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REVIEW ARTICLE

Type 2 diabetes mellitus and recent treatment options in adolescents and young adults

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ABSTRACT

Although type 2 diabetes mellitus (T2DM) has historically been thought of as a disease that mostly affects adults, its incidence among adolescents and young people has been rising in tandem with the rising rates of childhood obesity. There is no evidence to support the best course of treatment for T2DM in this age group despite the undeniable benefits of lifestyle adjustment for obese kids. Early diabetes start is linked to extended exposure to the disease and a greater likelihood of chronic issues, which impact more individuals during their working years and highlight the negative social effects of the condition. Additionally, there is mounting evidence that juvenile diabetes cohorts exhibit an aggressive phenotype that contributes to the early onset of problems that negatively affect life quality and negatively impact long-term results, increasing the possibility of a future public health emergency. Relevant studies were identified through a systematic search of PubMed, ScienceDirect, and Google Scholar for articles published between 2019 and 2025 using the keyword "Adolescents and (T2DM or Insulin Resistance)". Type 2 diabetes in young people is a serious global public health issue now. Many significant obstacles must be overcome to treat T2DM that develops in young people, including a lack of effective treatment alternatives and limitations in carrying out therapeutic research. The US Food and Drug Administration has approved metformin, glimepiride (Amaryl), and insulin as treatments for teenagers and young adults with type 2 diabetes, despite therapeutic medication studies. Given modified pharmaceutical laws, it is probable that further anti-diabetic drugs will be included in the arsenal of treatment choices available to teenagers and young adults with T2DM. The epidemiology and current understanding of the pathophysiology, risk factors, consequences, and therapy of T2DM in adolescents and young adults are discussed in this review.

Keywords: Type 2 diabetes mellitus, treatment option, physical lifestyle, obesity, pathophysiology, adolescent, insulin

INTRODUCTION

Over the past three to four decades, type 2 diabetes mellitus, or T2DM, has become a new condition for adolescents and young people.[1] Type 2 diabetes, which accounted for a very small proportion of all new cases of diabetes in this age group range, was detected in nearly all adolescents and young people with diabetes prior to this increase.[2] Insulin resistance and hyperglycemia are hallmarks of beta cell loss caused by T2DM, a chronic, progressive illness. Adolescents with prediabetic states, such as impaired glucose tolerance (IGT) and impaired fasting glucose (IFG), usually have these conditions before being diagnosed with T2DM.[3] The risk of complications from diabetes is predicted to be substantial in the upcoming years and decades, despite the lack of trustworthy data due to the disease's new onset in young people.[4] T2DM was shown to be prevalent in all racial and ethnic groups, particularly American Indians and other indigenous peoples, according to a study conducted on people under the age of 18.[5] Over the past few decades, sedentary lifestyles, an increase in the incidence of fetal diabetes exposure, and the growing frequency, severity, and earlier onset of teenage obesity have all been major contributors to young-onset T2DM.[6] Compared to people who develop T2DM at maturity, those who have it in childhood or adolescence frequently have a more aggressive course, with a larger chance of treatment failure, rapidly developing comorbidities, and a faster decline in β-cell activity. Furthermore, there are insufficient therapeutic choices for kids and teenagers with T2DM.[7] Metformin, glimepiride (Amaryl), and insulin were the only pharmaceutical treatments that regulatory organizations advised until recently.[8] In young onset T2DM there are significant knowledge gaps regarding etiology, clinical courses, and treatment optimization of type 2 diabetes, a developing condition with difficulties in clinical care and research programs.[9] In obese people, peripheral and hepatic insulin resistance, which is followed by a steady decline in beta-cell function, leads to abnormal glucose metabolism. Compared to adults, teenagers have an even greater correlation between obesity and T2DM.[10] Through the use of oral glucose tolerance tests (OGTTs) and hyperglycemic clamp techniques, it was shown in one study that beta-cell activity in adolescents with T2DM decreased relatively quickly, by roughly 20–35% annually.[11] In contrast, beta-cell function loss in individuals with type 2 diabetes has been reported to occur at a rate of 7–11% annually.[12] Furthermore, compared to type 1 diabetes mellitus (T1DM), early-onset T2DM is associated with a markedly increased risk of severe cardiovascular events, T2DM comorbidities, and mortality.[13] At the start of the trial, microalbuminuria was detected in 6.3% of participants; at the end of the follow-up, 16.6% of teenagers had microalbuminuria. [14] Nephropathy represented 54.8% of the total incidence of T2DM-related comorbidities, while neuropathy and retinopathy were 32.4% and 51%, respectively. The clinical progression of type 2 diabetes in children and adults was compared in two other studies that also investigated how significant microvascular and macrovascular problems are affected by young-onset type 2 diabetes.[15,16]

We explore potential reasons to explain the aggressive metabolic phenotype seen in young adults with type 2 diabetes, and we discuss available treatment options and the challenges associated with implementing them in this population group.[17]

METHODS

The standard systematic-review approach was followed in the conduct of this review, and PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) guidelines were followed in its reporting.[18] For type 2 diabetes mellitus (T2DM) in adolescents and young adults, we examined the biomedical literature for studies, clinical trials, guidelines, and systematic reviews that addressed the disease's epidemiology, pathophysiology, and available pharmacological and non-pharmacological treatments. PubMed, ScienceDirect, SpringerLink, and Oxford Academic were among the electronic databases that were examined; the search was limited to English-language papers and included publications from 2019 to 2025.[19] We also checked the reference lists of included papers and pertinent reviews, as well as the websites of significant professional associations and regulatory bodies, to document changes to regulations and guidelines.[20]

Free-text terms for the population and condition (Type 2 diabetes, T2DM, adolescent, youth, young adult, pediatric) and controlled

vocabulary (e.g. MeSH) Medical Subject Headings were combined with intervention and outcome terms (e.g. metformin, insulin, GLP-1 receptor agonist, SGLT2 inhibitor, behavioral therapy, bariatric surgery, treatment, management, glycemic control, weight loss).[21] Type 2 diabetes [MeSH] or type 2 diabetes or T2DM and (adolescent or young adult) and (therapy or management or insulin or GLP-1 or SGLT2 or DPP-4 or bariatric) was a typical PubMed search string that was used. Each database's syntax was taken into consideration when crafting the search strings.[22] The search initially yielded 81 articles. After removing duplicates, inaccessible full texts, and articles not relevant to the review objectives, 1 article was excluded. A total of 80 articles were selected for analysis and synthesis. The selected articles were reviewed to identify key findings related to the risk factors, pathophysiology, pharmacological treatment, and initial treatment according to presentation and hyperglycemia severity of T2DM in adolescents and young adults.

Risk factors of T2DM

Puberty

Type 2 diabetes mellitus is incredibly common before the age of ten. However, it is most prevalent in people between the ages of 10 and 18, who are most likely going through adolescence.[23] The corresponding hormonal alterations in young children cause either an increase in insulin resistance or a physiological decrease in insulin sensitivity. To make up for this, there must be a corresponding rise in insulin secretion. [24] Teenagers who have low beta-cell function for a variety of reasons, however, might not be able to make up for it and end up with hyperglycemia.[25] Vulnerable teenagers are therefore more susceptible to developing T2DM. Factors that contribute to the prevalence of T2DM include a complex interplay of metabolic, genetic, and environmental factors.[26] Epidemiological research shows that reducing the main modifiable risk factors—obesity, inactivity, and poor diet—can prevent many T2DM cases, even though there is a significant genetic basis for an individual's predisposition to the disease caused by non-modifiable risk variables (race and family history/genetic predisposition).[27]

Childhood diet and obesity

Serbis et al.[28] noted that puberty and other known risk factors, such as sex and heredity, cannot account for the recent rise in the prevalence of T2DM in adolescents. Rather, environmental factors are implicated, most likely the obesogenic milieu that is causing childhood obesity to become more prevalent.[29] Increased visceral fat linked to obesity raises insulin resistance via a few pathways, including lipotoxicity and adipokine production. Currently, 37.3% of men, 39.8% of women, 24.8% of boys, and 23.6% of girls suffer from the worldwide epidemic of overweight and obesity.[30] Changes in lifestyle are largely responsible for the rising prevalence of obesity and type 2 diabetes in pre- and early adolescence, even though the causes of obesity in children and adolescents are complicated.[31] The main causes among young people are the rising consumption of high-calorie sugar-filled beverages, and a decline in physical activity. Frequent drinking of sweetened beverages raises energy intake by roughly 15%, while children, adolescents, and young people become more obese due to larger portion sizes, easier access to fast food, and targeted snack advertising.[32] The extensive use of fructose syrup generated from corn as a sweetener in "fizzy" beverages has a significant effect on young people's development of obesity, insulin resistance (IR), hyperglycemia, and other cardio-metabolic risk factors.[33]

Physical activity

A higher risk of obesity is linked to physical inactivity. However, it is challenging to measure the secular changes in leisure time activity among teenagers and younger people due to methodological flaws and a lack of trustworthy baseline data.[34] However, playing video games, watching television, and using superior transportation all lead to sedentary habits.[35] Adolescents' physical activity levels drop even more than those of younger children, and only a small percentage reach recommended levels.[36] For example, recent surveys conducted in Europe and South America show that 80% of 13 to 15-year-olds engage in moderate to vigorous exercise for at least 45 minutes each day, with girls being less active than boys. Young people who are physically inactive are more likely to develop metabolic syndrome, insulin resistance, and type 2 diabetes.[37]

The Bogalusa Heart Study, which involved young adults between the ages of 20 and 38, found a negative correlation between risk factors for insulin resistance and leisure-time physical activity.[38] Similarly, there was a high correlation between physical inactivity and the risk of type 2

diabetes, hypertension, and metabolic syndrome in the Cardia research, which involved individuals aged 18 to 29. The projected metabolic advantages of aerobic activity are relatively lower in those with type 2 diabetes, even if aerobic exercise can postpone or prevent the development of the disease in older adults.[39]

Lifestyle modification

A technical study and a set of clinical practice guidelines on the management of T2DM in children and adolescents were recently published by the American Academy of Pediatrics. For young people with type 2 diabetes, the Academy of Nutrition and Dietetics Pediatric Weight Management Evidence-based Nutrition Practice Guidelines should be followed.[40] Children should be encouraged to exercise moderately to vigorously for at least 60 minutes each day, and their non-academic screen time should be limited to less than two hours per day. Despite these guidelines, young people with type 2 diabetes tend to be far less active, be more sedentary, and have poorer levels of cardiorespiratory fitness than their peers without the disease. In addition, young people with type 2 diabetes have poorer food quality than their peers with type 1 diabetes.[41] They are less likely to reach the recommended daily consumption of less than 10% of calories from saturated fat, consume fewer micronutrients, and report consuming more than they would want to. They consume twice as many sugar-sweetened beverages as their peers with type 1 diabetes.

Balanced Diet According to the American Diabetes Association (ADA) should restrict calories and high-glycemic-index foods, be high in fiber, whole grains, and legumes, and contain both saturated and reduced trans fats.[42] Glycemia has been demonstrated to improve and maintain improvements with decreases in glycated hemoglobin (HBA1C) when people lose a little amount of weight through a lower calorie diet and greater physical exercise.[43] Adolescents with type 2 diabetes benefit greatly from exercise as well. The benefits of increased physical exercise include improved insulin sensitivity, greater muscle uptake, and a reduced requirement for insulin medication.[44-46] To reduce sedentary activities, screen time should be limited to no more than one or two hours each day. To address the psychological requirements of young people, patient and family education should be conducted in an age-appropriate and culturally sensitive way, with an emphasis on nutrition and exercise. Reinforcement is necessary for healthy actions to result in long-lasting lifestyle changes.[47] The mainstay of managing type 2 diabetes in adolescents is lifestyle modification; however, only 12% of adolescents with T2DM can attain sufficient metabolic control with lifestyle modification alone.

Polycystic ovarian syndrome

Compared to teenage girls of normal weight, those who are overweight or obese are more likely to have polycystic ovarian syndrome (PCOS).[48] Type 2 DM (4.7%) and poor glucose tolerance (35%) are highly prevalent in adolescent girls with PCOS and obesity. In the current cohort, oligomenorrhea affected up to 23% of teenage girls.[49] These girls had lower levels of estradiol and sex hormone-binding globulin but greater levels of androgen.

When combined with lifestyle changes, metformin can help girls with PCOS and T2DM by reducing hyperandrogenism and improving menstrual regularity and metabolic dysfunction.[50] However, all of the females in the current trial were taking metformin, therefore it could not be shown how menstruation or sex steroids were impacted differently by the three treatment groups: metformin alone, metformin plus lifestyle changes, and metformin plus rosiglitazone.[51] The mainstay of treatment for hyperandrogenism and anovulation in PCOS, hormonal combined oral contraceptive pills (COCPs) have no contraindications in young women with T2DM, even though some of them have been linked to poor metabolic status and cardiovascular (CV) risk.[52] Adolescent PCOS can be identified by combining clinical or laboratory signs of hyperandrogenism with oligo- or amenorrhea, even though polycystic morphology detected by pelvic ultrasound is not a reliable indicator of the condition.[53]

Non-alcoholic fatty liver disease

Up to 45% of children with type 2 diabetes have non-alcoholic fatty liver disease (NAFLD). Eight percent of non-diabetic teenagers with NAFLD died or needed a liver transplant after 19 years, according to longitudinal research.[54]

Furthermore, 7.5% of kids with NAFLD research conducted by multiple diagnostic centers had type 2 diabetes, and 24.4% had pre-diabetes. Additionally, young-onset T2DM has been found to have a higher histological severity of NAFLD than adults, with a higher chance of developing cirrhosis, liver failure, and hepatic fibrosis. It is

crucial to screen out non-NAFLD causes of chronic liver disease because transaminase values show poor specificity for NAFLD, despite having strong sensitivity for detecting advanced stages of hepatitis or fibrosis.[55] It is advised to measure alanine transaminase (ALT) and aspartate transaminase (AST) upon diagnosis and yearly after that to check for the existence of potential NAFLD in young people with type 2 diabetes. Although liver ultrasonography can identify liver fat greater than 30%, its sensitivity is low in people who are extremely obese and have lower levels of fat infiltration.[56] Spectroscopy using magnetic resonance is the non-invasive diagnostic with the highest sensitivity for identifying liver fat, and liver biopsy is still the gold standard. Note that non-invasive fibrosis assessment methods, such as transient elastography and scores such as fibrosis-4 should not be utilized since they have not been proven to work in kids or teenagers.[57]

Pathophysiology of T2DM in adolescents and young adults

In teens and young adults, insulin resistance and progressive pancreatic β-cell dysfunction—which are impacted by genetic, environmental, and lifestyle factors—combine to cause type 2 diabetes mellitus (T2DM) (Figure 1). Compared to adults, the disease tends to progress more aggressively in this age range, with problems starting earlier.

To maintain normal glucose levels, pancreatic β-cells first secrete more insulin in response to the increasing insulin resistance. But as time passes, these β-cells start to lose their ability to compensate, which results in a relative lack of insulin and increasing hyperglycemia.[58] The frequently aggressive nature of type 2 diabetes in younger people can be explained by the fact that this β-cell degeneration seems to happen more quickly in adolescents than in adults.

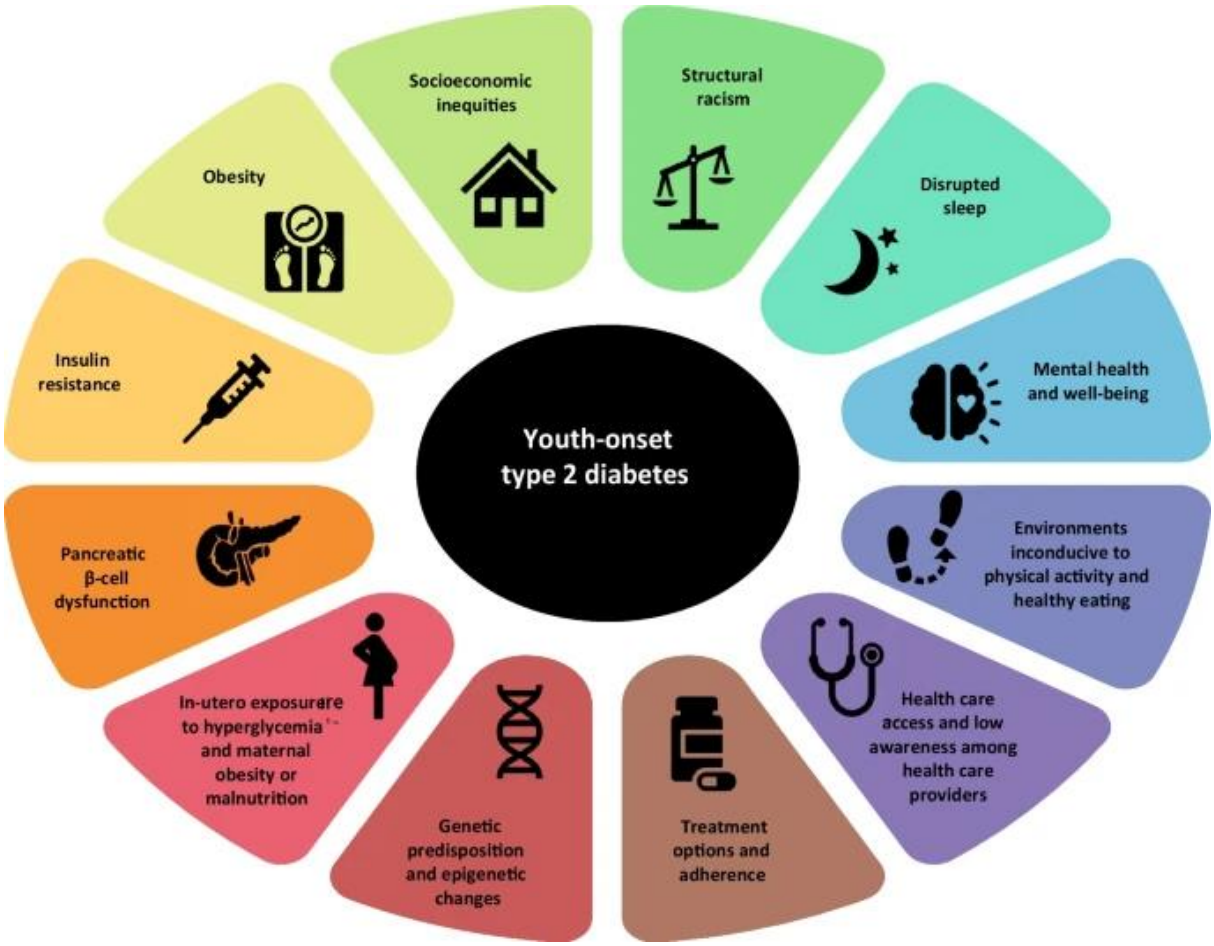

Figure 1. Youth-onset type 2 diabetes: an overview of pathophysiology, prognosis, prevention and management [60]

A major contributing factor to this pathophysiology is obesity, particularly central adiposity. In addition to being a store of fat, dysfunctional adipose tissue also functions as an active endocrine organ, lowering levels of protective adiponectin and secreting pro-inflammatory cytokines such as interleukin-6 and tumor necrosis factor-α.[59] This inflammatory milieu speeds up the loss of β-cells and exacerbates insulin resistance. Another factor is added by puberty, when growth hormone and sex hormones induce physiological insulin resistance to naturally rise.

Rapid progression of T2DM in adolescents and young adults

Evidence of decreased β-cell function signals the progression to glycemic failure, even though obesity and insulin resistance are important beginning causes. Compared to adults, adolescents with type 2 diabetes experience a quicker progression to glycemic failure.[61] Their pathophysiology includes reduced insulin sensitivity and a faster rate of β-cell function loss than in adults. In the RISE research, young people experienced a 30%–35% loss of β-cell function, compared to 11% for those with adult-onset type 2 diabetes.[62] Although the precise cause of this rapid β-cell function reduction, insulin resistance, and glucolipotoxicity brought on by fat, as well as excess growth hormone during puberty, is unknown, they are thought to be contributing factors. Insulin sensitivity indicators did not significantly differ between adults with T2DM and those with young onset.[63] The RISE trial found that, in contrast to adults, early insulin administration did not reverse the loss of β-cell function. This suggests that insufficient glycemic control is not causing this accelerated progression.[64]

Pharmacological treatment-approved options

Treating young people with type 2 diabetes is still difficult. In 2019, liraglutide, a glucagon-like peptide 1 rheumatoid arthritis receptor agonist (GLP-1 RA) was approved for use in children 10 years of age and following 52 weeks of treatment due to satisfactory safety data and 1.3% placebo-corrected decrease in HbA1c.[65] Prior to this the regulatory bodies had only approved metformin and insulin as pharmacological treatment options. Following a modest trial of young people in Europe aged 10 to 24, the indication for the sodium-glucose co-transporter 2 (SGLT-2) inhibitor dapagliflozin was expanded to include children aged 10 and up.[66,67] Exenatide, dulaglutide, and dapagliflozin all caused a placebo-corrected decrease in HbA1c of -0.85%, -1.4%, and -0.75%, respectively.[68] The dipeptidyl peptidase (DPP-4) inhibitor linagliptin did not result in a clinically significant decrease in HbA1c in a recent study of young people (ages 10–17) with type 2 diabetes who were treated with metformin and/or insulin and had a mean baseline HbA1c of roughly 8%.[98] In a randomized clinical trial on persons with T1DM, the SGLT-2 inhibitor empagliflozin had a slight impact on HbA1c only when combined with insulin or metformin therapy.[70] The safety profiles of linagliptin and empagliflozin were comparable to those of adults with T2DM.[71]

Type 2 diabetes in young people can now be treated with more than just insulin and metformin, thanks to recent research. According to the TODAY trial, only roughly half of teenagers were able to maintain sustained glycemic control with metformin alone. Intensive lifestyle intervention did not enhance results, while rosiglitazone did. Subsequent studies showed that GLP-1 receptor agonists work well in this age group.[72] Liraglutide and once weekly dulaglutide both significantly decreased HbA1c when compared to a placebo, and they both had gastrointestinal side effects that were comparable to those seen in adults. In more recent times, dapagliflozin-induced SGLT2 inhibition has also been shown to enhance glycemic control and be well tolerated by adolescents and young adults. According to the most recent evidence, tirzepatide, a dual GIP/GLP-1 agonist, significantly lowers body weight and HbA1c in adolescents while maintaining a safety profile that is in line with adult research (Figure 2).

Approach to pharmacotherapy of T2DM in adolescents and young youth

Compared to adult-onset T2DM, the disorder in adolescents and young adults has distinct problems due to the disease's rapid progression, early β-cell loss, and elevated risk of complications. Although lifestyle change is still the mainstay of treatment, early pharmaceutical intervention is frequently necessary to establish and sustain glycemic control.[74] Individualized treatment with close observation of safety and effectiveness in this age group is the focus of current guidelines approved by the FDA, the American Diabetes Association (ADA), and the International Society for Pediatric and Adolescent Diabetes (ISPAD).[75]

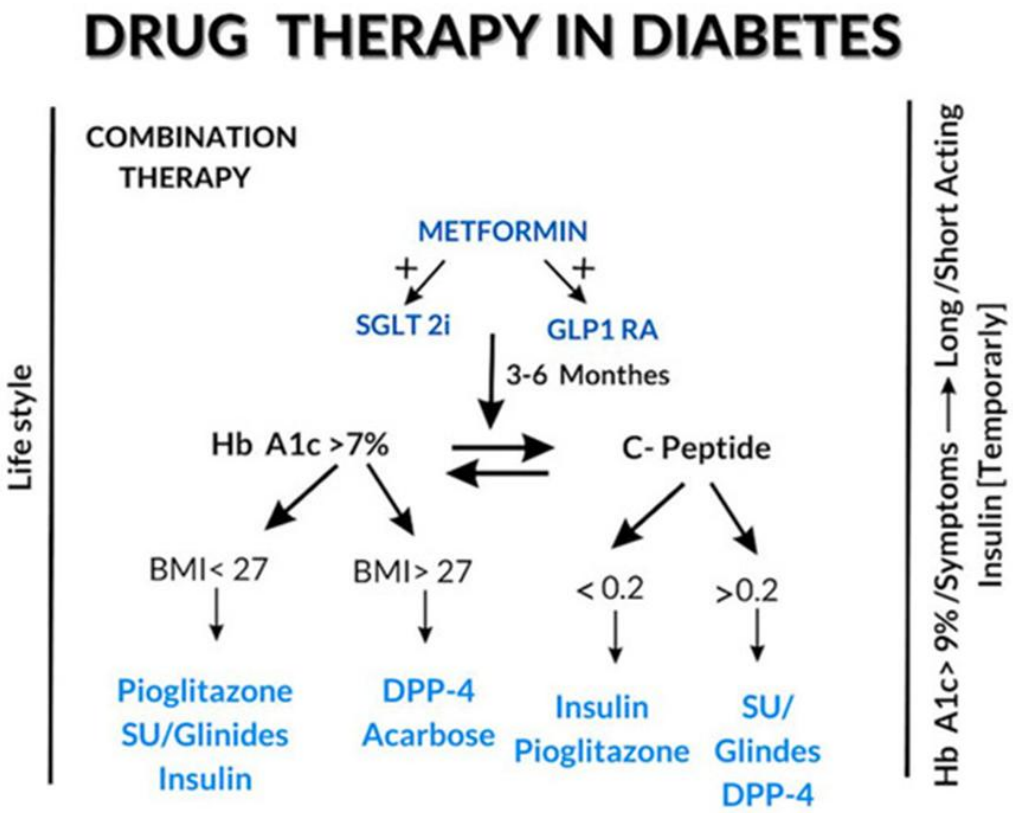

Figure 2. Drug-treatment for diabetes. The algorithm outlines current recommendations for diabetes treatment, incorporating the initiation of combined drug therapy and adjusting medications based on the patient's response [73]

Pharmacologic and lifestyle management are the first steps in the treatment of T2DM in young people. Young people with type 2 diabetes should be included in a developmentally and culturally appropriate lifestyle program that aims to reduce weight by promoting good eating habits and engaging in vigorous physical exercise for 30–45 minutes five days a week. Reducing childhood obesity is linked to a lower HbA1C. Weight loss was associated with a lower HbA1C one year following diagnosis in patients on metformin and those on insulin-containing regimens, according to a recent study of young people with type 2 diabetes.[76]

Continuous difficulties and observation

Even with treatment, glycemic control tends to deteriorate with time unless treatment is intensified early because many teenagers with type 2 diabetes have a rapid loss of β-cell function.[77] Frequent glucose monitoring (especially if using insulin), close monitoring for glycated hemoglobin (HbA1c) every three months, and screening for comorbidities (lipids, hypertension, kidney disease risk) are essential.[78]

Initial treatment according to presentation and hyperglycemia severity

First-line treatment for adolescents with type 2 diabetes is metformin plus lifestyle modification if they are metabolically stable (glycated hemoglobin HbA1c <9.0% [212 mg/dl]) and do not exhibit signs of severe hyperglycemia, acidosis, or ketosis.[79] Metformin is frequently given if an adolescent has a higher glycated hemoglobin level (HbA1c ≥9.0%) but no ketoacidosis. Insulin, particularly basal insulin, is administered right away. Insulin is started immediately (usually basal + bolus or full regimen) if there is ketoacidosis or significant metabolic decompensation until metabolic stability is reached; metformin may be administered later.[80]

Recommendations to patients

Prioritize getting enough sleep, at least seven hours each night, and consume nutritious food and beverages. Increase the number of fruits and vegetables consumed each day. Choose foods with a low glycemic index, such as fruits, legumes, whole grains, green salad with olive oil

dressing, and most vegetables. Refined carbs (white bread, rice, white potatoes, pasta, etc.) should be avoided. Limit saturated fatty acids (SFAs) and stay away from trans fats. A common component of diabetes treatment is taking insulin or other diabetes medications. Medicines can help you manage the disease in addition to choosing nutritious foods and beverages, exercising, and controlling your stress levels. Given the limitations, we advise screening for type 2 diabetes in children and adolescents with risk factors using a combination of A1C and random or fasting blood glucose.

CONCLUSION

Compared to T2DM that develops in adults, T2DM in children and adolescents presents unique features, demography, and disease development, making it an emerging global public health concern. Compared to adults, it exhibits lower rates of response to oral medication. Since type 2 diabetes in children and adolescents is a relatively new condition, data based on prevention, the best treatment strategies, and population monitoring is trailing the steady increase in incidence. There are few therapeutic options available to manage type 2 diabetes in young people and prevent problems from developing. An expert diabetes team with experience in providing the necessary diabetes education, aggressive treatment, and monitoring is necessary for the best management of young people with type 2 diabetes. Since metformin is the only oral drug authorized for use in young people with type 2 diabetes, it is the recommended first-line oral treatment for stable patients. Since type 2 diabetes in young people is extremely difficult to treat once diagnosed, primary prevention should be a top priority for health care resources and efforts.

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Conflict of Interest

There are no conflicts of interest

Author Contribution

MNB is responsible for conception, writing the manuscript and acquisition and collection of data. MRA is responsible for conception, critical revision of paper and analysis, and interpretation of data. IM is responsible for study design and methods used, MA is responsible for acquisition, collection of data, writing of manuscript and analysis, interpretation of data. All authors have read and approved the final manuscript.

Data Availability Statement

Ther were no new data generated data sharing is not applicable.

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Declaration of the Use of AI in Scientific Writing

The usage of artificial intelligence (AI)-assisted technologies to assist with the scientific writing process has been beneficial for this manuscript. For language improvement, grammatical correction, summarization, paraphrasing, and structuring of scientific text, OpenAI's ChatG T was utilized. The authors alone were responsible for the conception, execution, and validation of all scientific concepts, experimental plans, analyses, interpretations, and results reported in this work. Original data creation, analysis, and crucial scientific decision-making were not done by the AI. The integrity and correctness of the information provided are entirely the writers' responsibility.

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