Review Article

Young Onset Type 2 Diabetes Mellitus: A Review

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Received: 17-02-2022; **Revised:** 22-04-2022; **Accepted:** 29-04-2022; **Published on:** 15-05-2022.

ABSTRACT

Diabetes is an increasing global problem. Youth onset type2 diabetes mellitus is increasing in many countries. Early onset type 2 diabetes is increasingly prevalent with significant impact on individual or healthcare service. The individuals with history of type 2 diabetes, obese and leading sedentary life style, black or minority or ethnic group has higher risk of type 2 diabetes mellitus. Individuals with type 2 diabetes have higher risk of complications. Specific symptoms in young people include growth impairment, unexplained loss of weight and wetting of bed. Obesity, particularly abdominal obesity, PCOS, pubertal age group and intrauterine exposure to hyperglycemia are among the risk factors for development of T2DM in children and adolescents. Symptoms of diabetes and random plasma glucose concentration, or glycated haemoglobin or fasting plasma glucose or 2 h plasma glucose during oral glucose tolerance test may be used for diagnosing diabetes. Initial treatment of youth-beginning sort 2 diabetes should incorporate metformin as well as insulin alone or in combination, in view of the metabolic status of the patient. Initial treatment of youth-beginning sort 2 diabetes should incorporate metformin as well as insulin alone or in combination, in view of the metabolic status of the patient. Early onset type 2 diabetes is more aggressive and has higher complications and comorbidities. Youth onset type 2 diabetes creates large personal and societal burden so adequate educational and psychological support should be given. This review on young onset diabetes mellitus provides knowledge on emerging epidemic.

Keywords: Young onset, obese, type 2 diabetes, psychological support.

QUICK RESPONSE CODE →

DOI: 10.47583/ijpsrr.2022.v74i01.004

DOI link: http://dx.doi.org/10.47583/ijpsrr.2022.v74i01.004

INTRODUCTION

Diabetes is a worldwide problem, estimated to have type 2 diabetes in more than 620 million adults by 2045. However, the incidence of youth onset type2 diabetes increasing annually by 7.1 percent in some countries. Youth onset type 2 diabetes generates large personal and societal burden. Compared with adults' type 2 diabetes young onset has risk of serious complications [1].

Diabetes is majorly divided into two types type 1also called as insulin-dependent diabetes mellitus and type 2 also called as noninsulin-dependent diabetes mellitus.[2]

The classic symptoms in youth onset type 2 diabetes are similar to adult-onset type 2 diabetes which include frequent urination and excessive thirst. Specific symptoms in young people include growth impairment, unexplained loss of weight and wetting of bed.[1]

Diabetes is a metabolic sickness which is described by hyperglycaemia resulting because of defects in insulin secretion and insulin activity. Chronic hyperglycaemia of diabetes is related with long term dysfunction, damage and failure of different organs mainly eyes, kidneys, nerves, heart and blood vessels.[3]

Over past three decades there has been ongoing increase in the prevalence of early onset of diabetes mellitus. Previously type 2 diabetes mellitus is considered as disease of older adults but now it is increasingly diagnosed in adolescents and young adults.[4]

The predominance of type 2 diabetes in youths or adolescents and young adults is drastically increasing. similarly earlier onset type 2 diabetes, the major leading risk factors are obesity, family ancestry, and sedentary way of life. Beginning of diabetes at a younger age is related with longer disease exposure and higher risk for chronic complications. Younger onset type 2 diabetes additionally affects more people of working age, complementing the unfavourable cultural impacts of the disease. Besides, evidence is accumulating that younger onset type 2 diabetes has a more aggressive disease aggregate, prompting untimely advancement of complications, with antagonistic consequences on quality of life and unfavourable impacts on long term results, raising the chance of future public health calamity.[5]

The occurrence of type 2 diabetes expanded by 4.8% each year. Pathologic processes related with diabetes, including the improvement of insulin obstruction and the weakening

of beta-cell function, progress more quickly in youth-onset type 2 diabetes than in adult beginning diabetes. These variables result in worse glycaemic control and an expanded risk of early diabetes-related complications.[6]

While onset of disease is fundamentally in adult, the increment in prevalence of obesity among youth has resulted in an increasing rate of beginning of type 2 diabetes in youth. Type 2 diabetes adds to a high burden of disease related inconveniences and comorbidities. disease pathogenesis is driven by both environmental and hereditary factors, with raise in hepatic glucose production, impaired insulin discharge, and insulin resistance acting as key drivers in the advancement of disease.[7]

Pathophysiology

The pathophysiology of type 2 diabetes is complex.[8] under normal conditions, glucose concentrations remain within normal range in fasting and feeding state. [9] the alteration in the balance between insulin secretion and insulin sensitivity are the most important factor in development of type 2 diabetes mellitus.[8] Glucose regulation is maintained by proper balance between insulin secretion and insulin sensitivity.[9] In normal individual, at given glucose tolerance there is a balance between insulin sensitivity and insulin secretion.[10] Gradual decrease in beta cell function on a background of insulin resistance results in type 2 diabetes mellitus.Adolescents with glucose dysregulation have more impairment in insulin secretion compared with decreased insulin sensitivity.[8] In individuals with normal glucose tolerance, decrease in insulin sensitivity of peripheral tissues results in a compensatory increase in insulin secretion and normoglycemia is maintained. Failure of this compensatory response can lead to glucose intolerance and diabetes.[11]

In beta cells special channels are present i,e. potassium channel. On which ADP is present potassium being a special regulatory unit of ADP. When ADP binds to K^+ Channel it will open and allows to escape K^+, so resting membrane of K^+ cell consistently losing cells and develops intracellular negativity of about -70Mv. If more glucose is entering into beta cells more ATP is generated these ATP will bind on ADP of K^+ channel and close the channel this is also known as ADP sensitive potassium channel. By blocking the channel, the positive ions retained in the cell and its negative charge has been depolarized. Now its value is -50Mv. As soon as glucose enters the cell ATP is increasing it will bind to ADP and closes the channel at that stage Ca^+ channel is opened, in generally Calcium ions move from high concentration to low concentration, as calcium moves into cell intracellular calcium ions will increase and moves the secretory vesicles towards the cell membrane and fuse them and releases Insulin, C-peptide, Amylin, and Proinsulin.

Investigations of insulin secretion and glucose disposal in young people with glucose dysregulation have distinguished that, in impaired fasting glycaemia (IFG), the insulin stimulated glucose removal is typical but first and second stage insulin secretion are around 50%and 30% lower, respectively. In impaired glucose tolerance (IGT) the principal stage insulin secretion is around 40% lower while second stage insulin secretion is preserved. if IFG and IGT co-exist, there is impairment in the two stages - around 55% lower first stage insulin and 30% lower second stage insulin secretion. In T2DM, glucose removal is impaired by ~30%, first stage insulin by ~ 75%, and second stage insulin by ~65% compared with youngsters with normal glucose tolerance.[8]

Further, the deterioration in β cell work in youth with T2DM is accelerated (~15% each year) than seen in adults. Accordingly, the people who have combination of IFG and IGT are probably going to have a higher risk of progression to T2DM compared those with either IFG or IGT in isolation.[12]

Risk Factors

The improvement of early stage T2DM represents a complex interaction among hereditary and environmental factors.[13]

Risk factors of type 2 diabetes mellitus in youth are two types. They are modifiable and non-modifiable.

Modifiable risk factors include obesity, low physical activity, high sedentary behavior, socioeconomic status.

Non modifiable risk factors include ethnicity, family history, less birth weight, low weight during birth, exposing of diabetes mellitus in the uterus, female sex, history of gestational diabetes.[14]

Obesity, particularly abdominal obesity, PCOS, pubertal age group and intrauterine exposure to hyperglycemia are among the risk factors for development of T2DM in children and adolescents.[15]

Obesity

Obesity and type 2 diabetes are growing factors among young adults. Most of the early onset of diabetes are obese compared to older adults which is a inverse linear relationship between BMI and age of diagnosis of type 2 diabetes mellitus.[16]

Family history

Hereditary predisposition has a significant impact in risk of creating diabetes. Some 84% young people with diabetes have family background of diabetes while 56-71% have affected parent or sibling. While all things considered, a hereditary predisposition builds risk of beginning of diabetes families regularly share a similar climate.[17]

Ethnicity

Internationally Japanese Hispanics and native Americans have higher risk of developing type 2 diabetes in young age.[18]

Low physical inactivity

Physical inactivity is an important element in diabetic epidemic in young adults.[19] Decrease in physical activity in adolescents leads to increased weight gain which is important factor in development of glucose dysregulation among young adults.[20]

Complications

People diagnosed with type 2 diabetes during youth have greater risk of developing complications at early stages and have higher rate of developing multiple complications within 15 years after diagnosing the disease. Within 15 years of diagnosis of type 2 diabetes 60 percent of people have at least one complication related to diabetes and nearly one third of people had two or more complications. According to TODAY (treatment options for type 2 diabetes in adolescents and youth) study showed that youth onset diabetes is different from adult-onset diabetes and it is more aggressive and more difficult to control in youth onset diabetes.[21]

Complications occur due to diabetes are nephropathy, neuropathy, retinopathy, cardiovascular morbidity and mortality, non-alcoholic fatty liver disease, type 2 diabetes in pregnancy, psychological burden.[13]

Nephropathy in diabetes is a concern not only because it can lead to end stage renal failure but also it is related to cardiovascular disease. Renal disease is the most common complication in early onset of type 2 diabetes mellitus.Microalbuminria is present in people at diagnosis 28 to 42% at 5 years after diagnosis and 60% 10 years after diagnosis.[22]people diagnosed with diabetes more than 18 year old has higher chance of microalbuminuria and hypertension than type 1 diabetes, despite a shorter duration of diabetes and lower HbA1c supporting the hypothesis that early onset type 2 diabetes is a more aggressive form of diabetes.[22]

Neuropathy develops earlier in type 2 diabetes than in type 1 diabetes. This aggressive complication can lead to foot ulceration as early as 2 years after diagnosis and amputation after 10 years of diagnosis.[23]

Premature development of retinopathy is associated with early onset of type 2 diabetes mellitus and found to be more severe than type 1 diabetes. A population-based cohort study found that severe incidence of retinopathy was significantly found in age group of 15 to 34. Retinal assessment of adolescents found that retinal abnormalities are more in type 2 diabetes mellitus.[23]

Cardiovascular problems are often found in early onset of type 2 diabetes mellitus. At time of diagnosis 26 % of adolescents have hypertension increasing to 50percent.researchers have found that 80% of adolescents have low high density lipoprotein level and 10 % have elevated triglycerides at time of diagnosis. Early onset type 2 diabetes has cardiovascular risk profile like overweight, hyperlipidaemia, hypertension similar to adult type 2 diabetes.[13]

Non-alcoholic fatty liver disease is a important marker of insulin resistance. It is found that in 50% of young people with type 2 diabetes non alcoholic fatty liver disease is the most common liver abnormality.[24]

Early onset of type 2 diabetes is found in number of women attending maternity services. Type 2 diabetes in pregnancy women has a significant impact on foetus and mother. It is related with large number of risks on mother and foetus and may lead to miscarriage, birth injury, neonatal hypoglycaemia, macrosomia and still birth. These risks are more in adolescents with type 2 diabetes.[13]

Psychological burden is more in youth with type 2 diabetes mellitus. They not only need to strive for glucose control and weight loss but also, they have to take multiple medications to avoid complications and complications at early stage of life. This combination of increased body weight, previous dieting and history of depression result in eating disorders.[25]

Diagnosis

If a person represents with classic type 2 diabetes symptoms or more than one of the indicators, a diagnostic blood test is recommended followed by type-differentiate test. Symptoms of diabetes and random plasma glucose concentration (>11.1 mmol/L,200mg/dl), or glycated haemoglobin (HbA_{1c}:.6.5%,48mmol/L) or fasting plasma glucose (FPG:7.0mmol/L,126mg/dl) or 2 h plasma glucose during oral glucose tolerance test (.11.1mmol/L,200 mg/dl) may be used for diagnosing diabetes. For its durability and lack of fasting requirement, the American diabetes association recommends HbA_{1C} as one of the diagnostic criteria of youth-onset type 2 diabetes mellitus.[1]

Though the person does not have classic symptoms, the American diabetes association recommends that they should be diagnosed if they are overweight for their age, family history of type 2 diabetes mellitus, race or ethnicity is native American, African-American, Latino, Asian American, or of pacific islander descent and maternal history of diabetes when child was in utero. Once diabetes is identified further tests are needed to determine the type.[26]

There are different tests performed to diagnose diabetes mellitus. Blood is taken from the person to perform the test.

A1c is a test which measures average blood glucose over past 2 or 3 months.

Random blood sugar test is the test used to check blood glucose levels after eating and blood sugar values are expressed in milligrams of sugar per decilitre (mg/dl) or millimoles of sugar per litre (mmol/L). if the blood sugar levels are 200mg/dl or higher then it is diagnosed as diabetes particularly if person have symptoms like frequent urination or extreme thirst.

Fasting blood sugar test which is also called fasting plasma glucose is a test which measures blood sugar on an empty

stomach. Before performing this test should not eat or drink anything except water for 8hours before test. A blood sample is taken and test is performed. If blood glucose level is less than 100mg/dl (5.6 mmol/L) then it is normal condition. If the blood glucose levels are between 100 to 125mg/dl (5.6 to 6.9 mmol/L) then it is diagnosed as prediabetes. If the blood glucose levels are 126mg/dl (7mmol/L) or higher it is diagnosed as diabetes.

Oral glucose tolerance test is used to check blood glucose before and 2 hours after drinking something sweet to know how body handles sugar in body. In this test person need to fast overnight and then drink the sugary liquid and then blood sugar levels are tested for two hours. If blood sugar levels are less than 140mg/dl (7.8 mmol/L) then it is normal condition. If the blood glucose levels are between 140 to 199 mg/dl (7.8 mmol/L to 11.0 mmol/L) then it is diagnosed as prediabetes condition. If the blood glucose levels are more than 200mg/dl (11.1 mmol/L and above) after two hours it is diagnosed as diabetes.[27]

Management

Treatment options like type of insulin, dose and frequency of insulin administration, blood glucose goals, frequency of self-monitoring, use of injections, nutritional management, physical activity levels differ among patients. The diabetes care team should determine the regimen that best suits the patient individual qualities and conditions.[28]

The treatment of type 2 diabetes mellitus in young adults is different from adults because in young adults' treatment mainly focuses on decreasing insulin sensitivity with advancing sexual maturity, physical growth and ability to provide self-management.[29] Diet and exercise for metabolic control are found to be effective in less than 10 percent of youth with type 2 diabetes and an oral medication or insulin is preferred. As onset of action of metformin is delayed about four weeks, patients with ketoacidosis, substantial ketosis or remarkable elevated blood glucose levels initially treatment is started with insulin and after blood glucose levels are controlled and symptoms subside metformin should be added and insulin may be stopped or discontinued if metabolic control is maintained.[30] In young adults increase in overweight is due to increased consumption of beverages with a high sugar content, reduction in physical activity and long hours watching television. Young adults with high BMI should be counselled to increase physical activity and reduction in weight gain. [28]

Adults with early-stage type 2 diabetes were 80% bound to start insulin treatment than those with usual onset type2 diabetes.

Basal-bolus treatment utilizing a combination of long-or intermediate acting and short-acting insulin gives adaptability and can further develop A1C levels. Insulin pumps can give considerably greater adaptability; however, they cost more and require more training for accurate use. Fixed-dose regimens give little adaptability and may not fit the way of life of young people. A pre-prandial insulin bolus depends on an insulin: carbohydrate proportion, and an insulin-adjustment portion should be administered for hyperglycaemia. Further adjustment of insulin or food intake might be required in anticipation of exceptional conditions like increase exercise. Patients should self-screen their blood glucose level before meals and at sleep time.[28]

All adolescent with type 2 diabetes and their families should receive exhaustive diabetes self-administration instruction/support that is support to youth with type2 diabetes and is socially competent.

Initial treatment of youth-beginning sort 2 diabetes should incorporate metformin as well as insulin alone or in combination, in view of the metabolic status of the patient. Starting treatment of the adolescent with obesity and diabetes should consider that diabetes type is frequently uncertain in the initial few weeks of treatment attributable to overlap in presentation and that a significant level of youth with type 2 diabetes will give clinically critical ketoacidosis. [31] Consequently, immediate treatment should address the hyperglycaemia and related metabolic confusions regardless of extreme diabetes type, with adjustment of treatment once metabolic compensation has been laid out and subsequent information, for example, immune response results, becomes available.[14]

Metformin is the preferred medication for initial treatment of type 2 diabetes in adults and youth. Asymptomatic youth with hypothetical type 2 diabetes who present in a stable metabolic state and have A1C <8.5% should to be started on metformin as initial treatment assuming that renal capacity is ordinary.[32] Asymptomatic patients with A1C ≥8.5% may likewise be given an underlying preliminary of metformin monotherapy at the prudence of the medical services supplier, particularly assuming that the patient and family circumstance propose the guarantee of brilliant adherence to way of life change suggestions. The prescribed way to deal with metformin initiation is to start with a dose of 500-1,000 mg/day and steadily raise it every 1 to 2 weeks, depending upon patient tolerability, to the suggested therapeutic dose of 1,000 mg b.i.d. More slower dose acceleration might be required assuming gastrointestinal side effects occur and, at times, the maximum dose may not be reachable. Extended-release metformin might have less gastrointestinal side effects and be more helpful for the patient, however there are no examinations in youth contrasting extended-release metformin with the standard metformin preparation.[14]

Youth with stamped hyperglycemia (blood glucose ≥250 mg/dL as well as A1C ≥8.5%) without acidosis at determination however who are indicative with polyuria, polydipsia, nocturia, and additionally weight reduction should be treated with at first with basal insulin while simultaneously initiating and titrating metformin. In patients with ketosis/ketoacidosis at diagnosis, treatment with subcutaneous or intravenous insulin should be started to quickly correct the hyperglycemia and the

metabolic insanity. Whenever acidosis is resolved, metformin should be started while subcutaneous insulin treatment is proceeded.[33]

Once glycemic stability is accomplished, insulin may not be required. limited information suggests that youths with type 2 diabetes who present at first with DKA, ketosis, or indicative hyperglycemia can be managed effectively with metformin alone, at first after a short course of insulin treatment to lay out glycemic stability.[34]

When the individualized glycemic target can never again be met with metformin alone, or if assuming metformin intolerance or renal deficiency develops, insulin treatment should be started. This should be possible alone or in combination with metformin, except if metformin is contraindicated. Since studies show that adherence with insulin treatment is a challenge in youth with type 2 diabetes, beginning with a single daily dose of a long-acting insulin analog ([glargine Lantus, Basalglar, Toujeo], detemir [Levemir], or degludec [Tresiba]) might be preferred. Premixed insulins might be suitable in some circumstances. The most significant adverse impact of insulin treatment in type 2 diabetes, as in type 1 diabetes, is hypoglycemia. Although the frequency of hypoglycemia in youth with type 2 diabetes is low, even with insulin treatment, patients treated with insulin should be taught about avoidance, acknowledgment, and treatment of hypoglycemia and should be instructed on the utilization of glucagon for treatment of extreme hypoglycemia. Likewise, since insulin might result in weight gain, association of a nutritionist in patient care and instruction is essential when insulin is started.[14]

Prevention

It is realized that T2DM is an ever-evolving disease that usually starts a very long time preceding clinical determination with an increase in insulin obstruction a period compensatory hyperinsulinemia and then a decrease in pancreatic capacity with decline in insulin secretion.[35]

Some life style modifications are needed like losing certain amount of weight.

Effective nonpharmacological involvement in prevention of type 2 diabetes mellitus includes increase in daily activity and decreasing caloric intake and increasing muscle mass. some researchers also included psychological and social support involvement intended to strengthen initiating and maintaining health behaviour.[36]

CONCLUSION

Young onset Type 2 diabetes mellitus is a progressive disease that can be prevented through life style management, maintaining diet, control overweight and obesity. Education of people is still key to control of this arising pandemic. Even though there are new concepts into pathophysiology of disease there is no cure of the disease and new medications are also being developed. Life style modifications can benefit the prevention or delaying in progression of type 2 diabetes mellitus. Regular usage of medications and life style modifications for diabetes should be maintained to improve quality of life of individuals.

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Source of Support: The author(s) received no financial support for the research, authorship, and/or publication of this article.

Conflict of Interest: The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.