

## Type 2 Diabetes Mellitus in the Young: A Paradigm Shift

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Type 2 diabetes Mellitus (T2DM) has changed from a disease of the old to a disease of the young and, to be more precise, from a disease of the parents to a disease of children. It has the potential to become a global public health issue with serious widespread health outcomes. As more and more children and young adults develop this devastating disease, it has become apparent that we have to learn much about who in the younger population is at risk to develop type 2 diabetes, how to manage, and, most importantly, how to prevent it from destroying future generations.

Type 2 diabetes mellitus (T2DM) is a chronic and progressive metabolic disorder characterized by insulin resistance, beta cell dysfunction and incretin hormonal dysregulation and is escalating to an epidemic proportion. It is estimated that 422 million adults had diabetes in 2014 and the prevalence has doubled since 1980 from 4.1 % to 8.6 % [1]. It is estimated that by 2030, around 552 million of the population would have developed type 2 diabetes mellitus and Asian subcontinent will contribute to 60% of this burden. Although type 1 diabetes is more common in children but type 2 diabetes is getting even more common in the young, a real challenge of the future. Traditionally, type 2 diabetes mellitus was considered to affect mainly the elderly aged more than forty years; however, the recent study has shown that the type 2 diabetes is being diagnosed increasingly in younger population as well because of rising trend in obesity and overweight in children and adolescents [2].

In the SEARCH study, the incidence of type 2 diabetes among children and adolescents varies greatly by ethnicity, with the highest rates observed among youths aged 15 - 19 years in minority populations. The reported incidence rate was 49.4 for Native Americans, 22.7 for Asian/Pacific Islanders, 19.4 for African Americans, 17 for Hispanics, and 5.6 for non-Hispanic whites [3]. In this study prevalence rate found to be lowest for Europe. Although the lowest prevalence of type 2 diabetes in Europe could be attributed to the differences in obesity rates between U.S. and European youth, the full explanation for these discrepancies remains unclear [4]. It is also notable that the incidence of T2DM in Japanese children from 1980 to 1990 had increased significantly to the extent that it has surpassed the number of type 1 diabetes mellitus [5]. In another study in Japan, more than 80 % of all new cases of diabetes in children and adolescents were diagnosed as type 2 diabetes mellitus [6]. In New York, from 1990 to 2000, the number of patients with early-onset type 2 diabetes mellitus increased nine times in African-American and Caribbean-Hispanic adolescents [7]. While in United Kingdom, from 2003 to 2006, incidence of type 2 diabetes mellitus increased from 5% to 12 % in individuals less than 30 years and 24 % in patients less than 40 years of age [8,9]. A clinic-based study from Jamaica found that 22 % of individuals diagnosed with diabetes prior to the age of 25 years had features consistent with T2DM [10]. In the Indian Council of Medical Research (ICMR) Registry of Diabetes in the Young in India, 25.3 % of individuals developing diabetes under the age of 25 years had a diagnosis of T2DM [11]. In another Indian study, it is found that type 2 diabetes in youth overlaps with monogenic forms of diabetes such as maturity-onset diabetes of the young, fibrocalculous pancreatic diabetes, and malnutrition-modulated diabetes, all of which are ketosis-resistant forms of youth-onset diabetes [12].

It has been postulated that the occurrence of type 2 diabetes in young is associated with complex interaction between genetic and environmental factors and people with obesity, sedentary lifestyle, family history of diabetes mellitus, and poor socioeconomic status

are the major reasons for the increase in early-onset T2DM [13,14]. Amongst all the factors mentioned, over weight and obesity are the most closely linked with the rising trend of early onset type 2 diabetes in younger population of the world, and play a central role in type 2 diabetes epidemic in adults across the globe [15]. The prevalence of obesity has rapidly increased in the last century and now ranks as one of the major causes of morbidity and mortality in the industrialized world [16,17].

The incidence of obesity has also significantly increased by 70% in the younger population ages from 18 - 29 years, indicating that the younger population has the quickest increase in the incidence of obesity and T2DM [18]. Based on Centers for Disease Control (CDC) criteria, obesity has risen among children to its current prevalence of ~17% (this is slightly higher than WHO criteria), and disproportionately affects ethnic minorities [19].

After matching for age, the young patients with type 2 diabetes mellitus develop a higher incidence of microvascular complications compared to the patients with type 1 diabetes mellitus and cardiovascular disease is a major contributor to morbidity and mortality and the leading cause of death among people with T2DM [20,21]. Hillier and Pedula confirmed that patients with early-onset T2DM present a higher risk of cardiovascular disease compared with patients with normal-onset T2DM [22].

Although numerous studies have been published that are related to the management of diabetes and its comorbidities in adults but only few studies are available to look into the management and complications of T2DM in the young. The Treatment Options for type 2 Diabetes in Adolescents and Youth (TODAY) study was designed to evaluate the efficacy of various treatments and provided a unique opportunity to study the disease progression and appearance of complications in a pediatric cohort with recent onset of the disease [23].

The study included 699 participants of ages from 10 to 17 years diagnosed with T2DM using the prevailing ADA criteria with illness duration of 2 years or less at the time of enrollment. In the TODAY study, hypertension was present in 11.6% of the population at baseline and increased to 33.8% by the end of the study. Prevalence of high-risk LDL-cholesterol rose from 4.5% at baseline to 10.7% at the end of the study. Microalbuminuria was found in 6.3% of the cohort at baseline and increased to 16.6%. Retinopathy was not assessed upon entry into TODAY, but was present in 13.9% of the TODAY cohort at the end of the study. Experience to date indicates that these complications and comorbidities are similar to that seen in adults, but occur on an accelerated timeline. So, it can be concluded that patients with early onset type 2 DM have a greater risk of developing microvascular and macrovascular complications, often at an earlier stage and with greater frequency than seen in type 1 diabetes mellitus. For this reason, obesity and T2DM in younger population have become major public health problems and if these metabolic disorders cannot be reversed, our society will face major challenges. That is, the burden of diabetes mellitus and its complications will affect many more individuals than currently anticipated, and the cost of diabetes mellitus to our society will cause us to consume enormous resources. Screening of high-risk groups may help in the early detection and prevention of complications of T2DM in young. Patients with early onset of type 2 diabetes mellitus merit an aggressive and supportive management in a multidisciplinary setting to prevent the development of significant morbidity and mortality during their most productive years.

Taking a life-course perspective is essential for type 2 diabetes prevention. Early in life, when eating and physical activity habits are formed and when the long-term regulation of energy balance may be programmed, there is a critical window for intervention to mitigate the risk of obesity and type 2 DM later in life [24,25].

Based on the above facts, primary prevention towards obesity should be given utmost priority and would require a comprehensive approach involving the schools, government and non-governmental agencies with a focus on healthier lifestyles. Schools have to focus on increasing children's physical activity and improving their nutrition and must have physical education curriculums designed to help optimize the health of children and should re-institute vigorous physical education programs for all children and in all grades. Nutrition counseling needs to be available so that children understand the importance of healthy eating. Furthermore, as an individual, all of us should play a role to put an end to the rise of this devastating disease in the young community.

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