A PROSPECTIVE STUDY ON ROLE OF CLINICAL PHARMACIST IN REDUCING SMOKING FREQUENCY AND PHYSIOLOGICAL ASSESSMENT IN DIABETIC PATIENT BY USING PHYSIOLOGICAL ASSESSMENT SCALE AT

SECONDARY CARE HOSPITAL

Dissertation submitted to

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

Chennai-600 032

In partial fulfillment of the requirement for the award of the degree of

MASTER OF PHARMACY

In

PHARMACY PRACTICE

Submitted by

REG. NO: 261640401

Under the guidance of

Dr. T. SUTHANTH B.PHARM, PHARM.D

DEPARTMENT OF PHARMACY PRACTICE

THE ERODE COLLEGE OF PHARMACY& RESEARCHINSTITUTE

ERODE

APRIL - 2018

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EVALUATION CERTIFICATE

This is to certify that dissertation work entitled "**A PROSPECTIVE STUDY ON ROLE OF CLINICAL PHARMACIST IN REDUCING SMOKING FREQUENCY AND PHYSIOLOGICAL ASSESSMENT IN DIABETIC PATIENT BY USING PHYSIOLOGICAL ASSESSMENT SCALE AT SECONDARY CARE HOSPITAL** "Submitted by **REG NO: 261640401**to THE TAMILNADU Dr.M.G.R.MEDICAL UNIVERSITY, CHENNAI, in partial fulfillment for the degree of **MASTER OF PHARMACY** is a bonafide thesis work carried out by the candidate at the department of pharmacy practice, The Erode college of pharmacyand Research institute, erode, was evaluated by us during the academic year **2017-2018.**

Examination center : The Erode College of pharmacy and Research institute, Erode.

Date:

Internal Examiner **External Examiner**

Convener of Examination

The Erode College of Pharmacy & Research Institute

Dr. T. SUTHANTH B.PHARM, PHARM.D
Department of pharmacy practice,
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Erode -638112.

This is certify to that dissertation work entitled "**A PROSPECTIVE STUDY ON ROLE OF CLINICAL PHARMACIST IN REDUCING SMOKING FREQUENCY AND PHYSIOLOGICAL ASSESSMENT IN DIABETIC PATIENT BY USING PHYSIOLOGICAL ASSESSMENT SCALE AT SECONDARY CARE HOSPITAL"** Submitted by **REG NO: 261640401** to THE TAMILNADU Dr.M.G.R.MEDICAL UNIVERSITY, CHENNAI. In partial fulfillment for the award of degree of **MASTER OF PHARMACY IN PHARMACY PRACTICE,** Is the bonafide work carried out under the guidance and direct supervision of **Dr. T. SUTHANTH B.PHARM, PHARM.D.,** department of pharmacy practice, the erode college of pharmacy and research institute, erode -638112, during academic year **2017-2018.**

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ENDORESEMENT BY THE PRINCIPAL

This is to certify that the investigation described in the dissertation entitled "**A PROSPECTIVE STUDY ON ROLE OF CLINICAL PHARMACIST IN REDUCING SMOKING FREQUENCY AND PHYSIOLOGICAL ASSESSMENT IN DIABETIC PATIENT BY USING PHYSIOLOGICAL ASSESSMENT SCALE AT SECONDARY CARE HOSPITAL"** submitted by**REG NO: 261640401**to THE TAMILNADU Dr.M.G.R. MEDICAL UNIVERSITY, CHENNAI. In partial fulfillment for the award of degree of **MASTER OF PHARMACY IN PHARMACY PRACTICE** is the bonafide work carried out under the guidance and direct supervision of **Dr. T. SUTHANTH B.PHARM, PHARM.D.,**Department of pharmacy practice, the Erode college of Pharmacy and Research institute, erode-638112, during the academic year **2017-2018.**

Place : Dr.V.GANESAN, M.Pharm.,

Ph.D.,

Date : PRINCIPAL

DECLARATION

The research work embodied in this dissertation work entitled "**A PROSPECTIVE STUDY ON ROLE OF CLINICAL PHARMACIST IN REDUCING SMOKING FREQUENCY AND PHYSIOLOGICAL ASSESSMENT IN DIABETIC PATIENT BY USING PHYSIOLOGICAL ASSESSMENT SCALE AT SECONDARY CARE HOSPITAL"** was carried out by me in the department of pharmacy practice, the erode college of pharmacy, erode, under the direct supervision of **Dr. T. SUTHANTH B.PHARM, PHARM.D.,** the erode college of pharmacy, erode. Those dissertation submitted to **THE TAMILNADU DR.M.G.R.MEDICAL UNIVERSITY,CHENNAI,** as a partial fulfillment for the award of **degree in Master of Pharmacy** in pharmacy practice during the academic year 2017-2018. The work is original and has not been submitted in part or full for the award of any degree or diploma of this or any other university.

Place: Reg.No.

261640401

Date

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I cannot express what I owe to my father (Saidalavi M), mother(Aleema KP), and my loving brothers and sisters always being with me, for making me what I am and for all the love and care they provided me without which I would not have been in a position to write this page.

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Place: Reg.no:261640401

Date:

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LIST OF TABLES

LIST OF CHARTS

LIST OF ABBREVATION

CVD	Cardiovascular Disease
BMI	Body Mass Index
HIV	Human Immunodeficiency Virus
COPD	Chronic Obstructive Pulmonary Disease
nAChRs	Neuronal Nicotinic Acetylcholine Receptors
CHD	Coronary Heart Disease
GAD	Glutamic Acid Decarboxylase
DM	Diabetes Mellitus
T1DM	Type 1 Diabetes Mellitus
T2DM	Type 2 Diabetes Mellitus
FPG	Fasting Plasma Glucose
HbA1c	Glycosylated Hemoglobin
OGTT	Oral Glucose Tolerance Testing
DPP4	Dipeptidyl Peptidase-4
SGLT2	Sodium-Glucose Co-Transporter 2
USFDA	US Food And Drug Administration

INTRODUCTION

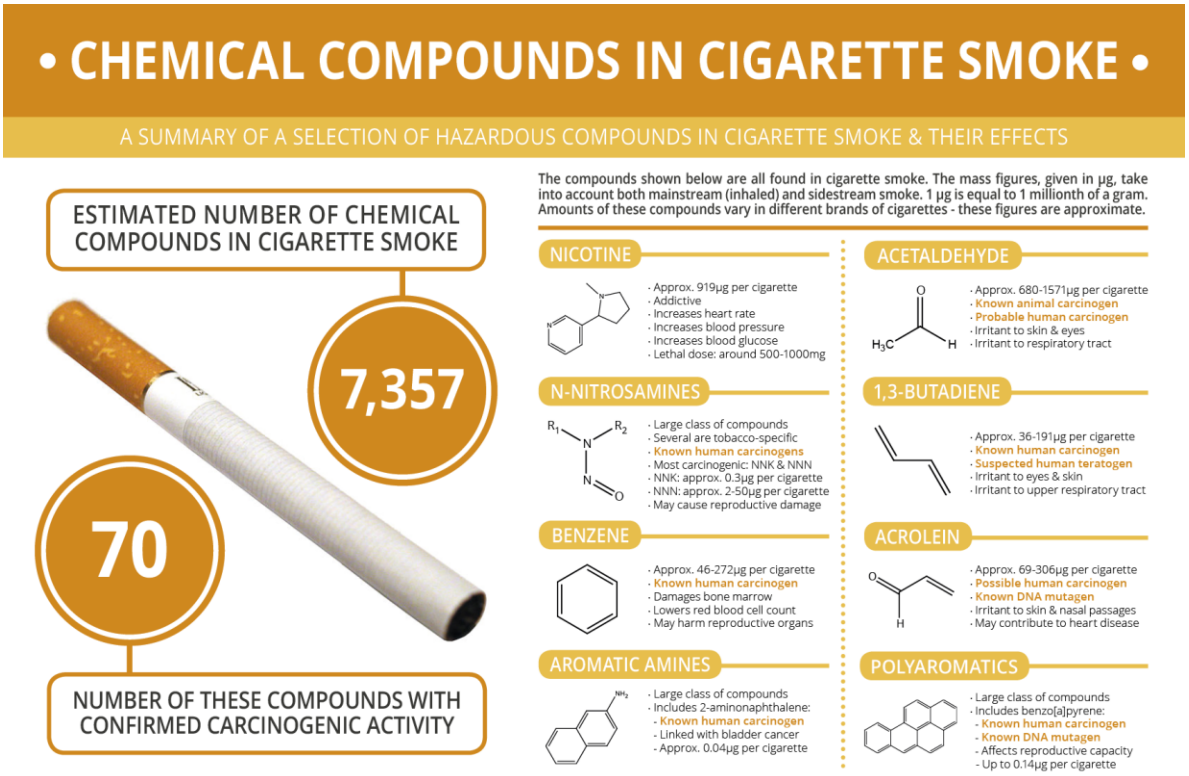
Background:

Cigarette smoking continues to be one of the leading causes of preventable global mortality. Tobacco use is a significant hurdle to development gains worldwide. It is the leading cause of preventable death. Worldwide, only two large and growing causes of death exist. One is HIV-1 infection, and the other is tobacco. On current consumption patterns, about 1 billion people in the 21stcentury will be killed by their addiction to tobacco. Smoking-related illness costs billions of dollars each year.

Hazards of Smoking:

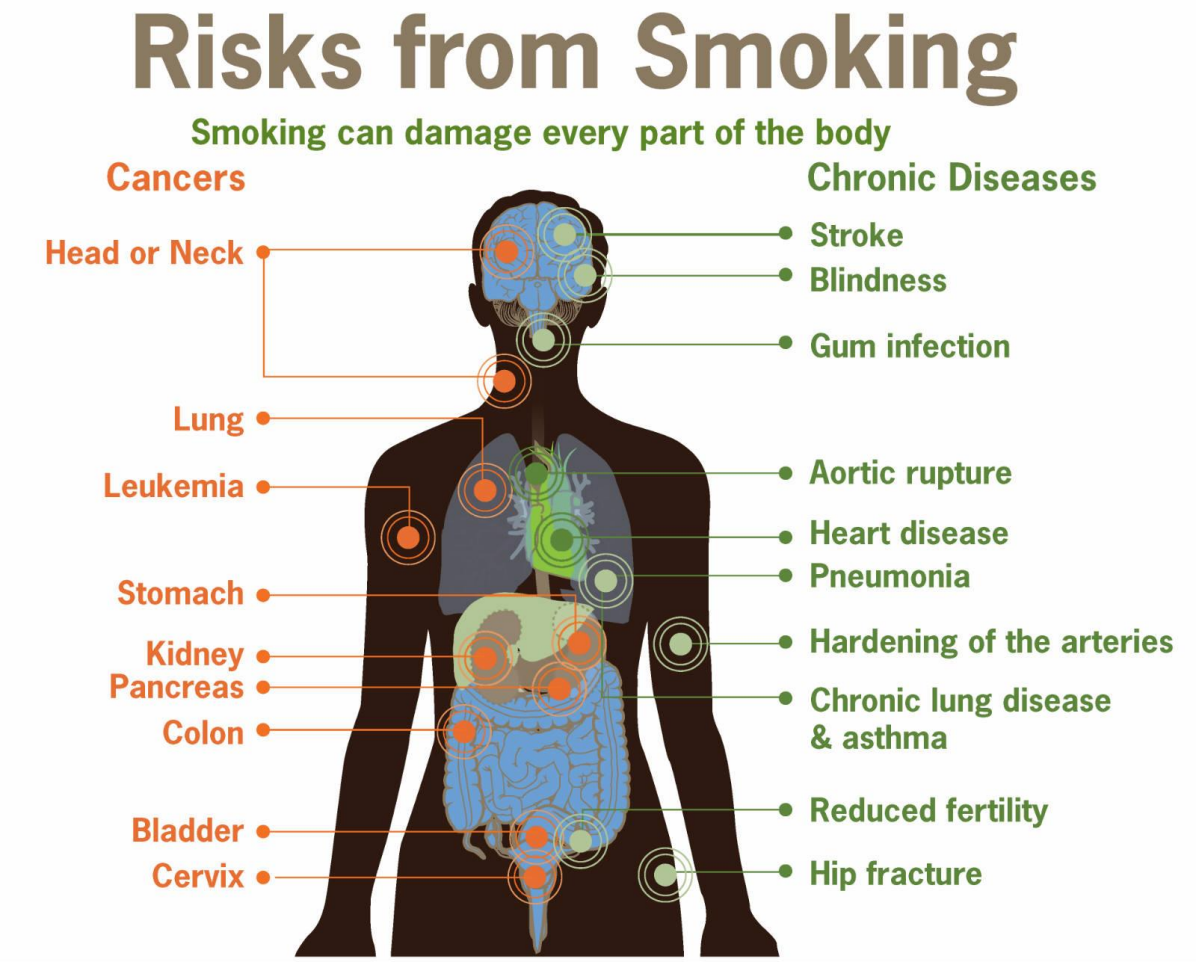
Tobacco is the biggest external cause of non-communicable disease and is responsible for even more deaths than adiposity globally. The risks in middle age are much greater for smokers who started in early adulthood than for those who started later. After 1950, cigarette consumption continued to rise for some decades in high-income countries, and it has risen among men (though generally not among women) in many low- and middle-income countries. Two thirds of all smokers live (in descending order of numbers of smokers) in China, India, the European Union (in which central tobacco legislation can influence 28 countries), Indonesia, the United States, Russia, Japan, Brazil, Bangladesh, and Pakistan. In India, manufactured cigarettes are now displacing bidis[1].

Smoking also increases the risk of cardiovascular disease, aortic aneurysm, Cohn's disease, gastric and duodenal ulcers, cataracts, and age-related macular degeneration. The two most common respiratory diseases caused by smoking are lung cancer and chronic obstructive pulmonary disease (COPD). According to a study of male British doctors between 1951 and 1991, smoking caused 81% of lung cancer deaths and 78% of deaths from COPD.



Psychological Effects of Smoking

Psychologically, for some people, the feel, smell, and sight of a cigarette and the ritual of obtaining, handling, lighting, and smoking the cigarette are all associated with the pleasurable effects of smoking[2]. Nicotine induces pleasure and reduces stress and anxiety. Smokers use it to modulate levels of arousal and to control mood. Smoking improves concentration, reaction time, and performance of certain tasks. With regular smoking, the smoker comes to associate specific moods, situations, or environmental factors — smoking-related cues — with the rewarding effects of nicotine. Typically, these cues trigger relapse[3]. The legal and social barriers constantly test a user's drive to smoke. A smoker is presented with nearly ubiquitous opportunities and frequent cues to both purchase and use tobacco because of mass marketing and promotion of tobacco[1].



Smoking Cessation:

"Most smokers identify tobacco use as harmful and express a desire to reduce or stop using it, and nearly 35 million want to quit each year"

There is substantial scientific evidence that smoking cessation helps recovery[4]. Quitting smoking has immediate and long-term health benefits. From the very first day of quitting, body begins to repair itself. Within days the smell and taste improves and breathing improves making exercise easier. Within one to nine months, coughing and shortness of breath also decrease. Peo-ple experience nicotine withdrawal differently. Some people find it more challenging than others. Many people find nicotine withdrawal is worst in the first 24 - 48 hours of quitting. Symptoms of nicotine withdrawal includes: Irritability and anxiety, Difficulty concentrating, Restlessness and

insomnia, Cravings, Dizziness, Appetite changes[5]. Smokers are finding difficulty in managing these symptoms as NRTs help in reducing symptoms, but not in carvings.

Cessation before middle age avoids more than 90 percent of the lung cancer risk attributable to tobacco, with quitters possessing a pattern of survival similar to that of persons who have never smoked. In the United Kingdom, among those who stopped smoking, the risk of lung cancer fell steeply with time since cessation.

GOVT INTERVENTIOENS TO RDUCE DEMAND FOR TOBACCO[1]:

Numerous studies, mostly from high-income countries, have examined the effect of interventions aimed at reducing the demand for tobacco products on smoking and other kinds of tobacco use.

- Tobacco Taxation[6]
- Restrictions on Smoking
- Health Information and Counter-advertising
- Bans on Advertising and Promotion
- Smoking Cessation Treatments
- Interventions to reduce the supply of tobacco
- Comprehensive tobacco-control Programs:
    - ✓ preventing initiation among youths and young adults
    - ✓ promoting cessation among all smokers
    - ✓ reducing exposure to passive tobacco smoke
    - ✓ identifying and eliminating disparities among population subgroup

THE IMPACT OF SMOKING ON THE DEVELOPMENT OF DIABETES AND ITS COMPLICATION

Smoking is one of the modifiable risk factors for many chronic conditions, such as cardiovascular disease (CVD), cancer, chronic obstructive lung disease, asthma and diabetes. Smoking cessation is one of the few interventions that can safely and cost-effectively be recommended for individuals with diabetes. In the guidelines from the American Diabetes Association, smoking cessation is recommended as one of the most important steps in preventingthe complications of diabetes.[7] Many studies haveshown that the adverse effects of smoking on diabetes mellitusare not only related to macrovascular complicationsbut also microvascular disease.Although smoking is known to decrease body weight[8], itis associated with central obesity[9]. Substances present intobacco smoke undoubtedly trigger free radical processes,interfere with vascular homeostasis and proper functioningof the vascular endothelium,and also increase inflammation/oxidative stress, in addition to directly damagingβ-cell function[10]. A growing body of the literature has shown linksbetween tobacco use and the development of diabetes.[11]

However, this literature is wide ranging and complex as tobacco products such as cigarettes contain 7357 chemical compounds and 10 to 10free radicals, and this is in addition to the well-known compounds such as carbon monoxide, tar, arsenic, lead and nicotine[12], leading to multiple pathways that may be involved in the pathogenesis. To complicate matters, each of these pathways is neither mutually exclusive nor linear, and there are a vast number of interactions between chemicals, and interconnectivity between the inflammatory and biochemical pathways that they induce. Since nicotine is the critical substance which exerts most of the adverse effects

Of smoking, we will concentrate on the role of this substance in this review. The prevalence of smoking in youth and adults is still high and remains one of the major health problems. Many Previous studies documenting the impact of smoking onhealth did not discuss separately the results for subgroupsof patients with diabetes, suggesting an estimated risk of complications that is similar to the general population. Understanding the hazardous effects of smoking on diabetes Mellitus may lead to increased emphasis on smoking prevention and smoking cessation as important strategies in the management of this condition.[13]

The relationship between diabetesand smoking

Diabetes is one of the most common metabolic disorders, underpinned by a combination of genetic, environmental and lifestyle factors. Many epidemiological studies indicatethat cigarette smoking is an independent risk factorfor type 2 diabetes.The 5-year-long *Insulin Resistance Atherosclerosis Study*confirmed the significant effect of cigarette smoking on the development of diabetes in adults. In the analyzedstudy, there were nearly a thousand non-diabetic and Declared healthy individuals examined. The study comprised sample with 25% smoking and 14% non-smokingpersons with diabetes. After considering the anthropometric, behavioral, metabolic, gender, race and hypertension relatedfactors, it was found that the risk of type 2 diabetes For smokers was statistically higher than for non-smokers.

In addition, a higher risk of diabetes was observed insmokers with normal glucose tolerance. There was also apositive correlation between the risk of developing type 2diabetes and smoking duration. Periods of intensive cigarette smoking favour the occurrence of hyperglycemia, Hyperinsulinaemia and hypertension.[14]Other work has also shown that cigarette smoking is a risk factor for type 2 diabetes. Men who smoke more thantwo packs of cigarettes per day have a 45% higher risk ofdeveloping diabetes when compared to men who never smoked. In contrast, women who smoke over 40 cigarettesper day have a risk of developing diabetes that can be as much as 75% higher when compared to non-smoking women. Quitting smoking reduces the risk to the level observed in non-smokers within 5 years for women andmore than 10 years for men.[15]Specific studies on the effect of smoking on the risk ofdiabetes in women have been scarce. The results from theNurses' Health Study in the United States (114,247 women,1,227,589 person-years follow-up) showed that the risk fordiabetes in smokers was 1.42 after adjustment for otherrisk factors.[16] Others have found that current and pastsmoking are associated with a risk of diabetes mellitus essentially in men, but much less in women, and the relationship between fasting glucose and smoking appears differentin men and women.[17] The longitudinal study ofJapanese males from 1984 to 1992 estimated the risk of developing type 2 diabetes was increased by threefold in those who smoked 16–25 cigarettes a day compared with those who never smoked, after controlling for other risk factors including alcohol consumption and obesity.[18] Afollow-up study of this Japanese male cohort, conducted from 1994 to 1999, has established that the level of consumption and the number of years smoked were positively correlated

with the development of type 2 diabetes and also to impaired fasting glucose, which often progresses to type 2 diabetes.[19]The study by Wannamethee et al. has demonstrated similar findings; the researchers studied 7124 men aged40–59 years over a period of 17 years. The cases of diabetes were determined on the basis of questionnaires sent systematically by the primary care physician. Over the course of the study, 290 cases of diabetes were observed.

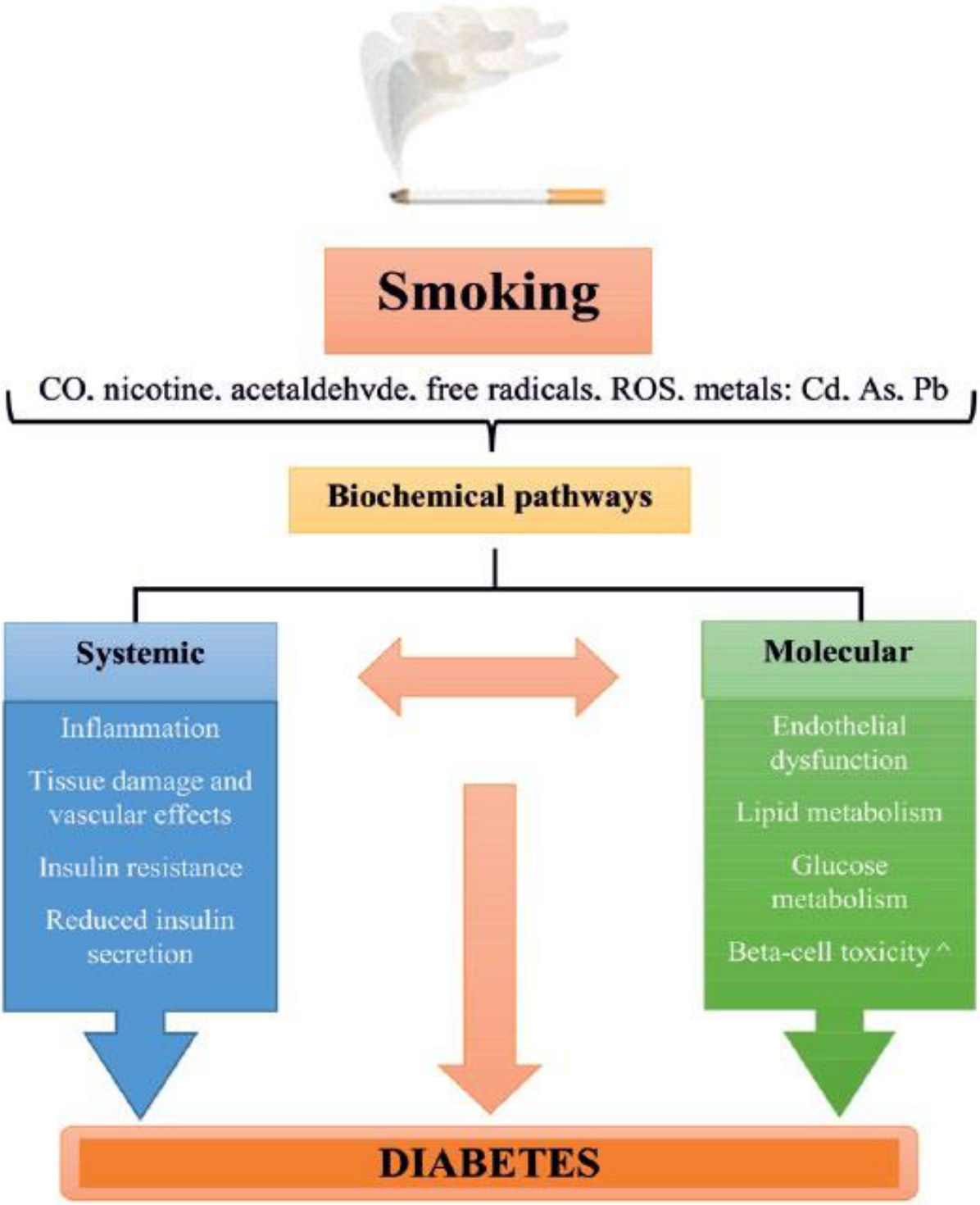
After taking into account factors such as age, body mass index (BMI), and others influencing the onset of diabetes, cigarette smoking was statistically demonstrated to increase the risk of this disease. In this study, however, there was no significant relationship between the duration.

Summary of pathways that link smoking cigarettes with diabetes pathophysiology.[20]

Reduced insulin secretion

The presence of neuronal nicotinic acetylcholine receptors (nAChRs) was discovered in the β cells of pancreatic islets. It was found that on the surface of islet cells in the pancreas, there are subunits of nAChRs, such as α-2, α-3, α-4, α-5, α-7 and β-2. Both in the case of acute (60 min) and chronic (48 h) exposure to nicotine, decreased β cell insulin secretion was observed. The findings suggest that nAChRs play an important role in controlling the hormone release by β cells. It was further found that exposure to nicotine concentrations above 1 μmol/L inhibits insulin secretion in isolated human islet cells.[21]

These findings indicate that functional nicotinic receptors are present in pancreatic islets and β cells and nicotine could, at least in part, negatively affect pancreatic β-cell function. Thus, the presence of neuronal nicotinic receptors sensitive to nicotine in pancreatic cells may be explained by the mechanism of toxic influence of nicotine on insulin-secreting β cells.


Smoking
CO. nicotine. acetaldehvde. free radicals. ROS. metals: Cd. As. Pb
Biochemical pathways
Systemic
Inflammation
Tissue damage and vascular effects
Insulin resistance
Reduced insulin secretion
Molecular
Endothelial dysfunction
Lipid metabolism
Glucose metabolism
Beta-cell toxicity ^
DIABETES

Many animal studies have demonstrated that nicotine may affect the development of pancreatic cells and contribute to the development of diabetes. Several studies have shown that nicotine can increase apoptosis of islet β cells in nicotine exposed animal models. In an experiment using an animal model, the impact of prenatal and postnatal exposure to nicotine on the function of β cells of pancreatic islets was analyzed. The study was conducted on pregnant rats that were injected with a solution of hydrogen tart rate nicotine, with the control group being injectedwith saline. The administration of nicotine and saline continued until the end of lactation, that is, for 21 days afterbirth. The study revealed that nicotine exposure can causeβ-cell dysfunction and increased β-cell apoptosis, mediated via the mitochondrial and/or death receptor pathway, which led to the development of impaired glucose metabolism.[22]Another study indicated that maternally derivednicotine can act via pancreatic nAChRs during fetal andneonatal development, leading to oxidative stress that inturn results in loss of pancreatic β cells. These results supportthe concept that β-cell apoptosis in fetal and neonatal pancreas can be induced by a direct effect of nicotine vianAChRs, and that this effect may be mediated through increased oxidative stress.[23]

Others found that exposure to nicotine during fetal and neonatal life stages caused an increase in body fat and dysglycaemia.In experimental animal models, glucose metabolism disturbances appeared at the age of 7 weeks inrates and persisted until the age of 26 weeks in rats exposedto nicotine during their prenatal and neonatal stages of life, with insulin resistance playing a role. Therefore, smoking can induce diabetes both by increasing insulin resistance and through reduction of insulin secretion. Each cigarette smoked leads to an inflammatory response in the body and if continued, chronic pancreatitis. Prolonged smoking destroys the exocrine part of the pancreas (the pancreas decreases morphologically), while the pancreatic islets become restricted and then destroyed.[24] The studies conducted by Sarles et al. showed that smokers are more predisposed to pancreatic calcification than nonsmokers. This fact was also confirmed by Cavallini et al,who showed that for smoking patients with chronic pancreatitis, there was a 20% increased risk of pancreatic calcifications when compared to non-smoking patients. Furthermore,it was observed that pancreatic calcifications are formed earlier in smokers than in non-smokers (median: 4.5 years earlier).[25]

Studies evaluating the pancreatic exocrine function in smoking patients with chronic pancreatitis showed a significant impairment in the activity of the pancreatic enzymes. For many

years, it was thought that both parts of the pancreas – the endocrine and the exocrine –operated independently and had different functions in thebody. Recent studies suggest that there is an interactionbetween the endo- and exocrine function of the pancreas. For example, insulin affects the synthesis and the secretionof enzymes by the exocrine pancreas in the acini receptor mechanism. Immuno histochemical localization of insulin and glucagon in pancreatic samples differs in smokers and non-smokers with chronic pancreatitis, with reduced insulin detection in the former group, particularly in the tail of the pancreas.

The significantly lower levels of insulin and the higherblood glucose levels in smokers with chronic pancreatitis in comparison to non-smokers coincided with the progressionof changes in the structure and dysfunction of the endocrine organ Chemical components of tobacco smoke may havedirect toxic effects on the pancreas and β-cell function, both in fetal life and adulthood. Because higher levels of inflammatory markers [C-reactive protein and interleukin-6 (IL-6)] herald the development of diabetes, smokingmay also contribute to the development of diabetes byincreasing levels of inflammatory markers.16 Furthermore, mitochondrial dysfunction, oxidative stress and inflammationare involved as underlying mechanisms for the directtoxicity induced by nicotine via nAChRs.[26-30]

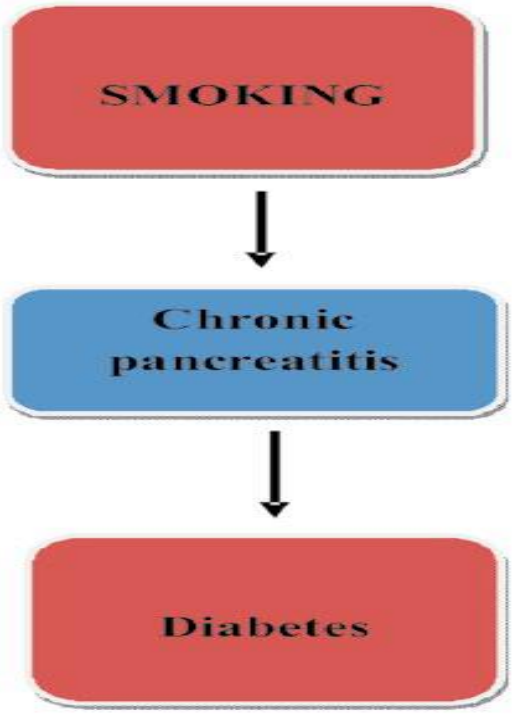
Increased insulin resistance

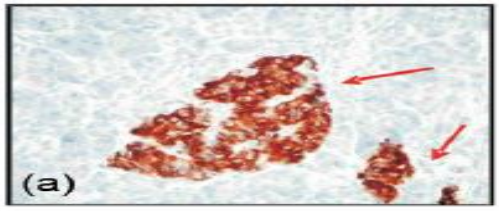
In healthy people, glucose levels are maintained within the normal range through proper insulin secretion by β cells and the sensitivity of peripheral tissues to the action of this hormone. Insulin resistance, metabolic syndrome and glucose intolerance are regarded as disturbances with a common background and strong interrelations. Increasing insulin resistance seems to be the primary factor especially in the pathogenesis of type 2 diabetes, which occurs many years before the appearance of overt hyperglycemia. In the early stages of increased insulin resistance, the islet β cells 'try' to compensate increasing secretion of insulin. Current evidence indicates that smoking increases insulin resistance, although exact mechanisms remain to be elucidated Numerous studies have shown the negative effects of cigarette smoking on peripheral insulin action, which appears to be 'dose dependent'. In healthy young men, acute smoking showed an increased insulin resistance. Smokers had a significantly increased homeostatic model assessment insulin resistance index an hour after smoking.

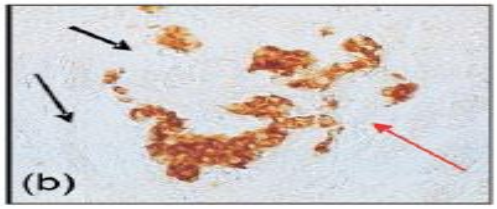
The smoking reduced insulin-mediated glucose uptake by 10%–40% in men who smoked compared with on-smoking men.

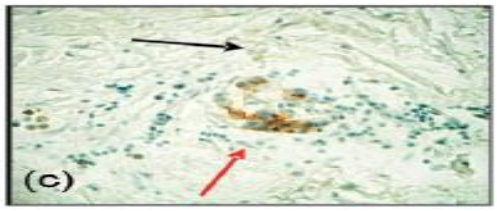
Additionally, in healthy men, chronic smoking was associated with high plasma insulin concentrations, independent of other factors known to influence insulin sensitivity. This observed increase in insulin resistance in smokers may be related, at least in part, to nicotine as long-term use of nicotine gum use is associated with hyperinsulinaemia and insulin resistance. The chronic smoking effect on insulin sensitivity was also evaluated in patients with type 2 diabetes, and the results of this study showed decreased peripheral glucose metabolism in smoking patients when compared to nonsmokers. Insulin and C-peptide responses to oral doses of glucose were significantly higher in smokers than nonsmoking patients, while the blood glucose was not significantly different. Thus, chronic cigarette smoking seems to increase significantly insulin resistance in type 2 diabetes, which may have implications for treating these patients.

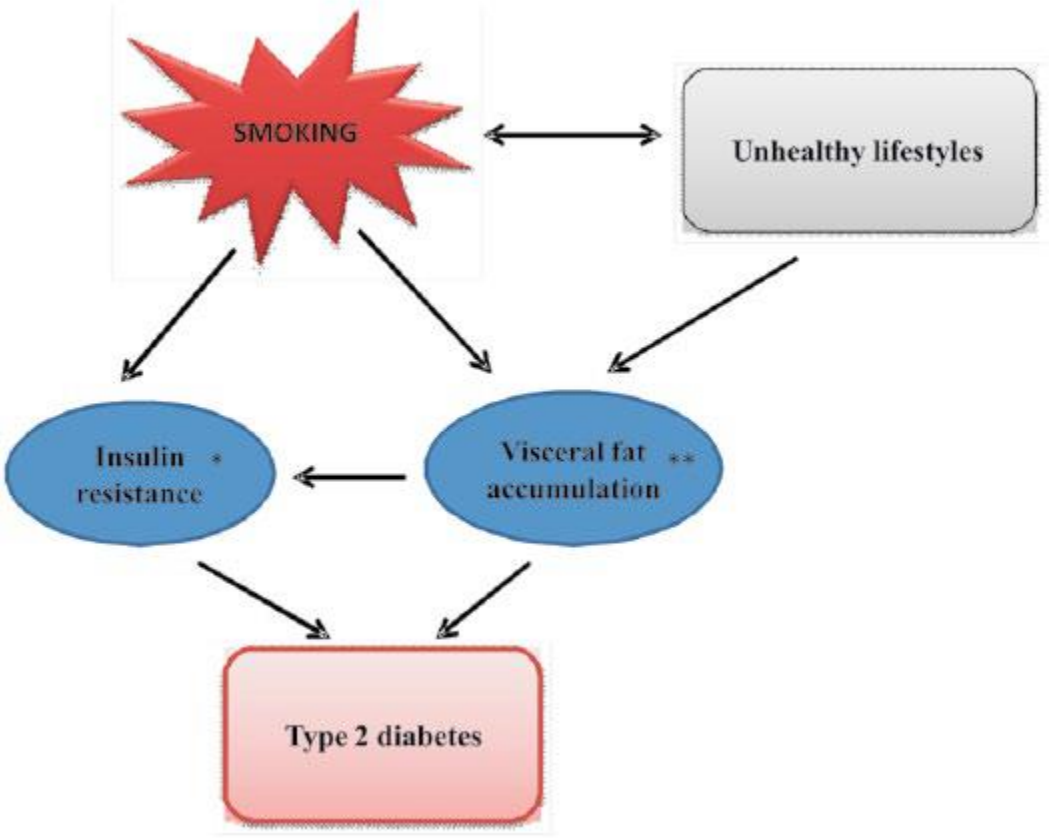
Human experiments using the glucose-clamp technique have found that an acute infusion of nicotine aggravates the insulin resistance response in people with type 2 diabetes, further implicating this agent in the observed changes in insulin sensitivity in smokers. On the positive side, the effect of smoking on insulin sensitivity may be partially reduced after quitting smoking. In non-obese men, insulin sensitivity improved 8 weeks after smoking cessation, despite an increase in body weight.[31]











Nicotine on islet beta-cells

Nicotine influences insulin secretion through nAChRs on beta-cells Recently, many studies have found neuronal nicotinic acetylcholine receptors (nAChRs)expressed on many different non-neuronal cell types includingpancreatic islet cells. Basal insulin secretion can be modulated by an endogenous pancreatic ganglionic mechanism. The effects of ganglion pre- and postsynaptic In AChRs antagonism were studied in the *in vitro* canine pancreas. Results suggest that nAChRs are present at the ganglionic level in the pancreas and modulate insulin secretion by a complex intraganglionic mechanism. Direct evidence of the presence of nicotinic receptors on islet beta-cells has also been obtained. In that study, expression of mRNA fornAChRs subunits α 2, α 3, α 4, α 5, α 7, and β 2 were detected in insulin secreting cells by reverse transcriptase polymerase chain reaction. Not only a long term exposure to nicotine but also acute exposure induced a reduction in insulin secretion in response to insulin-secreting agonists including

tolbutamide. These studies suggest that nAChRs are playing an important role in controlling insulin release. Yoshikawa *et al* also has shown that acute exposure to nicotine at concentrations of higher than 1 moll/L inhibited high-glucose-induced insulin release in isolated human islets, although these concentrations of nicotine failed to decrease the glucose-induced insulin release from rat islets. On the other hand, the exposure to nicotine for 48 h inhibited insulin releases even at basal glucose levels in rat and human islets. These findings indicate that functional nicotinic receptors are present in pancreatic islets and beta cells and nicotine could, at least in part, negatively affect pancreatic beta-cell function. Thus, the presence of neuronal nicotinic receptors sensitive to nicotine in pancreatic cells may be a switch to modulate pancreatic cells physiological function by acetylcholine and can be involved in tobacco toxicity.

Nicotine increases apoptosis of islet β-cells

There are several lines of studies have shown that nicotine can increase apoptosis of islet β-cells in nicotine exposed animal models. In a rat model, prenatal nicotine exposure affected early endocrine pancreas and adipose tissue development in pups before weaning. Results proved a direct association between fetal nicotine exposure and offspring metabolic syndrome with early signs of dysregulations of adipose tissue and pancreatic development. Another two studies revealed that nicotine exposure can cause β-cell dysfunction, increased β-cell apoptosis, and loss of β-cell mass, which is mediated via the mitochondrial and/or death receptor pathway.

This nicotine-induced apoptosis may lead to the development of postnatal dysglycemia and obesity. Recently, Bruin *et al* also showed that nicotine exposure caused beta-cell apoptosis and loss of β-cell mass. Moreover, this study indicated that maternally derived nicotine can act via pancreatic nAChRs during fetal and neonatal development to induce oxidative stress in the pancreas thus to induce loss of pancreatic β-cells. These results support that beta-cell apoptosis in the fetal and neonatal pancreas can be induced by a direct effect of nicotine via nAChRs and that this effect may be mediated through increased oxidative stress. All these studies in animal models have indicated that prenatal or neonatal exposed to nicotine will lead to loss of pancreatic β-cells, thus less insulin secretion. Mitochondrial dysfunction, oxidative stress, and inflammation are involved as underlying mechanisms for the direct toxicity induced by nicotine.

THE EFFECT OF SMOKING ON INSULIN ACTION

The exact mechanism for why smoking increases the risk of diabetes and deteriorates glucose homeostasis has not been fully elucidated, but the available evidence shows that smoking increases insulin resistance.

In healthy young men, acute smoking showed an increased insulin resistance . Smokers had a significantly increased homeostatic model assessment insulin resistance index an hour after smoking . The smoking reduced insulin mediated glucose uptake by 10% to 40% in men who smoked compared with non-smoking men . In type 2 diabetic subjects, insulin and C-peptide responses to oral glucose load were significantly higher in smokers than non-smokers and the insulin resistance, as determined by the euglycemic clamp technique, was positively correlated in a dose dependent manner . Thus smoking induced insulin resistance in patients with type 2 diabetes, as well as healthy subjects.

In addition to increased insulin resistance, smoking also showed dyslipidemia prone to atherosclerosis. Smokers had higher fasting triglycerides and lower high density lipoprotein cholesterol levels, and an increased proportion of small dense low density lipoprotein particles. Fibrinogen levels and plasminogen activator inhibitor 1 activity were also elevated in smokers .

In terms of glucose homeostasis, smoking has a negative effect on glucose control. In a population-based prospective study, cigarette smoking was positively associated in a dose dependent manner with elevated HbA1c after adjustment for possible confounding by dietary variables. This finding was also reported in patients with diabetes in Sweden; smoking type 1 and type 2 patients had a higher mean HbA1c but a lower mean body mass index than non-smokers.[32-38]

SMOKING AND DIABETIC MICROVASCULAR COMPLICATIONS

The smoking effects on micro vascular diabetes complications vary across reports. Generally, several studies have shown that smoking has an adverse effect on diabetic nephropathy, but the influence of smoking independently with glucose control, on retinopathy and neuropathy are unclear.

SMOKING AND NEPHROPATHY

Several studies have demonstrated that smoking promotes diabetic microal buminuria and exacerbates diabetic nephropathy. In the study by Biesenbach et al., [39] a 13-year follow-up study, the progression of nephropathy was clearly increased in smokers. The authors showed that smoking was a risk factor for diabetic kidney disease, independent of age, sex, and duration of diabetes and HbA1c levels.

In prospective studies by Chuahirun and Wesson[40] and Chuahirun et al.,[41] the adverse effects on diabetic neprhropathy in type 2 patients were confirmed, even in optimal hypertensive patients.

SMOKING AND RETINOPATHY

The association of smoking and diabetic retinopathy has not been clear. It was reported that retinopathy has been associated with glycemic control and not smoking state. Some studies have reported no association with smoking and retinopathy in type 2 diabetes.[42]The United Kingdom Prospective Diabetic (UKPD) study to determine risk factors related to the incidence and progression of diabetic retinopathy followed patients over 6 years from diagnosis. The development of retinopathy was associated with glycemia and higher blood pressure, but not smoking. Thus in type 2 patients, the effects of smoking on diabetic retinopathy has not been as clear as with nephropathy.[43]

SMOKING AND NEUROPATHY

There are few studies about smoking and diabetic neuropathy. Smoking may affect diabetic neuropathy differently according to the type of diabetes. In type 2 diabetic patients, smoking was not a risk factor in the presence of polyneuropathy or sensory neuropathy as diagnosed by symptom and sign. It was reported that there was no relationship between current or previous levels of smoking and the severity and duration of chronic painful neuropathy. But in the study by Tamer et al., while smoking was not associated with neuropathic complaints, using electromyography-supported neuropathy examination there were significant relationships with smoking, as well as HbA1c. Therefore, more studies are needed to evaluate the association between smoking and neuropathy.[44-47]

SMOKING AND MACROVASCULAR COMPLICATIONS

Smoking has been shown to be a significant risk factor for all-cause mortality, and for mortality due to CVD and coronary heart disease (CHD) in diabetics. Smokers die on average 8 to 10 years younger than non-smokers, as age is entered into most multi-regression analysis.

DIABETES MELIITUS

DEFINITION

Diabetes mellitus (or diabetes) is a chronic, lifelong condition that affects your body's ability to use the energy found in food.

All types of diabetes mellitus have something in common. Normally, your body breaks down the sugars and carbohydrates you eat into a special sugar called glucose. Glucose fuels the cells in your body. But the cells need insulin, a hormone, in your bloodstream in order to take in the glucose and use it for energy. With diabetes mellitus, either your body doesn't make enough insulin; it can't use the insulin it does produce, or a combination of both.

Since the cells can't take in the glucose, it builds up in your blood. High levels of blood glucose can damage the tiny blood vessels in your kidneys, heart, eyes, or nervous system. That's why diabetes -- especially if left untreated -- can eventually cause heart disease, stroke, kidney disease, blindness, and nerve damage to nerves in the feet.[48]

TYPES

There are three major types of diabetes: type1 diabetes, type2 diabetes, and gestational diabetes.[49]

Type 1 Diabetes(T1DM)

Type 1 diabetes is also called insulin-dependent diabetes. It used to be called juvenile-onset diabetes, because it often begins in childhood. It is an autoimmune condition. It's caused by the body attacking its own pancreas with antibodies. In people with type 1 diabetes, the damaged pancreas doesn’t make insulin.

SYMPTOMS FOR T1DM

- Above average thirst
- Tiredness during the day
- Polyuria

- Unexplained weight loss
- Genital itchiness

CAUSES FOR T1DM

This type of diabetes may be caused by a genetic predisposition. It could also be the result of faulty beta cells in the pancreas that normally produce insulin.

A number of medical risks are associated with type 1 diabetes. Many of them stem from damage to the tiny blood vessels in your eyes (called diabetic retinopathy), nerves (diabetic neuropathy), and kidneys (diabetic nephropathy). Even more serious is the increased risk of heart disease and stroke.

DIAGNOSIS FOR T1DM

- Ketone test
- GAD autoantibodies test
- C-peptide test

TREATMENT FOR T1DM

Treatment for type 1 diabetes involves taking insulin, which needs to be injected through the skin into the fatty tissue below. The methods of injecting insulin include:

- Syringes
- Insulin pens that use pre-filled cartridges and a fine needle
- Jet injectors that use high pressure air to send a spray of insulin through the skin
- Insulin pumps that dispense insulin through flexible tubing to a catheter under the skin of the abdomen

A periodic test called the A1C blood test estimates glucose levels in your blood over the previous three months. It's used to help identify overall glucose level control and the risk of complications from diabetes, including organ damage.

Having type 1 diabetes does require significant lifestyle changes that include:

- Frequent testing of your blood sugar levels
- Careful meal planning
- Daily exercise
- Taking insulin and other medications as needed

People with type 1 diabetes can lead long, active lives if they carefully monitor their glucose, make the needed lifestyle changes, and adhere to the treatment plan.

Type 2 Diabetes (T2DM)

Type 2 diabetes mellitus is a metabolic disorder that results in hyperglycemia (high blood glucose levels) due to the body: Being ineffective at using the insulin it has produced; alsoknown as insulin resistance and or being unable to produce enough insulin.

T2DM characterized by the body being unable to metabolize glucose (a simple sugar).This leads to high levels of blood glucose which over time may damage the organs of the body.T2DM is also known as non-insulin dependent or adult-onset diabetes due to its occurrence mainly in people over 40

Causes

T2dm occurs when the hormone insulin is not used effectively by the cells in body. Insulin is needed for cells to take in glucose from the bloodstream and convert it into energy

Ineffective use of insulin results in the body becoming resistant to insulin-also known as insulin resistance, which in turn causes hyperglycemia

In advance t2dm may causes damage to insulin producing cells in the pancreas, leading to insufficient insulin production for your body's needs

Risk factors

- Being overweight or obese
- Eating an unhealthy diet
- Physical inactivity
- Having a first-degree relative with type 2 diabetes
- Having high blood pressure or raised cholesterol level

The like hood of developing T2DM is also influenced by genetics and environmental factors for example, research show that

- If either parent has T2DM, the risk of inheritance of T2DM is 15%
- If both parents have T2DM ,then the risk of inheritance is 75%

Symptoms for T2DM

- Excessive thirst
- Frequent urination
- Increased hunger
- Extreme tiredness
- Sudden loss of muscle mass

Gestational Diabetes

Diabetes that's triggered by pregnancy is called gestational diabetes (pregnancy, to some degree, leads to insulin resistance). It is often diagnosed in middle or late pregnancy. Because high blood sugar levels in a mother are circulated through the placenta to the baby, gestational diabetes must be controlled to protect the baby's growth and development.

According to the National Institutes of Health, the reported rate of gestational diabetes is between 2% to 10% of pregnancies. Gestational diabetes usually resolves itself after pregnancy. Having gestational diabetes does, however, put mothers at risk for developing type 2 diabetes later in life. Up to 10% of women with gestational diabetes develop type 2 diabetes. It can occur anywhere from a few

weeks after delivery to months or years later. With gestational diabetes, risks to the unborn baby are even greater than risks to the mother. Risks to the baby include abnormal weight gain before birth, breathing problems at birth, and higher obesity and diabetes risk later in life. Risks to the mother include needing a cesarean section due to an overly large baby, as well as damage to heart, kidney, nerves, and eye.[50]

DIAGNOSIS OF DIABETES

Accurate tests are available to doctors to definitively confirm a diagnosis of diabetes. Before tests are conducted, a diagnosis may be suspected when patients report certain symptoms. Doctors will evaluate these symptoms by asking questions about the patient's medical history.

Doctors may also carry out a physical examination, including checks for complications that could have already developed - examining the feet for changes in sensation, for example.

Testing can be part of routine screening for people at risk of the disease, who may show up as having prediabetes. The US Department of Health and Human Services recommends diabetes testing for anyone overweight at the age of 45 years and over, alongside anyone under the age of 45 with one or more of the following risk factors:

- Hypertension (high blood pressure)
- High cholesterol
- History of diabetes in the family
- African-American, Asian-American, Latino/Hispanic-American, Native American or Pacific Islander background
- History of gestational diabetes (diabetes during pregnancy) or delivering a baby over 9 lbs.

Blood tests for diabetes diagnosis

Diagnoses of diabetes are confirmed through 1 of 3 types of blood test.

One of three blood tests can be used to confirm a diagnosis of diabetes,

- Fasting plasma glucose (FPG) levels - a blood test after 8 hours of no eating
- Glycosylated hemoglobin (HbA1c) - to measure a marker of the average blood glucose level over the past 2-3 months
- Oral glucose tolerance testing (OGTT) - a test used less frequently that measures levels before and 2 hours after consuming a sweet drink (concentrated glucose solution).

Glycosylated hemoglobin is often abbreviated to A1C, and this blood test is also used in the monitoring of diabetes management

To make an initial diagnosis, an HbA1c reading must be 6.5% or higher. An A1C result between 5.7% and 6.4% indicates prediabetes and a risk of type 2 diabetes.

The HbA1c is the preferred blood test for diagnosis because - while it is more expensive than the FPG test - it has advantages, including,

Urine tests for diabetes were once common but are no longer considered reliable.

- Greater convenience (no need for fasting)
- Less day-to-day variation during stress and illness.

When the fasting plasma glucose test is used to confirm symptoms, diabetes is diagnosed at levels equal to or above 126 mg/dL(7.0 mmol/L).

For oral glucose tolerance testing, the plasma glucose levels after 2 hours need to be equal to or above 200 mg/dL (11.1 mmol/L) for a diabetes diagnosis.

Another blood test is the random plasma glucose test - taken regardless of time and eating - which diagnoses diabetes if the level is at least 200 mg/dL (11.1 mmol/L).

Unless the clinical picture is clear, a positive blood test should also be repeated to rule out laboratory error.

Urine tests for diabetes diagnosis

Urine tests are no longer used to make a diagnosis of diabetes, although they were once common. Blood tests are used instead because urine tests are not sensitive or specific enough and offer only a crude indication of high blood sugar levels.

A urine sample may be used, however, to test for ketones, particularly in people with type 1 diabetes who exhibit certain symptoms. Here, the test can pick up ketoacidosis, a complication of diabetes.

Treatments for Diabetes

Type 2 diabetes has a number of drug treatment options to be taken by mouth known as oral antihyperglycemic drugs or oral hypoglycemic drugs.
Oral diabetes drugs are usually reserved for use only after lifestyle measures have been unsuccessful in lowering glucose levels to the target of an HbA1c below 7.0%, achieved through an average glucose reading of around 8.3-8.9 mmol/L (around 150-160 mg/dL).
The lifestyle measures that are critical to type 2 diabetes management are diet and exercise, and these remain an important part of treatment when pills are added.
People with type 1 diabetes cannot use oral pills for treatment, and must instead take insulin

is the most widely used oral antihyperglycemic drug and reduces the amount of glucose released by the liver into the bloodstream.
Oral antihyperglycemic drugs have three modes of action to reduce blood glucose levels:

- Secretagogues enhance insulin secretion by the pancreas
- Sensitizers increase the sensitivity of the peripheral tissues to insulin
- Inhibitors impair gastrointestinal absorption of glucose.

Each class of antihyperglycemic drug has a different adverse event or safety profile, and side effects are the main consideration when it comes to choosing a medication.

Possible side effects range from weight gain, through gastrointestinal ones such as diarrhea, to pancreatitis and more serious problems. Hypoglycemia is also a possible adverse event.

Biguanides

Metforminis usually the first treatment offered, however, and it is the most widely used oral antihyperglycemic. Metformin is a sensitizer in the class known as biguanides; it works by reducing the amount of glucose released by the liver into the bloodstream and increasing cellular response to insulin. A metformin pill is usually taken twice a day

This drug is a low-cost antihyperglycemic with mild side effects that can include diarrhea and abdominal cramping. Metformin is not associated with weight gain or hypoglycemia.

Sulphonylureas

Which are secretagogues that increase pancreatic insulin secretion. There are several drug names in this class, including:

- Chlorpropamide
- Glimepiride
- Glipizide
- Glyburide.

Again, the choice of drug is an individual one. In the case of sulphonylureas, the choice depends on daily dosing and the level of side effects. These drugs are associated with weight gain and hypoglycemia.

Glitazones (also known as thiazolidinediones)

Glitazones are sensitizers - they increase the effect of insulin in the muscle and fat and reduce glucose production by the liver.

Two glitazones are available: pioglitazone and rosiglitazone. These drugs can have the side effects of weight gain or swelling and are associated with increased risks of heart disease and stroke, bladder cancer and fractures.

In the UK, rosiglitazone was withdrawn from the market over concerns about adverse events. In 2015, it remains available in the US, with information on its safety provided by the US Food and Drug Administration (FDA).

Alpha-glucosidase inhibitors

They are intestinal enzyme inhibitors that block the breakdown of carbohydrates into glucose, reducing the amount absorbed in the gut.

Available as Acarbose and Miglitol, they are not usually tried as first-line drugs because of common side effects of flatulence, diarrhea and bloating, although these may reduce over time.**Dipeptidyl peptidase-4 (DPP4) inhibitors**

DPP4 includesAlogliptin, Linagliptin, Saxagliptin and Sitagliptin.

Also known as gliptins, DPP4 inhibitors have a number of effects, including stimulating pancreatic insulin (by preventing the breakdown of the hormone GLP-1). They may also help with weight loss through an effect on appetite.

These drugs do not increase the risk of hypoglycemia. Mild possible side effects are nausea and vomiting.

Sodium-glucose co-transporter 2 (SGLT2) inhibitors

SGLT2 includeCanagliflozin and Dapagliflozin. They work by inhibiting the reabsorption of glucose in the kidneys, causing glucose to be excreted in the urine (glycosuria).

SGLT2s may also cause modest weight loss. Side effects include urinary infection.

Meglitinides

These include Repaglinide and Nateglinide. They stimulate the release of insulin by the pancreas. Meglitinides are associated with a higher chance of hypoglycemia and must be taken with meals three times a day. As a result, these drugs are less commonly used.[51]

AIM&OBJECTIVES

Aim:

To identify role of clinical pharmacist in reducing smoking frequency and physiological assessment in diabetic patient by using physiological assessment scale

Objectives:

The main objectives of the study is,

- To assess the physiology of smokers in DIABETIC patients by using physiological assessment scale
- To counsel the diabetic patient about the harmful effect of smoking
- To reduce the frequency of smoking in diabetic patients

REVIEW OF LITERATURE

A literature review is a summary of previous research on a topic. My literature review focused on the smoking frequency and physiological assessment in diabetic patient

- **Mariola Śliwińska-Mossoń, et.al.,** .conducted a study on The impact of smoking on the development of diabetes and its complications. In this review they summarized that the Diabetes is one of the most common metabolic disorders and emerges secondary to an interaction between genetic, environmental and lifestyle factors. This work provides an overview of the impact of smoking on the development of vascular complications in this condition and also provides an overview of the potential role of smoking in predisposition to diabetes. There are many studies documenting the impact of smoking on health (not focused on patients with diabetes), suggesting that the health exposure in these individuals is at least comparable to that observed in the general population. Distinct studies of smoking in patients with diabetes have unambiguously confirmed an increased prevalence and a higher risk of early death associated with the development of macrovascular complications. Smoking is also associated with premature development of microvascular complications and may contribute to the pathogenesis of type 2 diabetes. It has been shown that smoking is a predictor of the progression of glucose intolerance at both the transition from normoglycaemia to impaired glucose tolerance status and the increased risk of developing diabetes. The mechanisms explaining the relationship between smoking and the development of diabetes are not fully understood, although a number of hypotheses have been put forward. Current evidence indicates that smoking cessation is not only important to prevent

macrovascular complications in diabetes, but also has a role in limiting microvascular disease and may also facilitate glycemic management in this condition.[52]

- **JoAnn Eet.al.,**studied a review article namely a prospective study of cigarette smoking and the incidence of diabetes mellitus among us male physicians. This review aims to determine the association between cigarette smoking and the incidence of type 2 diabetes mellitus. They concluded that Smokers had a dose-dependent increased risk of developing type 2 diabetes mellitus: compared with never smokers,in these prospective data from the Physicians' Health Study support the hypothesis that cigarette smoking is an independent and modifiable determinant of type 2 diabetes mellitus. The biologic plausibility of this association lends further credence to a causal interpretation, and the found that type 2 diabetes can be added to the list of major adverse health outcomes linked to smoking. Strategies to prevent the adoption of cigarette smoking or to facilitate smoking cessation may also reduce the incidence of diabetes and its complications. Populations at high risk of type 2 diabetes mellitus should be considered for special targeted smoking interventions. Guidelines for physicians (27) to ask about tobacco use and to assist smokers to quit could help reduce the burden of diabetes as well as the even larger burdens of cardiovascular disease and cancer.[53]
- **Carole Willi, MD, et.al.,**studied the association between active smoking and the incidence of type 2 diabetes. In this observational study they reported risk of impaired fasting glucose, impaired glucose tolerance, or type 2 diabetes in relationship to smoking status at baseline; had a cohort design; and excluded persons with diabetes at baseline. Here concluded that active smoking is associated with an increased risk of type 2 diabetes.[54]
- **Navidad Canga, Bsc, et.al.,** studied a review article namely Intervention Study for Smoking Cessation in Diabetic Patients. This review aims to evaluate the effectiveness of a nurse-

managed smoking cessation intervention in diabetic patients.They concluded thata structured intervention managed by a single nurse was shown to be effective in changing the smoking behavior of diabetic patients. The higher effectiveness of our intervention could be explained not only by the longer time spent with each patient but also because the intervention followed the guidelines of the Agency for Health Care Policy and Research, which include face-to-face counseling, behavioral therapy techniques, NRT, and relapse prevention The participants in this study were probably particularly resistant to change. They had been diagnosed with diabetes several years before, and they had received health professionals' advice to quit smoking repetitively. Therefore, many previous interventions by health professionals had failed.[55]

- **S. GOYA WANNAMETHEE;PHD,et.al.,** concluded a prospective study on Smoking as a Modifiable Risk Factor for Type 2 Diabetes in Middle-Aged Men. The study aimed to examine the effects of cigarette smoking, giving up smoking, and primary or secondary pipe or cigar smoking on the risk of type 2 diabetes. The study that concluded that Cigarette smoking is an independent and modifiable risk factor for type 2 diabetes. Smoking cessation is associated with weight gain and a subsequent increase in risk of diabetes, but in the long term, the benefits of giving up smoking outweigh the adverse effects of early weight gain.[56]
- **Nwaokoro Joakin Chidozieet.al.,** conducted a study on the effect of smoking on Type 2 Diabetic Patients in Federal Medical Center Owerri, in Southeastern Nigeria.the study concluded that the comprehensive programs should be initiated to prevent smoking in type 2 diabetic patients such as: regular physical activity, health education on diabetes, smoking cessation, home blood sugar monitoring - minimize smoking impact to body organs that may lead to many complications. Only a low proportion of Type 2 diabetic patients were smokers

due to lack of proper awareness and education on the effect of smoking on diabetes, the disease is spreading widely and silently in Nigeria and other countries in world. More than half of the patients found that smoking did not give improvement rather than worsens their Type 2 diabetes. People with diabetes already have an increased risk of developing diabetic related complications and this will further elevate if they smoke.[57]

- **Carole Clair, MD MSc, et. al.,** conducted a cohort, cross-sectional and case–control studies on The Effect of Cigarette Smoking on Diabetic Peripheral Neuropathy: A Systematic Review and Meta-Analysis. This review aims to study was to assess the relationship between smoking and DPN in persons with type 1 or type 2 diabetes. They concluded that the smoking may be associated with an increased risk of developing DPN. This is an important finding, as this exposure is a modifiable behavior to be targeted in clinical practice based on diabetes guideline recommendations. Future research should be focused on evaluating the impact of smoking cessation on improvement of diabetic neuropathy, and on helping to establish a causal link between exposure and outcome.[58]
- **Xi-tao XIEet.al.,** conducteda study on nicotine effects on insulin action and insulin secretion, indicating the impact of nicotine on type 2 diabetes development. The study concluded that nicotine exposure could induce a reduction of insulin release, and negatively affect insulin action, suggesting nicotine could be a cause for development of insulin resistance. Mitochondrial dysfunction, oxidative stress, and inflammation are involved as underlying mechanisms of nicotine induced pancreatic β-cells loss. These evidences together indicate that cigarette smoking can affect insulin action and pancreatic cell function. To facilitate the development of diabetes, besides the well-known risk for cardiovascular and

other disease. Thus, in diabetes care, smoking cessation is important for glycemic control and limiting the development of diabetic complications.[59]

- **Maija Feodorof, et.al.,** conducted that a study on Smoking and progression of diabetic nephropathy in patients with type 1 diabetes. The purpose of the study contains to evaluate the effect of cumulative smoking on the development of diabetic nephropathy. Study included 3613 patients with type 1 diabetes, participating in the Finnish Diabetic Nephropathy Study. The 12-year cumulative risk of microalbuminuria, macroalbuminuria and end-stage renal disease (ESRD) was estimated for current, ex- and nonsmokers. Cox regression analyses, with multivariable adjustments for other risk factors for diabetic nephropathy, were used to evaluate the risk at different stages of diabetic nephropathy based on the cumulative amount of smoking in pack-years. In the current smokers, one pack-year increased the risk of macroalbuminuria with a HR of 1.025 (1.010–1.041) and the risk of ESRD with a HR of 1.014 (1.001–1.026) compared with nonsmokers, in the fully adjusted model. In the ex-smokers, the risk of macroalbuminuria and ESRD was no different from the risk in nonsmokers after multivariable adjustment. The study concluded that Current smoking is a risk factor for the progression of diabetic nephropathy and the risk increases with the increasing dose of smoking. Ex-smokers seem to carry a similar risk of progression of diabetic nephropathy as nonsmokers.[60]
- **Eric B Rimm, et.al.,** this prospective study concluded that the Cigarette smoking may be an independent, modifiable risk factor for non-insulin dependent diabetes mellitus. Moderate alcohol consumption among healthy people may be associated with increased insulin sensitivity and reduced risk of diabetes. After controlling for known predictors of diabetes we found positive association between smoking and the subsequent risk of diabetes. This study

included an increased risk among current and former smokers, supporting experimental evidence that smoking exerts both short term effect on insulin sensitivity and long term effect on insulin secretion. The study confirm results in women for both alcohol consumption and smoking and support laboratory evidence that, compared with men who abstain, men who take up to three drinks day are more insulin sensitive and may be at lower risk of diabetes. These findings from large prospective cohort of men suggest that factors in addition to obesity can modify the incidence of diabetes.[61]

- **Julie C Wil, et.al.,** conducted a study on Cigarette smoking and diabetes mellitus: evidence of a positive association from a large prospective cohort study.The purpose of this study was to determine whether greater frequency of cigarette smoking accelerated the development of diabetes mellitus, and whether quitting reversed the effect. The study concluded that a dose-response relationship seems likely between smoking and incidence of diabetes. Smokers who quit may derive substantial benefit from doing so. Confirmation of these observations is needed through additional epidemiological and biological research.[62]
- **Jiang N, et.al.,** conducted a study on Smoking and the risk of diabetic nephropathy in patients with type 1 and type 2 diabetes: a meta-analysis of observational studies. The observational study aimed to assess the effects of tobacco smoking on the development of M.Th.study concluded that A total of nineteen observational studies (1 case-control, 8 cross-sectional and 10 prospective cohort studies) were identified, involving more than 78,000 participants and a total of 17,832 DN cases. Compared with never-smokers, there was an augmented SRR (95% CI) of DN in ever-smokers in patients with T1DM (1.31 [1.06-1.62]; P = 0.006) and T2DM (1.44 [1.24-1.67]; P < 0.001), respectively. In patients with T1DM, the SRR (95% CI) was 1.25 (0.86-1.83) for microalbuminuria only, 1.27 (1.10-1.48) for

macroalbuminuria only, and 1.06 (0.97-1.15) for end-stage renal disease (ESRD) .The meta-analysis suggests evidence for cigarette smoking as an independent risk factor for the development of DN in patients with both T1DM and T2DM.[63]

- **GIOVANNI TARGHER, et.al.,** concluded a study on Cigarette Smoking and Insulin Resistance in Patients with Noninsulin-Dependent Diabetes Mellitus. This cross-sectional study shows that chronic cigarette smoking can exert a deleterious impact on insulin sensitivity in patients with NIDDM and may bring a more complete expression of the insulin resistance syndrome. Because insulin resistance has been involved, by direct or indirect mechanisms, in the pathogenesis of hyperglycemia and macroangiopathy, smoking cessation in NIDDM patients might favorably affect not only cardiovascular risk, but also long-term metabolic control. The study compared NIDDM subjects who stopped smoking or continued to smoke, are needed to substantiate this hypothesis, especially because smoking cessation often results in weight gain, and this might adversely affect insulin sensitivity. It concluded that the smoking status should be carefully considered in case-control studies, including subjects with NIDDM.[64]
- **Ying Wang, et.al.,** conducted a study on Passive Smoking and Risk of Type 2 Diabetes: A MetaAnalysis of Prospective Cohort Studies. This review aims to explore whether an association exists between passive smoking and risk of type 2 diabetes. In conclusion found that the present meta-analysis suggests that passive smoking is associated with an increased risk of T2DM. However, considering the limited number and moderate quality of included studies, further well-designed studies are warranted to confirm this observed association.[65]
- **Toshimi Sairenchi, et.al.,** conducted a prospective study on Cigarette Smoking and Risk of Type 2 Diabetes Mellitus among Middle-aged and Elderly Japanese Men and Women in

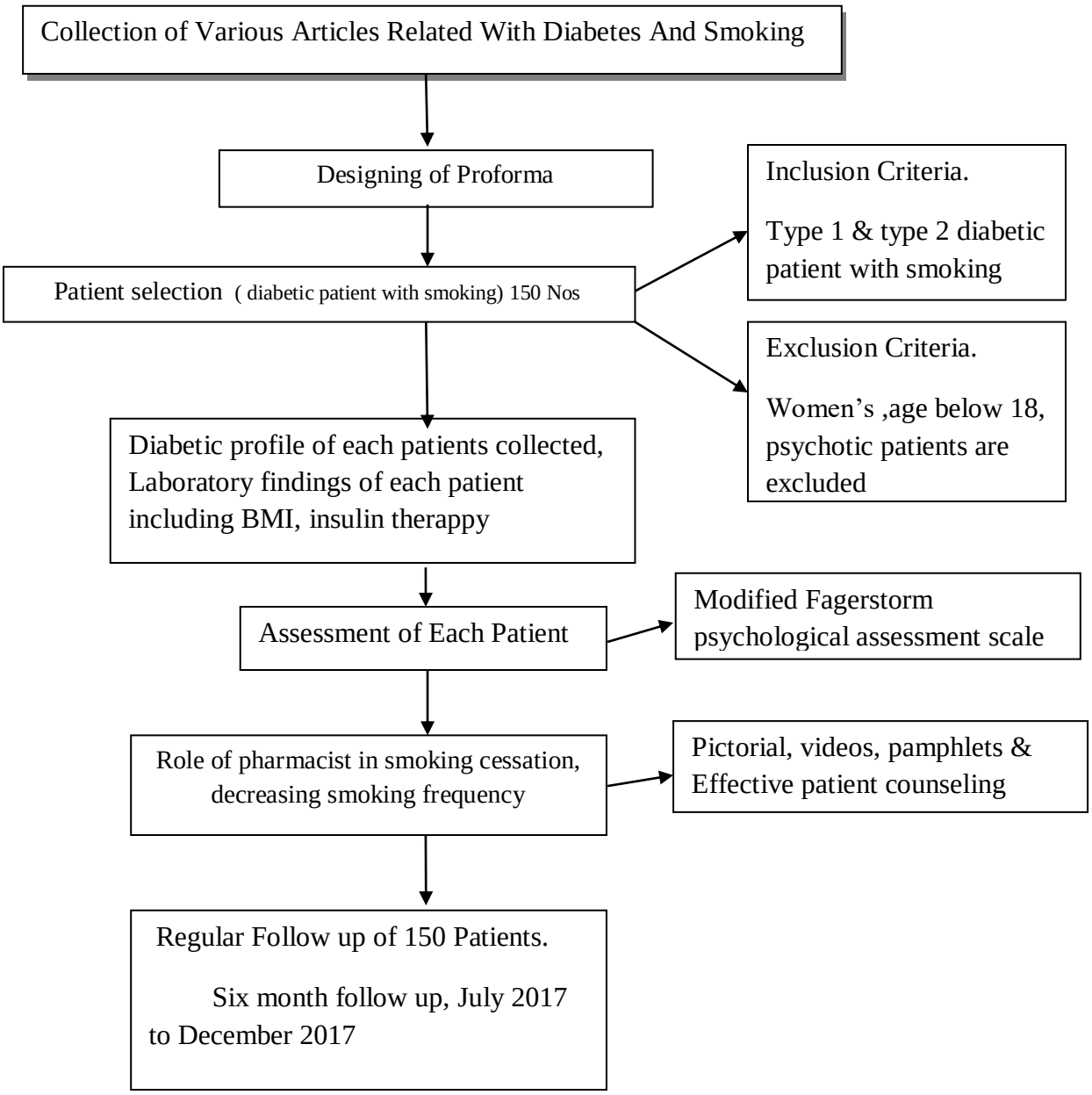
japan.the purpose of the study included that for examination of sex- and age-specific relations between smoking and risk of type 2 diabetes mellitus. Then the study showed that current smoking was associated with a 20–40 percent increased risk of diabetes mellitus, of which 99 percent was type 2 diabetes (13), among men and a 40–50 percent increased risk for both age subgroups (40–59 years and 60–79 years) among women and concluded that cigarette smoking was associated with increased risk of type 2 diabetes mellitus among both middle-aged and elderly men and women.[66]

- **D Haire-Joshu,et.al.,** conducted a study on smoking and diabetes. The objective of this review is to summarize the literature on diabetes and smoking related to epidemiological risks, efficacy and cost-effectiveness of different cessation approaches, and implications for clinical practice. This study concluded thatthere is a clear need to increase the frequency of smoking cessation advice and counselling for patients with diabetes given the strong and consistent data on smoking prevalence; combined risks of smoking and diabetes for morbidity, mortality, and several complications; and the proven efficacy and cost-effectiveness of cessation strategies.[67]
- **Deborah j. Toobert, PhD, et.al.,** reviewed a study on The Summary of Diabetes Self-Care Activities Measure, Results from 7 studies and a revised scale. The study was done to review reliability, validity, and normative data from 7 different studies, involving a total of 1,988 people with diabetes, and provide a revised version of the Summary of Diabetes Self-Care Activities (SDSCA) measure. in this study was found that the Participants were typically older patients, having type 2 diabetes for a number of years, with a slight preponderance of women. The average inter-item correlations within scales were high (mean = 0.47), with the exception of specific diet; test-retest correlations were moderate (mean = 0.40). Correlations

with other measures of diet and exercise generally supported the validity of the SDSCA subscales (mean = 0.23).the reviewed study was concluded that The SDSCA questionnaire is a brief yet reliable and valid self-report measure of diabetes self-management that is useful both for research and practice. The revised version and its scoring are presented, and the inclusion of this measure in studies of diabetes self-management is recommended when appropriate.[68]

- **Saito K, et.al.,** conducted a study on Effect of smoking on diabetes mellitus and dyslipidaemia (effect of smoking on glucose and lipid metabolism).in this study was found that Smoking is one of the important risk factors of cardiovascular disease. Its effects on arteriosclerotic diseases act not only directly but indirectly, by worsening control of blood pressure, lipid metabolism and glucose metabolism. And in patients with diabetes, it affects both macroangiopathy and diabetic microangiopathy (especially diabetic nephropathy) adversely. This study was concluded that the all effects and mechanisms of smoking on metabolic diseases are not yet unclear. But smoking cessation improves lipid metabolism and may improve glucose metabolism and may decrease risk of impaired glucose tolerance, type 2 diabetes, and diabetic microangiopathy. All patients with metabolic diseases must quit smoking for control of diseases and prevention of arteriosclerotic disease as soon as possible.[69]

PLAN OF WORK


Collection of Various Articles Related With Diabetes And Smoking
Designing of Proforma
Patient selection (diabetic patient with smoking) 150 Nos
Inclusion Criteria.
Type 1 & type 2 diabetic patient with smoking
Exclusion Criteria.
Women's ,age below 18, psychotic patients are excluded
Diabetic profile of each patients collected, Laboratory findings of each patient including BMI, insulin therappy
Assessment of Each Patient
Modified Fagerstorm psychological assessment scale
Role of pharmacist in smoking cessation, decreasing smoking frequency
Pictorial, videos, pamphlets & Effective patient counseling
Regular Follow up of 150 Patients.
Six month follow up, July 2017 to December 2017

METHODOLOGY

Study Period:

- This study is carried out for a period of six months (July 2017 to December 2017).

Study Design:

It is a prospective study and carried out in patients arriving in Tirupur Govt. Hospital.

Sample Size:

A total of 150 patients with diabetic and smoking from the general medicine ward of Government Headquarters Hospital, Tiruppur were included in the study

Study Method:

- The Study is to be conducted in Govt. Headquaters Hospital, Tirupur- 18.
- The study method involves selection of patients based on the inclusion criteria.
- The data collected will be analyzed using suitable statistical tools.

Inclusion Criteria:

- Smokers of any age, who are affected by Diabetes
- Type 1 and Type 2 diabetes patients registered in the hospital
- Patients with co-morbiditie

Exclusion Criteria:

- Patient who are not willing to participate.
- Psychiatric patients.
- Ladies.
- Age below 18 yrs.

Design of patient consent form:

The consent from the patient was obtained before inclusion to the study. The consent was prepared in English as well as in local language.

Data collection:

The data collection will be done during the interview with patients at an interval of once in every two months in order to understand patient details including past medical history, past medication history, social history, marital status, occupation, family history, Diabetic profile , history of present illness etc. Laboratory investigation and other relevant details of related to the study will be included.

Diagnosis/questionnaire:

A complete smoking history is a prerequisite for providing support and motivation in smoking cessation for DIABETIC patients. This history results in a higher number of patients who successfully cease smoking, but it is currently not taken often enough. Tobacco consumption should therefore be assessed and documented regularly (level of recommendation ⇑⇑, that is: strongly recommended).

To determine the extent of dependence, the *Modified Fagerstrom psychological assessment scale* is particularly suitable of 6questions, the 2 main ones are:

- How soon after you wake up do you smoke your first cigarette?
- How many cigarettes do you smoke each day?

Modified Fagerstrom psychological assessment scale:

1. How many cigarettes a day do you smoke?
   a. Over 26 cigarettes a day (2)
   b. About 16-25 cigarettes a day (1)
   c. About 1-15 cigarettes a day (0)
   d. Less than 1 a day (0)

2. Do you inhale?

a. Always (2)

b. Quite often (1)

c. Seldom (1)
d. Never (0)

3 How soon after you wake up do you smoke your first cigarette?

a. Within the first 30 minutes (1)

b. More than 30 minutes after waking but before noon (0)

c. In the afternoon (0)

d. In the evening (0)

4. Which cigarette would you hate to give up?

a. First cigarette in the morning (1)

b. Any other cigarette before noon (0)

c. Any other cigarette afternoon (0)

d. Any other cigarette

in the evening (0)

5. Do you find it difficult to refrain

from smoking in places where it is forbidden (church, library, movies,

etc.)?

a. Yes, very difficult (1)

b. Yes, somewhat difficult (1)

c. No, not usually difficult (0)

d. No, not at all difficult (0)

6. Do you smoke if you are so ill that you are in bed most of the day?

a. Yes, always (1)

b. Yes, quite often (1)

c. No, not usually (0)

d. No, never (0)

7. Do you smoke more during the first 2 hours than during the rest of the day?

a. Yes (1)

b. No (1)

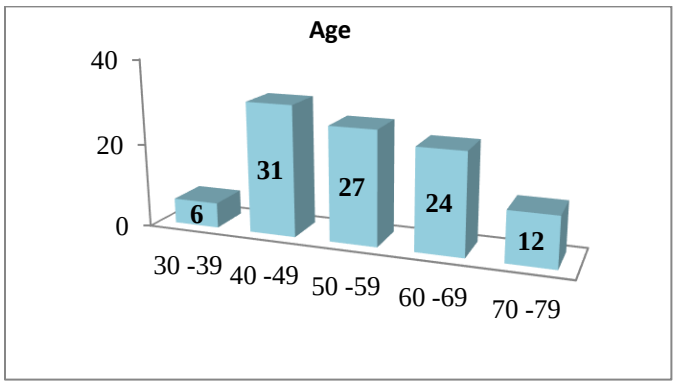
RESULTS

Age Wise Classification:

Table:1

Age	No Of Patients	Percentage
30 -39	9	6
40 -49	46	31
50 -59	40	27
60 -69	36	24
70 -79	19	12

Figure:1

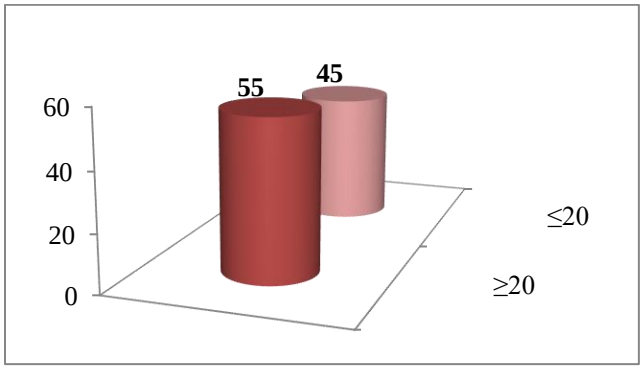


Dialy Cigarettes :

Table:2

No of Cigarettes	No Of Patients	Percentage
≥20	82	55
≤20	68	45

Figure:2

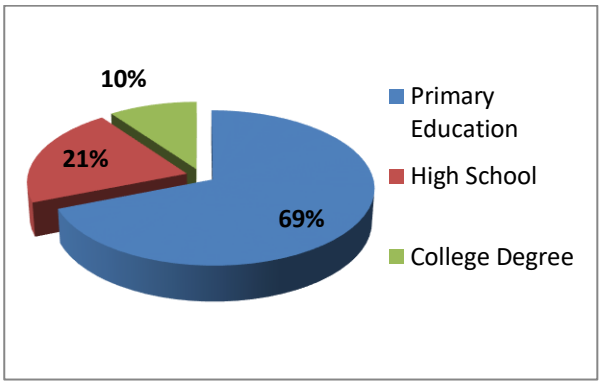


Education Level :

Figure:3

Table:3

Education	No Of Patients	Percentage
Primary Education	104	69
High School	31	21
College Degree	16	10

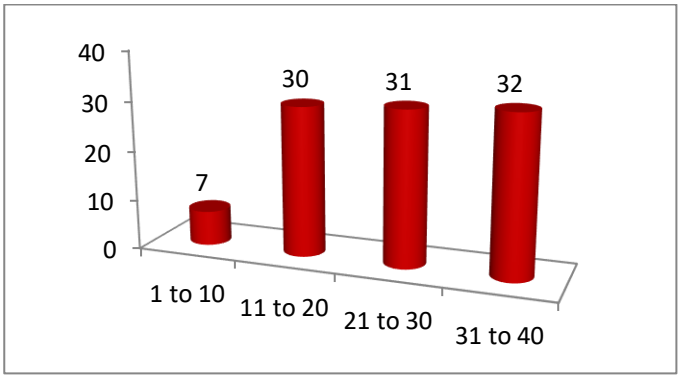


Smoking Years:

Figure:4

Table:4

Year	No Of Patients	Percentage
1 to 10	11	7
11 to 20	45	30
21 to 30	47	31
31 to 40	47	32

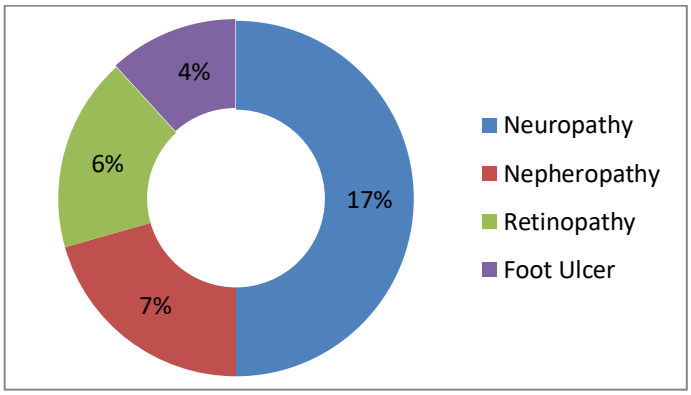


Diabetic Complication:

Figure:5

Table:5

Complication	No Of Patients	Percentage
Neuropathy	26	17
Nephropathy	11	7
Retinopathy	9	6
Foot Ulcer	5	4

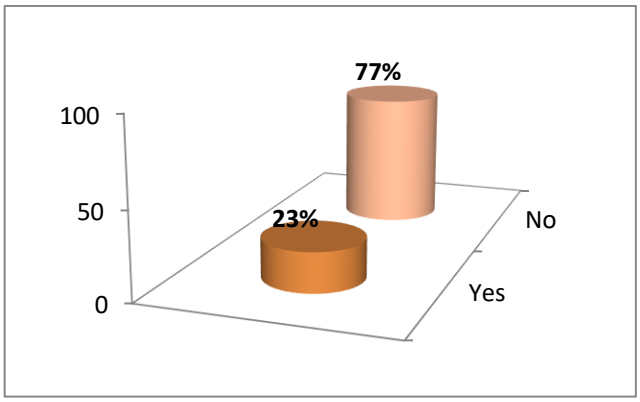


Insulin Therapy:

Figure:6

Table:6

Insulin	No Of Patients	Percentage
Yes	35	23
No	115	77

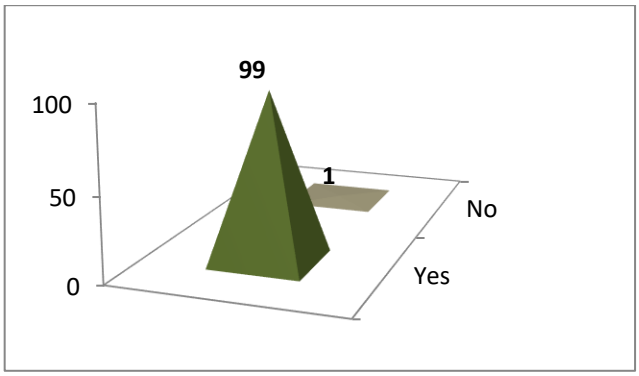


Oral Hypo Glyciemic Agents:

Figure:7

Table:7

OHGs	No Of Patients	Percentage
Yes	149	99
No	1	1

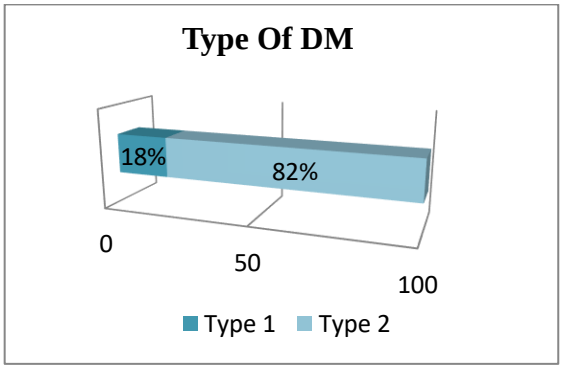


Type Of DM:

Figure:8

Table:8

Type	No Of Patients	Percentage
Type 1	28	18
Type 2	122	82



Diabetic Duration:

Table:9

Duration	No Of Patients	Percentage
Below 3	11	8
3 to 10	14	70
Above 10	35	22

Figure:9

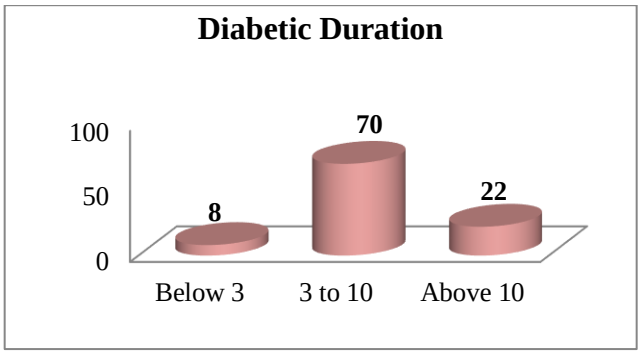


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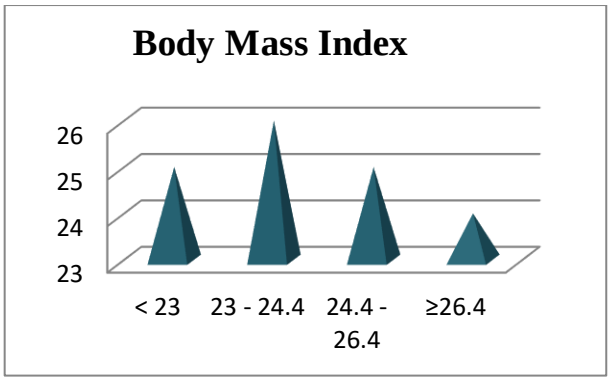
Table:10

Range	No Of Patients	Percentage
< 23	37	25
23 - 24.4	39	26
24.4 - 26.4	38	25
≥26.4	36	24

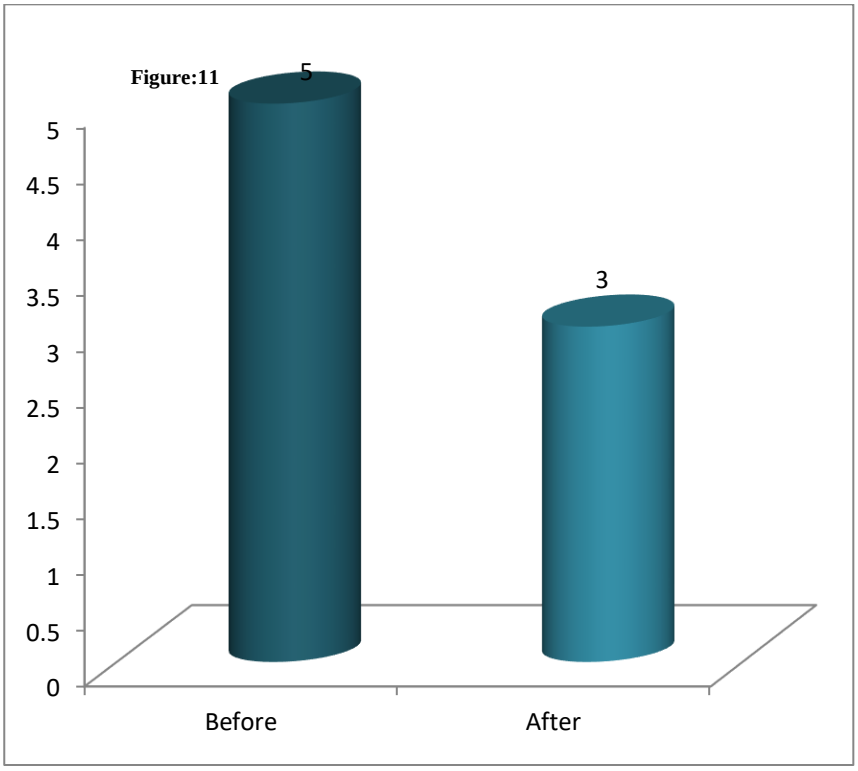
Figure:10



FS Scale Score:

Table:11

Before	After
5	3

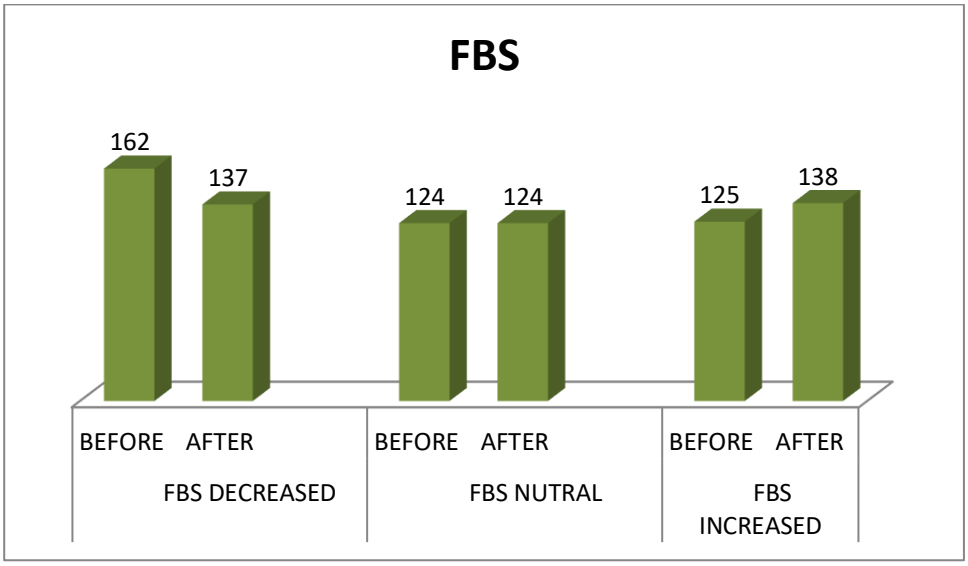


FBS:

Table:12

FBS DECREASED		FBS NEUTRAL		FBS INCREASED	
Before	**After**	**Before**	**After**	**Before**	**After**
162	137	124	124	125	138

Figure:12

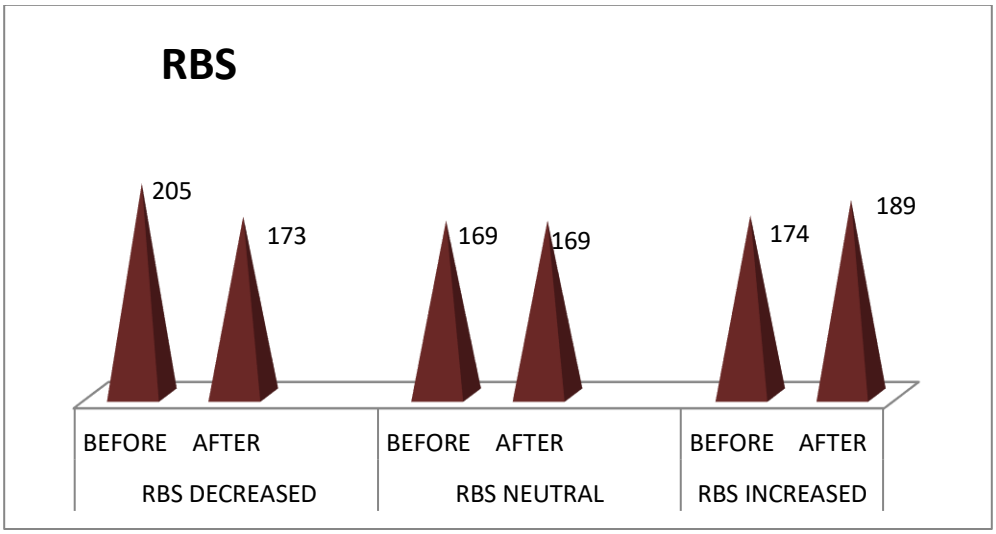


RBS:

Table:13

RBS DECREASED		RBS NEUTRAL		RBS INCREASED	
Before	**After**	**Before**	**After**	**Before**	**After**
205	173	169	169	174	189

Figure:13

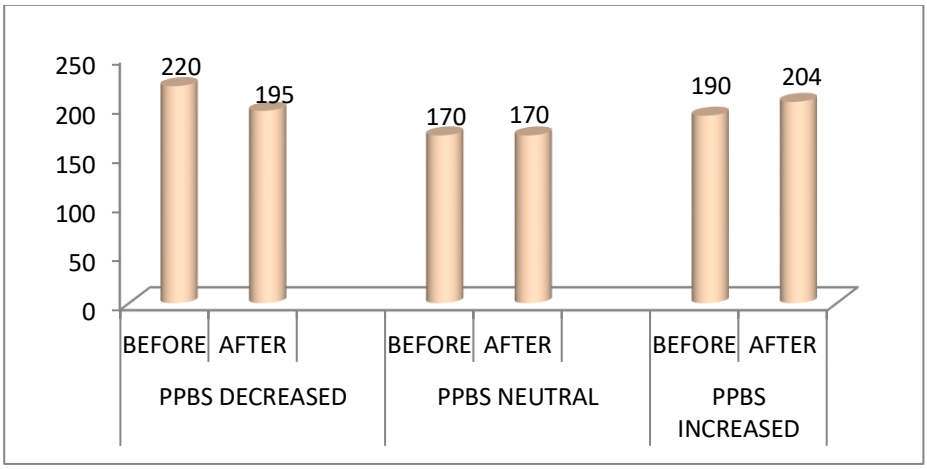


PPBS:

Table:14

PPBS DECREASED		PPBS NEUTRAL		PPBS INCREASED	
Before	**After**	**Before**	**After**	**Before**	**After**
220	195	170	170	190	204

Figure:14

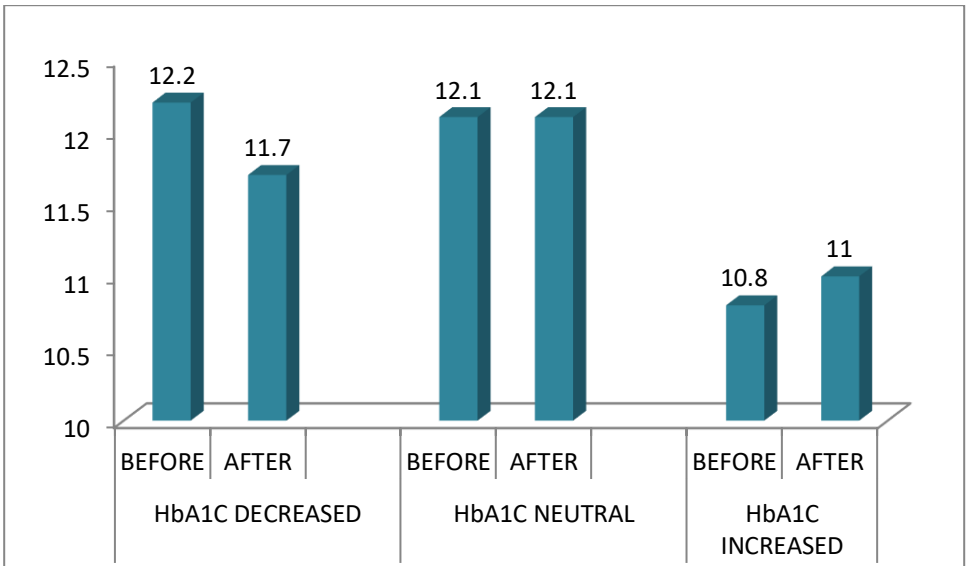


HbA1c:

Table:15

HbA1C DECREASED		HbA1C NEUTRAL		HbA1C INCREASED	
Before	**After**	**Before**	**After**	**Before**	**After**
220	195	170	170	190	204

Figure:15



Discussion

- Table 1 & Figure 1shows that age group from 40 to 49 are more prone to be affected by Diabetes with the percentage of 31 among smokers followed by 50-59, 60-69, 30-39 & 70-79 with the corresponding percentage of 27, 24, 6 & 12 respectively. The author states that the incidence of Diabetes Mellitus is increasing above 40 yrs of age groups.
- Table 2 & Figure 2 indicate that 55% of the patient population were Heavy smokers with ≥20 cigarettes per day.
- Table 3 & Figure 3 denote that 69% of the patient population were found to be with only the Primary education and remaining patients are having high school , college degree Education with the percentage of 21 and 10 respectievly .
- Table 4 & Figure 4 signify that 32%, 31% and 30% & 7% of patients were 31-40 , 21-30, 11-20 & 1-10 respectively.
- Table 5 & Figure 5 represents that Neuropathy were found to be more predominant in Diabetic patients rather than other complications of Nephropathy, Retinopathy & Foot Ulcer on among Diabetic smokers with the percentages of 17, 7, 6& 4 respectively
- Table 6 & Figure 6 signifies that , A minimum of patients were treated with Insulin .A less number of patients of 35 with the percentage of 23 .
- Table 7& Figure 7 shows that Oral Hypo Glyciemic agents were prescribed for most of the patient with 99% of prescription. the oral Hypo Glyciemic agents were found to be the most comfortable treatment for the diabetes followed by the insulin in some kind of patients .
- Table 8 & Figure 8 shows that type2 diabetes were mostly founded in all over the diabetic patients which here studied .Here the numbers of type 2 diabetic patient were

found to be 122 from all among 150 diabetic patients with the percentage of 81 and type 1 diabetes is just 22%

- Table 9 & Figure 9 Indicates that the diabetic duration were found highly in 3-10 years .Here 104 patients were in 3-10 years under diabetes ,Other patients were under diabetes either above 10 years or below 3 years with the percentage of 22 & 8 respectively
- Table 10 & Figure 10 shows the Body Mass Index of diabetic patients .Were the body mass index are found 25%, 26%, 25%, & 24% at the range of <23, 23-24.4, 24.4-26.4, ≥26.4 are respectively.
- Table 11 & Figure 11 Indicates that the overall Modified Fagerstrom Psychological assessment score were reduced as the effect of various counseling aids & methods and regular follow up of DIABETIC patients, by which the table proves that counseling plays an important role in reducing the smoking frequency among DIABETIC patients. The author stated that smoking cessation ranks among the most effective medical interventions. Hence through appropriate counseling aids and with the help of a pharmacist, the patient can find it little bit easier at least in reducing the number of cigarette smoking and thereby, it may help the DIABETIC patients in reducing or managing the severity of the disease.
- The individual scores of individual questions from Modified Fagerstrom Psychological assessment scale were reduced. Thereby indicating that there is a specific role for a pharmacist in patient care especially in reducing smoking among DIABETICpatients.
- Table 12 & Figure 12 shows that the Fasting Blood Sugar (FBS) were decreased after the counseling and follow up of each patients indicates the positive results in such patients.

The average of FBS founded for the decreased number of patients were turn 162 to 137 only for the limited patients.

- Table 13 & Figure 13 shows the Random Blood Sugar level were Increased, neutral, decreased for different group of patients and the averages of increased and decreased were found to be 174-189 and 205-173 respectively. It gives a positive results in such contemplator patients.
- Table 14 & Figure 14 Indicates the Post Prandial Blood Sugar(PPBS) level were Increased, Decreased on different group of patients and the averages of increased and decreased were found to be 190-204, 220-195.These indicates a positive results in counseling.
- The Table 15& Figure 15 shows the decreasing , increasing and neutral levels of laboratory results as HbA1C (glycated protein) . Were the decreased and increased levels are 12.2-11.7, 10.8-11 respectively. It indicates the positive result in counseling the patients and proves that counseling plays an important role in patient care.

CONCLUSION

- The present study shows that the modified Fagerstrom scale questionnaire scores were decreased after the appropriate counseling aids given to the patients than the first observation. Hence a clinical pharmacist can not only save the patients but also serve the public in smoking cessation and also to avoid the consequent effect of second hand smoking.
- Our study suggest that a structured intervention properly conducted by the pharmacist can achieve a significant increase in smoking cessation incidence among diabetic patients.
- Also the study signifies that reducing in the numbers of smoking frequency will definitely help the patient to manage their further complications of the disease.
- This study shows that the role of clinical pharmacist is vital in reducing smoking frequency in which many patients fails to do by their own, even though they are ready to quit. And the psychological assessment in DIABETIC patients made a positive result in reducing smoking frequency.
- The study shows that the laboratory values such as FBS, RBS, PPBS & HbA1c are decreased in some patients. It Indicated that this counselling reduced the diabetic risk by reducing the smoking frequency.
- Also, by means of these results our study shows that the contemplation of patient or participation of patients in counseling programs as contemplation can make a positive change in decease condition

DRAWBACKS

- The study Population is low; hence it is difficult to attain a statistical significant result since the chances of error were more.
- Also the study period was less to draw a definite conclusion for the study. Hence other pathological, physiological and life style strategies may markedly interfere with the study results.

BIBLIOGRAPHY

1. Prabhat Jha, Frank J. Chaloupka, James Moore, Vendhan Gajalakshmi, et al. Disease Control Priorities in Developing Countries: Tobacco addiction.
2. NIH.
3. Neal L. Benowitz, M.D. Nicotine Addiction. NIH Public Access, N Engl J Med. 2010 June 17; 362(24): 2295–2303. doi:10.1056/NEJMra0809890.
4. American Academy of Addiction Psychiatry, Nicotine Dependence
5. Nicotine dependence and withdrawal. TOBACCO CESSATION
6. WHO report on the global tobacco epidemic, 2015: Global Tobacco Control: A Development Priority.
7. Ko SH, Kim SR, Kim DJ,etal., Clinical practice guidelines for type 2 diabetes in Korea. Committee of Clinical Practice Guidelines, Korean Diabetes Association. 2011; 35:431–436.
8. Canoy D, Wareham N, Luben R, et al.,Cigarette smoking and fat distribution in 21,828 British men and women: Obes Res. 2005;13:1466–1475
9. Morrow JD, Frei B, Longmire AW,et al., 2nd Increase in circulating products of lipid peroxidation in smokers:N Engl J Med. 1995;332:1198–1203.
10. Spector TD, Blake DR,et al., Effect of cigarette smoking on Langerhans' cells. Lancet. 1988;2:1028.
11. Noma K, Goto C, Nishioka K,et al.,Smoking, endothelial function, and Rho-kinase in humans. Arterioscler Thromb Vasc Biol. 2005;25:2630–2635.
12. Rafacho BPM, Azevedo PS, Polegato BF, et al. Tobacco smoke induces ventricular remodeling associated with an increase in NADPH oxidase activity. Cell Physiol Biochem 2011; 27: 305–312.
13. Bajaj M. Nicotine and insulin resistance: when the smoke clears. Diabetes 2012; 61: 3078–3080.
14. Foy CG, Bell RA, Farmer DF, et al., Smoking and incidence of diabetes among U.S. adults: findings from the Insulin Resistance Atherosclerosis Study. Diabetes Care 2005; 28: 2501–2507
15. Will JC, Galuska DA, Ford ES, et al., Cigarette smoking and diabetes mellitus: evidence of a positive association from a large prospective cohort study. Int J Epidemiol 2001; 30: 540–546

16. Rimm EB, Manson JE, Stampfer MJ, et al., Cigarette smoking and the risk of diabetes in women. Am J Public Health 1993; 83: 211–214.
17. Beziaud F, Halimi JM, Lecomte P, et al., Cigarette smoking and diabetes mellitus. Diabetes Metab 2004; 30: 161–166.
18. Kawakami N, Takatsuka N, Shimizu H, et al.,Effects of smoking on the incidence of non-insulin-dependent diabetes mellitus. Replication and extension in a Japanese cohort of male employees. Am J Epidemiol 1997; 145: 103–109.
19. Nakanishi N, Nakamura K, Matsuo Y, et al., Cigarette smoking and risk for impaired fasting glucose and type 2 diabetes in middle-aged Japanese men. Ann Intern Med 2000; 133: 183–191
20. Wannamethee SG, Shaper AG, Perry IJ, et al.,Smoking as a modifiable risk factor for type 2 diabetes in middle-aged men. Diabetes Care 2001; 24: 1590–1595
21. Yoshikawa H, Hellström-Lindahl E and Grill V. Evidence for functional nicotinic receptors on pancreatic β cells. Metabolism 2005; 54: 247–254
22. Bruin JE, Gerstein HC and Holloway AC. Long-term consequences of fetal and neonatal nicotine exposure: a critical review. Toxicol Sci 2010; 116: 364–374.
23. Bruin JE, Petre MA, Lehman MA, et al., Maternal nicotine exposure increases oxidative stress in the offspring. Free Radic Biol Med 2008; 44: 1919–1925.
24. Holloway AC, Lim GE, Petrik JJ, et al., Fetal and neonatal exposure to nicotine in Wistar rats results in increased β cell apoptosis at birth and postnatal endocrine and metabolic changes associated with type 2 diabetes. Diabetologia 2005; 48: 2661–2666
25. Cavallini G, Talamini G, Vaona B, et al.,Effect of alcohol and smoking on pancreatic lithogenesis in the course of chronic pancreatitis. Pancreas 1994; 9: 42–46.
26. Milnerowicz H, Sliwińska M, Jabłonowska M, et al., Effect of tobacco smoking on amylase activity in patients with pancreatitis. Przegl Lek 2004; 61: 1071–1072.
27. Sliwińska-Mossoń M and Milnerowicz H. Tobacco smoking and the diseases of pancreas. Przegl Lek 2005; 62: 1163–1166.
28. Sliwińska-Mossoń M and Milnerowicz H. Influence of tobacco smoking on lipase activity in patients with pancreatitis. Przegl Lek 2005; 62: 1058–1061.

29. Sliwińska-Mossoń M and Milnerowicz H. The activity of thermolability amylase in serum nonsmoking and smoking healthy persons and patients with pancreatitis. Przegl Lek 2008; 65: 491–494.
30. Sliwińska-Mossoń M and Milnerowicz H. Electrophoretic pattern of alpha-amylase isoenzymes in serum of nonsmoking and smoking normal persons and patients with pancreatitis. Przegl Lek 2009; 66: 641–643
31. Diabetes & Vascular Disease Research 2017, Vol. 14(4) 265–276 © The Author(s) 2017 Reprints and permissions: sagepub.co.uk journalsPermissions.nav: 10.1177/1479
32. Seet RC, Loke WM, Khoo CM,et al.,Acute effects of cigarette smoking on insulin resistance and arterial stiffness in young adults. Atherosclerosis. 2012;224:195–200.
33. Facchini FS, Hollenbeck CB, Jeppesen j,et al.,Insulin resistance and cigarette smoking. Lancet. 1992;339:1128–1130.
34. Eliasson B, Mero N, Taskinen MR,et al., The insulin resistance syndrome and postprandial lipid intolerance in smokers. Atherosclerosis. 1997;129:79–88.
35. Targher G, Alberiche M, Zenere MB,et al.,Cigarette smoking and insulin resistance in patients with noninsulin-dependent diabetes mellitus. J Clin Endocrinol Metab. 1997;82:3619–3624.
36. Eliasson B, Attvall S, Taskinen MR,et al., The insulin resistance syndrome in smokers is related to smoking habits. Arterioscler Thromb. 1994;14:1946–1950.
37. Sargeant LA, Khaw KT, Bingham S,et al., Cigarette smoking and glycaemia, Int J Epidemiol. 2001;30:547–554.
38. Nilsson PM, Gudbjornsdottir S, Eliasson B,et al.,Smoking is associated with increased HbA1c values and microalbuminuria in patients with diabetes: data from the National Diabetes Register in Sweden. Diabetes Metab. 2004;30:261–268.
39. Biesenbach G, Grafinger P, Janko O,et al.,Influence of cigarette-smoking on the progression of clinical diabetic nephropathy in type 2 diabetic patients. Clin Nephrol. 1997;48:146–150.
40. Chuahirun T, Wesson DE. Cigarette smoking predicts faster progression of type 2 established diabetic nephropathy despite ACE inhibition. Am J Kidney Dis. 2002;39:376–382.
41. Chuahirun T, Khanna A, Kimball K,et al.,Cigarette smoking and increased urine albumin excretion are interrelated predictors of nephropathy progression in type 2 diabetes. Am J Kidney Dis. 2003;41:13–21.

42. Guillausseau PJ, Massin P, Charles MA,et al.,Glycaemic control and development of retinopathy in type 2 diabetes mellitus: a longitudinal study. Diabet Med. 1998;15:151–155.
43. Mitchell BD, Hawthorne VM, Vinik AI. Cigarette smoking and neuropathy in diabetic patients. Diabetes Care. 1990;13:434–437.
44. Harris M, Eastman R, Cowie C. Symptoms of sensory neuropathy in adults with NIDDM in the U.S. population. Diabetes Care. 1993;16:1446–1452.
45. Benbow SJ, Williams G, MacFarlane IA. Smoking habits and painful diabetic neuropathy. J Diabetes Complications. 1997;11:334–337.
46. Tamer A, Yildiz S, Yildiz N,et al., The prevalence of neuropathy and relationship with risk factors in diabetic patients ,Med Princ Pract. 2006;15:190–194.
47. Stratton IM, Kohner EM, Aldington SJ,et al.,risk factors for incidence and progression of retinopathy in type II diabetes over 6 years from diagnosis. Diabetologia. 2001;44:156–163.
48. https://www. Webmd.com/diabetes/guide/types-of-diabetes-mellitus
49. https://www.diabetes.co.uk/diabetes-types.html.
50. https://www.medicinet.com/diabetes-mellitus/article.htm#what –is-type-2-diabetes
51. https://www.medicalnewstoday.com/info/diabetes/diagnosis-of-diabetes.php
52. Mariola Śliwińska-Mossoń and Halina Milnerowicz Diabetes & Vascular Disease Research 2017, Vol.14(4)265–276
53. JoAnn E. Manson, Umed A. Ajani,etal.,Prospective Study of Cigarette Smoking and the Incidence of Diabetes Mellitus among US Male Physicians THE AMERICAN JOURNAL OF MEDICINE Vol 109;10Nov 2000.
54. Carole Willi,Patrick Bodenmann,William A. Ghali,et al., Active Smoking and the Risk of Type 2 Diabetes A Systematic Review and Meta-analysis JAMA. 2007;298(22):2654-2664.
55. NAVIDAD CANGA,JOKIN DE IRALA, EDUARDO VARA, etal.,A Intervention Study for Smoking Cessation in Diabetic Patients DIABETES CARE, Vol 23,10 Oct 2000
56. S. GOYA WANNAMETHEE, PHD1 A. GERALD SHAPER, etal.,Smoking as a Modifiable Risk Factor for Type 2 Diabetes in Middle-Aged Men DIABETES CARE, Vol24,9,SEP 2001
57. Nwaokoro Joakin, Ede Alison Okorie1, O. Emerole.etal., Study on the effect of smoking on Type 2 Diabetic Patients in Federal Medical Center Owerri, Southeastern Nigeria Asian Journal of Medical Sciences Jul-Sep 2014 Vol 5(3)

58. Carole Clair, MD MSc1 , Marya J. Cohen,etal.,The Effect of Cigarette Smoking on Diabetic Peripheral Neuropathy: A Systematic Review and Meta-Analysis 30(8):1193–203 DOI: Society of General Internal Medicine 2015
59. Xi-tao XIE1 , Qiang LIU2 , Jie WU2 ,etal., Impact of cigarette smoking in type 2 diabetes development Acta Pharmacologica Sinica (2009) 30: 784–787;
60. Maija Feodoroff,Valma Harjutsalo,Carol Forsblom,etal.,Smoking and progression of diabetic nephropathy in patients with type 1 diabetes Acta Diabetol (2016) 53:525–533
61. Eric B Rimm, June Chan, Meir J Stampfer,etal., Prospective study ofcigarette smoking, alcohol use, and the risk of diabetes in men BMJ VOLUME 310 4MARCH1995
62. Julie C Will Deborah A Galuska Earl S,etal., Cigarette smoking and diabetes mellitus: evidence of a positive association from a large prospective cohort study International Journal of Epidemiology,Vol30(3) 1 June 2001, Pages 540–546.
63. Jiang N, Huang F, Zhang X.etal.,nephropathy in patients with type 1 and type 2 diabetes: a meta-analysis of observational studies.Oncotarget. 2017 Oct 4;8(54):93209-93218.
64. Giovanni Targher,Maria Alberiche Marina B.etal., Cigarette Smoking and Insulin Resistance in Patients with Noninsulin-Dependent Diabetes Mellitus. The Journal of Clinical Endocrinology & Metabolism, Vol82(11)1 November 1997, Pages 3619–3624.
65. Ying Wang, Jie Ji1,Yu-jian Li,etal.,Passive Smoking and Risk of Type 2 Diabetes: A MetaAnalysis of Prospective Cohort Studies, PLOS ONE July 2013, Vol 8(7)
66. Toshimi Sairenchi1, Hiroyasu Iso2, Akio Nishimura.etal., Cigarette Smoking and Risk of Type 2 Diabetes Mellitus among Middle-aged and Elderly Japanese Men and Women American Journal of Epidemiology 2004;160:158–162
67. D Haire- Joshu, R E Glasgow and T L Tibbs Diabetes Care 1999 Nov; 22(11): 1887-1898.
68. DEBORAH J. TOOBERT, PHD SARAH E.etal., The Summary of Diabetes Self-Care Activities Measure DIABETES CARE, VOL 23,(7), JULY 2000
69. Saito K, Sone H. Effect of smoking on diabetes mellitus and dyslipidemia Nihon Rinsho. Japanese journal 2013 Mar;71(3):443-8.

PATIENT PROFORMA

Name : Age: Gender:

IP NO: DOA: DOD: Ward:

Address : Mob No:

Reason for admission :

Past medical history :

Smoker: Y/N year: Alcoholic: Y/N BMI:

Marital status : Financial status: Occupation :

Co morbidities :

Diabetic profile:

Type of diabetes:

Diabetic complication if any:

Use of insulin:

Profile	**Initial**	**2nd follow up**	**3rd follow up**
FBS			
RBS			
PPBS			
HbA_1C			

Psychological Assessment score:

Before counseling	**After counseling**

Modified Version of the Fagerstrom Tolerance Questionnaire (mFTQ)

1. How many cigarettes a day do you smoke?
   a. Over 26 cigarettes a day (2)
   b. About 16-25 cigarettes a day (1)
   c. About 1-15 cigarettes a day (0)
   d. Less than 1 a day (0)

2. Do you inhale?
   a. Always (2)
   b. Quite often (1)
   c. Seldom (1)
   d. Never (0)

3. How soon after you wake up do you smoke your first cigarette?
   a. Within the first 30 minutes (1)
   b. More than 30 minutes after waking but before noon (0)
   c. In the afternoon (0)
   d. In the evening (0)

4. Which cigarette would you hate to give up?
   a. First cigarette in the morning (1)
   b. Any other cigarette before noon (0)
   c. Any other cigarette afternoon (0)
   d. Any other cigarette in the evening (0)

5. Do you find it difficult to refrain from smoking in places where it is forbidden (church, library, movies, etc.)?
   a. Yes, very difficult (1)
   b. Yes, somewhat difficult (1)
   c. No, not usually difficult (0)
   d. No, not at all difficult (0)

6. Do you smoke if you are so ill that you are in bed most of the day?
   a. Yes, always (1)
   b. Yes, quite often (1)
   c. No, not usually (0)
   d. No, never (0)

7. Do you smoke more during the first 2 hours than during the rest of the day?
   a. Yes (1)
   b. No (1)

PATIENT CONSENT FORM

Participant written informed consent

I understand that my participation is voluntary and that I may withdraw from this study at any time without giving any reason or to decline to answer any particular question in the study. I consent the members of the study to have access to my response and to publish the result, provided my identity is not revealed. I voluntarily agree to participate in the study.

Participant signature with date