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Review Article

Why Indians More Susceptible to Diabetes?

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Abstract

This review aims to investigate the facts behind the augmented susceptibility of the Indian population towards type 2 diabetes. The high rate prevalence of diabetes has been associated with rapid socioeconomic progress and urbanization in India. Epidemiology of diabetes prevalence reveals that the urban population is more vulnerable to diabetes due to risk factors like lifestyle changes, food habits, sedentary work, and high stress levels. These risk factors are equally responsible for obesity, diabetes, and cardiovascular disease globally. The key point is Indians are predisposed to insulin resistance, higher abdominal adiposity, waist circumference despite lower body mass index. The Indian population has low metabolic capacity and insulin resistance syndrome, which can be attributed to the low birth weight and less lean mass in adulthood. Some population-specific risk-alleles contribute to the elevated prevalence of diabetes in Indians, like the FTO (fat mass and obesity) gene, which is again environment-dependent, resulting in a much stronger relationship of obesity with diabetes among South Asians. Indians tend to have a larger waist and waist to hip ratio, excess body fat, and abdominal adiposity despite a moderate level of obesity, indicating the predisposition to diabetes at a younger age than in Europeans.

Keywords: *Type 2 Diabetes; Epidemiology; Prevalence; Genetic Factors; Insulin Resistance; Obesity*

Introduction

India has earned the status of being the diabetic capital of the world. Around 463 million people have diabetes globally, out of which 77 million belong to India as per 2020, International Diabetes Federation (IDF) data. Prevalence of diabetes is high in Asia as it is estimated that 20% of the global diabetic population resides in South-East Asia. The prevalence rate of diabetes in the Indian population is 8.9%, according to the IDF. Unfortunately, about half of these vulnerable populations remain undiagnosed as having diabetes [1]. The current scenario of diabetes in India is likely to worsen in the coming decades. By 2030 diabetes may affect up to 85 million individuals in India, with most people between 40 and 59 years of age [2]. The prevalence of diabetes among India's urban population is highest in the world, comparable to other high prevalence countries like West Asia and the Pacific [3].

Diabetes prevalence in India

Studies have reported higher diabetes prevalence in urban adults as compared with rural adults in India. Indians tend to develop diabetes at a younger age as patients younger than 45 years account for 36% of all diabetics in India [4]. Chronic diabetes leads to other complications, and this could threaten the national economy by increasing health expense burden. Recent studies have reported urban and rural diabetes prevalence rates of 8 - 20% and 5 - 15%, respectively. The prevalence was similar in male (12%) and female (11.7%)

populations. Both in urban and rural India, diabetes prevalence rates are increasing rapidly with an estimation of 2:1 to 3:1. Prevalence rates of diabetes had increased from 1% to 10-13.2%, correspondingly, in rural areas of India from 1970 to 2000 [5]. Regional studies have reported higher prevalence of diabetes in Southern India than the north, east, and central India [6]. Atre [7] reported a high prevalence of diabetes in economically and epidemiologically advanced states such as Tamil Nadu and Kerala. The difference in diabetes prevalence across India could be due to dissimilar urbanization and lifestyle factors such as food habits and obesity levels [8].

India is experiencing rapid socioeconomic progress and urbanization. Diabetes prevalence in India is more related to the Social Development Index of the cities than to geography. Cities with lower poverty and better social development indices have a greater prevalence of diabetes than other cardiometabolic risk factors [9]. These results are similar to the studies reported from China and other middle-income countries [10], though prevalence rates in India are 50 - 80% higher than in China (10%). Approximately 14% of the Indian population is prediabetes, harboring future diabetes [11].

Diabetic prevalence studies conducted in India

Ahmad., *et al*. [12] screened the prevalence of diabetes mellitus amongst high-risk age group populations in Kanpur's urban and rural areas. The overall prevalence of diabetes was 7.1%, and the maximum percentage of diabetes cases (41.66%) was in the age group of 56 - 60 years. A higher prevalence of diabetes was observed in the obese (56.25%), sedentary (87.5%), and in persons having a family history (35.41%) of diabetes.

Ramachandran., *et al*. [13] has associated urbanization in India with a high Prevalence rate of diabetes and cardiovascular risk factors. This study reports a significant increase in diabetes in the city and in periurban villages based on a population survey in Southern India. Ongoing lifestyle changes in periurban villages are likely to enhance the risk of diabetes and cardiovascular disease.

Gupta., *et al*. [14] assess the risk of diabetes on above 20 years adults in rural areas of Tamil Nadu using the Indian diabetes risk score (IDRS). IDRS assess modifiable (waist circumference, physical activity) and non-modifiable risk factors (age, family history) parameters for diabetes. Around 43% of the population were found in the high-risk category for the development of diabetes. People with sedentary and mild physical activity along with positive family history had a higher risk for diabetes.

A population-based cohort study was conducted between 2007 and 2011 among adults above 25 years in Pondicherry villages. Diabetes incidence was found to be 2% per year in adults of rural Pondicherry, with the rate increasing twice in males compared to females. Increasing age, obesity, alcohol use, and family history directly correlates with the development of diabetes, where almost one-third of the case occurred in people aged below 40 [15].

Gupta., *et al*. [16] conducted a population-based study in 11 cities in different regions of India to determine the prevalence of diabetes along with awareness, treatment and control of cardiovascular risk factors. Participants were evaluated for demographic, biophysical, and biochemical risk factors. The results showed that in the urban Indian middle class, more than one-fourth of patients have undiagnosed diabetes. Cardiovascular risk factors like hypertension, hypercholesterolemia, low HDL cholesterol, hypertriglyceridemia, smoking and tobacco use are highly prevalent. There is low awareness towards treatment and control of hypertension and hypercholesterolemia in patients with diabetes.

Tripathy., *et al*. [17] reported the prevalence of diabetes and prediabetes in Punjab, North India, as part of a large household Non-Communicable Disease Risk Factor Survey, including urban and rural areas. Around 15% of the general adult population have diabetes or are prediabetes, calling for urgent attention. Poorly controlled undiagnosed cases of diabetes in the community is a significant burden. There is a need to identify the large pool of undiagnosed diabetic people and offer early treatment to avoid complications.

Oruganti., *et al*. [18] conducted a cross-sectional study among 400 adults aged between 30 and 60 years residing in the Rukmini Nagar slum area of Belagavi city, Karnataka. About 30% of the respondents were at a high risk of developing diabetes, and the prevalence of newly diagnosed cases was 10.25%.

Singh., *et al*. [19] conducted a cross-sectional survey in villages under Chittoor District, Andhra Pradesh, on individuals above 15 years. The magnitude of diabetes in the community was 9.23%, with another 14.67% to be at a higher risk of developing diabetes. Increasing age, family history, hypertension, obesity, waist circumference, and body mass index directly correlate with diabetes occurrence.

Epidemiology of diabetes prevalence in India

In India, the epidemiological transition occurred paired with the economic boom, which has changed the dietary patterns, and along with added physical inactivity and environmental factors, the risk is elevated. Urban population, no matter rich or poor, are vulnerable group having a higher risk for diabetes mellitus due to adoption of urbanized lifestyle like changed food habits, sedentary working pattern, and work-related stress [20]. Studies done in north India showed an increase in diabetic risk factors among urban slum residents. A study done in the urban slums of Chennai city showed the prevalence of diabetes to be 20.8%. Due to epidemiological and social transition, the number of people living in urban slums may increase due to unplanned urbanization and rural unemployment.

Recent epidemiologic studies in India points to a greater burden on the health sector from diabetes in the coming years. Diabetes pandemic preventive measures in India is far from ideal as nearly half of people with diabetes remain undetected, accounting for the progression of complications at diagnosis. Early screening can differentiate an asymptomatic individual at high risk to develop diabetes from one at low risk. Despite a large number of diabetic patients in India, preventive awareness is low. Therapeutic care for diabetes management should be individualized with early consideration of combination drug therapy. Regular exercise, yoga, active lifestyle, mindful eating, and stress management can be beneficial in the management of diabetes [21].

Higher risk of diabetes in Indians

Indian population has an increased tendency of insulin resistance, greater abdominal adiposity, higher waist circumference despite lower body mass index. The higher rate of impaired glucose tolerance contributes to a greater risk of developing non-communicable diseases at a relatively younger age. Despite high under-nutrition rates, Indians develop diabetes at a younger age and at lower body weights than other ethnic populations. Despite India's population's diversity, a number of common factors can be attributed to the high-risk pattern of diabetes prevalence. The possible reasons for the escalation in diabetes in Indians are i) poor glycemic control, ii) increased insulin resistance, iii) genetic factors, and iii) environmental factors.

Poor glycemic control

Glycemic control depends on the 'metabolic capacity' of the body. The determinant components of metabolic capacity are the function of the pancreas producing insulin and muscle mass influencing glucose clearance rate. Pancreatic insulin production, paired with muscle glucose clearance capability, can resolve the 'metabolic load' created by high body fat, high dietary glycemic load, and sedentary behavior. Metabolic load depends on adiposity, dietary glycemic load, and lifestyle, maintaining normal glycemic control, and presence of any chronic inflammation deleterious to beta-cell function [22]. Elevated diabetic risk among Indian populations can be correlated with high metabolic load imposed by westernized lifestyles coupled with low metabolic capacity. The low metabolic capacity of the Indian population can be attributed to the low birth weight, which is associated with short stature and low lean mass at adulthood. Underlying causes are increased population density and wide adoption of vegetarian diets related to the thin physique of Indian populations. Sedentary behavior and high glycemic diets along with the low metabolic capacity of the Indian population have elevated the susceptibility to truncal obesity. Improving metabolic capacity may require multiple generations, but efforts can be made to reduce the metabolic load [23].

Increased insulin resistance

Greater degree of insulin resistance is one of the crucial factors contributing increased Type 2 diabetes prevalence in Asian Indians compared to matched age, sex, and body mass index of Europeans [24] and Caucasians [25]. Yajnik., *et al*. [26] demonstrated that low birth weight contributes to insulin resistance among Indians. Insulin resistance clustered with a metabolic syndrome-like abdominal obesity, glucose intolerance, dyslipidemia, and hypertension is called insulin resistance syndrome (IRS). Indian population has been reported with a high prevalence of IRS, which is higher in urban than the rural population. The prevalence of IRS in the middle-income group was significantly higher than the low-income group. Age, body mass index, central obesity, cholesterol, triglycerides, physical inactivity, and higher socioeconomic status positively correlated with IRS in this study [27]. Gupta., *et al*. [28] reported overall IRS prevalence to be 12.8%. The diabetic population has a greater prevalence of obesity, central obesity, hypertension, hypertriglyceridemia and low HDL and IRS compared with normal subjects.

Genetic factors

Neel [29] correlated genetic susceptibility of diabetes with the influential 'thrifty genotype' hypothesis, which proposed that metabolic differences in population arise through differential ancestral exposure to cycles of 'feast and famine', developing differential susceptibility to diabetes in modern environments. The genetic basis of type 2 diabetes is polygenic, and over 100 genes have already been associated with diabetes. Multiple genes located on different chromosomes contribute to Type 2 diabetes susceptibility. Studies reported testing the hypothesis that population-specific risk-alleles contribute to the elevated prevalence of diabetes in South Asians, though the evidence is limited. Evidence also signifies the importance of shared risk-alleles, which may act differently among South Asians compared with other populations. The FTO (fat mass and obesity) gene is associated with obesity and diabetes risk in Europeans, Africans, and Asians [30]. FTO's effect appears to be environment-dependent, resulting in a much stronger relationship of obesity with diabetes among urban relative to rural South Asians population [31].

Ethnic variations have a possible role in the genetic susceptibility of diabetes. Genetic studies on Asian Indians indicate that several genes (e.g. TCF7L2), appear to predispose Indians to diabetes. In contrast, other genes, which protect against diabetes and insulin resistance to Caucasians, do not appear to protect Indians. Asian Indians have some unique clinical and biochemical characteristics that are collectively referred to as the 'Asian Indian phenotype' responsible for diabetes susceptibility [32].

Epigenetic influences demonstrate the effects of pre-conceptual and gestational nutrition on lifelong metabolic factors of a person. The 'thrifty phenotype' hypothesis emphasizes a link between life-course plasticity and diabetes risk, proposing that poor growth in early life can reduce glucose tolerance in adulthood [33]. Low birth and early life weight have been associated with subsequent diabetes risk [34]. Birth weight of babies in India is among the lowest globally [35]. Variability in maternal phenotype and birth weight has been associated with elevated diabetes risk in Indians [36].

Environmental factors

With the urbanization rate being 35%, India is undergoing a rapid epidemiological transition with increased urbanization. This will have significant implications on the present and future non-communicable disease patterns in the Indian population. Over the last 50 years, socioeconomic development in India has resulted in a dramatic change in lifestyle from traditional to modern practices. This has led to physical inactivity due to technological advancement, affluence leading to consumption of fat, sugar, calories diets, and a high level of mental stress. All these adversely influence insulin sensitivity and lead to obesity. Numerous environmental factors can also interact with genes to induce glucose metabolism imbalance.

Eating a 'normal' diet can make animals obese if their ancestors had been undernourished for several generations. The middle classes from developing countries like India are more susceptible than westerners to Type-2 diabetes, obesity, and cardiovascular disease in the

current changing environment due to the nutrition endured by their ancestors. Mohan [37] suggests that the prevalence of type 2 diabetes in Indians may be due to environmental and lifestyle changes accompanied with industrialization and migration from rural to urban. Since 1970, several studies compared urban and rural populations in India, showing a higher prevalence of diabetes among urban residents in southern and northern parts of India [38,39]. As there is marked variation in living conditions across the country, it is essential to assess urbanization and socioeconomic factors on the prevalence of diabetes in India. Results demonstrate that there is a marked increase in diabetes prevalence with affluence, even in urban areas. Studies have confirmed that the prevalence of diabetes in India is lower among the low-income group than among more affluent people [40].

Conclusion

Significant determinants of diabetes risk factors are age, body-mass index, waist-hip ratio, low physical activity, and family history of diabetes. The driving forces behind the worldwide epidemic rate of diabetes are urbanization, economic development, the resultant increase in GDP, sedentary lifestyle, unhealthy diet, and genetic susceptibility. Despite a relatively lower prevalence of generalized obesity, Indians tend to have a larger waist and waist to hip ratio. Indians also tend to have excess body fat, giving up a greater degree of truncal adiposity and abdominal obesity. Abdominal obesity is associated with a characteristic metabolic profile of high plasma insulin levels and insulin resistance, causing a higher prevalence of diabetes. Indians have increased body fat for any given waist circumference and for any given body fat, they have increased insulin resistance indicating the predisposition to diabetes.

Indians accumulate a higher metabolic load with the respective increase in BMI due to a relatively higher fat to lean mass ratio for any given BMI level. Low average birth weight and reduced ability to clear glucose deriving from the lower lean mass, Indians, have a reduced capacity to tolerate this load. Asian Indians develop Type 2 diabetes at lower BMI levels, one to two decades earlier, and have more substantial heritability factors susceptibility compared with Europeans. Diabetes onset in Indians at a younger age than in Europeans also indicates reduced metabolic resilience.

The challenge is how to escape this vicious cycle of metabolic dysregulation. While in theory, higher nutritional intake by the mother during pregnancy may protect the offspring against diabetes, but in practice, this may overload maternal glycemic control and cause gestational diabetes. So as a preventive measure, public health policies must constrain the exacerbation of the general population's metabolic load from early childhood. Efforts should prioritize for the prevention of excess weight gain and the development of abdominal obesity. Encouraging an active lifestyle and shifting toward nutritious diets with low glycemic index and fat content will help. The particular challenge is how to achieve reductions in metabolic load and the promotion of metabolic capacity enhancement in the coming generations. The persisting problem of child malnutrition in India should be addressed through the provision of public health promotion policy.

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