

## High Risk Factors of Cardiovascular Diseases in Type 2 Diabetes

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### Abstract

Diabetes mellitus is a group of metabolic diseases characterized by hyperglycemia and hypoglycemia that result from defects in insulin secretion. The prevalence of type 2 diabetes mellitus is rapidly increasing all over the world. Cardiovascular disease (coronary heart disease, stroke, Myocardial infarction) is the most important cause of mortality and morbidity among patients with type 2 diabetes. The accelerated Atherosclerosis and cardiovascular disease in diabetes is likely to be multifactorial and therefore several therapeutic approaches can be considered. The number of people with type 2 diabetes is increasing due to population growth, aging, obesity, hypertension, unhealthy diet, smoking and alcohol consumption and increasing urbanization and physical inactivity.

**Keywords:** Diabetes Mellitus; Hyperglycemia; Hypoglycemia; Cardiovascular Diseases; Obesity; Hypertension; Alcohol Consumption.

**Abbreviations:** HDL: High Density Lipoproteins; LDL: Low Density Lipoproteins; BMI: Body Mass Index;

### Introduction

Diabetes mellitus, a common metabolic disease with a rising global prevalence, is associated with long-term complications [1]. The disease is one of the most important public health challenges for the 21<sup>st</sup> century. More than 150 million adult persons are affected worldwide, and the number is expected to double in the next 25 years. The increase will be much higher in developing countries. For instance, between 1995 and 2025, the number of diabetic patients is expected to increase by 170% in the developing countries, compared to only 42% in developed ones [2].

Diabetes mellitus is a group of metabolic diseases characterized by hyperglycemia that result from defects in insulin secretion, or action, or both. The prevalence of type 2 diabetes mellitus is rapidly increasing all over the world. The number of people with diabetes is increasing due to population growth, aging, urbanization, and increasing prevalence of obesity and physical inactivity [3].

Insulin Resistance occurs as a result of disturbances in lipid metabolism and increased levels of circulating fatty acids that accumulate within the insulin sensitive tissues such as muscle, liver and adipose tissues. Increased fatty acid flux has been suggested to be strongly associated with insulin resistant states such as obesity and type 2-diabetes [4]. Insulin is one of the most extensively studied proteins in many fields. Efforts in studying the molecule have been recognized widely, beginning with the Nobel Prize in 1923 to Banting and Macleod for the discovery of insulin [5].

### Types of Diabetes

Type 1 diabetes when a person has diabetes, either: their pancreas does not produce the insulin they need. A perfect Glycemic control in T1D is achieved in less than one-third of children only, the major challenge being a steady supply of basal insulin that mimics the physiological endogenous pancreatic insulin secretion [6]. Most cases of Type 1 diabetes mellitus (T1DM) are thought to result from selective autoimmune destruction of pancreatic beta cells. In keeping with the autoimmune etiology, other autoimmune diseases occur with increased frequency [7].

Type-2 diabetes their body cannot use this insulin effectively – is

the most common form of the disease typically afflicting obese adults. Patients with type-2 diabetes may be able to control their disease through diet and exercise alone or may require oral medications and/or insulin injections. The recommendations for initial treatment of type 2 diabetes include lifestyle adjustments and oral anti-diabetic medications [8].

Type 2 Diabetes is a progressive disease and deterioration of Glycemic control is partly due to a gradual loss of  $\beta$ -cell function and mass. Currently, pharmacological agents for treating type 2 Diabetes comprises drugs acting on insulin-resistant organs or on the pancreas [9].

### Glycemic control

Glycosylated hemoglobin (HbA1c) as a marker for average blood glucose levels over the previous months prior to the measurement is an important predictor of diabetes complications. The role of improved Glycemic control in reduction micro vascular and neurological complications of diabetes was demonstrated in many observational and randomized controlled clinical trials [10].

### Hypoglycemia

Recently, weekly blood glucose and, more importantly, Glycemic variability have been explored as means of assessing Glycemic control and altering management in type 2 diabetes [11]. Low blood glucose or hypoglycemia is the most common immediate health problem for patients with diabetes. Therefore, there is an urgent need to innovate new approaches that will sustainably stabilize the metabolic syndrome, or to an even greater extent, restore metabolic health; preferably, without requiring severe lifestyle curtailment and escalating doses of pharma therapeutic agents [12].

It occurs when the body gets too much insulin, too little food, a delayed meal, or more than the usual amount of exercise.

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Recognizing the determinants of poor Glycemic may contribute to a clearer understanding of modifiable antecedents of diabetes-related complications and may help to achieve improved Glycemic control and improve patient function and outcomes [3].

### Hyperglycemia

Hyperglycemia occurs when the body gets too little insulin, too much food, or too little exercise; Diabetes mellitus (DM) refers to a group of common metabolic disorders that share the phenotype of hyperglycemia. Depending on the etiology of the DM, factors contributing to hyperglycemia include reduced insulin secretion, decreased glucose utilization, and increased glucose production [13].

Hyperglycemia is associated with excessive free radical generation and oxidant stress. Oxidant stress may be linked to diabetes via altered NO production and action. NO, an endothelium-derived relaxing factor is a pleiotropic intercellular messenger regulating many cellular functions [14]. The diabetes complications are equally associated with the both types of DM. However, the severity of the disease is related to the long term exposure to uncontrolled Glycemic [15].

Diabetic patients have reduced Na<sup>+</sup>/K<sup>+</sup> ATP as activity resulting in elevated intracellular Ca<sup>2+</sup> concentration and platelet hyperactivity. Hyperglycemia is associated with increased PKC activity [16], and superoxide anion production as well as reduced antioxidant (glutathione) levels and NOS activity.

### Long Term Effects of Diabetes

Diabetes is a debilitating disorder world-wide and a root cause for several serious complications such as cardiovascular diseases, cerebrovascular diseases, renal disorders, inflammation and immunity, and obesity. Insulin, the protein hormone synthesized by the  $\beta$ -cells of the pancreas is one of the prime hormones is responsible for the glucose uptake/utilization by the cells in the body and also tightly maintains the homeostasis of the glucose in circulation [17]. T2DM represents about 90-95% of all the diabetic populations and can be unchained by several factors such as the obesity, high calorie diet and lack of physical activity [18]. Numerous studies have demonstrated that statins reduce the incidence of stroke in patients at high risk for cardiovascular events [19].

Micro vascular complications include effects on small vessels, including arterioles, capillaries and venues. The development of these complications starts early and accounts for morbidity in the form of retinopathy, neuropathy and nephropathy in Type 2 DM The present study was to determine prevalence and focused on presence risk factor affecting on diabetic vascular complications among type 2 diabetic outpatients in tertiary center [20].

Attempts to improve Glycemic control reduce the incidence of macro vascular events both in type 1 and type 2 DM [21]. The incidence and progression of micro vascular complications correlate with the Glycemic control and lower glycated hemoglobin (HbA1c) levels are associated with the reduction of cardiovascular risks [22].

### Diabetes and Specific CVD

While death rates of cardiovascular disease have been in decline for the past 30 years, it remains one of the highest causes of mortality in the United States, accounting for 1 in every 2.9 deaths annually. Each day, 2400 Americans will die of cardiovascular disease, which amounts to 1 death every 37 seconds [23].

Cardiovascular disease is the leading cause of morbidity and

mortality in patients with diabetes mellitus. Patients with diabetes mellitus have a 2 to 4 time's higher risk of cardiovascular disease and up to a 3 times increase in mortality than non diabetics. The accelerated rate of atherosclerosis seen in diabetes mellitus predisposes patients to coronary artery disease and to higher rates of myocardial infarction and death [24]. Common risk factors were documented including high blood pressure, diabetes, previous stroke and myocardial infarction, cardiovascular disease, hyperlipidaemia, atria fibrillation, periphery artery occlusive disease (PAOD), current smoking and alcohol consumption [25].

### Myocardial infarction

Myocardial infarction is a rare complication of valve surgery, most commonly mitral valve replacement [26]. Myocardial infarction rates are increased among diabetics of all ages. The prevalence of unrecognized myocardial infarction and silent myocardial ischemia detected by a treadmill exercises stress test was increased in patients with diabetes mellitus [27].

Myocardial viability represents a state of impaired contractility with the potential for recovery when blood supply is adequately restored. Traditionally, the evaluation of regional myocardial function was performed by visual assessment of the degree of thickening and inward displacement of individual myocardial segments. Obviously limited by inter and intra observer variability, poor visualization of some myocardial segments [28]. Three acute large vessel stroke patients presents to the emergency department [29].

### Atherosclerosis

Cardiovascular diseases (CVD) remain the leading cause of death in the US despite the efforts in prevention and treatment. Low plasma HDL cholesterol (HDL-C) is consistently associated with increased risk of atherosclerotic disease. Assessment of apolipoproteins, lipoprotein particle size and number allows a further characterization of CVD risk [30].

Obesity is associated with an increase risk for cardio metabolic diseases such as atherosclerosis and type 2 diabetes [31]. Atherosclerosis is characterized by chronic inflammation affecting the arterial intima. Therefore certain cytokines and chemokines can be considered markers of CVD risk as well.

### Lipoproteins

High-density lipoproteins, which transport cholesterol away from arteries, are protective. Low-density and very low-density lipoproteins, in contrast, can penetrate the arterial wall and deposit cholesterol within the artery, contributing to heart disease [32].

Atrioventricular (AV) block can be defined as a delay or interruption in the transmission of an impulse from the atria to the ventricles, and can be transient or permanent. It has been reported many causes for AV block including drugs, electrolyte disturbances, infiltrative malignancies, hyperthyroidism, and rheumatologic disorders.

Congestive heart failure and myocardial infarction are frequently reported cardiac signs and symptoms due to the accumulation of glycosphingolipids in vascular endothelial and smooth muscle cells and in cardiomyocytes [33].

Atherosclerosis does not increase the systemic vascular resistance, but can generate localized plaques that can trigger sudden occlusions of coronary arteries by thrombus formation, unlike the gradual narrowing of the lumen of the pulmonary vasculature [34].

## Osteoporosis

The number of patients with diabetes mellitus and osteoporosis is rapidly increasing in industrialized countries where Western-style aging societies are prevalent. Although the incidence of osteoporosis and type 2 diabetes mellitus is known to increase in prevalence with aging, both diseases were traditionally viewed as separate entities. However, the relationship between diabetes and osteoporotic fractures is recently and increasingly becoming recognized [35].

Normal serum Zinc and good Zinc dietary intake alone is not enough to improve osteoblastic function, but optimization of glucose metabolic profile in addition may help to improve osteoblasts activity and prevent bone complications [36].

## Cardiovascular Risk Factors in Type 2 Diabetes

Individuals with type 2 diabetes are at higher risk of cardiovascular diseases (CVD) than those without type 2 diabetes. Diabetes is a chronic disease with severe complications and is a growing health issue in Europe and Sweden as well as in other parts of the world. The prevalence of diabetes in Sweden, mainly type 2, is about 4.5%. For Diabetes hypertension and obesity is well-known major and independent cardiovascular risk factors [37].

For insulin sensitization, metformin is a commonly used drug for treating type 2 diabetes. As against these sensitization drugs, diet plays an important role in controlling glucose levels. Fiber foods and gums were found to bring glycemic control in diabetic subjects [38].

## Unhealthy diet

Type 2 diabetes mellitus is a chronic disease with severe late complications and high mortality. The increasing prevalence of Type 2 diabetes is mainly due to reduced physical activity and consumption of unhealthy food and larger portion sizes in genetic susceptible individuals [39] and present in every country regardless of their stage of development, and afflicts people in all socio-economic classes.

Long term complications of diabetes include effects on the eyes, kidneys nerves, and blood vessels that can lead to blindness, neuropathy and Hypertension with organ damage is frequently observed [40].

## Heavy alcohol consumption

Heavy alcohol intake increases the risk of hypertension and cardiovascular disease, but the relationship between alcohol consumption and type 2 diabetes remains controversial [41]. Some studies suggested no association between alcohol intakes and type 2 diabetes. Systolic and diastolic heart function, myocardial creatine phosphokinase leakage and myocardial antioxidants after ischemia/reperfusion were examined [42].

Other studies have shown that heavy drinking can increase blood glucose level or risk of type 2 diabetes. Some epidemiologic studies [43] have showed that proper quantities of alcohol consumption was a protective factor for coronary heart disease.

Mechanisms of protective effect of proper quantities of alcohol consumption on type 2 diabetes may be the same as on coronary heart disease. This protective effect on type 2 Diabetes or coronary heart disease may be explained by a viewpoint that moderate alcohol consumption can increase insulin sensitivity and high HDL-C.

## Dyslipidemia

Type of dyslipidemia that is most characteristic of type 2 diabetic

subjects is elevated triglycerides and decreased HDL cholesterol levels, although all lipoproteins have compositional abnormalities. Therefore, the primary target of therapy in diabetic patients is lowering LDL cholesterol (or possibly, non-HDL cholesterol). The goal here is weight reduction and increased exercise. However, for selected patients, combining a fibric acid (or low-dose nicotinic acid) with a statin also can be considered [44].

## Obesity

Obesity is the most important modifiable risk factor for type 2 diabetes mellitus and most patients with diabetes are overweight or obese. It is well known that excess bodyweight induces or aggravates insulin resistance, which is a characteristic feature of type 2 diabetes [45]. Over 30% of surgical patients are obese (BMI>30) and it is estimated that over ten million surgeries involving obese patients will be performed in 2010 (National Hospital Discharge Survey data) [46].

Obesity is associated with the development of a broad group of malignant, metabolic, cardiovascular, and neurological disorders. Of importance in the treatment of and prevention of diabetes mellitus, myocardial infarction, peripheral vascular disease, and cerebral infarction, obesity is a major factor in the development of metabolic syndrome. However, potential explanations for this rise in the prevalence of obesity include a sedentary life style, increased number of daily meals, the presence of an eating disorder, a changing job market, or an effect of a yet unidentified environmental agent or exposure [47].

To determine the proportion of patients with Type 2 diabetes mellitus (T2DM) who lost 5-10% of their body weight as part of their initial management. To determine associations between metformin uses, it is advised for dietary and physical modification on weight loss [48].

## Hypertension

Patients with comorbid hypertension and type 2 Diabetes are common, have a greatly increased risk of premature cardiovascular and renal morbidity and mortality, and are likely to increase substantially in number over the next 10–15 years. We suggest the need for more aggressive management strategies for these patients, regardless of their baseline blood pressure, including the early use of combination therapy with blockers of the renin–angiotensin system [49]. Hypertension was seen in 32 % of diabetic patients in this study which was similar to the previous study of 32.1% at the end of 2007 in the same center [50]. High blood pressure (HBP) is the leading cause of end-stage renal disease. Hypertension and obesity have been regarded as the most common cause of increased mass in general population [51].

Aggressive blood pressure control may be the most important factor in preventing adverse outcomes in patients with type 2 diabetes. The Appropriate Blood Pressure Control in Diabetes (ABCD) Trial is a prospective randomized blinded clinical trial that compares the effects of intensive versus moderate blood pressure control on the incidence and progression of type 2 diabetic complications.

## Lifestyle

Patients with type 2 diabetes often have negative self-concepts, feel hopeless and, therefore, become lax about following their regimen. This study shows that quality of life education can have positive effect on diabetes self concept, and prevent physical and side effects of type 2 diabetes [52].

Affective and behavioral neuropsychiatric disturbances are



frequently encountered in post-stroke patients [53]. Type 2 diabetes affects approximately 8 percent of adults in the United States. Some risk factors--elevated plasma glucose concentrations in the fasting state and after an oral glucose load, overweight, and a sedentary lifestyle--are potentially reversible. All diabetic patients if given proper education and guidance regarding foot care would be able to make a significant improvement in their life style which is helpful to avoid amputations [54].

## Conclusion

It is well known that type 2 diabetes is frequently associated with cardiovascular risk factors (CVRF), such as hypertension and dyslipidemia, and that the prevalence of other factors, such as smoking, sedentary lifestyle, and obesity is greater than in the non diabetic population. The objective of this study was to describe the association of type 2 diabetics with modifiable cardiovascular risk factors and the degree of control of these in a population of type 2 diabetics. Integrated and multifactorial intervention in type 2 diabetic patients can achieve clinically significant reductions in cardiovascular diseases.

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