Journal of Diabetes and Its Complications 30 (2016) 951–957

Contents lists available at ScienceDirect

Journal of Diabetes and Its Complications

journal homepage: WWW.JDCJOURNAL.COM

Diabetes complications in childhood and adolescent onset type 2 diabetes—a review

Anandakumar Amutha, Viswanathan Mohan *

Madras Diabetes Research Foundation & Dr. Mohan's Diabetes Specialities Centre, WHO Collaborating Centre for Non-communicable Diseases Prevention and Control, Gopalapuram, Chennai, India

ARTICLE INFO

Article history:
Received 15 October 2015
Received in revised form 9 January 2016
Accepted 7 February 2016
Available online 9 February 2016

Keywords:
T2DM
Complications
Children
Adolescents
Retinopathy
Nephropathy

ABSTRACT

Diabetes mellitus is one of the most common endocrine disorders in children. Earlier, diabetes in children was almost exclusively type 1 diabetes. Recently, the scenario has changed and increasing numbers of children and adolescent T2DM are being diagnosed. As the epidemic of T2DM shifts to children and adolescents, there is an increased risk of development of micro and macrovascular complications. This could potentially affect the economy of the nation apart from posing a large burden to the individual and his or her family. Prevention and treatment are especially important, given the fact that onset at an early age increases the risk of developing micro and macrovascular complications due to increased duration of exposure to hyperglycemia and other metabolic abnormalities. Diagnosing children and adolescents with T2DM early and instituting good control of all risk factors could yield good results in the prevention of long term complications of diabetes. This review focuses on the prevalence of complications of diabetes among children and adolescents with T2DM.

1. Introduction

Globally there is a rapid increase in the prevalence of adult type 2 diabetes (T2DM). Unfortunately there is also a parallel increase of T2DM among children and adolescents (Urakami et al., 2007). The main driver of this epidemic is the increasing rates of obesity among children, consequent to sedentary lifestyle, and this increase largely rises in those with a parental history of T2DM (Kitagawa, Owada, Urakami, & Yamauchi, 1998; Likitmaskul et al., 2003; Mohan, Jaydip, & Deepa, 2007; Ramachandran, Snehalatha, Satyavani, Sivasankari, & Vijay, 2003; Urakami et al., 2005). The shift in age at diagnosis of T2DM in children and adolescents has serious implications, as it not only affects the health of the youth, but it also has the potential to pose a huge socio economic burden on the society at large as they grow into adults. Developing T2DM during childhood or adolescence places them at markedly increased risk for developing diabetes complications and mortality in early adulthood. An extensive list of studies was summarized in the long term outcomes in youth with diabetes especially in type 1 diabetes (White, 2015), whereas only limited follow up studies are available with respect to complications in children and adolescents with T2DM. The purpose of the article was to review studies on the micro and macrovascular complications in childhood and adolescent onset T2DM.

2. Methods

Due to limited published articles related to our topic, we did an extensive literature search on studies done in children and adolescents with T2DM. The types of studies were not restricted owing to the rarity of the topic. Mostly they were all clinic based cohort studies on diabetes complications like diabetic retinopathy, diabetic nephropathy, diabetic neuropathy etc., especially on children and adolescents with age onset of T2DM at or below 19 years. The online search engines used were Google scholar, PubMed (MEDLINE), EBSCO, Ovid, Science direct, Web of science, Proquest and IDF Diabetes Atlas for articles in English using subject headings and key words like “childhood onset T2DM”, “children with T2DM and complications”, “adolescent onset T2DM with complications”, “youth onset T2DM with complications”, “young onset T2DM”,“microvascular complications”, “diabetic retinopathy”, “diabetic nephropathy” and “diabetic neuropathy” which were published in the previous years.

The inclusion criteria used were as follows:

1. Studies on children and adolescents with onset of T2DM at or below 20 years.

Conflict-of-interest: A. Amutha and V. Mohan declare that they have no conflict of interest

* Corresponding author at: Madras Diabetes Research Foundation & Dr. Mohan's Diabetes Specialities Centre, WHO Collaborating Centre for Non-communicable Diseases Prevention and Control, 4, Conran Smith Road, Gopalapuram, Chennai, 600086, India. Tel.: +91 44 4396 8888; fax: +91 44 2835 0935.

URL's: drmohans@diabetes.ind.in, http://www.drmohansdiabetes.com, http://www.mdrf.in (V. Mohan).

http://dx.doi.org/10.1016/j.jdiacomp.2016.02.009
1056-8727/

2. If any one of the diabetes complications like diabetic retinopathy, diabetic nephropathy (micro or macroalbuminuria) and diabetic neuropathy was assessed, those studies were included.
3. Only articles published in English language were included.

3. Microvascular complications

3.1. Diabetic retinopathy (DR)

DR is the most common microvascular complication of diabetes posing a serious threat to vision in T2DM. DR is the affection of the small vessels on the retina due to prolonged uncontrolled hyperglycemia leading to appearance of microanuerysms and/or hemorrhages and/or exudates and/or abnormal vessels on the retina. This condition may occur with or without other systematic complications of diabetes, and its prevalence increases with the duration of diabetes. Even though the severity of hyperglycemia may be greater in T1DM, among adolescents with T2DM as the disorder may be for several years the risk for retinopathy may be higher and indeed DR may even be present at two of diagnoses of T2DM. Hence there is a need for screening for retinopathy even at the time of diagnosis of adolescents with T2DM (Eppens et al., 2006).

Prevalence rates of DR among T1DM and T2DM vary widely in different studies due to various reasons including case mix. In a clinic based study from Australia, DR was significantly more frequent in individuals with T1DM than in those with T2DM (20 vs. 4%, $p = 0.04$) (Eppens et al., 2006). Similarly Scott et al. (2006) also reported that 10 vs. 4% of those with T1DM and T2DM respectively had background retinopathy. In both these studies, the duration of diabetes among T2DM was shorter than in T1DM. The SEARCH study (Mayer-Davis et al., 2012) reported a prevalence of 42% with DR among those who had more than 5 years duration of diabetes and with a mean age of 21 years. The TODAY study (TODAY Study Group, 2013b), reported the prevalence of DR to be 13.7% with a mean duration of 4.9 years but none of them had macular edema, or proliferative diabetic retinopathy. These prevalence rates are higher than previously reported among Pima Indians, in whom DR was detected only after 20 years of age (Krakoff et al., 2003).

There are very few studies on the prevalence of retinopathy in childhood diabetes. In 1990, a study from Kerala diagnosed eight patients with T2DM (then called as non insulin dependent diabetes) who had the onset of diabetes at below 20 years. Among them, two (25%) had diabetic retinopathy with duration of diabetes between 6 and 30 years (Abraham & Geevarghese, 1990). From Chennai, at a tertiary diabetes specialty center (Amutha, Datta, Unnikrishnan, Anjana, & Mohan, 2012) reported that the prevalence of DR increased from 4.2% among those with diabetes duration of ≤5 years to 81.5% in those with duration of diabetes >15 years and two patients had DR at the time of diagnosis of diabetes. In one of our recent studies on youth onset diabetes (Rajalakshmi et al., 2014), the age and gender adjusted prevalence of retinopathy in T1DM-Y and T2DM-Y was 62.5 and 65.8% respectively. Among the T2DM-Y, 22.7% of them were adolescents with T2DM (age at onset 10–19 years) and the prevalence of overall DR was found to be 32.4% (Fig. 1).

3.2. Diabetes nephropathy

Diabetic nephropathy is the leading cause of chronic renal failure and end stage renal disease (ESRD) (Ayodele, Alebiosu, & Salako, 2004). This is due to the increasing prevalence of T2DM, longer lifespan of diabetic patients and improved therapeutic options which allow the patients to live long enough to develop chronic complications including nephropathy. Less than 20% develop ESRD as most of the T2DM patients succumb earlier to coronary artery disease.

Diabetic nephropathy is characterized clinically by urinary albumin excretion, progressing through various stages of albuminuria and finally to ESRD. Microalbuminuria (MIC) is defined as an albumin excretion rate of 30–299 μg/mg of creatinine, which is currently the earliest detectable stage of nephropathy at which appropriate interventions can delay, or retard, the progression. Overt diabetic nephropathy is clinically defined as presence of persistent proteinuria of ≥500 mg/day or if MIC is ≥300 μg/mg of creatinine usually along with diabetic retinopathy and accompanying hypertension, and in the absence of any other renal disorder.

Screening for microalbuminuria should be done at the time of diagnosis of diabetes and at yearly intervals thereafter (American Diabetes Association, 2014). Persistent microalbuminuria is seen in approximately 10% of children and adolescents (Pinhas-Hamiel & Zeitler, 2007) which later progresses to overt nephropathy. Nephropathy occurs at all the age groups and it is not related to age at diagnosis of diabetes (Krakoff et al., 2003). In a clinic based study, we found that the prevalence of microalbuminuria increased from 8.7 to 29.5% when the diabetes duration increased from ≤5 to >15 years, while the prevalence of overt nephropathy increased from 9 to 34.4%, respectively (Amutha et al., 2012). The development of diabetic microalbuminuria and nephropathy at younger age is preventable which predisposes these individuals to a higher risk for cardiovascular complications which in turn could lead to a reduction in life expectancy. Longitudinal studies on the progression of microalbuminuria, risk factors, mechanisms and treatment options of nephropathy in youth onset T2DM are urgently needed to reduce this complication potentially especially in high risk populations (Afkarian, 2015; Solis-Herrera, Triplitt, & Lynch, 2014).

3.3. Diabetic neuropathy

Neuropathy is one of the commonest complications of diabetes (Vinik, Park, Stansberry, & Pittenger, 2000). Diabetic neuropathy is defined as the presence of symptoms and/or signs of peripheral nerve dysfunctions after exclusion of other causes. It is a heterogeneous condition that encompasses a wide range of peripheral nerve dysfunction whose development might be attributed to diabetes per se or to factors associated with the disease. It can be assessed non invasively by several tests varying from simple assessment of pin-prick perception to more detailed assessment using several different modalities including clinical signs and symptoms, sensory tests or electro diagnostic tests (Bhadada, Sahay, Jyotsna, & Agrawal, 2001). It is one of the most common and is referred to as the 'painful complication' of diabetes

Clinical neuropathy in adolescence is rare, although subclinical neuropathy demonstrated by abnormalities of vibration perception threshold or nerve conduction studies have been reported in 20 to 57% of adolescents with diabetes. The prevalence of neuropathy increased from 3 to 49.2% in those with diabetes duration of ≤5 and >15 years duration respectively in a clinic based study (Amutha et al., 2012). Some studies suggest that there is no difference among the rates of diabetic neuropathy in T1DM and T2DM, although, it tends to develop at a more rapid rate among T2DM adolescents (Eppens et al., 2006; Karabouta, Barnett, Shield, Ryan, & Crowne, 2008).

The prevalence of microvascular complications in children and adolescent onset T2DM in various published studies is summarized in Table 1.

4. Macrovascular complications

4.1. Cardiovascular disease (CVD) and mortality

Cardiovascular disease (CVD) is the major cause of death among patients with T2DM (Moss, Klein, & Klein, 1991; Stamler, Vaccaro,