



Introduction to Diabetes and Prevalence in India

6

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Diabetes is a chronic progressive disease associated with different co-morbidities. The availability of insulin or effective use of insulin in the body is the major cause of this disease. Enhanced blood sugar or hyperglycemia is the manifestation of this disease. If not treated timely, diabetes can damage cardiac system, blood vessels, vision, renal function and nerves leading to increased risk of cardiac disease, stroke and may cause neuronal, retinal, and kidney disease. The overall risk of morbidity and mortality among diabetes affected people is more than double compared to non-diabetic people (WHO n.d.).

Mainly two types of diabetes exist. Type 1 diabetes is associated with deficient insulin production. It is diagnosed in the early childhood and symptoms include frequent urination, enhanced thirst, hunger, weight loss, vision changes, and fatigue. Treatment of type 1 diabetes is the daily administration of insulin.

Among diabetic population, ~90% of people are comprised of type 2 diabetes. Type 2 diabetes occurs mainly due to obesity, enhanced plasma lipid (dyslipidemia), stress, and sedentary life style (lack of enough physical activity). Symptoms are initially not that severe like type 1 diabetes but increase slowly but progressively. Generally the disease is diagnosed in the late and in the advanced stage. So, type 2 diabetes is known as a silent killer disease.

Insulin resistance occurs when body cannot use insulin effectively resulting enhanced insulin secretion from the pancreatic β -cells causing hyperinsulinemia. Overtime, enhanced insulin resistance leads to impaired fasting glucose (IFG) and impaired glucose tolerance (IGT). This is known as prediabetic stage. IFG condition is diagnosed when fasting plasma glucose level ranges from 6.1 to 6.9 mmol/L (110–

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125 mg/dL) and 2 h plasma glucose is measured as >7.8 mmol/L (140 mg/dl) where as in the case of IGT, the fasting plasma glucose level is measured as <7.0 mmol/L (126 mg/dL) and 2 h plasma glucose ranges from 7.8 mmol/L (140 mg/dL) to 11.1 mmol/L (200 mg/dL). If untreated, insulin resistance increases drastically and rapid progressive degeneration of pancreatic β -cells leads to the decreased secretion of insulin resulting the transformation of prediabetic stage into full blown diabetic condition. Diabetic condition is detected when measured plasma glucose level in fasting condition is ≥ 7.0 mmol/L (126 mg/dL) or 2 h plasma glucose level is 11.1 mmol/dL (200 mg/dL). Ultimately, in the last stage of type 2 diabetes, the level of secreted insulin is measured below the normal level. During this stage, the patients are administered daily with exogenous insulin (Fig. 6.1).

Epidemiological and scientific data are now emerging which suggest that there may exist differences in the genesis of diabetes in Indians relative to the western population. Multiple risk factors such as genetic susceptibility, thin-fat phenotype, low birth weight, fetal programming, urbanization, sedentary life style, socioeconomic transition, smoking, and alcohol contribute to the origin of Indian insulin resistance syndrome. Indians are thinner with less muscle mass but are centrally obese with higher plasma free fatty acids, triglycerides, and insulin, characteristic of insulin resistance. Obesity and being overweight are relatively lower in Indian population than Western population but at a given Body Mass Index (BMI), Indians have a higher body fat composition (thin-fat phenotype) compared to other populations (Radha and Mohan 2007; Anjana et al. 2014).

A new susceptibility locus at 2q21 was identified in Indians in a genome-wide association study for type 2 diabetes (Tabassum et al. 2013). Study also identified that the common variants of IL6, LEPR, and PBEF1 are associated with obesity in Indian children (Tabassum et al. 2012). Several genetic variants have been detected in genome-wide association studies of single-nucleotide polymorphism (SNPs), which may be associated with β -cell dysfunction and insulin resistance (Khardori et al. n.d.). About 40 independent loci have been identified and found to be associated with increased type 2 diabetes (Wheeler and Barroso 2011). A subset of them are: TCF7L2, MTNR1B, FSADS1, PPAR γ , KCNJ11 (Nielsen et al. 2003); FTO and IGF2BP2 (Ukkola et al. 2001); HHEX, SLC30A8 (Sladek et al. 2007), and WFS1 (Sandhu et al. 2007). Genetic variants in incretin hormone—gastric inhibitory polypeptide (GIPR) might also affect type 2 diabetes (Saxena et al. 2010) and has been found to be associated with reduced β -cell function. A clear association of genetic defects with some form of diabetes have been proposed. Maturity Onset Diabetes of Youth (MODY) syndrome has been deserved to be associated with β -cell dysfunction for 2–5% of type 2 diabetes. Eleven MODY subtypes have been identified to date (Winckler et al. 2007).

In 2015, worldwide prevalence of diabetes was ~422 million (8.5% of adults aged 20–79) (WHO 2016) and it is projected to reach ~642 million in 2040, which is equivalent to one in every ten adults (International Diabetes Federation 2015; Kaveeshwar and Cornwall 2014). The prevalence of diabetes in India was ~33 million in 2005, ~69 million in 2015 and predicted to reach ~98 million in 2030 (Tripathy et al. 2017; Ramachandran 2005). About 7.8% of Indians above

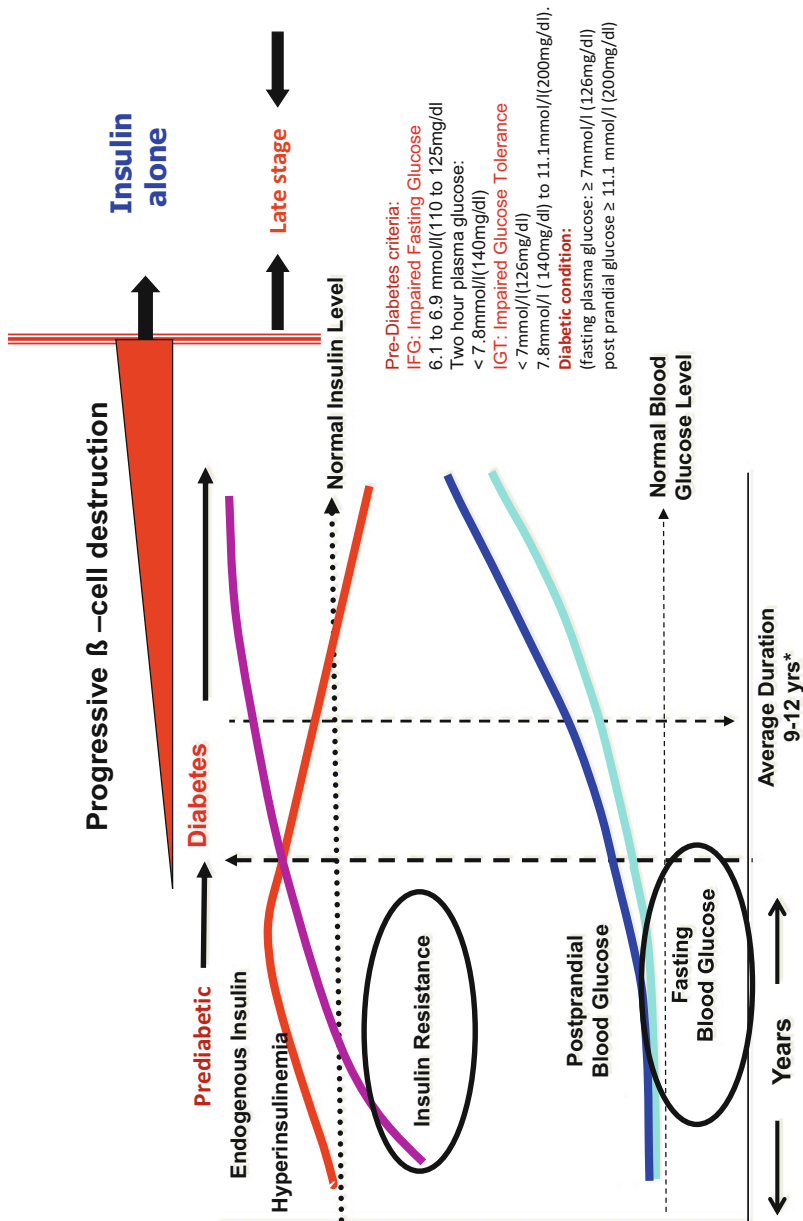


Fig. 6.1 Progressive nature of type 2 diabetes mellitus

18 years has been found to have high blood glucose levels or are being treated for diabetes (WHO 2014). Approximately 36.5 million impaired glucose tolerant adults were reported in India in 2015 and India ranks highest in the list of top ten countries having impaired glucose tolerance (International Diabetes Federation 2015). Prevalence of impaired blood glucose in India is greater than the impaired glucose tolerance (Anjana et al. 2011). A study was conducted by Indian Council of Medical Research-India (ICMR-INDIAB) on >20-year-old adults covering 15 different states of India. It reveals that frequency of diabetes is different among states in India. It varies from 4.3% in Bihar to 13.6% in Chandigarh (Anjana et al. 2017). In 2012, National Nutrition Monitoring Bureau carried out the third repeat survey involving adult men and women of India in different states. Their report showed that in Indian adult men and women, prevalence of diabetes is 8.2% and 6.8%, respectively. States of Kerala, Tamil Nadu, and Gujarat showed higher prevalence (8.2–16.4%) among male and females (ICMR 2012).

References

- Anjana RM et al (2011) Prevalence of diabetes and prediabetes (impaired fasting glucose and/or impaired glucose tolerance) in urban and rural India: phase I results of the Indian Council of Medical Research-India DIABetes (ICMR-INDIAB) study. *Diabetologia* 54:3022
- Anjana RM et al (2014) Physical activity and inactivity patterns in India – results from the ICMR-INDIAB study (Phase-1) [ICMR-INDIAB-5]. *Int J Behav Nutr Phys Act* 11:26
- Anjana RM et al (2017) Prevalence of diabetes and prediabetes in 15 states of India: results from the ICMR-INDIAB population-based cross-sectional study. *Lancet Diabetes Endocrinol* 5 (8):585–596. [https://doi.org/10.1016/S2213-8587\(17\)30174-2](https://doi.org/10.1016/S2213-8587(17)30174-2). Erratum in: *Lancet Diabetes Endocrinol*. 2017;5(8): e5
- ICMR (2012) Diet and nutritional status of rural population, prevalence of hypertension and diabetes among adults and infant and young child feeding practices – report of third repeat survey. National Institute of Nutrition, ICMR, Hyderabad
- International Diabetes Federation (2015) IDF diabetes atlas, 7th edn. International Diabetes Federation, Brussels
- Kaveeshwar SA, Cornwall J (2014) The current state of diabetes mellitus in India. *Australas Med J* 7:45–48
- Khadori R et al (n.d.) Type 2 diabetes mellitus. <https://emedicine.medscape.com/>. Accessed 4 Mar 2019
- Nielsen EM et al (2003) The E23K variant of Kir6.2 associates with impaired post-OGTT serum insulin response and increased risk of type 2 diabetes. *Diabetes* 52(2):573–577
- Radha V, Mohan V (2007) Genetic predisposition to type 2 diabetes among Asian Indians. *Indian J Med Res* 125(3):259–274
- Ramachandran A (2005) Epidemiology of diabetes in India--three decades of research. *J Assoc Physicians India* 53:34–38
- Sandhu MS et al (2007) Common variants in WFS1 confer risk of type 2 diabetes. *Nat Genet* 39 (8):951–953
- Saxena R et al (2010) Genetic variation in GIPR influences the glucose and insulin responses to an oral glucose challenge. *Nat Genet* 42(2):142–148
- Sladek R et al (2007) A genome-wide association study identifies novel risk loci for type 2 diabetes. *Nature* 445(7130):881–885
- Tabassum R et al (2012) Common variants of IL6, LEPR, and PBEF1 are associated with obesity in Indian children. *Diabetes* 61:626–631

- Tabassum R et al (2013) Genome-wide association study for type 2 diabetes in Indians identifies a new susceptibility locus at 2q21. *Diabetes* 62:977–986
- Tripathy JP et al (2017) Prevalence and risk factors of diabetes in a large community-based study in North India: results from a STEPS survey in Punjab, India. *Diabetol Metab Syndr* 9:8. <https://doi.org/10.1186/s13098-017-0207-3>
- Ukkola O et al (2001) Insulin like growth factor 2 and IGF-binding protein 1 (IGFBP1) gene variants are associated with overfeeding-induced metabolic changes. *Diabetologia* 44 (12):2231–2236
- Wheeler E, Barroso I (2011) Genome-wide association studies and type 2 diabetes. *Brief Funct Genomics* 10(2):52–60
- WHO (2014) Global status report on non-communicable diseases 2014. World Health Organization, Geneva
- WHO (2016) Global report on diabetes. WHO, Geneva
- WHO (n.d.). <http://www.who.int/mediacentre/factsheets/fs312/en/>. Accessed 24 Mar 2016
- Winckler W et al (2007) Evaluation of common variants in the six known maturity-onset diabetes of the young (MODY) genes for association with type 2 diabetes. *Diabetes* 56(3):685–693



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