among diabetic patients, placing them at heightened risk of CV complications. Therapy that is targeted to modify these risk factors can improve CV outcomes, but this can be a challenging to achieve. The guidelines pertaining to these risk factors typically vary from the guidelines for non-diabetic patients and the recommendations often change or differ depending on what organization publishes them. In addition, the research on how these different risk factors affect the CV risk profile of diabetics can be unclear, and at times, contradictory.

CONCLUSION

As the prevalence of DM continues to rise, associated CVD - through both traditional CV risk factors and the direct effects of DM on CVD - can also be expected to rise. Accordingly, proper control and treatment of DM, along with aggressive treatment of associated CV risk factors is central to curbing the growing prevalence and progression of DM and CVD. Additional research is needed to better understand the disease process and its effects on CV health in order to improve medical management and CV outcomes in diabetic patients.

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