ISSN-E: 2617-9563

“Diabetes mellitus in children”

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ISSN-E: 2617-9563

Abstract:
Context: the outlook for kids with type 1 diabetes is dismal. Those who do receive a diagnosis often have a short life expectancy (less than a year). The purpose of this study was to determine what characteristics of children and adolescents with type 1 diabetes were associated with better glucose management.
A hospital-based cross-sectional study was conducted with 76 children and adolescents (41 girls and 35 boys, mean age 15.1 3.1 years) with type 1 diabetes who were enrolled in the "Changing Diabetes in Children" (CDiC) programme and were seen at the clinics for children living with type 1 diabetes.
Results: The study population had a mean HbA1c of 10.3 ± 2.9%. There was a significant decrease in the mean HbA1c from diagnosis (11.1%) to the study period (10.3%) (p = 0.011). Multivariate analysis indicated that having a mother as the primary caregiver (OR 0.02, 95% CI 0.002 – 0.189) and minimal/moderate caregiver involvement in insulin injection (OR 26.8, 95% CI 4.4 – 56.1) were independent predictors of glucose control

الملخص:
السياق: النظرة المستقبلية للأطفال المصابين بداء السكري من النوع الأول قاتمة. غالبًا ما يكون متوسط العمر المتوقع لأولئك الذين يتلقون التشخيص قصيرًا (أقل من عام). كان الغرض من هذه الدراسة هو تحديد خصائص الأطفال والمراهقين المصابين بداء السكري من النوع الأول والتي ارتبطت بإدارة أفضل للجلوكوز.
أجريت دراسة مقطعية مستعرضة في المستشفى على 76 طفلاً ومراهقًا (41 فتاة و 35 فتى ، متوسط العمر 15.1 3.1 سنة) مصابين بداء السكري من النوع 1 والذين تم تسجيلهم في برنامج "تغيير مرض السكري عند الأطفال (CDiC) "وشوهدوا في عيادات الأطفال المصابين بداء السكري من النوع الأول.
النتائج: كان لدى مجتمع الدراسة متوسط HbA1c 10.3 ± 2.9٪. كان هناك انخفاض كبير في متوسط HbA1c من التشخيص (11.1٪) إلى فترة الدراسة (10.3٪) (p = 0.011). أشار التحليل متعدد المتغيرات إلى أن وجود أم كمقدمة رعاية أولية (OR 0.02، 95٪ CI 0.002 - 0.189) ومشاركة مقدم الرعاية الأدنى / المعتدل في حقن الأنسولين (نسبة الرجحان 26.8 ، 95٪ CI 4.4 - 56.1) كانت تنبئًا مستقلاً عن التحكم في الجلوكوز.

1. Introduction:

One of the most common metabolic diseases, diabetes mellitus (DM) has been on the rise worldwide in recent decades. Type 2 diabetes mellitus (DM2) is the most common form and is characterized by insulin resistance and an inadequate compensatory response of insulin secretion. Type 1 diabetes mellitus (DM1) is characterized by progressive absolute insulin deficiency and can be identified by genetic and pancreatic islet autoimmunity markers.

Diabetic ketoacidosis, hyperosmolar hyperglycemic state, and chronic microvascular (retinopathy, nephropathy, peripheral and autonomic neuropathy), and macro vascular (coronary atherosclerotic vascular, cerebral and peripheral vascular disease) complications negatively impact the quality of life and survival of patients with diabetes and are part of the disease's natural history. About 1 million individuals every year, primarily in low-income regions, lose their lives to this disease. (Neu, A., et.al, 2019)

This article's goals are to (1) raise awareness about the alarming rise in the number of children diagnosed with diabetes, and (2) provide an up-to-date overview of the disease's pathophysiology, progression, and control in order to aid in the preparation of response strategies to what is likely to become a major public health issue in the near future.

Types of diabetes mellitus (diabetes) in children are like those in adults, but children also have unique psychosocial challenges that can make managing their condition more difficult.

Two-thirds of all newly diagnosed cases of childhood diabetes are of the type 1 variety. One in every 350 children will be diagnosed by age 18; the frequency has recently been rising, especially in children younger than 5 years old, making it one of the most frequent chronic childhood disorders. Type 1 diabetes can develop at any age, but it is most common in children between the ages of 4 and 6 and again between the ages of 10 and 14.

Although previously uncommon, type 2 diabetes in children has been on the rise alongside childhood obesity rates (see obesity in children). Symptoms are most common after adolescence, specifically between the ages of 15 and 19. (see obesity in adolescents). (Pereira, P. F., et.al, 2014)

Previously known as MODY, monogenic forms of diabetes are rare (between 1 and 4 percent of all occurrences) and distinct from types 1 and 2.

Prediabetes is characterized by blood glucose levels that are higher than normal but do not yet meet diagnostic criteria for diabetes due to poor glucose regulation. However, in teenagers who continue to gain weight, prediabetes is more likely to develop into full-fledged diabetes rather than resolving on its own (reversal to normal after 2 years in 60% of those with prediabetes). The metabolic syndrome is linked to prediabetes (impaired glucose regulation, dyslipidemia, hypertension, obesity). (Nadella, S., et.al, 2017)

2. Causes of Type 1 and Type 2 Diabetes in children:

Patients are typically classified as having either type 1 or type 2 diabetes, with the latter being the more common kind and the one used to determine therapy. This classification system takes into account the patient's clinical history (age, family history, body habitus), clinical presentation, and laboratory results (antibodies). However, this system of categorization does not perfectly capture the clinical diversity of patients, and some people cannot be definitively categorized as having type 1 or type 2 diabetes at diagnosis. A progressive decrease of beta-cell activity leading to hyperglycemia is a hallmark of both type 1 and type 2 diabetes, and it can be caused by both hereditary and environmental factors.

Insulin production is severely reduced or eliminated in persons with type 1 diabetes due to the autoimmune death of pancreatic beta-cells, which may be initiated by environmental exposure in those who are genetically predisposed. The overall incidence of diabetes is between 4% and 8% (30% to 50% in monozygotic twins), however the risk is enhanced by 15 times for people who are close relatives. Young people with type 1 diabetes are more likely to develop other autoimmune diseases, including thyroid disease and celiac disease. Type 1 diabetes susceptibility is inherited and is determined by a large number of genes (about 60 risk loci have been discovered). The increased incidence of type 1 diabetes in some racial and ethnic groupings can be explained by the greater frequency of susceptibility genes among those ethnicities (eg, Scandinavians, Sardinians). (Dabelea, D., et.al, 2014)

The pancreas secretes insulin in people with type 2 diabetes, but the amount produced isn't enough to fulfil the body's increasing need due to insulin resistance (ie, there is relative insulin deficiency). Hyperglycemia symptoms in teenagers who have previously been compensated for their condition are commonly seen during the time of onset, which coincides with the peak of physiological pubertal insulin resistance. Instead of being caused by the body's immune system attacking and destroying beta cells, the condition results from the cumulative effects of a wide range of genetic and environmental factors.

Type 2 diabetes is distinct from both type 1 and type 2 diabetes in children and is also distinct from type 2 diabetes in adults. Beta-cell dysfunction and the onset of diabetes-related problems progress more rapidly in young people.

Type 2 diabetes risk factors:

- Obesity
- Native American, Black, Hispanic, Asian American, and Pacific Islander heritage
- Family history (60 to 90% have a 1st- or 2nd-degree relative with type 2 diabetes)

Patients with monogenic diabetes usually have a family history of the disease since the underlying genetic abnormality is passed down in an autosomal dominant fashion. There is no beta-cell death by the immune system or insulin resistance, unlike in type 1 and type 2 diabetes. The majority of cases emerge prior to the age of 25. (Xu, G., et.al, 2018)

3. Developmental Pathophysiology of Childhood Diabetes:

Hyperglycemia and poor glucose utilization in skeletal muscle are hallmarks of type 1 diabetes, which is characterized by an insulin deficiency. In order to get the energy needed, the body breaks down muscle and fat. Ketones, which are produced when fat is broken down, can lead to academia and, in extreme cases, life-threatening acidosis (diabetic ketoacidosis [DKA]).

However, up to 25% of children with type 2 diabetes present with DKA, and even fewer with hyperglycemic hyperosmolar state (HHS), also known as hyperosmolar hyperglycemic nonketotic syndrome (HHNK), in which severe hyperosmolar dehydration develops. The risk of developing HHS increases at times of increased stress or infection, when patients deviate from their prescribed treatment plans, or when certain medications already have an adverse effect on glucose metabolism (eg, corticosteroids). At the time of diagnosis, type 2 diabetes may also be accompanied by other metabolic derangements, such as those linked with insulin resistance. (Ma, R. C. W., et.al, 2017)

- Dyslipidemia (leading to atherosclerosis) (leading to atherosclerosis)
- Hypertension
- Ovary cysts and polycystic ovary syndrome.
- Sleep apnea with obstruction
- Definition of NASH (nonalcoholic fatty liver disease) (fatty liver)

The risk of cardiovascular disease is greatly amplified by atherosclerosis, which often first appears in early adulthood but can sometimes begin in infancy and adolescence.

The underlying abnormality in monogenic causes of diabetes varies. Defects in transcription factors (such as hepatic nuclear factor 4-alpha [HNF-4-] and hepatic nuclear factor 1-alpha [HNF-1]) that regulate pancreatic beta-cell function account for the vast majority of cases. Hyperglycemia becomes more severe with age, insulin secretion is diminished but not lost, and there is no insulin resistance. Glucosidase defects are the cause of another type of inherited diabetes. Fasting hyperglycemia caused by glucosidase abnormalities is not significantly worsened by ageing and occurs despite normal insulin production and appropriate glucose tolerance. (Friedman, J. E., 2018)

4. Diabetic Signs and Symptoms in Children:

The first symptoms of type 1 diabetes can range from being asymptomatic (hyperglycemia) to being potentially fatal (diabetic ketoacidosis). However, symptomatic hyperglycemia without acidosis is much more common in children, and is characterized by polydipsia, polyuria, and frequency of urination that lasts for days to weeks. In children who are not yet toilet-trained, parents may notice an increase in the frequency of wet or heavy diapers as a symptom of polyuria. In addition to stunted growth, almost half of children who have enhanced catabolism also lose weight. Ketonemia can cause nausea, vomiting, and blurred vision (from the lens and vitreous humour being in a hyperosmolar condition), and it can also cause fatigue and weakness. (Ly, T. T., et.al, 2014)

Type 2 diabetes has a wide range of possible symptoms. Oftentimes, children show no symptoms or only mild ones, and the disease is only discovered through routine screening. Despite this prevalent misperception, some children have a severe form of symptomatic hyperglycemia (also known as HHS or diabetic ketoacidosis [DKA]).

4.1 Complications of diabetes in children:

Patients with type 1 diabetes often have diabetic ketoacidosis, with prevalence ranging from 1--10% annually. This is typically due to the patient failing to take their insulin as prescribed. Additional factors that increase the likelihood of developing DKA include previous bouts of DKA, stressful social situations, depression or other psychological problems, coexisting sickness, and the use of an insulin pump (because of a kinked or dislodged catheter, poor insulin absorption due to infusion site inflammation, or pump malfunction). Clinicians can aid in mitigating risk by disseminating information and offering guidance.

Children with diabetes and their families are disproportionately affected by mental health problems. There is a significant percentage of children (up to 50%) who suffer from some sort of mental health issue. Adolescents who are trying to manage their weight often suffer from eating problems and resort to unhealthy measures like skipping insulin

injections. Poor glycemic control can also stem from psychological issues that make it difficult for youngsters to follow their prescribed food and/or medication schedules. To better understand and treat the psychosocial factors that contribute to poor glycemic control, a multidisciplinary team should include social workers and mental health professionals. (Papatheodorou, K., et.al, 2018)

Symptoms of vascular problems almost never present themselves clinically in young children. However, poor glycemic control is the biggest long-term risk factor for the development of vascular problems in type 1 diabetes, and these changes in pathology and function may already be present a few years after the onset of the disease. Diabetes can cause a variety of microvascular problems, including as nephropathy, retinopathy, and neuropathy. Children with type 2 diabetes are more likely to experience microvascular complications than those with type 1 diabetes, and with type 2 diabetes, these consequences may already be apparent at diagnosis or early in the disease's progression. Although neuropathy is more common in children whose diabetes has been present for a long time (5 years) and whose condition is poorly managed (glycosylated hemoglobin [HbA1c] > 10%), it can also occur in young children whose diabetes has been present for a relatively short time and is well managed. A stroke, heart attack, or coronary artery disease are all examples of macro vascular problems. (Cameron, F. J., et.al, 2015)

5. Childhood diabetes diagnosis:

Diagnosis of diabetes and prediabetes in children and adolescents is similar to that in adults, and relies on the presence or absence of symptoms in addition to fasting or random plasma glucose levels and/or HbA1c levels (see Table: Diagnostic Criteria for Diabetes Mellitus and Impaired Glucose Regulation). Traditional diabetic symptoms and blood glucose levels can help doctors make a diagnosis of diabetes. Fasting plasma glucose 126 mg/dL (7.0 mmol/L); fasting is defined as no caloric intake for 8 hours. Random plasma glucose 200 mg/dL (11.1 mmol/L).

If diabetes can be diagnosed using other methods, an oral glucose tolerance test is unnecessary and should be avoided. When necessary, 75 grammes of glucose dissolved in water (1.75 g/kg) should be used for the test. The test has the potential to aid in the diagnosis of type 2 or monogenic diabetes in children who are symptom-free, have little symptoms, or whose symptoms are atypical.

For the most accurate diagnosis of type 2 diabetes, the HbA1c criterion should be used, and hyperglycemia should be verified. HbA1c screening test findings should be interpreted with caution, even though they are widely utilized for the diagnosis of type 2 diabetes in children. Several studies have questioned the validity of using HbA1c as a screening test because of its limited sensitivity for detecting children with dysglycemia, and the data favoring HbA1c as a screening tool are drawn from adults (prediabetes or diabetes mellitus). Alternative measures, such as fructosamine, may be more appropriate in children with hemoglobinopathies, such as sickle cell disease. (Dabelea, D., et.al, 2017)

5.1 Primitive testing and inspection:

An electrolyte and glucose blood test, together with a urinalysis, should be the first line of testing for patients suspected of having diabetes but who otherwise appear healthy. Calcium, magnesium, phosphorus, and hematocrit levels, as well as a venous or arterial blood gas, are also measured and tested for in patients who are critically ill. (Melillo, R., et.al, 2020)

5.2 Diagnosis of diabetes type:

Types of diabetes should be confirmed with other tests like

- levels of C-peptide and insulin (if not already taking insulin)
- A1c levels (if not already done)
- Pancreatic islet cell protein autoantibody testing

Glutamic acid decarboxylase, insulin, insulinoma-associated protein, and zinc transporter ZnT8 are among enzymes that can be targeted by autoantibodies. Over 90% of people with a new diagnosis of type 1 diabetes have at least one of these autoantibodies; in contrast, the absence of antibodies is highly predictive of type 2 diabetes. Ten to twenty percent of children with the type 2 diabetes phenotype have autoantibodies and are categorized as type 1 diabetes because they are more likely to need insulin therapy and are at greater risk of developing additional autoimmune illnesses.

Recognizing monogenic diabetes is crucial because its therapy is distinct from that of type 1 and type 2 diabetes. Children with a strong family history of diabetes who do not exhibit any of the classic features of type 2 diabetes, such as mild fasting (100 to 150 mg/dL [5.55 to 8.32 mmol/L]) or postprandial hyperglycemia, being young and not obese, and lacking autoantibodies or signs of insulin resistance, should be considered for the diagnosis (eg, acanthosis nigricans). Monogenic diabetes can be confirmed through genetic testing. Some types of monogenic diabetes can worsen with age, thus this screening is crucial. (Huffhines, L., et.al, 2016)

5.3 Testing for complications and other disorders:

Antibody testing for celiac disease, thyroxine, and thyroid antibodies should be performed on patients with type 1 diabetes to rule out the possibility of other autoimmune illnesses. It is recommended that subsequent testing for thyroid disease and celiac disease be performed every 1–2 years. There is no need for routine screening for other autoimmune disorders that may occur in children with type 1 diabetes, including primary adrenal insufficiency (Addison disease), rheumatologic disease (e.g. rheumatoid arthritis, systemic lupus erythematosus, psoriasis), other gastrointestinal disorders (e.g. inflammatory bowel disease, autoimmune hepatitis), and skin disease (e.g. vit

Because children with type 2 diabetes frequently have comorbidities such as fatty liver, hyperlipidemia, and hypertension at diagnosis (unlike those with type 1 diabetes, in whom complications develop over many years), it is important to perform liver tests, a fasting lipid profile, and a urine micro albumin: creatinine ratio at the time of diagnosis. It's especially important to check kids who show signs of complications:

- Check for nonalcoholic steatohepatitis if you're overweight
- If you snore or nod off throughout the day, you might have obstructive sleep apnea.
- If you have hirsutism, acne, or irregular periods, you may have polycystic ovary syndrome. (Wolraich, M. L., et.al, 2019)

5.4 Screening for diabetes:

Screening for type 2 diabetes or prediabetes by testing HbA1c is recommended for children at risk who are asymptomatic and less than 18 years old. This screening should begin at the age of 10 (or earlier if puberty was experienced earlier) and be repeated every three years.

A child is at risk if they are overweight (BMI > 85th percentile for age and sex, or weight for height > 85th percentile) and have at least 2 of the following:

- History of type 2 diabetes among first- or second-degree relatives
- Afro-American, African-American, Hispanic, Asian, and Pacific Islander ancestry
- Telltale insulin resistance symptoms and related disorders (eg, acanthosis nigricans, hypertension, dyslipidemia, polycystic ovary syndrome, or small-for-gestational-age birth weight)
- Cases of diabetes or gestational diabetes in the mother. (Jonas, D. E., et.al, 2022)

6. children's Diabetic Care:

The goals of treatment are to normalize blood glucose levels while decreasing the number of hypoglycemia episodes and to prevent or delay the development and progression of problems; intensive education and treatment in childhood and adolescence may assist achieve these goals.

Certain socioeconomic characteristics are related to poor glycemic control and increased hospitalization rates. Low-income and non-Hispanic Black children continue to be at higher risk of complications and unfavorable outcomes due to poor glycemic control, despite technological advancements that have improved the quality of care and glycemic control for many patients with diabetes. Optimal glycemic control in children with type 1 diabetes may be affected by social determinants of health such as socioeconomic level, neighborhood and physical environment, dietary environment, health care, and social context. (Chiang, J. L., et.al, 2018)

6.1 Lifestyle modifications:

Some examples of healthy lifestyle changes that assist patients in general are:

- eating at set times and maintaining a steady caloric intake
- Reducing consumption of processed foods and animal fats
- The importance of doing more exercise

In most cases, it's preferable to refer to one's eating regimen as a "meal plan" or "good food selections" rather than Promoting heart-healthy diets that are low in cholesterol and saturated fats is the main focus.

Carbohydrate counting (in which parents estimate the quantity of carbohydrate in an upcoming meal and use that amount to determine the pre-prandial insulin dose) and basal-bolus regimens have altered the meal planning process for people with type 1 diabetes. There are no hard and fast rules on what a person should eat under this plan. Instead than prescribing a theoretically optimal diet that the child is unlikely to follow, meal plans are based on the child's real eating habits, and insulin dose is matched to actual carbohydrate intake. The insulin: carbohydrate ratio varies from person to person and also changes with factors including age, exercise level, sexual maturity, and duration of diabetes. The ability to precisely tailor insulin dosages has been made possible by recent technological developments. An approximate age guideline would be:

- From infancy up to five years old, 1 unit of insulin every 30 g of carbohydrate is recommended.
- Insulin dosage for children 6-12: 1 unit every 15 g of carbohydrate
- Insulin dosage for adolescents: 1 unit for every 5-10 grammes of carbohydrate

Patients with type 2 diabetes should be urged to lose weight to improve insulin sensitivity. Children between the ages of 3 and 13 have caloric needs that can be roughly estimated as 1000 + (100 child's age in years). Eating better and controlling weight can be as easy as taking the following steps.

- Reducing consumption of processed foods and beverages rich in added sugar (eg, processed candies and high fructose corn syrups)
- meal skipping is discouraged
- Reducing the size of meals and snacks
- Reducing access to high-calorie, high-fat foods Raising fibre consumption through increased consumption of fruits and vegetables. (Tuso, P., 2014).

6.2 Glucose and HbA1c target levels:

To strike a compromise between the necessity to normalize glucose levels and the danger of hypoglycemia, plasma glucose targets (see Table: Glucose and HbA1c Target Levels in Children and Adolescents with Type 1 Diabetes) are defined. The goal for patients after the honeymoon period (those without any remaining beta-cell function) is to have at least half of their blood glucose readings within the normal range (70–180 mg/dL [3.9–10 mmol/L]) and at least ten percent below range.

Age, length of diabetes, availability of diabetes technology (e.g., insulin pumps, continuous monitoring systems), comorbid conditions, and psychosocial situations should all be taken into account while setting treatment goals. Aggressive treatment efforts can be hampered by the possibility of hypoglycemia in children who either are ignorant of the condition or are too young to recognise its signs. HbA1c target levels 6.5% [48 mmol/mol] should be reserved for select patients in whom they may be achieved without substantial hypoglycemia and without detrimental affects on well-being, whereas a less strict target level (7.5% [58 mmol/mol]) should be explored for such patients.

Lower HbA1c levels during adolescence and young adulthood are associated with a lower risk of vascular problems, hence over time, the HbA1c target levels for children and adolescents with type 1 diabetes have been lowered in an effort to reduce complications. Even though most kids should have a HbA1c target of 7% (53 mmol/mol), a lot of kids and teens still don't. (Van Loocke, M., et.al, 2021)

HbA1c levels can be reduced through the use of continuous glucose monitoring (CGM) systems or increased self-monitoring of blood glucose levels (up to 6 to 10 times per day) because patients are better able to adjust insulin for meals, have an improved ability to correct hyperglycemic values, and possibly detect hypoglycemia earlier, preventing overcorrection (ie, excessive carbohydrate intake as treatment for hypoglycemia, resulting in hyperglycemia). When used correctly, CGM that is scanned intermittently can replace self-monitoring of blood glucose and insulin therapy.

The percentage of time that blood glucose levels are within the normal range (the time-in-range) is correlated well with HbA1c levels. Commonly used in conjunction with HbA1c, time-in-range is a treatment goal for evaluating the success of an insulin regimen. An adjustment of 0.8 percentage points in HbA1c is about equivalent to a 10% shift in time-in-range. HbA1c levels of 5.9% (41 mmol/mol), 6.7% (50 mmol/mol), 7.5% (58 mmol/mol), and 9% (75 mmol/mol) are all associated with time-in-ranges of 80%, 70%, 60%, and 40%, respectively (1).

CGM provides information related to adherence, information related to glycemic variability, information related to glucose management indicator, and information related to time-in-range in addition to information related to average sensor glucose, time-above-range (> 180 mg/dL [> 10 mmol/L]), and time-below-range (70 mg/dL [3.9 mmol/L]). In addition, CGM provides information related to time-in-range (eg, active CGM time, days worn). (DiMeglio, L. A., et.al, 2018)

It is recommended that CGM measurements generated from use over the most recent 14 days be utilised in conjunction with HbA1c level. Data obtained through CGM can be reported in a format that is standardised. The ambulatory glucose profile, often known as the AGP, is a standardised report that includes the mean glucose, the amount of time spent within range, and the amount of time spent below range. When utilising the AGP to monitor glycemia, a goal of time-in-range of > 70% with a time-below-range of 4% can be used as a glycemic control objective. This goal can be used in conjunction with the aim of a HbA1c target of 7% (53 mmol/mol), which is another glycemic control goal. In addition, there is a report known as the glucose management indicator, which calculates an estimated HbA1c based on the mean glucose levels measured by a CGM and uses data that is at least 14 days old.

The HbA1c target levels for children and adolescents with type 2 diabetes are the same as the targets for type 1 diabetes, which are less than 7% (less than 53 mmol/mol). In people who have type 2 diabetes, the target level of glucose in their blood while they are fasting should be less than 130 mg/dL (7.2 mmol/L). Children who do not meet the objectives for HbA1c and/or fasting glucose are potential candidates for enhanced treatment (eg, with insulin, liraglutide). Patients who have had diabetes for a shorter period of time and those who are treated with lifestyle interventions or metformin alone and achieve significant weight loss may be candidates for more stringent targets for

haemoglobin A1c (less than 6.5%, or less than 48 mmol/mol) and fasting blood glucose (less than 110 mg/dL, or less than 6.1 mmol/L). (Tansey, M., et.al, 2016)

6.3 Type 1 diabetes insulin regimens:

Insulin is essential to the treatment of diabetes type 1, the most severe form of the disease. The formulations of insulin that are available are very similar to those that are used in adults. Insulin should generally be administered prior to meals, with the exception of very young infants, whose food intake during any given meal can be difficult to anticipate. The appropriate dosage must be based on the patient's age, degree of activity, pubertal status, and the amount of time that has passed since the first diagnosis. Because they still have some beta cells functioning, many diabetic patients see a temporary reduction in the amount of insulin they need to take within the first few weeks after receiving their diagnosis (honeymoon phase). After this initial adjustment period, which can take anywhere from a few months to two years, insulin requirements will normally fall into the range of 0.7 to 1 unit/kg/day. Patients require greater doses (up to 1.5 units/kg/day) to counteract insulin resistance produced by increased pubertal hormone levels throughout puberty. This is because insulin resistance is induced by increasing pubertal hormone levels. (Šoupal, J., et.al, 2016)

Types of insulin regimens include:

- Treatment protocol including multiple daily injections (MDI) using a basal-bolus regimen
- Therapy with an insulin pump
- A regimen consisting of fixed forms of MDI or a regimen consisting of premixed insulin (less common)

In order to achieve better metabolic control, the majority of persons who have type 1 diabetes should be treated with MDI regimens (consisting of three to four injections per day of basal and prandial insulin) or insulin pump therapy as part of intensive insulin regimens.

The basal-bolus regimen is most often considered to be the optimal MDI regimen. In this treatment plan, children receive a daily baseline dose of insulin, which is subsequently supplemented by doses of short-acting insulin before each meal. These doses are determined by the predicted carbohydrate intake as well as the glucose levels that have been assessed. The daily basal dose can be administered as a single injection of a long-acting insulin (glargine, detemir, or degludec), and supplemental boluses can be administered as separate injections of rapid-acting insulin. For younger children, the basal dose may be administered more frequently than once every 12 hours (usually aspart or lispro). Injections of glargine, degludec, or detemir are not allowed to be coupled with rapid-acting insulin and are commonly administered before dinner or before going to bed.

In insulin pump therapy, the basal insulin is delivered at a rate that is either fixed or variable by a continuous subcutaneous infusion of rapid-acting insulin (CSII) through a catheter that is placed under the skin. CSII is an abbreviation for continuous subcutaneous infusion of rapid-acting insulin. In addition to delivering boluses for meals and corrections, the insulin pump also administers boluses. The basal dose helps keep blood glucose levels in range between meals and during night. The use of an insulin pump to administer the basal dose provides the user with the greatest amount of flexibility because the pump may be set to deliver a variety of different rates at various times throughout the day and night. (Yavuz, D. G., et.al, 2015)

When compared to MDI regimens, insulin pump therapy has the potential to provide greater benefits in terms of glycemic control, patient satisfaction, and safety. This makes it an increasingly popular treatment option for diabetic youngsters. This technique is generally favored for use with younger children (toddlers and preschoolers), as it provides an increased degree of control to a greater number of children as a whole. Some people find that using the pump is cumbersome, while others get sores or infections at the location where the catheter is inserted. In order to prevent lipohypertrophy in children, it is important to rotate the sites of injection and pump use. A condition known as lipohypertrophy is characterized by the buildup of fatty tissue lumps under the skin. Because they make it more difficult for insulin to be consistently absorbed into the body, the lumps tend to form at insulin injection sites that have been abused. This can lead to variations in the amount of glucose in the blood.

There is a trend away from using MDI regimens that have more rigid shapes. They are options that can be taken into consideration in the event that a basal-bolus regimen is not feasible (eg, because the family needs a simpler regimen, the child or parents have a needle phobia, lunchtime injections cannot be given at school or daycare). As part of this treatment plan, children often get an injection of neutral protamine Hagedorn (NPH) insulin before eating breakfast, dinner, and before going to bed, and they get an injection of rapid-acting insulin before eating breakfast and supper. This method requires fewer shots overall than the basal-bolus method since NPH and rapid-acting insulin can be combined into a single injection. However, this regimen offers less flexibility, necessitates a defined daily schedule for mealtimes and snacktimes, and has been mainly superseded by the analogue insulins glargine and detemir as a result of the reduced risk of hypoglycemia they present.

The preparations used in premixed insulin regimens are either 70/30 (consisting of 70% insulin aspart protamine and 30% regular insulin) or 75/25 (consisting of 75% insulin lispro protamine and 25% insulin lispro). Premixed regimens are not a good choice, but they are simpler and may improve adherence because they require fewer injections. This is because there are fewer injections to be administered. Children receive doses that are predetermined twice a day, with breakfast accounting for two thirds of the total daily dose and dinner accounting for one third. Premixed regimens, on the other hand, offer significantly less flexibility in terms of the timing and quantity of meals. Additionally, due to the fixed ratios, these regimens are less exact than other types of regimens.

In order to maximise glycemic control and thereby limit the risk of long-term vascular problems, clinicians should utilise the most intense management approach that children and their families are able to adhere to. (Mochizuki, M., et.al, 2017)

6.4 Controlling the side effects of type 1 diabetes:

Among children on an aggressive insulin regimen, hypoglycemia is a common but serious complication. Multiple episodes of moderate hypoglycemia occur often in youngsters, and most of them treat themselves with 15 g of fast-acting carbs (eg, 4 oz of juice, glucose tablets, hard candies, graham crackers, or glucose gel).

About 30% of children each year experience hypoglycemia, with most having had an episode by the age of 18. Severe hypoglycemia is defined as an episode requiring the aid of another person to provide carbs or glucagon. If neuroglycopenic symptoms (such as erratic behaviour, confusion, or trouble concentrating) prevent you from taking in any food or liquids, you could try taking some carbohydrates orally. Seizures, unconsciousness, and even death can result from untreated hypoglycemia. When a child's blood sugar drops below a certain threshold or drops rapidly, a real-time continuous glucose monitor can sound an alarm and save their life (see Monitoring glucose and HbA1c levels). (McKnight, J. A., et.al, 2015)

Intercurrent sickness is the most common cause of ketonuria/ketonemia, but insufficient insulin treatment or missed doses can also lead to this complication. Early detection of ketones in the urine or capillary blood using ketone test strips is important for preventing the development of diabetic ketoacidosis and reducing the likelihood of a kid or family member requiring admission to an emergency room or hospital. Testing for ketones in the blood rather than the urine may be the preferred method in certain cases, including in younger children, individuals with recurrent DKA, insulin pump users, and those for whom collecting a urine sample is problematic. If your child becomes unwell (regardless of their blood sugar level) or if their blood sugar is abnormally high (usually > 240 mg/dL [13.3 mmol/L]), you should have them tested for ketones. When combined with other symptoms such as abdominal discomfort, vomiting, drowsiness, or rapid breathing in children, a urine ketone level of 1.5 mmol/L or higher, or a blood ketone level of > 1.5 mmol/L, can indicate DKA. Ketone levels in the blood or urine that are below 1.5 mmol/L also need to be addressed.

When ketones are detected, additional short-acting insulin is given to the child every two to three hours (usually 10 to 20 percent of the entire daily dose) until the ketones are gone. It's important to prevent dehydration, thus extra fluids should be given as well. Sick-day management refers to the process of monitoring blood ketones and administering extra fluids and insulin when a person is ill and/or hyperglycemic. If the child's clinical status worsens, or if ketones worsen or don't resolve after 4 to 6 hours, parents should phone their doctor or head to the emergency room (eg, respiratory distress, continued vomiting, change in mental status). (Fisher, L., et.al, 2015)

6.5 Type 2 diabetes treatment:

Modifying one's diet and level of physical activity are crucial, just as they are for people with type 1 diabetes.

Children with more advanced diabetes (HbA1c > 9% [> 75 mmol/mol]) or DKA are begun on insulin therapy, which may involve glargine, detemir, or premixed insulin. Metformin is typically initiated concurrently if acidosis is absent. As endogenous insulin production improves during the first weeks of treatment, insulin doses may be reduced rapidly; in many cases, insulin may be discontinued few weeks after achieving satisfactory metabolic control.

Only metformin, an insulin sensitizer, is currently FDA-approved for use in individuals with hyperglycemia who are younger than 18. Some teenagers may benefit from the use of other oral medications approved for adults, although these options are more expensive and there is less data supporting their use in young people. To reduce the risk of side effects including nausea and diarrhoea, metformin should be taken at a low dose at first. The recommended starting dose is 500 mg once daily for 1 week, with subsequent increases of 500 mg per week for the following 3 to 6 weeks until the maximum target dose of 1000 mg twice day is reached. Maintaining a HbA1c level of 7% (53 mmol/mol) is the target of treatment, with a target of 6.5% (48 mmol/mol) being optimal. If metformin alone is insufficient, basal insulin or liraglutide should be added to the treatment plan. About half of adolescents with type 2 diabetes who initially respond to metformin alone end up needing insulin. Rapid-acting prandial insulin may be added to the treatment plan if individuals still aren't meeting their goals while on metformin and basal insulin combination therapy.

HbA1c levels can be lowered with the use of glucagon-like peptide-1 (GLP-1) receptor agonists such liraglutide and extended-release exenatide in children and adolescents aged 10 and up with type 2 diabetes. Injectable noninsulin antihyperglycemics like these decrease gastric emptying and increase insulin release in response to elevated blood sugar levels. 0.6 mg of subcutaneous liraglutide once daily is the starting dose, with 0.6 mg weekly increases possible up to 1.8 mg once day if needed for control. Patients may be more likely to take their weekly subcutaneous 2 mg dose of extended-release exenatide. Weight loss is facilitated by both medications, possibly through reduced appetite and delayed stomach emptying. Nausea and vomiting are the most prevalent gastrointestinal side effects of GLP-1 agonists. If HbA1c goals aren't fulfilled after 3 months of treatment with metformin alone, liraglutide and exenatide can be administered instead or in addition. The aggressive treatment of type 2 diabetes may include the use of liraglutide and exenatide instead of or in addition to insulin. (Marín-Peñalver, J. J., et.al, 2016)

7. Methods:

7.1 Study design/ population:

All children and adolescents ages 0-18 who visited the hospital's clinics for young people with diabetes throughout the study's January through August data collection period were included in this cross-sectional study. This kind of clinic was established to keep an eye on these kids and give them the care they need. These clinics also provide education for patients and their loved ones on how to better manage glucose levels.

7.2 Sample size:

The primary purpose of this research was to use binary logistic regression to determine characteristics that predict successful glucose management among children with type 1 diabetes. This study's sample size was calculated using Hsieh's sample size formula/tables, which rely on dichotomous covariates and a dichotomous dependent variable to determine sample sizes229, 230. HbA1c, an indicator of glucose control, was used as the primary outcome variable (Y) in this study, with values of 0 indicating optimal control and 1 indicating suboptimal control of glucose levels. BGM adherence, a key dichotomous covariate (X) in our investigation, was also given values of 0 and 1 to represent good BGM adherence and poor BGM adherence, respectively.

7.3 Statistical analysis:

SPSS 20.0 for Windows was used for the statistical analysis. Kolmogorov-Smirnov (K-S) tests were performed to check the normality of continuous variables. By using the WHO AnthroPlus programme, the anthropometric variables (height, weight, and BMI) were adjusted for age and gender using Z scores.

8. Results:

This study included 76 children and adolescents (35 boys and 41 girls) and 73.7% had been living with diabetes for more than 2 years. Gender distribution in the first age tertile was almost equal, while there was unequal distribution of boys and girls in the other age tertiles. Table 3.1 shows the main characteristics of the study population. More than 50% of the study participants were females. The mean age at diabetes diagnosis was 15.1 (95% CI 14.4 – 15.8) years with girls having a slightly higher mean age at diagnosis compared to boys (15.4 ±2.6 vs 14.8 ±3.7 years). However, this was not statistically significant. The mean duration of diabetes for the study population was 3.8 (95% CI 3.1 – 4.5) years. Also, a majority of the study participants were living with both biological parents, had a mother as the primary caregiver and received three or more insulin injections daily. In addition, more than 80% of the patients were of low/middle socioeconomic status with a majority of them from the rural area. In addition, 2 patients said they had visited a herbalist for the treatment of diabetes.

Variables	N	Frequency		Mean	(95%CI)
		%	(95%CI)		
Age Tertiles				15.1	(14.4 – 15.8)
First tertile (4 – 14 years)	25	32.9	(23.4 – 44.1)		
Second tertile (15 – 16 years)	25	32.9	(23.4 – 44.1)		
Third tertile (> 16 years)	26	34.2	(24.5 – 45.4)		
Gender					
Male	35	46.1	(35.3 – 57.2)		
Female	41	53.9	(42.8 – 64.7)		
Body mass index (BMI) (kg/m^2)				23.3	(22.1 – 24.5)
Underweight (< 18.5)	6	7.9	(3.7 – 16.2)		
Normal (18.5 – 25.0)	52	68.4	(53.7 – 77.8)		
Overweight + obese (> 25.0)	18	23.7	(15.5 – 34.4)		
Family structure					
Both parents living together	46	60.5	(49.3 – 70.8)		
Single parent	17	22.4	(14.5 – 32.9)		
Not living with parents	8	10.5	(5.4 – 19.4)		
Orphan	5	6.6	(2.8 – 14.5)		
Primary caregiver					
Mother	45	59.2	(48.0 – 69.6)		
Father	10	13.2	(7.3 – 22.6)		
Sibling	9	11.8	(6.4 – 21.0)		
Other	12	15.8	(9.3 – 25.6)		
Caregiver education					
No formal education	16	21.1	(13.4 – 31.5)		
Primary school	20	26.3	(17.7 – 37.2)		
Secondary/High school	29	38.2	(28.1 – 49.4)		
University	11	14.4	(8.3 – 24.1)		
Duration of diabetes (years)				3.8	(3.1 – 4.5)
< 2	20	26.3	(17.7 – 37.2)		
2 – 5	37	48.7	(37.8 – 59.7)		
> 5	19	25.0	(23.4 – 44.1)		
Insulin Regimen					
2 daily injection	31	40.8	(30.4 – 52.0)		
Multiple daily injection	45	59.2	(48.0 – 69.6)		
Degree of urbanization					
Urban	30	39.5	(29.3 – 50.7)		
Rural	46	60.5	(49.3 – 70.8)		
Socioeconomic status					
Low	53	69.7	(58.7 – 78.9)		
Middle	9	11.8	(6.4 – 21.0)		
High	14	18.4	(11.3 – 28.6)		

We found that among the patients in our sample, 18.4 percent kept their insulin in the refrigerator, 51.3% kept it in a pot of charcoal/sand or cold water, and 30.3 percent kept it at room temperature.

Although individuals who kept their insulin in the refrigerator had better glycemic control (10.8%, 95% CI 9.9 - 11.8) than those who kept their insulin in a pot of charcoal/sand or cold water, the difference was not statistically significant (p = 0.265). Glycemic control appeared to be equivalent across individuals who refrigerated their insulin and those who left it at room temperature.

Adolescents' mean score on a knowledge assessment of diabetes was 65.4% (SD 14.6%), and this score rose in a linear fashion with increasing diabetes duration. In spite of it, it was inconsequential. The following table summarises the findings of an evaluation of adolescents' knowledge of diabetes. The teen's educational background also played a role

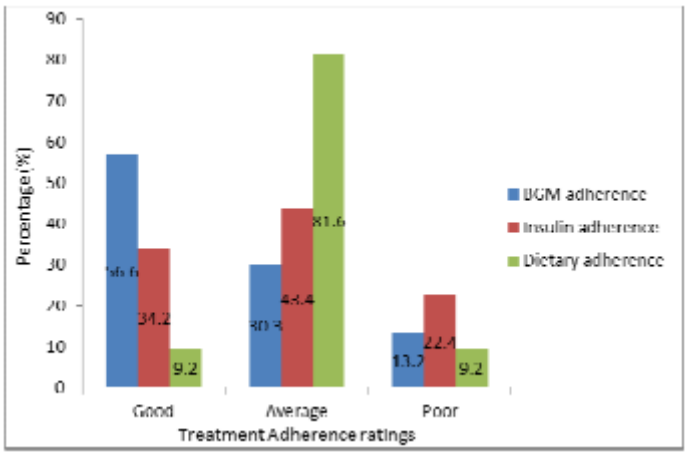
in how well they understood diabetes. In comparison to adolescents who had completed an appropriate level of education for their age, those who had not completed formal education or who had dropped out of school had a lower mean score on the diabetes knowledge exam. The significance of HbA1c in the therapy of T1D was also understood by all the teenagers. However, being aware of HbA1c levels had no effect on glycemic management.

Diabetes characteristics	Score		*p*-value*
	Mean (%)	95%CI	
Age tertiles			
First	65.9	(62.1 – 69.7)	0.367
Second	62.2	(59.1 – 65.3)	
Third	67.9	(64.9 – 70.8)	
Duration of diabetes			
< 2 years	59.2	(51.6 – 66.7)	0.079
2 to 5 years	67.5	(63.5 – 71.6)	
> 5 years	67.7	(60.1 – 75.2)	

All the kids and teens who visited the clinic had access to insulin thanks to the CDiC initiative. However, 14.5 percent of the kids and teens in the survey said they had forgotten to pick up their insulin at least once in the previous three months.

In addition, 11.8 percent of people stated they would be able to buy insulin in the event of a shortage at the clinic.

How regularly people follow their prescribed treatments. Less than 40% of the study population had good insulin adherence, whereas 22.4% had poor adherence. More than half of the people in the research also had good BGM adherence. Most patients (81.6%) followed the clinic's recommended diet plan to an average degree. It was also discovered that most teenagers had trouble lowering their carbohydrate intake.



9. Discussion:

The primary goal of treating type 1 diabetes is to keep blood sugar levels within a healthy range, as this reduces the risk of both immediate and long-term problems. However, the patient, their family, and the healthcare practitioner still face difficulties in the management of type 1 diabetes in children and adolescents. Optimizing glycaemic control is emphasised in the current guidelines for managing the condition to lessen the chances of both immediate and long-term consequences.

The goal of this research is to determine what characteristics of kids with type 1 diabetes are associated with tight glucose control. This research shows that having a mother as the primary carer for a kid with type 1 diabetes increases the likelihood that the child will maintain good glycemic control. Multivariate analysis further demonstrated that children whose caretakers were only mildly involved in the insulin injection process were at increased risk for poor glycemic control as shown by HbA1c.

The current treatment standard for patients with type 1 diabetes involves many daily injections of insulin, as was the case in our trial.

Surprisingly, greater glucose control was seen with twice-daily insulin injections compared to three or more injections each day. Even though this seems illogical at first, it may indicate that children who were not well controlled were the ones who were converted to numerous daily injections of insulin, as the "default" therapy is twice-day injections. The reasons why paediatric patients were shifted to receiving several injections were not documented.

Research has shown that a patient's HbA1c level can be predicted by the frequency with which they attend their diabetes clinic. In our research, we found that the more often a patient saw their doctor, the better they were able to

keep their blood sugar levels under control. Patients who do not attend appointments as scheduled are more likely to experience treatment noncompliance and develop diabetes-related problems. Regular checkups with a doctor enable for more frequent insulin dosage adjustments and more educational opportunities, if needed.
Similar to how frequent visits to the diabetes clinic have been shown to enhance glycaemic management in most but not all studies.

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