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MÉMOIRE

Présenté par

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En vue de l'obtention du

Diplôme de MASTER

En Nutrition et Diététique

Thème

STUDY OF LIPID PROFILE IN NON-OBESE TYPE 2 DIABETIC MEN FROM WESTERN ALGERIA-TLEMCEN

Soutenu le 12 /06/2022, **devant le jury composé de :**

Président	HADJ MERABET Djahida	MAB	Université de Tlemcen
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ملخص

أجرينا دراسة مقطعية لتحديد مستوى الدهون في الدم لدى الرجال غير البدينين المصابين بداء السكري من النوع 2 (DT2) من غرب الجزائر -تلمسان. تم الحصول على البيانات البيوكيميائية والقياسات البشرية من 30 مريضًا. التحليل كان في مختبرات مختلفة داخل تلمسان بين 2019-2022. وجد أن 50٪ يعانون من ارتفاع في الدهون الثلاثية و30٪ لديهم فرط كوليسترول الدم. ارتبط محيط الخصر ومدة الإصابة بمرض السكر بارتفاع كوليسترول الدم وزيادة الدهون الثلاثية وارتفاع ضغط الدم الانبساطي على التوالي. لم تكن ملامح الدهون مرتبطة بمؤشر كتلة الجسم والرياضة والنظام الغذائي في مرضى DM الذين تمت دراستهم.

الكلمات الدالة : دهون الدم، DT2 ، محيط الخصر ، فرط كوليسترول الدم ، ارتفاع الدهون الثلاثية ، PAD ، مؤشر كتلة الجسم ،DM ، النظام الغذائي

Résumé

Nous avons réalisé une étude transversale pour déterminer le profil lipidique sérique chez les hommes non obèses diabétiques de type 2 (DT2) de l'ouest algérien-Tlemcen. Les données biochimiques et anthropométriques de 30 patients ont été obtenues. Les analyses des échantillons ont été effectué dans différents laboratoires de Tlemcen entre 2019-2022. Il a été constaté que 50% avaient une hypertriglycéridémie et 30% avaient une hypercholestérolémie. Le tour de taille et la durée du diabète étaient respectivement associés à l'hypercholestérolémie, l'hypertriglycéridémie et pression artérielle diastolique (PAD). Les profils lipidiques n'étaient pas associés à l'IMC, au sport, au régime chez les patients DM étudiés.

Mots clés : lipides sériques, DT2, hypertriglycéridémie, hypercholestérolémie, tour de taille, PAD, IMC, DM, régime.

Summary

we carried out a cross-sectional study to determine the serum lipid profile in non-obese type 2 diabetes mellitus (T2DM) men from western Algeria-Tlemcen. Biochemical and anthropometric data from 30 patients were obtained. Sample analyses were performed at various laboratories within Tlemcen between 2019-2022. It was found that 50% had hypertriglyceridemia and 30% had hypercholesterolemia. Waistline and duration of diabetes were associated with hypercholesterolemia, hypertriglyceridemia and diastolic BP; respectively. Lipid profile was not associated with BMI, sport, diet in the DM patients studied.

Keywords: serum lipid, T2DM, hypertriglyceridemia, hypercholesterolemia, waistline, diastolic BP, BMI, DM, diet.

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DEDICATION

This dissertation is dedicated to both my parents. My father, the late NYAGA Muthaura did not only raise and nurture me, but he also devoted himself dearly over the years to my education and intellectual development. Incidentally, he met his demise about the same moment I was finalizing this dissertation on 23 April 2022; his memory will be forever a comfort and a blessing. To my mother, Beth NYAGA has been a source of motivation and strength during moments of despair and discouragement. Her motherly care and support have been shown in incredible ways recently.

To my sisters Audensia NYAGA, Priscilla NYAGA you have been the best. Life is full of changes but a sister's love is forever.

NYAGA

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ABREVIATIONS AND ACRONYMS

DM : Diabetes mellitus

T1DM : Type 1 diabetes mellitus

T2DM : Type 2 diabetes mellitus

GD : Gestational diabetes

ADA: American Diabetes Association

IDF: International Diabetes Federation

AHA: American Heart Association

CDC: Centre of Disease Control

MENA: Middle East and North Africa

GBD: Global Burden of Disease

US: United State

DALYs: Disability-adjusted life years

WHO: World Health Organisation

CVD: Cardiovascular Diseases

BMI: Body Mass Index

TG: Triglyceride

VLDL-C: Very Low Density Lipoprotein Cholesterol

HDL-C: High Density Lipoprotein Cholesterol

KDPS: Korean Diabetes Prevention Study

DTH: Delayed Type Hypersensitivity

NCEP: National Cholesterol Education Program

PG: Plasma Glucose

FPG: Fasting Plasma Glucose

HbA1c: Glycated Haemoglobin

OGTT: Oral Glucose Tolerance Test

IFG: Impaired Fasting Glucose

G-3-P: Glycerol-3-Phosphate

GDI: Glucose Disposition Index

NGT: Normal Glucose Tolerance

Apo-B: Apo-Lipoprotein-B

FA: Fatty Acids

FFA: Free Fatty Acids

TAG: Triglyceride

IDL-C: Intermediate Density Lipoprotein Cholesterol

INSR: Insulin Resistance

WAT: White Adipose Tissue

CETP: Cholesterol Ester Transfer Protein

HTN: Hypertension

SBP/DBP: Systolic/Diastolic Blood Pressure

HSBP: High Systolic Blood Pressure

RAAS: Renin-angiotensin-aldosterone

ER: Endoplasmic Reticulum

DCET: Diabetes Control and Complication Trials

NGSP: National Glycohemoglobin Standardization Program

Micro: Microvascular

CKD: Chronic Kidney Disease

DFU: Diabetic Foot Ulcers

DR: Diabetic Retinopathy

DME: Diabetic Macular Edema

DN: Diabetic Nephropathy

BRB: Blood Retinal Barrier

cm: Centimetre

ml/min: milliliter per minute

pmol/l: picomol per litre

mg/dl: Milligram per decilitre

mmol/l: Millimoles per litre

g: grams

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GENERAL INTRODUCTION

Introduction

Diabetes mellitus (DM) is a chronic metabolic disease characterized by the increase of blood sugar level, a condition referred to as hyperglycaemia**,(Ghafar et al., 2021).** It mostly occurs when the pancreas is unable to produce insulin enough to regulate the blood sugar in the body or when the pancreas produces enough insulin, but the body cannot effectively use it**(WHO, 2021b).** DM has become a global epidemic. It is approximated that 6% of world's population which is more than 420 million people either live with type 1 or type 2 diabetes mellitus (T1DM, T2DM).**(WHO, 2021b).**

According to International Diabetes Federation (IDF Atlas), more than one in every 10 adults globally are living with diabetes. They also reported that in some countries one in every five adults is diabetic.**(*IDF Diabetes Atlas 2021 – 10th Edition*, 2021)** It is estimated that since 2000, the prevalence of diabetes in adults between the age of 20-79 years has tripled, from approximately 151 million which was 4.6% of world's population to 537 million (10.5%) of today's world population. If an immediate action is not taken to compact the increase of diabetes, it is predicted that 643 million people will be diabetic by the year 2030 (11.3% of the world's population) and if by then still no sufficient action taken, the number would increase to an estimated 783 million (12.2%) by the year 2045**(Kotwas et al., 2021).** In the region of Middle East and North Africa (MENA) which comprises of Algeria as one of the countries, in the year 2021, 73 million people were living with diabetes and if no sufficient action taken to address this situation, it is predicted that the number would raise to 95 million and 136 million people by the 2030 and 2045; respectively with an increase of 87% **.(*IDF Diabetes Atlas 2021 – 10th Edition*, 2021) (Figure1)**

Globally the mortality and Disability-adjusted life years (DALYs) related with diabetes demonstrated an increased tendency in most of Global Burden of Disease (GBD) regions. The highest mortality age-standardized was in Oceania, Sub-Saharan Africa, Central Latin America and Caribbean; respectively. The diabetic burden geographical distribution in the year 2017 varied by countries, the highest being China (89.5 million), India (67.8 million), United States (30.7 million), Indonesia (21.0 million), and Mexico (13.1 million) while the five countries where most deaths were recorded were India (254,555), China (153,185), Indonesia (97,005), the United States (68,558), and Mexico (64,067); respectively.**(Lin et al., 2020)**

In the US population, it was estimated that 34.2 million people both adults and children counting for 10.5% of US population had diabetes. Among this number, 34.1 million or 13.0%

were adults aged 18 years and above of all US adults. About 7.3 million adults aged 18 years and above had undiagnosed diabetes, this represents 2.8% of US adults population and 21.4% of all diabetic adults in the US**.(*National Diabetes Statistics Report 2020. Estimates of Diabetes and Its Burden in the United States.*, 2020).**

Algeria is the ninth most populated country in Africa with an estimated population of 43.4 million people in 2017, among this Algerian population it is estimated that 29% of them are aged 15 years and below, while 6% of the population is 65 years and above, this population is expected to increase by ~40% by the year 2050**(*The Diabetic Retinopathy Barometer Report*, 2017).** Algeria has an estimated of more than 1.7 million adults living with diabetes, which is ~5% of people with diabetes, in MENA region. Deaths related to diabetes were 14,067 people in Algeria in the year 2015, which is ~4% of all deaths, in this region**.(*IDF Diabetes Atlas 2021 – 10th Edition*, 2021)**

Algeria was ranked number seven as one of the countries with the most prevalence of T1DM and 10th country with most children living with T1DM**.(Khater et al., 2021)** In the year 2017, the prevalence of diabetes increased by 6.9% in Algeria, this is an estimated 1,782,000 diabetics. According to published epidemiological data, it is evidence that the prevalence of diabetes is rapidly increasing in Algeria where a huge proportion (31.51-40.82%) of patients living with T2DM were also affected by obesity**.(Boukli Hacene et al., 2020)**

Lipid abnormalities in diabetic patients are often common and are an important factor in the increased cases of cardiovascular health problems**(Stamouli et al., 2014).** The main objective of the study of lipid profile in diabetic patients is to summarize the benefits of dyslipidaemia treatment for the diabetic patients, the purpose of dyslipidaemia treatment is to minimize overabundance of cardiovascular mortality and morbidity of diabetic patients.**(Rahmoun et al., 2019).**

The main aim of our study was to present and describe the lipid profile, find the relationship of lipid profile with anthropometric and biochemical variables such as (BMI, lifestyle, other pathologies, sports etc.) in non-obese type 2 diabetic men from the region of western Algeria (Tlemcen)

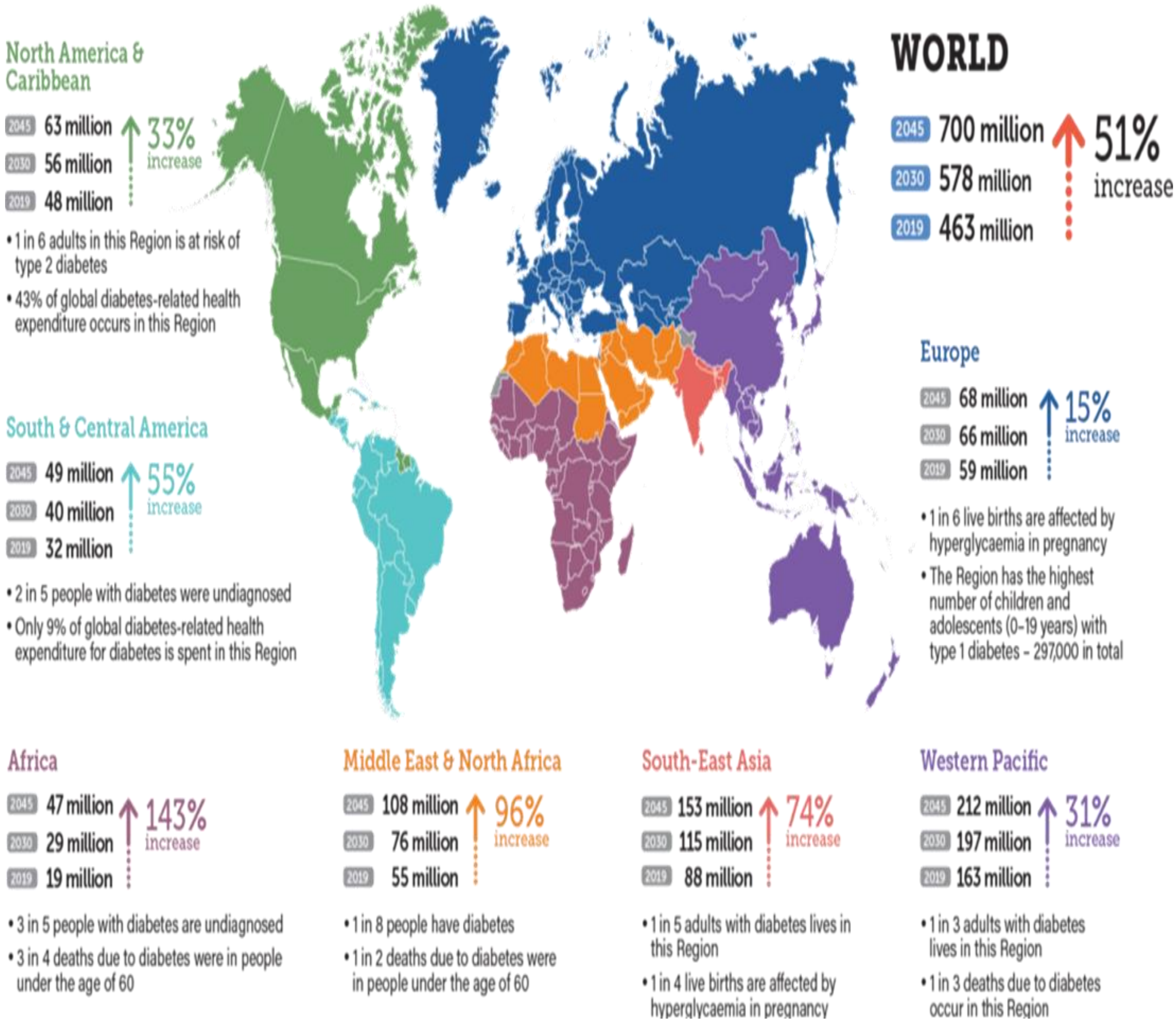

Figure 1: Showing distribution of diabetes cases worldwide and per region in 2019, 2030 and 2045. **(Idf Diabetes Atlas 9th Edition 2019, HD Png Download - Kindpng, 2019)**

LITERATURE REVIEW

1. Chapter 01

1.1 Diabetes

In 2019, World Health Organization (WHO) considered diabetes as the pandemic of 21st century up to March 2020 when they announced coronavirus disease 2019 (COVID-19) as a pandemic**.(Bounihi et al., 2021a).**

Three countries of North Africa, Tunisia, Morocco and Algeria has encountered nutritional transition for the last few years which has left the countries with increased cases of metabolic disorders such as obesity and overweight as well as prevalence of their comorbidities such as cardiovascular diseases (CVDs) and (T2DM).**(Belhayara et al., 2020)**

According to Centre of Disease Control (CDC), diabetes can be defined as long-lasting and a chronic health condition that affects the ability of our bodies to convert the food that we ingest into energy. Normally our bodies breakdown the ingested food in our digestive systems into glucose and it is released in our bloodstream resulting in the levels of our blood sugar to go up, a condition described as hyperglycaemia. Since our blood sugar level is high, it signals our pancreas to release insulin hormones which regulates our blood sugar and lets our body cells use it as energy**.(CDC, 2022)**

In Algeria, a large proportion of T2DM patients with an estimated percentage of (31.51-40.82%) are affected by obesity. In addition, poor control of blood glucose, cholesterol and blood pressure (BP) has also been reported in such patients and as a result urgent intervention is required to compact diabesity.**(Bounihi et al., 2021a)**

Undiagnosed diabetes or poor managements can lead to serious health complications such as damage of the kidney, heart, eyes, blood vessels, increased heart diseases, stroke nerves or premature death. It is estimated that 77% worldwide deaths which are diabetes-related occur in Sub-Saharan Africa in patients aged 61 years or younger.**(Dessie et al., 2020)**; the rising of type 2 diabetes is alarming and it is becoming a big challenge to the public health especially in the MENA region, this region has seen rapid shift in its eating habits for the past decades adopting more westernized unhealthy dietary habits in place of their traditional Mediterranean diet.**(Hwalla et al., 2021)**

1.2 Classification of diabetes

DM is basically classified into 3 main categories,**(Diamond et al., 2022)** all types of diabetes are defined by a common feature “hyperglycaemia”, but natural history, pathogenic mechanisms, aetiology and treatment for various categories of diabetes are different. To date it is still difficult to classify some types of diabetes but others are easily classified by their exclusive and specific features.**(World Health Organization, 2019)**

The importance of classifying DM to specific types is to offer a basis for epidemiological studies, give a guideline to the clinical care decisions and also facilitate research of etiopathology.**(American Diabetes Association, 2021)**

1.2.1 Type 1 diabetes

T1DM is a multifactorial autoimmune and insulin dependent disease which occurs as a result of destruction of beta cells of the islets of Langerhans in the pancreas.**(Grabia et al., 2021)** T1DM affects both genders male and females equally. Despite the fact that it is commonly occurring in childhood, it can as well occur in adults where 84% of patients living with diabetes type 1 are all adults. The rate of destruction of beta cells varies from one person to another where in some is slow and rapid in others.**(World Health Organization, 2019)**

As a result of destruction of beta cells in the pancreas, the insulin production is reduced leading to less intake of glucose into the cells and more glucose in the bloodstream. T-cells attacks beta cells located in the pancreas precisely in the islet of Langerhans which are specialized in producing insulin, due to Type 4 Cell-Mediated Hypersensitivity**(Gicchino et al., 2021).** The activation and migration of T lymphocytes into the pancreas activates insulitis macrophage which activates the production of cytokines leading to cell-mediated delayed-type hypersensitivity (DTH) response causing anti-glutamic acid antibody, anti-islet cell antibody and anti-insulin antibody production.**(Venkatesan, 2021)**

Due to high level of glucose in the bloodstream starving the cells, lipolysis occurs in the adipose tissue converting fat to fatty acids while the muscle tissue degrades the proteins leading to loss of weight. The liver further converts the fatty acids to ketone bodies causing Diabetic Ketoacidosis providing energy for cells while subsequently increasing the blood acidity which causes Hyperkalaemia, Kussmaul Respiration and High anion gap.**(Hawkins, 2019)**

T1DM symptoms may include Glycosuria, polyphagia, polydipsia and polyuria**.(Haris et al., 2021)**

1.2.2 Type 2 diabetes

According to WHO, T2DM commonly affects low and middle-income countries and it accounts for 90% and 95% of all diabetes cases making it a serious global health challenge, due to rapid evolution in relation to unplanned and increasing urbanization, rapid social, economic and cultural changes, reduced physical activities, ageing population and unhealthy lifestyle and behavioural patterns**(World Health Organization, 2019).**

T2DM was previously known to mostly occur in adults but recent research shows an increasing number of adolescents and children being affected**(Hur et al., 2021)**

In patients with T2DM their production of insulin by the pancreas is normal but the body tissues have become resistant to insulin leading to less intake of glucose by the cells and more glucose level in the bloodstream**(Tao et al., 2015)**. There are various reasons which can lead to insulin resistance such as obesity, Genetics and lifestyle but up to date the precise causes are not yet fully documented.**(Diamond, 2022)** Beta cells increase the production of insulin levels causing increase in the number of beta cells also known as (beta hyperplasia) and increase of their size which is referred to as (beta hypertrophy), all the mechanisms are as a result of the body trying to balance the level of the glucose in the bloodstream. This leads to degradation of beta cells (hypotrophy) which leads to decrease in production of insulin.**(A & G, 2021)**

The degeneration of beta cells causes Hyperosmolar Hyperglycaemic symptom; a syndrome which is characterized by severe dehydration, hyperglycaemia and hyperosmolality.**(Tomita, 2016)** Symptoms of T2DM include Glycosuria, polydipsia, polyphagia and polyuria. Before these clinical symptoms are manifested, the patients level of blood glucose is above normal but not too high to be considered being diabetic, this stage is referred to as prediabetes.**(Lim et al., 2020)** This stage is associated with hypertension(HTN), dyslipidaemia with high triglyceride (TAG) or low high density lipoprotein (HDL) cholesterol and can gradually worsens, if the patients become obese or stressed, but it can as well improve and the blood glucose become normal, if the patients adopted a healthy lifestyle and engaged in more physical activities**.(American Diabetes Association, 2020)**

1.2.3 Gestational diabetes

It is mostly diagnosed during the second or third trimester of pregnancy, gestational diabetes (GD) is also characterized by insulin resistance which occurs as a result of high production of placental hormones such as progesterone, oestrogen, cortisol, leptin, and placental growth hormones leading to increase of glucose levels in the bloodstream. Hyperplasia and hypertrophy of pancreatic beta cells occurs to maintain the glucose homeostasis.**(Yang & Wu, 2022)**

CLASSIFICATION	PATHOGENESIS	
1. Type I	• β-cell destruction • Absolute insulin deficiency • Autoantibodies • Islet cell autoantibodies • Insulin autoantibodies	• Glutamic acid decarboxylase autoantibodies • Tyrosine phosphatase IA-2 and IA2B autoantibodies
2. Type II	• Insulin resistance with an insulin secretary defect	• Relative insulin deficiency
3. Other	• Associated with secondary conditions • Genetic defects of β-cell function • Pancreatic disease • Endocrine disease	• Drug or chemical induced • Insulin receptor abnormalities • Other genetic syndromes
4. Gestational	• Glucose intolerance during pregnancy	• Due to metabolic and hormonal changes

Figure 2: Classification of diabetes mellitus **(Ng & Gupta, 2019)**

1.3 Diagnosis

According to Korean Diabetes Prevention Study (KDPS), adults over 40 years and in those aged 30 years and above should be screened for DM annually by using 2h-plasma glucose (PG), fasting plasma glucose (FPG) and glycated haemoglobin (HbA1c) levels during 75g oral glucose tolerance test (OGTT). When screening diabetes by use of HbA1c criteria, it should be carried out by use of a method that is certified by National Glycohemoglobin Standardization program (NGSP) and traceable to the Diabetes Control and Complication Trials (DCCT) assay**.(American Diabetes Association, 2020).**

To diagnose GD, the abnormal glucose tolerance is those of Coustan and Carpenter criteria.**(A & G, 2021).** An FPG level of 100 to 125 mg/dL signals impaired fasting glycaemia (IFG), while a 2h-PG value of 140 to 199 mg/dL after a 75g oral glucose load or HbA1c levels of 5.7% to 6.4% is defined to be prediabetes.**(Hur et al., 2021)**

Tableau 1: Diagnosis and criteria for diabetes.**(World Health Organization, 2019)**

i.	FPG ≥ 126 mg/dL (7.0 mmol/L) when an individual has not ingested any calorie for at least 8h is referred to as fasting.
ii.	During 2-h OGTT ≥ 200 mg/dL (11.1 mmol/L. An equivalent of 75g anhydrous glucose load dissolved in water should be used to perform this test.
iii.	AIC ≥ 6.5% (48 mmol/mole) and the method should be NGSP certified and standardized to the DCCT assay.
iv.	If classic symptoms of hyperglycaemia crisis are observed in patients a random plasma glucose ≥200 mg/dL (11.1 mmol/L) can be considered.

Tableau 2: Diagnosis criteria of GDM using a 100-g or 75-g glucose load.**(American Diabetes Association, 2021)**

		mg/dl	**mmol/l**
i.	100-g glucose load fasting ,1-h,2-h,3-h	95,180,155,140 respectively	5.3,10.0,8.6,7.8 respectively
ii.	75-g load fasting,1-h,2-h	95,180,155 respectively	5.3, 10.0, 8.6 respectively

1.4 Risk factors of type 2 diabetes

According to studies published recently, T2DM was described as a complex disorder which is mostly affected by genetic and environmental factors; inactive lifestyle and intake of calories dense foods are the common environmental factors associated with T2DM. DM can also be genetically inherited.**(AL-Eitan et al., 2020)**

1.4.1 Age

According to American Heart Association (AHA), T2DM mostly occurs in middle aged adults after the age of 40 years, is when the risk of pre-diabetes and T2DM is at its peak. But in recent years, children and adolescents are being diagnosed with T2DM.**(American Heart Association, 2021**)

1.4.2 Glycaemia

Adipose tissue and skeletal muscles reduce their glucose uptake leading to presence of excess glucose in the blood stream. This results in hyperglycaemia which is associated with prediabetes and insulin resistance and if it is not well managed it can lead to T2DM**.(Diamond, 2022)**

1.4.3 Genetic factors

Having a family history of T2DM increases the chances of developing T2DM in individual's lifetime. Apart from genetic predisposition, parents can also pass poor health habits and other lifestyle choices to their children which are associated with the development of T2DM.**(Rachel Nall, 2019)**

1.4.4 Environmental factors

1.4.4.1 Obesity

In most developed countries, the incidence of obesity as increased and a noticeable prevalence of T2DM has been also reported. High body mass index (BMI) or an excess of adipose tissue which is associated to many metabolic abnormalities resulting in insulin resistance is the strongest risk factor for T2DM. Recent studies have shown that visceral adiposity independently could be a T2DM risk predictor.**(Zheng et al., 2018)**

1.4.4.2 Diet

In the past few years, poor and unhealthy dietary habits which increases the risk of obesity have been widely adopted worldwide, these habits increase the chances of progressing from prediabetes to diabetes. If a prediabetes individual adopts high carbohydrates diet, he challenges the glucose lowering ability; thus accelerating the development of T2DM. Other diets such as saturated fat, trans fats, high fats and low fibre diet lead to dyslipidaemia, a condition that causes insulin resistance resulting in hyperglycaemia hence development of T2DM.(**Diamond, 2022)**

1.4.4.3 Sedentary lifestyle

Physical activities help the body to effectively use its insulin hence lowering insulin resistance. Being physically inactive is one of the modifiable risk factors for prediabetes and T2DM in recent years. Every individual is recommended to at least spend 75 or 150 minutes per week of vigorous-intensity or moderate-intensity aerobic physical activities to help reduce the risk of diabetes.**(American Heart Association, 2021)**

1.4.5 Smoking

Individuals who smoke have an estimated 37% higher risk of developing T2DM as compared to non-smokers.**(Y. Zhang, Pan, et al., 2020).** Every year smoking causes approximately 8 million deaths in both active and non-active smokers. The increase of nicotine in the body due to smoking reduces the intake of glucose by the muscles which leads to development of insulin resistance resulting in T2DM.**(Ismail et al., 2021).**

1.5 Complications and consequences of diabetes mellitus

DM leads to various acute and chronic complications which reduces the quality of live and may also lead to premature death.**(Salci et al., 2017)**

1.5.1 Diabetic macroangiopathy

Diabetic macroangiopathy which is characterized by accumulation of VLDL in the blood vessels can result in cerebro-cardiovascular diseases leading to death in patients with diabetes.**(Feng et al., 2018)** Diabetic macroangiopathy is characterized by vascular homeostasis alterations which occurs as a result of vascular smooth muscle and endothelial cell dysfunction. Risk factors such as dyslipidaemia, arterial HTN and obesity in presence of insulin resistance and hyperglycaemia play a crucial role in development of atherosclerosis.**(Madonna et al., 2018a)** Other factors such as smoking, cholesterol levels, oxidative stress and increased low-density lipoprotein (LDL) leads to vascular endothelial dysfunction; hence resulting in the development of atherosclerosis (figure 3).**(Katakami, 2018)**

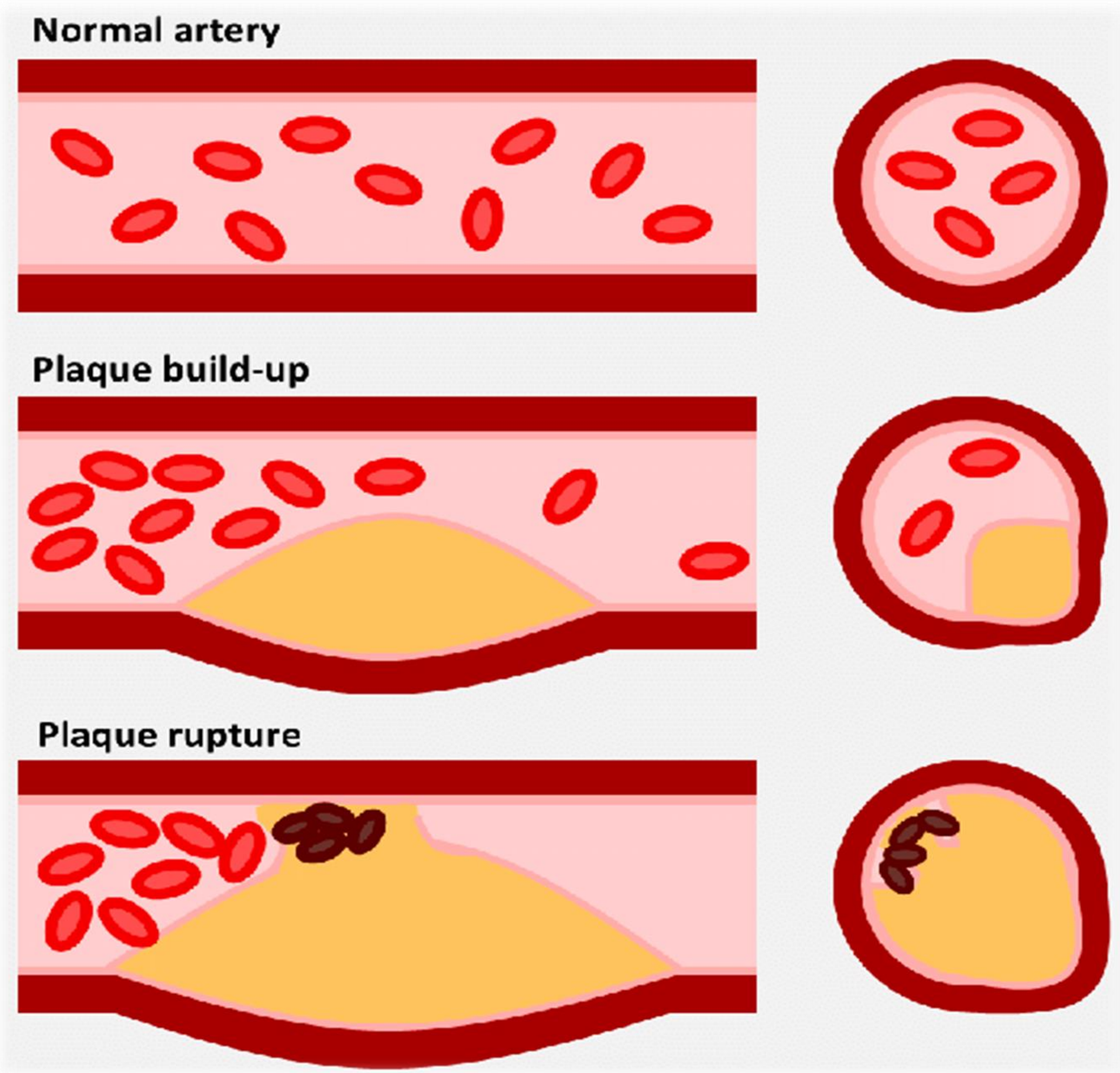

Figure 3: Development of atherosclerotic plaque**.(Liam-Ward, 2019)**

1.5.2 Diabetic microangiopathy

Recent studies have reported an increased prevalence of microvascular complications in patients with diabetes. About 38% among T2DM patients manifest symptoms of chronic kidney disease (CKD), while more than 30 % live with peripheral neuropathy and another 30 % have retinopathy**(Madonna et al., 2018b)**. Microvascular are characterized by hyperglycaemia but also hyperlipidaemia, and high BP plays a role in their development.**(Avogaro & Fadini, 2019)**

Diabetic foot ulcers (DFU) which is a chronic wound progression on the lower limbs as a result of dysfunction of skin microcirculation leading to the lower parts of the body such as fingers to have limited blood flow; hence lacking enough macrophage and lymphocytes (T-cells and B-cells) which help in healing of wounds**.(Sharma et al., 2020)**

1.5.3 Diabetic retinopathy

According to recent study, it has been reported that 35% of patients with diabetes worldwide have diabetic retinopathy (DR). Among the leading causes of impaired vision or blindness in the world, DR was ranked fifth and its prevalence is expected to increase in the future.**(Hammes, 2018)**

There are several risk factors for DR but the most common include presences of HTN, disease duration and poor glycaemic control (high levels of HbA1c), other possible risk factors are cataract surgery, high BMI as well as puberty.**(Simó-Servat et al., 2019)**

DR is characterized by abnormal vascular symptom in the retina. Macular edema (DME), which is defined by thickening or swelling of macular as a result of sub- and intra-retinal fluid accumulation in the macula caused by the breakdown of the blood-retinal barrier (BRB), is the common cause of loss of vision. Retinal blood vessels in response to hyperglycaemia undergo blood vessel dilatation, which changes the flow of blood. Hyperglycaemia is associated with the development of retinal microvascular damages.**(W. Wang & Lo, 2018)**

1.5.4 Diabetic neuropathy

Diabetic neuropathy is among neurodegenerative disorder characterized by the damage of the autonomic and peripheral nervous systems originating distally from the lower extremities such as limbs and it is always accompanied by pain. Half of the patients living with diabetes develop diabetes neuropathy with time. Distal symmetric polyneuropathy which mostly affect the lower limbs and hands is the most prevalent form of diabetes neuropathy.**(Feldman et al., 2019)**

Several pathological lipid and glucose metabolism alterations occur as a result of dyslipidaemia and hyperglycaemia which leads to neuronal dysfunction, hence contributing to development of diabetic neuropathy.**(El et al., 2019)**

1.5.5 Diabetic nephropathy

Diabetic nephropathy (DN) is characterized by high mortality and morbidity and it is the most common and severe DM complication. High BP and chronic hyperglycaemia are among the risk factors of diabetes nephropathy.**(Samsu, 2021)**

1.6 Anatomy of the pancreas and the liver

The liver and the pancreas are two essential organs which are involved in the body physiological metabolism by their ability to secrete important hormones, such as angiotensinogen, insulin and glucagon respectively, and they are directly involved in the development of DM.**(Pashaei et al., 2021)**

1.6.1 Pancreas

The normal pancreas of an adult in a heathy state weighs approximately 100g, with the volume of 72.4 ± 25.8 cm^3 and the length of 14 to 25cm and it is elongated in shape and lobular.**(Atkinson et al., 2020)** It is divided into four parts(figure 4):

- ❖ Uncinate process (which is located in the ventral lobe of the head)
- ❖ The head
- ❖ Body and tail
- ❖ The neck

Most tissues of the pancreas play a major role in its exocrine function, which involves the secretion and production of digestive enzymes via a complex ductal tree into the duodenum.**(Marshall, 2020)** The pancreas is composed of various cells such as acinar cells, which makes up the largest part (about 85% of the pancreas), their main role is to secrete digestive enzymes such as lipase, trypsin and amylase which are essential for the digestion of fat, protein and carbohydrates; respectively**(Judge & Dodd, 2020)**. Between meals pancreatic secretions are secreted at a low rate of about (0.2-0.3ml/min) and they increase during meals to around (4.0ml/min) attaining a volume of ~2.5l daily.**(Tomita, 2012)**

Other tissues found in the pancreas are the endocrine secretory tissues also referred to as islet of Langerhans which are located between the cluster of acinar cells**(Titchenell et al., 2017)**. Islet of Langerhans makes around 1-2% of the pancreas mass and they weigh about 1gram**(Jones, 2016)**. Among all the endocrine cells 40-60% of them are insulin producing beta-cells while the rest are delta, alpha, epsilon and pancreatic polypeptide secreting cells. The contribution of the endocrine pancreas to DM is due to its ability to secrete two important hormones insulin and glucagon, which play a major role in the regulation of energy metabolism.**(Atkinson et al., 2020)**

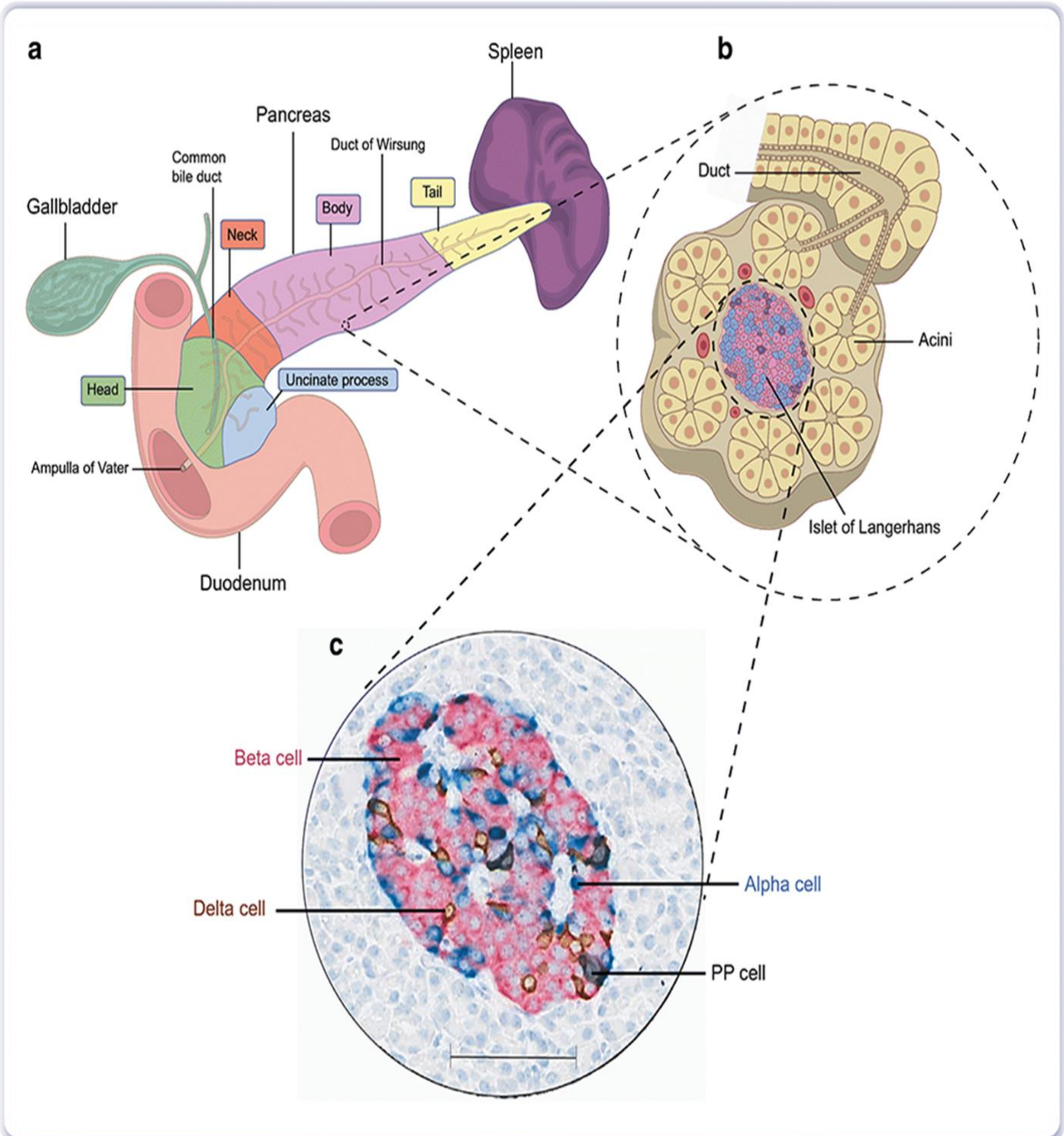

Figure 4: Anatomy of the pancreas. **(Atkinson et al., 2020)**

1.6.2 The liver

The liver is one of most critical organs (figure 5), which is the centre of numerous physiological processes not limited to endocrine control of growth signalling pathways, macronutrient metabolism, lipid and cholesterol homeostasis. During feeding, the liver has the capacity to store glucose in form of glycogen and during fasting periods, it allows gluconeogenic pathways to take place and provide the body with the required blood glucose.**(Petrov & Basina, 2021)**

The liver is composed of various types of cells, such as binary epithelial cells (cholangiocytes), Kupffer cells, stellate cells, hepatocytes and liver sinusoidal endothelial cells which help it carry its important physiological functions (figure 5). The majority of the liver volume is occupied by the hepatocytes and they perform most of the liver functions.**(Trefts et al., 2017)**

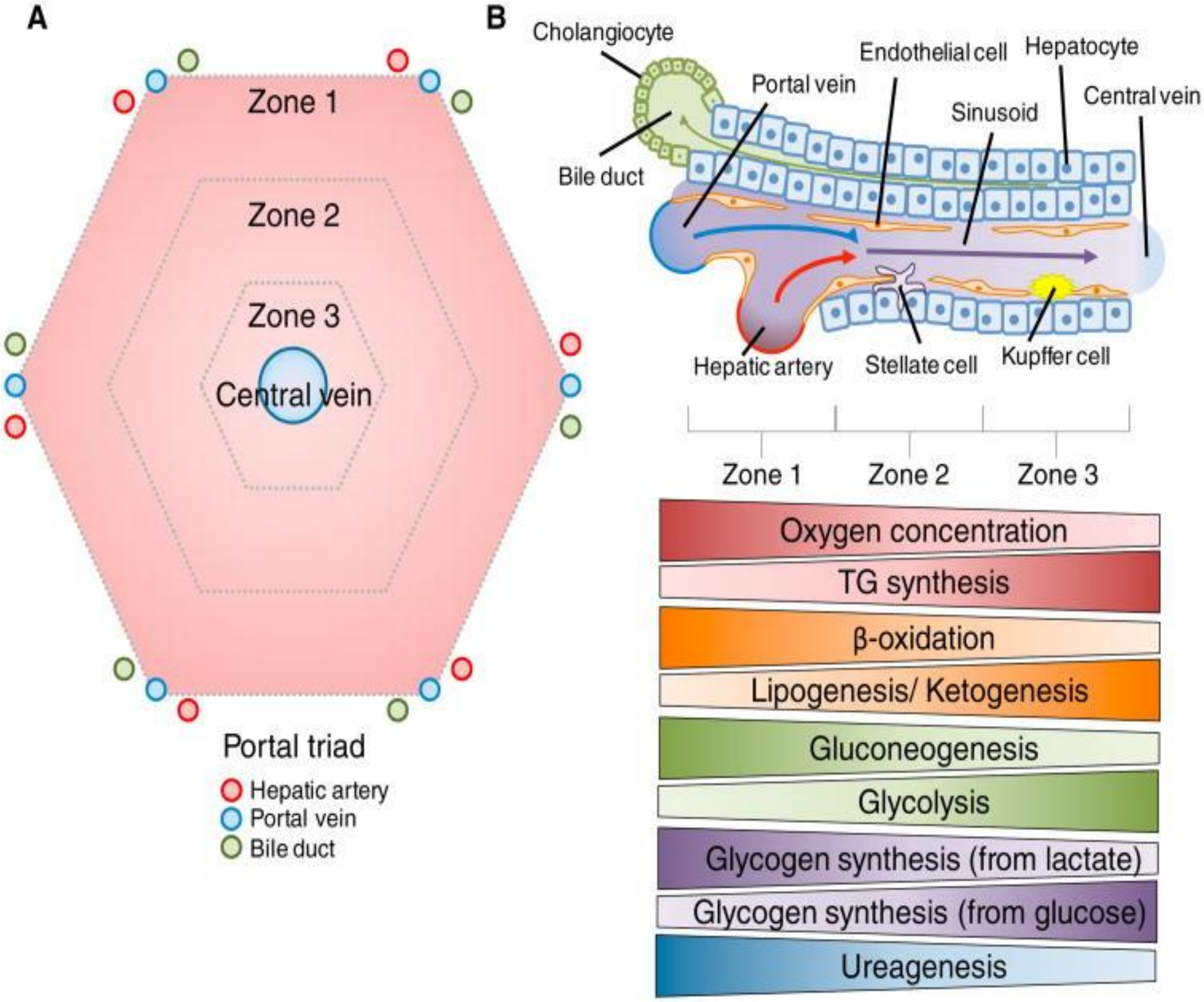

Figure 5: Showing the organisation of the liver**.(Trefts et al., 2017)**

1.7 Lipoprotein metabolism

Metabolites such as carbohydrates, fatty acids (FA) and proteins goes through biochemical process known as Krebs cycle where they are oxidized to produce energy to be used by the body. **(Jones, 2016).**

There are two main sources of FA, either from endogenous or dietary sources. Bile acid emulsifies dietary TG in the intestinal lumen after their hydrolysis by the pancreatic lipase. The enterocytes take up the emulsified lipid molecules and resynthesizes them into TG. **(Petersen et al., 2017)** This resynthesized TG are packaged into chylomicrons and they are secreted into the lymphatic system aimed to reach the plasma. The adipose tissue and muscles take up most of the chylomicron TG due to their lipoprotein lipase activity. The liver converts glucose into FA in case there is abundance of carbohydrates in a process referred to as *de novo* lipogenesis (DNL) (figure 6). **(Alves-Bezerra & Cohen, 2017).** When plasma insulin concentrations are low during fasting state, white adipose tissue initiates lipolytic program which increases the level of fatty acids in the plasma making it available for uptake by the liver. FA go through esterification within the hepatocyte to produce cholesterol and glycerol-3-phosphate (G3P), which generate cholesterol esters and TG respectively.**(Petersen et al., 2017)**

Intestinal chylomicrons (CM) and VLDL derived from the liver are the two classes of lipoproteins rich in TG which transport lipids to other cells. CM transport dietary lipids, while VLDL delivers endogenous lipids to peripheral tissues. In healthy individuals, in the liver, insulin has proven to inhibit the synthesis of VLDL**.(Ramasamy, 2014)**

During intravascular lipolysis , VLDL are transformed into other products including LDL and IDL.**(Packard et al., 2020)**

LDL particles in the blood, which are formed after the remodelling of VLDL in the liver and plasma, transfer cholesterol to lipid requiring cells.**(Röhrl & Stangl, 2018)**

LDL is referred to as bad cholesterol due to its harmful effect on the body due to its ability to accumulate in the blood vessels**(Chandel, 2021).**

Excess cholesterol accumulating in the peripheral tissues (e.g., macrophage in the aortae) is removed by HDL, where it is transported back to the liver to be excreted into the faeces via the bile. The intestine and the liver secrets two major HDL-associated apoA-l and apoA-ll into the plasma. These two apolipoproteins are then lapidated to form lipid poor, nascent HDL, discoidal. Cholesterol from cell membranes and other lipoproteins is taken up by nascent HDL.**(H. Zhang et al., 2014)**

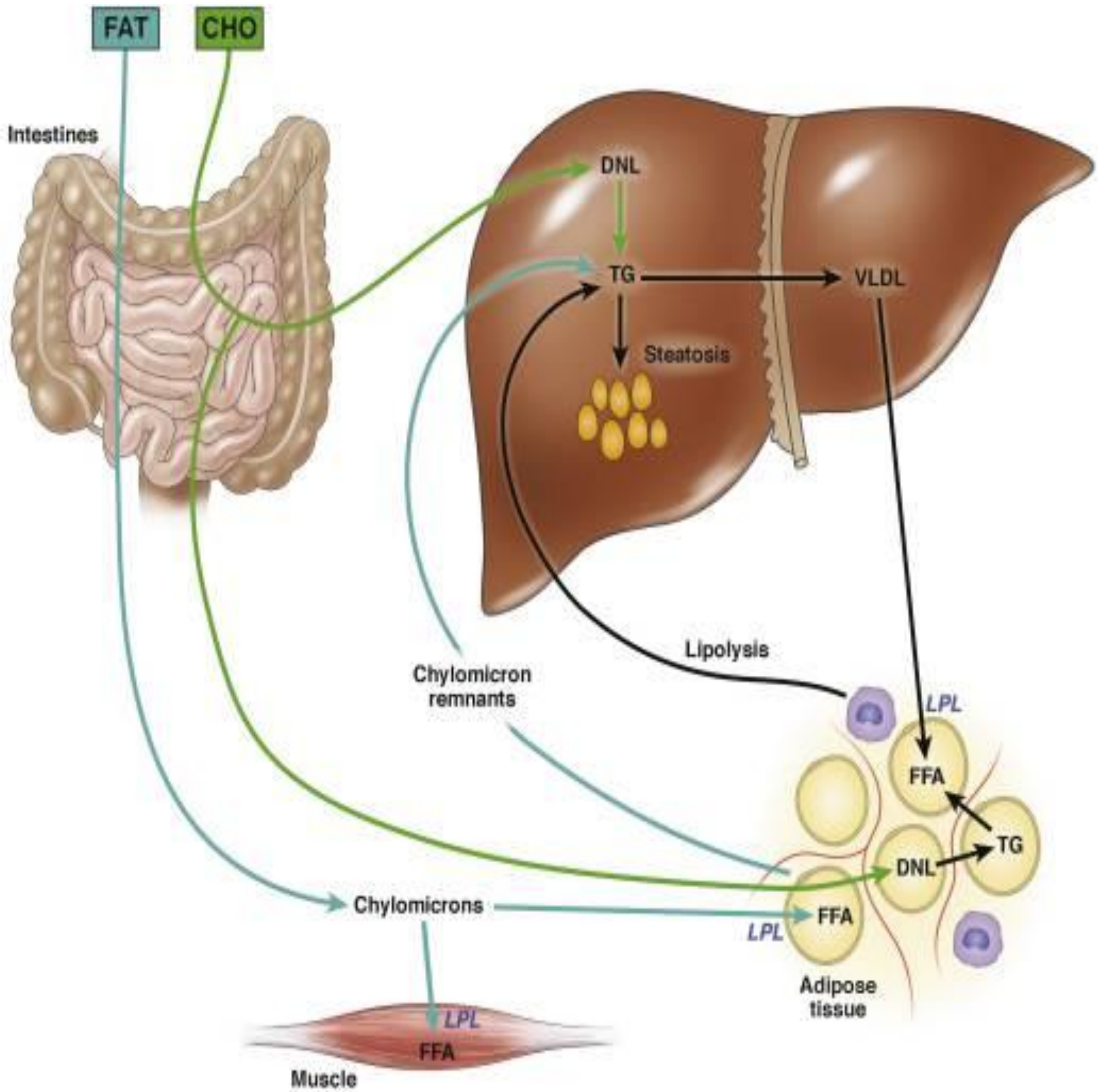

Figure 6: Showing route of dietary carbohydrates and fats to the liver and adipose tissue**.(Duwaerts & Maher, 2019)**

1.8 Pathophysiology of type 2 diabetes

According to recent studies, the dysfunction of β-cells leads to abnormally high levels of glucose in the bloodstream.**(Kautzky-Willer et al., 2016a)** The body is unable to maintain physiological glucose level if the amount of insulin secreted by β-cells is reduced. In the second scenario, liver increases the production of glucose, but muscles, adipose tissue and the liver have a limited uptake of glucose due to insulin resistance (IR). Insulin resistance increases the risk of β-cell dysfunction. The presence of insulin resistance and β-cells dysfunction result in hyperglycaemia which leads to progression to T2DM.**(Galicia-Garcia et al., 2020a)**

The glucose disposition index (GDI) normalizes the response of the β-cells to any degree of insulin resistance (IR). If insulin sensitivity of the peripheral tissues decreases in an individual with normal glucose tolerance (NGT), beta-cells increases the secretion of insulin to maintain normoglyceamia. If the beta-cell cannot increase the secretion of insulin to maintain the normoglyceamia, it will result in glucose intolerance and diabetes.**(Banday et al., 2020)**

1.8.1 Insulin signalling and resistance

A window of optimal physiological level is exhibited by most of endocrine hormones and if the levels of these hormones are either below or above their physiological range, the functions of the organism are compromised. In the case of insulin which is a good example of endocrine hormone both hyperinsulinemia and hypoinsulinemia are detrimental to functions of the body**(Di Pino & DeFronzo, 2019).** The normal levels of circulating insulin in healthy individuals is estimated to be approximately 25 and 70 pmol/l (25-75% percentile).**(Kolb et al., 2020)**

The storage and utilization of glucose in skeletal muscles is promoted by insulin where it increases the transport of glucose and net glycogen. Glycogen synthesis and expression of lipogenic genes in the liver is promoted by the presence of insulin while limiting the expression of gluconeogenic genes and finally the increase of glucose transport, lipogenesis in the white adipose tissue and suppression of lipolysis occurs as a result of insulin secretion.**(Sbraccia et al., 2021).** Insulin binds to insulin receptor on the plasma membrane of skeletal muscles, liver and white adipose tissue to exert its physiological effects. Insulin receptor which composes of two isoforms A and B can be described as a heterotetrameric receptor tyrosine kinase with two insulin binding extracellular alpha subunits.**(Fazakerley et al., 2019)** The two insulin binding sites of insulin receptor have a negative cooperativity where insulin binding on one site inhibits the ability of the other site to bind with insulin. The secretion of insulin signals the liver, adipose tissue and skeletal muscles that there is high concentration of glucose in the bloodstream and they accordingly respond by the increased uptake of glucose by cells for use of energy.**(Petersen & Shulman, 2018)**

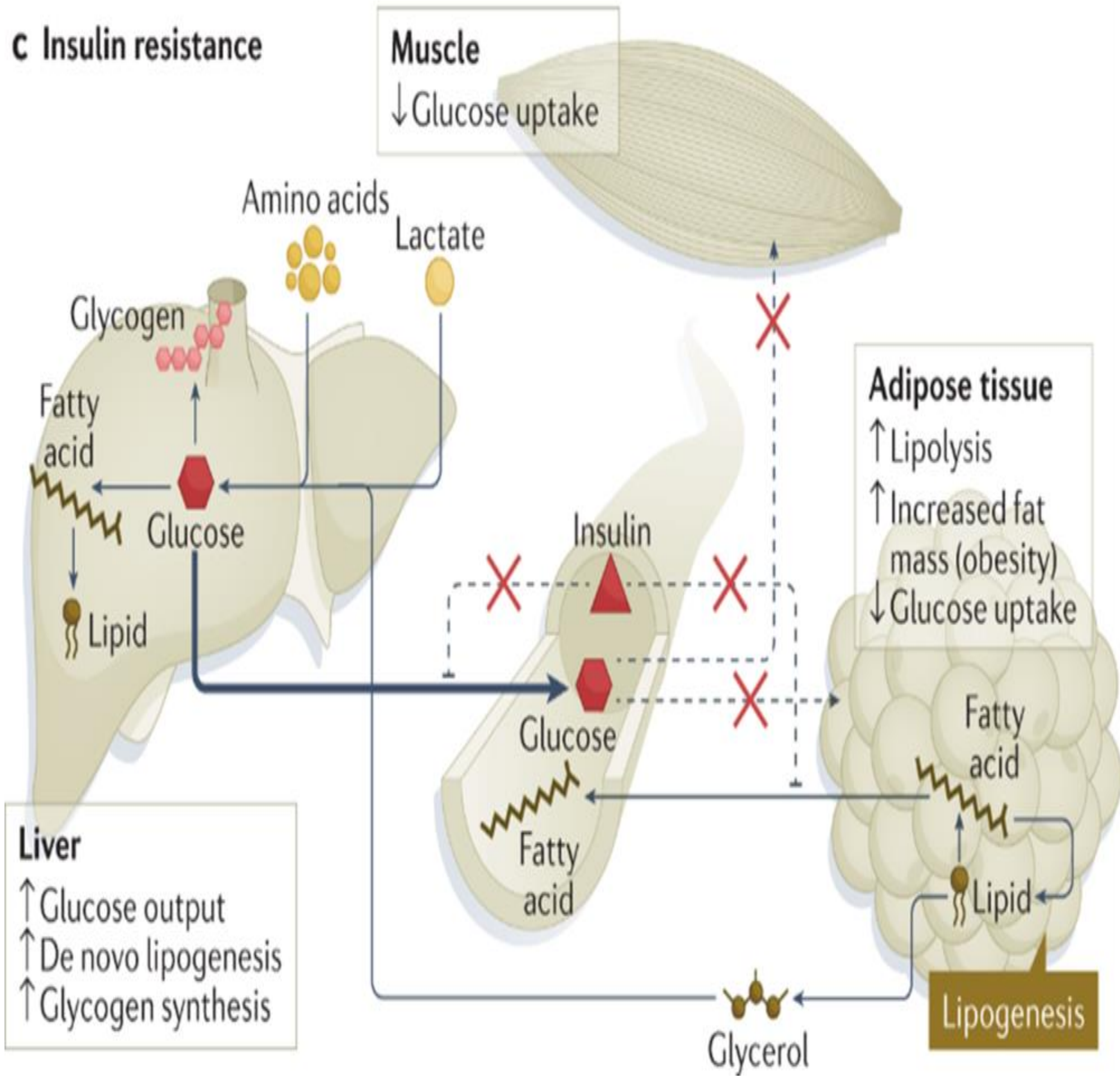

Figure 7: showing mechanism of insulin signalling and resistance.**(Di Pino & DeFronzo, 2019)**

1.8.2 Insulin deficiency

Hyperglycaemia is characterized by the malfunction of the feedback loops between insulin secretion and insulin action. The body is unable to maintain physiological glucose level due to reduced secretion of insulin which is reduced as a result of beta-cells dysfunction. In the case of insulin resistance there's an increased production of glucose in the liver and the uptake of glucose in the adipose tissue, muscle and liver is decreased.**(Ruegsegger et al., 2018)**

According to recent evidence hyperglycaemia, obesity and hyperlipidaemia leads to chronic inflammation and insulin resistance, beta-cells are subject to various toxic pressures due to their genetic susceptibility differences, which include endoplasmic reticulum stress, amyloid stress, metabolic/oxidative stress, inflammatory stress and inflammation which lead to a loss of islet integrity. Insulin precursors or insulin itself undergo defects during their synthesis or disruption of secretion mechanism resulting in dysfunction of insulin secretory which leads to the failure of beta-cells and developing of T2DM**.(Galicia-Garcia et al., 2020b)**

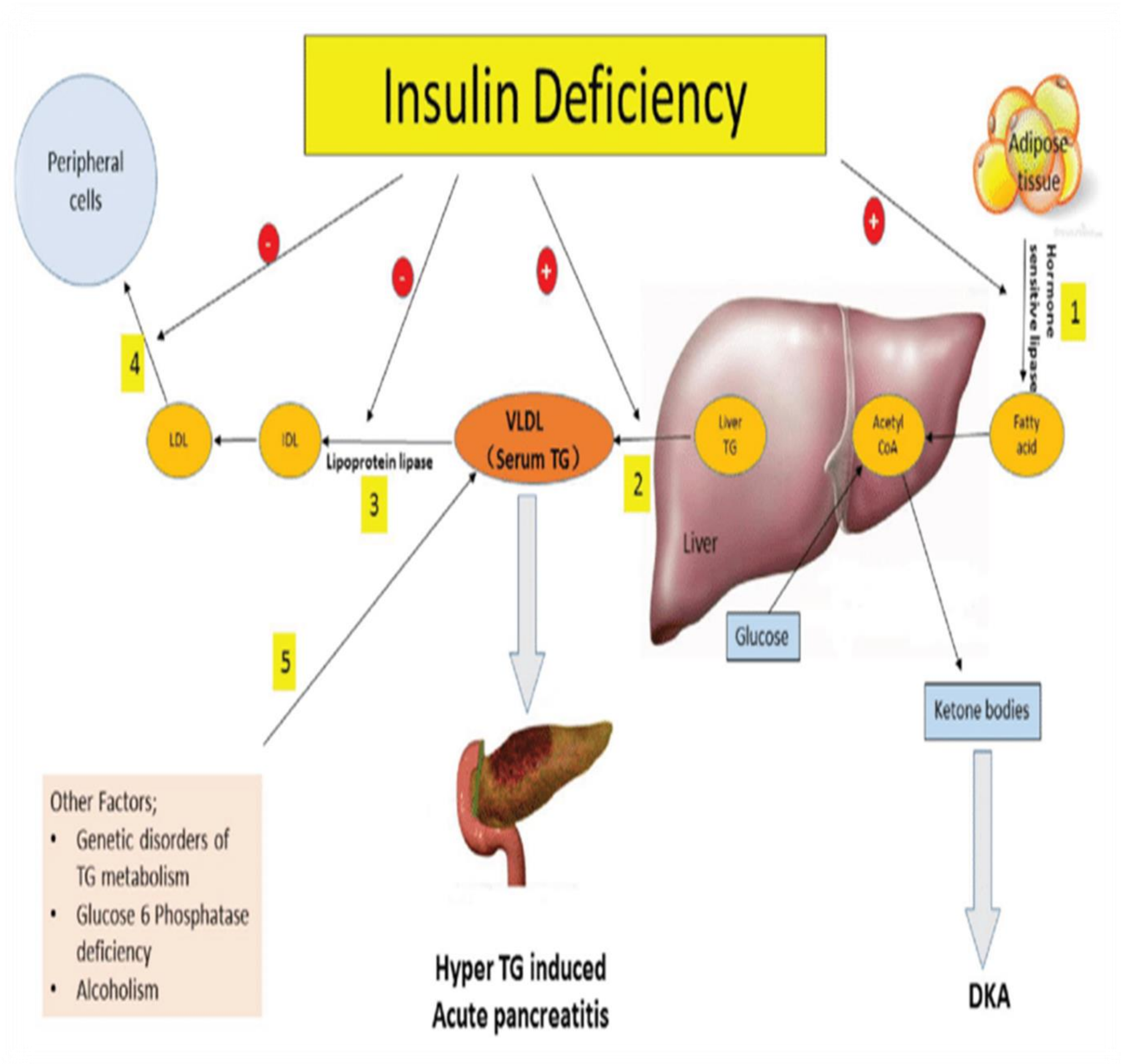

Figure 8: Showing insulin deficiency.**(Y. Wang et al., 2016)**

1.9 Sex and gender differences in development of type 2 diabetes

The recent prevalence of T2DM in the world today has been a great concern for public health, and scientists have taken the task to find every possible risk factor associated to this prevalence, and sex and gender difference is one of the factors they have evaluated its correlation with T2DM.**(Wild et al., 2004)**

Sex hormones such as oestrogen have shown a significant impact in development of T2DM (figure 9). Oestrogen has been reported to stimulate insulin secretion and synthesis as well as offering protection to beta-cells by preventing apoptosis which could be caused by lipotoxicity or oxidative stress. All these important roles of oestrogen put women at a lesser risk of developing T2DM as compared to men.**(T. Li et al., 2021)**

According to cross-sectional and prospective studies available, it is reported that the prevalence of T2DM is more frequent in men with lower BMI and age than women, whereas obesity which is one of the most risk factor associated with T2DM is more likely to occur in women than men.**(Kautzky-Willer et al., 2016b)**.

Males with the habit of being physically inactive present a higher possibility of consuming alcohol as well as their energy intake daily is increased as compared to women making them more vulnerable to develop T2DM.**(Shepard, 2019)**

The localization of adipose tissue in different body parts plays a major role in fat distribution in both genders. Women store most of their adipose tissue in subcutaneous sites which gives them an advantage in body composition and ectopic fat deposition as compared to men who store fat around visceral sites which puts them at a higher risk of developing visceral obesity which is directly associated with T2DM development.**(Tramunt et al., 2020)**

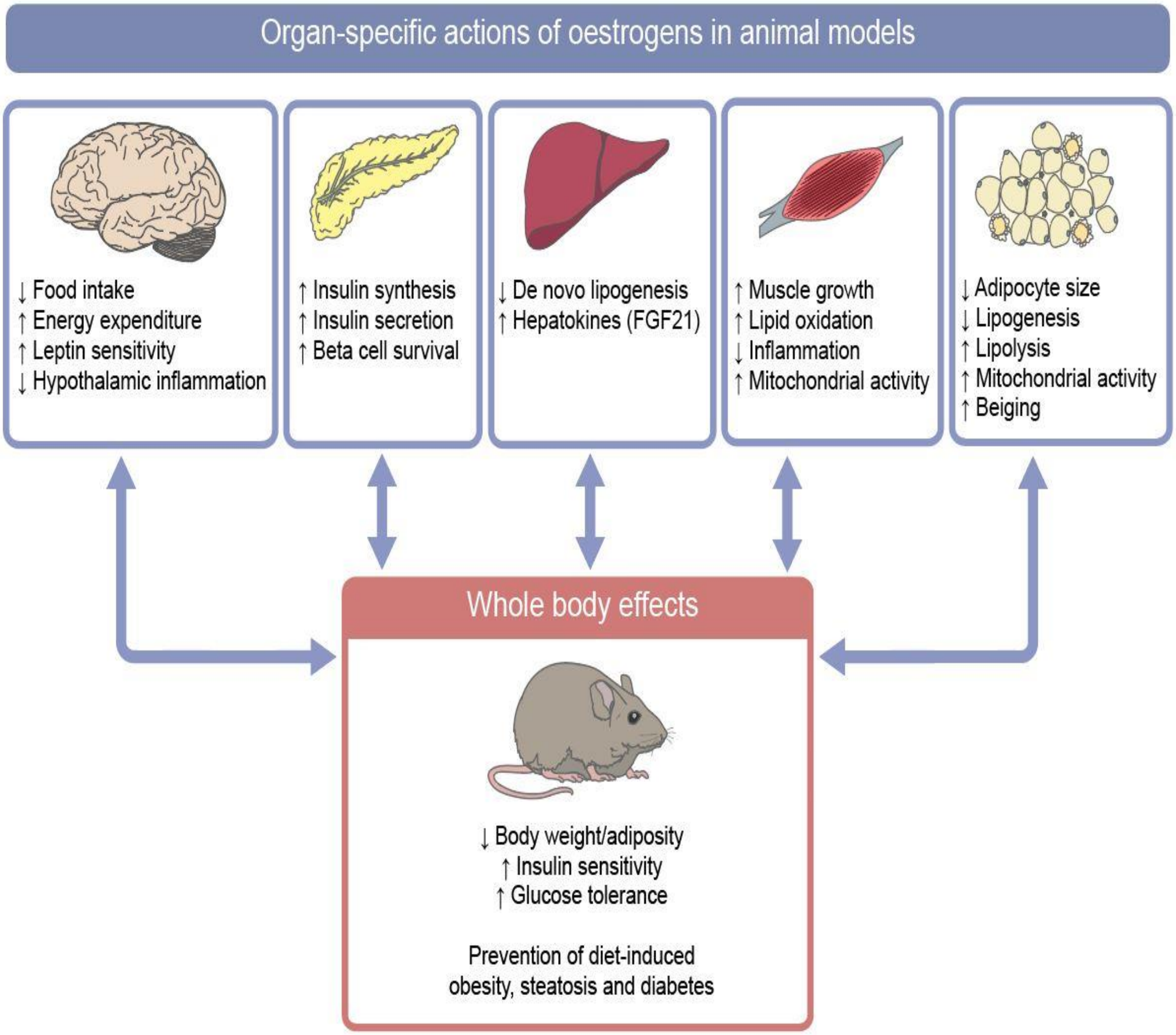

Figure 9: Showing effect of oestrogen on various organs in animal model **.(Tramunt et al., 2020)**

2. Chapter 02

2.1 Diabetes and dyslipidaemia

According to the published study on the world population, the proportion of elderly people aged over 60 years is expected to double outnumbering the younger generation aged 5 years and below by the year 2050. This generation will be vulnerable to cardiovascular diseases.**(Achila et al., 2021)**. Diabetic dyslipidaemia is multifactorial characterized by elevated LDL-cholesterol, postprandial and fasting triglycerides, predominance of small dense LDL, low HDL-cholesterol and poor glycaemic control.**(L. Wu & Parhofer, 2014a)**

Among patients living with T2DM, 65% of them manifest more than 100mg/dl levels of LDL-C at baseline making the prevalence and incidences of diabetic dyslipidaemia and DM relatively equivalent.**(Athyros et al., 2018)**

In case of excess accumulation of TC, cholesterol will eventually assemble in LDL particles, this accumulation results in their longer circulation in the blood stream. This results in oxidation of the particles which leads to stiffness of cell membranes and increased atherosclerotic risk.**(Röhrl & Stangl, 2018)**

It is reported that among all the deaths related to T2DM, 50% are directly associated with coronary heart diseases (CHD)**.(Pokharel et al., 2017)**

2.1.1 Pathophysiology of dyslipidaemia

Cholesterol homeostasis and lipid metabolism are regulated by insulin hormone. At the same time, risk factors such as hyperglycaemia, obesity and metabolic syndrome in patients with T2DM worsen the dysregulated lipid metabolism.**(Sunil & Ashraf, 2020)**

Intermediate-density lipoprotein cholesterol (IDL-C), chylomicron remnants, chylomicrons, VLDL-C make up circulating TGs.**(Opoku et al., 2021).** Patients with T2DM have high circulating free fatty acid (FFA) flux resulting from the process of lipolysis which is promoted by insulin deficiency due to insulin resistance (figure 10).**(Rhee et al., 2021)**

Elevated FFA are associated to destruction of beta-cells of islet of Langerhans and insulin deficiency due to their ability to promotes insulin resistance. hepatic secretion of the TG-rich VLDL-C and production of TG is promoted by increased FFA flux in the liver.**(E et al., 2021)**

The adipocytes increase the level of FFA as a result of the loss of suppressive effects of insulin on lipolysis. The presences of high level of FFA flux in the liver leads to the secretion and assembly of VLDL resulting in hypertriglyceridemia. In the blood, TG in VLDL is transferred to both LDL and HDL. HDL rich in TG are easily cleared from the circulation by the kidney, leaving only a low level of HDL to accept cholesterol. Insulin resistance results in decreased hepatic glycogen synthesis, in the glucose metabolism. This is due to decreased activation of glycogen synthase enzyme, glucose delivery and increased hepatic gluconeogenesis by the liver.**(Ormazabal et al., 2018)**

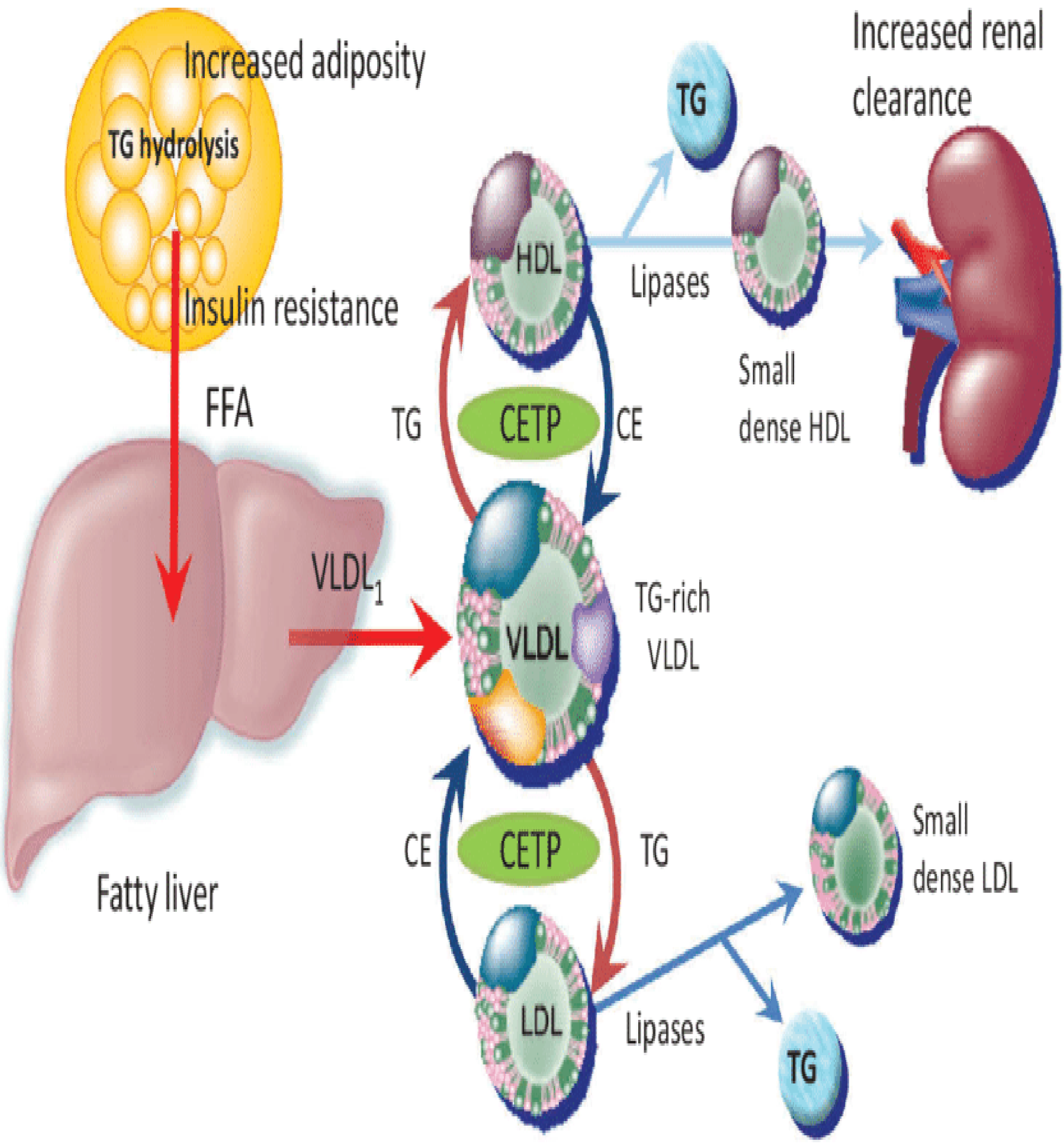

Figure 10: Showing mechanism of dyslipidaemia.**(Brian, 2020)**

3. Chapter 03

3.1 Diabetes and hypertension.

Diabetes and HTN are an invisible epidemic which mortality exceeds that of communicable, maternal and perinatal diseases, have been reported to be on high prevalence in industrialized countries**(Tsimihodimos et al., 2018)**. Diabetes and HTN in most cases exist together. These two diseases DM and HTN are among chronic diseases which can result in premature death, if their detection and treatment is not well managed.**(Nielen et al., 2009).** It is estimated that 70% of type 2 diabetic patients are affected by HTN, while individuals with pre-existing HTN have a 2.5 chance of developing T2DM.**(Climie et al., 2019)**

By the year 2025, HTN is expected to increase to 1.5 billion globally and 125.5 million in sub-Saharan Africa. In the continent of Africa, the prevalence of HTN is estimated to be 33.3% in Northern Africa region and 27% in the whole of sub-Saharan Africa. The MENA region shows the highest age standardized prevalence of HTN of 12.2% in the world. A four-fold increase in mortality rate is associated with the presence of both HTN and diabetes. A sustained high BP ≥ 140/≥ 90mmHg is defined as HTN.**(Abdelbagi et al., 2021)**

Individuals with T2DM experience both microvascular and macro-vascular complications as a result of elevated arterial BP. Various factors such as BMI, age and ethnicity determines the magnitude of T2DM and HTN prevalence**(Alloubani et al., 2018)**. Other factors such as insulin resistance contribute to development of T2DM and HTN where approximately 50% of those with HTN show systemic insulin resistance.**(Pavlou et al., 2018)**

3.1.1 Mechanism of hypertension in diabetes patients

Based on ACC/AHA and ADA guidelines, in 2020 the prevalence of HTN was at 66.0% to 76.3% in DM adults. The risk of developing HTN increases with the presences of DM. **(Lastra et al., 2014)**

A Na+/H+ channel is opened as a result of insulin action; this channel facilitates the exchanges of hydrogen ions out of the cell and the transport of sodium ions into the cell. The reabsorption of sodium from renal tubules increases due to hyperinsulinemia which is caused by insulin resistance, this increase leads to elevated BP.**(Ohishi, 2018)** The increase of circulatory fluid volume which is caused by hyperglycaemia can also lead to elevated BP. The increase of renin excretion as a result of hyperinsulinemia activates the sympathetic nervous system as well as increase the peripheral vascular resistance and cardiac output, this changes increase circulatory fluid volume leading to the elevation of BP.**(Pavlou et al., 2018)**

The co-existence of diabetes and HTN is characterized by insulin resistance, hyperglycaemia and dyslipidaemia which result in cardiovascular diseases (CVDs) complications such as Atherosclerosis, a condition which can result in increased peripheral arterial resistance and narrowing of blood vessels which defines the development of HTN**(Sanchez & Musso, 2021).** Other studies have stated that inappropriate renin-angiotensin-aldosterone system is associated with insulin resistance**.(Abdelbagi et al., 2021)**

Insulin resistance, abnormal renal sodium handling hyperinsulinemia, over-activation of renin-angiotensin-aldosterone system (RAAS) are among well-known pathophysiological mechanisms which contribute the coexistence of DM and HTN. Risk factors for T2DM such as hyperinsulinemia and insulin resistance play a major role in the development of HTN. **(Mortada, 2017)** One of major components of renin-angiotensin-aldosterone system (RAAS) known as Angiotensin II plays a role in the skeletal muscles by causing insulin resistance which results in decreased blood flow and inhibition of intracellular insulin signalling pathways as well as decreasing the secretion of insulin by beta-cells of the pancreas. In a study carried out on animal models Angiotensin II showed a capacity to cause beta-cells dysfunction through overexpression of proinflammatory cytokines and endoplasmic reticulum stress.**(Yildiz et al., 2020)**

MATERIALS AND METHODS

4. Materials and methods

4.1 Principal objectives

Our main objectives for our study were as follows:

- To summarize the benefits of dyslipidaemia treatment for the diabetic patients
- To describe the lipid profile in non-obese type 2 diabetic men.
- To evaluate correlation between pairs of lipid parameters and other parameters such as (BMI, SBP, DBP etc.) in non-obese type 2 diabetic men in the region of Tlemcen.

4.2 Type of study

We carried out a descriptive study of lipid profile on a population of type 2 diabetic men.

4.3 Study population and sample size

4.3.1 Geographical presentation of study area

The study area is located in the Wilaya of Tlemcen. It is geographically limited by the Mediterranean Sea to the north, to the west by the Kingdom of Morocco, to the northeast by the Mtella plain (Wilaya of Ain Témouchent) and to the east by the mountains of Daya (Wilaya of Sidi Belabes) and finally to the south by the high plains of the Wilaya of Naama.

The Wilaya of Tlemcen (north-west Algeria) is characterized by four (04) large distinct natural units which can be identified as follows: a coastal unit, the sublittoral plain, a set of high steppe plains.

The towns in which we conducted our study are divided into these sets, which present specific characteristics concerning the climate, the water network and land use. It has 949,132 inhabitants over an area of 10,182 km². The population density of the Wilaya of Tlemcen is therefore 93.2 inhabitants per km².

Tlemcen, Maghnia and Mansourah are the largest towns in the Wilaya of Tlemcen among the 53 towns that compose it. The dry and cold semi-arid climate is the main climate of the Wilaya of Tlemcen**(*Worlddata.Info,* 2022).** The Wilaya of Tlemcen is divided into 20 daïras: the daïra of Aïn Tallout, the daïra of Bab El Assa, the daïra of Beni Boussaid, the daïra of Beni Snous, the daïra of Bensekrane, the daïra of Chetouane, the daïra of Fellaoucene, the daïra of Ghazaouet, the daïra of Hennaya, the daïra of Honaïne, the daïra of Maghnia, the daïra of Mansourah etc. (figure 11)

Figure 11: Showing the geographical location of Wilaya of Tlemcen.(***Worldmap*, 2019**)

Our study targeted non-obese type 2 diabetic men from Western part of Algeria-Tlemcen. A total of 30 participants were involved.

4.3.2 Inclusion criteria

- ✓ All male individuals with T2DM
- ✓ Adults aged between 54years and 88 years old residing in Tlemcen.
- ✓ Subjects with all the information from the provided questionnaire.
- ✓ Consent to participate.

4.3.3 Exclusion criteria

We excluded from our sample any person:

- ✓ With T1DM
- ✓ Obvious cognitive disorders
- ✓ Patients with obesity

4.4 Data collection

All the data needed for our study was collected between the year 2019 and 2022. The samples were analysed in medical laboratories within Tlemcen such as EPSP (ROAG), AGHADIR, EPSP Chetouane and EPH Remchi. When it was not possible to visit these identified locations due to the outbreak of covid-19 the necessary analyses were carried out from private laboratories.

- ❖ Visiting participants were required to answer a standard questionnaire intended to collect information about age, lifestyle factors, medical history etc.
- ❖ General clinical measurements such as height, weight, BP (average of two reading) was recorded for all participants. Weight and height were recorded.
- ❖ The blood samples were carefully analysed for biochemical parameters (glycaemia, cholesterol, HDL-C, LDL-C, TAG)

4.5 Biochemical parameters

4.5.1 Glycaemia

Abnormal values for glycaemia (Fasting blood glucose: ≥ 126 mg per dL (7.0 mmol per L) HbA1c measurement: ≥ 6.5 percent were determined according to ADA criteria.**(American Diabetes Association, 2020)**

4.5.2 Lipid parameters

Abnormal values (TC: ≥ 170mg/dL; HDL: ≤ 40mg/dL; LDL: ≥110mg/dL and TG: ≥ 90mg/dL were determined according to established criteria [cholesterol levels: Expert panel, National cholesterol Education Program (NCEP)].**(Kuhar, 2002)**

- **Calculation of LDL cholesterol (LDL-C)**

The LDL cholesterol concentration in the sample is calculated by the "FRIEDWALD" formula, provided that the TG concentration is less than 4 g/l.

LDL-C (g/l) = total cholesterol-HDL-C – (TG/5).(Kuhar, 2002)

NB: LDL-C should be measured by direct assay if triglycerides are ≥ 4 g/l.

4.6 Statistical analyses

The processing and calculation of the results as well as correlation between the parameters were carried out by the software Minitab version 16.2.3 and Excel 2016. We used ANOVA one-way factor and Pearson correlation to find the relationship between lipid profile and to compare them with other parameters such as Age, BMI, Diet, SBP, DBP etc.

Indeed, Microsoft Word was used for the design of the texts, the data entry and the presentation of the tables and figures of the results. Minitab was used to design plot of correlation while Microsoft excel was used to design the histograms for all the parameters of our study.

RESULTS

5. Results

5.1 Description of the study population based on various considerable parameters.

5.1.1 Description of study population by Age

Based on the total number of our study population, we were able to group all the patients according to age where we had two groups of those with the age of (≤65 years) and those with the age of (>65 years).

We found 16 patients representing 53.33% of the total population who were ≤65 years and the other 14 patients representing 46.67% were above the age of >65 years. (Figure 12)

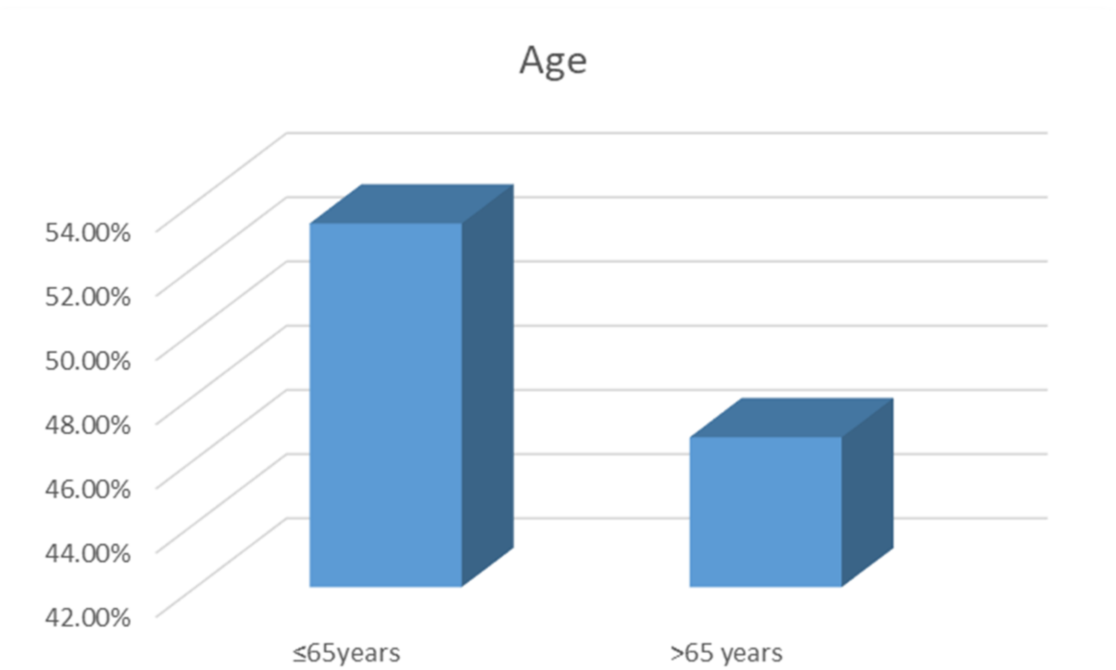

Figure 12: Description of study population according to Age

5.1.2 Distribution of study population according to their BMI.

Our study population was divided into two categories based on their BMI. The first category was those who had normal weight while the second category was for those who were overweight.

Among 30 patients who participated in our study, 11 of them which represented 36.7% had normal weight while the rest 19 (63.3%) were overweight. The category of each group was determined according to CDC criteria where a BMI of between 18.5-24.9 was considered as normal/healthy weight, while a BMI of between 25.0-29.9 was considered as overweight. The distribution of BMI is well illustrated in (figure 13).

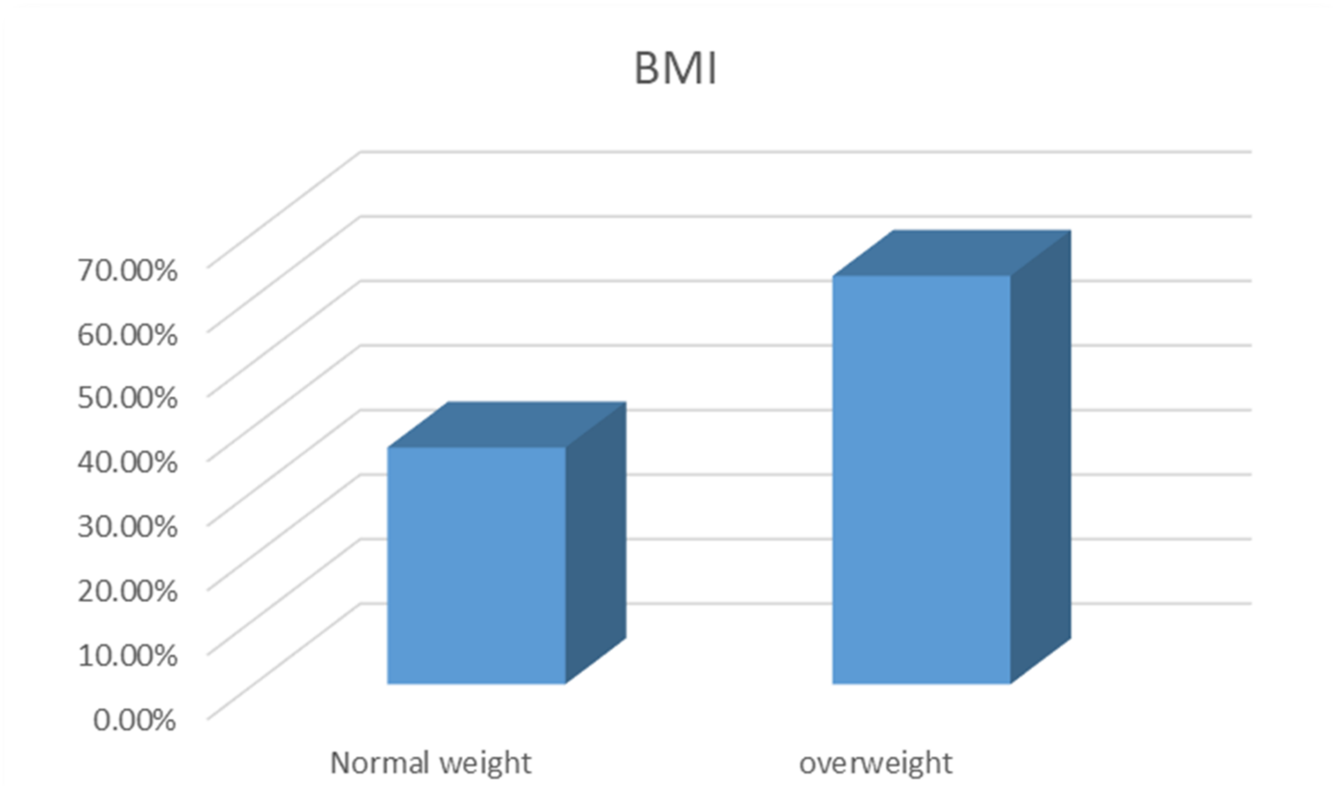

Figure 13: Distribution of study population according to BMI

5.1.3 Description of study population based on diet.

In order to understand the lifestyle (nutrition) of all the patient, we included questions intended to find out those who were on any kind of diet in their life. Those who followed a diet were supposed to respond (YES) to this question and those who did not follow any diet responded by saying (NO).

Out of 30 patients, only 10 of them which is 33.3% were following diet while the rest 20 which is 66.7% of the study population did not follow any diet in their daily life. (figure 14)

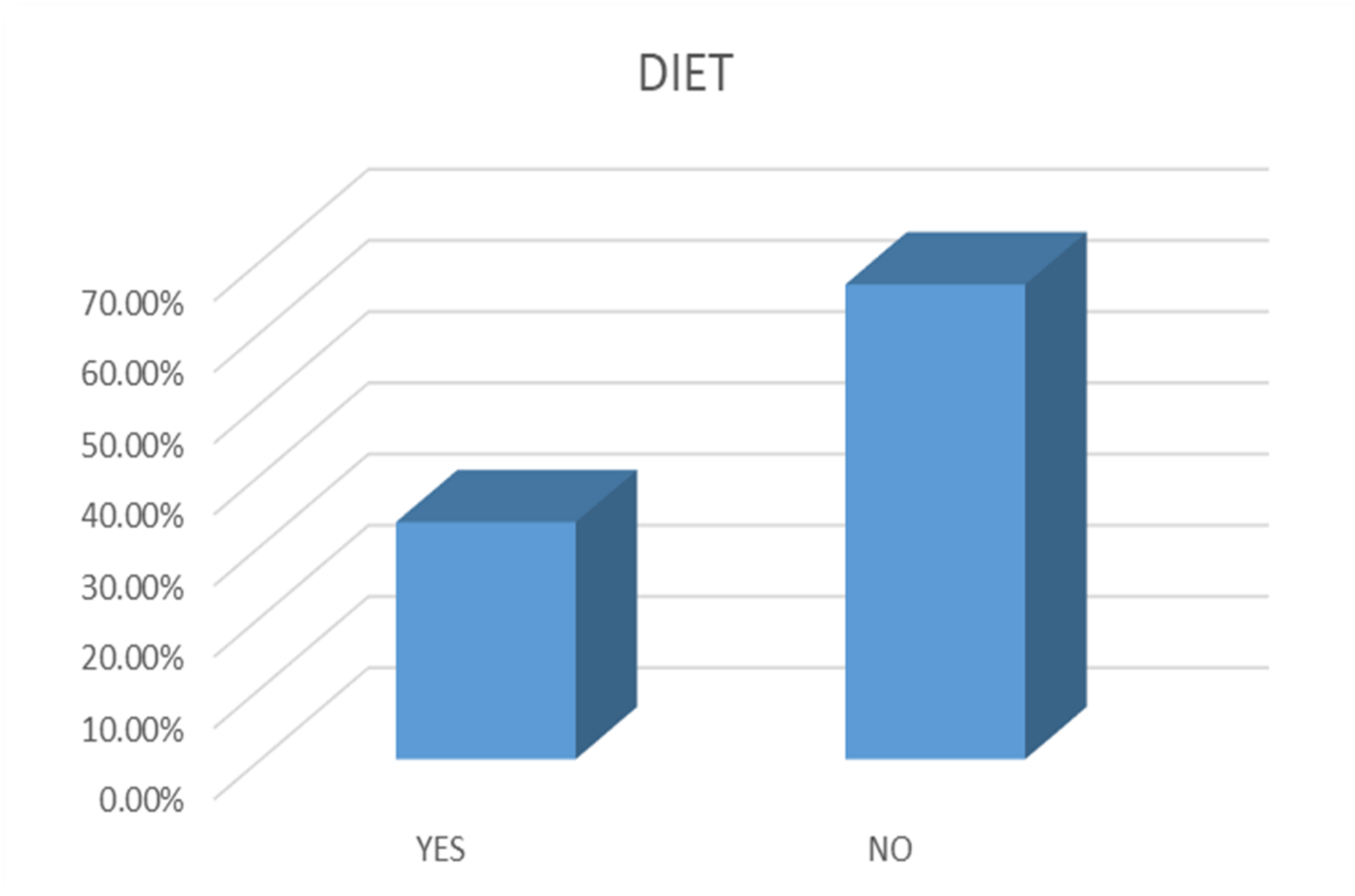

Figure 14: Distribution of study population according to diet

5.1.4 Description of study population based on diet result.

After identifying those who were on diet, we further took into consideration the impact the diet had on their health. For this question, the patients were supposed to respond either by (no effect) if the diet they were following did not show any positive impact on their health, those who noticed a minimum impact of their diet responded by (moderate) and those who their diet showed maximum positive impact on their heath responded by (excellent).

Among the 30 patients, 20 of them which was 66.7% did not follow any diet hence they were not considered in the category of diet result, only 10 patients were taken into consideration.

Out of those who followed the diet, 1 patient which represents 3.33% did not notice any impact of their diet. Five other patients which is 16.67% noticed moderate impact from their diet while the rest 4 patients representing 13.33% of study population, their diet showed excellent results. (figure 15)

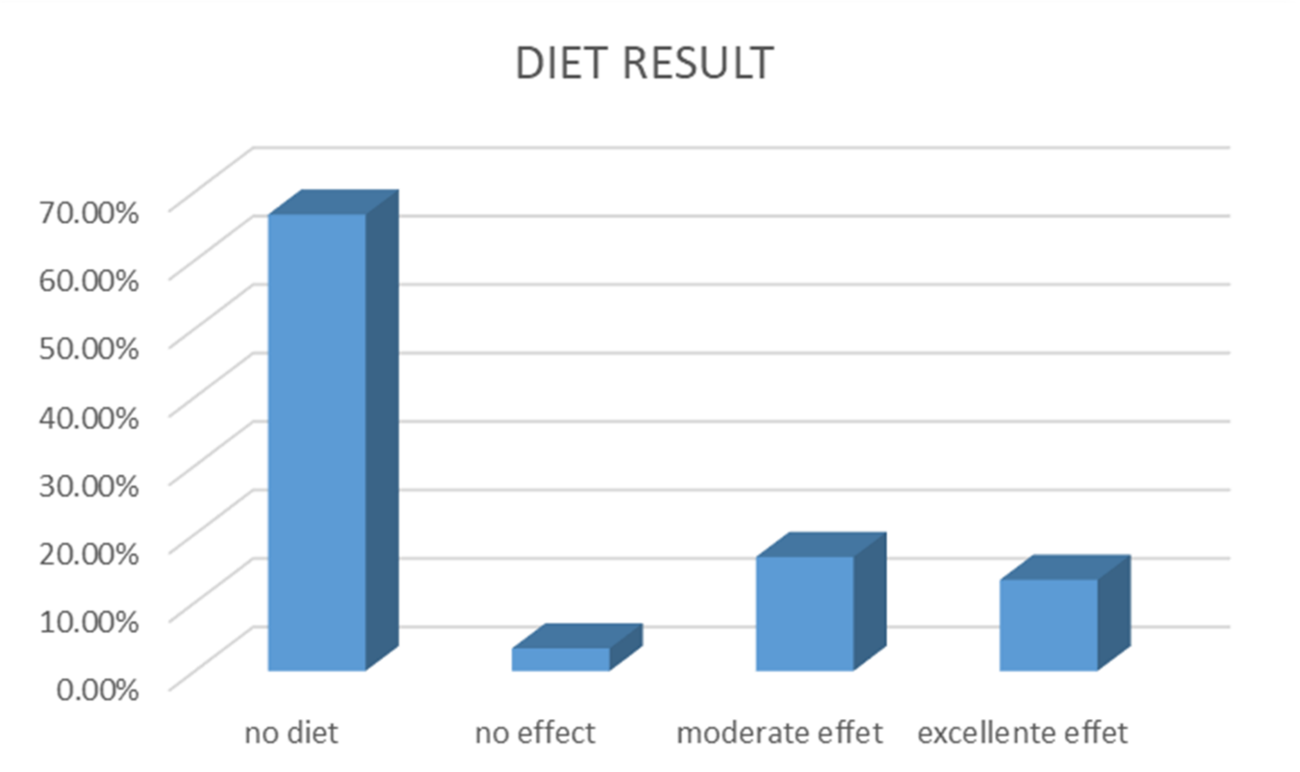

Figure 15: Description of study population based on their diet result

5.1.5 Description of study population based on sport activities.

To accomplish our goal of identifying the patients among all the 30 participating patients who were involved in physical activities, we asked a question to every patient intended to know whether they were taking part in any sportive activity in their life. Those who practiced any sport activity responded by (YES) while those who did not take part in any sportive activity responded by (NO).

Out of the 30 patients who took part in our study, 2 among them which represented 6.7% took part in sportive activities while the rest 28 patients representing 93.3% did not practice any sportive activity in their daily life. (figure 16)

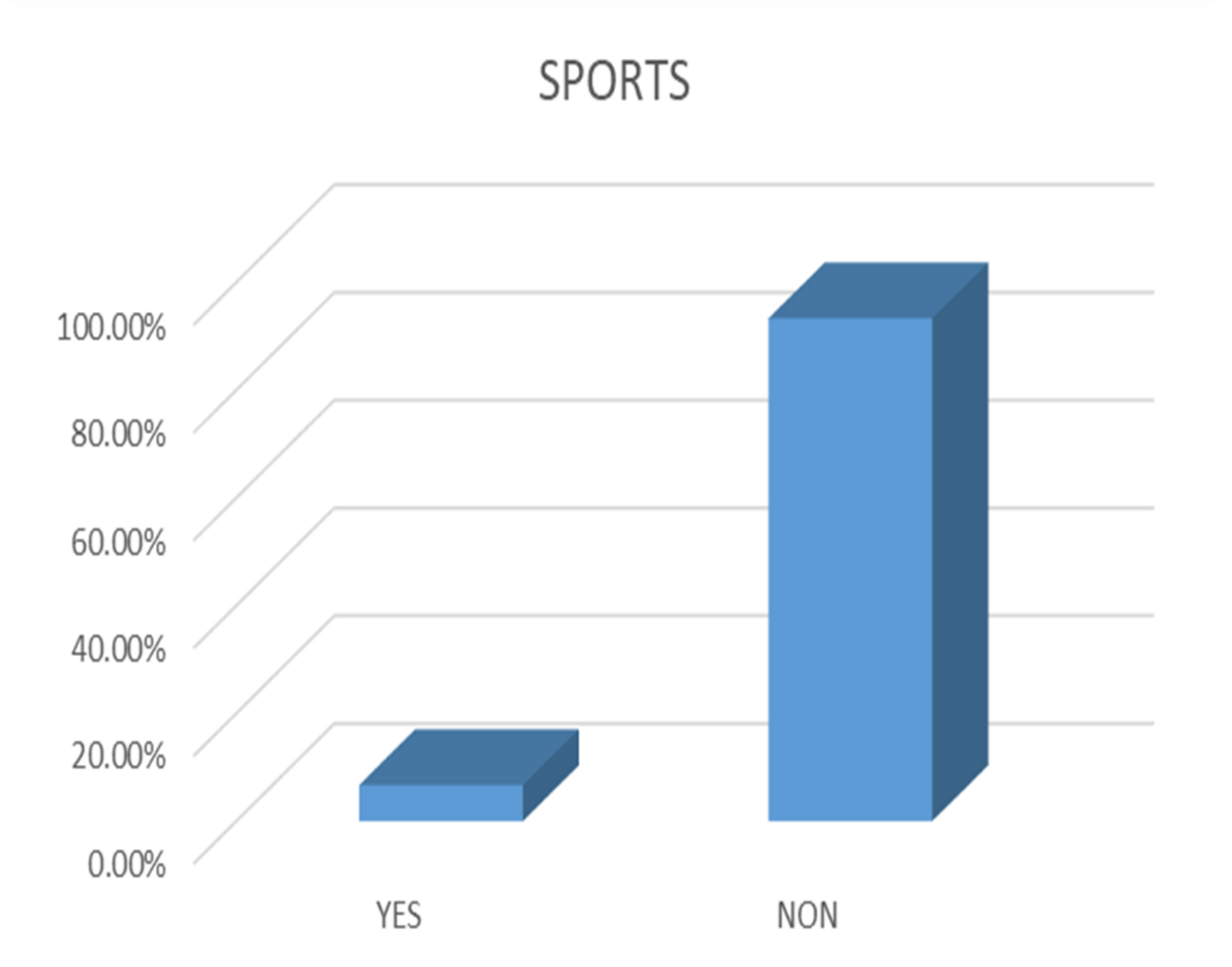

Figure 16: Description of study population based on sport activity

5.1.6 Description of study population based on other pathologies

We intended to find out if all 30 patients had other pathologies other than type 2 diabetes. Every patient was required to respond by mentioning the number of other pathologies; if any.

We found that 16 patients, which represented 53.3%, had only type 2 diabetes without other pathologies. Two patients (6.7%) had only one other pathology other than type 2 diabetes. Other 7 patients representing 23.3% of the study population had 2 other pathologies. Another 2 patients representing 6.7% had three other pathologies. Another 2 patients, which is 6.7%, had 4 more other pathologies other than type 2 diabetes, and 1 patient representing 3.3% had six other pathologies other than type 2 diabetes. (Figure 17)

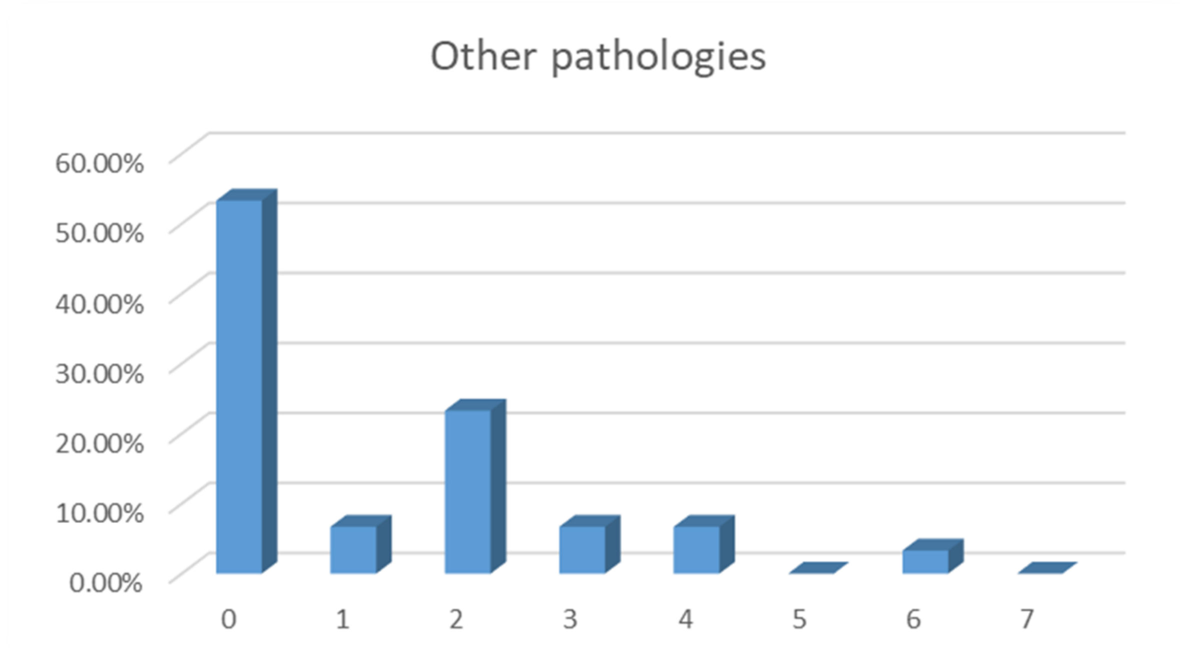

Figure 17: Description of study population based on other pathologies

5.1.7 Description of study population according to total cholesterol level.

After analysing the level of total cholesterol in all 30 patients, we categorized the results into two categories. The first category comprised of those who had normal total cholesterol and the second category comprised of those who had hypercholesterolemia.

These two categories were based on the criteria published by **(Rhee et al., 2021),** any level ≤ 200 mg/dl was considered desirable or normal total cholesterol while any level above 200 mg/dl was considered borderline high or hypercholesterolemia.

Out of 30 patients, 21 of them which represented 70% of the total number, had desirable or normal total cholesterol level. The rest 9 patients, which was 30% of the total patients, had borderline high or hypercholesterolemia. (Figure 18)

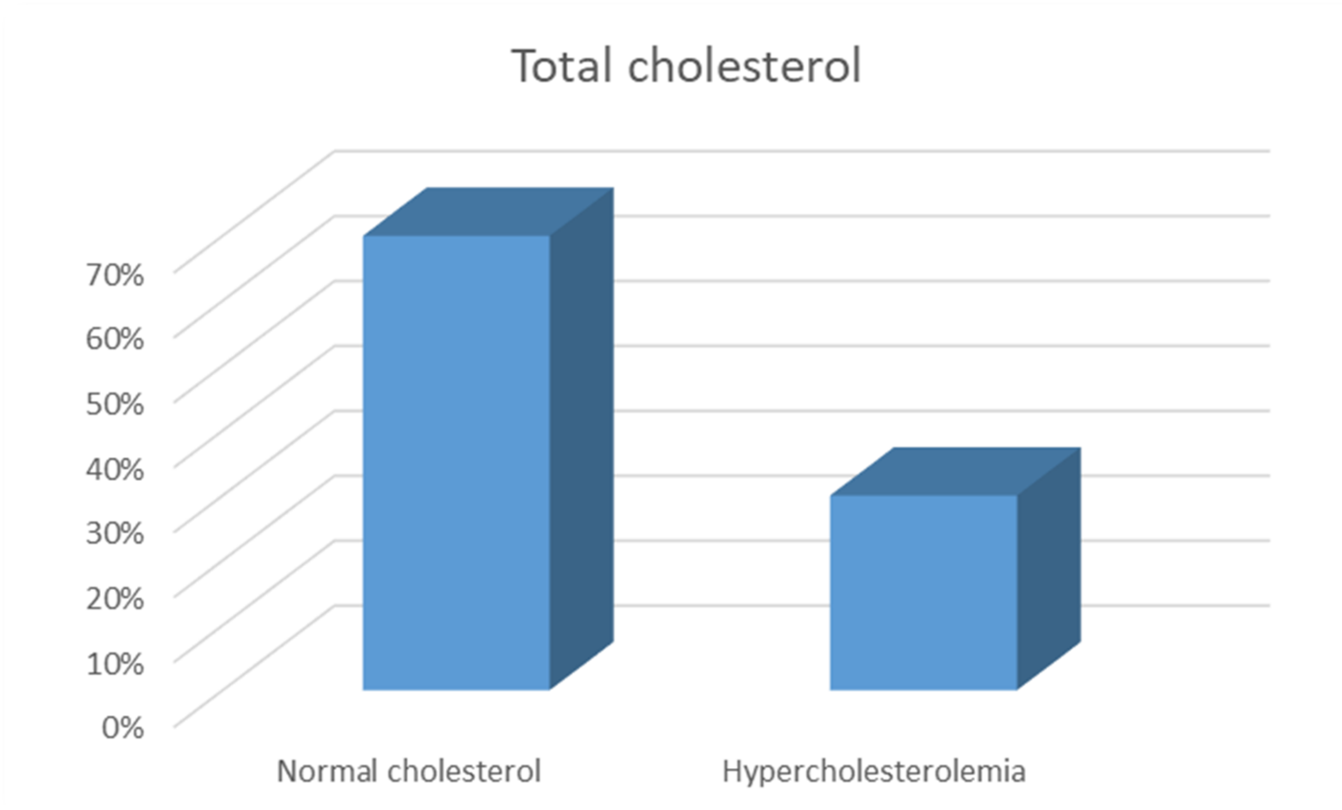

Figure 18: Description of study population based on their total cholesterol levels

5.1.8 Distribution of study population according to their LDL level

We were able to group the study population into two categories. The first category constituted of patients with normal LDL range below 129 mg/dL. While the second category comprised of those with high LDL level ranging above 130 mg/dL.**(Rhee et al., 2021)**

Among the 30 participating patients, 24 of them representing 80% of the study population had normal LDL level, while the rest 6 of the population representing 20% of total population had high LDL level. (Figure 19)

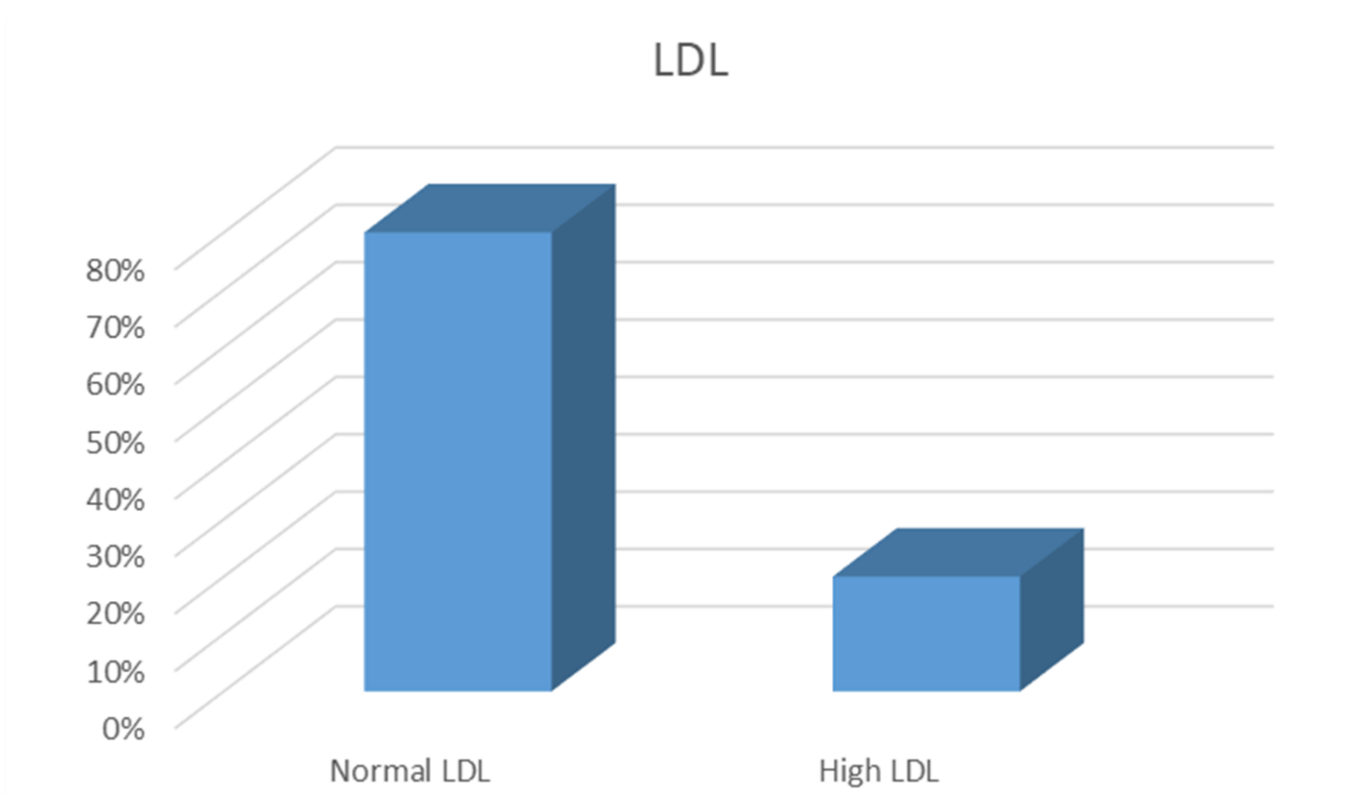

Figure 19: Description of study population based on their LDL level.

5.1.9 Description of study population according to their HDL level

After the analyses of the HDL level of every patient, we were able to group them into two categories. The first category was those who had a desirable or better HDL level of 40mg/dL and above while the second category was those with poor HDL level ranging below 40mg/dL.**(Rhee et al., 2021)**

Out of 30 patients, 12 of them representing 40% of the total population had poor HDL level, while the rest 18 patients, which was 60% of the total population had better or desirable HDL level. (figure 20)

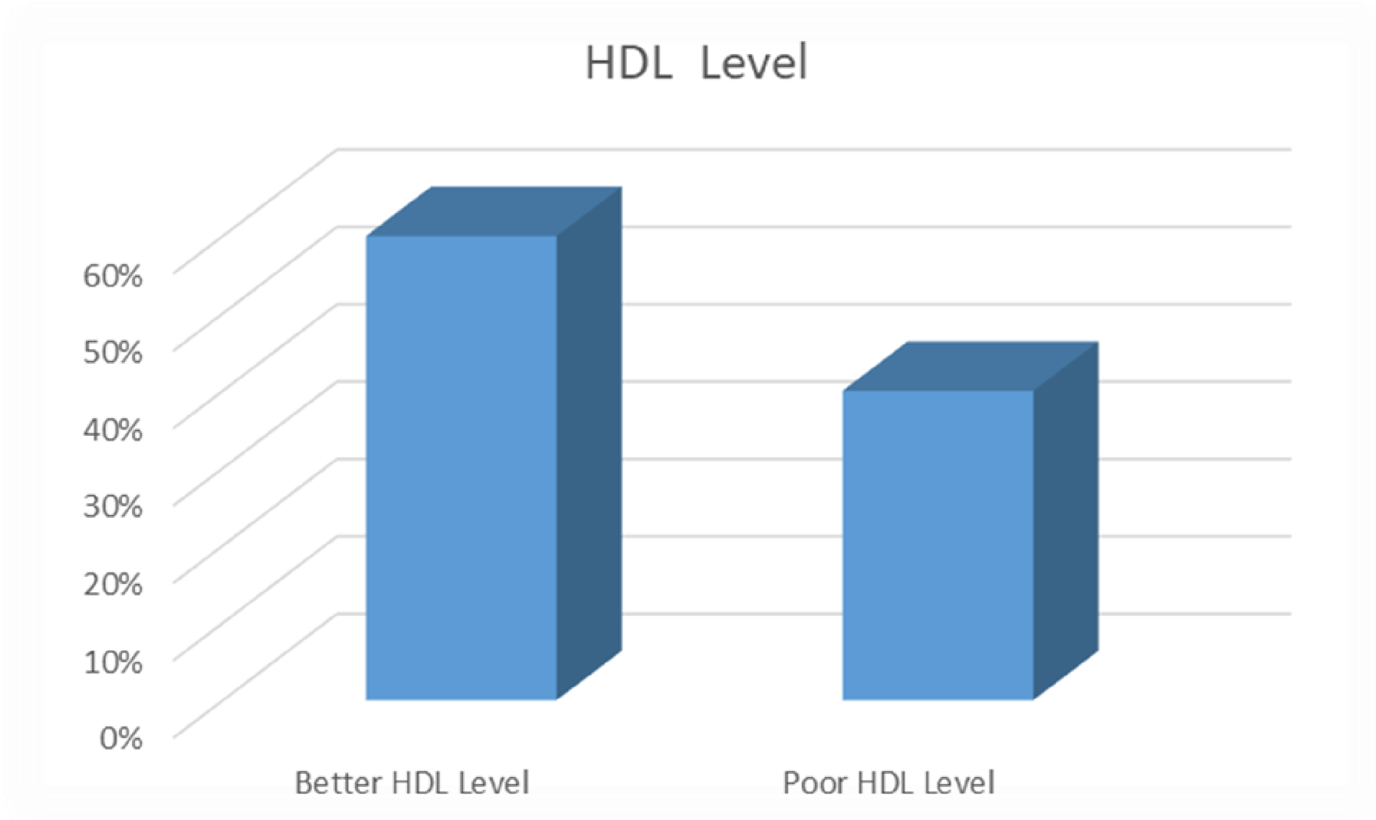

Figure 20: Description of study population according to their HDL level

5.1.10 Description of study population based on their TG level

Our population was categorized according to their TG level, where we were able to group them into two groups. The first group comprised of those with normal/desirable TG level of below 150mg/dL. While the second group they had high TG level ranging above 150mg/dL. **(Rhee et al., 2021)**

We found that 15 out of 30 patients representing 50% of the total population, had normal TAG level, while the rest 15 patients representing 50% of total study population had high level of TAG. (Figure 21)

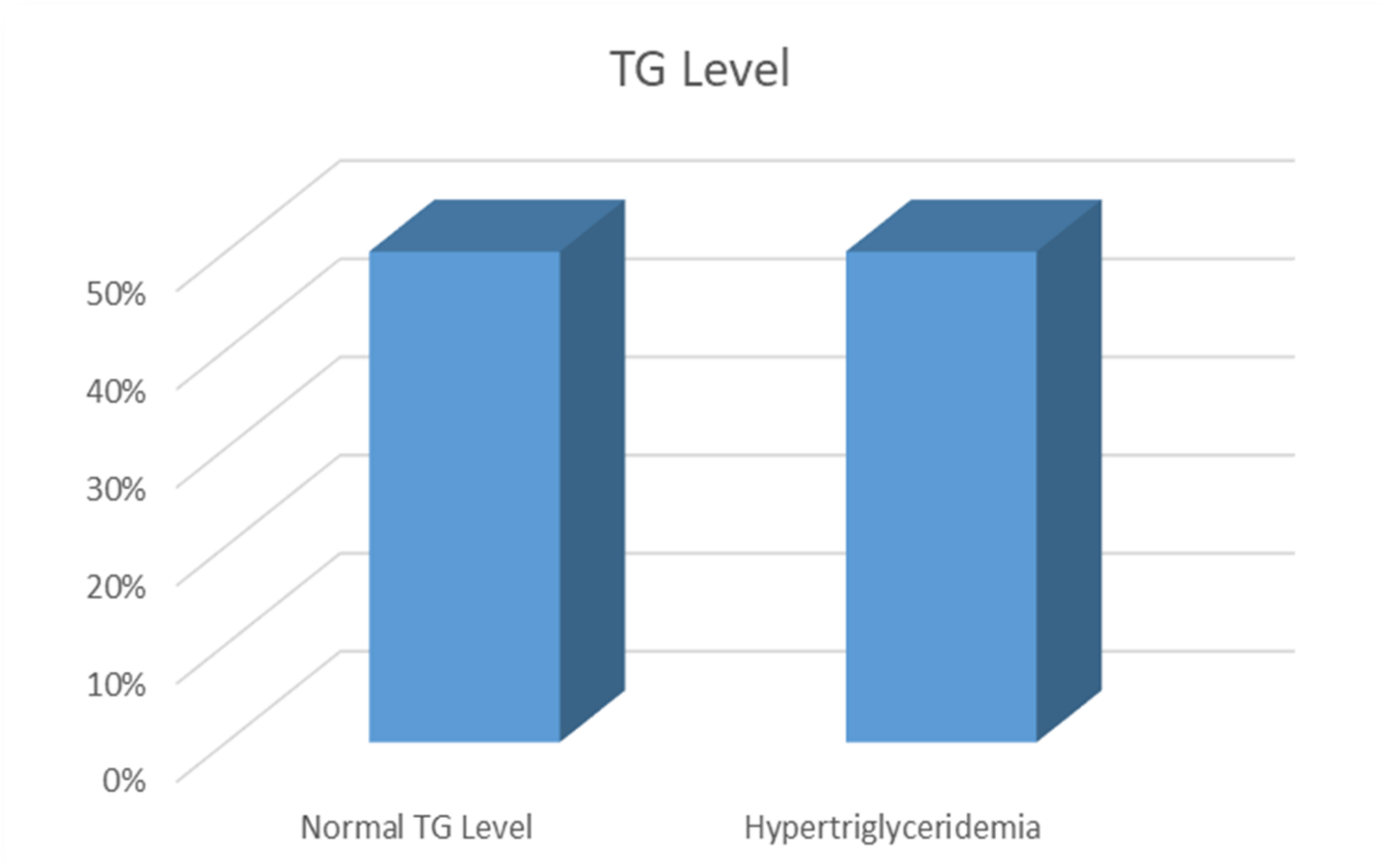

Figure 21: Description of study population according to their TG level

5.1.11 Description of study population according to their systolic BP

Our study population was described and categorised according to their systolic BP. Based on the results obtained, we were able to categorize all the 30 patients into two categories. The first category comprised of patients with normal systolic BP ranging below 120mmHg while the second category constituted of those with high systolic BP ranging over 120mmHg based on (National Institute of Health) criteria.

After evaluating all the systolic BP from the 30 patients, we found that 8 patients representing 26.7% of the total study population had normal systolic BP, while the rest 22 patients (73.3%) had high systolic BP. (figure 22)

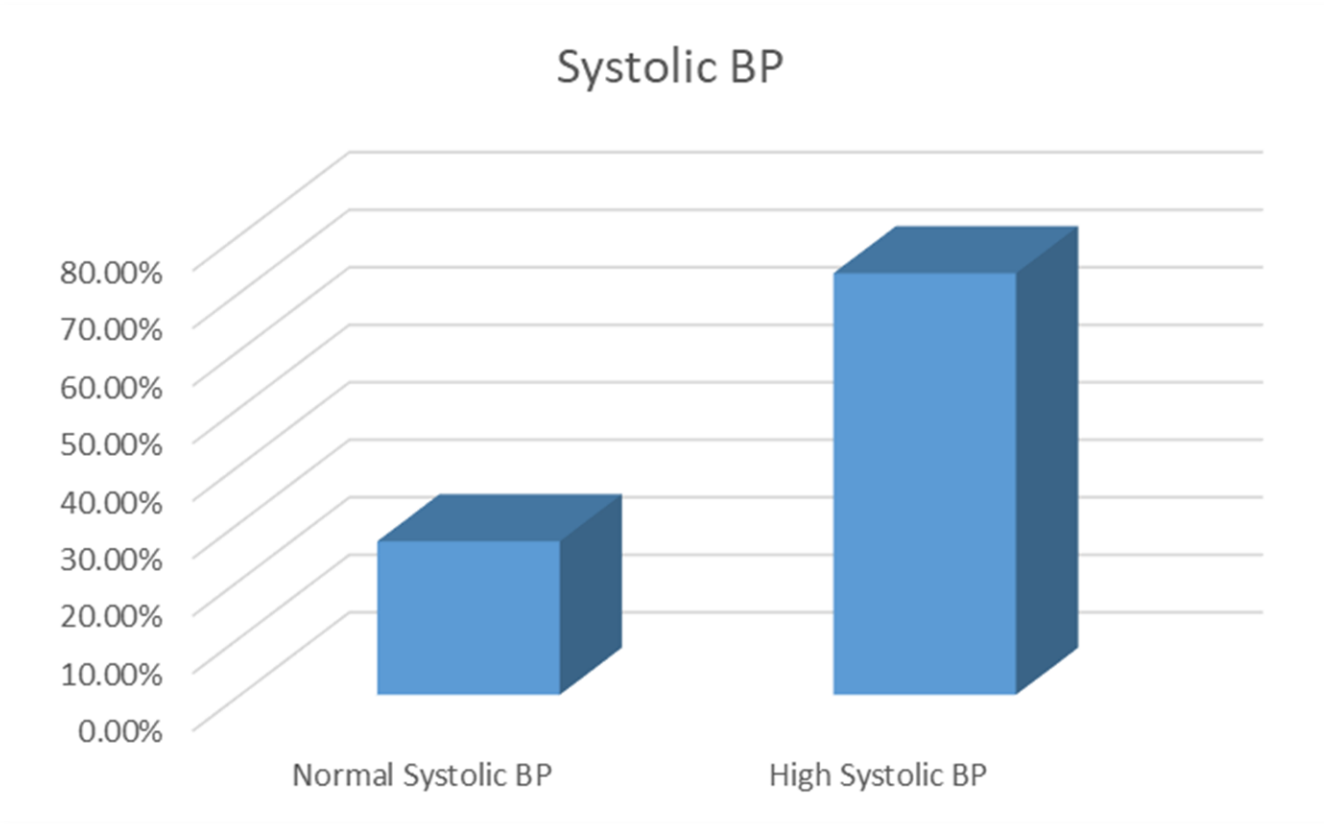

Figure 22: Description of study population according to their systolic BP.

5.1.12 Description of study population according to their diastolic BP.

All the reading of diastolic BP was carefully recorded and the results enabled us to categorize our patients into two groups. The first group comprised of those with normal diastolic BP ranging below 80mmHg, while the second group comprised of those with high diastolic BP of 80mmHg according to (National Institute of Health) criteria.

We found that 21 patients, which was 70% of the study population had normal diastolic BP, while the rest 9 patients representing 30% of the total study population, had high diastolic BP. (Figure 23)

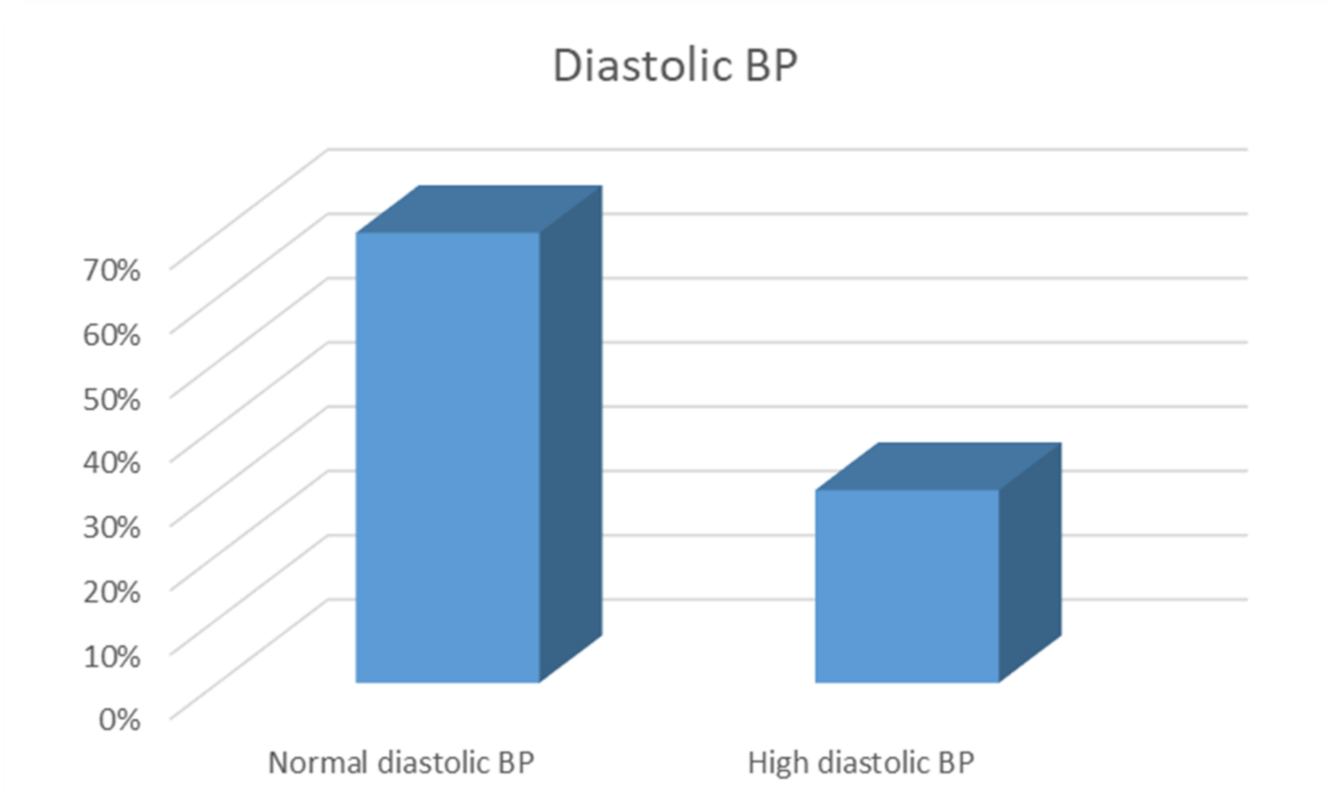

Figure 23: Description of study population according to their diastolic blood pressure

5.1.13 Description of study population according to waist circumference

The measurements for each patient's waist circumference were carefully recorded in order to determine the risk factor for aggravation and associated diseases such cardiovascular diseases (CVD) since high waist circumference is among the risk factors for T2DM.

We were able to group our patients into two groups based on the waist circumference results. The first group constituted of those with normal waist circumference ranging below 94cm(37in) while the second group comprised of those with high waist circumference ranging above 94cm(37in) according to (British Heart Foundation) criteria.

We found that 27 patients, representing 90% of our study population had normal waist circumference while the rest 3 patients representing 10% of study population had high waist circumference. (Figure 24)

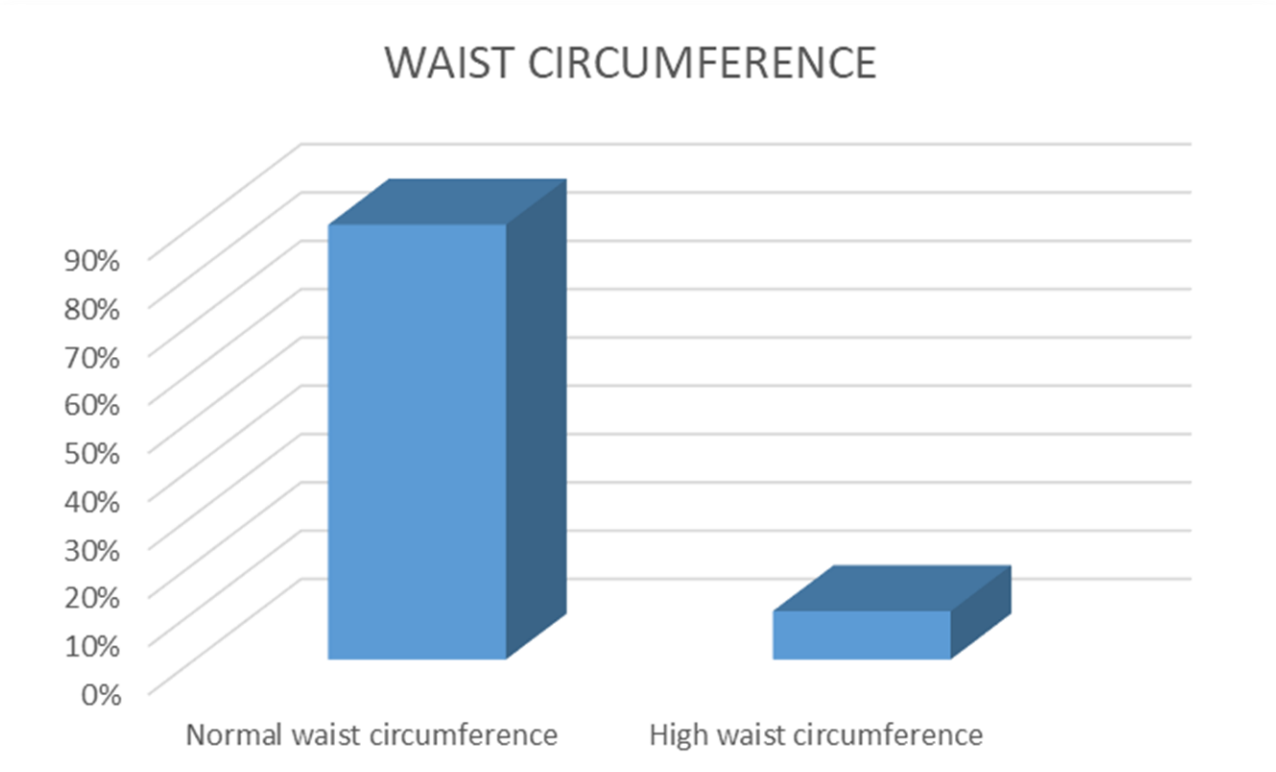

Figure 24: Description of study population according to their waist circumference

5.1.14 Description of study population according to their Glycated Hemoglobin (HbA1c)

Blood samples of all patients were tested to determine the level of glycated haemoglobin (HbA1c.

Based on the results obtained we were able to describe our study population into two groups. The first group were those who had glycated haemoglobin ranging between 5.7% to 6.4%, which signalled normal HbA1c. The second group had glycated haemoglobin ranging 6.5% and above, which means they had elevated level of HbA1c.

We found 2 patients, which represents 6.67% of the total study population, had normal level of HbA1c, while the rest 28 patients representing 93.33% of the population had high HbA1c. (Figure 25)

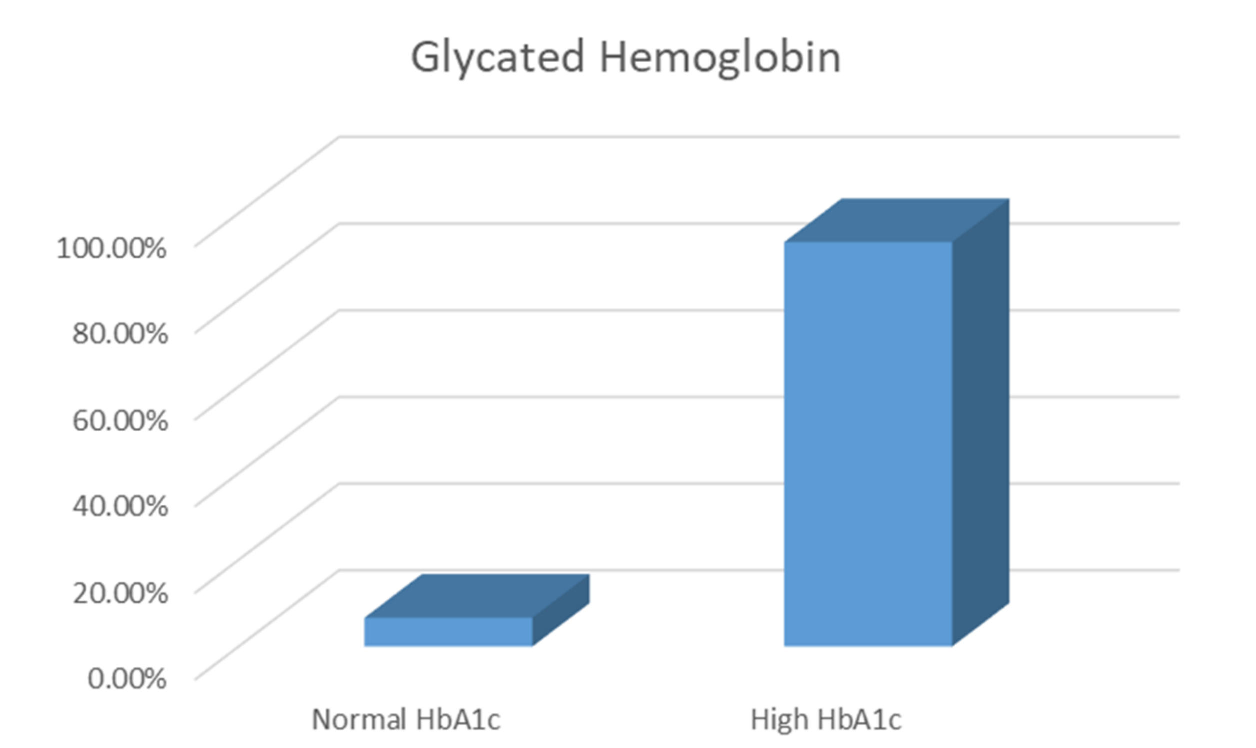

Figure 25: Description of study population according to glycated haemoglobin test (A1c)

5.1.15 Description of study population according to fasting blood glucose.

All the participating patients were tested for their blood glucose to determine the level of their fasting blood glucose. The results helped us to identify the level of glucose in the blood stream of all the patients.

We were able to categorize our study population into two categories based on the results obtained. The first category comprised of those patients with normal fasting blood glucose ranging between 100 to 125 mg/dL. The second category comprised of patients with high fasting blood glucose ranging 126mm/dL or higher.

We found 6 patients, which is 20% of the total study population, had normal glycaemia while the rest 24 patients representing 80% of our study population, had high level of blood glucose. (figure 26)

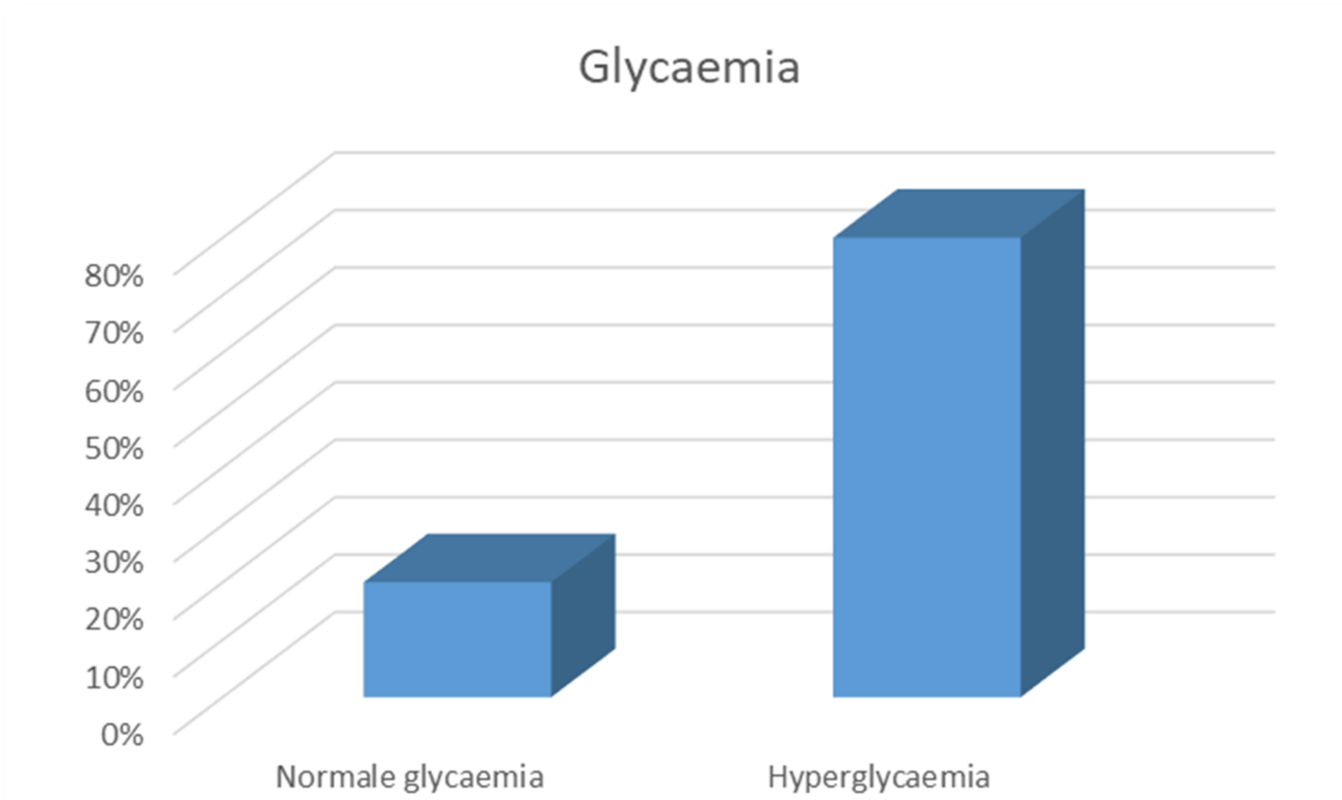

Figure 26: Description of study population according to their glycaemia

5.2 The correlation and relationship between lipid profile and various parameters

We intended to find out whether there was any correlation between lipid profile and various general parameters such as Age, BMI, and Waist circumference obtained from all participating patients. As well as between glycaemia, HbA1c and other parameters. Significant correlations were considered at (*p<0.05*). (Table 03)

- For Pearson correlation (r) value ranges between [-1;1]

Tableau 3: Correlation between lipid profile and various general parameters.

		AGE	BMI	Duration	Diet	Waist circumference	Sport
Total chol	**r**	-0.192	0.149	-0.130	-0.176	0.421	0.223
	p	0.310	0.433	0.492	0.351	**0.021**	0.237
LDL	**r**	-0.049	0.147	-0.201	-0.149	0.135	0.340
	p	0.797	0.439	0.287	0.431	0.476	0.066
HDL	**r**	-0.167	0.132	0.038	-0.025	0.001	0.119
	p	0.379	0.486	0.841	0.895	0.995	0.530
TG	**r**	-0.278	0.193	-0.343	0.024	0.575	-0.091
	p	0.137	0.306	0.063	0.901	**0.001**	0.634
Other pathologies	**r**	-0.305	0.176	-0.175	-0.045	0.223	-0.206
	p	0.102	0.353	0.356	0.812	0.235	0.275
SBP	**r**	-0.248	0.062	-0.216	-0.015	0.108	0.172
	p	0.186	0.744	0.253	0.939	0.570	0.363
DBP	**r**	-0.144	0.077	-0.474	-0.163	-0.135	0.205
	p	0.448	0.687	**0.008**	0.389	0.476	0.277
Glycaemia	**r**	-0.181	0.094	-0.043	-0.171	0.097	0.001
	p	0.337	0.623	0.821	0.366	0.610	0.994
HbA1c	**r**	0.126	-0.011	0.008	-0.002	-0.089	-0.120
	p	0.506	0.954	0.965	0.993	0.641	0.528

5.2.1 Correlation between waist circumference and lipid profile

5.2.1.1 Waist circumference and total cholesterol

According to the results obtained after drawing a fitted line plot we have seen that the distribution of all the points has a recognizable pattern which signifies that the two variables waist circumference and total cholesterol or TG have a positive correlation with r>0 (r=0.421, 0.575); respectively. (Figure 27, 28)

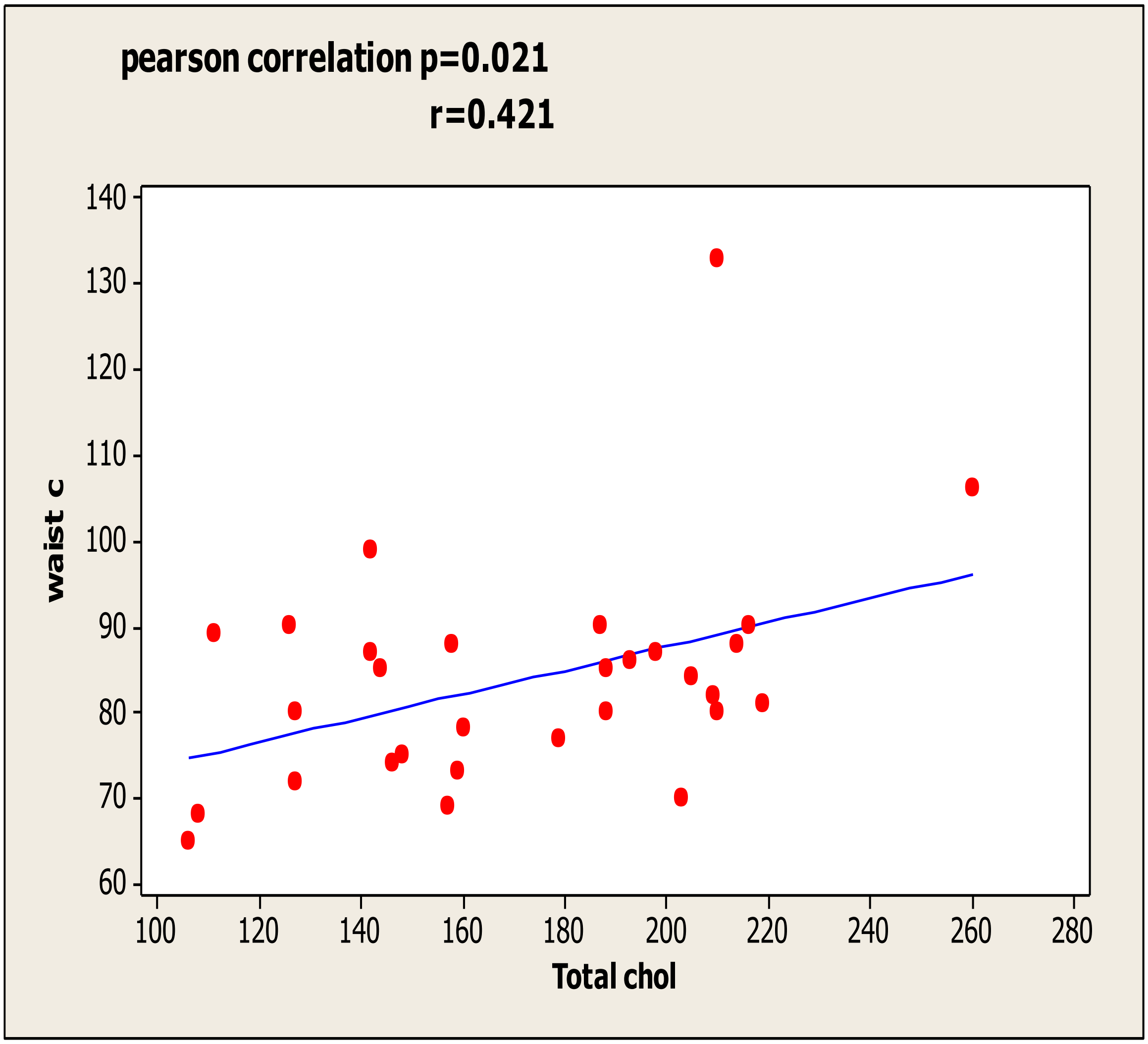

Figure 27: Correlation between waist circumference and total cholesterol

5.2.1.2 Waist circumference and TG

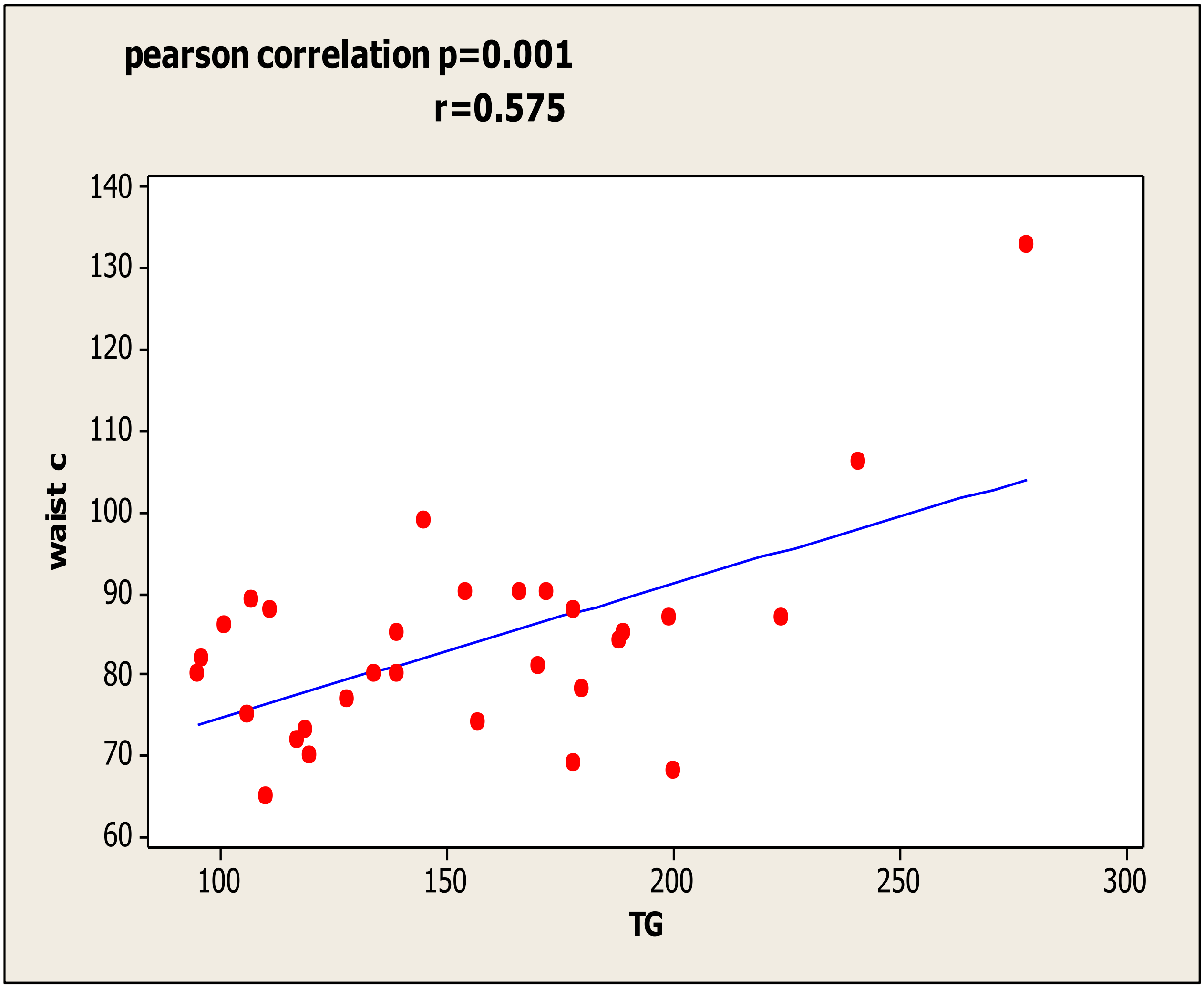

Figure 28: Correlation between waist circumference and TG

5.2.2 Correlation between diastolic BP and long-term diabetes

5.2.2.1 Diastolic BP and duration of diabetes

Diastolic BP and duration of diabetes showed a negative correlation with r<0 (-0.474) meaning that one increases while the other decreases. (Figure 29)

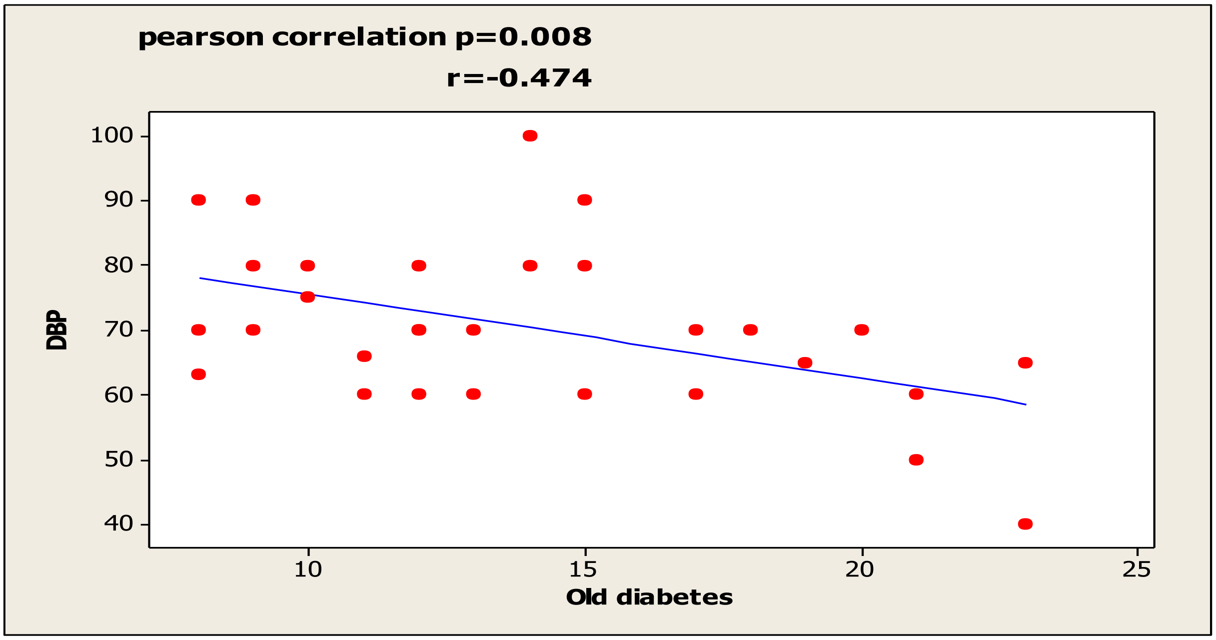

Figure 29: Correlation between long term diabetes and diastolic BP

5.2.3 Correlation between two quantitative variables

We intended to find out if there is a significant correlation between quantitative variables and other quantitative variables. We correlated systolic BP against TAG, diastolic BP against TAG, glycaemia against systolic BP and glycaemia against TAG. (Table 04)

We found no significant correlation between all these variables with r<0(-0.125, -0.071, -0.188) r>0 (0.080, 0.025); respectively.

Tableau 4: Correlation between quantitative variables

		TG	GL
SBP	**r**	-0.125	-0.071
	p	0.512	0.710
DBP	**r**	0.080	-0.188
	p	0.676	0.319
TG	**r**		0.025
	p		0.895

DISCUSSION

6. Discussion

6.1 Description of study population based on various parameters

T2DM is a pathology with high prevalence in adults as compared to adolescent. After the age of 65 years, the risk of developing T2DM is at 10-20%. **(Diyane et al., 2013)**

According the study carried out in the middle east region including (Qatar, Kuwait, Oman, Turkey) they found that most of their diabetic patients were ≤65 years**(Meo et al., 2019).** This study was consistent with our findings where we found 53.33% of our patients were ≤65 years.

Other studies from UK were different as compared to our findings where they reported that most of their patients were aged 65 years and above.**(Kautzky-Willer, 2021)**.

Most of T2DM patients in the world are overweight**(Franz et al., 2015).** According to the findings of a cross-sectional study involving 240 T2DM patients from Iran, it was reported that 54.6% of their patients were overweight**(Golabi et al., 2021).** This finding was in agreement with our study where we found 63.3% of our patient to be overweight. Individuals with normal weight can also develop T2DM.**(Ding et al., 2019)**

The adoption of quality diet such as Mediterranean diets can play an essential role in prevention of diseases such as T2DM. T2DM has a direct association with lifestyle and diet.**(Martín-Peláez et al., 2020)**

Our results showed that 66.7% of the study population did not follow any diet. This could have put them at a more unfavourable position and they become vulnerable to diseases such as T2DM. Diets rich in calories, high in fat and cholesterol increases the risk of T2DM.**(Palau et al., 2020)**

Those patients who were on diet 13.33% of them reported excellent effect of the diet on their health, our results were in line with a recent work on healthy diet with positive impact on heath as reported in recent work of **(Martín-Peláez et al., 2020)**

T2DM is directly associated with sedentary lifestyle which leads to gaining of excessive weight and as a result of overweight, our body tissues and muscles become resistant to insulin hormone; hence poor regulation of blood glucose which is directly associated with T2DM.**(Franz et al., 2015)**

Most of our patients did not take part in any sport activities; hence they had increased risk of developing diabetes. As reported by various studies, inactive lifestyle increases the risk of diseases and other health complication and engaging in physical activities can improve one's health by around 60% as reported by **(*WHO*, 2020)**

Based on the results of our study very few patients had other associated pathologies. We found less than 25% of our study population had other associated pathologies.

T2DM has been reported to be highly associated with other pathologies such as obesity, HTN, late-onset Alzheimer's dementia (LOAD). This may be as a result of change in lifestyle or increase in aging population in the world today.**(Hayden, 2019)**

One of the risk factors of cardiovascular diseases CVD in patients with diabetes is dyslipidaemia.**(Gonzalez-Aldaco et al., 2020)** Diabetic patients are characterized by high concentration of LDL, low HDL levels, hypertriglyceridemia. This is as a result of increased free fatty acid flux where hydrolysis of TAG occurs releasing fatty acids in the blood stream due to insulin resistance caused by DM.**(Mooradian, 2009)**

In our study, we found that lipid profiles are different as reported in various published literatures. We found a minimal cases of abnormal lipid changes. Only 20% of patients who had high concentration of LDL, 40% had high level of HDL, 30% had hypercholesterolemia while we found 50% with hypertriglyceridemia.

A study carried out on 2293 patients from rural Bangladeshi reported significant high proportions 58.7% of their study population had high TG, high T-chol, high LDL-C and low HDL-C.**(Bhowmik et al., 2018)**

The rise of LDL in patients with T2DM can be as a result of lipolysis of very-low density lipoprotein (VLDL) which after supplementation of triglyceride by cholesteryl ester transfer protein, along with hepatic lipase mediated hydrolysis of triglyceride and phospholipids which lead to increased LDL production**.(Haile & Timerga, 2020)**

In this study, we found hypertriglyceridemia (50%) to be the highest lipid parameter abnormally expressed. Our finding was in accordance with other studies done in Sudan (48.8%) and in Hyderabad (60%). This finding can be as a result of high secretion of hepatic VLDL as well as due to delayed clearance of TAG rich lipoproteins as a result of insulin resistance and hyperglycaemia. It can also be as a result of adipose tissue releasing free fatty acid in the blood stream of diabetic patients.**(Samimagham et al., 2021)**

HTN is one of modifiable risk factors of DM where it is estimated that 2 in every 3 diabetic patients have high BP**(Yamazaki et al., 2018).** High BP in patients with diabetes occurs as a result of accumulation of VLDL in the blood vessels leading to stiffen and narrowing of the vessels hence increase of pressure resulting in high BP.**(Y. Zhang, Nie, et al., 2020).** Previous studies have reported that both systolic and diastolic BP variability is an independent predictor of macro and microvascular complications specifically nephropathy in patients with T2DM.**(Ceriello & Prattichizzo, 2021).** Other studies have also reported a significant correlation of maximum morning high systolic blood pressure (HSBP) which was associated with development of diabetes nephropathy.**(Okamura et al., 2019)**

This was found in our study where 73.3% of our patients had high systolic BP, but we found high diastolic BP in less than 30% patients. Our study was in accordance with a cross-sectional study carried out on 96 T2DM patients from Benin city (Nigeria) where they reported 64.6% of their patients had high systolic BP and less than 46% had high diastolic BP.**(S. Ogedengbe et al., 2016)**

Waistline is one of the predictors for DM. We found that large number 90% of our patients had a normal waistline of <94cm/(37in).

Men with large waistline were 22 times likely to develop DM than those with normal waistline.**(Márk & Dani, 2016)**

According to recent study on 2,665 T2DM Chinese men aged 40-90 years; it was reported that 72% of study population had high waistline, this study was different from our finding.**(Cui et al., 2016)**

Diabetic is characterized by high levels of fasting blood glucose and HbA1c. This is as a results of insulin resistance/deficiency which is common in all diabetic patients.**(Incani et al., 2015)**

We found 93.33% of our population had elevated HbA1c as well as 80% of them had hyperglycaemia. This finding was in agreement with other published studies about DM.**(Kidwai et al., 2020)**

6.2 Pearson correlation between lipid profile and various considerable parameters

Based on the results we obtained after we carried out Pearson correlation between lipid profile and other anthropometrical and biochemical variables, we found a significant positive correlation between 3 different pairs of correlation. We found a positive linear correlation between total cholesterol vs waistline ($p=0.021$), TG vs waistline ($p=0.001$) and DBP vs duration of diabetes ($p=0.008$); respectively.

Similar finding of a significant positive correlation was reported between waistline with total cholesterol and TG; respectively in a study carried out by **(Biadgo et al., 2017),** but in their study they did not find any correlation between duration of diabetes and DBP.

In another study involving 296 subjects, a positive correlation was reported between BMI and TC, TG and LDL.**(Ghorbanian, 2012).** Our finding did not correspond to this study and other studies done in Iran and Saudi Arabia.**(Guo et al., 2019; Musina et al., 2020)**

Another cross-sectional study involving 140 T2DM Pakistani men aged 35-70 year, a significant positive correlation between LDL, TC, and BP was reported.**(Amin et al., 2016)** Our finding was different from these findings where we did not find any significant correlation between lipid profile with BP.

In another study carried out on Chinese population of 32,004 patients, they reported a co-existence of high BP and abnormal glucose in DM patients**(Jr et al., 2018)**. They demonstrated an association between hypertriglyceridemia and HTN in patients with poor glycaemic control and this finding was consistent to our study.

Waistline was reported to have significant positive correlation with SBP**(Golabi et al., 2021)** Contrary to this finding, we did not find any correlation between waistline and BP.

Another positive correlation was reported between TG with HTN ($r=0.2$, $p=0.001$) as well as with fasting blood glucose ($r=0.013$, $p<0.001$)**(Haile & Timerga, 2020).** Contrary to this finding, we did not find any positive correlation between TG with fasting blood glucose and HTN (r=-0.025, p=0.895), (r=0.025, p=0.512); respectively.

CONCLUSION

The current study gives further insight into a comprehensive risk assessment for T2DM in Algerian men, increasing our understanding of the effect of serum lipid profile, BMI and waistline, including TC, HDL-C, TG, on T2DM. We also found that waistline, DBP, TG and duration of diabetes are key variables relating to T2DM.

Various parameters such as waistline are predictors of T2DM and showed a significant correlation with lipid profile. However, this relationship needs to be assessed in a large sample because variables such as life history, medical history may have significant influence on this association.

LDL-C, high BMI, high systolic BP, TG, HbA1c and glycaemia were significantly elevated in our study population indicating a need to promptly address this increase in order to manage T2DM and reduce the morbidity related to T2DM.

Sedentary life and lack of diet plan were identified as risk factors of T2DM among men from western Algeria and adopting better lifestyle, including sport activities could improve their quality of life.

In recent years, eating behaviours have changed in most countries, from a healthy, balanced diet to a diet high in sugar, fat, and poor-quality protein. This habit puts the general population at a vulnerable position with high risk of various metabolic-related disorders, such as excess body fat around the waist, high blood sugar and abnormal cholesterol levels. All these metabolic disorders increase the risk of various diseases, such as T2DM, CVDs, HTN etc. There are several factors that are causing these changes, among them: working environment, stress. Healthy lifestyle needs to be adopted by the general population to lower the risk of these diseases and improve the quality of life.

In Africa, it was reported that 3 in 5 deaths associated to diabetes occur in patients aged 60 years and below. In 2019, 19 million patients were living with diabetes in Africa, and if no proper measures will be taken to manage these DM cases, an increase of 143% is predicted by the year 2045, reaching 49 million cases of DM. This increase is a big public health challenge to all African countries. Health professionals need to implement sustainable policies both in public institutions and private sectors in order to improve the lifestyle of the general population.

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APPENDICES

Nutrition questionnaire

1. General information

Patients name: ……………………………

Age:………………………………….

Weight:……………………….

Height:…………………………

Waistline:…………………………

BMI:……………………..

2. Medical history

Duration of diabetes………………………………..(years)

3. Dietary habits

Have you been on diet?. …….Yes………No

If yes, what was the diet results?….excellent,……..moderate,……….no effect.

4. Physical activities

Do you participate in sporting activities?………yes……No.

ملخص

أجرينا دراسة مقطعية لتحديد مستوى الدهون في الدم لدى الرجال غير البدينين المصابين بداء السكري من النوع 2 (DT2) من غرب الجزائر -تلمسان. تم الحصول على البيانات البيوكيميائية والقياسات البشرية من 30 مريضًا. التحليل كان في مختبرات مختلفة داخل تلمسان بين 2019-2022. وجد أن 50٪ يعانون من ارتفاع في الدهون الثلاثية و30٪ لديهم فرط كوليسترول الدم. ارتبط محيط الخصر ومدة الإصابة بمرض السكر بارتفاع كوليسترول الدم وزيادة الدهون الثلاثية وارتفاع ضغط الدم الانبساطي على التوالي. لم تكن ملامح الدهون مرتبطة بمؤشر كتلة الجسم والرياضة والنظام الغذائي في مرضى DM الذين تمت دراستهم.

الكلمات الدالة : دهون الدم، DT2 ، محيط الخصر ، فرط كوليسترول الدم ، ارتفاع الدهون الثلاثية ، PAD ، مؤشر كتلة الجسم، DM ، النظام الغذائي

Résumé

Nous avons réalisé une étude transversale pour déterminer le profil lipidique sérique chez les hommes non obèses diabétiques de type 2 (DT2) de l'ouest algérien-Tlemcen. Les données biochimiques et anthropométriques de 30 patients ont été obtenues. Les analyses des échantillons ont été effectué dans différents laboratoires de Tlemcen entre 2019-2022. Il a été constaté que 50% avaient une hypertriglycéridémie et 30% avaient une hypercholestérolémie. Le tour de taille et la durée du diabète étaient respectivement associés à l'hypercholestérolémie, l'hypertriglycéridémie et pression artérielle diastolique (PAD). Les profils lipidiques n'étaient pas associés à l'IMC, au sport, au régime chez les patients DM étudiés.

Mots clés : lipides sériques, DT2, hypertriglycéridémie, hypercholestérolémie, tour de taille, PAD, IMC, DM, régime.

Summary

we carried out a cross-sectional study to determine the serum lipid profile in non-obese type 2 diabetes mellitus (T2DM) men from western Algeria-Tlemcen. Biochemical and anthropometric data from 30 patients were obtained. Sample analyses were performed at various laboratories within Tlemcen between 2019-2022. It was found that 50% had hypertriglyceridemia and 30% had hypercholesterolemia. Waistline and duration of diabetes were associated with hypercholesterolemia, hypertriglyceridemia and diastolic BP; respectively. Lipid profile was not associated with BMI, sport, diet in the DM patients studied.

Keywords: serum lipid, T2DM, hypertriglyceridemia, hypercholesterolemia, waistline, diastolic BP, BMI, DM, diet.