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TYPE 2 DIABETES MELLITUS AND ITS ASSOCIATED RISK FACTORS

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ABSTRACT
Diabetes Mellitus is a metabolic disorder characterized by abnormally high blood glucose levels known as hyperglycemia due to a defect in insulin secretion, insulin action or both. Diabetes Mellitus continues to increase as a result of rapid cultural and social changes. Indians are also believed to have a greater degree of insulin resistance and a stronger genetic predisposition to diabetes. Type 2 Diabetes Mellitus carries a high risk of large vessel atherosclerosis commonly associated with hypertension, hyperlipidaemia and obesity.[6] According to the latest statistics and predictions for the future, more than 60% of the diabetics live in Asia. Among the diabetic persons in Asia, 51 million live in India. Diabetes Mellitus occurs at least 10 to 15 years earlier in developing countries, especially in India compared to developed countries. The genetic predisposition, urbanization, physical inactivity and altered diet leading to obesity are likely to be the primary reasons for the risk in diabetes. This review paper is focussed on the risk factors associated with type 2 Diabetes Mellitus.

KEYWORDS: Type 2 Diabetes Mellitus, Risk Factors, Hyperglycemia.

INTRODUCTION
Diabetes mellitus (DM) is a metabolic disorder characterized by abnormally high blood glucose levels known as hyperglycemia[1] due to a defect in insulin secretion, insulin action or both. Insulin deficiency results in chronic hyperglycaemia with disturbances of carbohydrate, fat and protein metabolism.[2] Etiology shows that factors contributing hyperglycemia are reduced insulin secretion, decreased glucose utilization and increased glucose production. The symptoms include polyuria, polydipsia, polyphagia, weight loss and blurred vision. The chronic hyperglycemia is also associated with long-term damage, dysfunction and failure of various organs like eyes, kidneys, nerves, heart and blood vessels.[3] DM occurs at least 10 to 15 years earlier in developing countries, especially in India compared to developed countries. The genetic predisposition, urbanization, physical inactivity and altered diet leading to obesity are likely to be the primary reasons for the risk in diabetes. This review paper is focussed on the risk factors associated with Type 2 DM (T2DM).

Type 2 Diabetes Mellitus – A Major Health Concern
Increased hepatic glucose production, diminished insulin secretion and impaired insulin action are three key defects in the onset of hyperglycemia in T2DM.[4] The risk for coronary heart disease (CHD) is two-to four-folds higher in T2DM patients compared to non-diabetic populations.[5] T2DM carries a high risk of large vessel atherosclerosis commonly associated with hypertension, hyperlipidaemia and obesity. Most of the T2DM patients die from cardiovascular complications.[7] T2DM is associated with aging, obesity and physical inactivity. Due to increasing incidence of obesity and physical inactivity among young people, the age of onset of T2DM is substantially lower than previously and the insulin resistance precedes the onset by years or decades.

Numerous epidemiologic studies have shown that people with one or more first-degree relatives who are affected with diabetes are 2 to 6 times as likely to have the disease compared with people who have no affected relatives.[8] Persons with a positive family history of diabetes, including children, might show early signs of defective insulin actions, glucose intolerance, lipid abnormalities, high BP, large weight gains, reduced β-cell function and impaired endothelial function.[9] Because DM and Cardiovascular Disease (CVD) share risk factors such as obesity and dyslipidemia and might even share etiology, people with a family history of diabetes show increased risk for CVD. Conversely, people with a family history of CVD might show early signs of insulin resistance and impaired glucose metabolism and ultimately, risk of diabetes.[10] Several studies have highlighted the presence of insulin resistance and CVD risk factors among children. For example, the Bogalusa Heart Study, in a series of cross sectional studies, demonstrated that cardiovascular risk factors are detectable in childhood and that signs of adult heart disease, including atherosclerotic lesions are

evident as early as the second and third decades of life.[11]

Epidemiology

According to International Diabetes Federation, around 415 million people had DM in 2015 and this number is expected to rise to 642 million by 2040. India is home to 69.1 million people with DM and is estimated to have the second highest number of cases of DM in the world after China in 2015.[12] The prevalence of DM in India ranges from 5–17%, with higher levels found in the southern part of the country and in urban areas.[13,14,15] DM continues to increase as a result of rapid cultural and social changes, which include: ageing populations, increasing urbanization, dietary changes, reduced physical activity and unhealthy behaviour.[16]

More than 60% of the diabetics live in Asia. Among the diabetic persons in Asia, 51 million live in India. During the period 1971-2000, studies from different parts of India reported a 10-fold increase in the incidence of diabetes in urban India (from 1.2% in 1971 to 12.1% in 2000). Studies using either the standard procedures recommended by American Diabetes Association (ADA) or World Health Organization (WHO) over the period 1990 to 2000, have shown the prevalence to increase from 5 to 15% among the urban populations, from 4.2 to 6.2% in semi urban populations and from 2 to 5% in the rural populations. In the last two decades, diabetes prevalence in urban areas has increased by three- to four-fold in many regions of India.[17,18] By 2030, urbanization is expected to reach nearly 50% in India and therefore the country will continue to have the largest number of diabetic subjects as a result of the rapid urbanization and economic development.[19]

Pathogenesis

Insulin resistance is a state in which the body does not respond to the action of insulin, even when enough insulin is secreted and nearly 90% of T2DM patients are insulin resistant. Insulin resistance, prediabetes and T2DM are linked by a similar pathogenesis. Initially, insulin resistance causes an increase in insulin secretion appropriately from the β-cells of the pancreas. This compensatory mechanism results in euglycemia with elevated fasting and/or postprandial serum insulin levels. The β-cells continue to compensate by increasing insulin levels, resulting in glucose homeostasis for up to 7 years.[20] As β-cells eventually exhaust and insulin levels become too low to meet the requirement of skeletal muscles and liver tissues, a mild postprandial hyperglycemia develops. As insulin resistance increases and the progressive loss of β-cells function continues, insulin secretion is decreased and resulting in IFG.

Risk Factors

DM occurs at least 10 to 15 years earlier in developing countries, especially in India compared to developed countries. The genetic predisposition, urbanization, physical inactivity and altered diet leading to obesity are likely to be the primary reasons for the risk in diabetes.

Age

Indians develop diabetes at younger age, at least 10 – 15 years earlier than Caucasian population. An analysis by the International Diabetology Group comparing the profile of T2DM in European and Asian populations showed that Indians had the strongest age associated risk factors for diabetes among all the groups. The association between age and diabetes was higher in the Indians than the populations of Europeans, Chinese and Japanese.[21] As per Indian Council of Medical Research – India Diabetes (ICMR-INDIAB) study, the prevalence of diabetes is more in the age group 25-34 years.[22] The Atherosclerosis risk in communities (ARIC) study also identified age as an important risk factor for the incidence of diabetes.[23]

Gender

Even though, there is no clear gender predisposition, some differences were observed in the prevalence rates. Particularly in rural India there seems to be a dramatic increase in diabetes in men.[19] As per ICMR-INDIAB study diabetes prevalence was higher in men compared to women.[22]

Family History

It is well accepted that T2DM is an inherited disease. The prevalence of diabetes increases with increase in family history of diabetes. The risk of the offspring developing diabetes with a parental history increases above 50% and it is around 40% if the proband has a diabetic sibling. About 75% of T2DM patients in India have a first degree family history including strong familial aggregation in this population.[24] Familial aggregation of diabetes with a high prevalence among first degree relatives and vertical transmission through more than two generations is commonly seen in Asian Indians.[25] In ARIC study, parental history of diabetes has been suggested as an important predictor of diabetes.[23] In the Framingham Offspring Study, the offspring with maternal diabetes were more likely to have a mild slowly progressive form of glucose intolerance compared to offspring with paternal diabetes.[26]

Hypertension

Hypertension has been suggested as an independent risk factor for diabetes. In ARIC cohort, the risk of developing diabetes was two- to four-fold greater in hypertensive individuals than normotensive after adjusting for obesity.[27] Elevated systemic blood pressure accelerates the progression of both microvascular and macrovascular complications in diabetes. Vasoactive hormone pathways, e.g. the renin-angiotensin-aldosterone system, appear to play a pertinent role in the progression of diabetes and diabetic complications. Hypertension is often associated clinically with diabetes either as part of the metabolic

syndrome or as a manifestation of diabetic nephropathy and the coexistence of these two conditions synergistically increases the risk of life-threatening cardiovascular events.[28]

Overweight

Overweight (BMI > 25kg/m2) plays a major role in the pathogenesis of T2DM by influencing insulin resistance. Obesity is also an independent risk factor for hypertension, dyslipidemia, and CVD which is the major cause of death in those with diabetes.[29] It has been shown that adiponectin reduces insulin resistance in individuals with progressive obesity. Elevated levels of adipocytokines such as tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6) and Resistin are observed with obesity and these adipocytokines have been suggested to increase insulin resistance. Various adipose tissue beds produce different amounts of these peptides. Therefore, greater accumulation of fat in the body will increase insulin resistance and increase the risk of developing T2DM.[20]

Physical Activity

The physical activity is inversely associated with T2DM. A meta-analysis combining ten prospective cohorts of physical activity of moderate intensity and T2DM suggested that brisk walking can substantially reduce the risk of T2DM.[30] ADA recommends at least 150 min/week of moderate-intensity aerobic physical activity (50-70% of maximum heart rate) and/or at least 90 min/week of vigorous aerobic exercise (>70% of maximum heart rate) to improve glycemic control and reduce the risk of CVD.[29] The habitual physical inactivity and low cardiorespiratory fitness are involved in the progression to T2DM. The exercise increases tissue sensitivity to insulin. In prospective cohort studies, persons who maintain a physically active lifestyle develop impaired glucose tolerance and T2DM less often than those who lead sedentary lifestyle.[31] The majority of people with T2DM are overweight and usually have other metabolic disorders of the insulin resistance syndrome, so the major aims of dietary and lifestyle changes are to reduce weight, improve glycaemic control and reduce the risk of CHD.

Alcohol

Several studies suggest that low-to-moderate amounts of alcohol intake may decrease development of diabetes by increasing insulin sensitivity and slowing glucose uptake from a meal.[32] One of the major risks with alcohol consumption in diabetes is the potential danger of hypoglycaemia, especially among those who use sulphonylureas. However, in many clinical studies, no alterations in glucose homeostasis were observed when moderate alcohol is consumed with meals.[33]

Smoking

Active smoking is associated with an increased risk of T2DM.[34] Cigarette smoking causes insulin resistance in peripheral tissues, whereas insulin secretion may be normal or over-stimulated. Smoking has been shown to cause elevations in blood glucose concentration and may increase insulin resistance. Current smokers also tend to have higher blood concentrations of glycosylated hemoglobin than the non-smokers.[35] Several studies have shown that smokers have less BMI than non-smokers and also they tend to have more central fat deposition which is associated with insulin resistance.[36]

CONCLUSION

DM occurs at least 10 to 15 years earlier in developing countries, especially in India compared to developed countries. The genetic predisposition, urbanization, physical inactivity and altered diet leading to obesity are likely to be the primary reasons for the risk in diabetes. Stress-free lifestyle and proper diet help in reducing the early occurrence T2DM.

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