

Possible mystery behind higher susceptibility of type 2 diabetes in Asian Indians: is it diet, genetics or something else

Abstract

Prevalence of type 2 diabetes and its life threatening complications i.e. cardiovascular diseases (CVDs) and hypertension, is increasing rapidly around the globe. India has largest diabetic population of diabetics in the world, and rapid growth is expected in coming years. Plethora of literature suggest that dietary, factors, physical activity, genetics, pollution/ environment and epigenetic play an important role in development of type 2 diabetes. But it's not known how this progression might have happened in Indian population to make them high susceptible for diabetes. Being from Indian background, here we want to point-out some possible and very normal practices in typical Indian people that might have made Asian Indian more vulnerable for diabetes. We are also discussing how these general practices might have changes genetic program in next generations. We will also give a brief insight for future research to ameliorate diabetes rate in Indian population.

Keywords: diabetes, insulin resistance, obesity, India, diet, genetics, epigenetic, pollution, environment, micro biome

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Background

Type 2 diabetes (T2D) and obesity is on high rise from last few decades around the globe. There are 170 billion people suffering from T2D, worldwide and this number is growing so fast and estimated to reach 355 billion by 2030.¹ India has largest population suffering from diabetes, and this population is on higher risk for development of cardiovascular diseases (CVDs).² The reason behind this high vulnerability of diabetes in Indian population is completely obscure.

Various factors i.e. genetics, diet and environment play a crucial role in development of diabetes or insulin resistance (Figure 1). In this report we will mention how genetics, diet, pollutants, gut flora and epigenetic might have played a role in increasing risk for diabetes in Indian population. In addition, we will also bring up some of the important research areas and major points to be explored to better understand the possible cause behind increased diabetes rate, hence proper strategies can be developed to ameliorate diabetes in Asian Indian population.

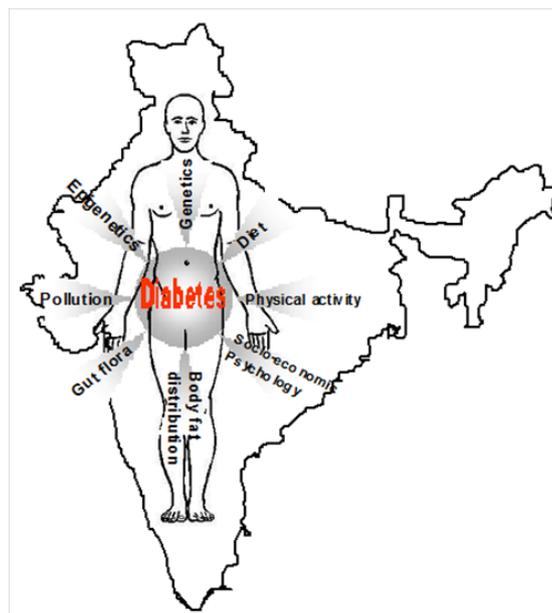


Figure 1 Factors associated with higher prevalence of diabetes in Asian Indian population.

Genetics

Genetics is an important factor that employs the significant role in pathology of metabolic diseases.³ In recent years we have learned a lot about involvement of genes in pathology of diabetes through genome wide association (GWAS) and other genetic studies.⁴⁻⁶ Although these GWAS studies have suggested various culprit genes involved in risk of diabetes, but their pure effects have been very mild.^{7,8} Technology has driven us to explore interaction of genetic factors with risk of diabetes, but better understanding its etiology and broader effects on pathophysiology of diabetes is obscure. Moreover ethnic variations in genetics have significant impact on diabetes risk therefore exploring genetic markers in Indian population associated with higher risk for diabetes might be of great interest in future genetic studies. Furthermore, adopting new genetic techniques i.e. next generation sequencing can give better information on rare genetic variants, and how they participate in diabetes pathology.

Diet and diabetes in Indians

Dietary habits and composition is a crucial player in pathophysiology of T2D.⁹ Indian diet has been enriched with oil fried foods and pure carbohydrates. It is well known that high energy nutrients i.e. fatty acids and sugars (fructose, glucose etc) directly interact with genomic expression networks (nutri genomics) and induces abnormal metabolic states i.e. diabetes and obesity.¹⁰ Therefore lining out detrimental food components or their appropriate amount will ameliorate the prevalence of diabetes in Indian population. The food regulatory agencies have to develop standards and recommendations for the type of diet and appropriate amount to eat by a health individual. Also research should be directed to find out the composition of diets that majority of Asian Indians are consuming and intervene the dietary components which are detrimental for normal metabolic functions. By this approach, diabetes progression can be ameliorated by decreasing consumption of such foods that are enriched with this kind of nutrients should be avoided in daily routine.

Physical activity

Decreased physical activity and increased energy intake lead to dramatic rise of obesity and insulin resistance.^{11,12} Due to modern technology era, the physical activity has been dramatically reduced without changing much in the food intake that results to create huge imbalance in energy intake versus expenditure (energy balance). Another factor in reducing physical activity is the cheap labor in India, which reflects by the higher occurrence of diabetes in high income group people. Socio-economic and psychological factors also play an important role in pathophysiology of diabetes and obesity.¹³ India is a growing country and majority of its population moving from rural areas to urban regions that results dramatic decrease in physical activity without changes in food habits, even increased consumption of energy dense foods and food frequency. Therefore, some health education programs need to be urgently initiated that can spread awareness about these detrimental factors of human life style and can be used to ameliorate risk of diabetes in next generation.

Body fat distribution

Adipose (fat) tissue is an important endocrine organ, which secretes various adipokines i.e. leptin, adiponectin, resistin and others that regulates whole body energy homeostasis, through regulation of food intake and energy expenditure.¹⁴ In mammal two type of adipose tissue exist i.e. white adipose tissue (WAT) and brown adipose tissue (BAT). WAT primarily participates in fat storage in the

form of triglyceride whilst BAT burns the fat to produce heat that is utilized for maintenance of body temperature.¹⁵ The location of these adipose tissues is different and sometime they found in the mixed forms. Increased WAT content is associated with increased insulin resistance, in contrast increased BAT content or activity decreases the risk of insulin sensitivity. Therefore, distribution and types of fat tissues in different regions of human body is important that makes dramatic difference in metabolic status of an individual. Abdominal adiposity has been a major factor associated with diabetes in Indian population¹³ and abdominal fat has been considered classical WAT that is less enriched with brown like cells. This might be the one reason for increased insulin resistance in adipose tissues of Indian people. This opens new avenues to investigate the types of adipose tissues and their distribution in India population. Also, fat accumulation in other metabolic organs i.e. muscles, liver and pancreas induces insulin resistance.¹⁶ Investigating the differential distribution of fat in different tissues of Indian subjects might give the important information about its association with higher risk of diabetes.

Gut micro biome

Association of gut-micro flora has been established with diabetes and obesity.^{17,18} Lean and insulin sensitive individuals have different gut flora than obese and insulin resistance people.¹⁷ The composition of gut flora in Indian population and its association with diabetes risk is highly obscure. Exploring the differences in gut flora and its association with diabetes susceptibility in Indian population will open the new line of studies for developing the successful strategies to modulate the gut flora in beneficial manner to ameliorate risk of diabetes and obesity. Bringing few recent studies in light which are suggesting that gut microbiome modulated via antibiotics in early life can increase insulin resistance and obesity later in life. Antibiotics use is highly unregulated in India, and early exposure of antibiotics in kids might be posing increasing threat for diabetes and obesity prevalence. Childhood as well as adult infections are also common in Indian peninsula, and few infections like viral, bacterial and fungal infections and certain acute infections are causing lifelong alterations in immune response i.e. low grade inflammation and gut microbiome.^{19,20} Abdominal or mesenteric fat is most abundantly increased fat types in Asian Indian population, and alternations in gut microbiome via either antibiotics or infections might changes mesenteric tissue metabolic functions in lifelong manner. Further in depth studies on role of infections in lifelong metabolic function and incidence of obesity and diabetes would be highly important to address these issues and bring them in practice to ameliorate the prevalence of these health ailments.²¹⁻²³

Pollution

Various pollutants have been described as endo-disruptants and also known to be associated with higher risk of diabetes and obesity in several studies.²⁴⁻²⁶ India being a developing country has very mild rules and regulations for pollution control thereby chances of dramatic increase exposure for people with pollutants might have pushed biological system to increase diabetes risk. Hence, investigating the potential pollutants that participate in diabetes and obesity risk in Indian population should be urgently studied and should be avoided for normal use. Also the impact of pollution on embryonic development has been significantly correlated with diabetes risk hence research and policy should be developed and encouraged to implement that can ameliorate the progression of these health ailments in developing countries like India.

Epigenetic

Increased risk of diabetes in Indian population can be explained by 'epigenetic theory'. Due to unregulated higher consumption of sugar and fat by pregnant women may have created the epigenetic changes in during embryo development in child that might result increased susceptibility for diabetes in next generation. Furthermore, Indian population being more insulin resistant, pregnant women have higher occurrence of gestational diabetes, that might imprint the epigenetic changes in developing embryo and results further higher susceptibility for next generation to these health ailments. In addition, unregulated pollution might also be creating various epigenetic changes in mother and embryo to increase susceptibility for diabetes in coming progeny, therefore, studies should be initiated to find-out the proper food and environment for pregnant mothers to avoid the circumstances of these epigenetic changes and also studies how these epigenetic changes can be reversed, so diabetes risk can be reversed.

Due to complex pathophysiology of diabetes and involvement of various factors i.e. genetics, diet, life style, environment, gut micro biome and epigenetic. We think initial studies controlling individual factors and establishing their strong effects on diabetes risk in Indian population should be carried out. After recognizing the potential factors and controlling those factors on single platform/protocol, next label studies can give new targets and avenues to develop strategies to ameliorate the risk of diabetes and prevent the population from these life threatening health ailments.

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Criteria for inclusion in the authors/ contributors list

HY and SJ both equally contributed to draft proofread and discuss this article.

Conflict of interest

Author declares that there is no conflict of interest.

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