THE RELATIONSHIP OF GLYCEMIC CONTROL TO THE OUTCOMES OF DENTAL EXTRACTION

A Dissertation submitted in

partial fulfillment of the requirements

for the degree of

MASTER OF DENTAL SURGERY

BRANCH – III

ORAL AND MAXILLOFACIAL SURGERY

THE TAMILNADU Dr. M.G.R. MEDICAL UNIVERSITY

CHENNAI – 600032

2015 – 2018

DECLARATION BY THE CANDIDATE

I hereby declare that this dissertation titled**"The Relationship of Glycemic control to the outcomes of dental extraction"**is a bonafide and genuine research work carried out by me under the guidance of**Dr.K.PRABHU SANKAR., M.D.S., Professor, Head of the Department,**Department Of Oral and Maxillofacial Surgery, Best Dental Science College, Madurai – 625104.

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This agreement herein after the "Agreement" is entered into on this day 29 ,Dec 2017, between the Best Dental Science College represented by its **Principal** having address at Best Dental Science College, Madurai – 625104, (hereafter referred to as, 'the College')

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"No one who achieves does so without acknowledging the help of others. The wise and confident acknowledge this help with gratitude."

-Alfred North Whitehead.

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Date:

Place: Dr.T.V.Avinash Balaji

List of Abbreviation

HgbA1c- glycosylated haemoglobin

BL- Buccolingual site

POD- Post Operative day

EPT-Epithelialization

IFG- Impaired Fasting Glucose

IGT- Impaired glucose tolerance

OGTT-Oral glucose tolerance test

IRMM-Institute for Reference materials and Measurements

NIDDM-Non Insulin dependent diabetes mellitus

BGL- Blood glucose level

RBS- Random Blood Sugar

CHO-Carbohydrate

DCCT- Diabetic control and complication trial

DM-Diabetes Mellitus

PMN-Polymorphonuclear leukocyte

SPSS- Statistical package for Social sciences

LIST OF CONTENTS

AIM

Aim

The aim of this study was to determine whether glycemic control influences healing after dental extraction.

OBJECTIVES

Objectives

To Assess the Epithelialization of extraction sockets and gross wound healing based on

1. PP Blood sugar level
2. HbA1c values .

Introduction:

Diabetes is a condition where the body either fails to produce insulin (type 1 diabetes) or the insulin that is produced is no longer as effective (type 2 diabetes). Insulin is a hormone produced in the beta cells of the islets of Langerhans within the pancreas. Insulin is released directly into the blood stream and is therefore part of the endocrine system. Insulin acts like a key which allows blood glucose to enter the cells around the body for use as an energy supply. Glucose is essential for the body to function properly. The brain is particularly affected by any reduction in blood glucose supply due to its lack of capacity for glucose storage. There are two types of diabetes : Type 1 diabetes and Type 2 diabetes. Type 1 diabetes accounts for approximately 15% of all diabetics is usually juvenile onset, but can occur at any age. In type 1 diabetics the beta cells in the pancreas undergo a chronic autoimmune destruction process which results in a long term lack of endogenous insulin. Scientists and researchers remain unsure as to the exact cause of type 1 diabetes but it is thought that a viral or other infection may trigger the autoimmune destruction. The resultant lack of insulin must be replaced via injection or via an insulin pump. This should be combined with knowledge of dietary carbohydrate values such that injected insulin can be adjusted to carbohydrate consumed to avoid large fluctuations in blood glucose levels.

Assigning a type of diabetes to an individual often depends on the circumstances present at the time of diagnosis, and many diabetic individuals do not easily fit into a single class. For example, a person with gestational diabetes mellitus (GDM) may continue to be hyperglycemic after delivery and may be determined to have, in fact, type 2 diabetes. Alternatively, a person who acquires diabetes because of large doses of exogenous steroids may become normoglycemic once the glucocorticoids are discontinued, but then may develop diabetes many years later after recurrent episodes of pancreatitis. Another example would be a person treated with thiazides who develops diabetes years later. Because thiazides in

themselves seldom cause severe hyperglycemia, such individuals probably have type 2 diabetes that is exacerbated by the drug. Thus, for the clinician and patient, it is less important to label the particular type of diabetes than it is to understand the pathogenesis of the hyperglycemia and to treat it effectively. Type 1 diabetes (beta -cell destruction, usually leading to absolute insulin deficiency) **Immune-mediated diabetes.** This formof diabetes, which accounts for only 5–10% of those with diabetes, previouslyencompassed by the terms insulin dependent diabetes, type 1 diabetes, or juvenile-onset diabetes, results from a cellular-mediated autoimmune destructionof the Beta-cells of the pancreas. Markers of the immune destruction of the beta-cell include islet cell autoantibodies, autoantibodiesto insulin, autoantibodies to GAD(GAD65), and autoantibodies to the tyrosinephosphatases IA-2 and IA-2. One and usually more of these autoantibodies are present in 85–90% of individuals when fasting hyperglycemia is initially detected. Also, the disease has strong HLA associations, with linkage to the DQA and DQB genes, and it is influenced by the DRB genes. These HLA-DR/DQ alleles can be either predisposing or protective. In this form of diabetes, the rate of beta-cell destruction is quite variable, being rapid in some individuals (mainly infants and children) and slow in others (mainly adults). Some patients, particularly children and adolescents, may present with ketoacidosis as the first manifestation of the disease. Others have modest fasting hyperglycemia that can rapidly change to severe hyperglycemia and/or ketoacidosis in the presence of infection or other stress. Still others, particularly adults, may retain residual beta-cell function sufficient to prevent ketoacidosis for many years; such individuals eventually become dependent on insulin for survival and are at risk for ketoacidosis. At this latter stage of the disease, there is little or no insulin secretion, as manifested by low or undetectable levels of plasma C-peptide. Immune mediated diabetes commonly occurs in childhood and adolescence, but it can occur at any age, even in the 8th and 9^{th} decades of life. Autoimmune destruction of beta-cell has multiple genetic

predispositions and is also related to environmental factors that are still poorly defined. Although patients are rarely obese when they present with this type of diabetes, the presence of obesity is not incompatible with the diagnosis. These patients are also prone to other autoimmune disorders such as Graves' disease, Hashimoto's thyroiditis, Addison's disease, vitiligo, celiac sprue, autoimmune hepatitis, myasthenia gravis, and pernicious anemia. **Idiopathic diabetes.** Some forms of type 1 diabetes have no known etiologies. Some of these patients have permanent insulinopenia and are prone to ketoacidosis,but have no evidence of autoimmunity. Although only a minority of patients with type 1 diabetes fall into this category, of those who do, most are of African or Asian ancestry. Individuals with this form of diabetes suffer from episodic ketoacidosis and exhibit varying degrees of insulin deficiency between episodes. This form of diabetes is strongly inherited, lacks immunological evidence for beta-cell autoimmunity, and is not HLA associated. An absolute requirement for insulin replacement therapy in affected patients may come and go. Type 2 diabetes (ranging from predominantly insulin resistance with relative insulin deficiency to predominantly an insulin secretory defect with insulin resistance) Type 2 diabetes, which accounts for 90–95% of those with diabetes, previously referred to as non–insulin dependent diabetes, type 2 diabetes, oradult-onset diabetes, encompasses individualswho have insulin resistance andusually have relative (rather than absolute) insulin deficiency At least initially, and often throughout their lifetime, these individuals do not need insulin treatment to survive. There are probably many different causes of this form of diabetes. Although the specific aetiologies' are not known, autoimmune destruction of beta-cells does not occur, and patients do not have any of the other causes of diabetes listed above or below. Most patients with this form of diabetes are obese, and obesity itself causes some degree of insulin resistance. Patients who are not obese by traditional weight criteria may have an increased percentage of body fat distributed predominantly in the abdominal region. Ketoacidosis seldom occurs

spontaneously in this type of diabetes; when seen, it usually arises in association with the stress of another illness such as infection. This form of diabetes frequently goes undiagnosed for many years because the hyperglycemia.

There are many other factors (apart from insulin and CHO) which can affect blood glucose levels. These are less easy to control or monitor and include: anti-insulin hormones, eg, adrenaline, growth hormone, cortisol and glycogen; exercise; and anxiety. The above factors alter from day to day and even hour to hour thus making good blood glucose control a far from simple goal. With Type 2 diabetes there are usually adequate levels (and sometimes even increased levels) of insulin but it is no longer as effective at the cellular level. Using the key analogy, it is as if the key is a bit rusty and it struggles to unlock the cell door to allow the blood glucose to enter. Blood sugar therefore becomes raised but as there is still some effective insulin the levels are not usually as high as with the Type 1 diabetes situation.Hence the undiagnosed Type 2 diabetic may misinterpret or even ignore their symptomsof lethargy, increased thirst and drinking, more infections and slower healing. Several pathogenic processes are involved in the development of diabetes. These range from autoimmune destruction of the beta-cells of the pancreas with consequent insulin deficiency to abnormalities that result in resistance to insulin action. The basis of the abnormalities in carbohydrate, fat, and protein metabolism in diabetes is deficient action of insulin on target tissues. Deficient insulin action results from inadequate insulin secretion and/or diminished tissue responses to insulin at one or more points in the complex pathways of hormone action. Impairment of insulin secretion and defects in insulin action frequently coexist in the same patient, and it is often unclear which abnormality, if either alone, is the primary cause of the hyperglycemia. Symptoms of marked hyperglycemia include polyuria, polydipsia, weight loss, sometimes with polyphagia, and blurred vision. Impairment of growth and susceptibility to certain infections may also accompany chronic hyperglycemia. Acute, life-threatening consequences of uncontrolled diabetes are hyperglycemia with ketoacidosis or the nonketotic hyperosmolar syndrome. Long-term complications of diabetes include retinopathy with

potential loss of vision; nephropathy leading to renal failure; peripheral neuropathy with risk of foot ulcers, amputations, and Charcot joints; and autonomic neuropathy causing gastrointestinal, genitourinary, and cardiovascular symptoms and sexual dysfunction. Patients with diabetes have an increased incidence of atherosclerotic cardiovascular, peripheral arterial, and cerebrovascular disease. Hypertension and abnormalities of lipoprotein metabolism are often found in people with diabetes. The vast majority of cases of diabetes fall into two broad etiopathogenetic categories. In one category, type 1 diabetes, the cause is an absolute deficiency of insulin secretion.

Individuals at increased risk of developing this type of diabetes can often be identified by serological evidence of an autoimmune pathologic process occurring in the pancreatic islets and by genetic markers. In the other, much more prevalent category, type 2 diabetes, the cause is a combination of resistance to insulin action and an inadequate compensatory insulin secretory response. In the latter category, a degree of hyperglycemia sufficient to cause pathologic and functional changes in various target tissues, but without clinical symptoms, may be present for a long period of time before diabetes is detected. During this asymptomatic period, it is possible to demonstrate an abnormality in carbohydrate metabolism by measurement of plasma glucose in the fasting state or after a challenge with an oral glucose load. The degree of hyperglycemia (if any) may change over time, depending on the extent of the underlying disease process A disease process may be present but may not have progressed far enough to cause hyperglycemia. The same disease process can cause impaired fasting glucose (IFG) and/or impaired glucose tolerance (IGT) without fulfilling the criteria for the diagnosis of diabetes. In some individuals with diabetes, adequate glycemic control can be achieved with weight reduction, exercise, and/or oral glucoseloweringagents. These individuals therefore do not require insulin. Other individuals who have some residual insulin secretion but require exogenous insulin for adequate glycemic control can survive

without it. Individuals with extensive cell destruction and therefore no residual insulin secretion require insulin for survival. The severity of the metabolic abnormality can progress, regress, or stay the same. Thus, the degree of hyperglycemia reflects the severity of the underlying metabolic process and its treatment more than the nature of the process itself

TREATMENT

Type 1

The Type 1 diabetic must take daily insulin injections to replace the lack of insulin. Previously animal (pork or beef) insulins were used. Synthetic human insulin was developed by the Eli Lilly company in 1980 using recombinant DNA technology. Further refinements to these resulted in the modern 'analogue' insulin. The slight alteration in the synthesised human insulin resulted in two types of analogue insulin.

Bolus or short-acting insulin

These dissolve more quickly into the bloodstream and are generally injected just before snacks or meals containing CHO. They have a rapid onset of action and their peak action lasts for 2-4 hours.

Basal or long-acting insulin

These are usually injected once or twice a day. Their onset of action is slow and peak action lasts for 4-12 hours with duration of action being 16 to 35 hours.

The basal insulin deals with the background level of glucose (caused by the anti-insulin hormones) found in the blood during the day. The bolus insulin, given just before eating, deals with the rise in glucose levels after eating. The dosage can be adjusted depending on the value of carbohydrates (CHO) in the meal. The diabetic patient should be conversant with carbohydrate values of different foods. Eating food that has not been prepared at home can sometimes be a best guess process but with experience, carbohydrate assessment becomes

more accurate. Regular blood glucose monitoring means that the levels of insulin can be altered to try to maintain blood glucose levels within the range 4-7 mmol/l before meals and <9 mmol/l for most of the time.

Type 2

With Type 2 diabetes treatment is aimed at increasing the effectiveness of the endogenous insulin using metformin and glitazones. Sulphonylureas, which act on the pancreas to help increase insulin production, may also be used. These drugs are supplemented by dietary changes and an increase in exercise to help to prolong the insulin production of the pancreas. Unlike Type 1 diabetes there is a definite genetic propensity to develop Type 2 diabetes. Fiske reported that people of South Asian or Afro-Caribbean origin have a higher incidence of Type 2 diabetes and their age of presentation is younger (aged 25) compared to Caucasians (aged 40). Putting on weight is a significant contributing factor to the increase in number of people with diabetes. With time, all patients with Type 2 diabetes will eventually need to inject insulin: the pancreas will produce less and less effective insulin and the ever increasing blood sugar levels will eventually necessitate insulin injections.

There is no consensus on the most accurate screening test for detection of diabetes. The most widely used screening tests include the fasting plasma glucose (FPG) test and the oral glucose tolerance test (OGTT). Both these tests involve measurement of blood glucose. However, the measurement of both OGTT and FPG require patients to fast overnight for at least 8 h and confirmation of diagnosis using FPG requires the test to be repeated at least twice. Furthermore, studies have shown that the sensitivity of FPG for diabetes diagnosis is not as high as expected, with nearly one-third of individuals with diabetes remaining undetected .OGTT is also costly, time-consuming and labour intensive and has low reproducibility that can add confusion and uncertainty to the confirmation of diabetes diagnoses. **Glycated** hemoglobin (hemoglobinA1c, HbA_{1c}, A1C, or Hb_{1c}; sometimes also referred to as

being Hb1c or HGBA1C) is a form of hemoglobin that is measured primarily to identify the three-month average plasma glucose concentration. The test is limited to a three-month average because the lifespan of a red blood cell is four months (120 days). However, since RBCs do not all undergo lysis at the same time, HbA1C is taken as a limited measure of 3 months. It is formed in a non-enzymatic glycation pathway by hemoglobin's exposure to plasma glucose.

HbA_{1c} is a measure of the beta-N-1-deoxy fructosyl component of hemoglobin.[1] The origin of the naming derives from Hemoglobin type A being separated on cation exchange chromatography. The first fraction to separate, probably considered to be pure Hemoglobin A, was designated HbA_0, the following fractions were designated HbA_{1a}, HbA_{1b}, and HbA_{1c}, respective of their order of elution. There have subsequently been many more sub fractions as separation techniques have improved. Normal levels of glucose produce a normal amount of glycatedhemoglobin. As the average amount of plasma glucose increases, the fraction of glycatedhemoglobin increases in a predictable way. This serves as an indicator that blood sugar is increasing and that action should be taken.

In diabetes mellitus, higher amounts of glycated hemoglobin, indicating poorer control of blood glucose levels, have been associated with cardiovascular disease, nephropathy, neuropathy, and retinopathy. A trial on a group of patients with Type 1 diabetes found that monitoring by caregivers of HbA_{1c} led to changes in diabetes treatment and improvement of metabolic control compared to monitoring only of blood or urine glucose. However, a trial designed specifically to determine whether reducing HbA_{1c} below the normal 6%, using primarily insulin and sulfonylureas (both known to easily drive blood sugar too low), would reduce the rate of cardiovascular events in type 2 diabetes found *higher* mortality—the trial was terminated early. The negative outcomes may well have been a result of the treatment approach, primarily insulin and sulfonylureas,

utilized in the "intensive" treatment group instead of LCHF, GlP-1 analogues & SGLT-2 inhibitors, none of which have these problems & lower cardiovascular mortality.

The accuracy of FPG and OGTT may be reduced by patient non-adherence to fasting, laboratory error and/or use of certain medications. The glycatedhaemoglobin (HbA1c) test has been suggested as an alternative screening test for Type 2 diabetes. HbA1c levels represent a 2–3-month average of blood glucose concentrations. The accuracy of HbA1c analysis may be influenced by the presence of haemoglobinopathy or renal failure, as well as laboratory error and/or use of certain medications, but, compared with the OGTT, HbA1c measurement is quicker and more convenient. HbA1c can be measured at any time of the day regardless of the duration of fasting or the content of the previous meal. HbA1c can also be analysed with a small blood sample using a portable device, although this is an expensive option currently . There is also the potential for blood obtained from a finger prick to be sent to a central laboratory for analysis, allowing screening of individuals in remote areas.

In 1995 the IFCC established a Working Group (IFCC WG-HbA1c) to achieve international standardization of HbA1c measurement. The activities achieved by this WG so far can be summarized as follows:

a) Highly purified HbA1c and HbA0 materials have been produced and these have been made available to the 14 laboratories of the IFCC network These primary reference materials will be available in 2007 through the Institute

for Reference Materials and Measurements (IRMM)

b) A reference measurement procedure for HbA1c has been developed. This method is based on the proteolytic digestion of red cell hemoglobin followed by quantitative peptide mapping by HPLC-mass spectrometry or HPLC-capillary electrophoresis. It has been voted on by the National Societies affiliated to the IFCC and published as an ‘‘approved IFCC reference measurement procedure’’

c) A network of reference measurement laboratories has been implemented. Two experiments are performed every year, in which materials are distributed to the laboratories for comparison purposes, and also to assign HbA1c values to candidate calibrators and controls. These studies have been performed since 1999 and have also been important in refining the reference measurement procedure, which is regularly updated as soon as new technical information becomes available. The network has developed a set of rules for the certification of reference values and for the calculation of the uncertainties of the calibrators.

d) Several comparison studies have been performed between the IFCC reference measurement laboratories and the existing DCMs. These studies found stable relationships between the IFCC and different DCM systems and the corresponding
regression equations (the ‘‘master equations’’) were published.

e) Secondary reference materials have been produced in the form of panels of fresh and frozen whole blood and distributed to the manufacturers and to laboratories performing DCMs to anchor their methods to the IFCC reference system.

The literature is replete with studies emphasizing the importance of strict glycemic control.Studies on diabetic and nondiabetic rats provide histologic evidence of delayed or inadequate wound healing after dental extractions5 and implant placement6 in the hyperglycemic group. A prospective study looking at implant failures in patients with NIDDM found that the duration of diabetes, not the preoperative plasma glucose or glycosylated hemoglobin level, was a statistically significant predictor of implant failure. This may imply that chronic glycemic control is a better predictor of outcome than is intraoperative blood glucose (BG) level. Despite expressed intuitive concerns regarding oral surgery in the poorly controlled diabetic patient, there are no prospective studies on complications or wound healing of diabetic patients after dental extractions. Therefore the

aim of this study was to determine whether glycemic control influences healing after tooth extractions.

REVIEW OF LITERATURE:

MacKenzie CR, et al[1] (1988)

The purpose of this study was to define the preoperative clinical characteristics that identify patients with diabetes mellitus at increased risk for postoperative complications, and inception cohort of diabetic patients undergoing surgical treatment was examined. Serious cardiac morbidity and death were predicted by the presence of pre-existing cardiac disease, specifically, congestive heart failure and valvular heart disease. Patients at increased risk for non-cardiac complications (infection, renal insufficiency and cerebral ischemic events) included 24 per cent of those patients with diabetic end-organ disease (retinopathy, neuropathy and nephropathy), 29 per cent of those with congestive heart failure or valvular heart disease and 35 per cent of those with peripheral vascular disease and infection. In patients who did not have such pre-existing conditions, serious noncardiac complications were rare (4 per cent). Neither the severity of the disease nor the degree of perioperative glucose control were associated with increased postoperative morbidity or mortality. Hence it was concluded that, among patients with diabetes mellitus who are undergoing surgical procedures, postoperative complications can be predicted by the presence of readily identifiable preoperative clinical characteristics.

H.Devlin et al[2] (1996)

concluded that the histologic observations suggest that in uncontrolled insulin dependent diabetes the formation of the collagenous framework in the tooth extraction socket is inhibited , resulting in delayed healing and increased alveolar destruction.

Brunner GA et al[3] .(1998)

The study was to evaluate the clinical and analytical accuracy of home blood glucose meters. Six blood glucose meters--Reflolux S (Boehringer Mannheim, Mannheim, Germany), One Touch II (LifeScan, Milpitas, CA), Glucocard Memory (Menarini, Florence, Italy), Precision QID (Medisense, Cambridge, U.K.), HaemoCue (HaemoCue, Angelholm, Sweden), and Accutrend alpha (Boehringer Mannheim, Mannheim, Germany)--were compared with a reference method (Beckman Glucose Analyzer II) under controlled conditions (glucose clamp technique). Validation of the blood glucose meters was

accomplished by clinically oriented approaches (error grid analysis), statistical approaches (variance components analysis), and by the criteria of the American Diabetes Association (ADA), which recommend a target variability of < 5%. A total of 1,794 blood glucose monitor readings and 299 reference values ranging from 2.2 to 18.2 mmol/l were analyzed (705 readings < 3.89 mmol/l, 839 readings between 3.89 and 9.99 mmol/l, and 250 readings > 9.99 mmol/l). According to error grid analysis, only Reflolux S and Glucocard M had 100% of estimations within the clinically acceptable zones A and B. Assessment of analytical accuracy revealed substantial differences between the glucose meters after separation of the data into defined glycemic ranges. None of the devices met the ADA criteria.it was concluded that to evaluate accuracy of blood glucose meters, error grid analysis, as well as statistical models, are helpful means and should be performed together. Analytical performance of currently available home blood glucose meters differs substantially within defined glycemic ranges.

RabeHesketh et al[4] (1998)

concluded that in type 2 diabetes there are improvements in long term glycaemic control and psychological distress but not in weight control or blood glucose concentration in people who receive psychological therapies.

Mark L Nevins et al[5] (1998)

concluded that the streptozotocin induced diabetic model produced altered blood glucose levels to allow the study of the effects of diabetes on osseointegration of titanium implants.

Laakso M[6] (1999)

This study reviews the long term complications caused by diabetes mellitus. Cardiovascular disease (coronary heart disease, stroke, peripheral vascular disease) is the most important cause of mortality and morbidity among patients with type 2 diabetes. Conventional risk factors contribute similarly to macrovascular complications in patients with type 2 diabetes and nondiabetic subjects, and therefore, other explanations have been sought for enhanced atherothrombosis in type 2 diabetes. Among characteristics specific for type 2 diabetes, hyperglycemia has recently been a focus of keen research. A recent meta-analysis of 20 studies on nondiabetic subjects has demonstrated that in the nondiabetic range of glycemia (<6.1 mmol/l), increased glucose is already associated with an increased risk for

cardiovascular disease. Similarly, 12 recent prospective studies have convincingly indicated that hyperglycemia contributes to cardiovascular complications in patients with type 2 diabetes. The recently published U.K. Prospective Diabetes Study has shown that intensive glucose control reduces effectively microvascular complications among patients with type 2 diabetes, but that its effect on the prevention of cardiovascular complications was limited. Given the fact that in the U.K. Prospective Diabetes Study, none of the treatment modalities was particularly effective in reducing glucose, this underestimates the true potential of the correction of hyperglycemia in the prevention of cardiovascular disease in type 2 diabetes. However, in addition to intensive therapy of hyperglycemia, other conventional risk factors should also be normalized to prevent cardiovascular disease in patients with type 2 diabetes.

Golden SH,et al[7].(1999)

This study was designed to assess the relationship of perioperative glycemic control to the subsequent risk of infectious complications. Although hyperglycemia is hypothesized to increase the short-term risk of infection, this hypothesis has not been well tested in a clinical setting. A total of 411 adults with diabetes who underwent coronary artery surgery from 1990 to 1995 in the cardiac surgery service of an urban university hospital were included in a nonconcurrent prospective cohort study based on chart review. Perioperative glycemic control was characterized by the mean of six capillary glucose measurements taken during the 36-h interval following surgery. The major outcomes studied were infections of leg and chest wounds, pneumonia, and urinary tract infections.It was concluded that in patients with diabetes who undergo coronary artery surgery, postoperative hyperglycemia is an independent predictor of short-term infectious complications. Physicians should consider a glucose concentration target of < or =200 mg/dl to reduce the risk of infection.

Sherita HG et al[8] (1999)

concluded that in patients with diabetes who undergo coronary artery surgery, post operativehyperglycemia is an independent predictor of short term infectious complications.

Olson JW, et al[9].(2000)

Diabetes mellitus, a prevalent disorder worldwide, is associated with systemic adverse sequelae, such as wound healing alterations, which may affect osseointegration of dental

implants. This prospective multicenter study assessed the success of 2-stage endosseous root-form implants (3 different implant systems) placed in the mandibular symphysis of 89 male type 2 diabetic subjects. The implants were uncovered approximately 4 months after placement, restored with an implant-supported, Hader bar clip-retained overdenture, and maintained at scheduled follow-up data collection examinations for 60 months after loading. Sixteen (9.0%) of the 178 implants failed. Life table methods calculated implant survival at approximately 88%, from prosthesis placement through the 60-month follow-up, and at approximately 90% from implant placement through the observation period. No implants failed between surgical placement and uncovering, 5 failed at uncovering, 7 failed after uncovering before prosthesis placement, and 4 failed after prosthesis placement. Fasting plasma glucose (FPG) and glycosylated hemoglobin (HbA1c) values were determined before implant placement (baseline) and approximately 4 months later at surgical uncovering (follow-up). The 5-year implant outcomes (successes versus failures) were analyzed against the following predictor variables: (1) baseline and follow-up FPG values, (2) baseline and follow-up HbA1c values, (3) subject age, (4) duration of diabetes (years), (5) baseline diabetic therapy, (6) smoking history, and (7) implant length. Regression analysis found only duration of diabetes ($P < .025$) and implant length ($P < .001$) to be statistically significant predictors of implant failure. There was no statistically significant difference in failure rates between the 3 different implant systems used. This study supports the use of dental implants in type 2 diabetic patients**.**

Joseph DH et al[10] (2001)

The purpose of this study was to determine the value of peer coaching and its influence on behavior change. Coaches who were known to be successfully managing their diabetes were paired with individuals who were struggling with behavior change associated with managing diabetes. The pairs were matched according to age, sex, and physical appearance. Coaches met initially with participants in a face-to-face meeting for 1 hour and talked with them once a week for 10 to 15 minutes for the next 8 weeks. The initial interview and subsequent phone conversations focused on the person's problems and efforts at behavior change. At the end of the study, the pairs participated in a videotaped focus group to discuss their views on coaching and its influence on behavior change. Participants reported that coaching was personal, useful in disease management, and helpful in their quest to establish and adhere to routines of care. Participants also reported making progress toward changing

their behavior related to diet, exercise, and blood glucose monitoring. Sustained behavior change was not measured. It was concluded that Peer coaching appears to have merit as a viable, low-cost intervention with the potential of helping individuals with diabetes who need to change their behavior.

Lalla RV et al[11] (2001)

The authors present relevant information about DM, including a recently revised nomenclature system, pathophysiology, complications, new diagnostic criteria, medical and dental management considerations, and associated oral condition. The prevalence of diabetes mellitus, or DM, in the United States is increasing steadily. The increasing longevity of the American population and more effective diagnostic protocols mean that the dental practitioner will be treating an increasing number of patients with the disease. There are many important medical and dental management issues that dentists should consider when treating patients with DM.

Aaron Vinik et al[12] (2002)

They have discussed the long term risk factors caused by diabetes mellitus. Cardiovascular disease (CVD) is the major cause of morbidity and mortality in patients with diabetes. Macrovascular events, including stroke, myocardial infarction (MI), and peripheral arterial disease (PAD), occur earlier than in nondiabetics and the underlying pathologies are often more diffuse and severe. Diabetic arteriopathy, which encompasses endothelial dysfunction, hypercoagulability, changes in blood flow, and platelet abnormalities, contributes to the early evolution of these events. Tight glucose and blood pressure control improves the vascular status of these patients by varying degrees. Antiplatelet agents have also been shown to be effective in the secondary prevention of cardiovascular events. In the ideal world, every risk factor would be addressed and each diabetic would have excellent glycemic control, a low normal blood pressure, a low LDL, and be prescribed an ACE inhibitor, together with aspirin and clopidogrel. If this is done, this emerging epidemic of macrovascular disease will be contained.

Taylor GW et al[13] (2004)

this study has reviewed the literature on the role of diabetes and its effects on dentition. Diabetes has been seen to have a destructive effect on the health of the periodontium there by cause been loss and tooth loss.

Douglas B et al[14] (2004)

concluded that diabetes mellitus is an increasingly common pathology that affects patients of all ages and results in significant morbidity and mortality rates.

Peel E et al[15].(2004)

this study used in-depth interviews with 40 newly diagnosed type 2 diabetic (T2DM) patients in Scotland, to explore their emotional reactions about diagnosis, and their views about information provision at the time of diagnosis. Data were analysed using a thematic approach. Our results showed three main 'routes' to diagnosis: 'suspected diabetes' route; 'illness' route; and 'routine' route. Those within the 'routine' route described the most varied emotional reactions to their diagnosis. We found that most patients, irrespective of their route to diagnosis, wanted more information about diabetes management at the time of diagnosis. We suggest that practitioners would benefit from being sensitive to the route patients follow to diagnosis, and prompt, simple but detailed advice about T2DM management would be helpful for newly diagnosed patients.

Blake DR et al[16] (2004)

They discussed the role of Point-of-care testing, or near patient testing, refers to testing of biochemical parameters with devices that provide rapid results so the data can be immediately used in clinical care. Because the diagnosis and, in particular, management, of diabetes mellitus is largely relegated to the outpatient setting (including self-care in the home, school and workplace), point-of-care testing is particularly relevant for this disease. Moreover, the need for timely (immediate) results for glucose monitoring makes point-of-care testing necessary for the management of diabetes in the inpatient and outpatient setting. The following review examines the role of various assays in the diagnosis and management of diabetes and discusses the role of point-of-care testing.

Calisti L et al[17] (2005)

In this study, Glycosylated hemoglobin (HbA1c) is a marker of evaluation of long-term glycemic control in diabetic patients and predicts risks for the development and/or progression of diabetic complications. Glycosylation process depends on the exposure to glucose, so on the half-life of erythrocyte. It was demonstrated, however that metabolic control concerning the last 90-120 days had only a 10% effect on the result of HbAlc; mean blood glucose of the last 30 days contributes for 50% of HbA1c value. Blood glucose value in the afternoon and in the evening better correlate with HbA1c levels if compared with blood glucose values in the morning. It is important to know that there may be, in the evaluation of HbAlc, interference in the dosage, due to a condition of uremia, hyperlipemia, bad conservation and hemolysis of the sample, increase of leucocytes and presence of anomalous hemoglobins. Moreover the use of different methods, the lack of a common calibration concerning the same methods and the variability of instrumentation do not make reproducible results yet, in different laboratories.

Maskari AY et al[18] (2005)

suggested that DM is a chronic disease affecting all age groups. It is one of the leading causes of mortality and morbidity worldwide.

Nathan DM et al[19] (2005)

In this study Intensive diabetes treatment and cardiovascular disease in patients with type 1 diabetes is assessed. It is concluded that Intensive diabetes therapy has long term beneficial effects on the risk of cardiovascular disease in patients with type 1 diabetes.

Winkley K et al[20] (2005)

concluded that psychological treatments can slightly improve glycaemic control in children and adolescents with diabetes but have no effect in adults.

Bennett CM et al[21] (2007)

In this study it is concluded that HbA1c and FPG are equally effective diagnostic tool for Type 2 diabetes.

Hoelzel W et al[22] (2007)

They have evaluated concluded a reproducible link between the IFCC RM and DCM HbA1c values.

John et al[23], (2007)

The measurement of glycated haemoglobin is cental monitoring of glycemic control in patients with diabetes. There are atleast 30 differnt laboratory assays commercially available to measure the portion of HbA1c in blood. In 1995 the IFCC established a working group (IFCC WG-HbA1c) to achieve internation standardisation of HbA1c measurement.

Hasniza Zaman Huri et al[24] (2008)

Self-monitoring of blood glucose (SMBG) has become a more common practice among type-2 diabetes patients, but there is limited information available regarding the patients practice and knowledge of SMBG. A cross-sectional survey was conducted on 285 outpatients at the University Malaya Medical Centre of Malaysia from November 2006 to February 2007, to assess patients practice in terms of timing, frequency, performance and utilization of blood glucose value from SMBG as well as the relationship between patients SMBG knowledge and demographic characteristics. It was concluded that Age had no significant influence in patients SMBG knowledge. Conclusion: More education programs pertaining to SMBG should be carried out, especially for patients with low education.

Ryan ME[25] (2008)

This article reviews the pathogenesis of periodontal disease as it relates to diabetes. The author discusses patient susceptibility in terms of risk and recommends risk assessment to determine optimal treatment strategies. The bridge between oral and systemic health exists and becomes more concrete as data continue to emerge in support of this relationship. The medical management of diabetes is affected by the presence of chronic infections, such as periodontitis. Patients with poorly controlled diabetes are at greater risk for developing periodontitis. The opportunity for systemic exposure to periodontal pathogens and proinflammatory mediators associated with periodontitis is discussed relative to their specific effects on patients with diabetes. The importance of good metabolic control in terms of risk for developing long-term complications of diabetes is presented and the impact of periodontitis on achieving adequate metabolic control is described. Special considerations for the management of patients with diabetes in the dental office are

reviewed, including the signs and symptoms of diabetes, risk assessment for diabetes, and the challenges of "tight control" with insulin and oral agents with regards to hypoglycemia. It is recommended by the author that a thorough medical history of the patient be obtained, that the patient's medications are known, that the dentist consults with the patient's physician to assess the patient's glycemic control, and that the patient's blood glucose levels and dietary intake be monitored before treatment. Finally, the author reviews the long-term complications of diabetes, particularly the oral complications that can affect overall health. The author concludes with the belief that the treatment of periodontal diseases should not be considered optional or elective but, instead, should be a necessary and integral part of a patient's overall healthcare program.

Srividyakidambi et al[26] (2008)

concluded that Diabetes mellitus is a chronic , systemic metabolic disorder in which the orosystemic connection is becoming more understood.

CC Azodo[27] (2009)

The importance of Improved knowledge of this DM among dental practitioner will translate to enhanced management of oral diseases, prevention of complication and overall improvement in quality of life of diabetic patients has been studied. Diabetes mellitus (DM) is a chronic, non-communicable disease with concomitant oral manifestations that impact on dental care. Approximately 40-80 persons in 2,000 adult population visiting dental practice are diabetic and about half are unaware of their condition. The average dentist attends to over 100 diabetic patients per year. 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 poorly controlled disease. Oral diseases and their treatments are known to affect glycemic control and insulin resistance in diabetic patient. By taking an active role in the diagnosis and treatment of oral conditions associated with DM, dentists also may contribute to the maintenance of optimum health in patients with this condition.Emphasis should therefore be placed on the multidisciplinary and team approach in diabetes mellitus patient management

Al-Maskari F et al[28] (2010)

The aim of the study was to estimate the direct annual treatment costs of DM and its related complications among patients in Al-Ain city, UAE. A sample of 150 DM patients were enrolled during 2004-2005, and their medical costs over the ensuing 12 months was measured, quantified, analyzed and extrapolated to the population in Al-Ain and UAE, using conventional and inference statistics. Overall, costs increased with age, diabetes duration and were higher for patients treated with insulin compared to those treated with oral hypoglycemic agents or with diet control only. It was concluded that DM direct treatment costs increased with the presence and progression of chronic DM related complications. Hospitalisation costs constituted a large proportion and were increasingly higher with the presence and progression of DM related complications. To reduce the impact on healthcare resources, efforts should be made to prevent progression to DM complications, by implementing guidelines for diabetes care, screening for complications and better management.

Aronovich et al[29] (2010)

In this study, in was analysed whether glycenic control influences healing after tooth extractions. It was a prospective observer blinded study. Epithelialization of extraction sites was assessed relative to the patient history, relative to the non fasting blood glucose levels and glycated haemoglobin levels. There was no statistical significant difference in the post extraction epithelialisation between the diabetic patients based on pre operative blood glucose levels, HbA1C levels or patients history. Hence glycemic control did not influence post extraction healing in diabetic patients.

L.Wray et al[30] (2011)

concluded that with the current rise in number of people with diabetes it is important for clinicians to have a background understanding of the diabetic condition.

S Huang et al[31] (2012)

concluded that the traditional view that diabetics have increased delayed healing was not supported. Type 2 diabetics on oral hypoglycaemics should be treated the same as non diabetic patients for extraction.

Dang MN et al[32] (2013)

This article reviews how epigenetic mechanisms may contribute to the development of autoimmune diseases with a focus on type 1 diabetes. Autoimmune diseases arise when the body mounts an immune response against 'self' cells and tissues causing inflammation and damage. It is commonly accepted that these diseases develop because of the interplay of genetic and environmental factors. Evidence for genetic factors includes the higher concordance of disease in monozygotic twins than in dizygotic twins. However, monozygotic twins may remain discordant for disease indicating a role for environmental factors. Environmental factors may alter gene expression via epigenetic mechanisms. This is particularly pertinent in type 1 diabetes in which DNA methylation and histone modifications have been associated with altered gene expression. The low disease concordance rate in adult-onset type 1 diabetes (<20%) suggests that environmental and epigenetic changes may play a predominant role. Defining the role of epigenetic changes could identify specific gene pathways and dysregulated expression of gene products that contribute to the pathogenesis of type 1 diabetes.

Yunan Tang et al[33] (2013)

In this study, research has been done on the clinical complications of type 2 diabetes that could be attributed, in part, to low-grade chronic inflammation. Before the development of type 2 diabetes, changes in the metabolism of glucose and fatty acids activate innate immune responses that give rise to systemic insulin resistance, which in turn perpetuates and establishes a state of chronic inflammation. As a result, type 2 diabetes is associated with tissue dysfunction and injury, deficiencies in clearing microbial infections, and impaired wound healing.Normally, inflammation protects against infection and injury but must be resolved to prevent inadvertent tissue damage. The resolution of inflammation is accomplished by time- and site-specific generation of proresolving mediators that control both the magnitude and the duration of the inflammatory response. Among the mediators of resolution, resolvins have emerged as critical players that exert potent anti-inflammatory actions by blunting excessive polymorphonuclear neutrophil (PMN) infiltration into tissues and decreasing proinflammatory mediator production. Unlike other anti-inflammatory mediators that suppress inflammation, resolvins also promote macrophage phagocytosis of apoptotic cells and microbes and stimulate the clearance of phagocytes to enable return to homeostasis. These events are critical for resolution of inflammation because lingering apoptotic cells or phagocytes can undergo secondary necrosis causing unwarranted tissue

damage. Hence, disruption of these endogenous pathways of resolution could give rise to chronic inflammation in type 2 diabetes. However, it is not known whether type 2 diabetes affects the resolution of inflammation and whether treatment with proresolving mediators would stimulate resolution and ameliorate clinical complications of type 2 diabetes, such as impaired wound healing.In summary, the results of the current study demonstrate that resolution of inflammation is altered in type 2 diabetes and that defective macrophage-mediated resolution could be restored by proresolving lipid mediator RvD1. Notably, local delivery of RvD1 enhanced wound closure in diabetic mice, suggesting that stimulating resolution has beneficial functional outcomes. As resolvins are currently in phase III clinical trials for the treatment of other inflammatory pathologies (i.e., dry eye), the results of this study could be readily translated into clinical therapy for accelerating wound healing in patients with diabetes. The findings of the current study also have wide implications for developing future strategies for the treatment of other diabetes complications and several chronic autoimmune and cardiovascular diseases associated with unresolved chronic inflammation

Anna Chapman et al[34] (2015)

This study presents the first systematic review and meta-analyses of psychological interventions for the management of glycemic and psychological outcomes of T2DM in China that uses both international and Chinese-language databases, in order to quantify the efficacy of interventions relative to control conditions. Type 2 diabetes mellitus (T2DM) is a complex metabolic condition that requires effective long-term management in order for patients to achieve optimal glycemic control and to prevent chronic complications. As lifestyle, behavioral, and psychological changes are fundamental to the management of T2DM, it is essential for health care teams and patients to work collaboratively to ensure patients adhere to clinical recommendations and the T2DM self-care regimen. Internationally, evidence-based guidelines recognize the importance of a structured and systematic approach to the management of T2DM in the primary care setting that incorporates psychological care within clinical recommendations. It is also widely recognized that compared to the general population, individuals with T2DM have a higher prevalence of clinical and sub-clinical levels of depression and anxiety, with the potential consequences being reductions in glycemic control, quality of life, and treatment adherence. In conclusion, this systematic

review and meta-analyses demonstrated that psychological interventions, namely, CBT, MI, and CCT, are effective in improving certain T2DM related outcomes in China. Considerable levels of heterogeneity and unclear risk of bias associated with the most included RCTs warrant caution when interpreting results. If China is to address the health issues associated with its burgeoning T2DM population and delay the progression of T2DM-related outcomes, psychological interventions are promising tools and should be utilized in the future.

Mohammad Hassan Akhavan Karbassi et al[35] , (2015)

This study evaluated and compared the relationship between socket blood sugar and post-extraction complications in type II diabetic and non-diabetic patients. This cross-sectional study was carried out on 80 diabetic and 80 non-diabetic patients in Yazd Dental School. All patients had posterior tooth extraction. Prolonged bleeding, pain, fever and swelling were studied at the end of 4th day and dry socket and lack of healing at the end of the 7th day after extraction. Data was analyzed with SPSS 13 software using chi squared, Mann-Whitney and Fisher's exact tests.The frequency of prolonged bleeding and incidence of dry socket between two groups at socket blood sugar levels under 126 mg/dL and comparison of the frequency of prolonged pain, fever and infection between two groups at socket blood sugar levels ≥126 mg/dL showed statistically significant differences (P<0.05). Swelling and lack of healing were not associated with diabetes mellitus in none of the socket blood sugar levels (P>0.1). It is concluded that dentists use glucometers to determine socket blood sugar levels in diabetic patients to predict and prevent complications after tooth extraction in diabetic patients.

Katie E. Rollins[36] (2015)

The aim of this systematic review was to establish the relationship between long-term preoperative glycemic control as measured by HbA1c and postoperative complications. Diabetes is a significant risk factor for surgical complications and also increases the prevalence of comorbidities, thereby increasing surgical risk. A systematic search was conducted to source articles published between 1980 and 2014 pertinent to the review. Full-text articles were included if they met the pre-determined criteria as determined by two reviewers. Studies reporting the impact of preoperative HbA1c levels on postoperative outcomes in all disciplines of surgery were included. Twenty studies, including a total of 19,514 patients with diabetes mellitus from a range of surgical specialties, were suitable for inclusion. Preoperative glycemic control did not have a bearing on 30-day mortality. There

were no significant differences in the incidence of stroke, venous thromboembolic disease, hospital readmission and ITU length of stay based on glycemic control. The majority of studies suggested no link between preoperative HbA1c levels and acute kidney injury or need for postoperative dialysis, dysrhythmia, infection not related to the surgical site and total hospital length of stay. The literature was highly variable with regards to myocardial events, surgical site infection and reoperation rates. It was concluded that elevated preoperative HbA1c was not definitively associated with increased postoperative morbidity or mortality in patients with diabetes mellitus. The studies included in this review were relatively heterogeneous, predominantly retrospective, and often contained small patient numbers, suggesting that good quality evidence is necessary.

Shariq I. Sherwani, et al[37] (2016)

Historically, HbA1c was first isolated by Huisman et al. in 1958 and characterized by Bookchin and Gallop[4] in 1968, as a glycoprotein. The elevated levels of HbA1c in diabetic patients were reported by Rahbar et al. in 1969. Bunn et al. identified the pathway leading to the formation of HbA1c in 1975. Using the HbA1c as a biomarker for monitoring the levels of glucose among diabetic patients was first proposed by Koenig et al. in 1976. Analysis of glycated hemoglobin (HbA1c) in blood provides evidence about an individual's average blood glucose levels during the previous two to three months, which is the predicted half-life of red blood cells (RBCs). The HbA1c is now recommended as a standard of care (SOC) for testing and monitoring diabetes, specifically the type 2 diabetes. it was concluded that HbA1c is an accurate and easy-to-administer test with on-the-spot results availability and can be an effective tool in establishing the diagnosis of diabetes, especially in low- and middle-income countries and hard-to-reach populations. Even though HbA1c has been endorsed for diagnosis of diabetes, in most of the countries worldwide, some testing strategies and cutoff ranges are still being debated. However, combination of FGT and HbA1c significantly enhances the diagnostic accuracy of these individual tests. The prognostic potential of HbA1c lies in its unique ability of assessing retrospective glycemic control as well as predicting the lipid profile in diabetic patients. As the epidemic of diabetes continues to grow worldwide, HbA1c test may continue to be implemented as part of the diagnostic and prognostic tool, leading to better patient care and successful clinical outcomes.

Keiichi Torimoto et al [38] (2017)

Their study was to determine the relationship between blood glucose profile at discharge and HbA1c levels at 12 weeks after discharge in patients who did not change their medications after discharge. For this purpose, we evaluated blood glucose profile at admission and discharge as measured with CGM in patients with type 2 diabetes who received inpatient diabetes education.

Hemoglobin A1c (HbA1c) is used as an index of chronic hyperglycemia in the diagnosis and treatment of diabetes mellitus. Many epidemiological studies have shown that HbA1c is associated with the risk of diabetic vasculopathy. HbA1c is the most important index of glycemic control, and has been used to set the goal of appropriate treatment for each patient. Generally speaking, the aim of the majority of inpatient diabetes education programs is to improve lifestyle habits and enhance treatment within a short period of time. Through such programs, patients learn the benefits of diet and exercise, and receive information about acute and chronic complications of diabetes and preventive measures. The primary goal of such programs is to achieve good long-term glycemic control; and HbA1c level after discharge is one of the most important indexes used to evaluate the effect of such programs. The HbA1c value reflects the net mean blood glucose level over the preceding 1 or 2 months, and does not reflect immediate changes in the blood glucose profile after treatment. In clinical practice, self-monitoring of blood glucose (SMBG) and continuous glucose monitoring (CGM) are often used to assess circadian variation in blood glucose and changes in blood glucose after treatment. Among the parameters measured by SMBG and CGM, the mean blood glucose level is reported to be strongly correlated with HbA1c[9], [10]. To our knowledge, however, there is little or no information on the relationship between blood glucose profile at discharge and HbA1c level after discharge. It was concluded that HbA1c level after discharge was associated with disease duration and MBG level at discharge. Furthermore, the study identified disease duration and postprandial hyperglycemia at discharge as significant factors that influenced the achievement of HbA1c <7.0%. Based on the data obtained using CGM, the present study showed that blood glucose profile at discharge might be useful in predicting HbA1c level after discharge for patients who received diabetes education during hospitalization. We consider that early treatment to improve blood glucose fluctuation and prevent postprandial hyperglycemia, in addition to lower mean blood glucose, is essential for achieving strict glycemic control.

MATERIALS AND METHODS:

We enrolled 100 diabetic patients who required dental extractions in this prospective observer-blinded study. Epithelialization of extraction sites was assessed relative to thepatient's history, non-fasting blood glucose levels, and glycosylated hemoglobin levels.

METHODOLOGY / PROCEDURES:

100 diabetic patients are included in the study those who require dental extractions in this prospective observer-blinded study. Epithelialization of extraction sites is assessed relative to the patient's history, Random blood glucose levels (RBS), and glycosylated hemoglobin levels (HbA1c) and results were evaluated student 't' test in SPSS software.

Inclusion criteria:were the presence of a fully eruptedtooth requiring extraction, diagnosis of diabetes mellitus and use of related medications, age of 18 years or

older, and American Society of Anesthesiologists status II or III.

Exclusion criteria:were recent antibiotic or steroid use, steroid-induced glucose intolerance, systemic immunodeficiency, chemotherapy and radiation therapy, nonlocalizedodontogenic infection, and surrounding tissue pathology or lesion.

INTERVENTIONS / DRUGS USED:

Local Anesthesia 1: 80000 (with Adrenaline) Lignox 2% for Dental Extraction procedure

Antibiotics: Amoxycillin 500 mg

Metrogyl 400 mg

NSAID's: T-Lac (Ketorolac)

Dolo 650mg

H2 receptor blocker: Rantac 150 mg

PROCUREMENT OF INVESTIGATIONAL DRUGS , STORAGE, DISPENSING, etc..: Nil

STUDY TERMINATION:

Study terminated by September 2017.

STUDY PARAMETERS:

Outcome variables recorded clinically at post operative days 0,7,14

Measured Outcome Variable

1. Greatest buccal-to-lingual width of extraction site in millimetres
2. Drainage (purulent or serosanguinous)
3. Dehiscence
4. Edema
5. Fluctuance
6. Tenderness
7. Erythema
8. Pain rating scale
9. Number of additional postoperative visits
10. Need for reoperation with description
11. Antibiotic prescribed postoperatively
12. Increased throbbing pain between PODs 3 and 5
13. Need for dry-socket dressing between PODs 3 and 5

TABLE 1

MALE	32
FEMALE	68

GRAPH 1

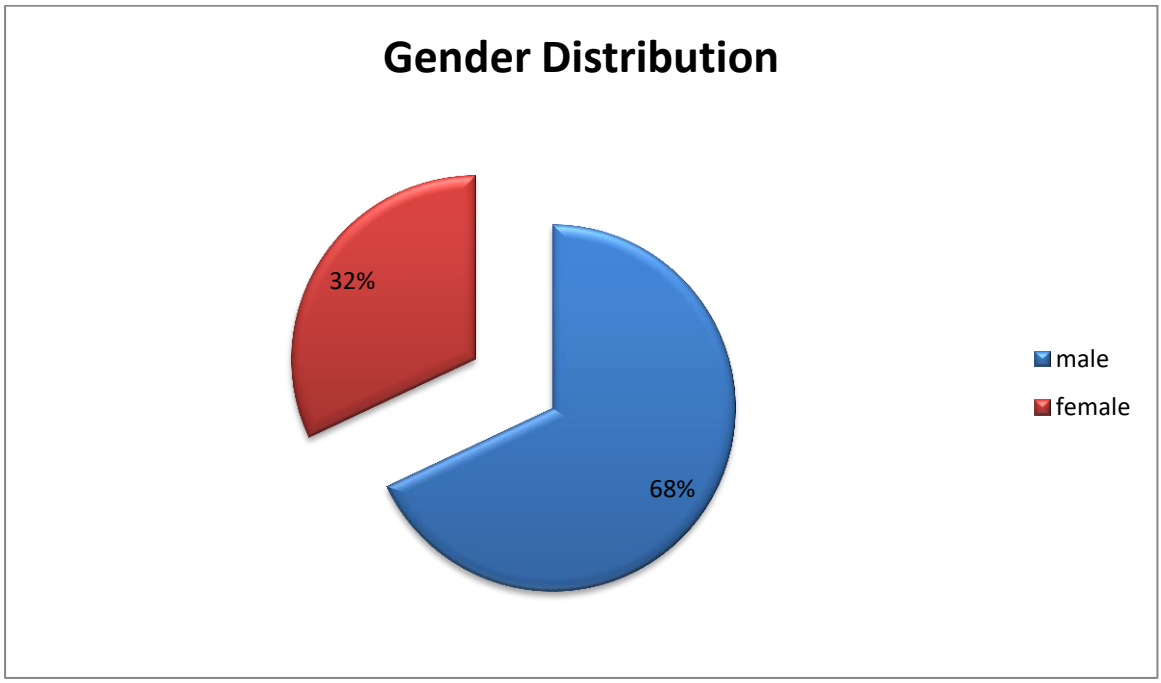


TABLE 2

≤ 5 Yrs	6-10 yrs	11-15 yrs	>15 yrs
46	22	14	26

GRAPH 2

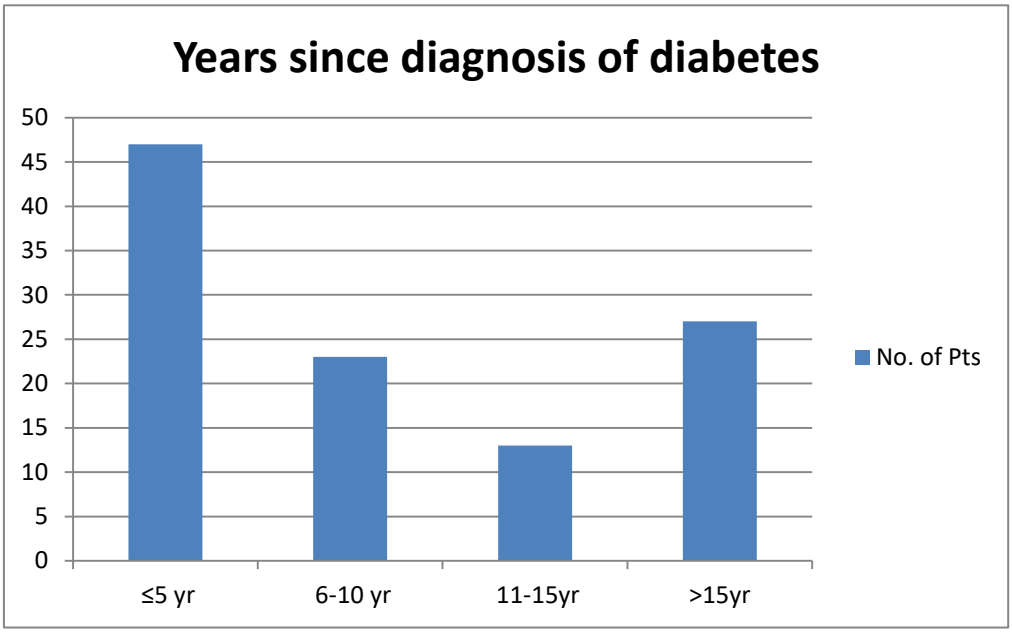


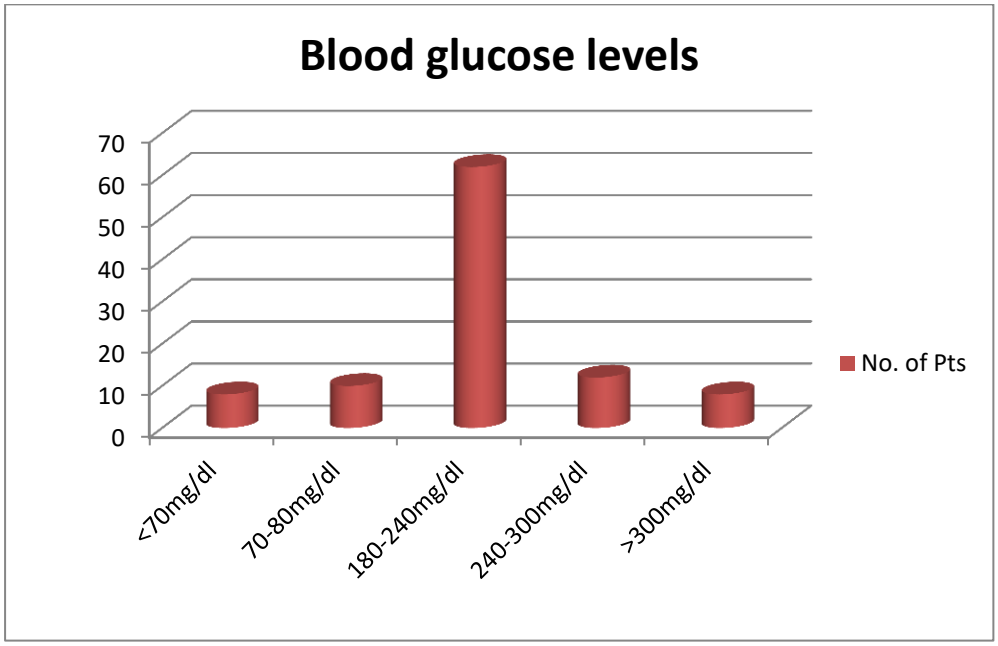
TABLE 3

Variable of Interest	BG Level ≤180 mg/dl [Mean {No. of pts}]	BG Level > 180 mg/dl [Mean{No. of pts}]	P Value
BL on POD 7	3.8 mm(18)	4.2 mm(82)	
BL on POD 14	2.4 mm(18)	2.6 mm(82)	
EPT1	3.2 mm(18)	2.8 mm(82)	
EPT2	4.6 mm(18)	4.4 mm(82)	

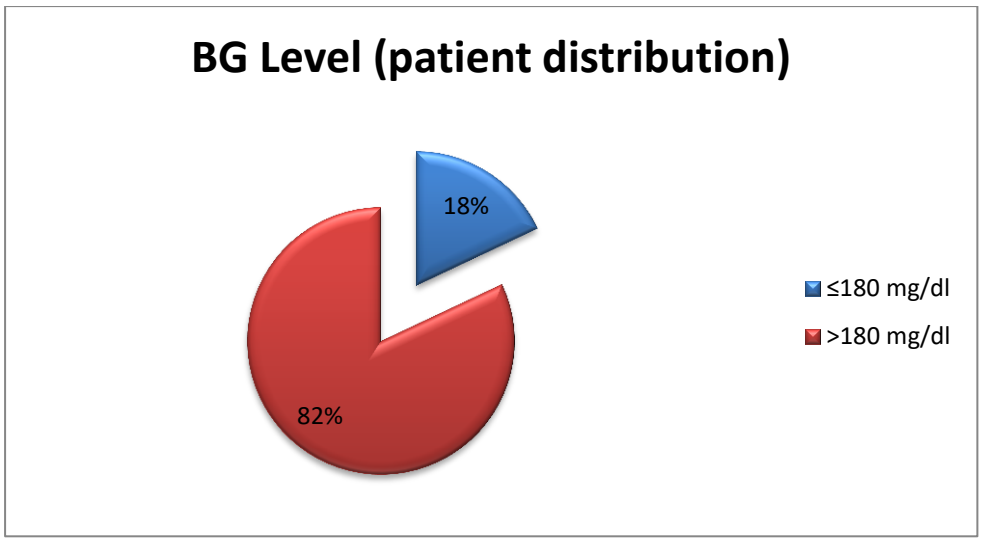
TABLE 4

Variable of Interest	HgbA1c ≤7% [Mean{No. of pts}]	HgbA1c of 7.1%-9% [Mean{No. of pts}]	HgbA1c >9% [Mean{No. of pts}]	P value
BL POD 7	3.8 mm(18)	3.9 mm(40)	4.1 mm(42)	
BL POD 14	1.9 mm(18)	2.1 mm(40)	2.3 mm(42)	
EPT1	3.2 mm(18)	3.1 mm(40)	2.9 mm(42)	
EPT2	5.1 mm(18)	4.9 mm(40)	4.7 mm(42)	

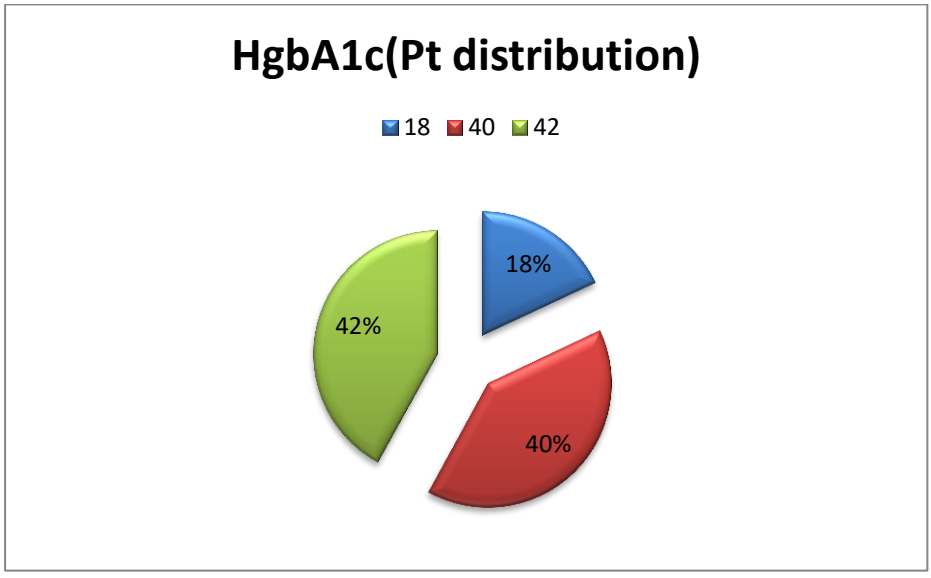
GRAPH 3


Blood glucose levels
70
60
50
40
30
20
10
0
<70mg/dl
70-80mg/dl
180-240mg/dl
240-300mg/dl
>300mg/dl
No. of Pts

GRAPH 4



GRAPH 5



RESULTS:

Of the 100 patients Males were 32, females 68 . The distribution of patients according to the number of years living with diabetes is shown in (Table 2/Graph 2). At the time of diagnosis 56 patients were prescribed with oral hypoglycemics, later 28 patients were switched ones to insulin. This was decided based on their glycemic control and the occurance of diabetes related complications.

Of the 100 patients 18 had proper BG level of 180mg/dl and 82 had levels greater than 180mg/dl (Graph 3/ Graph 4). All patients had updated their HbA1c levels who were divided into three groups 7% or less, 7.1 % to 9% and greater than 9 % (Graph 5).

The distribution of extraction comprised of 64 maxillary tooth and 36 mandibular teeth of with 18 anterior tooth and 82 posterior tooth were extracted.

All patients had a 1 and 2 week follow up. The mean age of extraction sockets of POD 0,7,14 was 7.00, 4.00, 2.5mm respectively. Only four patients had pain at the site of extraction socket required local topical application of antibiotics and oral care. No other complications were reported.

There was no stastistically significant difference in the rate of postextraction epithelialization between the diabetes patients with the operative BG level of 180mg/dl or less and those with greater than 180mg/dl. (Table 3). There was also no statistically significant difference in the rate of post extraction epithelialization between diabetic patients with glycosylated Hb level of 7 % or less, 7.1% to 9 % or greater than 9% (Table 4).

Statistical analysis of the patient data comparing the the diabetes patients with the operative BG level of 180mg/dl or less and those with greater than 180mg/dl was done using a Student ‘t’ test. The two tailed P value equals 1.000. by conventional criteria, this

difference is considered to be not statistically significant. The Student ‘t’ test comparing the between diabetic patients with glycosylated Hb level of 7 % or less, 7.1% to 9 % or greater than 9% was also found to be statistically in significant.

Discussion:

Traditionally in dentistry diabetics are considered to have increased healing problems related to dental extractions, periodontal surgery and wearing ill-fitting dentures[39]. They are also considered more likely to have infections. Although this may be so for poorly controlled Type 1 diabetics, there is only anecdotal support for this view for Type 2 diabetics on oral hypoglycaemics. There are no evidence based studies such as case controlled cohort studies for dental surgery in Type 2 diabetes. This is an important evidence based deficiency as Type 2 diabetics constitute 90% of all diabetic patients. A study comparing well controlled with poorly controlled diabetics, as measured by blood glucose level (BGL), haemoglobinAlc (HbAlc) and end organic scores was published. It found no difference in healing. Diabetes is a common metabolic disorder characterized by an inability to regulate blood glucose due to insulin deficiency or resistance. Type 1 diabetes (previously known as insulin-dependent, juvenile or childhood- onset) is characterized by deficient insulin production whereas Type 2 diabetes (formerly called non-insulin-dependent or adult-onset) results from relative insulin deficiency and tissue insulin resistance causing abnormal BGLs despite secondary hyperinsulinaemia[40,41]. In the AusDiab Study of 2002 it was found that 7.4% of Australian adults were diabetic and a further 16.4% were prediabetic[42]. For every two known diabetics it has been found that there is at least one unknown diabetic. This number is increased by the two prediabetic states of impaired fasting glucose (IFG) and impaired glucose tolerance (IGT). Patients with prediabetes do not meet the criteria for being diagnosed with diabetes but have glucose levels higher than those considered normal.[43] For IFG, it is a fasting BGL of 6.1–7 mmol/L and for IGT, it is a non-fasting BGL of 7.8–11.0 mmol/L. Each year, 3–10% of people with prediabetes will go on to

develop diabetes. The clinically relevant BGLs are 7.8 mmol/L for prediabetes and 11.0 mmol/L for diabetes.

Another useful measure of long-term glycaemic control is the haemoglobinAlc (HbAlc) test where the target is 6.5–7.0%, with above 8.0% being an indicator of poorer control. It is recommended that dentists determine the stability of known diabetics by means of the BGL and HbAlc, either by patient history, advice from their medical practitioner or by directly performing the tests prior to commencing surgery[44]. Poor glycaemic control predisposes to development of a range of complications that have been broadly categorized as macrovascular, microvascular and neuropathic[45]. Microcirculatory deficiencies, in particular, can have significant bearing on wound healing following surgical procedures. An intact microcirculation is required for tissue nutrition, removal of waste products, inflammatory responses and temperature regulation. In diabetics, changes to the capillaries such as thickening of the basement membrane result in altered permeability, impeded migration of leucocytes and impaired hyperaemia, causing underperfusion during tissue stress and tissue hypoxia[46,47]. These changes can adversely affect the outcome of surgery, resulting in poor wound healing and wound infection[48,49]. This has been most clearly documented in relation to cardiothoracic procedures where poorly controlled diabetic patients undergoing coronary bypass surgeries experienced increased morbidity and mortality, [50] increased rates of postsurgical infections[51] and worse hospital outcomes[52,53]. Conversely, maintenance of tight perioperative glycaemic control for coronary bypass patients has been shown to significantly decrease infections and other adverse outcomes[54]. It has been shown that diabetic complications can occur during prediabetes, particularly microangiopathy such as diabetic retinopathy[55]. It is for these reasons that known diabetics are offered counseling on nutrition and lifestyle including smoking cessation.

In dentoalveolar surgery, diabetic patients could be expected to suffer similar complications to those observed in other surgical procedures. However, the oral environment with the forces of mastication, high bone turnover, high vascularity, saliva and the constant reservoir of microorganisms is distinct from other parts of the body, thereby making generalizations from other surgical sites limited[56]. There have been a limited number of studies using experimentally induced diabetes in rats. These animals have an uncontrolled insulin dependent diabetic state and not surprisingly dental extraction wounds heal poorly, often with alveolar destruction[2]. However, this does not represent a current clinical situation in an advanced country such as Australia unless both the patient and their treating dentist completely mismanage an unstable Type 1 diabetic state. This may occasionally occur and the patient ends up in hospital, requiring specialist management. Such cases are not reported but the two consultant oral and maxillofacial surgeons in this study have encountered such cases.

Presently, diabetes mellitus has become a serious health problem worldwide,Affecting246 million people all over the world[57] . Based on World Health Organization (WHO) estimates, approximately 333 million people will suffer from diabetes mellitus by 2025[58] .Diabetes mellitus is characterized by abnormal metabolism of carbohydrates, lipids and proteins. The resultant hyperglycemia causesmicro vascular complications and a number of clinical neuropathies. Diabetes is classified into Type I and II with prevalence rates of 5% and 95%, respectively. Uncontrolled diabetes will increase the complications in future and severely affecting the patients' quality of life. In recent years, widespread national programs have been designed to prevent the incidence, complications and disabilities of diabetes which increase the rate of mortality . The oral healthcare professions, as a component of the healthcare team have an important role in screening and monitoring patients with diabetes mellitus. Half of

the diabetic patients require surgery at a period of their lives and two-thirds of these patients will experience some complications in relation to infections. Diabetic patients have experienced complications associated with tooth extraction, periodontal surgeries and ill-fitting dentures. Poor regeneration of soft tissues and a delay in osseous tissue healing are well known complications of oral surgeries in diabetic patients. Therefore, management and treatment of diabetic patients undergoing oral surgeries are more difficult. Delayed angiogenesis, decrease in blood flow, compromised innate immunity, decrease in the production of growth factor and psychological stress have been reported as factors cause delay in the healing of oral ulcers[59] .

In most cases, diabetes makes the patient susceptible to oral and dental problems and complications, including various oral soft tissue injuries and inflammatory conditions[60] Some of the possible complications after tooth extraction in diabetic patients are edema, discomfort, prolonged hemorrhage, trismus, infection and alveolar osteitis[61]. Hyperglycemia makes the patients susceptible to infections and further complications by decreasing the function of leukocytes and affecting the endothelium [62]. It should be pointed out that a large number of studies have evaluated the relationship between tooth loss and tooth extraction and diabetes. The results of these studies have shown that tooth loss and tooth extraction are significantly more common in diabetic patients compared with healthy subjects[63]. Since complications after tooth extraction will decrease the patients' quality of life, the present study was designed to evaluate the relationship between the glucose level in tooth socket blood and complications after tooth extraction in patients with Type II diabetes and healthy controls.

Latham et al[64] reported a significant relationship between postoperative infection and postoperative blood sugar levels in their subjects (P=0.007). Stratton et al[65] reported each 1% decrease in HbA1C causes37% decrease in micro vascular complications (P<0.001). In

addition, the results of studies by Carson et al[66] , Huang et al (P=0.0136) , Liao et al [67](P=0.003) , Del Toro et al[68] (P=0.003) , Hirsch et al[69] (P<0.05) and Bower et al[70] (P<0.042) were consistent with the present study in relation to the significant differences in the incidence of infection between diabetic and non-diabetic groups. Because of microvascular and macro vascular changes and immune deficiency in diabetes, risk of infection will increase . A study by Latham et al showed history of diabetes increases the infection at surgery site 2.7 folds compared to non-diabetic subjects. In this study, no relationship was found between the blood sugar control (HbA1C) and the incidence of infection (P=0.09). In relation to swelling no similar study was found. Dry socket occurs due to disturbance in the blood flow and in patients with diabetes the incidence of dry socket is higher due to micro angiopathy . In addition, absence of significant differences between the diabetic and non-diabetic subjects at socket blood sugar levels ≥126mg/dL might be attributed to the fact that despite no history of diabetes in the non-diabeticgroup, an increase in the socket blood sugar levels might be considered as a risk factor of dry socket; therefore, no significant differences were observed between the two groups. Huang et al reported similar socket healing processes after tooth extraction in diabetic and nondiabetic subjects. Joshipura[71] evaluated epithelialization of the socket in patients with different levels of bloodglucoseand reported no significant differences in epithelialization between them. Aronovich etal reported that the control level of blood glucose had no effect on socket healing after tooth extraction. Fernandes et al[72] evaluated the healing process after tooth extraction in patients with Type II diabetes and reported that 60 days after tooth extraction the socket epithelialization was complete in all the subjects despite poor control of blood glucose levels and neutrophils dysfunction. Graves et al[73]evaluated oral ulcers created in diabetic and non-diabetic mice and concluded that the epithelial coverage of ulcers, the connective tissue structure and the

density of fibroblasts were significantly poor in the diabetic subjects compared to the nondiabeticsubjects (P<0.05).

In our study, of the 100 patients , males were 32, females 68 . Of the 100 patients 18 had proper BG level of 180mg/dl and 82 had levels greater than 180mg/dl. All patients had updated their HbA1c levels who were divided into three groups 7% or less, 7.1 % to 9% and greater than 9 %. All patients had a 1 and 2 week follow up. The mean age of extraction sockets of POD 0,7,14 was 7.00, 4.00, 2.5mm respectively. Only four patients had pain at the site of extraction socket required local topical application of antibiotics and oral care. No other complications were reported. There was no stastistically significant difference in the rate of postextraction epithelialization between the diabetes patients with the operative BG level of 180mg/dl or less and those with greater than 180mg/dl. There was also no statistically significant difference in the rate of post extraction epithelialization between diabetic patients with glycosylated Hb level of 7 % or less, 7.1% to 9 % or greater than 9%. Our results were comparable to the results obtained by Aronovich et al (2010).

They reported a decrease in fibroblast proliferation secondary to increased apoptosis on one hand and an increase inpolymorphonuclear leukocytes (PMN) counts secondary to the inability of the diabetic tissue to eliminate the inflammation and return to the normal state on the other hand as reasons for a delay in healing.In addition, Hirsch et al compareddiabetic and non-diabetic animals in relation totissue healing and reported that on the 12thday after ulceration there was a significantdifference between the two groups (P<0.001).In the present study, gross wound healing and epitheliasation was evaluated on the 7th day and 14 th day after tooth extractionbased on the patients' symptoms and signs inrelation to the presence and absence of pain oran unpleasant feeling during tooth extraction.

CONCLUSION:

Diabetes mellitus can be a life threatening disease when seen in a chronic scenario. Long standing diabetic patient have a greater chance for the oral infection spreading into fascial planes of the head and neck resulting in fulminant infection. This study has concluded that healing of extraction socket is not greatly influenced by glycemiccontrol.However presiding factors like patients oral hygine and patients abilty and cooperation to maintain and monitor blood sugar level periodically has been emphasized

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ANNEXURE 2

INFORMATION SHEET

We are conducting a study on "**THE RELATIONSHIP OF GLYCEMIC CONTROL TO THE OUTCOMES OF DENTAL EXTRACTION".** The identity of the patients participating in the research will be kept confidential throughout the study. In the event of any publication or presentation resulting from the research, no personally identifiable information will be shared.

Taking part in the study is voluntary. You are free to decide whether to participate in the study or to withdraw at any time; your decision will not result in any loss of benefits to which you are otherwise entitled.

The results of the special study may be intimated to you at the end of the study period or during the study if anything is found abnormal which may aid in the management or treatment.

Name of the patient Signature / Thumb impression

Name of the investigator Signature

Date

ANNEXURE 3

INFORMED CONSENT FORM

THE RELATIONSHIP OF GLYCEMIC CONTROL TO THE OUTCOMES OF DENTAL EXTRACTION

Name: Age/Sex Op.No: Date:

Address:

I, _____ aged _____ have been informed about my role in the study.

1. I agree to give my personal details like name, age, sex, address, previous dental history & the details required for the study to the best of my knowledge.

2. I will co-operate with the dentist for my intra oral examination & extra oral examination.

3. I will follow the instructions given to me by the doctor during study.

4. I permit the dentist to take blood sample, photos, intraoral radiographs & I accept to undergo bone regenerative procedures as required for the study.

5. If unable to participate into study for reasons unknown, I can withdraw from the study.

In my full consciousness & presence of mind, after understanding all the procedures in my own language, I am willing & give my consent to participate in this study.

Name of the patient: Name of the investigator:

Signature/Thumb impression Signature

ஆராய்ச்சி ஒப்புதல் கடிதம்

பெயர் :

தேதி :

வயது :

புறநோயாளி எண் :

பாலினம் :

ஆராய்ச்சி சேர்க்கை எண்:

கீழ்க்காணும் நிபந்தனைகளுக்கு நான் ஒப்புதல் அளிக்கிறேன்

1. என் பெயர், வயது, பாலினம் , முகவரி, பல் சம்மந்தப்பட்ட சிகிச்சை மற்றும் என்னுடைய முழு விவரத்தினை கொடுக்க நான் முழு மனதுடன் ஒப்புக் கொள்கிறேன்
2. என்னுடைய வாயின் உள்பகுதி (அல்லது) வெளிபகுதியை மருத்துவர் பரிசோதனை செய்ய ஒத்துழைக்கிறேன்.
3. நான் மருத்துவர் அளிக்கும் விதிமுறைகளை தவறாமல் கடைபிடிப்பேன்.
4. மேற்கண்ட ஆராய்ச்சிக்காக என் இரத்தம, புகைப்படம், பற்கள் சம்பந்தப்பட்ட எக்ஸ்ரே மற்றும் ஈறு அறுவை சிகிச்சை எடுக்க மருத்துவருக்கு அனுமதி அளிக்கிறேன்.
5. நான் மேற்கண்ட ஆராய்ச்சியில் பங்குபெற முடியவில்லை என்றால் ஆராய்ச்சியில் இருந்து விலகிக் கொள்வேன்.

மருத்துவரின் ஆராய்ச்சி சம்பந்தப்பட்ட விவரங்களை முழுமையாக புரிந்து கொண்ட பிறகு, என் முழு மனதுடனும் மற்றும் சுய நினைவுடனும் இந்த மருத்துவ ஆராய்ச்சியில் பங்கு கொள்ள சம்மதிக்கிறேன்.

நோயாளியின் பெயர் கையொப்பம்

ஆராய்ச்சியாளரின் பெயர் கையொப்பம்

ANNEXURE 4

THE RELATIONSHIP OF GLYCEMIC CONTROL TO THE OUTCOMES OF DENTAL EXTRACTION

CLINICAL PROFORMA

Op No: **Sl. No:**

Date:

Name: **Age/ Sex:**

Address: **Occupation:**

Chief Complaint:

Medical history:

Dental history:

Family history:

Personal History:

HbA1c