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Commentary

Young-onset diabetes: An Indian perspective

Diabetes in young has been classically defined as onset of diabetes <35 yr of age[1]. Sahoo *et al*[2] in this issue through a protocol-based evaluation [assessment of β-cell reserve, diabetes autoantibodies, genetic testing for maturity-onset diabetes of young (MODY) if fitting clinical criteria, genetic testing for mitochondrial diabetes] and close follow up of patients with diabetes in young, over a period of two years, determined that the most common aetiologies for diabetes mellitus (DM) in young were type 2 diabetes mellitus (T2DM, 40%), type 1 DM (T1DM, 40%), fibrocalculous pancreatic diabetes (FCPD, 15%), MODY (2%), flatbush diabetes (2%) and mitochondrial diabetes (1%).

An exponential increase in T2DM prevalence in India in the last 30 years has played a major role in contributing to the increased burden of diabetes in young in this part of the world[3]. The prevalence of T2DM in India is 8-10 per cent with an additional 15 per cent having pre-diabetes[3]. T2DM in Indian patients is characterized by lower body mass index (BMI), increased body fat, increased clinical and biochemical measures of insulin resistance and systemic inflammation, coupled with one of the highest global rates of pre-diabetes progression to T2DM (14-18, 6 and 2.5% p.a. in India, Finland and USA, respectively), highlighting a more aggressive diabetes phenotype in Indians[3-5]. T2DM onset in Indians is nearly two decades earlier than in the west[3,4]. This also explains the high prevalence of T2DM in young as has been documented by Sahoo *et al*[2].

Tropical calcific pancreatitis, better known as FCPD, is predominantly limited to tropics characterized by pancreatic intra-ductal calcifications, ketosis-resistant lean diabetes, progressive and irreversible destruction of pancreatic parenchyma, good initial response to oral diabetes medications and high-risk of carcinoma pancreas in the long run[6,7]. Aetiopathogenesis is multifactorial with malnutrition, cassava intake, micronutrient deficiencies and serine protease inhibitor Kazal type 1 gene variations[6-9]. FCPD contributes significantly to the burden of diabetes in young in this part of the world as has been highlighted by Sahoo *et al*[2]. This is a novel message as conventionally FCPD has been considered to occur after 30-35 yr of age. Further studies with regard to the burden of FCPD in young are needed from other parts of India, especially West Bengal, Kerala and Tamil Nadu.

MODY is not uncommonly missed in young Indians with diabetes, especially in those with strong family history. These patients are often misdiagnosed as T1DM and treated with insulin. More frequent use of genetic studies would increase the diagnosis of MODY. Number of MODYs (attributed to specific genes) has increased significantly in recent years from six to more than 13 different specific genes[10,11]. However, it is likely that MODY would not be as common in India as seen in certain ethnic groups like the Scandinavians[10]. In the study by Sahoo *et al*[2], two per cent occurrence of MODY may be an under representation. Limiting the genetic testing for MODY to only those with classical clinical history and pedigree analysis suggestive of MODY, may explain the lesser diagnosis of MODY in the current study. It is now well known that many patients with MODY may present *de novo* with the absence of strong family history of diabetes[11,12].

Another form of diabetes, which is unique to South Asia, is the flatbush diabetes[13]. These patients present with very high blood glucose values, varying degree of ketosis, have one of more features of insulin resistance, initially respond poorly to oral antidiabetes medications, and are well managed with insulin in the acute setting. Once glycaemic control is achieved in a few weeks, insulin can be commonly stopped in these patients and they do well with oral antidiabetes medications for long periods of time similar to T2DM.

At present, it would be safe to say that the two most common forms of diabetes in young are T1DM and T2DM, each having an almost similar prevalence of 40-45 per cent; FCPD and flatbush diabetes contributing to 5-15 per cent of all diabetes and up to 10 per cent being contributed by MODY and other genetic forms of diabetes. The increasing prevalence of childhood obesity is also contributing to the burden of T2DM in young. This is in contrast to nearly three decades back when the predominant form of diabetes in young was T1DM. However, it must also be kept in mind that in the actual population, the proportion of people with T2DM in 'diabetes with young cohort' is likely to be higher, as the above prevalence rates have been obtained from hospital-based studies, where only people with more severe disease reach hence are subject to referral bias.

Till routine and affordable genetic testings are available in India, a more judicious use of clinical phenotype, such as restricting measurement of diabetes autoantibodies [glutamic acid decarboxylase (GAD) antibody, IA2 antibody, ZnT8 antibodies] and C-peptide (fasting/one hour post-mixed meal) to non-obese patients with diabetes without a family history of diabetes or features of the metabolic syndrome (central obesity, increased dorsal pad of fat, skin tags, acanthosis, fatty liver, polycystic ovary syndrome, high triglycerides and low high-density lipoprotein cholesterol) would be more pragmatic and cost-effective in deciding the medications best suited for establishing the type of diabetes and diabetes management (oral antidiabetes agents vs. early insulin therapy). Many times, a judicious follow up over 1-2 years also helps in establishing the type of diabetes in a patient.

***Conflicts of Interest*:** None.

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