Influence of diabetes mellitus on apical periodontitis
Sonakshi E. Charles¹, Rahul Pandey¹, Prateeksha S. Ellis², Everard S. Charles³

¹Department of Conservative Dentistry and Endodontics, Institute of Dental Sciences, Bareilly, Uttar Pradesh, India,
²Consultant, Sewa Mandir Health Foundation, Ajmer, Rajasthan, India, ³Senior Consultant, Dr. GK Srivastava Hospital, Bareilly, Uttar Pradesh, India

INTRODUCTION
Diabetes mellitus (DM) is a disorder where metabolism of glucose, fat, and protein is disturbed. This can be attributed to impaired insulin secretion, a different level of insulin resistance, or both. This condition is due to either profound or absolute insulin deficiency or due to resistance of the uptake by the tissues.¹ Insulin facilitates the entry of glucose, which circulates in the blood stream, into the body cells by causing an increased glucose transport across the cell membrane. Glucose is transported across the cell membrane by a family of specialized transport proteins, the so-called glucose transporters.²

PATHOPHYSIOLOGY OF DIABETES
A diabetic is more susceptible to bacterial infections, and once invaded, there is a greater likelihood that more serious infections will occur with insulin intake disruption.³ This susceptibility is caused by a generalized circulatory disorder due to a lack of insulin that controls glucose metabolism, leading to insufficient blood supply to the injured regions. In addition, the increased blood sugar at the injury site can improve the multiplication of bacteria with final cell death and apoptosis, as well as the clearance of leukocytes while stopping the recruitment of polymorphonuclear leukocytes.⁴

CONSEQUENCES AND COMPLICATIONS OF DIABETES
Other organ complications related to DM are opthalmic, renal, cardiovascular, cerebrovascular, and peripheral neurological disorders. Various aspects of the immune system are impaired and wound healing is impaired in DM. These aspects include,
above all, the dysfunction of leukocytes.[7] As diabetes is the third most common systemic disease among patients who are looking for dental treatment, its effect on the tooth tissue is noticeable.[6]

Impairment of Immunity

During an inflammatory reaction, leukocytes adhere to endothelial cells due to the presence of adhesion receptors on leukocytes and endothelial cells. Before leukocytes migrate into tissues, they are tightly adhered to the vessel endothelium before.[7] Accordingly, impairment in molecule responsible for adhesion of leukocytes is the reason for the abnormal leucocyte functioning in DM, which leads to reduced interactions between leukocytes and endothelial cells and a reduced number of leukocytes in inflammatory lesions. Decreased chemotactic activity of leukocytes is observed in pulp with having more chances of obligate anaerobic bacterial infection.[8]

Vascular System Impairment

Formation of oxygen-free radical brings about most of the changes in metabolic functions, which reduces opposition to oxidative stress.[9] Diabetes leads to hyperglycemia and induces the formation of superoxides, which contribute to the pathogenesis of microvascular and macrovascular complications. In DM, there is overall disruption in the circulatory system. There are atheromatous deposits in the lumen of the blood vessels. Along with this there is thickening of the basement membrane of the blood vessel wall lining is also seen, especially in vessels with narrow diameter like capillaries. Such changes bring about deterioration in the leucocyte response as well as in their antimicrobial property. These complications at the vascular level leads to improper functioning of the humoral and cellular bases of immune system.[10]

Prolonged diabetes can lead to angiopathy and the basement membrane of the gingival vessel thickens along with impair blood circulation to the pulp.[11] There is absence of collaterals in pulp circulation, making it highly susceptible to infection, particularly the spread of periodontal infection to the pulp through the periapical route.[12] The circadian rhythm of pulp sensitivity has also changed in diabetics.[13] Due to constraint microbial activity of immune cells along with lack of collateral circulation, there is increased probability of pulp infection and necrosis in patients with DM.[10,14,15] This complication of infection occurs through the process of anachoresis. If the pulp is already chronically inflamed, the introduction of bacteria and toxins through pressure on the dentinal tubules can lead to a pulp and periapical infection.

RELATIONSHIP BETWEEN INFLAMMATION AND DIABETES

The ability of pulp to repair and nutrition to the tissue is also affected due to compromised vascular system in diabetic patient. This creates a suitable anaerobic environment for microbes to inhabit. Inflammatory process progresses in diabetics at a faster and rate. This leads to precipitation of uncontrolled form of diabetes. Management of such a condition usually requires alteration in the form and dosage of medication. Removal of the inflammatory condition usually requires less insulin to control diabetes. It is therefore a matter of course to eliminate all types of infections, as well as pulpal infections. The problem can be more complicated if the teeth are not carious or if the pain symptoms occur bilaterally without pulp response during the pulp test of the neighboring teeth. This condition is often referred to as diabetic odontalgia.[16] There is unexplained odontalgia which can indicate an undetected DM condition and because diabetes leads to circulatory disorders with ischemia, pulp necrosis can occasionally occur.

OTHER COMMON ORAL MANIFESTATIONS

A diabetic with uncontrolled levels of blood glucose levels can also present with oral manifestations of this disease which includes, dryness of mouth, increased risk of secondary infections, delayed healing, more incidence and aggressiveness of caries, candidiasis, inflammation of gums, increased susceptibility to periodontal disease, and burning mouth syndrome.[17] High risk of periodontal disease is a consequence of change in host immune response, bacteria in subgingival region, metabolism of collagen, and vascular system.[18] Changes in taste sensations have been described in some diabetics. This has been attributed to altered glucose receptors or early manifestations of diabetic neuropathy. There is also an increase in saliva and glucose that can affect oral microflora and can cause increased caries development and periodontitis.[19,20] An unusual clinical finding in DM is glossodynia, tongue pain is often associated with xerostomia, and this can be the early clinical sign of DM.[21]

EFFECT OF APICAL PERIODONTITIS (AP) ON DM

AP is an inflammatory condition surrounding the tooth root apex, due to pulp infection. This poses significant clinical challenges associated with the same systemic disorders associated with periodontal disease.[22] Few common features between periodontitis and AP are that both the conditions are of chronic type, both have multibacterial infections that have similar microbial agents. There is release of high levels of cytokines with predominant Gram-negative microbes in both the diseases.[22,23] It can therefore, assumed that periapical lesions are similar to periodontitis and can lead to impaired insulin metabolism and poor blood sugar control.[24] Diabetes pathogenesis is promoted by inflammation, and there is reciprocating association of diabetes and chronic periodontitis. Stronger inflammatory responses in diabetics causes elevation in blood sugar levels, which leads to an uncontrolled diabetic state.[25] In such condition dose adjustments of insulin or oral medications is needed to control the raised blood sugar levels. When the inflammatory condition is eliminated, then less dosage of insulin is required to maintain normal levels. Therefore, it is crucial to abolish all infections.
The activation of intracellular pathways of macrophages and neutrophils and regulation of prostaglandin, tumor necrosis factor-alpha and cytokines such as IL-1, IL-6, and IL-8 are due to release of lipopolysaccharide from anaerobic Gram-negative bacteria. Then, there is reaction between the free fatty acids and advanced glycosylation products (AGEs) with the released cytokines when these cytokines enter the systemic cycle.[29] This is peculiar to Type 2 DM. When these inflammatory pathways are triggered in the defense cells of body tissues, there is change in metabolic control and elevation in total insulin resistance, in patients with Type 2 diabetes and chronic AP. Diabetes significantly affects oral tissue and influences inflammation mediators and metabolic pulpal changes. Pulp and periradicular tissue.[24,27] Bender et al. reported that there is impaired healing and repair and the size of the lesion increases progressively even after initiation of endodontic management of uncontrolled diabetic patients.[16]

**SEQUEL OF DM ON AP**

There is increased risk of developing AP in patients with DM.[18] Diabetics who have received insulin have a tendency toward intensified symptomatic form of periradicular disease. Flare is also observed in diabetics undergoing endodontic treatment. Effective intra-canal medicaments should be implied during endodontic management of diabetics, especially where there is a pre-operative periradical lesion.[23] In diabetic patients, inflammation of the periodontal ligament in the apical region, alveolar bone, and root resorption is more intense. Calcifications of unspecified shape are also seen sometimes. The periradicular lesions are larger and the inflammatory response is more severe in diabetics than in non-diabetic patients.[28] Poorly controlled diabetes has delayed healing compared to fair and well-controlled diabetes along with resorptive conditions. This indicates that evolution of periradicular lesions is because of the metabolic effects of DM.

**MICROBIOTA OF AP WITH DIABETES**

In diabetic patients marked that increase in the concentration of Prevotella intermedia and Porphyromonas gingivalis was found. Fusobacterium nucleatum, Peptostreptococcus micros, and Streptococcus spp. were one of the most common microorganisms isolated. An association between pre-operative pain and Streptococcus species and the combination of Streptococcus spp. and F. nucleatum was also seen. An interrelation between Porphyromonas endodontalis and Porphyromonas gingivalis with diabetes has also been established.[30]

**CONSIDERATIONS FOR DIABETIC PATIENTS TAKING ENDODONTIC THERAPY**

When reviewing the medical history, a doctor should know the main signs of DM which are polydipsia, polyphagia, polyuria, decrease in body weight, and malaise and contact a doctor for diagnosis and treatment. In diabetics, doctors should determine how well the diabetic condition can be controlled. With acute infections, however, special considerations must be made. Diabetic patients who are not on insulin may need insulin. Diabetic patients who take insulin to control blood sugar levels may need to increase the insulin dosage only after physician’s consult. This only needs to be done after consulting the doctor concerned.[30] Acute oral inflammatory manifestations in diabetic patients should be managed with providing incision which facilitates drainage, complete removal of pulpal tissue, providing antibiotic regimen, and oral rinses with lukewarm water.

For endodontic procedure of well-controlled, diabetic patient should be given morning scheduled. This is because in morning there are elevated levels of endogenous cortisol (cortisol increases). For patients on insulin, their schedule should not overlap when there is maximum insulin effect. As in such a situation, the patient is at the maximum risk of having episode of hypoglycemia. Before commencing of any treatment procedure, make sure that the patient has had his medication and meal as normal. Sedating the patient should be kept as an alternative if the patient is experiencing emotional or physical stress. An increase in the stress levels at the time of procedure can lead to release of increased levels of cortisol and adrenaline which may ultimately precipitate as hyperglycemia.[31] Appointments of long duration should not be given. Consultation of the patient’s physician is recommended if any procedure of long duration had to be undertaken. A track of blood sugar level should be kept during long surgical procedures. During dental treatment diabetic patient usually has encounter with episodes of hypoglycemia. Hypoglycemic episodes should be considered as a medical emergency. It should be managed with oral carbohydrates (15 g) such as orange juice (6 ounces) or 3-4 teaspoons of table sugar, preferably powdered. If the patient is not able to take through oral route, then through subcutaneous or intramuscular route glucagon (1 mg) should be given. Infection control with root canal debridement and filling should be done for patients presenting with AP.[32] Endodontic treatment of periradicular pathosis in a diabetic can have history of increased pre-operative symptoms. Such cases should incorporate use of proper intracanal medicament during root canal treatment.

Glucose control is also influenced by Vitamin D. It has a positive effect on insulin metabolism. Vitamin D also plays an important part in regeneration of alveolar bone and periradicular tissue inflammation. Vitamin D can play a therapeutic function in endodontic treatment in diabetic patients.[31] It can be used as a therapeutic approach in diabetics. Periapical lesion of a patient with controlled DM heals in a similar way as that of a non-diabetic patient.[16] There is high incidence of having residual lesion in Type 2 diabetics.[34] The final outcome of endodontic treatment is not satisfactory in diabetics and there is greater chance of treatment failure.

**PROGNOSIS OF ENDODONTIC TREATMENT IN DIABETICS**

Diabetic patients with pre-operative periapical involvement have unfavorable success rate. They also stated that usually
such patients report with pre-operative pain. Diabetes also have higher incidence of flare-ups during treatment phase or postoperatively.\(^{27}\) Residual lesion is observed in diabetic patients who had undergone endodontic treatment.\(^{34,35}\)

**CONCLUSION**

Diabetes being one of the most common systemic disease and apical periodontitis being one of the most common dental disease can have significant influence on each other. This relationship poses problems in controlling blood sugar levels as well as increases the intensity and chances of inflammation. Such a condition also responds to the healing phase poorly. While managing such patients greater emphasis should be given to keep diabetes under control and to eliminate all types of infection.

**REFERENCES**