

REVIEW OF LITERATURE

The elderly is a diverse population with a range of physiological profiles, functional capacities, and life expectancies. Elderly type 2 DM appears to be caused by a number of causes, including genetic make-up, prolonged life expectancy resulting in decreased insulin production, and the alteration of specific environmental factors causing central obesity. The final one is in charge of insulin resistance, the primary contributor to metabolic syndrome and type 2 DM in adults and the elderly. The most significant contributing variables are the eating problems that characterize modern lifestyles in combination with a lack of physical activity. It is widely recognized that eating can have additional health benefits for the prevention and treatment of various diseases in addition to providing nutrients for nourishing the body. Regular consumption of functional foods may be linked to improved anti-oxidant, anti-inflammatory, insulin sensitivity, and anti-cholesterol activities, all of which are important for managing and preventing T2DM. Amongst many functional foods, pumpkin seeds are apparent to be having protective effect against type 2 diabetes and dyslipidaemia due to its unique composition.

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Section 2.1 Non communicable diseases

Non communicable diseases (NCDs) are chronic diseases having long duration which is the result of combination of genetic, physiological, environmental and behavioural factors. They are chronic in nature. If they are untreated, it can also resulted into premature death. Non communicable diseases (NCDs) kill 41 million people each year, equivalent to 74% of all deaths globally. Each year, 17 million people die from NCD between the ages of 30 and 69 years; over 86% of these "premature" deaths occur in low- and middle-income countries. (WHO Factsheet, 2022).

Diabetes, cardio-vascular diseases, cancers and chronic respiratory diseases are major types of Non-communicable disease (NCDs). People of all age groups and regions got affected due to Non-communicable diseases. Rapid urbanization, increased industrialization, unhealthy diets and lack of physical activity are major responsible factors of Non-communicable diseases.

High blood pressure, obesity, uncontrolled diabetes, hyperlipidaemia, physical inactivity and smoking are the modifiable risk factors of NCDs while age, gender, ethnicity and genetic factors are non-modifiable risk factors. Non-modifiable risk factors can also classified as biological, behavioural and social factors. In which, biological factors includes being obese or overweight, hyperlipidaemia, hypertension and insulin resistance. Unhealthy diets, smoking, use of tobacco, lack of physical activity are comes under behavioural factors whereas socioeconomic and cultural parameters are part of social factors.

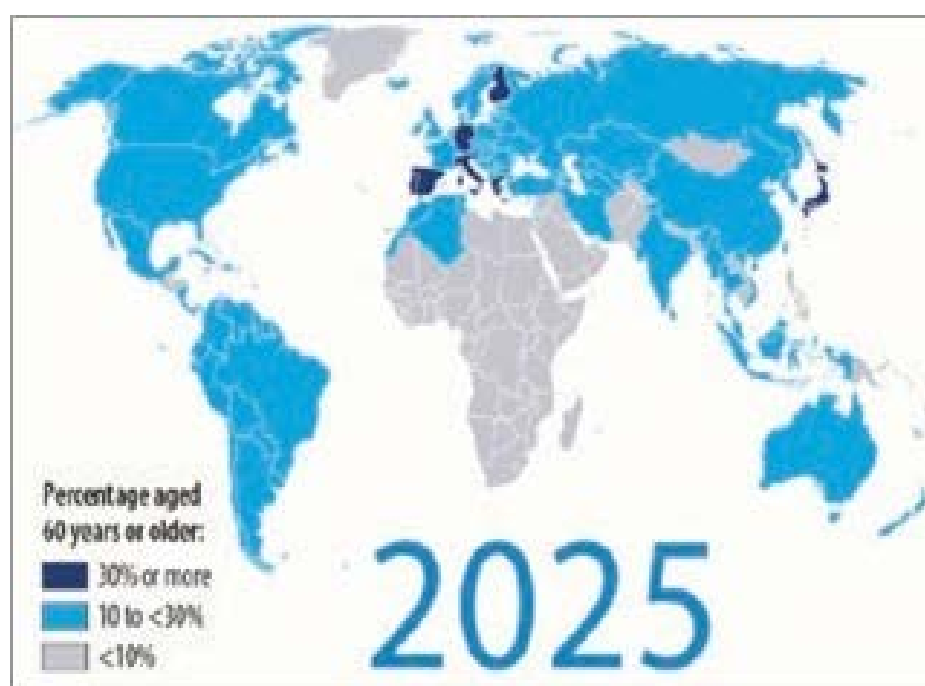
NCDs are referred as “Rich and noble disease” but their impact is affecting on economical development and also affecting the quality of life of severely ageing population. Among developing countries like India, burden of NCDs is growing rapidly.

NCDs threaten progress towards the 2030 Agenda for Sustainable Development, which includes a target of reducing premature deaths from NCDs by one-third by 2030. Poverty is also one of the major contributors of occurrence of NCDs in low-middle income countries. Vulnerable and socially disadvantaged people die sooner than others because of the exposure with harmful products such as tobacco and alcohol, unhealthy diets and limitation for accessing health services due to unavailability of resources.

According to one of the study conducted in Nigeria, prevalence of hypertension, diabetes and dyslipidaemia were 35.3%, 4.6% and 47.1% respectively, which highlights the need for actions and policies to tackle the NCDs (Israel Oluwaseyidayo Idris, 2020) Approximately 6.1 million deaths were reported due to NCDs and out of that 2.76% deaths were due to type 2 diabetes (Noncommunicable Diseases. Both sexes, all ages, 2019).

Increased life expectancy and easy access to health care facilities has increase the life expectancy and as result, there is a rapid ageing of population worldwide. One of the recent report published by World Health Organization stated that population above 60 years of age are expected to live for more 15 years and it will be double by year 2050. Older population will account for one third of total population in many high-income countries and in some low and middle-income countries of Asia-pacific group (World report on ageing and health, 2015). For geriatric population, good health helps to assure independence, security and good productivity in later years. However, occurrence of NCDs can diminishes quality of life, increase health care cost and pressure on family members.

Figure 2.1.1 Projection of old age population worldwide



Section 2.2 Diabetes

A collection of common metabolic conditions known as diabetes mellitus (DM) share the phenotype of hyperglycemia and are characterised by disturbances in the metabolism of carbohydrates, fats, and proteins due to deficiencies in insulin secretion, insulin action, or both. A complicated interplay of genetic and environmental variables results in the development of several unique forms of DM. Reduced insulin secretion, decreased glucose utilization, and increased glucose production are all variables that might contribute to hyperglycemia depending on the cause of the diabetes. The ailment "Madhumeha," which would be equivalent to the current name "Diabetes mellitus," is mentioned in ancient Indian scriptures, indicating that diabetes must have existed in India even before 2500 BC. According to the Indian Council of Medical Research India Diabetes Study (ICMR-INDIAB study), there were 62.4 million diabetics in India in 2010.

Nearly one-fifth of all persons with diabetes worldwide, according to the World Diabetes Atlas, reside in the South-East Asia Region. According to recent estimates, there are currently 78.1 million adults worldwide who suffer with diabetes, 69.2 million of them reside in India. By 2040, there will be 123 million diabetics in India, accounting for 12.1% of the adult population.

IGT is also present in an additional 36.5 million people, and by 2040, this number will reach 65.3 million. In the South East Asian area, India has the second-highest prevalence of diabetes among adults (9.1%). In India, diseases associated with diabetes claim the lives of almost 1.1 million people annually. According to IDF estimates, more over half (52.1%) of all diabetics in India are ignorant of their condition (Sharma et al, 2017).

According to the IDF Diabetes Atlas 10th edition (2021), approximately 537 million adults aged between 20-79 years are living with diabetes in 2021 are projected to rise upto 643 million by 2023 and by 2045 figure will reach to 783 million. 3 in 4 adults are suffering from diabetes in low and middle income countries. Diabetes caused 6.7 million death world wide in a year.

Prevalence of Diabetes in world

Figure 2.2.1 World-wide prevalence of Diabetes Mellitus

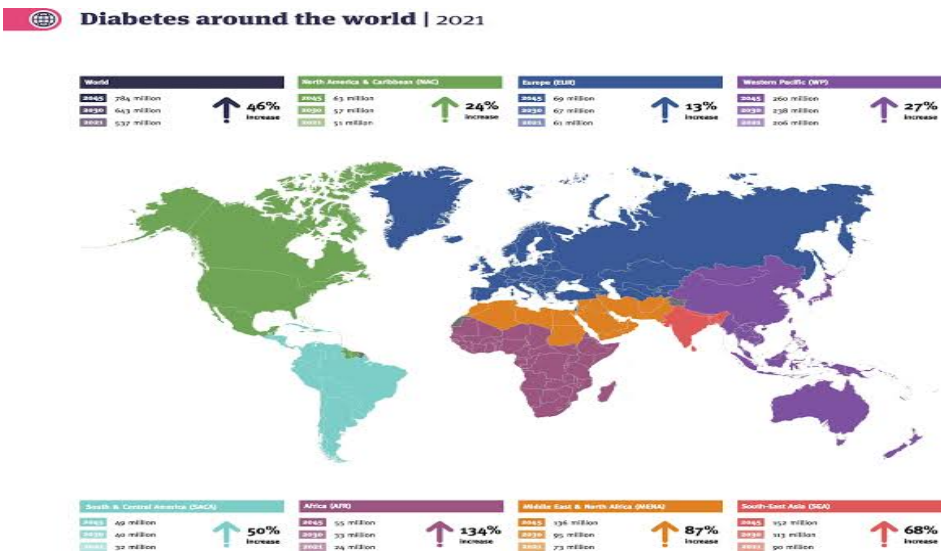


Figure 2.2.2 Top ten countries showing prevalence of Diabetes mellitus

Table 3.4 Top 10 countries or territories for number of adults (20–79 years) with diabetes in 2021 and 2045

2021			2045		
Rank	Country or territory	Number of people with diabetes (millions)	Rank	Country or territory	Number of people with diabetes (millions)
1	China	140.9	1	China	174.4
2	India	74.2	2	India	124.9
3	Pakistan	33.0	3	Pakistan	62.2
4	United States of America	32.2	4	United States of America	36.3
5	Indonesia	19.5	5	Indonesia	28.6
6	Brazil	15.7	6	Brazil	23.2
7	Mexico	14.1	7	Bangladesh	22.3
8	Bangladesh	13.1	8	Mexico	21.2
9	Japan	11.0	9	Egypt	20.0
10	Egypt	10.9	10	Turkey	13.4

Source: IDF Diabetes Atlas, 2021-10th edition

Indian scenario

Figure 2.2.3 % Prevalence of Diabetes in different states



Source: ICMR INDIAB study, 2017

Regional scenario (Gujarat)

As per one of the study conducted in Sonapat, The age range of 46 to 60 years was shown to have the highest prevalence of diabetes (41.96%). In this age group, the mean fasting plasma glucose was 149.36 19.51 for men and 147.43 18.19 for women. Male and female mean 2 hour postprandial plasma glucose values were 259.94 51.36 and 259.65 51.39, respectively. (Madaan, 2014).

Gujarat has the second-highest prevalence of diabetes after Tamil Nadu because the Gujarati population is genetically predisposed to the condition, and the main causes include a lack of physical activity and poor eating habits. According to research by the Indian Council of Medical Research, diabetes prevalence rates among rural populations were quite low and variable, ranging from 0.4% in Himachal Pradesh to 1.3% (Kerala), 1.5% (Delhi), and 3.9% in Gujarat (Gupta et al. 2007).

In one of the research carried out in Gujarat's Gandhinagar district's Raysan village. It was a community-based study that was carried out through a home-to-home survey, interviewing participants, and effective communication. The data collection form was created to collect information on demographics, medical history, medication history, and results of previous biochemical investigations. There were 34 diabetics in Raysan Village, which had a total population of 2673. Therefore, Raysan Village has a 1.27% prevalence rate for diabetes mellitus. Of the 34 diabetics, 23 were men and 11 were women (patel et al 2016).

Another study was carried out to map the prevalence of non-communicable diseases in the free-living populations of Vadodara and Godhra, and it was shown that Godhra had a little higher prevalence of diabetes (19%). Additionally, in both cities, the frequency was higher in male individuals than in females (Iyer et al,2011).

In order to determine the influence of nutrition, lifestyle, and manners on the condition, a survey of DM patients in the Saurashtra region was done. To determine the main causes of the DM, 250 diagnosed patients from the Saurashtra region of Gujarat, India, were chosen for the current study. The results of the study's observation show that specific food and lifestyle practises in this region are to blame for the development of DM (Rohit Sharma, 2012)

According to one of the hospital based study conducted in Ambala district of Haryana revealed that, the age group of people over 70 years old had the highest prevalence of Diabetes mellitus (DM), or 5.99%. In study, the gender-specific prevalence of diabetes was 6.07% for men and 4.06% for women. This study's findings about the increased prevalence of diabetes among the male participants are consistent with findings from other research (Nitesh Pradhan, 2018).

In order to define the profile of patients with type 2 diabetes mellitus, Similar kind of an above hospital-based observational study was carried out in the Ahmedabad district of Gujarat state, India, between August 2006 and January 2009. The study involved 622 type 2 diabetics who had just received their diagnosis. Variables like sociodemographic parameters, presenting symptoms, risk factors (hypertension, obesity, dyslipidemia, and glycemic status), family

history of diabetes, physical activity, and behavioural profile were all covered by the questionnaires. The following parameters were measured: blood pressure, body mass index (BMI), glycosylated haemoglobin levels, and fasting lipid profile. According to this study's findings, type 2 diabetes mellitus is a significant burden in Gujarat, which is consistent with Simon's 2010 findings.

Above study suggested that in Gujarat, lifestyle adjustment interventions like diet, exercise, and patient education are crucial (Patel et al ,2011).

The prevalence of diabetes in and around the city of Vadodara has also been the subject of numerous studies at our department (faculty of family and community sciences, department of Foods and Nutrition). According to the studies, the prevalence of diabetes in Vadodara city's industrial population rose from 10.4% in 2004 to 15.3% in 2005.

Additionally, the majority of studies in India come from the south, while just a small number come from the north. Gujarat has seen few comparison studies. Few studies have been conducted to evaluate the population's cultural diversity and its effects on lifestyle choices and comorbidities. Another community-based cross-sectional study that used a house-to-house survey and was carried out in Ahmedabad found that 7.33% of urban residents had diabetes mellitus. The majority of the study's participants (53.64%) were aged 45 to 60. (Koria et al,2013).

The situation of diabetics in India is worse than other nations due to lack of awareness and information about diabetes and its management, as shown by various studies that show a greater prevalence of diabetic problems due to changes in lifestyle and nutrition transition. Although there have been numerous studies on diabetes education programmes conducted elsewhere, there is relatively little information available on comparable studies conducted in India.

Section 2.3 Types of Diabetes Mellitus

Diabetes mellitus, more often known as diabetes, is a dangerous, long-term (or "chronic") disorder that manifests as elevated blood glucose levels when the body is unable to create any, sufficient amounts of, or utilise the insulin that is produced. There are mainly 3 types of Diabetes:

Type 1 Diabetes Mellitus

Type 1 Diabetes Mellitus is also known as “Insulin-dependent” or “Juvenile onset” diabetes mellitus. The immune system of the body destroys the pancreatic beta-cells that produce insulin, which results in type 1 diabetes. As a result, either very little or no insulin is produced by the body. People with type 1 diabetes require daily insulin injections to maintain a healthy blood glucose level. Abnormal thirst, excessive hunger, dry mouth, tiredness, lack of energy, blurred vision, weight loss, recurrent infections and delayed wound healing are most common symptoms of type 1 diabetes mellitus. The reasons for the occurrence of diabetes are still unknown, it may occur due to genetic factors, environmental factors, viral infections, early events in womb (IDF, 2021).

Type 2 Diabetes Mellitus

Type 2 Diabetes Mellitus is also known as “Non-insulin dependent” or “Adult onset” Diabetes Mellitus. In type 2 diabetes, insulin resistance, or the body's cells' failure to adequately respond to insulin, is the original cause of hyperglycemia. Insulin resistance causes the hormone to become less effective, which eventually causes an increase in insulin production. The inability of the pancreatic beta cells to meet demand over time can result in inadequate insulin production. Type 2 diabetes mellitus have similar types of symptoms as type 1 diabetes but sometime it can be asymptomatic as well. Overweight, Obesity, increasing age, family history and unhealthy diet are risk factors for type 2 diabetes mellitus. Type 2 diabetes is highly prevalent and on the rise all over the world. This increase is brought on by population ageing, economic growth, and growing urbanisation, which promote sedentary behaviour and increased consumption of foods linked to obesity. Use of oral Hypoglycaemic drugs, healthy diets, physical activity and

lifestyle modifications are important to control blood sugar levels of type 2 diabetic patients.

Gestational Diabetes mellitus

GDM has long been referred to as any level of glucose intolerance that begins or is initially noticed during pregnancy. The criteria was applicable whether or not the problem remained after pregnancy and did not rule out the potential that undiagnosed glucose intolerance may have preceded or started concurrently with the pregnancy, even though the majority of cases resolve with delivery. Although its limitations were known for a long time, this definition made it easier to develop a consistent approach for the detection and categorization of GDM. The proportion of pregnant women with undiagnosed type 2 diabetes has increased as the continuous obesity and diabetes epidemic has raised the prevalence of type 2 diabetes in women of reproductive age (ADA, 2020). GDM typically manifests during pregnancy as a temporary disease that goes away after the baby is born. Any lifestyle intervention should begin no later than three years after the pregnancy in order to reap the greatest benefits for the prevention of type 2 diabetes, given the high risk of early onset and the fact that prior GDM increases the risk of cardiovascular disease (CVD), with or without type 2 diabetes (IDF, 2021).

Section 2.4 Pathophysiology of Diabetes Mellitus

One of the most prevalent metabolic illnesses, Type 2 Diabetes Mellitus (T2DM), is brought on by a confluence of two main factors: improper insulin secretion by pancreatic beta-cells and improper insulin response in insulin-sensitive organs. The molecular mechanisms involved in the synthesis, release, and detection of insulin are carefully regulated activities because they are necessary for maintaining glucose homeostasis. A metabolic imbalance that is the cause of the disease's onset can result from flaws in any of the mechanisms involved in these processes. Cellular integrity must be protected, and the pathways and mechanisms involved in β -cell physiology must be strictly controlled, to maintain optimal β -cell function. The main features of T2DM are examined in this review, along with the molecular mechanisms and pathways involved in insulin metabolism that result in T2DM and insulin resistance (Galicia-Garcia U, 2020). Therefore, defect in any above mechanism leads to pathogenesis of Diabetes mellitus.

A high-calorie Western diet raises blood sugar levels and causes circulating very-low-density lipoproteins (VLDLs), chylomicrons (CMs), and their remnants (CMRs) to be triglyceride-rich (TG). Reactive oxygen species (ROS) concentrations increase as a result, which triggers the aberrant production of inflammatory chemicals. Given that oxidative stress is a well-known inducer of inflammation, the two processes interact synergistically after a large meal, amplifying any negative postprandial consequences (Dali-Youcef N., 2013).

To prevent, control, treat, or reverse the pathophysiology of T2DM and its problems, it is essential to understand the mechanisms involved in each stage of the development and complications of T2DM.

Section 2.5 Risk factors

As people become older, type 2 diabetes and prediabetes are more common. The following are the two most significant causes of hyperglycemia: age-related declines in insulin production and increasing insulin resistance brought on by alterations in body composition and sarcopenia. Elderly diabetics are a diverse population with varying life expectancies, co-occurring chronic illnesses, and the capacity to self-manage blood glucose or administer an injection. Individualized treatment should be provided. To achieve specific therapeutic goals, older patients with long-term diabetes and severe chronic comorbidities require a more lenient approach. Avoiding hypoglycemia, ensuring the therapy's safety, and gaining the patient's approval should all be additional objectives (Mordarska & Zawada, 2017).

Compared to other generations, people aged 65 and older have a higher chance of developing diabetes. Additionally, data indicate that the prevalence of diabetes among the elderly has recently increased (Vrdoljak D et al, 2014). Pre-diabetes and diabetes are recognised to be strongly influenced by social and economic factors, including income, education, occupation, levels of physical activity, being overweight or obese, health behaviors, living conditions, and other demographic factors (Williams ED et al, 2010).

Aside from genetics and family history, the risk factors for diabetes include ethnicity, age, obesity, physical inactivity, eating poorly, and behavioural behaviours. The beginning of diabetes complications can be prevented or delayed by maintaining stable blood sugar, blood pressure, and blood lipid levels. Due to numerous problems and obstacles, including a lack of a multisectoral approach, surveillance data, a lack of awareness of diabetes, its risk factors, and complications, access to health care settings, a lack of affordable medication options, etc., the prevention and management of diabetes and associated complications is a significant challenge in India. To stop the diabetes epidemic and lower complications associated with diabetes in India, effective primary prevention and health promotion are required at both the individual and population levels (Pradeepa R, 2021).

One of the study conducted by Anying Bai et al (2021) assessed Prevalence and risk factors of diabetes among adults aged 45 years or older in China. Study findings reported that factors such as age, place of residence, BMI, history of hypertension, stroke, and coronary heart disease, ADL disability, and lower/upper extremity functional restriction were substantially linked to a higher risk of diabetes and pre-diabetes. Males aged 45 to 55 had a higher prevalence of diabetes than females did. Females were more prevalent in other age groups. It's stated that beyond the age of 45, more women become overweight or obese, but more men become overweight earlier in life (Pickett K et al, 2005).

Section 2.6 Management of Diabetes

Diabetes patients need ongoing care that goes beyond a standardised drug intake and involves more complex disease management. In particular, managing type 1 diabetes necessitates making frequent treatment choices, such as varying insulin dosages based on blood glucose levels, food intake, and degree of exercise. This necessitates the use of medical technology, proper patient handling, and the conversion of measurement data into sensible therapeutic choices.

The long-term management of diabetes may only partially benefit from the pharmacological strategy to treating T2DM. For the disease to be managed effectively, individuals must make significant changes to their lifestyles and receive therapeutic therapies. These include of adjustments to one's physical activity level, nutritional changes, stress management, and sleep improvement.

Pharmacological treatment

Hemoglobin A1c levels are reduced by 0.6% to 1.5% by all FDA-approved drugs for the treatment of hyperglycemia in type 2 diabetes. Although there are some differences among the recommendations made by the various associations, they all adhere to a similar set of principles, including the following: (1) establish a glycemia or haemoglobin A1c goal; (2) begin metformin therapy in most patients; (3) use combination therapy to achieve the glycemic goals; (4) avoid hypoglycemia; and (5) comprehend adverse effect profiles of medications.

The effectiveness of metformin in decreasing blood sugar, as well as its safety record, weight neutrality, and affordable price, support its usage as first-line therapy. The dosage of metformin medication should be adjusted to reduce gastrointestinal side effects. Cohort studies and a single modest cardiovascular outcomes trial also point to metformin's cardioprotective effects (Holden SE, 2016).

Similar to sulfonylureas, short-acting insulin secretagogues (repaglinide, nateglinide) increase insulin secretion. However, because of their quicker action, they might encourage insulin secretion more during meals than during other times. They therefore seem to have a lower risk of hypoglycemia and may be particularly

effective at lowering postprandial hyperglycemia. Weight gain is possible, albeit it seems to be less than with sulfonylureas. These medications are unlikely to work for patients who have not responded to previous oral medications (such as sulfonylureas or metformin).

Biguanides

Metformin and other biguanides lower plasma glucose via reducing hepatic glucose synthesis (gluconeogenesis and glycogenolysis). They are regarded as peripheral insulin sensitizers, but the stimulation of peripheral glucose absorption may just be a side effect of their hepatic effects on glucose decreases. In addition to lowering cholesterol levels, biguanides may also reduce nutritional absorption from the gastrointestinal tract, boost beta-cell sensitivity to blood glucose, and lower levels of plasminogen activator inhibitor 1, all of which have an antithrombotic impact. The only biguanide that is commercially accessible in the US is metformin.

It can be used safely with other medications and insulin and is at least as effective as sulfonylureas at lowering blood sugar. It also seldom results in hypoglycemia. Furthermore, metformin does not lead to weight gain and may possibly encourage weight loss through hunger suppression. But the medication frequently produces gastrointestinal side effects (such dyspepsia and diarrhoea), which for most people pass over time. Vitamin B12 malabsorption is a less frequent side effect of metformin, but clinically severe anaemia is uncommon.

Metformin is contraindicated in patients at risk of acidemia even though it seldom contributes to life-threatening lactic acidosis (including those with significant renal insufficiency, hypoxia or severe respiratory disease, alcohol use disorder, other forms of metabolic acidosis, or dehydration). During surgery, the administration of IV contrast, and any significant illness, the medication should be avoided. Many patients on metformin monotherapy eventually need to take another medication.

Thiazolidinediones

Thiazolidinediones (TZDs; pioglitazone, rosiglitazone) are insulin sensitizers that

reduce peripheral insulin resistance, but it is unclear how exactly they work. The medications interact with a nuclear receptor called PPAR-gamma, which is largely found in fat cells and is involved in the transcription of genes that control lipid and glucose metabolism. TZDs can also reduce triglycerides, raise HDL levels, and possibly have anti-inflammatory and anti-atherosclerotic effects. In terms of lowering haemoglobin A1C, TZDs are just as effective as sulfonylureas and metformin. Treatment of nonalcoholic fatty liver disease may benefit from TZDs (NAFLD).

Anti-alpha-glucosidase agents

The intestinal enzymes that hydrolyze dietary carbohydrates are competitively inhibited by alpha-glucosidase inhibitors (acarbose, miglitol); as a result, carbohydrates are digested and absorbed more slowly, decreasing postprandial plasma glucose. Because they may produce dyspepsia, flatulence, and diarrhoea, alpha-glucosidase inhibitors are less successful than other oral medications at lowering plasma glucose, and patients frequently discontinue taking them. However, the medications are generally safe and are compatible with insulin and all other oral medications.

Inhibitors of dipeptidyl peptidase-4

By blocking the enzyme dipeptidyl peptidase-4 (DPP-4), which is involved in the breakdown of endogenous glucagon-like peptide-1 (GLP-1), dipeptidyl peptidase-4 inhibitors (e.g., alogliptin, linagliptin, saxagliptin, sitagliptin) prolong the activity of endogenous GLP-1. The small intestine produces the peptide GLP-1, which promotes insulin production and suppresses glucagon release. By extending its activity, GLP-1 decreases plasma glucose. DPP-4 inhibitors are generally regarded as safe and well-tolerated, but there is a modest increase in the risk for pancreatitis. With DPP-4 inhibitors, the haemoglobin A1C reduction is not significant.

Sodium-glucose co-transporter 2 inhibitors

Canagliflozin, dapagliflozin, and empagliflozin are SGLT2 inhibitors that limit glucose reabsorption in the proximal tubule of the kidney, resulting in glycosuria

and a decrease in plasma glucose. SGLT2 inhibitors may also reduce blood pressure and result in a little amount of weight reduction. Recent research has demonstrated that in people at higher risk for cardiovascular disease, SGLT-2 inhibitors reduce mortality, serious adverse cardiovascular events, and hospitalizations for heart failure. Additionally, it has been demonstrated that SGLT-2 inhibitors can stop the course of chronic kidney disease in those with diabetes, a low glomerular filtration rate, or albuminuria.

Genitourinary infections, particularly mycotic infections, are the most frequent side effects. There can also be symptoms of orthostasis. Patients with type 1 and type 2 diabetes have been linked to SGLT-2 inhibitors for producing diabetic ketoacidosis (DKA), and ketoacidosis can happen at lower blood glucose levels than with other causes of DKA. Canagliflozin has been linked in one significant study to an increase in lower limb amputations.

Dopamine agonist

A dopamine agonist called bromocriptine reduces haemoglobin A1C by roughly 0.5% through an unidentified mechanism. Despite being licenced for type 2 diabetes, it is not frequently used due to possible side effects.

Injectable Antihyperglycemic Drugs

The effects of GLP-1, a peptide produced in the small intestine that boosts glucose-dependent insulin secretion and slows stomach emptying, are mimicked by GLP-1 receptor agonists. Additionally, GLP-1 agonists may decrease hunger, encourage weight loss, and increase beta-cell proliferation. Incretin hormones exenatide, lixisenatide, liraglutide, dulaglutide, albiglutide, and semaglutide are a few examples. There are formulations for twice-daily, once-daily, and weekly administration. GLP-1 agonists frequently cause gastrointestinal side effects, particularly nausea and vomiting. A small increase in the risk of pancreatitis is also brought on by GLP-1 agonists. Because they have been shown to raise the incidence of medullary thyroid carcinoma in tested rodents, they should not be used in people who have a personal or family history of the disease.

Amylin analog

The pancreatic beta-cell hormone amylin, which aids in controlling postprandial glucose levels, is mimicked by the amylin analogue pramlintide. Pramlintide delays stomach emptying, inhibits postprandial glucagon secretion, and increases satiety. It is administered intravenously and combined with insulin for usage during meals. Type 1 diabetic patients receive 30 to 60 mcg subcutaneously before meals, whereas type 2 diabetic patients receive 120 mcg.

Non-Pharmacological treatment

Even though patients with T2DM have a wide range of pharmaceutical therapy choices, non-pharmacological therapies should always be taken into account to change the pathophysiological mechanisms of the disease. In managing T2DM, appropriate dietary changes together with consistent physical activity are crucial since they not only improve glycaemic outcomes but also have positive effects on conditions like dyslipidemia, hypertension, OSA, and cardiovascular illnesses.

Type 2 diabetes mellitus disease load is a major public health concern. Low- and middle-income countries (LMICs) have a greater prevalence and mortality rate from diabetes mellitus than high-income nations. A balanced diet and more physical activity are two crucial and effective ways to delay the onset of diabetes mellitus.

Physical activity

Exercise is a planned, organised, and repetitive physical activity carried out with the aim of enhancing physical fitness. Physical activity is defined as any body movement that increases energy expenditure beyond the baseline. In addition to lowering the risk of cardiovascular morbidity and mortality, physical activity increases insulin sensitivity, body weight, cardiovascular risk factors, physical fitness, cholesterol levels, blood pressure, and general wellness.

Among T2DM patients, physical exercise is strongly correlated with controlled glucose levels. It has been discovered that regular, moderate physical activity is an

efficient strategy to manage diabetes' long-term complications. These activities include going for walks, gardening, and doing regular housework. The best physical activity for those with T2DM is walking because it offers excellent glycemic control with little physical strain for people who are already physically frail (H., 2016).

Changes in sedentary behaviours are another highly justified lifestyle change for T2DM patients. An extremely low amount of energy is expended while one is sedentary. In T2DM patients, prolonged periods of inactivity are linked to uncontrolled glucose levels. Therefore, it's important for diabetics to spend less time sitting down, which can be done by doing more physical activity. Additionally, regular aerobic exercise is known to lower HbA1c levels in diabetic patients (Snowling NJ, 2006).

Through a number of processes, including the numerous rise in mitochondrial densities, higher sensitivity to insulin, improved compliance of blood vessels, and lung functions with increased cardiac output, aerobic exercise tends to improve health outcomes in patients (Garber CE, 2011).

In addition to enhancing glycemic control in T2DM patients, exercise significantly lowers blood pressure and body weight. By lowering total cholesterol and low-density lipoprotein (LDL) cholesterol and raising high-density lipoprotein (HDL) cholesterol, it improves the unfavourable lipid profile. These, in turn, lower the risk of certain cardiovascular events that are common among T2DM patients.

Dietary modifications and Medical Nutrition Therapy

Diabetes, a condition marked by a sustained rise in blood glucose level, is characterised by insufficient insulin secretion and insulin action as two key causes. Vascular problems in type 2 diabetes are greatly influenced by diet and a sedentary lifestyle. Nutritional intake is reprogrammed as a result of dietary alteration, which has been shown to be successful in managing diabetes and its consequences. Dietary changes alter a number of molecular players involved in the regulation of autophagy, the signalling of nutrients, and energy metabolism (Oza M et al, 2021).

High intakes of sweets, fried foods, and red meat are strongly associated with insulin resistance and the subsequent emergence of T2DM. Contrarily, consumption of vegetables strong in antioxidants, fibre, and other nutrients is associated with a decreased risk of developing type 2 diabetes (T2DM) (Abdali D, 2015).

Patients with diabetes who are obese have a different average calorie consumption. Typically, a nonobese diabetic patient should consume 1,500–2,500 calories on average each day, but obese diabetics should consume 800–1,500 calories on average each day. Refined sugar consumption should be kept to a minimum for T2DM patients. In these people, non-nutritive sweeteners like aspartame and saccharine can work well as sugar substitutes. Additionally, it is advised to limit consumption of foods high in saturated fats and cholesterol and to replace them with meals high in polyunsaturated fats. Changes in eating habits, such as spreading meals out over the day in modest portions rather than eating one or two large meals, can also prevent severe postprandial increases in blood glucose levels. (M., 2014). When diabetes patients adopt a Paleolithic diet (a diet high in lean meat, fish, fruits, and vegetables) into their daily routines, their ability to handle glucose improves noticeably (Nicholson AS, 1999).

To enhance glycemic control, lifestyle changes based on exercise to build muscle strength, weight loss in obese individuals, and a diet low in sugar and fat are equally significant in young people. Especially sugar-sweetened beverages should be avoided by senior individuals since they are linked to a higher risk of type 2 diabetes in people with impaired glucose tolerance. Products with added sugar appear to have an impact on body weight, insulin resistance, and the pancreatic beta cells' capacity to counteract it.

Together, small but significant eating pattern modifications among diabetic individuals represent a viable strategy to reduce the long-term effects of diabetes. Additionally, a successful use of nutritional therapy in people with diabetes might be a profitable strategy to obtain better diabetes management with better health outcomes.

Weight management

Dieting and weight loss attempts have grown more popular among the public, but the main issue is retaining the reduced weight. Adults with type 2 diabetes mellitus (T2DM) must lose weight in order to control their diabetes, however it has proven challenging to measure the advantages of weight loss in T2DM patients. T2DM's pathophysiology involves complex interactions across numerous organ systems, each of which has its own hormones and feedback loops. Adiposity raises insulin resistance, which causes T2DM to develop or worsens symptoms. Hence, a variety of therapies (such as food, exercise, drugs, and surgery) can lead to weight loss, each of which may have a different physiological and psychological effect (Stumvoll M et al, 2005).

In a meta-analysis, Franz et al (2015) acknowledged that the majority of lifestyle programmes were unable to lose this much weight, but concluded that 5% weight loss seemed sufficient to have positive impacts on glycemic management. In a study conducted in 2016, comparing two different energy-restriction diets, Carter et al. discovered that a 1% change in body fat was responsible for a 3% change in HbA1c. In a meta-analysis, Gummeson et al. developed a model that claimed that each kilogramme of weight lost typically resulted in a 0.1-point drop in HbA1c, and that this drop was larger in patients with poor baseline glycemic control in 2017.

Role of macronutrients

The Asian Indian diet is likewise heavy in carbohydrates. Due to urbanisation and migration, convenience foods that are processed, refined, and high in fat are becoming more popular, and both AIs living in India and those living abroad are engaging in less physical activity (Misra A et al, 2011).

AIs are very susceptible to insulin resistance (IR), impaired glucose tolerance (IGT), type 2 diabetes (T2DM), and associated aftereffects. The results of the study suggested that those at risk for T2DM may benefit from adhering to a macronutrient distribution of roughly 50:30:20 percent of total kilocalories from carbohydrates, fat, and protein, or from a higher intake of dietary protein, while assuring the quality of those macronutrients. Future research is needed to establish

the association between diet quality and diabetes status (Pandya A et al, 2021).

Health benefits of a Mediterranean diet in diabetes

One of the foundations for the prevention and advancement of many diseases, including diabetes, is diet. Western nations are seeing an epidemic of type 2 diabetes (T2D), which makes people more susceptible to other illnesses including cancer and cardiovascular disease. Diet and lifestyle choices are linked to T2D. The traditional Mediterranean diet has demonstrated health advantages for diabetes and other cardiovascular risk factors.

The MD is essentially a plant-based diet, which is well known for its many health advantages, particularly in the treatment of cancer and cardiovascular illnesses. People who have diabetes benefit from the MD as well.

This eating style, collectively referred to as MD, was adopted in the Mediterranean region's olive-growing areas in the late 1950s and early 1960s (particularly in Greece and Italy). It is used to define the traditional eating style of people who live in nations surrounding the Mediterranean (A., 2001). The MD includes high amounts of olive oil, fruits, nuts, whole grains, vegetables, legumes, chicken, fish, whole-fat dairy products, and red meat, as well as low to moderate amounts of wine.

Cooking with seasonal and local ingredients and interacting with others over meals are characteristics of the traditional Mediterranean diet. It includes a daily abundance of vegetables, a range of minimally processed whole grain bread, other cereals, and legumes as the main sources of protein, nuts and seeds, fresh fruit as the typical daily dessert, and treats made with nuts, olive oil, and honey that are only consumed on special occasions. The main sources of fat are cold-pressed extra-virgin olive oil (EVOO), nuts, and seeds. consuming little to moderate amounts of dairy products (mostly local cheese and yoghurt); moderate amounts of fish, poultry, and eggs; rarely eating red meat (about once a week); and drinking moderate amounts of wine, usually with meals (Tosti V et al, 2018).

The MD is proven to be protective not only in healthy people but also in people with cardiovascular disease and women who have a history of gestational diabetes

(Karamanos B, 2013). MD was observed to significantly lower the incidence of T2DM by 52% in the PREDIMED-Reus nutrition intervention study among non-diabetic adults with high cardiovascular risk (Salas-Salvado J, 2011). MD has been found to help T2DM patients achieve glycaemic control, lessen insulin resistance and cardiovascular risk factors (BMI, blood pressure, cholesterol, inflammatory markers, and adhesion molecules), and improve liver and sexual function. One clinical trial and nine prospective studies were included in the meta-analysis conducted in 2014 by Kolooverou and colleagues. They discovered that among people with a maximum or minimum adherence score on the Mediterranean diet, the risk of T2D was decreased by 23%.

In conclusion, every aspect of the Mediterranean diet—many of which share similar physio-pathological pathways—could be engaged in processes relating to diabetic homeostasis. The Mediterranean diet adherence could play a role on T2D-related mechanisms, such as anti-inflammatory/antioxidant activities, glucagon-like peptide agonist chemicals, and alterations in gut flora. Overall, interactions and synergies between various nutrients and their derived metabolites may strengthen their individual effects, making the Mediterranean diet an essential tool in the primary and secondary prevention of diabetes. It is crucial to stress the significance of this diet within the framework of a healthy lifestyle.

Sustained hyperglycemia brought on by reduced insulin production and/or cell insulin resistance in pancreatic beta-cells is the primary physio-pathological mechanism of type 2 diabetes (T2D) (IR). This indicates either inadequate insulin production, a failure of insulin to deliver glucose to the cells, or both. The result is a dysregulation of protein, lipid, and carbohydrate metabolism, which leads to macro- and microvascular problems (DeFronzo R.A et al 2015).

Sleep and Chronopharmacology

Although maintaining a healthy diet and exercising regularly greatly improves the management of T2DM, these factors cannot be seen as the only factors contributing to the worsening of diabetes occurrences. Another lifestyle habit that can be changed is sleep, which has been shown to have an impact on energy levels and metabolic health. Optimizing sleeping habits is essential for managing

diabetes. According to a population-based study, insomnia or little sleep (less than 5 hours) may raise your chance of developing type 2 diabetes (Vgontzas AN, 2009).

Similar studies have shown that T2DM patients with poor sleep have higher HbA1c levels (>7%) and insulin resistance. Diabetes' onset, progression, and control are all significantly impacted by disturbed circadian rhythms and sleep-wake cycles. Due to chronic sleep deprivation and circadian rhythm disruption, shift workers are more likely to develop metabolic diseases (De Bacquer D, 2009).

In addition, a significant risk of T2DM is linked to a developed inclination for napping as a result of inadequate or poor nocturnal sleep (Xu Q, 2010).

One study found that restoring sleep patterns could significantly reduce the insulin response to a normal meal when sleep and circadian rhythms were experimentally altered. (Buxton OM, 2012).

Study conducted by Arora et al (2015) reported connection of Short sleep with changes in the hormones leptin and ghrelin, which enhance the desire for carbohydrate-rich foods and increase calorie intake. Additionally, lack of sleep causes oxidative stress, orexin (also known as hypocretin) release, stimulation of the sympathetic nervous system, increased cortisol release, and a simultaneous decrease in growth hormone secretion, all of which contribute to significant hyperglycaemia.

Section 2.7 Glycaemic Index and Glycaemic Load

For foods containing carbs, there is a rating system called the glycaemic index (GI). It demonstrates how rapidly each food lowers your blood sugar (glucose) level when consumed alone.

The rate of glucose entry into the circulation, the amount absorbed, the rate of glucose disappearance from the circulation due to tissue uptake, and hepatic control of glucose release all play a role in the normal physiological phenomenon known as the glycemic response (GR), which occurs after eating (Triplitt, 2012).

When a person takes a certain amount of a food that contains a set amount of carbohydrates, the GI provides information about the GR that might be anticipated (usually 50 g). According to this system, GR is characterised as the rise in blood glucose levels that occurs after eating and is measured as the incremental area-under-the-blood-glucose-curve (iAUC) over a two-hour period. Since the GR of the food is expressed as a percentage of the GR of a reference food, the GI value is really supplied as a relative GR (usually a glucose solution or white bread)

$$GI = (iAUC_{\text{test food}} / iAUC_{\text{reference food}}) \times 100$$

The amount of food ingested greatly influences how much GR is produced; for example, if a lot of a food with a low or high GI is consumed, the GR will be high, and if a little bit of a food with a low or high GI is taken, the GR will be low. In order to estimate the GR, the idea of the glycemic load (GL), which considers the GI and the amount of readily available carbohydrate in a serving of food, was developed (Salmerón, 1997).

$$GL = GI \times \text{available carbohydrate in a given amount of food}$$

Foods have been categorised by GI into low (GI 55), medium (GI 56-69), and high (GI 70) categories and by GL into low (GL 10), medium (GL 11–19), and high (GL 20) categories in order to apply the ideas.

Eating a diet limited in carbohydrates has been linked to greater HDL cholesterol levels and, in large cohort studies, a lower risk of developing diabetes and cardiovascular disease. Positive correlations between the food glycemic index and

the incidence of breast and colon cancer have also been shown in case-control studies. Despite data inconsistencies, enough convincing evidence has been accumulated to contend that the food glycemic index may be crucial for the management and prevention of chronic diseases (David JA Jenkins, 2002).

According to the results of the systematic review and meta-analysis, individuals with type 2 diabetes who follow low-GI diets have better control over their HbA1c and fasting blood glucose levels than those who follow higher-GI diets or control diets. The results of the meta-analysis and sensitivity tests have shown significant differences ($p < 0.001$ and $p < 0.001$, respectively) between low-GI diets and higher-GI diets or control diets in relation to glycated haemoglobin, despite the fact that the results of the individual studies were occasionally different with respect to the variables of interest. In addition, after meta-analysis, changes in fasting blood glucose levels between the low-GI diet and the higher-GI diet or control were significant ($p < 0.05$) (Ojo, 2018).

The altered post-prandial metabolism is linked to a cluster of metabolic and cardiovascular risk factors known as the metabolic syndrome. Low-GI foods' advantageous effects on post-meal metabolism may be helpful not only in the treatment but also in the prevention of this illness. The insulin resistance syndrome's clusters of risk variables are recognised contributors to CHD risk. The presence of hyperinsulinemia is a standalone risk factor for CHD. Exercise, weight loss, pharmacological therapies, and other strategies are used to modify insulin sensitivity. As approximately 55% of total energy should come from carbohydrates, it is crucial to find out how much of an impact this will have on insulin sensitivity. There is substantial evidence that low-GI, high-fiber diets influence not only overall insulin sensitivity but also adipose tissue insulin sensitivity in CHD patients and CHD risk individuals (Frost et al. 1998).

Foods' carbohydrate content Eating carbs may raise blood glucose levels, particularly after meals. Thus, a diet high in carbohydrates may be harmful to glycemic control in patients with diabetes, whether they have type 1 or more severe types of type 2. This could lead to microvascular and macrovascular problems.

However, not all foods high in carbohydrates cause hyperglycemia when eaten. Even when ingested in portions containing the same quantity of carbohydrates, different postprandial blood glucose responses to diverse carbohydrate-containing diets have been shown in both healthy and diabetic participants. This suggests that the reported variability in postprandial blood glucose levels following ingestion of the various carbs-containing diets by both healthy and diabetic people could be due to changes in the specific components of carbohydrates (Gabriele R et al., 2008).

Around 70–80% of the total carbohydrates in typical diets come from starch. Starches are divided into three groups for nutritional purposes based on how quickly and thoroughly they digest: rapidly digestible starch (RDS), slowly digested starch (SDS), and resistant starch (RS) (Sajilata, M et al., 2006).

The starch component known as RDS is rapidly absorbed and processed in the duodenum and proximal small intestine, which causes a spike in blood sugar and typically results in a subsequent episode of hypoglycemia. With a low initial glycemia and a subsequent gradual and extended release of glucose, SDS is the starch component that is digested slowly but thoroughly in the small intestine to offer sustained energy availability. Human studies demonstrate that RS can have significant health advantages, including lowered blood glucose levels and better insulin sensitivity in type 2 diabetic individuals (Nurgent AP, 2005).

In the presence of water, starch heated to a temperature of around 50 °C causes the granule's amylose to enlarge, amylopectin's crystalline structure to break down, and the granule to rupture. Starch swells and the surrounding matrix becomes thicker as a result of the polysaccharide chains taking on a random structure. The starch becomes easily digested as a result of the gelatinization process. The starch will become more fluid and have a higher GI as the gelatinization increases; this could also have an impact on the GL.

Controversial findings were produced by a number of research done in the past ten years on the impact of dietary fibre on insulin sensitivity. Pereira et al (2002) assessed insulin sensitivity in 11 obese hyperinsulinaemic patients in a randomised cross-over trial. According to their research, eating whole grains

improved postprandial insulin sensitivity compared to eating refined grains.

Protein-rich diets stimulate the release of more insulin, which lowers postprandial blood glucose levels. Hence, some foods' natural protein content may be the cause of their starches' resistance to hydrolysis, which gives them lower GIs. The case of pasta in cereals and gluten, which block the activity of pancreatic amylases and result in lower GIs, is a typical example.

It has been proven that different methods of food processing have an impact on how easily starch is absorbed, which may have an impact on the GIs of certain foods. Processing methods might influence resistant starch production by affecting the retrogradation and gelatinization processes. For instance, it has been noted that roasted and fried dishes have higher GIs than boiling items (Deepa G et al., 2010).

Food takes longer to exit the stomach and enter the intestine when it is fat. Foods high in fat may have a lower GI than similarly sized diets without fat because they delay the pace at which dietary carbs are processed in the intestine. For instance, the GI of baked potatoes is 85, French fries are 75, and potato chips are 57 (Brand-Miller JC, 2003).

The particles in starchy meals are considerably more easily hydrolyzed by digestive enzymes when they are ground, which raises their GI. For instance, differences in the reported GI of rice are caused by particle size (Urooj A et al., 1999).

One of the important elements linked to a number of diseases, including diabetes, has been identified as diet. The prevention and management of diabetes as a whole, including diet alone, diet with oral hypoglycemic medications, or diet with insulin, all revolve around diet. It has been suggested that the idea of GIs and GL can be a helpful aid in the management of diabetes. This health inference stems from blood glucose levels and diabetics' insulin responses, which are directly related to how quickly carbs are digested.

Section 2.8 Health problems of geriatric population

According to World Health Organization (WHO) report, there was approximately 1 billion old age population in 2019, which can increase up to 1.4 billion by 2030 and 2.1 billion at the end of year 2050. This rise is occurring at unprecedented pace and can accelerate in coming decades especially in developing countries like India. (WHO Factsheet, 2021).

India is the world's second most populous country experienced a dramatic demographic shift in the elderly population (above 60 years of age). In 2011 census, elderly population above age of 65 years found to be 5.3%. Furthermore, majority of population who are now between 65-75 years of age are going to be in age group of above 75 years of age group in a decade (Gambert SR, 2006). As per United Nations Department of Economics and Social Affairs, 91.6 million elderly population reported in India during year 2010 with an annual addition of 2.5 million elderly between 2005 and 2010 (United Nations Department of Economic and Social Affairs, 2008).

Every person in the every country of world should have an opportunity to live a healthy and prosperous life. Ageing is natural process of life characterized by series of physiological, mental and metabolic changes in the body. Ageing process also affects the capacity of cells for its regeneration. The National Commission on Population estimates that India's elderly population share, which was close to 9% in 2011, is expected to increase quickly and reach 18% by 2036. India needs to start preparing and providing for the elderly now if it wants to guarantee them a good quality of life in the near future. Worldwide, the life expectancy of old age people has increased due to improved health facilities and easy accessibility of health care services. Therefore, Indian elderly are likely to suffer more from chronic illness compare to acute illness. There is a rise in occurrence of Non-communicable diseases. Heredity, unhealthy diets, physical inactivity, smoking influences the quality of life.

Elderly people may suffer from physical and mental health problems due to impaired physical and mental functions. Poor cultural, economical, educational and health conditions can results in poor quality of life. Type 2 diabetes mellitus,

high blood pressure, cardiovascular disorders, cerebrovascular diseases, osteoporosis are the most common health problems among elderly people.

The elderly population is more susceptible to the health ailment diabetes. One-half of older adults have prediabetes, and more than one-quarter of people over 65 have diabetes. The proportion of older adults living with these illnesses is predicted to rise sharply in the future decades (National Diabetes Statistics Report, 2020).

The care of diabetes in older persons necessitates routine evaluations in the medical, psychological, functional, and social realms. In comparison to older persons without diabetes, those with diabetes have increased rates of early death, functional disability, rapid muscle atrophy, and concomitant diseases such as hypertension, coronary heart disease, and stroke. Although the findings of screening tests may have an impact on targets and therapeutic methods, screening for diabetic complications in older individuals should be tailored to each individual and repeated on a regular basis.

Although controlling hyperglycaemia in older diabetic patients may be crucial, therapeutic attention on comprehensive cardiovascular risk factor management is more likely to lead to higher decreases in morbidity and death. Strong evidence from clinical trials supports the efficacy of treating hypertension in older persons, with the majority of cases indicating that hypertension should be treated to customised target values. The benefits of these therapies for primary and secondary prevention are expected to apply to older persons whose life expectancies are equal to or greater than the time periods of the clinical trials. Nevertheless, there is less evidence to support lipid-lowering therapy and aspirin therapy (Gencer B et al, 2020).

An ideal preventive health programme should incorporate a variety of elements, such as education about illness conditions and methods for preventing and managing them, a healthy diet and regular exercise. Additionally, meditation, prayer, and motivational techniques should be used to foster a good outlook and a sense of wellbeing.

To create a personalised care plan, the requirements of older persons with

diabetes and their care takers should be assessed. The quality of life of these individuals may be compromised by impaired social functioning, which also raises the possibility of functional reliance. The patient's living condition must be taken into account because it may have an impact on diabetes management and support requirements. The COVID-19 pandemic has drastically changed the quality of life of all the age groups. Generally, older adults experiences more of anger, loneliness, anxiety, excessive worry and loneliness. Therefore, it is easy to conclude that old age population may experience negative outcomes of COVID-19 pandemic. One of the study conducted among old age population to assess the effect of CoVID-19 pandemic reported psychological symptoms, sleep disturbances and physical deterioration. Apart from that decreased social life was observed during COVID-19 pandemic associated with increased depression and reduced quality of life (Audrey Lebrasseur, 2021).

Due to a sedentary lifestyle and less physical exercise, older adults who originate from middle-class and upper-class families are more likely to acquire obesity and its associated consequences. In a survey of 206 old patients at a Delhi tertiary care hospital's geriatric clinic, roughly 34 percent of males and 40.3% of women were found to be fat (Singh P et al 2014).

In conclusion, a number of issues affecting the elderly in India have emerged as a result of current demographic trends, fast urbanization, and lifestyle changes. A comprehensive strategy and coordinated efforts from the health and health-related sectors are required to improve the quality of life for the aged.

Section 2.9 Diabetes among geriatric population

Elderly diabetics carry a heavy health burden. The resulting difficulties make matters more difficult. Life duration and quality of life are negatively impacted. The Medicare system is dealing with increased workload.

India is sometimes referred to as the "diabetes capital" of the world, and the impact has been disproportionately felt in metropolitan areas. Now, a new study has demonstrated how much — 26.1% of urban respondents 60 years of age or older have been given a diagnosis of excessive blood sugar levels (LASI report, 2021).

Diabetes mellitus is no longer disease but now it has become the global problem, a major epidemic of the 20th century. Higher proportions of old age populations are affecting due to diabetes mellitus. This tremendous rise may due to the increased life expectancy, rapid urbanization, physical inactivity, modern lifestyle and obesity. Diabetes mellitus has affected all over the world, around 50 million people in the world are suffering from diabetes mellitus and out of that, 50% population is from developing countries. Prevalence of diabetes increases with age. In India, 20% of old age population is suffering from diabetes mellitus while 25% of old age population is suffering from impaired glucose tolerance (IGT) (Harris MI, 1987).

Together with hypertension, type 2 diabetes mellitus (T2DM) is the illness that most severely affects the aged population. The quality of life for the elderly and the cost of healthcare for society are both severely impacted by diabetes and its consequences. Diabetes makes older persons more susceptible to cardiovascular death. Diabetes management in the elderly calls for particular consideration and care. According to the most recent surveillance data, depending on the diagnostic criteria employed, the prevalence of diabetes among U.S. persons aged 65 years ranges from 22 to 33% (A consensus report, 2012).

Older diabetics experience co-morbidities and DM problems more frequently than their younger counterparts. Cardiovascular problems brought on by ageing and precocious atherosclerosis unique to DM are the most common, while cognitive

and visual deficits, particularly Alzheimer disease and other forms of dementia, are the most distressing. Insulin resistance brought on by inactivity and food problems appears to be a risk factor for both DM and Alzheimer disease. Barriers to care for DM therapy include depression, memory issues, and physical and visual impairments (Chentli et al., 2015).

Sarcopenia, often known as the universal and involuntary loss of skeletal muscle mass, is linked to ageing. This causes a loss of muscle strength and eventually makes it difficult for the elderly person to do daily duties. One of the main ways that insulin works is by making it easier for the muscle to absorb glucose. Lean tissue mass that is less metabolically active, less lean body mass, and decreased physical activity all result from a decrease in lean body mass (Kesavadev JD et al., 2002).

Due to vitamin and/or gonadal deficiency, elderly persons typically suffer severe osteoporosis. Bone demineralization is also a result of inadequate nutrition brought on by loneliness, depression, dental issues, and/or socioeconomic issues. One of the most prevalent deficits among the elderly is a lack of vitamin D. Via insulin resistance and insulin insufficiency, it encourages diabetes. Additionally, it puts them at risk for additional carcinogenic, cardiovascular, and metabolic illnesses. Additionally, proximal muscle weakness, falls, and fractures are all strongly correlated with vitamin D insufficiency. Low vitamin D levels are particularly dangerous for the elderly. Due to decreased outdoor activity and a less diversified diet with reduced natural Vitamin D content, solar exposure is typically restricted (Hosseini-nezhad A et al., 2013).

According to American Diabetic Association (ADA), 34.2 million Americans around 10.5% population had diabetes in 2018. Moreover, 14.3 million American seniors above age of 65 years were reported in America.

According to one of the study conducted in 2017, 178 had diabetes out of 580 subjects, which indicates around 30.42% prevalence of diabetes among 65 years and above age group of NEERI hospital of Nagpur city. 80% of diabetic population were also suffering from hypertension and 64% of subjects were obese irrespective of gender (Beckett N et al, 2008).

Although controlling hyperglycemia in older diabetic patients may be crucial, therapeutic attention on comprehensive cardiovascular risk factor management is more likely to lead to higher decreases in morbidity and death. Clinical trials have produced compelling evidence supporting the benefits of treating hypertension in older persons.

The management of a senior's lifestyle should take into account their level of fragility. Diabetes is linked to decreased muscle mass, poor muscle quality, and rapid muscle mass loss in the ageing population, which may cause sarcopenia and/or osteopenia (Park SW et al, 2006). Additionally acknowledged as a separate risk factor for frailty is diabetes. Due to physiologic vulnerability, functional or psychological stressors, and an increased risk of poor health outcomes, frailty is characterised by a reduction in physical performance. Inadequate dietary consumption, especially insufficient protein intake, can increase an older person's chance of developing sarcopenia and frailty. In order to manage frailty in people with diabetes, they must consume enough protein and follow an activity regimen that combines resistance, weight-bearing, and aerobic exercises.

Section 2.10 Quality of life of diabetic population

The chronic metabolic disease type 2 diabetes mellitus (T2DM) has a significant negative influence on several aspects of quality of life (QoL), including social, physical, and mental health.

Every diabetic patient's life is different, and the many regulations the disease forces them to abide by leave them feeling psychologically overburdened. Since each person has a unique perspective of their physical, emotional, and social well-being that includes both a cognitive element of satisfaction and an emotional element of happiness, it is crucial to evaluate the quality of life (QoL) of patients. Many factors related to both short-term and long-term diabetes management can either negatively or positively impact quality of life. The most significant aspects that have an impact on the patient's quality of life are the microvascular and macrovascular problems and the extended duration of the illness caused by the condition.

It has already been established that psychological health is a reliable indicator of general welfare, including physical health and QOL. The psychological state can be used to direct treatments for enhancing QOL in senior diabetic patients as well as strategies for sustaining health-promoting habits, according to a study by Nedeljkovic et al. during 2011. In a study by Gomez et al (2019), depression was identified as a crucial factor in reducing the QOL of diabetes patients.

Body mass index (BMI) and sociodemographic characteristics like age, gender, marital status, income level, and level of education, as well as adherence to a rigorously prescribed diet and exercise plan, might have a substantial positive or negative link (Timar, 2016).

One of the study conducted in India stated that patients who got less extensive therapy with OHA monotherapy or a combination of one or more OHA, T2DM patients who received more intensive therapy with insulin or insulin combined with OHA had more deteriorated QoL across the majority of the domains (John, 2019).

Despite advances in medical science and the emergence of specialised trends in

geriatrics, it has been demonstrated that many parts of the elderly's personalities and psychological challenges remain unknown, and many of their psychological and physical problems remain neglected. It has not been thoroughly studied how to predict the QOL of senior diabetic patients, especially in underdeveloped nations.

Diabetes distress is an unfavourable emotion associated with diabetes management that can impair diabetes self-care and management.

Distress associated with having diabetes (DRD), also known as diabetes-specific distress, is the emotional reaction to having the disease, the stress of having to manage it constantly, and its long-term effects. It is linked to lower levels of general emotional health and self-care. Type of diabetes, insulin therapy, social repercussions, dietary restrictions, and obesity can all affect it differently. Mild diabetic anxiety can become severe diabetes anxiety and/or depression if left untreated.

Additionally, it can result in detrimental medical and psychological outcomes, such as decreased physical activity, poorer dietary choices, failing to take prescribed medications, less frequent blood glucose self-monitoring, an elevated HbA1c, more frequent severe hypoglycemia, and a lower quality of life.

Study conducted by Almeida et al., in 2016 demonstrated impact of long-term on the patient's quality of life. The correlation between diabetes and depression is "J-shaped," meaning that the longer the duration of diabetes, the higher the risk for depression with an odds ratio of 1.92. This is true even if the cause-and-effect relationship between diabetes and depression is not well understood.

According to a study conducted during 2016 by Nanayakkara N et al., stated that it is crucial to give patients—especially the elderly—social support so they can improve their quality of life and self-care skills. These patients need additional assurance in addition to being at a higher risk for discomfort, especially when they must adhere to stringent food guidelines, remember medications, or even take care of themselves. Diabetes burnout may be correlated with disengagement from self-care activities (such as skipping insulin doses/tablets or failing to monitor blood glucose), unhealthy or uncontrolled eating, risk-taking behaviours, nonattendance

at clinic consultations, or lengthy gaps between clinic appointments.

The primary variables influencing diabetic distress in young individuals with type 2 diabetes were gender, age, occupation, smoking, and complications. Self-management, ageing, smoking, and diabetes complications were among them, and they were responsible for 35.42% of the overall variation in diabetes discomfort. Study's findings are crucial in determining the best targeted treatments for reducing diabetes discomfort and enhancing patients' quality of life (Yanfen Hu et al., 2020).

Section 2.11 Functional foods

Public and consumers are becoming more health conscious nowadays and looking for a new ways to stay healthy. This awareness has grown the field of Functional foods and its researches for the prevention of health and various disease conditions.

Functional foods are the foods, which have additional health benefits beyond its normal functions and nutrition. Functional foods can be whole, fortified, enriched or enhanced, which provide health benefits beyond the provision of essential nutrients.

The International Life Sciences Institute defines them as “Foods that, by virtue of the presence of physiologically-active components, provide a health benefit beyond basic nutrition”.

The tenet, “Let food be thy medicine and medicine be thy food” was embraced 2500 years ago by Hippocrates, The father of medicine. However, this “Food as medicine” philosophy fell into relative obscurity in the 19th century with the advent of modern drug therapy. In the 1900s, the important role of diet in disease prevention and health promotion came to the forefront once again (Clare M, 2002).

Functional foods have no specific definition, which is accepted universally. The concept of functional food was first discovered in the Japan in 1980s when they were facing escalating health care costs, The Ministry of Health and Welfare initiated a regulatory system to approve certain foods with documented health benefits in hopes of improving the health of the nation's aging population (S, 1996).

Table 2.11.1 Definitions of Functional food by different organizations

Organization	Definition
Academy of Nutrition and Dietetics	Foods defined as whole foods along with fortified, enriched, or enhanced foods that have a potentially beneficial effect on health when consumed as part of a varied diet on a regular basis at effective levels.”
International Food Information Council	“Foods or dietary components that may provide a health benefit beyond basic nutrition and may play a role in reducing or minimizing the risk of certain diseases and other health conditions.”
Institute of Food Technologists	“Foods and food components that provide a health benefit beyond basic nutrition (for the intended population”.
European Commission	“A food that beneficially affects one or more target functions in the body, beyond adequate nutritional effects, in a way that is relevant to either an improved state of health and well-being and/or reduction of risk of disease. It is part of a normal food pattern. It is not a pill, a capsule or any form of dietary supplement”
Health Canada	“A functional food is similar in appearance to, or may be, a conventional food, is consumed as part of a usual diet, and is demonstrated to have physiological benefits and/ or reduce the risk of chronic disease beyond basic nutritional functions
Japanese Ministry of Health, Labour, and Welfare	FOSHU [food for specified health uses] refers to “foods containing ingredient with functions for health and officially approved to claim its physiological effects on the human body. FOSHU is intended to be consumed for the maintenance / promotion of health or special health uses by people who wish to control health conditions, including blood pressure or blood cholesterol.”

(Kristi M.Crowe, 2013)

There are many plant foods or physiological ingredient of foods which have been studied so far for its functional properties. Today market is flooded with variety of functional foods. Most of the functional foods are available in the form of leaves, seeds, bark, flowers, etc. major companies are interested in developing functional

food products in health and wellness market. This market will continue growing for decades and decades due to interest in self-care, health and for the prevention of diseases.

Academic, private research institutes and industries around the globe to identify how functional food ingredient might help to prevent chronic disease by reducing health care cost and for the improvement of quality of life of many consumers.

Functional foods when consume as a part of balance diet, proposed as a possible alternative method of weight management and obesity prevention also helps to improve metabolic consequences like increased blood glucose and lipid levels (Konstantinidi & Koutelidakis, 2019).

Today consumers are demanding foods, which are produced sustainably, fresh, natural and safe for the consumption.

Functional foods contains biologically active components and its regular consumption is associated with certain health benefits to prevent and manage several Non-communicable diseases such as Type 2 diabetes mellitus, Blood pressure, Hyperlipidaemia, etc. Functional foods contains nutraceuticals, polyphenols, terpenoids, flavonoids, alkaloids, sterols, pigments, and unsaturated fatty acids, which have the protective role in management of Non-communicable diseases (Alkhatib A, 2017).

Type 2 diabetes mellitus is a metabolic disorder, which results into hyperglycaemia, insulin resistance, destruction of beta cells of the pancreas. It can also results into oxidative stress and various sub-clinical inflammations.

Type 2 diabetes is a complicated metabolic disorder having various types of complications. Several animal and human trails supported that use of functional foods, nutraceuticals can significantly reduce hyperglycaemia, and adipose tissue metabolism modulate carbohydrate and lipid metabolism. It may also help to reduce dyslipidaemia, insulin resistance and can prevent long-term complications of diabetes such as retinopathy, Cardiac problems, nephropathy and neuropathy (Mirmiran P., 2014)

Prevalence of Diabetes is increasing day by day around the globe and causing significant increase in morbidity profile, mortality rate and other complications of diabetes. There is an important role of several lifestyle modifications such as healthy diets, physical exercise and use of specific foods having functional properties. Use of such foods makes it important to investigate the role of functional foods in the treatment of diabetes mellitus.

Several studies has shown that regular consumption of such functional foods can be considered as functional in terms of glycaemic control, regulation of blood pressure, activation of antioxidant enzymes, gut microbiota and also helps to suppress over production of several inflammatory markers and cytokine.

Section 2.12 Role of functional foods in Diabetes

Non-communicable illnesses are a significant public health and socioeconomic issue in developing nations. They represent the main obstacle to growth in the twenty-first century. According to World Health Organization (WHO) fact sheets, lifestyle diseases such as cardiovascular diseases, diabetes, obesity, cancer, osteoporosis, respiratory diseases, and gastro-intestinal diseases cause 56.5 million deaths yearly and account for 59 percent of the worldwide burden of disease.

The understanding of how nutrition affects health and wellbeing has greatly increased over the past several decades and is frequently linked to certain food components. Interest in healthy eating among consumers is now more focused on the potential health advantages of particular meals and food components. Furthermore, scientific data supports the notion that some of these might benefit our health and wellbeing in addition to meeting our nutritional needs.

Concept of healing with medicinal plant is an old one. People are going back to use non-pharmacological treatments for the disease control. The oldest evidence on use of herbal plant for therapeutic purpose was found near Nagpur around 5000 years old. It was based on 12 recipes for drug preparation by using around 250 various plants. Out of that, some of them were alkaloids such as henbane, poppy and mandrake (K, 2009).

Emperor Shen Nung circa 2500 BC has mentioned the use of dry medicinal plants for therapeutic purpose such as camphor, ginseng, jimson weed, Rhei rhizoma and cinnamon bark in his Chinese book on roots and grasses “Pen T’Sao” (C, 2006).

Vedas, The Indian holy book also mentioned about use of plant for treatment. Numerous plants and spices are most commonly used even today such as nutmeg, pepper and clove.

The Ebers Papyrus has mentioned the use of around 700 plants species and drugs for therapy such as pomegranate, Senna, garlic, fig, coriander, juniper, aloe and castor oil plant in his book circa 1550 BC (L, 1954).

According to the Holy book Bible and Jewish book the Talmud, there is a use of aromatic plants during myrtle and incense (Z., 1999).

Medicinal properties can be derived from many parts of the plants such as bulbs, flowers, fruits, seeds, bark, roots, essential oils, gums, leaves, tuber, rhizome and wood.

Table 2.12.1. Different parts of plant having anti-diabetic activity

Part of the plant	Name of the plant
Aerial parts	Artemisia pallens, Bidens pilosa, Bixa orellana, Teramnus labialis
Bark	Cinnamomum zeylanicum, Croton cajucara
Bulb	Allium cepa, Allium sativum
Flower	Cassia auriculata, Gentiana olivier, Musa sapientum
Fruit	Carum carvi, Coriandrum sativum, Embellica officinalis, Juniperus communis, Momordica charantia, Xanthium strumarium
Leaves	Aloe barbadensis, Annona squamosa, Averrhoa bilimbi, Azadirachta indica, Beta vulgaris, Camellia sinensis, Cassia alata, Eclipta alba, Eucalyptus globulus, Euphrasia officinale, Ficus carica, Gymnema sylvestre, Gynura procumbens, Ipomoea aquatica, Mangifera indica, Myrtus communis, Memecylon umbellatum, Morus indica, Ocimum sanctum
Rhizome	Nelumbo nucifera
Roots	Clausena anisata, Glycerrhiza glabra,

	Helicteres isora, Pandanus odoratus
Seed	Acacia arabica, Agrimony eupatoria, Lupinus albus, Luffa aegyptiaca, Lepidium sativum, Mucuna pruriens, Punica granatum
Stem	Amaranthus spinosus, Coccinidium fenestratum
Tubers	Ipomoea batata
Whole plant	Abies pindrow, Achyranthus aspera, Ajauga iva, Aloe vera, Anacardium occidentale, Andrographis paniculata, Capsicum frutescens, Cryptolepis sanguinolenta, Enicostemma littorale, Ficus religiosa

(Bhushan MS, 2010)

Among the different parts from plant, seeds of many plants are used for medicinal purposes. Seeds can be used as medicinal drugs in various forms such as raw, roasted, paste, powder, infusion, oil extracted from seeds, isolates or decoctions. Seeds can find inside the fruit or sometime used by their own.

In a botanical sense, a nut is actually considered as a fruit having hard shell and seed. Many times these seeds are referred as nuts in culinary use. Nuts and seeds are rich in energy, vitamins and minerals. Most of the nuts and seeds are great source of healthy fats including omega 3 fatty acids. They also contains vegetable protein, fibre and relatively low in carbohydrates (low glycaemic index). Nuts and seeds are best source of magnesium, which is important for the regulation of blood glucose levels. Presence of phytonutrients like flavonoids and phytosterols in seeds exhibit antioxidant properties. When seeds consumed in moderation, it acts beneficial for the prevention and management of diabetes.

Nuts and seeds are a very good alternative to more common processed snack foods like potato chips, crackers and cookies, and can be a useful snack food for diabetics.

Section 2.13 Role of Various seeds in Diabetes Management

Chia seeds (*Salvia hispanica*)

Some of the researches indicates that chia seeds are having beneficial effects on lipid profile, high blood pressure, diabetes and inflammation due to its high fibre, amino acids and fatty acid profile. Several studies provided evidences for antioxidants activities as well. Some of the researches shown that chia seeds exhibit the capacity to scavenge the free DPPH radicals and can neutralize over 70%. Supplementation of 40gm chia seeds per day for 12 week has significantly reduced systolic blood pressure compared to control group among type 2 diabetic subjects (Eman Zaid Marzouq Alwosais, 2021).

Figure 2.13.1 Chia seeds



Nigella sativa seeds

These seeds are belongs from Family Ranunculaceae. It is very popular in various traditional therapies like Unani, Tibb, Ayurveda and siddha. It has been widely used as antihypertensive, diuretics, digestive, anti-diahoreal, appetite stimulant, analgesics, anti-bacterial and to treat skin disorders. The therapeutic properties of this plant are due to the presence of thymoquinone, which is major bioactive component of the essential oil (Aftab Ahmad, 2013). One of the study conducted in 2010 revealed that a dose of 2 gm/ day of Nigella sativa might be a beneficial adjuvant to oral hypoglycaemic agents in type 2 diabetic patients (Abdullah O Bamosa, 2010).

Figure 2.13.2 Niger seeds



Fenugreek seeds (*Trigonella foenum-graecum*)

Fenugreek seeds are known to have antioxidant, hypoglycemic and nephroprotective effects and acts as a stabilizer especially due to its novel furostanolic saponins content. Fenugreek seeds has shown 63% reduction in fasting plasma glucose levels after the intervention period of 90 days (Narsingh Verma, 2016). One of the study conducted by Nazila Kassaian et al revealed that supplementation of fenugreek seed powder along with hot water for 10gm per day has shown 25%, 30% and 30.6% reduction in FBS, TG and VLDL levels among type 2 diabetic subjects (Nazila Kassaian, 2009).

Furthermore, supplementation of powdered fenugreek seed around (15gm) was soaked in water and given which have shown significant reduction in postprandial glucose levels and plasma insulin level (Madar, Abel, Samish, & J Arad, 1988).

Figure 2.13.3 Fenugreek seeds



Garden cress seeds (*Lepidium sativum*)

Garden cress seeds belongs to Brassicaceae family and its scientific name is *Lepidium sativum*. It has been extensively used to cure many health problems

such as kidney problems, hypertension, diabetes and prevention of cancer. Presence of alkaloids in garden cress seeds found effective in the treatment of diabetes. Significant reduction in fasting blood glucose levels, lipid profile, total cholesterol, LDL cholesterol was observed among alloxan induced diabetic and hyperlipidemic male Wistar rats (Dave, 2018).

Figure 2.13.4 Garden Cress seeds



Sunflower seeds (*Helianthus annuus*)

Sunflower plant belonging to the family of Asteraceae of the genus, *Helianthus*. The botanical name of the sunflower seeds is *Helianthus annuus*. Crunchy, nutty and delicious sunflower seeds are appraised as a healthy food due to an incredible source of calories, minerals, vitamins and essential fatty acids. Sunflower seeds are having good fatty acid profile. Several researches proven that sunflower seeds may play an important role to improve the lipid profile and to prevent cardiovascular disorders. Supplementation of 2gm of sunflower seeds for 6 months showed a positive and a faster decrease in FBS level from 186.2 mg/dl to 109.9 mg/dl among type 2 diabetes patients of Punjab. Further it have also improved the HDL cholesterol levels to improve heart health (B & P, 2016).

Figure 2.13.5 Sunflower seeds



Flax seeds

Flax seeds are one of the most versatile seeds we know. Flax seeds have gain popularity due to its health benefits. Flax seeds are rich in omega 3 fatty acids and lignin. Being rich source of antioxidants, fibre content and fatty acid profile making it as an effective intervention for diabetes. Presence of dietary phytoestrogens (isoflavones and lignans) reduces risk of chronic diseases such as diabetes by affecting the regulation of inflammatory pathways (Bhathena SJ, 2002).

One of the study conducted in 2016 have no significant reduction in FSG, insulin concentration, HOMA-IR, beta-cell function, and IS but have significantly reduced blood pressure after the 12-week supplementation of 20 g or 40 g flaxseed powder among pre-diabetic patients (Afrooz Javidi, 2016). Another study published in a year 2013 shown to have an impact on fasting blood glucose in prediabetes individuals but not effective in long-term blood glucose control (Hutchins AM, 2013). However one of the study conducted by U V Mani et al evaluated effect of flax seeds on diabetes where 10gm of flax seeds powder shown reduction in fasting blood glucose by 19.7% and glycated haemoglobin by 15.6% which suggests the therapeutic potential of flax seeds in diabetes management (Uliyar Vitaldas Mani, 2011).

Figure 2.13.6 Flax seeds



Section 2.14 Pumpkin and pumpkin seeds

Classification of pumpkin includes;

Family: Cucurbitaceae

Botanical Name: Cucurbita (Pumpkin)

Cucurbita-Moschata (Pumpkin seeds)

Kingdom: Plantae

Order: Cucurbitales

Family: Cucurbitaceae

Genus: Cucurbita

Colour: Light yellow-orange to bright orange

Best Season: Throughout the year

Figure 2.14.1 Pumpkin



Table 2.14.1 Names of the pumpkin in different languages

Pumpkin	English
Kohlu	Gujarati
Kaddu	Hindi
Lal bhopla	Marathi
Kumbra	Bengali
Kumbala	Kannada
Paarimal	Kashmiri
Mathan or Chakkara kumbalanga	Malayalam
Kakharu	Oriya
Sitaphal	Punjabi
Purangikka i or Pooshanikai	Tamil
Gummadi kayi	Telugu
Dangaree	Sanskrit

(Venkaiah, 2017)

An abundant source of nutrients and a well-known multipurpose food, pumpkin has recently given scientists fresh insights. Primary and secondary metabolites, such as proteins, carbohydrates, monounsaturated fatty acids, polyunsaturated fatty acids, carotenoids, tocopherols, tryptophan, delta-7-sterols, and numerous other phytochemicals, are abundant in the pumpkin fruit, including the flesh, seed, and peel (Maria B et al, 2022). Pumpkin belongs to the family of “Cucurbitaceae”, consumed traditionally in different forms such as cooked vegetable, frozen or sometime it can be canned. All over the world, pumpkin has grown for the purpose of either as vegetable consumption or for its medicinal properties. They are mostly grown in tropical and sub-tropical regions including squash and cucumbers. Worldwide there are three types of pumpkins namely “Cucurbita pepo”, “Cucurbita maxima” and “Cucurbita moschata” (Lee YK, 2003). Cucurbitaceae family consists of 80 genera and almost 800 species (Giampan, 2007).

Pumpkin has been conventionally used in most of the countries such as China, India, Argentina, Pakistan, Yugoslavia, America and Brazil. Pumpkins are also used in Halloween festivals and as thanksgiving feast in most of the parts of USA.

According to few reports available, pumpkin flour used extensively as supplement in the form of cereal flour, bakery products, soups, noodles and sauces. Pumpkin can be consumed by using different cooking methods such as boiling, steaming, roasting and baking.

Pumpkin seeds

In recent time, seeds and nuts of plants got tremendous attention due to its various health benefits. Among different seeds, pumpkin seeds are the seeds belongs to “Cucurbitaceae” family. Pumpkin seeds are versatile and most of the plants of pumpkin can be consumed like seeds, leaves, flowers and even fleshy shell.

Figure 2.14.2 Pumpkin seeds



A rising amount of attention has been paid to seeds and nuts in recent years because of the high nutraceutical and therapeutic potential of their bioactive components. The same is true for pumpkin seeds. The Cucurbitaceae family includes pumpkins with oily seeds. Although most people think of pumpkin seeds as agricultural waste, they are actually nutrient powerhouses with intriguing nutraceutical qualities. Pumpkin seed consumption has grown. After being roasted and salted, seeds are eaten as snacks straight away. Additionally, they are utilised as food additives in the baking sector.

Pumpkin seeds are thrown out by most of the industries, as agricultural waste. Pumpkin seeds are commonly known as “pepitas”. They look flat and mostly encased in yellowish white cover of husk. Pumpkin seeds are nutritionally adequate seeds. Pumpkin seeds are loaded with variety of nutrients and particularly they are rich in Proteins, Vitamins and Minerals. Pumpkin seeds can be consumed as snacks in roasted or unroasted form. Fried and salted Pumpkin seeds are also available in the market and sell as “Pepitos”.

Although tiny, pumpkin seeds are incredibly rich in beneficial nutrients and

nutraceuticals, including amino acids, phytosterols, unsaturated fatty acids, phenolic compounds, tocopherols, cucurbitacins, and priceless minerals. These bioactive substances are all necessary for a healthy life and overall wellbeing.

Section 2.15 Nutritional Composition of Pumpkin seeds

Pumpkin seeds are rich in fatty acids such as linoleic, oleic, palmitic and steric which covers more than 95% of total fatty acids and most of fatty acids are unsaturated. Unsaturated fatty acid profile has been studied extensively due to the protective effects against cardiovascular disorders. They are also having important role in healthy growth and development of brain tissues and nervous system. They are reported to have beneficial role in reducing inflammation, amelioration of blood pressure, arthritis, cancer and heart diseases. Alpha linoleic and linoleic fatty acids are not synthesized by the human body so important to be supplied from the diet (J. Plat, 2019).

Pumpkin seeds contains 35% of crude protein and having significant role in health due to composition of amino acids. Amino acids are building proteins and plays very important role in the physiological functions of the body. Studies reveled that protein isolates of pumpkin seeds resemble with soybean due to its high bioavailability of amino acids (L. Rezig, 2013).

Pumpkin seeds are rich in different vitamins and minerals. They are low in sodium while they are rich in potassium, calcium, manganese, phosphorus, magnesium and contains few trace elements such as zinc, copper and iron. Out of these, few minerals possess antioxidant activities and acts as cofactors during anti-oxidation process. Presence of low sodium and high potassium in pumpkin seeds can also implicate for the management of pumpkin seeds and cardiovascular diseases by using pumpkin seeds (J. Dotto, 2019). Zinc is an important mineral for the male reproductive health, as structural protein and for cellular growth, which present in huge amount in a pumpkin seeds.

The pumpkin seed oil contains a good amount of phenolic compounds, which are attracting researchers due to their promising health effects to humans. Phenolic compounds are synthesized as secondary metabolic products in plants. Presence of

hydroxyl function group having radical scavenging activity making it more suitable for reducing risk of oxidation induced degenerative diseases (E.I. Fawzy, 2018). Various studies found that tyrosol; vanillin, caffeic, ferulic and vanillic acids are present dominantly in pumpkin seeds. Small amounts of protocatechuic, luteolin, syringic and trans-p-coumaric acids. Anti-oxidizing potential could be compromised sometimes because phenolics are susceptible to metabolic transformations to form complexes. Sometime, these complexes are less effective due to blocking of the phenolic hydroxyl groups responsible for its anti-oxidizing role (D. Pericin, 2009).

Pumpkin seeds are also rich in Vitamin E. it includes the presence of four tocopherols and tocotrienol isomers (α , β , γ , and δ). Pumpkin seeds are rich in γ – tocopherol and contains small amounts of α -tocotrienol, β - and γ –tocotrienols. Tocotrienols and tocopherols are two powerful antioxidants having ability to deactivate highly active free radicals by releasing H^+ ions from its ring (S.K. Bharti, 2013).

Despite the significant advancements in pumpkin seed research over the years, there were little studies on their usefulness in animal models, mechanisms of action, and safety profile. To close the information gap on the safety of pumpkin seeds as a functional food ingredient, more research is required.

Section 2.16 Health benefits of pumpkin seeds

Supplementation of pumpkin seeds, pumpkin seeds isolates, pumpkin seed flour, pumpkin seed oil have proven its different medicinal properties by using animal models. Presence of proteins, Vitamins, Minerals, trace elements and phytonutrients are responsible for its protective effect in cancer prevention, management of NCDs like blood pressure, diabetes and cardiovascular diseases and to improve mental health.

Based on available literature, health benefits of pumpkin seeds are summarized below:

Anticarcinogenic effect

Cancer is one of the major health concern threatening people around the globe. Cancer results due to the abnormal cell growth and cell division in the body. Imbalance between free radicals and antioxidant defense results into progression of cancer. Cancers can be treated by different methods such as chemotherapy, organ removal, radiation therapy and use of immunosuppressant. All the list methods have side effects to the body and therefore there is a strong interest to use plant-based therapy for the prevention and treatment of cancer.

One of the study conducted on wistar rats found that supplementation of ethanolic pumpkin seed extract in 1,2- dimethyl hydrazine have positive effects to cure colon cancer among rats. Furthermore, study described that the extract is cytotoxic in nature which is effective in the treatment of cancer (K.Y. Chari, 2018). Study conducted by B. Jayaprakasam (2003) reported anti-proliferative activity of pumpkin seeds to treat colon, breast and lung cancers.

Supplementation of pumpkin seed isolate shown dose dependent inhibitory effect against the prostate cancer (Shuai Ren, 2012). Some researchers believe that presence of anti-cancer properties in pumpkin seeds are due to flavonoids and cucurbitacin concentrations.

Anti-diabetic effects

Diabetes is one of the serious non-communicable disease growing worldwide

characterized by elevated blood glucose levels due to the failure of cells to utilize glucose effectively. It increases social and economical issues at family and national level. Diabetes can be controlled by regular physical exercise, appropriate diet, restriction of smoking and by consuming different seeds.

Supplementation of pumpkin seed oil among mild and severe diabetic wistar rats significantly lowered the blood glucose levels by 26.15% and 39.33% respectively due to stimulating action of insulin release from beta cells of the pancreas (Kumari Srivastava, 2017).

Mixture of flax seeds and pumpkin seeds shown reduction in plasma and kidney malondialdehyde level, which possessed hypoglycaemic and antioxidant activities among alloxan-induced diabetic rats (P. Gutierrez, 2016). This study indicates that mixture is having antioxidant and hypoglycaemic properties.

Studies conducted by (N Marbun, 2018) and (Bayat A, 2014) revealed that pumpkin seed extract has a positive effect on sugar control, lipemic control and beta cells of pancreas. This activity is might be due to the presence of bioactive compounds like steroids, flavonoids, triterpenoids and polyphenolic compounds.

One of the study conducted in year 2008 claimed that presence of polysaccharides in ungerminated pumpkin seeds and proteins from germinated pumpkin seeds are having hypoglycaemic effect (M. Gu, 2008).

Pumpkin seeds are rich in fibre, which helps to regulate blood glucose levels and reduces the need for insulin when diet of diabetic patient is rich in fibre rich foods.

Number of studies on hypoglycaemic and anti-lipemic effects of pumpkin seeds are reported so far but more clinical trials are required to establish the strong association between mechanism of action, dosage and to evaluate associate health benefits.

Antidepressant effect

Depression is one of the most common yet serious illness, which can affect your mind, body and act. Depression results into feeling of sadness and negativity

reduced appetite, lack of sleep and sometime even suicidal thoughts. Some plants have been reported anti-depressant effect.

LaChance and Ramsey (2018) claimed 47% of antidepressant food score (AFS) in pumpkin seeds which indicates antidepressant potential in it. Another study conducted by George in 2012 reported significant anti-depressive potential by using pumpkin seed extracts (PES) through forced-swimming and tail-suspension tests on rats. Furthermore, researchers are focusing on clinical and animal trials to reveal the antidepressant effects of pumpkin seeds as there are only limited sources exist in this area.

Antihyperplastic effect on prostate gland

Benign prostatic hyperplasia (BPH) can be defined as Non-cancerous enlargement of the prostate occurred due to proliferation of both stromal and epithelial cells after the age of 40 years. Several herbal medicines have been used to treat BPH since ages. Supplementation of pumpkin seed oil on rats shown positive effect to inhibit testosterone-induced hyperplasia of the prostate (M. Gossell-Williams, 2006). Furthermore, one of the study conducted in 2019 reported International Prostate Symptom Score (IPSS) of 14.8 in sixty men patients by 30% after supplementing oil free hydroethanolic Pumpkin seed Extract (PSE) (Martin Leibbrand, 2019).

Anthelmintic effect

Helminthic infections are widely present in America, East Asia, China and Saharan regions of Africa. It can impose a huge health risk on the community. Mostly all the gastrointestinal parasites are found to be pathogens and among them, Helminthic is highly rampant. Effective Anthelmintic are required to treat this deadly pandemic problem. There are some evidences on pumpkin seeds claiming Anthelmintic effect. Study conducted on infected mice indicated lethal activity in *Heligmosoides bakeri* after supplementation of pumpkin seed extracts (M. Grzybek, 2016) significant suppression on the number of adult *H. nana* worms and their egg production (A.O. Alhawiti, 2019).

Extract of pumpkin seeds and areca nuts shown ability to exterminate

Taeniasaginata and Taeniasolium (T. Li, 2012). From above literature, it can be stated that pumpkin seeds having Anthelmintic effect but only few studies have conducted so far therefore more studies are recommended in this area.

Anti-hypertension effects

Study conducted in Egypt on supplementation of pumpkin seed oil among rates have shown positive effect as amlodipine drug to treat the hypertension. Presence of tryptophan in pumpkin seeds might be responsible for the anti-hypertensive effect (Vasdev, 2010).

Anti-lipidemic effects

It has been found that composition of fatty acids and oils in seeds plays a very important role to improve the lipid profile. One of the study conducted during 2012 found that supplementation of pumpkin seeds for 37 days increased HDL cholesterol as well as reduction (47%) in LDL and total (78%) cholesterol among atherosclerotic rates (Abuelgassim, 2012). Presence of high concentration of phytosterols might be responsible for this effect. Among various nuts and seeds, pumpkin seeds have the third highest phytosterols content (Phillips, 2005). Administration of 2gm of pumpkin seed oil among post-menopausal women for 12 weeks reported 16% increase in HDL cholesterol and 7% reduction in blood pressure (Gossell-Williams, 2011).

Pumpkin seed oil helps to increase the elasticity of blood vessels and to strengthen them. Pumpkin seeds are also rich in stanols and plant sterols having important role in the prevention of arthrosclerosis. High fibre content present in pumpkin also helps to give protection against heart diseases. Abundant distribution of vitamin K in pumpkin seeds useful for the prevention of arthrosclerosis (Levin, 2012).

Unsaturated fatty acids like oleic acids and linoleic acids have significantly reduced cholesterol levels in blood among rates that is because pectin is responsible for the reduction in cholesterol levels by facilitating excretion of bile acids leading to synthesis from cholesterol in the liver, which ultimately helps to reduce the levels (Fernandez, 1990).

An activity of lipoprotein lipase in heart and fat tissues enhanced by pectin. This phenomena result into higher absorption of VLDL and chylomicrons in other tissues than liver to promote breakdown. Cholesterol is very important for the biosynthesis and LDL contains more amount of cholesterol, likely to deplete more followed by decrease in cholesterol levels (Sedigheh, 2011).

Anti-inflammatory effects

Presence of beta-carotene among pumpkin seeds are responsible for its anti-inflammatory properties. Regular consumption of pumpkin seeds provides protection against inflammation of joints (McCaffrey, 2012).

γ -tocopherol in pumpkin seed is responsible for having anti-inflammatory properties which can be used to treat arthritis and other painful conditions (Jeznach, 2012).

Bone protection effect

Pumpkin seeds are rich in zinc. Zinc plays a very vital role in immunity and to support bone density especially to the osteoporosis patients. Pumpkin seeds are used widely to prepare snacks to protect bones from the recurrent fractures (Gold, 2009).

Hypotriglyceridemic effects

Pumpkin seeds are rich in L-Arginine and due to this, they are having protective effect against atherosclerosis. Pumpkin seeds extract has been found having a strong Hypotriglyceridemic effects (Ardabili, 2011).

Relief from anxiety effects

Serotonin is a neurotransmitter plays important role for good mood and to promote wellbeing. Tryptophan is present in pumpkin seeds, which converts into serotonin to relieve the anxiety. It also promotes sleep and relieves anxiety (Shapiro, 2012).

From above literature it can be stated that pumpkin seeds are having health benefits to treat diabetes, blood pressure, cardiovascular disease, inflammation, to boost

immunity, having protective role for prostate, cancer management and to improve mental health. The conversion of these agri-cultural wastes to valuable elements can be a huge footstep towards the improvement of quality of life.

Therefore, the further researches and studies are recommended to generate evidences for the clinical use of pumpkin seeds in disease prevention. Thus, in the light of review carried out present study was planned to evaluate glycaemic and lipemic properties of pumpkin seeds on humans.