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CARDIOVASCULAR RISK FACTORS ASSOCIATED IN DIABETES AND HYPERTENSION PATIENTS

Kuldeep Dhaked*[1] and Yogesh Kumar Sharma[2]

[1]Research Scholar, Department of Pharmacology, Jaipur College of Pharmacy, Jaipur, Rajasthan, India.
[2]Associate Professor, Department of Pharmacology, Jaipur College of Pharmacy, Jaipur, Rajasthan, India.

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***Corresponding Author**
Kuldeep Dhaked
Research Scholar, Department of Pharmacology, Jaipur College of Pharmacy, Jaipur, Rajasthan, India.

ABSTRACT

Diabetes is a chronic disease that occurs when the body cannot produce enough or effective insulin. Patients with type 2 diabetes are disproportionately affected by cardiovascular disease, with a significantly increased risk of cardiovascular morbidity and mortality compared to non-diabetics. Much of this additional risk is related to the higher prevalence of known risk factors such as hypertension, dyslipidemia, and obesity in these patients. However, the improvement in cardiovascular disease in patients with type 2 diabetes is not only due to a higher prevalence of traditional risk factors. Cardiovascular disease is characterized by a complex combination of several traditional and unconventional risk factors that play a key role in the initiation and progression of atherosclerosis over its long natural history, from endothelial function to clinical events. Increases in people with type 2 diabetes. The aim of this review is to highlight the weight of traditional and non-traditional risk factors for cardiovascular disease in the context of type 2 diabetes mellitus and to discuss their place in the etiology of excess cardiovascular disease in these patients.

KEYWORDS: Risk factors Cardiovascular disorders, Type 2 diabetes mellitus, Blood pressure, Obesity, Postprandial Hyperglycaemia.

INTRODUCTION

Diabetes mellitus (DM) is a chronic disease that occurs when the body fails to produce enough insulin or use it effectively, and is caused by a genetic predisposition combined with environmental factors.[1] In 2011, 366 million people had DM half of these (183 million) are undiagnosed.[2] The number of people with diabetes is increasing worldwide and is expected to reach 552 million by 2030.[2]

DM is an established risk factor for cardiovascular disease (CVD). Individuals with type 2 diabetes (T2DM) have higher rates of cardiovascular morbidity and mortality and are disproportionately affected by CVD compared to non-diabetic patients.[3] Diabetic vascular disease increases the incidence of coronary artery disease (CAD) and stroke by 2- to 4-fold and improves the risk of heart failure by 2- to 8-fold.[4] Patients with type 2 diabetes and no history of CAD have a risk of cardiovascular events similar to that of patients with a history of myocardial infarction.[5] However, subsequent studies have revealed mixed results.[6] further suggesting that diabetic conditions may not equate to CVD in all situations, hence the risk of CVD prevention in people with diabetes. The need for a multivariate approach is emphasized as a good basis.[6] for stability.[7] There is a gradient in CVD risk, and the acquisition of this gradient depends on the combination of many risk factors.[7] Much of this excess risk is associated with a better prevalence of known risk factors such as hypertension, dyslipidemia, and obesity in these subjects. Over the past decade, conclusive evidence has accumulated that treatment of traditional risk factors is critical in reducing CVD risk for people with type 2 diabetes.[8,9] Inadequate control of most cardiovascular risk factors in the diabetic population.[10] supports the need for more aggressive targeting of modifiable cardiovascular risk factors, particularly in patients with pre-existing cardiovascular disease. I am here. However, the improvement in cardiovascular disease in patients with type 2 diabetes is not simply due to a higher prevalence of traditional risk factors. Therefore, other non-traditional risk factors may be important for patients with type 2 diabetes.[11] Some studies have shown possible association of non-traditional risk factors in type 2 diabetes, independent of traditional risk factors.[12] In addition, therapies such as insulin sensitizers and statins that are currently used to manage type 2 diabetes have differential effects on many of these nontraditional risk factors.[13,14] The relative magnitude of these risk factors has been extensively reviewed in the literature.[15]

Traditional	Nontraditional
Dyslipidaemia	Insulin resistance and Hyperinsulinemia
Hypertension	Postprandial Hyperglycaemia
Obesity	Glucose variability
Abdominal obesity	Microalbuminuria
Physical exercise	Haematological factors
Cigarette smoking	Thrombogenic factors
	Inflammation C-reactive protein
	Homocysteine and vitamins
	Erectile dysfunction
	Genetics and Epigenetics

Table 1: Cardiovascular risk factors in Diabetes Mellitus.

Possible Risk Factor of Diabetes

Obesity

Obesity or overweight is associated with the accumulation of adipose tissue with various detrimental effects on both physical and psychological health.[9] Obesity is associated with many chronic diseases, such as hypertension, diabetes mellitus, dyslipidemia, osteoarthritis, sleep apnea, cerebrovascular and cardiovascular diseases, as shown in Table 1. Concomitant use with other chronic diseases.[10] According to data from the WHO (World Health Organization), the global rate of obesity is 10% for men and 14% for women. Information According to the National Health and Nutrition Examination Survey (NHANES), the prevalence of obesity and overweight increased from 55.9% to 64.5% between 1988 and 1994, and increased from 22.9% to 22.9% between 1999 and 2000. increased to 30.5%.[10] This index has been found to be closely related to insulin resistance and diabetes.

High Blood Pressure

Hypertension is very common in people with diabetes and is one of the most common diseases worldwide. Sixty percent of patients with type 2 diabetes have hypertension.[22,23] The coexistence of the two conditions increases the probability of both complications, both microvascular and macrovascular. Macrovascular complications include myocardial infarction and stroke, and microvascular complications include retinopathy and nephropathy.[24]

Traditional Risk Factors

Dyslipidemia

The incidence of dyslipidemia is increased in diabetic patients.[31] A proposed underlying pattern observed in the development of dyslipidemia in diabetic patients is low levels of triglycerides, LDL (low-density lipoprotein), and HDL-C (high-density lipoprotein cholesterol).[32] One of the hallmarks of dyslipidemia in diabetes is elevation of LDL-P or ApoB relative to LDL particles. Because LDL particles are more atherogenic, they also increase the risk of associated kidney disease.[33]

Association between dyslipidemia and cardiovascular risk in type 2 diabetes

A large body of data from case-control studies, genetic studies, and large observational studies suggest that elevated TG-rich particles and their residues, low HDL-C, and cardiovascular risk are causally related.[31,32] Even in patients with normal LDL-C levels, the results of statin trials confirm the position of low HDL as an independent cardiovascular risk marker.[33,34] The incidence of cardiovascular events was significantly higher in individuals with dyslipidemia: LDL-C > 2.6 mmol/L, HDL-C ≤ 0.88 mmol/L and TG ≥ 2.3 mmol/L, similar to the intervention with fenofibrate.[35,36] Study of Event Reduction in Diabetes (FIELD) and Study of Cardiovascular Risk Management in Diabetes (ACCORD).

Recommendations	Class	Level
Blood pressure control is recommended in patients with diabetes mellitus and hypertension to lower the risk of cardiovascular events	I	A
It is recommended that a patient with hypertension and diabetes mellitus is treated in an individualized manner, targeting a blood pressure of < 140/85 mmHg	I	A
It is recommended that a combination of blood pressure lowering agents is used to achieve blood pressure control	I	A
A RAAS blocker (ACE-I or ARB) is recommended in the treatment of hypertension in diabetes mellitus, particularly in the presence of proteinuria or microalbuminuria	I	A
Simultaneous administration of two RAAS blockers should be avoided in patients with diabetes mellitus	III	B

Table 2: Recommendations for blood pressure control in diabetes.

Management of dyslipidaemia, significance in the Prevention of CVD in T2DM

As the development of atherogenic dyslipidaemia precedes the onset of overt Glycaemia and the clinical diagnosis of diabetes, early effective intervention is recommended to reduce the risk of premature CVD. In T2DM large data exists on action mechanism and efficacy of statins in the prevention of CVD events.[39] The Collaborative Atorvastatin Diabetes Study assessed the benefits of a statin in T2DM patients and at least one of the following risk factors: albuminuria, retinopathy, hypertension or current smoking.[40]

Residual risk in people on LDL-lowering therapy

Patients with T2DM at the LDL-C target are still at a significant risk of CVD events.[31] This residual risk is associated to several factors as increased on TGs-rich proteins, decreased HDL-C and small, dense LDL particle with Data of FIELD study demonstrated that fenofibrate Therapy did not decrease the primary endpoint (nonfatal myocardial infarction and CAD-related death), but total CVD events were decreased from 14% to 12.5% (P = 0.035).[35,43] However, a subgroup analysis of dyslipidaemic people (TGs > 2.3 mmol/L and HDL-C ≤0.9 mmol/L) in this study showed a 27% reduction in CVD risk.[35] In both ACCORD and FIELD, treatment with Fenofibrate was related with a strong reduction of TGs (22%), whereas increase of HDL-C remained less than expected (2% and 2.4%, respectively). The clinical benefits of fibrates on major CVD events have been confirmed in meta analyses; but not on cardiovascular mortality.[43,44] The effects seem to be appeared to an improvement in TGs.[45]

Direct effects due to inhalation of smoke from tobacco products
Impaired insulin sensitivity based on influence of haemodynamic dysregulation in capillary vascular bed
Impaired insulin sensitivity due to increase in inflammatory markers secondary to bronchitis and pulmonary infections caused by smoking
Impaired beta-cell function due to toxic effects of tobacco smoke
Lipotoxicity due to influence of increased triglyceride levels
Hypercortisolaemia and increase in abdominal fat tissue
Elevated sympathetic nervous activation
Indirect effects on glucose metabolism
Unhealthy lifestyle in smokers (poor diet, lack of physical activity)
Increased alcohol consumption (toxic effects on beta cells)
Psychosocial stress and impaired sleep associated with smoking
Impaired fetal growth in smoking pregnant women, associated with increased diabetes risk in offspring in adult life

Table 3: Mechanism for the influence of smoking on risk of Type 2 Diabetes.

Blood pressure

Arterial hypertension is present in more than 60% of T2DM patients.[46] This is directly linked to:

(1) Increased Renin-angiotensin-aldosterone system activity;
(2) Hyperinsulinemia associated to increased renal reabsorption Of sodium; and
(3) Increased sympathetic tone.[47]

Aging, Obesity, and the onset of renal disease also promote an Increase in the prevalence of hypertension. Hypertension and DM are additive risk factors for CVD. While The diagnosis of diabetes doubles the cardiovascular Risk in men and more than triples the risk in women, Hypertension quadruple cardiovascular risk in diabetic Patients.[5,48]

Obesity and abdominal obesity

Generalised obesity assessed by the body mass index (BMI), and abdominal obesity determined by the waist Circumference (WC), are related with a variety of CVD Risk factors. Clinical guidelines do not indicate whether BMI or the WC measurements have identical utility in Predicting cardiovascular risk in individuals with T2DM Compared to non-diabetic patients.[66,67]

The impact of obesity on both atherogenesis and in Novel procoagulant and prothrombotic cardiovascular Risk factors is of particular interest in cases of T2DM, as They contribute to increased CVD mortality in these individuals.[68-72]

In diabetic patients the coexistence of multiple variables such as diabetic duration, glycaemic control and The drugs used for achieving it, lipid profile, BP or the Existence of risk behaviours such as smoking or alcohol Use may confound the impact of obesity on the risk of CVD.[73]

A-ASK:	Systematically inquire about smoking status at every opportunity
A-ADVISE:	Unequivocally urge all smokers to quit
A-ASSESS:	Determine the person's degree of addiction and readiness to quit
A-ASSIST	Agree on a smoking cessation strategy, including setting a quit date, behavioral counseling, and pharmacological support
A-ARRANGE	Arrange a schedule for follow-up

Table 4: The strategic "five As" for smoking cessation.

Physical Training

Regular exercise is associated with a lower risk of cardiovascular morbidity and mortality in both primary and secondary prevention. However, it should be noted that this type of testing is often influenced by other lifestyle changes associated with exercise (eg, smoking cessation, balanced diet, etc.).[76,77]

About smoking

Smoking is associated with poor metabolic control in patients with diabetes,[90,91] which is associated with an increased risk of developing macrovascular and microvascular complications and increased mortality in diabetes.[92,93]

The proposed mechanisms for the effects of smoking on type 2 diabetes risk are summarized in Table 3. autonomic nervous system.[98,99] Nicotine decreases insulin sensitivity directly or indirectly through these and possibly other mechanisms. Furthermore, smoking increases circulating free fatty acid levels,[95] which is an additional negative factor for insulin-mediated glucose uptake.

Unconventional risk factors

Insulin resistance and hyperinsulinemia

IR is an important marker of DM2 and is found in multiple organs, including skeletal muscle, liver, adipose tissue, and heart. The development of hyperglycemia and diabetes usually precedes IR by several years. Obesity plays a key role in this phenomenon, providing an important link between DM2 and adiposity.[106] A significant proportion of the population with DM2 is obese.[107]

Hyperinsulinemia resulting from IR precedes the onset of DM and may coincidentally be associated with vascular disease.[108–111]

Postprandial hyperglycemia and blood sugar fluctuations

Postprandial hyperglycemia has been shown to be associated with an increased risk of cardiovascular events in patients with and without DM2.[122–125] Postprandial glucose fluctuations, particularly when postprandial TG levels are elevated, are pathophysiologically associated with increased OS, systemic inflammation, and endothelial dysfunction, all of which are associated with atherosclerosis and cardiac disease. are Postprandial hyperglycemia is also associated with retinopathy, cognitive impairment in the elderly, and certain cancers.[128] Relatedly, elevated postprandial blood glucose concentrations strongly increase both atherogenesis and cardiovascular events, even when fasting blood glucose levels are controlled.[122–125,129]

Two studies have examined the predictive power of blood glucose in later cardiovascular events. The Intervention Diabetes Study.[130] was a population-based multicenter study conducted in 1139 newly diagnosed DM2 subjects aged 30 to 55 years and followed for 11 years. Later blood glucose levels were shown to be an independent predictor of death. However, HbA1c was not considered in this study. On the other hand, the San Luigi Gonzaga Diabetes Study,[122] which followed 505 DM2 patients for 14 years, showed that both subsequent blood glucose and HbA1c predicted cardiovascular events and all-cause mortality. Postpartum blood sugar. Blood glucose in cardiovascular events after HbA1c correction.

Microalbuminuria

The term microalbuminuria (MA), urinary albumin excretion of 30–300 mg/24 h, was introduced to identify subjects at high risk for early cardiovascular death and progressive renal disease. In DM2 individuals, AM is an early clinical sign suggesting vascular injury to the glomerulus. MA is now also reported as an important risk factor for CVD and is the largest and most widely used marker of diabetic nephropathy in clinical practice. It is also a marker of organ dysfunction and appears to be associated with an increased risk of cardiovascular morbidity and mortality in DM2 patients.[137] Increased albumin excretion is now believed to be a manifestation of systemic renal endothelial dysfunction.[138] According to various studies, the prevalence of AM is up to 19% in DM2.[139–142]

The epidemiology of AM shows a close association with systemic and glomerular endothelial dysfunction and vascular disease. Damage to the glycocalyx, the protein-rich surface layer of the glomerular endothelium,

probably represents an early stage in the development of diabetic AM.[143]

Hematological and thrombogenic factors

Atherothrombosis, defined as the formation of a blood clot in a preexisting atherosclerotic plaque, is the leading cause of death in the Western world. Diabetes is recognized as an independent risk factor, and atherothrombosis accounts for 80% of deaths in these patients.[165,166] It is a consequence of the progression of atherosclerosis, whose main manifestations are sudden cardiac death, myocardial infarction, stroke, and peripheral arterial ischemia.[167]

Diabetes is associated with a hypercoagulable state, which becomes more pronounced after birth. Hyperactivated platelets act at the damaged endothelial interface, increasing the availability of thrombus precursors, reducing anticoagulant substances, and reducing fibrinolysis.[168] The UKPDS has clearly shown that macrovascular events account for more than 50% of all-cause mortality in patients with type 2 diabetes.[169] Atherosclerosis develops more rapidly and aggressively in diabetes, and interactions between the vessel wall and hypercoagulability lead to more frequent thrombotic events.[170,171]

Inflammatory C-reactive protein

Atherosclerotic coronary heart disease and other forms of CVD are not only the leading cause of death in type 2 diabetes, but also the leading cause of lifetime morbidity and costs. If diabetes develops in a patient with established CAD, the absolute risk of future events is very high. Inflammation is implicated in the pathogenesis of cardiovascular disease, type 2 diabetes, and cancer. Different biochemical parameters can be used to assess CVD risk in people with type 2 diabetes of different ages.[182] CRP is an acute phase protein produced in the liver. Its release is stimulated by cytokines (interleukin-6 and tumor necrosis factor-alpha). Its elevated levels are associated with the presence and severity of CAD and renal dysfunction in patients with type 2 diabetes.[183] The measurement of high-sensitivity CRP levels (hsCRP) represents an interest in the detection of CVD in patients with type 2 diabetes.[184] Elevated concentrations of hs-CRP are associated with the development of IR, T2DM, and CVD. In particular, inflammation, which is strongly associated with endothelial dysfunction, is accepted as one of the cardiovascular risk factors grouped under IR syndrome or metabolic syndrome. Furthermore, low-grade inflammation may play an important role in the pathobiology of the metabolic syndrome.[185,186] The exact mechanisms associating IR with inflammation remain unclear. Several studies have focused on finding elevated levels of Hs-CRP in type 2 diabetic patients with features of the metabolic syndrome.[187-190] Elevated hs-CRP is strongly associated with BMI, serum lipids, fasting blood glucose, and WC,[191-197] which are hallmarks of the metabolic syndrome, suggesting a role for obesity and abdominal obesity in the development of inflammation related to the metabolic syndrome. showing possibilities. Patients with DM2. The strong association of IR and inflammation in atherogenesis indicates that therapies that address both parameters, such as thiazolidinediones, may be beneficial in reducing diabetes-related macrovascular complications.[198]

Homocysteine and Vitamins

Homocysteine (HC) is a sulfur-containing essential amino acid derived from methionine. Vitamins B6, B12, and folic acid act as coenzymes in methionine and GH metabolism, and individual deficiencies can lead to hyperhomocysteinemia (HHC).[219] Therefore, there is a negative correlation between plasma levels of GH and levels of vitamin B6, B12 and folic acid.[220] Plasma GH levels are higher in men, increase after menopause in women, and increase with age in both sexes.[219] Elevated GH levels may be associated with decreased and/or inhibited renal clearance and metabolism of substances resulting from exogenous metabolism, but may also be associated with chronic kidney disease through mechanisms that are not yet fully understood.

In patients with type 2 diabetes, elevated GH levels are associated with an increased risk of cardiovascular events,[223] independent of other risk factors such as age and kidney function.[222,223] The close relationship between HC and CVD supports a role for atherosclerosis.[224] For some authors, high levels of GH are consistent not only with aging and male gender, but also with the development of DM.[225] GH levels do not seem to correlate with anthropometric indices such as body weight, BMI, percentage of body fat.

Erectile dysfunction

Men with DM have a higher prevalence of erectile dysfunction (ED) compared with the general population.[269] In these individuals, the prevalence of ED augments with Age and duration and severity of disease.[269,270] ED and Atherosclerosis are frequent complications of DM.[271] There are close relations between ED and atherosclerosis In patients with T2DM, and ED might serve as a clinical marker for coronary, peripheral, or cerebrovascular Diseases in these subjects.[272] Several studies have found A positive correlation between ED and the risk of cardiovascular events.[273,274] The total cardiovascular risk increases severity of ED in T2DM patients without having Overt CVD.[275] A cohort study concluded that the presence of ED in men with T2DM and without clinically Overt CVD predicted CHD,[276] and another study indicates that ED appears to be robustly and independently related with silent CAD in apparently uncomplicated T2DM subjects,[272] Moreover, a meta-analysis of observational studies concludes that the presence of ED was related with an elevated risk of cardiovascular events in diabetic men.[277]

Genetics and epigenetics

T2DM is an independent risk factor for developing CVD With the relative risk of CVD mortality of 4.9 in women And 2.1 in men, relative to non-diabetics subjects. Genetic and environmental factors contribute to this risk. In the past decade, genome-wide association studies had Elevated the number of common single-nucleotide polymorphisms, which confirmed the relationship between T2DM and CVD.

Haptoglobin polymorphisms and CVD in T2DM

Haptoglobin (HP) has been involved in both T2DM, And T2DM related CVD. HP binds to ApoA1 in the same location as lecithin-cholesterol acyltransferase (LCAT); this lead to a decrease LCAT activity and consequently limiting HDL maturation. This inhibits reverse Cholesterol transport causing HDL to become proatherogenic.

CONCLUSION

The related CVD could also be predicted to increase as The incidence of DM keeps growing, due to both the Conventional factors of risk of DM and the direct impact On CVD. Appropriate treatment and management of DM together with successful therapy of related risk factors are therefore important for reducing DM and CVD's Increasing prevalence and advancement. Further work to Enhance knowledge of the disease state and its impact on CV function is required to boost medical treatment and CV results in people with diabetes.

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