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Diabetes associated with high blood pressure

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BY

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الاية

بسم الله الرحمن الرحيم

يَرْفَعِ اللَّهُ الَّذِينَ آمَنُوا مِنكُمْ وَالَّذِينَ أُوتُوا الْعِلْمَ دَرَجَاتٍ وَاللهُ بِمَا تَعْمَلُونَ خَبِيرٌ

صدق الله العظيم

Dedication:

I dedicate this work of my work to the one who taught me to give, to the one whose name I carry with all pride, and I hope that God will extend his life to see fruits that have come to be harvested after a long wait .

My dear father

To my companions in life, to the meaning of love, tenderness and devotion, to the smile of life and the secret of existence, to whom Her prayers were the secret of my success, my dearest friends

My beloved mother

To those who had great credit for encouraging and motivating me, and from whom I learned perseverance and diligence, to those who mattered and on whom I relied, and through whose presence I gained limitless strength and love, to those with whom I learned the greater meaning of life .

"My brothers and sisters

To those who showed brotherhood and were distinguished by loyalty and giving. To those who accompanied them on the happy and sad paths of life. I walked to those who were with me on the path to success .

With God’s success and prayers from my mother, there are only a few steps left to finish my career. Thank you to everyone who extended a helping hand to me

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ABSTRACT

The coexistence of diabetes and hypertension is known to have a multiplicative effect on adverse clinical outcomes with respect to both microvascular and macrovascular disease. Effective management of diabetes should therefore include a multifaceted approach combining optimal control of blood pressure and lipids with appropriate glycemic control. The pathophysiology of hypertension in diabetes involves maladaptive changes in the autonomic nervous system, vascular endothelial dysfunction, enhanced activation of the renin-angiotensin-aldosterone system, immune function alterations, and harmful environmental factors. Multiple high-quality randomized controlled trials have shown improvement in morbidity with lowering of elevated blood pressure in people with diabetes. Attention must be paid to individual risk factors and co-morbidities with a goal of less than 130/80 mm Hg in most patients with diabetes who are at higher risk of cardiovascular disease (CVD) than those without diabetes. Good glycemic control, optimizing weight, and promotion of exercise as well as lessening harmful environment factors such as air pollution exposure are integral components of the approach to blood pressure control in these patients.

Contents

1. introduction

Statistics from the Centers for Disease Control and Prevention (CDC) and National Health and Nutritional Examination Survey (NHANES) database show that the incidence of Type 2 diabetes mellitus (T2DM) has risen steeply in the last few decades. It is estimated that diabetes affects 34.2 million people in US 10.5% of US population. 73.6% of individuals with diabetes aged 18 years or more have hypertension. The coexistence of hypertension and diabetes in a large population of patients is not coincidental; individuals with T2DM often display a constellation of metabolic derangements termed the cardiometabolic or cardiorenal metabolic syndrome (1). This syndrome comprises a cluster of CVD risk factors including T2DM, hypertension, dyslipidemia, central obesity, and chronic kidney disease. The coexistence of hypertension and diabetes in these individuals substantially increases the risk for cardiovascular disease (CVD), cerebrovascular accident (CVA), retinopathy, and nephropathy (2). The rising prevalence of obesity and sedentary lifestyles in the US are the major driver of both diabetes and hypertension and the resulting health care costs are a serious public health concern. Increasingly, the role of environmental factors such as food deserts and environmental pollution in the promotion of diabetes, hypertension, and CVD is being appreciated. These harmful environmental factors especially affect minorities and other disadvantaged populations.

2.1 Diabetes

Diabetes mellitus is a group of chronic metabolic conditions characterized by a set of longterm metabolic irregularities, which arise from either the body's resistance to the activity of insulin or its inability to produce the hormone. This inability results in elevated blood sugar levels. The chronic

hyperglycemia associated with diabetes can cause damage, malfunction, and deterioration of several organs in the body, including the eyes, kidneys, nerves, heart, and blood vessels. (3). According to the American Diabetes Association (3), diabetes ranked as the seventh leading cause of death in the United States, with 282,801 death certificates citing diabetes as the cause of death. Diabetes is the primary cause of kidney failure, lower limb amputations, and adult blindness. (4) Additionally, diabetes is associated with a range of complications that affect multiple body tissues, including peripheral vascular disease, diabetic neuropathy, diabetic foot problems, diabetic retinopathy, and nephropathy. (5; 6). Often, insulin secretion and defects in insulin action coexist, making it challenging to identify the primary cause of hyperglycemia. (7) Risk factors for diabetes are more diverse; some are modifiable, and others are not. Nonmodifiable risk factors for type 2 diabetes include age, race or ethnicity, family history (genetic predisposition), history of gestational diabetes, and low birth weight. (8)

2.2 Prevent and treatments

type 1 diabetes cannot currently be prevented. Effective approaches are available to prevent type 2 diabetes and to prevent the complications and premature death that can result from all types of diabetes. These include policies and practices across whole populations and within specific settings (school, home, workplace) that contribute to good health for everyone, regardless of whether they have diabetes, such as exercising regularly, eating healthily, avoiding smoking, and controlling blood pressure and lipids.

The starting point for living well with diabetes is an early diagnosis – the longer a person lives with undiagnosed and untreated diabetes, the worse

their health outcomes are likely to be. Easy access to basic diagnostics, such as blood glucose testing, should therefore be available in primary health care settings. Patients will need periodic specialist assessment or treatment for complications.

3.1Hypertension

Hypertension is a cardiovascular syndrome that arises from various complex and interconnected factors. (9). High blood pressure refers to the consistent elevation of the force of blood flowing through the blood vessels. (10). Hypertension is an established independent risk factor for cardiovascular disease (CVD) and contributes to 1 in 7 deaths. The cost associated with hypertension in the United States from 2014–2015 was approximately $56 billion (11). High blood pressure (BP) is the most critical risk factor for cardiovascular disease (CVD), ranking first in global disability-adjusted life-years and associated with approximately 1,000 deaths per day (12). Effective blood pressure management has been shown to decrease the incidence of stroke, heart attack, and heart failure. Hypertension is a major risk factor for cardiovascular disease and a major modifiable risk factor for dementia (13). The causal relationship between hypertension and diabetes is not clear as studies have shown a bidirectional relationship between these two metabolic diseases. (14). Some studies have shown that the prevalence of hypertension is high in diabetic patients (15) while others have shown an increased prevalence of diabetes in hypertensive populations. (16). Hypertension and diabetes share common risk factors such as endothelial dysfunction, vascular inflammation, arterial remodeling, atherosclerosis, dyslipidemia, and obesity. Studies suggest that individuals with diabetes have a prevalence of hypertension that is approximately 1.5- 2.0 times higher than those without diabetes, as reported by (17).

3.2 symptoms of high blood pressure

Often, people with high blood pressure do not have noticeable symptoms. If the blood pressure is greatly elevated, a person may experience the following. However, each individual may experience symptoms differently. Symptoms may include:

- Headache
- Dizziness
- Blurred vision

The symptoms of high blood pressure may resemble other medical conditions or problems. Always consult your doctor for a diagnosis.

3.3 Preventing high blood pressure

The American Diabetes Association recommends the following to help prevent the onset of high blood pressure:

- Reduce your salt intake
- Engage in stress-relieving activities
- Exercise regularly
- Get to and stay at a healthy weight
- Avoid excessive alcohol intake
- Stop smoking and avoid exposure to secondhand smoke
- Monitor your blood pressure

3.4 Treatment for high blood pressure

Specific treatment for high blood pressure will be determined by your doctor based on:

- Your age, overall health, and medical history

- Extent of the disease
- Your tolerance for specific medications, procedures, or therapies
- Expectations for the course of the disease
- Your opinion or preference

Treatment may include exercise, a balanced diet, and quitting smoking, as well as medications prescribed by your doctor.

4.Type 2 Diabetes Mellitus and Hypertension

The prevalence of obesity and type 2 diabetes (T2D) continues to rise worldwide as lifestyles associated with low energy expenditure and high caloric intake are increasingly adopted, particularly in lower-income and developing countries. It is predicted that the number of cases of T2D will rise from 415 million to 642 million by 2040(18).(Hypertension is even more common, rising in prevalence in the same countries, with a recent worldwide estimate of 1.39 billion cases.(19)

Although T2D and hypertension can be simply diagnosed at the bedside, they are each complex and heterogeneous phenotypes associated with an elevated risk of life-threatening cardiovascular disease (CVD). Their frequent coexistence in the same individual is not a coincidence, because aspects of the pathophysiology are shared by both conditions, particularly those related to obesity and insulin resistance. For example, in the San Antonio Heart Study, 85% of those with T2D had hypertension by the fifth decade of life, whereas 50% of those with hypertension experienced impaired glucose tolerance or T2D.20

Diabetes is associated with both macrovascular (involving large arteries such as conduit vessels) and microvascular (involving small arteries and capillaries) disease. Chronic hyperglycemia and insulin resistance play an

important role in the initiation of vascular complications of diabetes and involve a number of mechanisms including (1) increased formation of advanced glycation end products (AGEs) and activation of the receptor for advanced glycation end products (RAGE) AGE-RAGE axis, (2) oxidative stress, and (3) inflammation.21 In addition, emerging evidence suggests a role for microRNAs (miRNAs) in the vasculopathy of diabetes (see further on).22 Hypertension is an important risk factor for diabetes-associated vascular complications, because hypertension itself is characterized by vascular dysfunction and injury (Fig. 1).

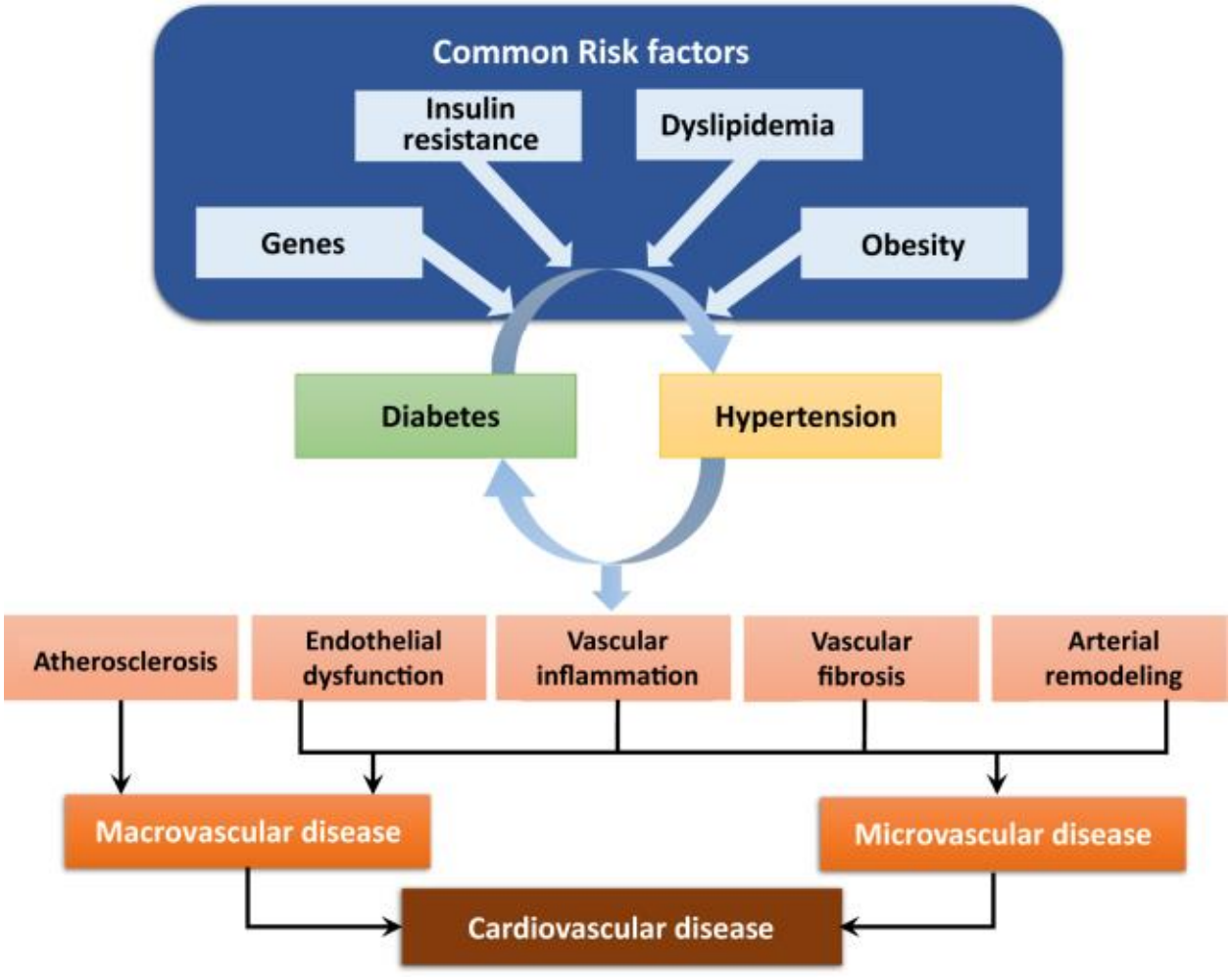

Figure 1

Vascular processes whereby diabetes and hypertension predispose to cardiovascular disease. Common risk factors promote diabetes and

hypertension, which are associated with atherosclerosis, vascular inflammation, endothelial dysfunction, and structural remodelling, which lead to macrovascular and microvascular disease. Vascular damage and endothelial dysfunction is amplified when diabetes and hypertension coexist.

5. Blood pressure targets in patients with diabetes

Major medical societies including the American Diabetes Association (ADA) recommend a target blood pressure of less than 130/80 mm Hg for patients with diabetes. The first trial to seek justification for this recommendation was the Normotensive Appropriate Blood Pressure Control in Diabetes (ABCD) trial. Although no specific blood pressure target was pursued, the mean attained blood pressure of 128/75 mm Hg in the intensive treatment group, was under the systolic target of 130 mm Hg. Over a follow up of five years, no significant difference was seen in creatinine clearance (primary outcome) or cardiovascular events when compared to the placebo group (mean blood pressure 137/81). The intensive treatment group did manifest significant reductions in progression of retinopathy, albuminuria, and absolute risk of stroke (26,27).

In conclusion, multiple high-quality randomized controlled trials have shown improvement in morbidity with correction of elevated BP in people with diabetes. Patients with T2DM appear to be particularly susceptible to the deleterious effects of hypertension in initiation and progression of CVD. In the treatment of hypertension in patients with diabetes attention must be paid to individual risk factors, co-morbidities, and patient preferences when considering lower treatment targets. A lower blood pressure target, for instance, might be more appropriate for a young person

who would likely benefit from a reduction in stroke risk and reduced progression of retinopathy without experiencing unwanted side effects of hypotension, syncope, and hyperkalemia that are encountered more commonly in the older popular

6 .Mechanisms of Vascular Complications in Diabetes and the Impact of Hypertension

A number of interacting mechanisms are in play as summarized in the following sections (Fig. 2).

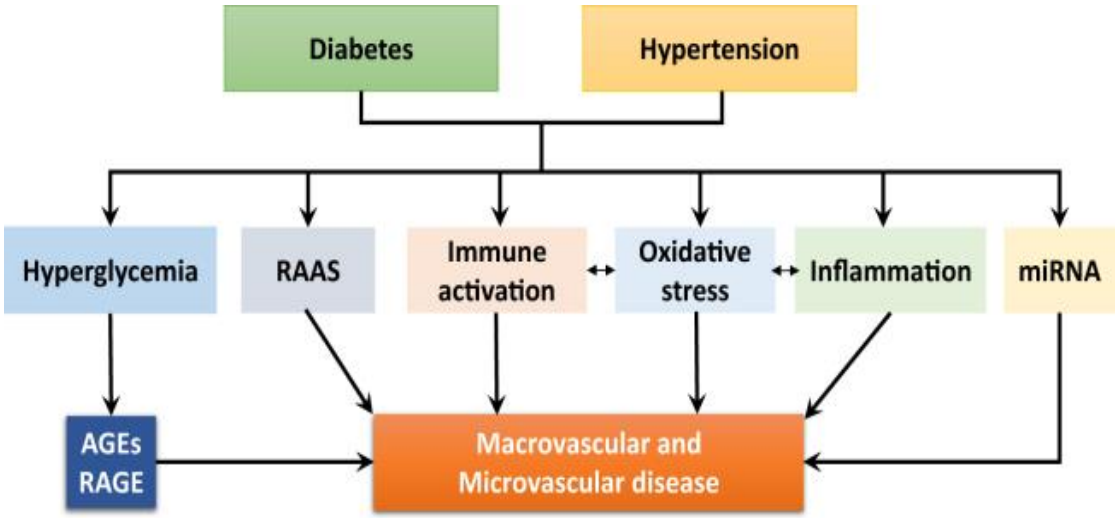

Figure 2

Putative mechanisms whereby diabetes and hypertension cause vascular disease. Immune cell activation and inflammation are mediated through oxidative stress. AGEs, advanced glycation end products; RAAS, renin-angiotensin-aldosterone system; RAGE, receptor AGE.

7. Macrovascular (or cardiovascular) disease with Diabetes

Macrovascular (or cardiovascular) disease with Diabetes of larger conduit arteries is a complex inflammatory process leading to myocardial

infarction, stroke, and peripheral artery disease. The primary pathologic process associated with macrovascular disease is atherosclerosis, which in diabetes is accelerated with extensive distribution of vascular lesions.(28)T2D confers an approximate 2-fold elevation in CVD risk, equivalent to that of a previous myocardial infarction.29,) Moreover, patients with T2D have poorer outcomes after an acute coronary syndrome and higher rates of reinfarction and heart failure.(30

Elevation of CVD risk begins at the stage of prediabetes in association with insulin resistance and impaired glucose tolerance) 31)

8. Microvascular disease

the **A**ction in **D**iabetes and **Va**scular Disease: Preterax and Diamicro**n** **C**ontrolled **E**valuation (ADVANCE) trial cohort has confirmed that the presence of microvascular complications increases the risk of cardiovascular complications in individuls with T2D.[32] Moreover, the coexistence of hypertension and retinopathy is a risk factor for the progression of nephropathy. There is evidence that treatment of hypertension with angiotensin II receptor blockers can reduce the progression of retinopathy in addition to well-known effects on nephropathy.[33]

9. pathophysiology of hypertension in diabetes

The pathophysiology of hypertension in diabetes can be traced to maladaptive changes and complex interactions between the autonomic nervous system, a maladaptive immune system, enhanced activation of the renin-angiotensin-aldosterone system (RAAS) as well as adverse environmental factors. The factors listed below play a major role in the

pathogenesis of hypertension and have been targeted for therapeutic interventions (34).

10.Sedentary Lifestyle, Excessive Caloric Intake and Insulin Resistance

Sedentary lifestyle and excessive caloric intake can lead to increased adiposity which has been associated with increased risk of worsening insulin resistance. Insulin resistance has been linked in turn to an increased vascular oxidative stress, inflammation, and endothelial dysfunction characterized by diminished vascular nitric oxide bioactivity, all of which promote vascular stiffness resulting in a persistent elevation of blood pressure and the promotion of CVD (35).

11. Role of Innate and Adaptive Immunity

There is emerging evidence that innate immunity and acquired immunity are involved in angiotensin II and aldosterone-induced hypertension and vascular disease (36). Animal studies suggest that intact T cell function is required for full expression of these adverse effects and that T cells and macrophages mediate the oxidative injury associated with these effects. On the other hand, the protective properties of T regulatory cells in animal models suggests a potential therapeutic role for these cells, although at this time such interventions are limited to the research setting.

12.Inflammation and the immune system

Links between inflammation and the immune system with metabolic dysfunction, hypertension, and cardiovascular morbidity are supported by extensive experimental data.[37] This encompasses a number of immune metabolic as

pects, including the key role of the tricarboxylic cycle or sphingosine-1-phosphate in the regulation of vascular inflammation.[38] Clinical studies have shown that patients with T2D have increased total leukocyte counts, particularly neutrophils and lymphocytes, that correlate with insulin sensitivity, which is in part mediated by inflammatory changes of adipose tissue. Inflammatory biomarkers are also useful in developing targeted cardiovascular therapies in the context of metabolic dysfunction.[39]

13.Treatment of diabetes mellitus and its cardiovascular complications

Once T2D has been diagnosed, the aim of achieving glucose control is principally to avoid microvascular complications. There are some benefits with respect to macrovascular complications, but this is dependent on the profile of individual drug classes and even appears to be different for agents within the same class.[40] The role of BP lowering to improve prognosis in T2D has been established since the UK Prospective Diabetes Study (UKPDS) in 1998.[41] However, more recently, more widespread use of glucose-lowering agents that reduce (rather than increase) weight, lower BP, and have beneficial “off-target” effects (as demonstrated in recent large cardiovascular outcome trials) facilitates cardiovascular risk factor control and is playing a role in improving the cardiovascular prognosis of T2D.[42]

Achieving glucose control in T2D begins with weight management. Particularly in the first 8 years after diagnosis, normal glucose tolerance can be restored if radical weight reduction can be achieved, most effectively using a very low-calorie liquid replacement diet.[43] In obese patients, this can also occur after successful bariatric surgery, particularly the Roux-en-Y procedure. The mechanism may involve reduction in

ectopic fat, and consequent relief from its proiabetesnflammatory effects, in and around the pancreatic islets of Langerhans.[44]

More recently introduced classes of glucose-lowering agents have heralded an exciting era in T2D pharmacotherapy because they are associated with weight reduction, BP reduction, and, importantly, reduced rates of major adverse events in long-term cardiovascular outcome trials.[45]

Conclusion

Diabetes is associated with an increased risk of CVD, which is exaggerated with coexistent hypertension. Many of the underlying molecular mechanisms, including oxidative stress, inflammation, and fibrosis causing microvascular and macrovascular complications of diabetes, also cause vascular remodelling and dysfunction in hypertension. Controlling comorbidities, especially hypertension, and targeting strategies to promote vascular health, may be especially important in reducing the microvascular and macrovascular complications of diabetes.

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