REVIEW

Diabetes Management

Emerging epidemic and challenges of Type 2 diabetes in young adults

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Practice points

- There is an exponential increase in prevalence of Type 2 diabetes (T2DM) in the younger people.
- Despite the young age and shorter duration of diabetes, mortality is twice as high as age-matched subjects with T1DM. Cardiovascular disease is the major cause of death.
- Approximately half of the population of young adults with T2DM has multiple cardiovascular risk factors such as hypertension or hyperlipidemia at diagnosis. Despite the constellation of risk factors, only a minority receive cardioprotective medications.
- Microvascular complications are also prevalent at the time of diagnosis and may take more aggressive course compared with T1DM or late onset T2DM.
- Evidence on self-management and structured education programs which underpin the successful management of this chronic condition for young people with T2DM is poor and therefore innovative approaches tailored to suit this group are much needed.
- Managing the disease *per se* and its related complications in this young group is a great challenge to clinicians. Gaps in understanding the natural history of the condition and lack of long-term randomized controlled trials on effective intervention leads to suboptimal treatment in this young cohort. Further research is needed in this area.

Type 2 diabetes is becoming increasingly prevalent in young adults. This trend is particularly pronounced in some ethnic groups. The characteristic phenotype with obesity, signs of insulin resistance and prevalence of cardiovascular (CVD) risk factors such as hypertension and dyslipidemia are very common in this subset of patients. Despite the young age of onset and short duration of diabetes, this group tends to develop diabetes related complications such as nephropathy and CVD early in the disease process. Thus, they represent a high risk population that require urgent attention. This article reviews the current understanding of what may be an emerging major medicosocietal problem and describes the challenges facing healthcare workers in managing this high risk group.

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Globally, the prevalence of diabetes is increasing rapidly [1]. It is predicted that the prevalence of diabetes in adults will rise from 6.4% in 2003 to 7.7% worldwide in 2025 of which Type 2 diabetes (T2DM) will account for more than 90% [2]. One of the concerns is that T2DM, once considered predominantly a disease affecting older people has grown exponentially in young adults under 40 years of age [3–5].

The rapid growth of T2DM in younger people raises both medical and societal concerns. Individually, the development of T2DM at a younger age represents a serious health problem due to extended exposure to adverse risk factors like hyperglycemia and other components of the metabolic syndrome. However, in a wider setting, this is becoming a public health issue, which invariably will have significant impact on both future healthcare policy and services.

Serious consideration needs to be made to address this evolving problem. Firstly, there is emerging evidence that the disease tends to be more aggressive in the younger age group with greater risk of major complications [6]. Secondly, there are very few evidence-based clinical interventions or health policies specifically targeting this age group in either detection or treatment of T2DM. Thirdly, well characterized physical and psychological morbidities associated with T2DM will undoubtedly have serious socioeconomic consequences which will impact upon this most productive segment of the society [7].

This review article aims to explore the magnitude of the evolving problem and challenges we face in managing T2DM in younger adults.

Epidemiology

Defining early onset of T2DM in young people is arbitrary. It is a very broad term encompassing development of T2DM in children, adolescents, youth and young adults. In the UK, NICE defines early onset as those who have T2DM under 40 years of age. In practical terms, early onset T2DM can generally be divided into pediatric and adolescent (≤18 years) population, youth (18–25 years) or younger adults (>25 years). Some published data define young adults as under 30 years of age whereas others view it as under 40–45 years. In this review, T2DM in younger adults will include the high-risk group up to 45 years of age as the CV risk profile and mortality in this cohort is significantly higher compared with those who are diagnosed with T2DM over 45 years of age [8].

It is recognized in literature that the age of onset of T2DM has decreased in the last two decades. Emerging evidence has shown that an increase in obesity along with sedentary life style have contributed to the downward shift in age of onset of T2DM. Although Type 1 diabetes (T1DM) remains the predominant form in young age group, T2DM is now increasingly diagnosed in children, adolescents and younger adults under 30 years of age [9] and particularly in blacks and minority ethnic groups such as American Indians, Hispanics, Asians and Pacific islanders [4]. An increase in prevalence of T2DM in children and adolescents has also been reported in several countries including China, India, Saudi Arabia, Australia [10–14] and it is predicted that this from of disease will be responsible for the majority of cases over the next 10 years [15].

Most evidence for the rising prevalence of T2DM in young people originates from USA **(Table 1)** and Japanese pediatric data. The SEARCH for Diabetes in Youth Study reported the annual incidence of T2DM among American youth as 3.7–19/100 000 [16–20] (i.e., approximately 1 in 2700–5000). T2DM accounts for as much as 45% of all newly diagnosed children and adolescents in certain ethnic groups [21]. There was a significant increase in prevalence of T2DM in children and adolescents (10–19 years) by 30.5% over 8 years between 2001 and 2009 in five areas of the USA [4,22]. In Japan, 50–75% of people with diabetes aged between 10 and 29 years have T2DM. Moreover, the incidence has approximately quadrupled in children 6–15 years of age [21].

A systematic review on global trends revealed a significant worldwide variation in the incidence and prevalence of T2DM in children and adolescents. For instance reported incidence varies from 0–330/100,000 person years depending on the age, gender, geography and ethnicity of the study population and geographical region. Such vast discrepancies may be due to population variance but undoubtedly also demonstrates a current lack of methodological standardization in reporting and disease definition [1].

In the UK, reports on the incidence and prevalence of T2DM in youth are derived from publications of either questionnaire surveys of pediatric units or general practice prescription analyses of oral diabetic therapies **(Table 1)**. A cross-sectional postal survey of pediatric diabetes centers in the UK reported the prevalence

Table 1. Prevalence estimates of Type 2 diabetes in adolescents and youth from USA and UK studies.

Study	Prevalence of T2DM	Age group	Year assessed	Source	Ref.
The SEARCH study (USA)	0.34/1000	<19 years	2001	Cross-sectional active surveillance and case ascertainment	[4,22]
The SEARCH study (USA)	0.46/1000	<19 years	2009	As above	[4,22]
Ehtisham (UK)	0.21/100,000	<16 years	2000	Cross-sectional questionnaire survey of pediatric diabetes centers	[3]
Hsia (UK)	1.9/100,000	<18 years	2005	Retrospective cohort study:analysis of antidiabetic prescription for children from GP data	[4]
Royal College of Pediatrics and Child Health (UK)	3/100,000	<18 years	2009	Cross-sectional survey by secondary care clinicians in England	[5]

T2DM: Type 2 diabetes mellitus.

of T2DM as 0.21/100,000 under 16 years of age in 2002 [23]. However, subsequent studies revealed an increasing trend of T2DM under 18 years of age with an estimated prevalence of 1.9/100,000 and 3/100,000 in 2005 and 2009, respectively [24,25]. A retrospective cohort study published in 2009 also reported an eightfold rise in prescriptions for oral diabetes medications from 1998 to 2005 in young adults under 18 years of age [24].

There are limited data available from adult diabetes services in the UK. A hospital based cross-sectional study carried out in Leeds in 2000 reported prevalence rate of 9/100,000 under 19 years old, which was the highest among comparable European countries [1]. The overall prevalence was 13/100,000 representing 5% of the diabetic population in their clinic under 30 years of age with T2DM [26]. Another study carried out in Sheffield in 2008 reported that 24% of their clinic population under 40 years of age were diagnosed with T2DM [27]. Similarly, in Leicester and Leicestershire, young T2DM under 35 years old represent 24% of the total secondary care clinic population [28].

Although there is no global census on prevalence of T2DM in young adults, all the available data so far illustrates a progressive rise in the burden of early onset T2DM.

Challenges in diagnosis & management

• Clinical presentation & diagnostic challenges

As the age of onset of T2DM is getting younger and traditional polarized concept around insulin deficiency and action become less applicable, making the correct clinical diagnosis becomes more of a challenge. Clinical features differentiating T1DM, T2DM and maturity onset diabetes of the young (MODY) are summarized in **Table 2**. Some commonly encountered diagnostic and management issues will be discussed in this section.

People diagnosed with T2DM at a younger age may present with a distinct or more extreme phenotype. Features of metabolic syndrome due to insulin resistance and other associated features such as acanthosis nigricans, polycystic ovarian syndrome (PCOS), nonalcoholic fatty liver disease (NAFLD) may often be present. Young people with T2DM are usually obese, from an ethnic minority background and have a family history of diabetes [4,28]. In addition, cardiovascular risk factors such as hypertension, dyslipidemia and nephropathy appear quite prevalent at the time of diagnosis and probably predate the development of glucose dysregulation [8] (see the 'Challenges of complications' section). This cohort tends to present insidiously with many being diagnosed as an incidental finding but some may present with overt symptoms of hyperglycemia.

In contrast to this insidious presentation, young people with T1DM typically present with profound and rapid onset hyperglycemia-related osmotic symptoms or even ketoacidosis. The majority of these patients do not have features of insulin resistance and describe significant preceding weight loss although it should be noted that obesity *per se* in young adults does not exclude T1DM. With the global rise in obesity, many young people with T1DM are becoming obese. Conversely, up to 30% of patients with T2DM, especially Afro-Carribean and Hispanic ancestry present with a mild form of diabetic ketoacidosis [29] even though the main driver to their diabetes is obesity-mediated insulin resistance. This creates a diagnostic dilemma at presentation.

Table 2. Clinical features differentiating Type 1 diabetes, Type 2 diabetes and maturity onset diabetes of the young (MODY) in young people.

	T1DM	T2DM	MODY
Prevalence (among young people with diabetes)	>90%	<10% (Japan 60–80%)	1–3%
Clinical features			
Onset	Usually acute onset	Usually insidious onset	Variable
Osmotic symptoms (polyuria, polydipsia, weight loss)	Pronounced	Often asymptomatic but can present with severe symptoms in some cases	Variable
Ketosis	Almost always present	Usually absent (except Afro-Caribbean origin)	Common in neonatal forms, rare in others
Body habitus	Usually not obese	Often obese	Usually not obese
Signs of insulin resistance	Rare	Often present	Rare
Association with other autoimmune disorders	Yes	No	No
Family history in parents	2–4%	80%	90%
Diagnostic aid biomarkers			
Antibodies	ICA, Anti-GAD, ICA 512 – positive	Negative	Negative
C-peptide	Negative	Positive	Normal range
C-peptide/creatinine ratio	Low	High	Normal
Treatment			
	Insulin	Oral hypoglycemic agents	Variable from diet to sulphonylurea to insulin

GAD: Glutamic acid decarboxylase; ICA: Islet cell antibody; MODY: Maturity onset diabetes of the young; T1DM: Type 1 diabetes; T2DM: Type 2 diabetes.
Adapted with permission from [5] and data taken from [1].

Misclassification can have serious clinical and psychosocial consequences. Incorrectly diagnosing T2DM in a young patient with T1DM could be life threatening if the situation is managed with oral diabetes medication rather than insulin. Likewise, misdiagnosing T1DM as T2DM can result in unnecessary life-long treatment with insulin, when alternative glucose lowering therapies may be more appropriate. In cases of diagnostic uncertainty, it is probably not unreasonable 'to err on the side of caution' and keep options open until further investigations (see below) can delineate the true etiology of the disease.

In addition, MODY due to single gene mutations is often misdiagnosed as T1DM or sometimes as T2DM. MODY should be considered in patients who require a very low dose of insulin and have a history of diabetes in successive generations. They may not be markedly obese or have signs of insulin resistance. Often, they are from an ethnic background with low prevalence of T2DM at a young age. Rarely people with MODY require insulin therapy and they can often be managed successfully with a low dose of sulphonylurea or dietary measures depending on the mutation identified. In addition, a subset of patients with T2DM diagnosed at a young age (i.e., those under 35 years of age with phenotype of T2DM) and not requiring insulin in the initial years may have latent autoimmune diabetes in adults (LADA) [30].

Biochemical tests are available to aid the diagnosis and guide the clinical management. A persistently high serum insulin and C peptide concentration is characteristic of T2DM and would be unusual in T1DM. However, this may not be apparent initially as there is an overlap in insulin and C peptide level between T1DM and T2DM at the time of diagnosis [31]. Detection of autoantibodies such as glutamic acid decarboxylase (GAD), islet cell (ICA) or insulin antibodies (IA) may be used to distinguish T2DM from T1DM. However, 15–45% of youth and adults with T2DM have T1DM associated antibodies [31]. In addition, patients with LADA may also have GAD and other islet cell antibodies [30]. Thus, the antibodies cannot be used as the sole diagnostic tool.

More recently postmeal urinary C peptide/creatinine ratio has been used to differentiate the two. The test is inexpensive, noninvasive and can be carried out easily in clinics or at home [32]. If MODY is strongly suspected, genetic testing for various types of MODY can be carried out in some centers, which may help to characterize the type of diabetes and also to tailor drug treatment. However, genetic testing takes time and therefore it may not be possible to formulate an accurate type of diabetes at the time of presentation.

Given the complexities mentioned, determining the type of diabetes at the time of diagnosis in young T2DM can be difficult. It may take months or years to establish the correct diagnosis. In case of diagnostic uncertainty, it is reasonable to keep options open until further information is available. When the patient is symptomatic, the safest option is to treat with insulin to prevent metabolic decompensation. However, a clear explanation of the diagnostic dilemma posed by certain atypical presentations together with the rationale for treatment changes over time should form part of normal diabetes practice.

• Challenges of complications

T2DM tends to behave more aggressively in younger adults with evidence of premature micro- and macrovasular diseases [5]. These complications occur despite the young age and relatively short duration of diabetes [3]. Life expectancy is reduced by 10 years if T2DM is diagnosed in a person under 40 years of age [33]. Excess mortality was also noted in youth with T2DM compared with the general population or youth of T1DM [34]. A small Canadian survey of young adults (18–33 years) who developed T2DM in childhood found that nearly 9% died during a 9-year follow-up period [35]. Mortality of 11% was quoted in an Australian study in youth (15–30 years) over a follow-up of over 20 years [36]. A significantly greater mortality was noted with twofold increase in risk for death in young people with T2DM compared with T1DM of similar age of onset (15–30 years), (11 vs 6.8%, p = 0.03) [36]. Death also occurred at a relatively young age of 52.9 years [36].

Microvascular complications

A clinical observation from a secondary cohort showed that people who were diagnosed with T2DM at a younger age developed significant diabetes related complications up to 20 years earlier, particularly microvascular complications, compared with those with late onset T2DM [27]. They may develop more diabetes related complications earlier than those with T1DM [36].

Nephropathy

Renal complications are common in young adults with T2DM. In a 30-year follow-up study, young adults with T2DM in Japan were reported to have a higher incidence of nephropathy than those with T1DM (44 vs 20.2%) [37]. In addition, despite having a shorter duration of diabetes and similar glycemic control, persistent micro- and macroalbuminuria was reported in 18.2 and 4.5% of the T2DM population versus 11.3 and 2.4% in T1DM cohort [38].

Compared with those with late onset of T2DM, younger patients are at a 20% higher risk of developing microalbuminuria at some point in the trajectory of the disease (HR: 1.2, 95% CI: 1.1–1.4) [8]. Approximately 17% of patients under 40 years with T2DM had microalbuminuria in a cross-sectional study in Leicester and Sheffield [39]. In a large, multiethnic, multicenter clinical trial of newly diagnosed children and adolescents of T2DM, the TODAY study, 6.3% of the participants already had microalbuminuria at base line, that is, within 2 years of diagnosis. The prevalence of microalbuminuria nearly tripled (16.6%) after 4 years of follow-up [40]. Six percent of the young onset T2DM required renal replacement therapy in the 9 years of follow-up in a Canadian survey of 51 young patients with T2DM [35].

Retinopathy

Data on prevalence of retinopathy in youth with T2DM are limited. The SEARCH study reported the prevalence of diabetic retinopathy as 42% in young people with T2DM compared with 17% for T1DM (OR: 1.5; 95% CI: 0.58–3.88; p = 0.4) [41]. In a large Swedish study of young adults, the incidence of sight threatening retinopathy was significantly higher in T2DM compared with an age-matched T1DM cohort [42]. In another observational study, around 15% of Japanese adults diagnosed with T2DM under 30 years of age developed proliferative retinopathy and 24% were blind by their thirty-fifth birthday [43]. Approximately 14% of young T2DM adolescents enrolled in the TODAY study were reported to have retinopathy

and long-term ophthalmological outcomes in this group are expected to be very poor [44].

Neuropathy

Studies reporting neuropathy in young adults are very sparse. A small UK study of 30 patients with T2DM aged between 13 and 35 years reported peripheral neuropathy in 40% and foot ulceration in 20% of subjects [45]. In contrast to a T1DM comparator group, 57% of young T2DM patients with mean duration of 4.6 years of diabetes had peripheral neuropathy while none was present in the T1DM cohort [46]. A similar percentage was quoted to have neuropathy in an Australian study again with short duration of diabetes (1.3 years) suggesting that incidence could be higher in young people with T2DM compared with T1DM [3].

• Macrovascular complications

Cardiovascular complications

There is increasing evidence that early onset Type 2 diabetes is a high risk condition of premature atherosclerotic [47] changes and premature cardiovascular disease (CVD) [48]. Although the absolute risk of CVD was higher in older adults with or without diabetes, younger adults with early-onset T2DM have a higher risk compared with age-matched controls.

At the time of diagnosis, subjects with either young or late onset T2DM will already experience a much higher frequency of macrovascular disease. However, younger adults with T2DM have eightfold higher risk of developing any macrovascular disease while the older adults with late onset T2DM have only fourfold risk compared with control subjects [8].

The risk of developing a myocardial infarction in young adults with T2DM is 14-fold higher than control subjects (HR: 14; 95% CI: 6.2–31.4) whereas it is only fourfold higher in those with late onset T2DM. Similarly, the likelihood of developing cerebrovascular disease is significantly higher in young T2DM compared with the background population [8].

Compared with patients with T1DM of similar age, more cardiovascular deaths were noted in young patients with T2DM (50 vs 30%; $p < 0.05$) despite a significantly shorter duration of the disease (26.9 vs 36.5 years; $p = 0.01$) and equivalent glycemic control [36].

Cardiovascular risk profile

Many young adults with T2DM have metabolic syndrome at the time of diagnosis and this is an important contributor to the marked increased risk of CVD. Young adults with T2DM are found to be more obese than those with late onset T2DM (BMI 37 vs 33 kg/m^2) [8]. Obesity *per se* is an independent risk factor for developing diabetes and CVD [49]. Furthermore, the combined effect of obesity and hyperglycemia from young age may have adverse cumulative effect on cardiac function. A pilot study where extensive phenotyping was carried out on young obese subjects with T2DM revealed a significant diastolic dysfunction on cardiac MRI suggesting early manifestation of diabetic cardiomyopathy [50,51]. In addition, hypertension and dyslipidemia were found to be prevalent in this group of young people with T2DM.

About 33–60% of young adults <18 years with T2DM have dyslipidemia which is significantly higher than nonobese and nondiabetic youths and 30–55% have hypertension at presentation [3,52,53]. A study comparing the CVD risk profile in UK primary care setting showed a similar adverse lipid profile and high systolic blood pressure in both young and late onset T2DM, 53% and 58% respectively [54]. In other hospital-based studies, young T2DM patients exhibit higher prevalence (60–90%) of multiple cardiovascular risk factors compared with other population.

In the TODAY clinical trial, 11.6% of the adolescents with T2DM had hypertension within 2 years of diagnosis (i.e., at baseline) and the prevalence nearly tripled (33.8%) at the end of study period in 4 years [40]. In addition, young T2DM subjects have an increased tendency to develop microalbuminuria, an independent risk factor for developing CVD.

A remarkably high prevalence of dyslipidemia was found at the base line in the TODAY study and both LDL and triglycerides levels increased in the first 12 months and remained at this higher level over next 24 months [55]. The proportion of youth prescribed lipid lowering agents also tripled during the same period.

Evidence has shown that the process of atherosclerosis begins in childhood or early adulthood and its rate of progression is determined by a discrete set of often modifiable risk factors (hypertension, dyslipidemia, obesity etc.) largely independent of age [56]. Thus it is not surprising that the co-existence of multiple risk factors at a young age will inevitably led to premature CVD disease and mortality in young T2DM subjects.

• Challenges in clinical management

The literature evaluating long-term outcomes and complications in young people with T2DM is very limited. This lack of evidence poses a further challenge for clinicians in formulating strategies and optimizing management plans to minimize the risk of complications. To the best of our knowledge, there is no published guidance focused specifically on young adults with T2DM.

At diagnosis, glycemic control tends to be worse in young T2DM < 45 years than older subjects (HbA1c 8.7 vs 8.1%) [8]. It continues to remain poor both within (8.3 vs 7.8%) and beyond 5 years of diagnosis (9.1 vs 8.6%) compared with older adults [57]. It is concerning to note that the proportion of young T2DM patients with suboptimal glycemic control was as high as 57% in the primary care setting in the UK [54].

Structured education

Dietary and life-style modifications are always recommended as the first line measures in managing T2DM. Structured education to support self-management is the key to long-term management of chronic conditions like diabetes. However, there are obstacles in successfully engaging young adults in education programs. Compared to people with late onset T2DM, younger adults are more likely to have depression and diabetes related distress [58]. This may impact on participation in structured education programs and self-management.

Glucose-lowering therapies

In theory, drug therapies available for glycemic control in early onset T2DM <45 years are the same as that of late onset T2DM. However, very few are licensed to be used in adolescents and younger adults mainly due to the lack of therapeutic trials that include this age group. Evidence so far predominantly originates from studies carried out on older adults over 50 years of age. Metformin and insulin are the commonly used therapies in adolescents and young adults.

In a multicenter double blind trial in 10–16 year old adolescents, use of metformin was found to be safe and resulted in HbA1c reduction of 1.2% over 16 weeks [59]. The sulphonylurea, glimepiride, results in similar improvement in HbA1c but with a weight gain of nearly 2 kg [60]. Both drugs were comparable in terms of safety profile over 26-week follow-up. However, there are no long-term studies of established oral therapies on how they may modify the prognosis or affect the complications.

In a 4-year follow-up of a large randomized controlled trial on adolescents with T2DM, treatment failure rate from metformin was found to be higher than in the older adults with T2DM. Furthermore, this study revealed that addition of rosiglitazone to metformin was superior to treatment with metformin alone or addition of life-style intervention to metformin therapy [61]. Half of the youth in the TODAY study were unable to maintain glycemic control when treated with metformin alone and needed insulin therapy [61]. Although the average time to requiring insulin was similar, young T2DM are 80% more likely to begin insulin therapy than those with late-onset T2DM [8].

Newer therapies such as DPP4 inhibitors, GLP-1 analogs or SGLT-2 inhibitors could be beneficial especially in young T2DM patients with obesity. GLP-1 analogs and SGLT-2 inhibitors are proven to reduce body weight in addition to lowering glucose in older adults with very low risk of hypoglycemia. However, there are no published studies using any of these newer agents in younger T2DM and therefore caution should be exercised in prescribing these agents in younger patients. For example, cases of diabetic ketoacidosis are reported in both T1DM and T2DM patients exposed to SGLT-2 inhibitors and the US FDA has recently issued a warning of associated risk of ketoacidosis with use of SGLT-2 inhibitors [62,63].

Therapies addressing CV risk factors

CVD is the major cause of mortality in young adults with T2DM and hence the rationale for aggressive cardioprotective treatment is convincing [27]. Evidence published so far on favorable outcomes after treating CVD risk factors are mainly based on studies of patients over 50 years of age. There are no randomized controlled trials in younger populations with T2DM to guide management. The lack of long-term data on CVD outcomes in young T2DM subjects may have led to reluctance amongst clinicians to expose young patients to life-long treatments for the fear of possible side effects. As a consequence, administration of cardioprotective treatment is suboptimal particularly in relation to primary prevention of CVD.

From the pediatric data, none of the 34% who were found to have hypertension received

antihypertensive treatment [64]. A cross-sectional study from two specialist centers in UK showed only 28 and 31% of young adults under 40 years of age were receiving antihypertensive and lipid lowering therapies [39].

Compared to patients with late onset T2DM, overall usage of cardio protective medications is lower in young adults. Only 39.6 and 23.9% received antihypertensive and statin therapy while 75.8 and 67% of patients with late onset T2DM had treatment although both cohorts had similar coexisting CV risk factors [65].

Evidence has shown that adverse risk of CVD is present soon after diagnosis [57]. However, the use of statins and antihypertensive treatment in young adults under 40 years is significantly lower within 5 years of diagnosis [57]. In the TODAY study, a third of the patients who were initially treated with angiotensin converting enzyme inhibitor (ACEI) required multiple antihypertensive medications during the follow-up period. The percentage requiring lipid lowering drugs tripled and the number achieving target levels declined [55] suggesting a progressive adverse CV risk profile despite treatment in this age group. This highlights that aggressive management of CV risk factors is essential to improve the long-term CV morbidity and mortality.

Female of reproductive age

Among younger patients, managing T2DM in women of child bearing age is a challenge. Firstly, 1 in 4 females with T2DM [64] has PCOS, which often affects fertility. Treatment with metformin can improve the chances of conception [39]. The UK Confidential Enquiry into Maternal Child Health (CEMACH) reported that a third of women in their study had T2DM and they were less likely to receive adequate pregnancy counseling, folic acid supplementation or a test for glycemic control 6 months prior to conception compared with those with T1DM [66]. This probably contributed to both poor neonatal and maternal outcomes with a twofold rise in congenital malformation and a threefold increase in perinatal mortality rates. Pregnancy loss as high as 40% was reported in Canadian adolescents with T2DM during a 9-year follow-up period [35]. Early and appropriate preconceptual counseling is therefore vital to improve the morbidity and mortality rate of both mother and fetus. A small intervention study of intensive preconception counseling on 13–19-year old girls with T2DM showed long-term sustained knowledge at 12 months that could improve reproductive health behaviors and outcomes [67].

Another limiting factor in this group of patients is choosing hypoglycemic medications. Metformin and insulin are safe options. However, the use of newer therapeutic agents such as DPP-4 inhibitors or GLP-1 analogs or SGLT-2 inhibitors requires adequate contraception as teratogenic effects are unknown. This will inevitably limit their use in a young woman with T2DM who wish to start or complete a family.

In addition, young women with T2DM are at 14-fold higher risk of having MI than the age and sex matched nondiabetic population [8]. Despite that, there is reluctance to treat women of childbearing age as aggressively as men due to the fear of possible teratogenic effects of medications. Stratification according to gender showed that significantly fewer women under 35 years were treated for hypertension (22 vs 43%, $p < 0.01$) and hyperlipidemia (16 vs 43%, $p < 0.01$) [39]. Clearly, the need for aggressive therapy is offset by the fear of teratogenicity, which can be minimized by prepregnancy counseling and the use of contraceptives. However, according to the general practice database (GPRD) data, although statin use increased from 14 to 55% over 6 years, use of contraceptives remained static at 11%. Only 9% of those on a statin were on oral contraceptive therapy [68].

Adherence

Another challenging factor in managing this group of young adults with T2DM is adherence to medication and follow-up appointments. Nearly 60% of young patients 10–19 years of age did not attend regular follow-up for 2 years in a Japanese study [69]. In another study, 65% was reported to have poor concordance with treatment and missing appointments [70]. Those who did not attend appointments had poorer glycemic control (HbA1c of 12%) [71] higher BMI, higher blood pressure and adverse lipid profile [69] than regular clinic attenders. Seamless transition from pediatric to adolescent and adult diabetes care is also imperative to support this young age group in order to reduce diabetes and related complications later in life. The American Diabetes Association (ADA) outlined the recommendations for both pediatric and adult healthcare providers to ensure that patients receive accessible, patient-centered, coordinated, comprehensive continuous effective care during the transitioning period [72].

Early detection or screening

Most of the guidance and healthcare policies in managing T2DM are targeted at older adults over 40 years of age to screen for diabetes and to treat them aggressively to reduce diabetes related complications. There are no specific worldwide policies to detect T2DM early in younger adults although it is considered as an emerging problem globally. In the UK, NICE recommends identifying young adults using risk assessment tools in high risk groups over 25–39 years of age in South Asians, Chinese, Afro-Caribbean, black Africans and other ethnic minorities [73].

Conclusion & future perspective

Type 2 DM is becoming increasingly prevalent in younger adults. Despite the young age of onset and shorter duration of diabetes, this group tends to develop diabetes related complications such as nephropathy and CVD early in the disease process [8] with high mortality at a relatively young age. However, there are many gaps in our understanding of the natural history of T2DM in young adults due to lack of both epidemiological and randomized controlled trial data. There are very few studies looking at how the clinical course differs by the age of onset of diabetes.

Based on the trend of exponential growth from available data so far, we speculate that T2DM in youth will continue to rise in the next decade both in developing and developed countries. Although we are not aware of any health economic analysis on the impact of developing diabetes at a younger age, this group will impose a huge health and economic burden on the society, not only from managing diabetes *per se* but also from treating related complications at an earlier age and for longer duration. Therefore, urgent adoption of early detection, prevention programs and standardized treatment are warranted in this age group.

Lack of evidence for intervention to either optimize glycemic control or to address CV risk factors also results in nonstandardized treatment and inevitable variations in standards of care. Well designed clinical trials are needed to guide glucose and CVD risk management in this young people who are otherwise heading for serious complications.

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