Diabetes Mellitus and Peripheral Vascular Disease

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ABSTRACT

Chronic complications or the long-term side effects of diabetes mellitus includes microvascular complications which affects smaller blood vessels such as retinopathy, nephropathy, neuropathy and macrovascular complications which affects larger blood vessels supplying the heart, brain, and extremities. Prevalence of Peripheral Vascular Disease (PVD) in diabetes ranges between 20% and 30%. Endothelial cell dysfunction, vascular smooth muscle cell dysfunction, inflammation, impaired platelet function and abnormal coagulation are the other key factors in progression of PVD in diabetes. Ankle Brachial Index can be used as a screening tool at regular intervals. Apart from the intensified multifactorial treatment of all modifiable risk factors, intensive therapy targeted at glycemic control and other modifiable cardiovascular risk factor is needed to prevent micro and macro vascular complications of diabetes, especially PVD.

Keywords: Complications, Diabetes, Peripheral Vascular Disease

INTRODUCTION

Diabetes is the most common metabolic disorder all over the world. The increasing incidence of diabetes gives India the "Diabetic Capital of the World".[1] Peripheral Vascular Disease (PVD) is one of the most common macro-vascular complications of Type II DM.[2] Nearly 50% of the patients with PVD are asymptomatic.[3] Diabetes explains for about 50% of all non-traumatic amputations in India especially due to diabetic foot. Early detection of vascular changes helps in effective handling of diabetes and its complications.

Diabetes

Normal maintenance of blood glucose and uptake by the cell is regulated by insulin hormone.[4] Type 1 diabetes happens when part or all of the insulin producing cells in the pancreas are destroyed resulting in little or no insulin. Type 2 diabetes arises when your body's cells battle the normal outcome of insulin, which is to enterprise glucose in the blood into the inside of the cells. This disorder is called insulin resistance. As a consequence, glucose starts to accumulate in the blood. Genetic and environmental risk factors influence inflammation, autoimmunity, and metabolic stress. Irrespective of the pathophysiology of diabetes mellitus, chronically raised blood glucose levels are attributing factors for the microvascular and macro-vascular complications. This will increase morbidity and risk of death in people with diabetes.[5] The epidemiological determinants and the risk factors of type II diabetes mellitus is listed below in Figure 1.[6]

Complications of Diabetes

Uncontrolled diabetes can cause metabolic imbalance that leads to acute or short-term complications that may necessitate immediate medical attention. This includes Ketoacidosis and Hyperosmolar Hyperglycaemic Non-ketotic Syndrome (HHNS). Chronic complications or the long-term side effects of diabetes mellitus includes microvascular complications, which affects the smaller blood vessels, such as retinopathy, nephropathy and neuropathy.[7] Macro-vascular complications affects larger blood vessels supplying the heart, brain and extremities.[8,9]

Peripheral Vascular Disease

Peripheral Vascular disease (PVD) is a comprehensive term surrounding a variety of atherosclerotic and aneurysmal conditions within the extra-coronary circulation. PVD is projected to affect up to 15% of the population aged above 65 years and considerably increases the risk of major cardiovascular events in affected patients. Based on the severity of PVD, the stages can be classified as compensation, rest pain, chronic non-healing ulcer, gangrene and amputation. These stages are characterised by decreased ankle blood pressure, angiogenesis, endothelial dysfunction and muscle fibre damage respectively.[10] The major difference between the normal artery and atherosclerotic artery are decreased blood flow, plague formation and narrowed artery.[11]

Prevalence of PVD in Diabetes Patients

The prevalence of PVD in Diabetes patients is difficult to assess as the pain perception is reduced with the simultaneous ongoing peripheral neuropathy.[12] There are not many studies available in the literature for studying the prevalence of PVD in Diabetes. In the United Kingdom Prospective Diabetes Study (UKPDS), 1.2% of the newly diagnosed type II diabetes patients had PVD (as defined as ABI less than 0.8) and the prevalence increased to 12.5% with 18 years of diabetes duration.[13] Other studies observed a prevalence between 20-30%.[14]

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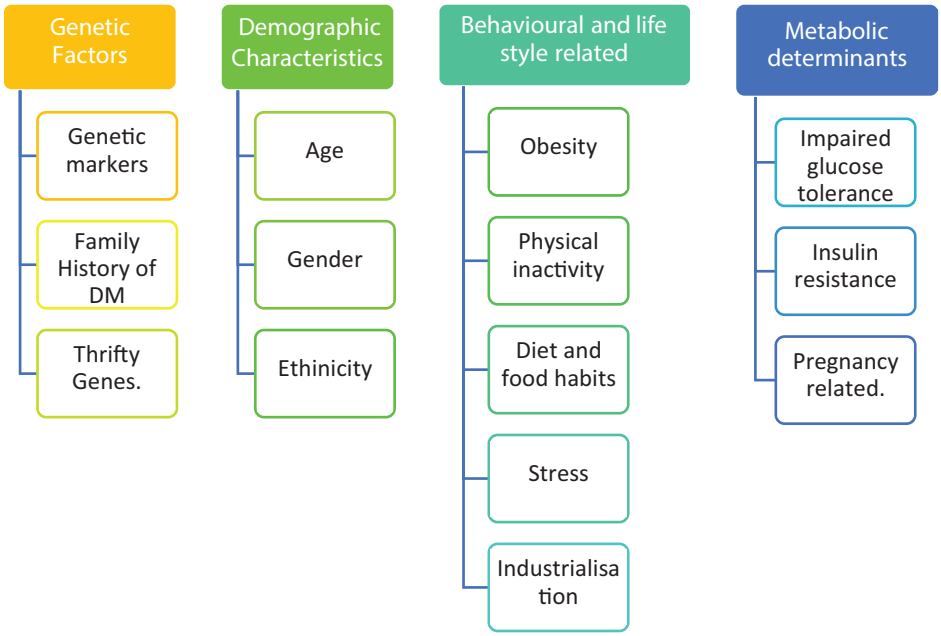

Figure-1: Risk Factors for Diabetes Mellitus

Risk Factors for PVD[15]

i Smoking
ii High blood pressure
iii Atherosclerosis
iv Diabetes
v High cholesterol
vi Older than age 60 years

Pathophysiology of PVD in Diabetes

The mechanism of actions of peripheral vascular disease include atherosclerosis, vascular remodelling, endothelial dysfunction and thrombosis which further leads to narrowing of vascular lumen, thickening of vascular wall, decrease in nitric oxide (NO) production and vascular blockade. All these mechanisms lead to reduction in vascular blood flow which in turn leads to the development of skeletal muscle ischemia and PVD.[16] Endothelial cell dysfunction causing defective synthesis of important bioactive substances such as nitric oxide (NO) – a potent vasodilator, other reactive oxygen species (ROS), prostaglandins, endothelin and angiotensin II (AII). Vascular smooth muscle cell dysfunction, inflammation, impaired platelet function and abnormal coagulation are the other key factors in progression of PVD in diabetes.[17]

Clinical Features of PVD

The classical symptom of PVD is pain in the legs during exertion such as walking, which is relieved by taking rest. Conversely, nearly up to 40% of individuals with PVD have no leg pain. Symptoms of pain, ache, or cramp during walking (claudication) can happen in the areas such as buttock, hip, thigh or calf. Physical signs in the leg that may indicate peripheral vascular disease comprise of muscle atrophy, hair loss, smooth shiny skin, decreased or absent pulses in the feet, non-healing ulcers or wounds in the extremities and coldness or numbness in the toes.[18] The six P's of Acute Limb Ischemia is shown in Figure 2.[19,20]

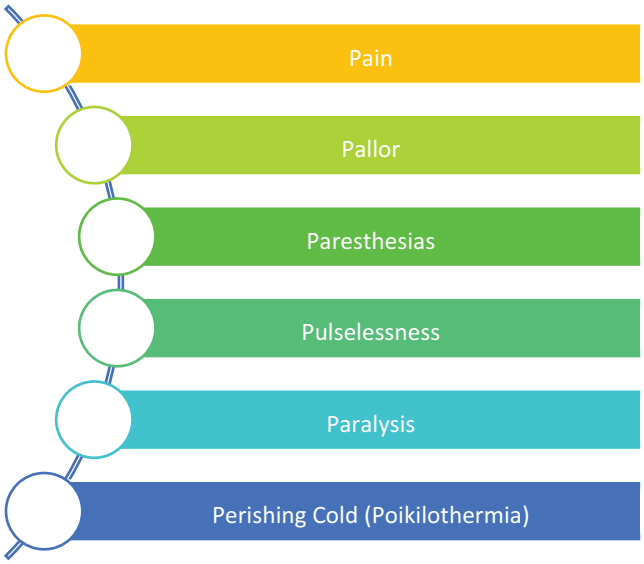

Figure-2: The six P's of Acute limb ischemia

Diagnosis

Endovascular evaluation includes physiological testing (skin perfusion pressure and transcutaneous oxygen monitoring) as well as anatomic evaluation (duplex doppler ultrasound, various types of angiography). The types of anatomical evaluation includes magnetic resonance angiography, computed tomographic angiography, contrast or catheter angiography, skin perfusion pressure test, transcutaneous oxygen monitoring.[21] Ankle Brachial Index (ABI) is an index calculated by ratio of systolic blood pressure measured at ankle to the systolic blood pressure measured in the arm. ABI measurement delivers a simple, reliable, acceptable, valid, non-invasive tool to assess vascular condition in diabetics with greater sensitivity and specificity.[22–24] PVD is defined as the presence of at least two of the following factors:

1. Ankle brachial index (ABI) < 0.8
2. Absence of both dorsalis pedis and posterior tibial

pulses at palpation in one or both the legs
3. Intermittent claudication.[13]

Life style Modifications

The following lifestyle modifications are needed for the treatment of peripheral vascular disease patients:[25]

a Cessation of smoking
b Improved control of diabetes
c Improved control of hypertension
d Improved control of lipids
e Weight loss management
f Regular physical activity and exercise.

Management of PVD

The management options of Peripheral vascular disease are broadly classified into non-pharmacological/conservative, Pharmacological/medical and surgical interventions. The individual interventions under the three categories are represented in the following figure 3.[26]

CONCLUSION

The risk of peripheral vascular disease (PVD) is higher, earlier, severe and diffuse in patients with diabetes mellitus due to the key factors like Endothelial dysfunction, vascular smooth muscle cell dysfunction, inflammation and hyper-coagulability which contribute in the pathogenesis of the disease. Apart from the intensified multifactorial treatment of all modifiable risk factors intensive therapy targeted at glycemic control and other modifiable cardiovascular risk factor is needed to prevent micro and macro-vascular complications of diabetes especially PVD.

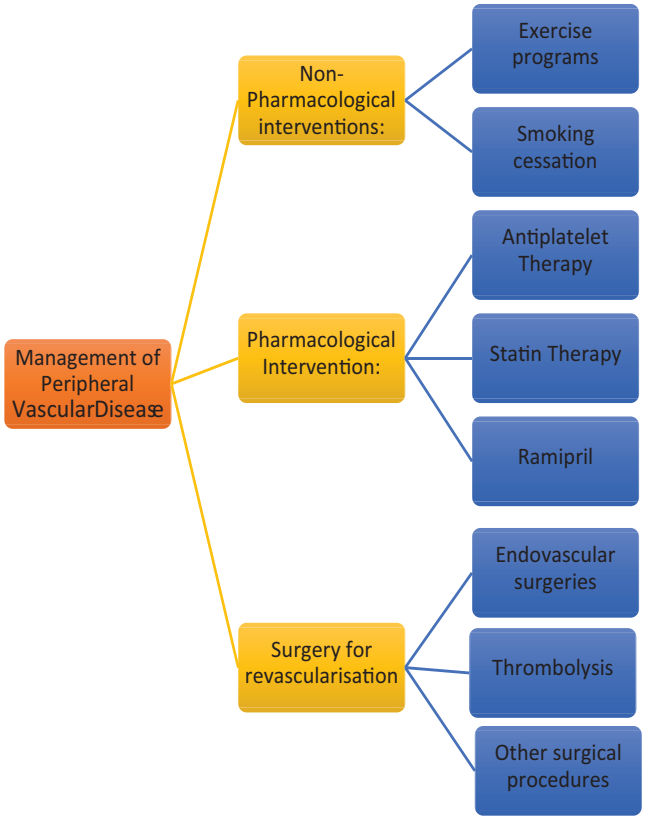

Figure-3: Management of Peripheral Vascular disease

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