

# Dental Care and Treatment of Children with Diabetes Mellitus - An Overview

## Abstract

Dental management of diabetic children aims at implementation of a preventive protocol, symptomatic relief of any oral manifestations of the disease and immediate provision of primary care. Appointments should be short, stress free and as traumatic as possible. Early morning appointments are preferred and patients should eat normal breakfast before appointment to prevent hypoglycemia. Conscious sedation is preferred over deep sedation. Insulin regimens should be adjusted by the diabetologist. Use of pulp capping and pulpotomy procedures in primary teeth is questionable in children with uncontrolled diabetes but vital pulp therapy may be preferred to a stressful extraction procedure under local anesthesia. In a non-vital tooth with evidence of infection, extraction is the only treatment of choice. Fixed or removable orthodontic appliances may be ideal, depending on the periodontal health of the patient. Prophylactic antibiotics may be recommended before surgical procedures. Vasoconstrictor drugs with local anesthesia to ensure profound anesthesia are advocated, but excessive adrenaline dosage is contraindicated to prevent an increase in blood glucose levels and for this reason glucocorticosteroids should be avoided. This article discusses an overview of the pathophysiology, signs, symptoms, diagnosis and treatment of diabetes as well as dental treatment considerations for children with diabetes.

**Keywords:** Children, Diabetes mellitus, Oral health, Management, Dental considerations

## Research Article

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**Abbreviations:** DM: Diabetes Mellitus; WHO: World Health Organization; IDF: International Diabetes Federation; GDM: Gestational Diabetes Mellitus; HbA<sub>1c</sub>: Glycated Haemoglobin Assay; CGM: Continuous Glucose Monitoring; MNT: Medical Nutrition Therapy; ROS: Review Of Systems; AAP: American Academy of Pediatrics

## Introduction

Diabetes mellitus (DM) is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action or both [1]. There is an increase in the prevalence of type 1 diabetes also, but the main cause of diabetic epidemic is type 2 diabetes mellitus, which accounts for more than 90 percent of all diabetes cases. World Health Organization (WHO) reported, India had 32 million diabetic people in the year 2000 [2]. The International Diabetes Federation (IDF) estimates the total number of diabetic subjects to be around 40.9 million in India and this is further set to rise to 69.9 million by the year 2025 [3]. The majority of cases of diabetes fall into two broad etiopathogenic categories now called type 1 and T2 DM.

It is important to note that the terms "juvenile-onset diabetes", "adult-onset diabetes", "insulin-dependent diabetes", "non-insulin-dependent diabetes", and acronyms IDDM and NIDDM no longer are used. The terms "type 1 DM" and "type 2 DM" are retained and should be written with Arabic rather than Roman numerals [4].

## Prevalence

Prevalence of DM has been steadily increasing in the United States. An estimated 6% of the US population has DM. Approximately 8 lakhs new cases are diagnosed each year. It is important for the dental practitioner to be aware of medical and dental considerations for this expanding patient population. Prevalence of diabetes in adults worldwide was estimated to be 4% in 1995, and is predicted to rise to 54% by the year 2025. In developing countries, the majority are in the age range of 45–64 years. In the developed countries, the majority of people with diabetes are aged 65 years. There are more women than men with diabetes [5].

## Etiologic Classification of DM

The American Diabetes Association's Expert Committee (1999) [1] classified DM based on the disease etiology as follows:

- i. Type 1 DM
- ii. Type 2 DM
- iii. Gestational diabetes mellitus and Other specific types

## Type 1 DM

It constitutes 5 to 10% of DM cases. Usually results from autoimmune destruction of the insulin-producing beta cells of the pancreas. It most commonly presents in childhood but one-fourth of cases are diagnosed in adults. But it can occur in any age and generally leads to absolute insulin deficiency. The incidence

of type 1 diabetes varies depending upon various factors like age, family history, environmental factors etc. Incidence rates in children <14 years ranging from 0.1/100,000 per year in China to 37/100,000 per year in Finland [6]. The incidence of childhood type 1 disease is rising worldwide, with reported annual increases of 2 to 5 percent in Europe, the Middle East, and Australia [7]. Symptoms are caused by hyperglycemia and include polyuria, polydipsia, and weight loss despite increased appetite initially. Children with type 1 diabetes often present with diabetic ketoacidosis (hyperglycemia and ketoacidosis). These patients have a high incidence of severe complications, including diabetic ketoacidosis and are also prone to other autoimmune disorders, such as Graves's disease, Hashimoto's thyroiditis and Addison's disease.

### Type 2 DM

It constitutes 90 to 95 % of DM cases. It usually begins as insulin resistance, a disorder in which the cells do not use insulin properly. As the need for insulin rises, the pancreas gradually loses its ability to produce insulin. Type 2 diabetes is associated with older age, obesity, family history of diabetes, history of gestational diabetes, impaired glucose metabolism, physical inactivity, and race/ethnicity. African Americans, Hispanic/Latino Americans, American Indians, and some Asian Americans are at particularly high risk for type 2 diabetes. Type 2 diabetes is increasingly being diagnosed in children and adolescents. Hyperosmolar non-ketotic acidosis may result due to prolonged hyperglycemia [4]. T2DM frequently goes undiagnosed for many years because the hyperglycemia develops gradually and in the earlier stages is not severe enough to produce the classic symptoms of diabetes; however, such patients are at increased risk of developing macrovascular and microvascular complications. The classic symptoms of polyuria, thirst, recurrent blurred vision, paresthesias, and fatigue are manifestations of hyperglycemia and osmotic diuresis and are present late in the course of disease. T2 DM is now considered to be a facet of Syndrome X (Reaven's syndrome) comprising of hyperinsulinemia, dyslipidemia, hypertension and hyperglycemia [1].

### Gestational Diabetes Mellitus (GDM)

A form of glucose intolerance that is diagnosed in some women during pregnancy. It is more common among obese women and women with a family history of diabetes. During pregnancy, gestational diabetes requires treatment to normalize maternal blood glucose levels to avoid complications in the infant. After pregnancy, 5% to 10% of women with gestational diabetes are found to have type 2 diabetes. In majority of cases, the glucose regulation will come to normal after delivery. Women who have had gestational diabetes have a 20% to 50% chance of developing diabetes in the next 5-10 years [4].

### Other Specific Types

These are relatively uncommon. They result from specific genetic conditions (such as maturity-onset diabetes of youth), surgery, drugs (glucocorticoids, thiazides), malnutrition, infections, and other illnesses. Excess amounts of cortisol, glucagon, epinephrine and growth hormone cause DM in people with pre-existing defects in insulin secretion. This type of diabetes

may account for 1% to 5% of all diagnosed cases of diabetes [1].

### Pathophysiology

Usually blood glucose levels are maintained within a range of 60-150 milligrams per deciliter, or mg/dl in healthy people throughout the day. Insulin plays a very important role in the regulation of blood glucose. Insulin is synthesized in the beta cells of the pancreas and is secreted rapidly into the blood in response to elevations in blood sugar such as after meal. Insulin serves the following functions such as it maintains glucose homeostasis by promoting uptake of glucose from blood into cells by its storage in the liver as glycogen. It also promoted the uptake of fatty acids and amino acids and their subsequent conversion into triglyceride and protein stores. Lack of insulin or insulin resistance which is seen in DM, results in an inability of insulin dependent cells to use blood glucose as an energy source. Stored triglycerides are broken down into fatty acids, which serve as an alternate source of fuel and an elevation in blood ketones leads to diabetic ketoacidosis. As blood glucose level is elevated (hyperglycemia), glucose is excreted in the urine and excessive urination (polyuria) occurs because of osmotic diuresis. Increased fluid loss leads to Dehydration and excessive thirst (polydipsia). Since cells are starved of glucose, there will be increased hunger (polyphagia) and cells are unable to take up glucose the diabetic patient frequently loses weight and these are the classic signs and symptoms of DM [1] (Figure 1).

### Complications

People with DM have an increased incidence of both microvascular and macrovascular complications.

- a. Acute complications
  - a. Ketoacidosis
  - b. The hyperglycemic hyperosmolar nonketotic syndrome
  - c. Hypoglycemia
- b. Chronic complications
  - a. Disorders of the microcirculation
    - i. Neuropathies
    - ii. Nephropathies
    - iii. Retinopathies
  - b. Macrovascular complications
  - c. Foot ulcers

People with poorly controlled DM may also have impaired wound healing and increased susceptibility to infections. Chronic hyperglycemia resulting in glycation of tissue proteins and excess production of polyol compounds from glucose is the causes of tissue damage [1].

### Diagnosis

The American Diabetes Association's Expert Committee on the diagnosis and classification of DM recently approved new criteria for the diagnosis of DM as follows [1,8] (Table 1):

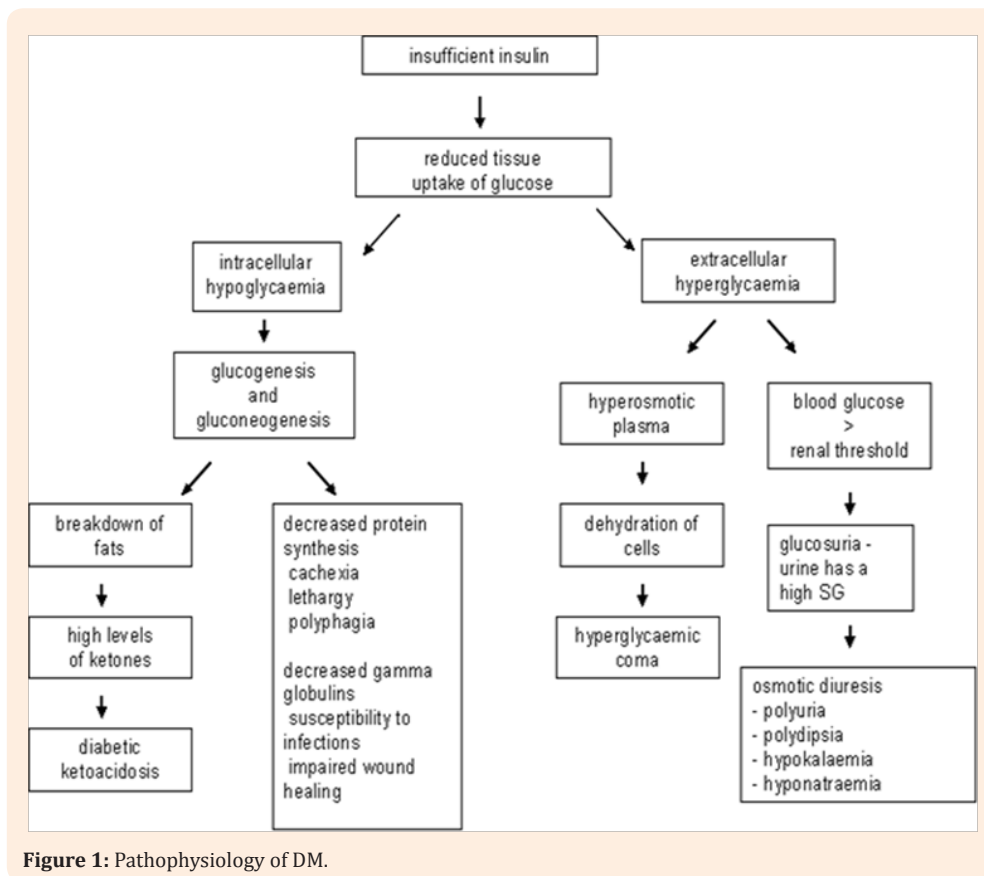


Figure 1: Pathophysiology of DM.

Table 1: American Diabetes Association Diagnostic Criteria For Diabetes18.

Testa	Threshold	Qualifier
Hemoglobin A1c or	· 6.5%	Lab NGSP-certified, standardized DCCT assay
Fasting glucose or	· 126 mg/dL (7.0 mmol/L)	No caloric intake for at least 8 hours
2-hour glucose or	· 200 mg/dL (11.1 mmol/L)	After 75 g of anhydrous glucose
Random glucose	· 200 mg/dL (11.1 mmol/L)	Plus classic hyperglycemia symptoms or crisis

NGSP: National Glycohemoglobin Standardization Program; DCCT: Diabetes Control and Complications Trial. Results must be confirmed by repeated testing.

The normal fasting plasma glucose level is now defined as less than 110 mg/dl.

ADA recommends that all the people older than age 45 years should be screened every 3 years.

### Medical Management

The objective of medical management in all diabetic patients is to maintain blood glucose levels as close to normal as possible.

The glycated haemoglobin assay (HbA 1c) reflects mean glycemic levels over the preceding 3/4 months and is currently used to assess whether the patient’s controlled metabolic levels remained within the normal target range.

Intensive treatment programs and comprehensive education in self-management includes:

- i. Diet control
- ii. Exercise
- iii. Frequent self-monitoring of blood glucose levels

### Insulin

It is used in all patients with type 1 and type 2 DM. Insulin preparations are classified according to their duration of action as Ultra-short, Short, Intermediate and long acting preparations (Table 2).

**Table 2:** Types of Insulin Preparations.

Main Types of Insulin Preparations				
Type	Onset	Peak	Duration	Comments
Rapid-acting insulin analogue Short-acting salubiregulc41 insulin)	5.15 min	30.60 min	2.5 hr	Can be injected at the start of a meal
Intermediate long-acting isophane or zinc insulin)	1-hr (NPH r Lente) 2-3 hr (Ultralente)	4-8hr 4-8hr	8.12hr (N PH) 8-24hr Ultralente	Used to control glucose levels between meals. May be combined with short-acting insulin
Long-acting insulin analogue	30-60min	No Peak	16-24hr	Usually taken once daily

Alternatively subcutaneous insulin infusion by means of computerized external pump may be used.

### Management of Type 1 Diabetes Mellitus

Insulin is the only therapy available for patients with type 1 diabetes. Insulin replacement in patients with type 1 diabetes has been less than optimal because it is not possible to completely reproduce the normal physiologic pattern of insulin secretion into the portal vein. The problem of achieving optimal insulin delivery remains unsolved with the present state of technology.

#### Type 1 Diabetes

In the past decade, two major advances have improved the care of patients with type 1 diabetes. First, we understand the unequivocal relationship between metabolic control and vascular complications [9-13]. suboptimal blood glucose control has a lasting harmful effect even if control improves later. Second, the development of new forms of insulin with more rapid onset or longer duration of action (insulin analogues) and new forms of delivery (eg. continuous pumps and aerosol sprays), as well as advances in glucose monitoring, provide more options for those affected.

#### Intensive Diabetes Management

Because of the relationship between suboptimal glycaemic control and vascular complications, intensive management to minimize hyperglycaemia is now recommended for all patients. This may include more frequent administration of insulin (up to four times daily) or use of different insulin types (eg. rapid- and long-acting insulin analogues), as well as more frequent blood glucose measurements and changes to insulin dose than in conventional therapy.

Intensive schedules need to be individualised to suit patient age and lifestyle. For example, adults and adolescents generally need intermediate-acting insulin before bed for night-time

control. Some school-aged children need short acting insulin at afternoon tea rather than lunch-time to prevent late-afternoon hyperglycaemia, while many preschool aged children can be managed with one dose of intermediate-acting insulin in the morning and small doses of rapid-acting insulin analogues to prevent hyperglycaemia later in the day. The imminent availability of long-acting insulin analogues will change these schedules considerably. Insulin pumps may be useful for some patients with frequent hypoglycaemia or hypoglycaemic unawareness. Intensive therapy is more demanding for patients and their families, and adherence is obviously critical to its success. Patient views are therefore central to management decisions. For example, an adolescent who struggles to comply with two injections a day is unlikely to manage four injections. In adolescents, good control improves quality of life and reduces the burden perceived by their parents [13].

Continuous glucose monitoring devices reveal the frequency of nocturnal hypoglycaemia and the limitations of conventional blood glucose monitoring. Both the new insulin analogues and continuous subcutaneous insulin therapy hold promise of improving control without the attendant risk of hypoglycaemia (Table 3).

Initial studies indicate that the long-acting analogues reduce the risk of nocturnal hypoglycaemia and produce a modest reduction in fasting blood glucose levels compared with intermediate-acting preparations [14].

#### Methods of Insulin Administration

##### Insulin syringes and needles

Single unit syringes (those with a needle fixed to the syringe to minimize dead space) are available for injection of insulin. 27 or 28-gauge, and more recently even 30- gauge attached needles have greatly reduced the pain of injections. Disposable syringes may be reused until blunting of the needle occurs (usually after three to five injections).

**Table 3:** Oral hypoglycemic agent characteristics.

Agent	Mode of Action	Adverse Effect
<b>Insulin Secretagogues - Drugs that primarily stimulate insulin secretion</b>		
Sulfonylureas (currently third generation [glipizide, glimepiride, etc.])	Bind to sulfonylurea receptors on the beta cells triggering release of insulin	Hypoglycemia Weight gain
	Duration of action and daily doses vary by agent	
Meglitinides (repaglinide, nateglinide)	Bind to sulfonylurea receptors	Generally none, but possible hypoglycemia
	Short duration of action, quick onset of action, taken 15 minutes before meals to target postprandial hyperglycemia	
<b>Insulin Sensitizers - Drugs that sensitize tissues (primarily liver and adipose tissue) to the action of insulin</b>		
Biguanides (metformin)	Decrease hepatic gluconeogenesis and increase peripheral glucose uptake	Diarrhea, abdominal pains
	Contraindicated in renal insufficiency and heart failure	Risk of lactic acidosis
	Promote weight loss and low risk of developing hypoglycemia when used alone	
Thiazolidinediones (rosiglitazone, pioglitazone)	Activate peroxisome proliferator-activated receptor $\gamma$ to affect glucose and lipid metabolism	Weight gain
	Improve peripheral glucose uptake in skeletal muscle and fat	Water retention
	Take as long as 6 to 12 weeks to attain optimal therapeutic effect	May precipitate congestive heart failure in susceptible people
	No significant risk of hypoglycemia	Possible increase in risk of experiencing bone loss
<b><math>\alpha</math>-Glucosidase Inhibitors - Drugs that principally affect absorption of glucose</b>		
Acarbose	Inhibit $\alpha$ -glucosidase in the gut and, thus, prevent breakdown of some complex carbohydrates into simple sugars that then cannot be absorbed	Bloating, diarrhea and flatulence due to action of colonic bacteria on undigested carbohydrates
Miglitol	Prevent postprandial glucose excursions	

### Pen devices

Pen devices contain cartridges of U 100 regular human insulin and retractable needles. Cartridges containing insulin lispro; regular insulin, NPH insulin and pre-mixed insulin are available for use with these pens [15].

### Sites for injection

Any part of the body covered by loose skin can be used as an injection site, including the abdomen, thighs, upper arms, flanks, and upper outer quadrants of the buttocks. Exercise facilitates insulin absorption when the injection site is adjacent to the

exercising muscle. Rotation of sites is advised to avoid delayed absorption when fibrosis or lipo hypertrophy occurs owing to repeated use of a single site. For most patients the abdomen is the recommended site for injection, since it provides a considerable area in which to rotate sites and there may be less variability of absorption with exercise than when the thigh or deltoid areas are used.

### New and Improved Insulin Delivery Devices

Advances in diabetes technology have helped to improve the outcomes of management of T1DM in last three decades.

#### Intranasal

Soluble insulin administered intranasally is rapidly absorbed when given along with a detergent substance to facilitate adsorption. Preliminary clinical trials have demonstrated its efficacy in reducing post-prandial hyperglycemia in subjects with type 1 diabetes. However, its absorption is limited to less than 10% of the administered nasal dose. This reduces its cost effectiveness, and most manufacturers have discontinued clinical trials until more progress is made in improving its bioavailability. Inhalers that can provide more precise delivery of drugs have been developed, and inhaled insulin is currently in phase III trials.

#### Insulin pumps and continuous subcutaneous insulin infusion

Insulin pump devices have become smaller and increasingly more sophisticated in their functionality. Insulin is delivered through a cannula placed subcutaneously and replaced with a 72 h frequency. A continuous basal rate is programmed into the pump and additional boluses of insulin can be administered 'at the push of a button. Smart pumps' have a more sophisticated computer incorporated into the insulin pump. The delivery of CSII through insulin pumps has been extensively investigated in the paediatric and young adult population [16].

#### Continuous glucose monitoring (CGM) systems

This system, through which a subcutaneous, glucose oxidase coated sensor measures interstitial fluid glucose concentrations and converts them to a plasma glucose estimate, provides a promising modality for future management of type 1 diabetes. A plot of plasma glucose concentrations over a 24 hours period are produced and can enable insulin adjustment to identify episodes of hyper or hypoglycaemia that may not have been identified using conventional capillary glucose monitoring. More recently, real-time CGM and CSII technologies have been combined in a single device and this exciting technology may represent a step towards an 'artificial pancreas' [17]. At present, insulins in the USA are available only in a concentration of 100 units/ml (U 100) while in India both U 100 and U40 are available and dispensed in 10 mL vials. However, despite advances, this technology is in its infancy and its current role in the management of type 1 diabetes is unclear.

#### Other modes of therapy in T1dm

Amylin analogues: Pramlintide is a synthetic analogue of amylin, a polypeptide hormone, co-secreted with insulin from

pancreatic  $\beta$  cells. It is injected pre prandially in addition to insulin and has shown modest improvements in post prandial hyperglycaemia with 20-30% decrease of insulin dose [18]. Treatment of type 1 diabetes with pramlintide is associated with fewer hypoglycaemic episodes and significant weight loss. Its use is limited by nausea and additional prick required besides insulin.

#### Pancreatic and islet transplantation

Whole-organ pancreatic transplantation for the treatment of type 1 diabetes has largely been reserved for those undergoing renal transplantation for end-stage diabetic nephropathy. While normalization of glycaemic control is achieved following successful transplantation, but this therapy carries the risk of pancreatic graft rejection and side effects of immunosuppression [19]. Islet cell transplantation provides a promising treatment option for type 1 diabetes.  $\beta$ -cells isolated from a donor pancreas are injected into the portal venous system where they then lodge within liver sinusoids. These  $\beta$  cells remain glucose sensitive and secrete insulin into the portal system, in the same way as occurs in the physiological situation [20]. Variable  $\beta$ -cell yield using this isolation technique requires harvest from more than one pancreas to provide sufficient tissue for successful transplantation. Nonetheless, with the future promise of engineered  $\beta$  cells using stem cell differentiation methods, this technique of cell delivery/transplantation may provide a successful long-term treatment of glycaemia in type 1 diabetes.

#### Immunotherapy

Pancreatic  $\beta$ -cell preservation using immune suppression or immune tolerance has been disappointing. When used as secondary prevention of type 1 diabetes, cyclosporine and anti-CD3 antibodies reduce the required insulin dose and prolong  $\beta$ -cell survival, as assessed by fasting and stimulated serum C-peptide concentrations [21]. However, both of these treatment modalities have unacceptable side effect problems, particularly given the age of the target population. GAD-alum immunization in an attempt to promote immune tolerance in subjects with diagnosed type 1 diabetes did not significantly reduce the requirement for insulin or improve fasting serum C-peptide concentrations [22], the use of these therapies requires more research before their introduction as main stream approaches to prevention of type 1 diabetes mellitus.

#### Other Advances

##### Education and psychological support

With the advent of intensive therapy and its greater demands on patients and their families, counseling and education are becoming even more important in achieving compliance, particularly in adolescents. However, as long-term risk of vascular complications can be predicted more accurately from HbA1c level, it is easier for doctors to counsel and encourage intensive management [1-4]. Furthermore, as doctors have become more certain about the need for intensive management, it is our impression that patients and their families have accepted and coped better with it. Indeed, mean HbA1c levels in Australian children have improved from 10% in the 1980s to around 8% in 2003 [23].

Coping-skills training has been shown to improve metabolic control and quality of life in adolescents.<sup>24</sup> This intervention, like all successful interventions in type 1 diabetes, needs to be intensive, and support must be sustained. The indispensable role of the diabetes educator and dietitian in the multidisciplinary team has long been recognized.

Dietary management and education is now more comprehensive and includes the concept of the glycaemic indices of food. 16 Educators' roles are becoming more specialised, both for different age groups and, as technology progresses, for different monitoring and delivery systems.

## Recent Advances In Therapy of Diabetes

### Management of Type 2 Diabetes Mellitus

**Non-pharmacological Therapy:** Non-pharmacological measures including diet, exercise and stress alleviation are as important interventions for the management of diabetes.

**Medical Nutrition Therapy (MNT):** A proper diet is important component of therapy in all patients with diabetes. In patients with *T2 DM* recommendations for caloric distribution is as follows: 55-60% energy from carbohydrate, 10-15% from protein and 20-25% from fats. This dietary distribution is also indicated in patients with type 1 diabetes on intensive insulin regimens in whom near normoglycemic control is less achievable on diets higher in carbohydrate content.

**Dietary Fiber:** Fibers such as cellulose or hemicelluloses, as found in bran, termed as insoluble fibers increases intestinal transit time and may have beneficial effects on colonic function. Soluble fibers such as gums and pectin's as found in beans, oatmeal, or apple skin, tend to decrease gastric and intestinal transit slowing glucose absorption thus decreasing hyperglycemia.

**Artificial Sweeteners:** The nonnutritive sweetener saccharin is widely used as a sugar substitute. Aspartame may prove to be the safest sweetener for use in diabetics which is 180 times as sweet as sucrose. A major limitation is its heat lability, which precludes its use in baking or cooking. These should be used in moderation.

**Fruits:** Fruits (whole) should be taken in moderation. However, very sweet fruits and fruit juices can be avoided.

**Alcohol:** Alcohol intake is best avoided and if used must be in moderation as it may worsen the dyslipidemia, neuropathy and glycemic control.

**Common Salt:** Pickles, papad, chatni and salty processed foods should be restricted as they contain more amount of salt. Permissible quantity of salt is 6 grams per day.

**Tobacco:** Smoking and the use of tobacco in any form should be prohibited.

**Physical activity:** In *T2 DM* exercise programme to achieve weight reduction and calorie counting is central to the management. The best form of exercise is a stepwise increase in aerobic exercises. All diabetics need to be evaluated to rule out any contraindication like CAD, proliferative diabetic retinopathy, autonomic neuropathy etc. before any exercise programme.

Brisk walking for 30-60 minutes or equivalent should be enforced regularly. Yoga, a traditional Indian system, has been demonstrated to have beneficial effect in diabetes. Some aspects of Yoga like, Asanas (involving postures), Pranayama (involving breath), Dhayana (meditation) and Bhavana (visualization) are beneficial but need to be learnt under expert guidance [25].

Table 3 shows characteristics of oral antidiabetic drugs. They are used in the management of mild to moderate type 2 DM. As the drug acts in different ways to lower blood sugar, they are often used in combination.

### Incretins

The recent introduction of the incretins, a group of intestinal peptides that enhance insulin secretion after ingestion of food, as novel oral antihyperglycaemic treatments may prove significant in older persons.

The newest group of oral agents used to treat patients with type 2 DM target the incretin pathway. This group includes dipeptidyl peptidase IV inhibitors. These agents prevent the rapid breakdown of two intestinally secreted hormones (glucagon-like peptide-1 and gastric-inhibitory peptide) that are released in response to meals. These hormones increase insulin secretion, decrease glucagon secretion and delay gastric emptying [26-28]. The incretin pathway is attenuated in patients with type 2 DM [29], and oral agents that specifically target the enzyme dipeptidyl peptidase IV increase their half-lives in the bloodstream. Naturally occurring incretins in humans have a short half-life and are not useful therapeutically. Exenatide is a synthetic analog of Gila monster incretin (exendin-4), and it targets the glucagon-like peptide-1 receptor. It is an injectable drug, however, and leads to weight loss, unlike insulin, which causes weight gain [30-33]. Of all the approved agents used to treat DM, only two (metformin and exenatide) consistently reduce weight, as well as improve glycemic control. All other agents tend to lead to weight gain.

These OHAs can be used alone or in combination with one another and with insulin. Regimens should complement each other and not produce the same effects; for example, combining a sulfonylurea with a meglitinide may not be effective because both act on the sulfonylurea receptors to release insulin. On the other hand, either of these can be combined with any of the insulin sensitizers or the incretin therapies. Use of combination therapies is common place for the control of DM [1].

### Counter Regulatory Hormones

These hormones increases blood glucose by stimulating hepatic glycogenolysis and gluconeogenesis. Agents that interfere with the secretion or action of counter regulatory hormones could potentially be therapeutically useful [34].

**a) Glucocorticoid antagonists:** Increased glucocorticoid concentrations can result in truncal obesity, insulin resistance and hyperglycemia, any approach to reduce the glucocorticoid action will reduce these adverse effects. Selective inhibitors of 11  $\beta$  - HSD1 have been shown to improve insulin sensitivity, glycemic control and plasma lipids in obese diabetic rodents [35].

**b) Insulin:** Insulin is required in patients with *T2 DM* who have developed sulfonylurea failure or those who are undergoing an acute infective or operative event.

Previously available treatments for *T2 DM* have improved glycaemic control but have been accompanied by weight gain and increased risk of hypoglycaemia. *T2 DM* is a progressive disease and more conventional agents do not address the decline of  $\beta$  cell function. Newer agents thus add to the choice of treatment options already available for *T2 DM* and are welcome, especially in light of the recent safety concerns with some of the more modern agents.

### Dental Management Considerations

The first step in managing the patient with medical problems is acquiring a thorough health history. The second step is for the clinician to fully understand the significance of the disease that may be endorsed by the patient. The dental clinician needs to understand the potential complications that can occur as a consequence of dental treatment of a medically compromised patient and when pretreatment or post-treatment medication or emergency care is indicated.

A comprehensive health history questionnaire should include questions about the patients cardiovascular, hematologic, neural and sensory, gastrointestinal, respiratory, dermal, mucocutaneous, and musculoskeletal, endocrine, and urinary systems as well as questions related to sexually transmitted diseases, drug use (eg, alcohol, tobacco), allergies, x-ray exposure or treatment, medications, and hospitalizations.

Preferably an oral history should also be obtained as a review of systems (ROS). This oral ROS often elucidates information that is only touched on by a questionnaire. The dental history should also include questions related to current oral conditions such as periodontal disease or oral ulceration and past dental treatment and potential complications from prior intervention including treatment failure and the delivery of anesthesia or post-treatment medication.

### Scheduling of Visits

In general morning appointments are advisable since endogenous cortisol levels are generally higher at this time. For patients receiving insulin therapy, appointments should be scheduled so that they do not coincide with the peaks of insulin activity, since that is the period of maximal risk of developing hypoglycemia.

### Diet

It is important for clinicians to ensure that the patient has eaten normally and taken medications as usual. If the patient skips breakfast owing to the dental appointment but still takes the normal dose of insulin, the risk of hypoglycemic episode is increased. For certain procedures (eg: conscious sedation) the dentist may request the patient to alter his/her diet before the procedure. In such cases, the medication dose may need to be modified in consultation with the patients physician.

### Blood Glucose Monitoring

Depending on the patient's medical history, medication

regimen and procedure to be performed, dentists may need to measure the blood glucose level before beginning a procedure. This can be done using commercially available electronic blood glucose monitors which possess high degree of accuracy. Patients with low plasma glucose levels (<70 mg/dl) should be given an oral carbohydrate before treatment to minimize the risk of a hypoglycemic event [36].

### During Treatment

The most common complication of *DM* therapy that can occur in the dental office is hypoglycemic episode. If insulin levels exceed physiological needs, the patient may experience a severe decline in his/her blood sugar level. Initial signs & symptoms include mood changes, hunger and weakness. These may be followed by seating, incoherence, and tachycardia. If untreated, possible consequences may include unconsciousness, hypotension, hypothermia, seizures, coma and death.

Controlling blood sugar (glucose) levels is the major goal of diabetes treatment, in order to prevent complications of the disease.

Type 1 diabetes is managed with insulin as well as dietary changes and exercise.

Type 2 diabetes may be managed with non-insulin medications, insulin, weight reduction, or dietary changes.

The choice of medications for type 2 diabetes is individualized, taking into account:

- i. The effectiveness and side effect profile of each medication.
- ii. The patient's underlying health status.
- iii. Any medication compliance issues.
- iv. Cost to the patient or health-care system.

Proper nutrition is a part of any diabetes care plan. There is no one specific "diabetic diet" that is recommended for all individuals. Pancreas transplantation is an area of active study for the treatment of diabetes. The clinician should measure blood glucose levels after immediate treatment.

### After Treatment

Clinicians should keep in mind about the post operative considerations. Patients with poorly controlled *DM* are at greater risk of developing infections may demonstrate delayed wound healing. Acute infections can adversely affect insulin resistance and glycemic control which in turn may further affect body's capacity of healing. Therefore, proper antibiotic coverage may be necessary for patients with overt oral infections. After treatment, oral antidiabetic medication or insulin may need to be appropriately adjusted in consultation with patient's physician if needed. Salicylates increase insulin secretion and sensitivity and can potentiate the effects of sulfonylureas, resulting in hypoglycemia. Hence should be best avoided.

A number of oral conditions have been associated in patients with poorly controlled *DM* which includes :

- I. Periodontal disease



- II. Salivary gland dysfunction
- III. Fungal infections
- IV. Oral burning and taste alterations
- V. Lichen planus and lichenoid reactions
- VI. Traumatic ulcers and irritation fibromas.

### Periodontal Disease

In 1999, the American Academy of periodontology reported about diabetes and periodontal diseases, indicating the risk of periodontitis is higher in poorly controlled DM [37].

This is the greatest dental problem in adult diabetic patients and is seen in its early stages. It is probably that its origin is in the capillary changes which occurs sooner or later in all diabetic patients and have been shown in the gingivae with consequent reduction in the blood supply. There is also the inherent susceptibility to infection though this is far less apparent in the controlled diabetic.

In the young patients under control, the gingivitis is reported to be often of a violaceous color which is a characteristic. The depth of gingival crevice is increased and there is some thickening of gingiva. There appears to be an increased tendency to calculus deposition and radiographs may show some degree of bone atrophy. In the older children, these lesions are more marked and progress towards the adult state of heavy calculus deposition, severe pocketing and loss of bony support. Periodontal abscesses may occur. Whenever local irritation, such as a fragment of calculus or an overhanging filling margin occurs there is a more marked inflammatory reaction than in the normal individual [8].

Several mechanisms have been proposed to explain the increased susceptibility to periodontal diseases, including alterations in host response, subgingival microflora, collagen metabolism, vascularity, gingival crevicular fluid and heredity patterns. Multiple pathophysiological mechanisms (compromised neutrophil function, decreased phagocytosis and leukotaxis) also have been implicated in the increased alveolar bone loss found in patients with diabetes [38]. Furthermore, poorly controlled diabetes, particularly in connection with tobacco use, is a risk factor for periodontal disease. Presence of severe periodontal infection may increase the risk of microvascular and macrovascular diabetic complications. Patients with poorly controlled DM have an increased rate of surgical wound infections and poor wound healing. Hence management of periodontal disease should be conservative and non-surgical. Since prevention plays a primary role in periodontal disease control in diabetic patients, they may need more frequent plaque control and scaling than nondiabetic patients [39]. Studies have shown that smoking increases the risk of periodontal disease, therefore tobacco use cessation counseling should be a part of the management of patients with DM [40].

### Salivary Gland Dysfunction

Literature reported that xerostomia in 40 to 80% of diabetic patients. Patients with poorly controlled DM have lower parotid flow rates than people with well-controlled nondiabetic control subjects. Impaired salivary uptake and excretion by salivary

scintigraphy in adults with type 2 diabetes was reported [41]. The cause is unknown, but may be related to polyuria or to alterations in the basement membranes of salivary glands [42]. Xerostomic complaints may be due to thirst, a common manifestation of diabetes. Saliva may be useful to diagnose and/or monitor systemic diseases, and it may be possible in the future to evaluate glucose levels or diabetes-specific autoimmune markers from oral fluids, thus eliminating the need for serum blood evaluation for diagnosis and monitoring [43]. Frequent sipping of water, ice chips or use of sugarless gums, saliva substitutes and also restriction of caffeine and alcohol intake may alleviate the dryness. Asymptomatic bilateral enlargement of the parotid glands have been reported in 24 to 48% of patients with DM [44,45].

### Dental Caries

Diabetic patients have more active dental caries than control subjects. Prevalence of dental caries is relatively higher in diabetic patients due to the elevated salivary glucose levels and xerostomia. However, low-carbohydrate diabetic diets should theoretically reduce caries prevalence [7]. Salivary cholesterol and triglycerides levels were significantly higher in children with type 1 diabetes mellitus [10]. Unstimulated and stimulated salivary flow rates remained significantly lower in diabetic children compared to controls [11]. Diabetes-induced changes in salivary glucose and albumin concentrations are indicative of caries development among diabetics [46]. Children with insulin-dependent diabetes mellitus have a lower salivary flow rate, pH and buffer capacity, but a higher glucose content and peroxidase, IgA, magnesium and calcium concentration, in comparison with healthy children [47].

### Fungal Infections

Diabetic people have an increased predisposition to manifestations of oral candidiasis including medial rhomboid glossitis, denture stomatitis, and angular cheilitis. While these associations have not been found consistently in all populations of subjects with diabetes [48], they may be due to chronic immunosuppression and require continued follow-up by health care practitioners. In patients with type 1 diabetes, chronic immunosuppression most likely is a sequelae of the disease, whereas in patients with type 2 diabetes, acute hyperglycemia causes alterations in immune responsiveness. Oral mucosal disorders represent an opportunity to coordinate diabetes care between physicians and dentists, which can improve the referral of patients to oral health practitioners [49].

Candidiasis has been found to be associated with poor glycemic control and use of dentures. This predisposition may be due to xerostomia, increased salivary glucose levels or immune dysregulation. *dohyphae*, a cardinal sign of oral *Candida* infection, have been associated significantly with cigarette smoking, use of dentures and poor glycemic control in adults with diabetes. Salivary hypofunction also may increase the oral candidal carriage state in adults with diabetes. Mucormycosis is a rare but serious systemic fungal infection that may occur in patients with uncontrolled DM. Nirmala et al reported a case of mucormycosis associated with a diabetes mellitus in a 14 year old boy [50]. Oral involvement usually appears as palatal ulceration or necrosis.

Treatment usually includes systemic antifungal therapy.

### Oral Burning and Taste Alterations

Taste is a critical component of oral health that is affected adversely in patients with diabetes [51]. Patients with diabetes have reported increased complaints of glossodynia and/or stomatopyrosis. Literature reported that 37 % of undiagnosed *type 2 DM* patients experiencing burning mouth or tongue. The burning may be due to peripheral neuropathy, xerostomia, or candidiasis. Good glycemic control may alleviate the burning sensation. Clonazepam may be beneficial in some patients with complaints of oral burning sensation [37]. Some diabetic patients have a mild impairment of the severe sweet taste sensation. This may be related to xerostomia or disordered glucose receptors [40]. Retinopathy and peripheral neuropathy that affects patients' hands may severely limit a patient's ability to perform oral hygiene procedures [52].

Patients may experience long-lasting oral dysesthesias, which could adversely affect oral hygiene maintenance. Peripheral neuropathies can impair the use of oral hygiene devices, and diabetic retinopathy can produce visual disturbances, ultimately leading to blindness, 51 which, in turn, also could impair daily oral and prosthesis hygiene. Dysphagia, another sequelae of diabetes, is caused by altered strength, speed and/or coordination of the cranial nerve musculature [53].

### Lichen Planus and Lichenoid Reactions

Prevalence of oral lichen planus is significantly higher in *type 2 DM* than *type 1 DM*. This may be a side effect of oral hypoglycemic agents or antihypertensive medications [54].

### Traumatic Ulcers and Irritation Fibromas

Guggenheimer and colleagues recently reported that people with *type 1 DM* have a higher prevalence of oral traumatic ulcers and irritation fibromas. These findings may be related to altered wound healing patterns in these patients [48].

Prior to dental treatment, the dentist must obtain a complete medical history, which indicates the type of diabetes suffered and frequent complications, the treatment received and the status of diabetes control. In 2009 consensus of the American Diabetes Association and the advocate glycated hemoglobin as the main parameter to assess the metabolic control. As a rule, a HbA1c <7%, a preprandial glycemia of 70- 130 mg/ dl and a postprandial glycemia <180 mg/ dl are indicative of good metabolic control. The well controlled diabetic patient can be treated similarly to a non diabetic patient, preferably receiving short morning appointments to reduce stress. They must not fast, in order to prevent hypoglycemia [1].

### Antibiotic Coverage

Patients with poorly controlled diabetes are at risk of developing oral complications because of their susceptibility to infection and sequelae, and likely will require supplemental antibiotic therapy. Anticipation of dentoalveolar surgery (involving mucosa and bone) with antibiotic coverage may help prevent impaired and delayed wound healing. Orofacial infections require close monitoring. Cultures should be performed for acute

oral infections, antibiotic therapy initiated and surgical therapies contemplated if appropriate (for example, incision and drainage, extraction, pulpectomy). In cases of poor response to the first antibiotic administered, dentists can select a more effective antibiotic based on the patient's sensitivity test results [55].

## Identification and Treatment of Hypoglycemia

### Identification

#### Symptoms

- Shakiness
- Anxiety
- Increased sweating
- Hunger

#### Signs

- Tremors
- Tachycardia
- Altered consciousness (lethargy and obtundation or personality change)
- Blood glucose level: < 60 mg/dl

### Treatment

#### Conscious patient

- Administer 15 mg of simple carbohydrates
- Repeat finger- stick glucose test in 15 minutes:
- Blood glucose level > 60 mg/dl: patient should be asked to eat or drink (for example, a sugar-sweetened beverage)
- Blood glucose level < 60 mg/dl: repeat treatment of 15 g of simple carbohydrates and check blood glucose in 15 minutes. Continue until achieving a blood glucose level > 60mg/ dl
- Ask the patient to report his/ her physician

#### Unconscious patient

##### With intravenous access

- Administer 5 to 25 g of 50% dextrose immediately
- Notify the patient's physician

##### Without intravenous access

- Apply glucose gel inside the mouth in a semi obtund patient or treat with 1 mg of glucagon intramuscularly or subcutaneously.
- Repeat the blood glucose test in 15 minutes
- Establish intravenous access and notify the patient's physician

### Monitoring Glycemic Control

Two critical steps are involved in treating patients with diabetes: establishing the diagnosis (*type 1* or *type 2* diabetes, and the form of therapy) and the level of disease control (well-controlled or poorly controlled). Most commonly, blood glucose

or HbA1c levels will be available from the physician's office. Medical updates must be recorded in the dental record at each visit to guide the clinician's treatment decisions. The dentist should be able to use a glucometer to measure blood glucose levels rapidly from a patient's fingertip. Finally, the dental office should be equipped with immediate sources of glucose in case a diabetic induced hypoglycemic event occurs.

### Communication with Physicians

Regular communication with physicians is a critical component of safely treating patients with diabetes. Communication must be bidirectional: physicians must be apprised of oral manifestations of the disease to help them regulate blood glucose levels, and dentists must be updated on glycemic control to help them maintain a patient's oral health. Treating patients with diabetes also represents an opportunity to expand a dentist's referral base. Physicians who treat children and adults with diabetes could be a good referral source of patients whose oral health care needs may not be satisfied adequately.

Dentists must be cognizant of the various methods of treating effectively the oral complications of diabetes mellitus. Many treatments are no different from those recommended for patients without diabetes. However, managing patients with diabetes does require more rigorous follow-up, more aggressive interventional therapy rather than observation, regular communication with physicians and greater attention to prevention. Patients with diabetes, particularly those with a history of poor glycemic control and oral infections, require more frequent recall visits and fastidious attention to acute oral infections [42].

### Dental Treatment

The two principal aims of dental care of a diabetic child are first, to eliminate and prevent any oral infection which may tend to upset the stability of the sugar balance, and second, to try to maintain healthy tissues.

It must be emphasized that the routine dental care of a child known to have diabetes mellitus is not a hazardous procedure and the possibility of a crisis due to either hypoglycemic or hyperglycemia in the dental surgery is fairly remote. Nevertheless, dentist must know how to deal with such an event should it occur, and should also take reasonable precautions to prevent the possibility. Whenever possible, appointments for routine treatment should be in the morning when the patient has had his insulin followed by his breakfast. He is more stable at this time of the day than at any other. If this is not feasible then care must be taken that the timing of his injections and meals are not altered in any way. It is as well to check with the patient or parent that these have been as normal, and that he has not been sick on the bus or that apprehension has not robbed him of his appetite without compensating.

The only crisis which may reasonably occur in the dental surgery is hypoglycemic attack, or insulin shock, which is usually the result of missing or postponing a meal following an insulin injection. As has previously been stated, the preliminary signs and symptoms are tremors, weakness, pallor and sweating accompanied by a hot or cold feeling and the patient feels clammy to the touch. This occurs in many normal children who

are apprehensive and is due to adrenaline release. If seen in the diabetic child, the dentist must be alerted to the possibility of hypoglycemic collapse and question the patient and parent immediately as to whether he should take sugar. These symptoms progress to restlessness, yawning, slurred speech and so on, and by this time treatment is really urgent as the next stage is coma and loss consciousness. Two teaspoonfuls of sugar in water should be given at once, but if not available immediately, then the quickest alternative must be given, such as concentrated orange squash or even biscuits, though the latter are much slower to be absorbed. If there is no improvement in five minutes, then repeat. If the hypoglycemic condition has progressed to unconsciousness the patient placed on his side or prone, and the recommended treatment is 50 ml of 50% of glucose given intravenously using a wide - bore needle because of the viscosity. Great care must be taken not to allow any to escape in to the surrounding tissue. This preparation may be obtained readily to administer in ampoules for such an emergency. Alternatively, an intramuscular injection of 1 mg of glucagon [adult dose] which is available ready packaged is probably a safer and more easily administered treatment than intravenous glucose for the dental practitioners who is unused to the latter technique. It has the great advantage of doing no harm if the diagnosis of insulin coma was wrong. Recovery of consciousness is usually rapid, within 15 minutes, and the patient should then be given carbohydrate by mouth to stabilize the recovery.

In the dental surgery a child under routine diabetic control is extremely unlikely to develop ketosis except in the presence of acute infection if he has obeyed his rules. Such condition only occurs if he is short of insulin and it is not of sudden onset but develops over several hours at its most rapid. In this case the patient and his parent will be aware of possibility, and he should go immediately to hospital, if possible to that responsible for him [48].

### Conservation

This presents no problems. Local anesthesia can be used normally since the usual adrenaline content of 1:80000 or less in the 2 to 4 ml of solution given is insufficient to make any material difference to the balance as a whole. On long treatment visits, the timing of insulin injections must be born in mind. Septic teeth which cannot easily be restored to a non-septic condition and non-vital teeth which cannot be properly supervised are better removed [46].

### Periodontal Treatment

Particular attention must be paid to the gingival condition. Scaling may need to be carried out frequently and must be thorough, though as non-traumatic as possible. Pockets should be eliminated by appropriate means. In Children, even where there is as yet no evidence of periodontal disease, preventive measures are important. Instructions in correct tooth - brushing and gum massage whenever necessary, the grinding of points of traumatic occlusion will assist the postponement of gingival diseases [37].

### Appliances

There is no contraindication to orthodontic treatment, though it is as well to reduce the wearing of appliance to a reasonable

minimum on general principles. If a prosthetic appliance is necessary, it must be kept under regular supervision and the patient's attention directed to the need for special care in brushing and massaging the gums [47].

### Oral Surgery

Extraction under local anesthesia usually creates no special problem in diabetic children under good insulin control. Many reports of dry sockets and slow healing are not applicable to young patients, but to older diabetics who have considerable vascular degenerations and severe periodontal diseases. In children the extraction is straightforward but the dentist should be assured that the patient's normal insulin and meal regime has been followed, and that he has not had any recent signs of blood-sugar instability. In the latter case, it would be wiser to refer him to his physician for advice and possibly have the extraction done on a day - admission basis at the hospital. As has been said already, normal local anesthetic solution with 1:80000 adrenaline is quite suitable in these children [46].

General anesthesia should never be used on a diabetic child as an out-patient in a dental surgery. This would require fasting for at least 3 hours before operation and would almost certainly precipitate insulin shock. If general anesthesia is indicated then the patient should be referred to his hospital physician for this to be arranged on an in-patient basis.

Any extraction which is accompanied by some degree of infection should be supported by an antibiotic, both to give the tissue additional help in combating it, and to remove a potential source of diabetic instability as soon as possible [1,9].

In January 2013, the American Academy of Pediatrics (AAP) [56] issued clinical practice guidelines on the management of type 2 diabetes in children and adolescents. The guidelines recommend insulin treatment in all patients who present with ketosis or extremely high blood glucose levels because it may not be clear initially whether these patients have type 2 or type 1 diabetes. Once a diagnosis of type 2 diabetes is confirmed, lifestyle modification and metformin treatment should be initiated (Table 4).

**Table 4:** Indications for use of continuous subcutaneous insulin infusion (CSII) in paediatrics [56].

Conditions Under Which CSII Should Be Considered
Recurrent severe hypoglycaemia
Wide fluctuations in blood glucose, regardless of HbA1c
Suboptimal diabetes control - HbA1c exceeding target range for age
Microvascular complications and/or risk factors for macrovascular complications
Good metabolic control but an insulin regimen that compromises lifestyle
Circumstances In Which CSII May Be Beneficial
Young children, especially infants and neonates
Adolescents with eating disorders
Children and adolescents with a pronounced dawn phenomenon
Children with needle phobia
Pregnant adolescents
Ketosis
Competitive athletes

### Conclusion

Diabetes mellitus have a significant impact in the delivery of dental care. It is important for dentists to be familiar with the medical management of patients with DM and to recognize the signs and symptoms of undiagnosed or uncontrolled disease. Dentists should contribute to the maintenance of optimum health in patients with this disease and they have the potential and the responsibility to assume an active role in the early identification,

assessment, and management of their patients who present with or are at risk of developing diabetes. They should implement inter professional education strategies in medical and dental training aiming to improve collaboration in the care of patients with diabetes.

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