INCIDENCE OF DIABETES AMONG SEDENTARY WOMEN AND ASSESSMENT OF VITAMIN D STATUS

DISSERTATION

***Submitted** in Partial Fulfillment of the Requirement for*

The Award of the Degree of

MASTER'S PROGRAMME IN

CLINICAL NUTRITION AND DIETETICS

BY

SHAHEEFA

(Register No: SM20MCN016)

DEPARTMENT OF CLINICAL NUTRITION AND DIETETICS

ST. TERESA'S COLLEGE (AUTONOMOUS)

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Signature of HOD ***Signature of Guide***

DECLARATION

I hereby declare that the thesis entitled "***INCIDENCE OF DIABETES AMONG SEDENTARY WOMEN AND ASSESSMENT OF VITAMIN D STATUS***" submitted in partial fulfillment of the requirement for the award of the Degree of Master's Programme in Clinical Nutrition and Dietetics is a record of original research work done by me under the supervision and guidance of Mrs. Ani Thomas Thottan, Head of department , Department of Clinical Nutrition and Dietetics , Women's Study Centre, St. Teresa's College(Autonomous), Ernakulam and that the thesis has not previously formed on the basis for the award of any degree work has not been submitted in part or full or any other degree/diploma/ fellowship or the similar titles to any candidate of any other University.

Place:

Date:

CERTIFICATE

I hereby certify that the dissertation entitled "***INCIDENCE OF DIABETES AMONG SEDENTARY WOMEN AND ASSESSMENT OF VITAMIN D STATUS***" submitted in partial fulfillment of the requirement for the award of the Degree of Master's Programme in Clinical Nutrition and Dietetics is a record of original research work done by Ms. Shaheefa during the period of her study under my guidance and supervision.

Signature of the HOD

Signature of the Research Guide

Mrs. Ani Thomas Thottan

Head of Department

Department of Clinical Nutrition and Dietetics,

Women's Study Centre

St. Teresa's College, Ernakulam

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ABSTRACT

ABSTRACT

Diabetes is a group of chronic diseases characterized by hyperglycaemia. Chronic hyperglycaemia in diabetes starts a cascade of events leading to micro and macrovascular complications, which affect many tissues and organs, causing retinopathy, nephropathy, neuropathy, cardiovascular diseases, and peripheral vascular diseases. Many medical researchers have supported the association between alteration in metabolism of serum minerals and vitamin D with the Type 2 Diabetes Mellitus and its complications. Still, relations and Association of these factors with the severity of disease is unsettled. For the study 150 sedentary women above 30 years were selected from Ernakulam district and among them incidence of diabetes and vitamin D status was identified, correlation between vitamin D status and diabetes mellitus was done. The objectives of the study were assessment of nutritional status of sedentary women, incidences of diabetes mellitus among sedentary women, identify hypovitaminosis D among selected subjects, correlate between vitamin D status among diabetic women and prepare suitable nutritional intervention tool against hypovitaminosis D. The questionnaire was distributed among the subjects for collecting more information. From that it gave a clear picture about their lifestyle. While assessing the dietary intake majority of subjects were calorie deficient and the consumption of vitamin D were also low. According to ICMR, majority of selected subjects were affected with diabetes mellitus and 85% were deficient in vitamin D. The relationship between vitamin D status and diabetes mellitus are considered statistically significant. Nutrition education was imparted to all the selected subjects by creating video with the importance, functions and risk factors of vitamin D, sources, and hypovitaminosis D in sedentary women, causes, symptoms, complications and management by sharing them to the selected subjects

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INTRODUCTION

Diabetes mellitus is a growing health problem worldwide. It is a metabolic disorder characterized by elevated blood glucose levels leading to defects in insulin secretion and insulin action, or both. Hyperglycaemia, or high blood sugar, is a common result of uncontrolled diabetes and over time can cause serious damage to the body, particularly the nervous system and blood vessels. Diabetes mellitus (DM) is a disease characterized by persistently elevated blood sugar levels. The main symptoms of diabetes mellitus are hyperglycaemia and glycosuria (elevated levels of glucose in the blood and urine, respectively), polyuria (abnormal urine production), polydipsia (excessive thirst), polyphagia (excessive hunger), sudden weight loss, and during acute episodes of diabetes mellitus. excess ketones in the blood and urine (ketonemia and ketonuria respectively). DM is mainly divided into two types, type 1 diabetes mellitus (T1DM), formerly known as insulin-dependent diabetes mellitus (IDDM), and type 2 diabetes mellitus (DM2), formerly known as non-insulin-dependent diabetes mellitus (NIDDM).

Chronic complications of diabetes mellitus can be divided into vascular and non-vascular complications. Vascular complications of DM are further divided into macrovascular and microvascular complications. Macrovascular disease is associated with atherosclerosis of the largest arteries, such as IHD, stroke, and peripheral vascular disease. Microvascular complications include diabetic retinopathy, neuropathy, and nephropathy. Diabetic retinopathy is a common but potentially blinding eye disease in which the vessels at the back of the eye change and become dysfunctional. Diabetic nephropathy (DN) or diabetic kidney disease is a syndrome characterized by the presence of pathological urinary albumin excretion, diabetic glomerular lesions, and loss of glomerular filtration rate (GFR) in diabetics. Diabetic neuropathy, a life-threatening complication, affects both peripheral and autonomic nerves and affects nearly half of the diabetic population.

Approximately 537 million adults at the age group (20-79 years) are residing with diabetes everywhere in the global wherein three in four adults with diabetes stay live in the low- and centre-income nations and nearly 1 in 2 human beings which debts for 240 million adults residing with undiagnosed diabetes all over the global. The international prevalence the diabetes mellitus has extended because of population aging, urbanization, and related lifestyle changes. Due to rise in the prevalence rate the number of human beings affected with

diabetes has doubled wherein 90% of the whole population is affected with type 2 diabetes mellitus.

Type 2 Diabetes Mellitus (T2DM) or “noninsulin-structured diabetes” or “person-onset diabetes” is a globally regularly occurring persistent metabolic disorder characterized by way of means of hyperglycaemia, relative insulin deficiency because of beta cell dysfunction, sub-chronic irritation, and peripheral insulin resistance.

Insulin resistance (IR) is a physiological circumstance wherein cells fail to respond to the ordinary movements of the hormone insulin. The body produces insulin, how, ever the cells within the body becomes resistance to insulin and are not able to use it as effectively, leading to hyperglycaemia. Beta cells within the pancreas eventually increase their production of insulin; in addition to contributing to hyperinsulinemia. This regularly stays undetected and might contribute to a diagnosis of Type 2 Diabetes. Insulin resistance is vital now no longer only, is it the maximum effective predictor of future development of a type 2 diabetes, it's also a therapeutic target once hyperglycaemia is present.

Diabetes-related cardiovascular complications are generally characterized by atherosclerosis and endothelial dysfunction. Both T2DM and impaired glucose tolerance (IGT) confer a 3 to eight-fold growth in CVD risk. Diabetes people are eight times more predisposed to cardiovascular diseases (CVDs) and the prevalence of myocardial infarction and stroke are 2 to four instances better in T2DM people in comparison to their non-diabetes counterparts. Susceptibility to a metabolic syndrome characterized by IGT, dyslipidaemia, obesity, hypertension, insulin resistance, and T2DM is the recognized reason for the better prevalence of CVDs in Indians.

Vitamin D is a sunshine vitamin, with the major form being vitamin D2(ergocalciferol) and vitamin D3 (cholecalciferol) acquired through diet. Cholecalciferol synthesis in the body takes place withinside the pores and skin from cholesterol mediated via way of means of a chemical response depending on sun exposure (ultraviolet radiation). Cholecalciferol is hydroxylated to form 25-hydroxycholecalciferol (calcifediol)in the liver, that's in addition to hydroxylated in the kidneys to form calcitriol (1,25-dihydroxycholecalciferol) (1,25(OH)2D), the biologically energetic form of vitamin D. Apart from bone health, vitamin D additionally performs a function in numerous different biochemical mechanisms in the human body. 1,25(OH)2D regulates over 200 genes, which encompass the ones concerned with insulin

production in the pancreas, renin production inside the kidney, the release of cytokines from lymphocytes, production of cathelicidin (own circle of relatives of antimicrobial peptides) in macrophages, increase and proliferation of each vascular smooth muscle cells and cardiomyocytes.

Vitamin D is a fat-soluble, secosteroid hormone required for proper regulation of many-body systems, normal growth and calcium homeostasis. Vitamin D has a first-rate function in glucose metabolism. These consist of insulin secretion, and insulin exocytosis and promote glucose uptake via way of means of peripheral tissues.

Vitamin D deficiency seems to be associated with the incidence of diabetes mellitus. Moreover, Vitamin D ought to lower the results of systemic inflammation in patients with type 2 diabetes in numerous ways, which include suppression of molecular-mediated immunity, stimulation of neurotrophic elements like nerve growth factor, the regulation of molecular proliferation, suppression of RAAS.

Vitamin D deficiency is presently a subject of severe interest, as vitamin D deficiency is extensively generic throughout all ages, races, geographical regions, and socioeconomic strata and has been proven to be related to high blood pressure and atherosclerosis and will increase the threat of non-musculoskeletal illnesses consisting of cancer, multiple sclerosis, CAD, stroke, T1DM, T2DM and CVD.

Vitamin D is now below particular research due expression of VDR in body tissues consisting of endothelial cells, vascular clean muscle cells, β- cells (beta cells) of the pancreas, T helper cells, macrophages, muscle groups, and adipose tissues. Vitamin D is proven to regulate gene transcription of many inflammatory factors and immune cells that would probably contribute to the development of persistent disease, recovery, or mortality. Inflammation and oxidative stress are taken into consideration as using elements for insulin resistance (IR), metabolic syndrome, diabetes mellitus, and vascular complications. The antioxidative and anti-inflammatory activity of vitamin D plays an essential function in insulin secretion and sensitivity. Vitamin D with the aid of using regulating the pro inflammatory factors and up-regulating anti-inflammatory factors has a potential to prevent endothelial disfunction of vascular smooth muscle cells, thereby lowering the CVD threat.

In current years, the function of vitamin D (Vit D), an important fat-soluble nutrient/steroid hormone in the regulation of non-skeletal disorder is gaining prominence. Vitamin D is regarded for its function in calcium and bone mineral homeostasis. Over the years, it's been implicated in diverse non-skeletal diseases. The extra skeletal phenomenon may be attributed to the presence of nutrition D receptors (VDRs) in nearly all cells and the identification of 1-α hydroxylase in extrarenal tissues. Over one thousand million humans worldwide are expected to be effected by the vitamin D deficiency (VDD) pandemic that paralleled the prevalence of obesity, T2DM and cardiovascular disease.

Aim and objectives

Aim of the study:

The aim of the study is to identify the incidence of serum Vitamin D (1,25-hydroxy Vitamin D) status of sedentary women aging between 30-55 years. The association between Vitamin D deficiency and Diabetes mellitus are also examined.

Objectives of the study:

1. Assessment of the nutritional status of sedentary women.
2. Incidences of Diabetes Mellitus among sedentary women.
3. Identify hypovitaminosis D among the selected subjects.
4. Correlate vitamin D status and diabetes among subjects.
5. Develop nutrition intervention tools and provide awareness on vitamin D status.

REVIEW OF LITERATURE

CHAPTER-2

REVIEW OF LITERATURE

The review of literature to the study on the "**Incidence of Diabetes Among Sedentary Women And Assessment Of Vitamin D** Status" is reviewed under the following headings.

2.1 The vitamin D and chronic disease connection

Epidemiological evidence supports an association between hypovitaminosis D and increased risk of mortality due to CVD, as well as an increased risk of hypertension, stroke, metabolic syndrome, and diabetes. There was also a significant linear trend between increasing serum 25(OH)D and these outcomes. Interestingly, the association between serum 25(OH)D and all-cause mortality was stronger in people with diabetes compared to those without diabetes.

This observation in diabetic patients suggests that raising serum 25(OH)D concentrations in this patient group may be of particular benefit in reducing mortality. (Parker J Hashmi O Dutton D, et al.,2010)

Recently, (Parker et al.,2010) reviewed the association of vitamin D status and cardiometabolic disorders (CVD, diabetes, and metabolic syndrome) in a meta-analysis of 28 independent, cross-sectional, case-control, and cohort studies published between 1990 and 2009 with a sample population of 99,745 participants. These investigators found a significant 55% reduction in risk of diabetes (9 studies), a 33% reduction in risk of cardiovascular disease (16 studies), and a 51% reduction in metabolic syndrome (8 studies) associated with high serum 25(OH)D concentration.

Although there appears to be a significant association between high serum 25(OH)D concentration and reduced risk of diabetes in observational studies, clinical intervention trials in which vitamin D status is increased by giving vitamin D supplements should provide a powerful test of the potential relationship between vitamin D and diabetes risk. (Chirsty S Maxwell et al.,2011)

2.2 Type 2 Diabetes Mellitus

2.2.1 Definition

Diabetes is a chronic, metabolic disease characterized by elevated levels of blood glucose (or blood sugar), which leads over time to serious damage to the heart, blood vessels, eyes, kidneys and nerves. The most common is type 2 diabetes, usually in adults, which occurs when the body becomes resistant to insulin or doesn't make enough insulin. In the past three decades the prevalence of type 2 diabetes has risen dramatically in countries of all income levels. Type 1 diabetes, once known as juvenile diabetes or insulin-dependent diabetes, is a chronic condition in which the pancreas produces little or no insulin by itself. For people living with diabetes, access to affordable treatment, including insulin, is critical to their survival. (WHO)

2.2.2 Risk factor

Obesity is considered to be one of the major risk factors of developing type 2 diabetes (Beane, 2011); however, there are other lifestyle aspects that contribute to type 2 diabetes. Lack of physical activity, alcohol consumption, smoking, and unhealthy eating habits can play a significant role in developing the disease.

T2DM risk factors include a complex combination of genetic, metabolic and environmental factors that interact with one another contributing to its prevalence. Although individual predisposition to T2DM due to non-modifiable risk factors (ethnicity and family history/genetic predisposition) has a strong genetic basis, evidence from epidemiological studies suggests that many cases of T2DM can be prevented by improving the main modifiable risk factors (obesity, low physical activity and an unhealthy diet) (Schellenberg et al., 2013).

2.2.2.1 Ethnicity and Family History/Genetic Predisposition

According to (Fuchsberger et al., 2016) Genetic predisposition plays an important part in the risk of developing T2DM. Over the past decade, several T2DM genome-wide association have shown the complex polygenic nature of T2DM in which most of these loci increase T2DM risk through primary effects on insulin secretion, and a minority act through reducing insulin action (Mn Carthy et al., 2010). (Dimas et al., 2014) grouped these variants on the basis of their potential intermediate mechanisms in T2DM pathophysiology, with four variants fitting a clear IR (insulin resistance) pattern; two reducing insulin secretion with fasting hyperglycemia; nine lowering insulin secretion with normal fasting glycemia; and one altering insulin processing. According to these data, the genetic architecture of T2DM is highly polygenic, and additional association studies are needed to identify most T2DM (Flannick et al., 2016). Interactions between susceptibility loci and environmental factors could underlie the missing heritability of T2DM thus the impact of a given genetic variant

can be modulated by the environmental factors (and vice versa) as evidenced by both observational studies and clinical trials (Franks et al., 2013).

2.2.2.2 Obesity, Low Physical Activity and Unhealthy Diet

Obesity (body-mass index [BMI]≥30 kg/m^2) is the strongest risk factor for T2DM (Bellou et al., 2018) and is associated with metabolic abnormalities resulting in IR. There exists an inverse linear relationship between BMI and the age at diagnosis of T2DM. The exact mechanisms by which obesity induces T2DM and IR remain to be elucidated; however, numerous factors have shown a significant role in the development of this pathological process, which involves both cell-autonomous mechanisms and inter-organ communications.

A sedentary lifestyle is another risk factor for T2DM as shown by the Women's Health Study and in the Kuipio Ischemic Heart Disease Risk Factor study, which showed a reduction of 34% and 56% reduction of developing T2DM in participants walking 2–3 h a week or at least 40 min a week, respectively. There are three primary benefits of physical activity on the delay of T2DM onset. First, the contraction of skeletal muscle cells induces an increase in blood flow into the muscle, enhancing glucose uptake from plasma (Venkataswamy et al., 2013). Second, physical activity reduces the notorious intra-abdominal fat, which is a known risk factor that promotes IR (Strasser, B, 2013). Finally, moderate-intensity exercise has been shown to improve glucose uptake by 40% and physical activity improves glucose uptake and insulin sensitivity but it can also improve or even reverse inflammation and oxidative stress, which are T2DM predisposing factors (Venkataswamy et al., 2013).

2.2.3 Role of vitamin D in type 2 DM

Epidemiological and observation evidence suggests that vitamin D (D3) supply inversely correlate with the risk for type 2 diabetes mellitus and once diabetic, serum 25(OH) D3 level correlate inversely with impaired glucose tolerance. Vitamin D3 improved insulin sensitivity (based on HOMAIR) and affected the course of Hb1Ac positively compared with placebo in patients with T2DM effect (Jehle et al. 2014). Diabetes Mellitus (DM) is becoming lifestyle related pandemic disease. Diabetic patients frequently show electrolyte disorder, especially diabetic ketoacidosis or non- ketoacidosis hyperglycaemic hyperosmolar syndrome. Such patients show 16 characteristic potassium, magnesium, phosphate and calcium depletion. The review, (Ahn et al. (2017) discusses homeostatic mechanism that links the calcium and DM.

Dalgård et al. (2011) reported that Vitamin D insufficiency is believed to be a risk factor for development of type 2 diabetes, and elder subjects are at more risk. Vitamin D status was assessed from serum concentration of 25-hydroxyvitamin D3 [25(OH)D3] in 20 668 Faroese residents of 70 – 74 years. Type 2 diabetes prevalence was determined from past medical histories, fasting plasma concentration of glucose, and glycosylated haemoglobin (HbA1c). It was seen that 70 (11%) new type 2 diabetic subjects, while 88 (13%) were previously

diagnosed. Subjects with vitamin D status, 20 ng/ml (50 nmol/L) double risk of newly type 2 diabetes after adjustment for BMI, sex, exposure to polychlorinated biphenyls, serum triacyl glyceride concentration, serum high density lipoproteins (HDL) concentration, smoking status, and month of blood testing. Besides, the HbA1c concentration decreased in higher serum 25(OH)D3 concentration autonomous of covariates. In older subjects, vitamin D sufficiency may give protection against type 2 diabetes. Since the investigation is cross sectional, mediation thinks about are expected to clarify whether vitamin D could be utilized to prevent development of type 2 diabetes. Vitamin D inadequacy may expand the risk of type 2 diabetes. Dele Skog et al. (2012) investigated whether serum concentrations of 25 hydroxyvitamin D [25(OH)D] would predict the development of prediabetes (impaired fasting glucose, impaired glucose tolerance or the two combined) and type 2 diabetes, either on their own or when combined with serum concentrations of IGF 1 or IGF binding protein 1 (IGFBP 1), which may interact with 25(OH)D. Men but not women with elevated of 25(OH)D level had a decreased or for developing type 2 diabetes after change for confounders (OR 0.52, 95% CI 0.30, 0.90), an impact represented by people with prediabetes, but not with normal glucose tolerance, at baseline. In both genders, movement from prediabetes to type 2 diabetes was reduced by about 25% per 10 nmol/l increase in 25(OH)D. A high insulin like growth factor binding protein 1 value was a superior indicator of a reduce risk of type 2 diabetes than high 25(OH)D for both genders, while high insulin growth factor (IGF) 1 concentration predicted a decreased risk only in men. High serum 25(OH)D concentration predict a reduced risk of type 2 diabetes in persons with prediabetes.

In a population-based study to establish research the relationship between levels of 25-hydroxyvitamin D and the occurrence of type 2 diabetes in a Spanish population it was seen that the frequency of diabetes in subjects with 25 hydroxyvitamin D levels ≤ 18.5ng/mL (percentile 25) was 12.4% versus 4.7% in subjects with levels > 18.5 ng/ml. The probability of having diabetes during the four years of follow-up was altogether lower in the subjects with more elevated levels of 25 hydroxyvitamin D. None of the subjects with levels higher than 30 ng/mL created diabetes. In this study a significant inverse relationship between serum 25-hydroxyvitamin D levels and the risk for type 2 diabetes was found in a population from the south of Spain (González-Molero et al. 2012).

2.2.4 Pathophysiology

Regarding the pathophysiology of the disease, malfunctioning of the feedback loops between insulin action and insulin secretion results in abnormally high glucose levels in blood. (Cerf et al., 2013) In the case of β-cell dysfunction, insulin secretion is reduced, limiting the body's capacity to maintain physiological glucose levels. On the other hand, IR contributes to increased glucose production in the liver and decreased glucose uptake both in the muscle, liver and adipose tissue. Even if both processes take place early in the pathogenesis and

contribute to the development of the disease, β-cell dysfunction is usually more severe than IR. However, when both β-cell dysfunction and IR are present, hyperglycemia is amplified leading to the progression of T2DM (Zheng et al., 2018).

2.2.4.1. Mechanisms Leading to T2DM and Pathophysiology

To safeguard proper β-cell function, cellular integrity must be ensured and the mechanisms and pathways implicated in the physiology of β-cell must be tightly regulated (Cerf et al., 2013)

β-cells are responsible for insulin production, which is synthesized as pre-proinsulin. In the maturation process, pre-proinsulin undergoes a conformational modification carried out with the help of several proteins in the endoplasmic reticulum (ER) to yield proinsulin (Bunney et al., 2017). Afterwards, proinsulin is translocated from the ER to the Golgi apparatus (GA), entering into immature secretory vesicles and being cleaved into C-peptide and insulin (Glibert et al., 2013)

Once matured, insulin is stored in granules until insulin release is triggered. Insulin release is primarily triggered by a response to high glucose concentrations. It is worth noting that some other factors can also induce insulin release such as amino acids, fatty acids and hormones (Boland et al., 2017). (Rorsman et al., 2018) When circulating glucose levels increase, β-cells take in glucose mainly through the glucose transporter 2 (GLUT2), a solute carrier protein that also works as a glucose sensor for β-cells. Once glucose enters, glucose catabolism is activated, increasing the intracellular ATP/ADP ratio, which induces the closing of ATP-dependent potassium channels in the plasma membrane. This leads to membrane depolarization and opening of the voltage dependent Ca^{2+} channels, enabling Ca^{2+} to enter the cell. The rise in the intracellular Ca^{2+} concentration triggers the priming and fusion of the secretory insulin-containing granules to the plasma membrane, resulting in insulin exocytosis (Seino et al., 2011).

2.2.4.2. Mechanisms Leading to β-Cell Dysfunction

β-cell dysfunction has been traditionally associated with β-cell death (Christensen et al., 2019) However, recent evidence suggests that the dysfunction of β-cells in T2DM might be due to a more complex network of interactions between the environment and different molecular pathways implicated in cell biology (Halban et al., 2014). In an excessive nutritional state, similar to that found in obesity, hyperglycemia and hyperlipidemia are often present, favoring IR and chronic inflammation. Under these circumstances, β-cells, due to

differences in their genetic susceptibility, are subject to toxic pressures including inflammation, inflammatory stress, ER stress, metabolic/oxidative stress, amyloid stress, with the potential of ultimately leading to a loss of islet integrity (Christensen et al., 2019).

An excess of FFAs and hyperglycemia lead to β-cell dysfunction by inducing ER stress through the activation of the apoptotic unfolded protein response (UPR) pathways (Yamamoto et al., 2019). In fact, lipotoxicity, glucotoxicity and glucolipotoxicity occurring in obesity, induce metabolic and oxidative stress that leads to β-cell damage (Halban et al., 2014). Stress derived from high levels of saturated FFAs can activate the UPR pathway by several mechanisms including inhibition of the sarco/endoplasmic reticulum Ca^{2+} ATPase (SERCA) responsible for ER Ca^{2+} mobilization; activation of IP3 receptors or direct impairment of ER homeostasis. In addition, sustained high glucose levels increase proinsulin biosynthesis and islet amyloid polypeptides (IAAP) in β-cells, leading to the accumulation of misfolded insulin and IAAP and increasing the production of oxidative protein folding-mediated reactive oxygen species (ROS) (Yamamoto et al., 2019). These effects alter physiological ER Ca^{2+} mobilization and favor proapoptotic signals, proinsulin mRNA degradation and induce interleukin (IL)-1 β release that recruits macrophages and enhances local islet inflammation (Halban et al., 2014).

As previously mentioned, insulin secretion has to be finely regulated to precisely meet metabolic demand. For that reason, proper islet integrity must be conserved in order to allow β-cells to respond to metabolic needs. Under pathogenic conditions, the mechanism described above can ultimately lead to disruption of islet integrity/organization, impairing optimal cell-to-cell communication within pancreatic islets, contributing to poor regulation of insulin and glucagon release and ultimately exacerbating the hyperglycemia. Defects in the synthesis of any insulin precursors, or insulin itself, as well as disruption of the secretion mechanism, can lead to insulin secretory dysfunction, the primary driver of β-cell failure, and a foundation of T2DM. For instance, reduced expression in the GLUT2 glucose transporter would affect the downstream signaling pathway (Hoang et al., 2015), while failure in the folding of proinsulin is another finding commonly linked to deficient insulin production and diabetes (Liu et al., 2018).

2.2.4.3. Pathological Conditions Perpetuating T2DM

Nutritional Factors

(Dali – Youcef et al., 2013) High-caloric Western diet contains large amounts of fats and carbohydrates that elevate blood glucose and circulating very-low-density lipoproteins

(VLDLs), chylomicrons (CMs) and their remnants (CMRs) that are rich in triglycerides (TG). This induces a spike in reactive oxygen species (ROS) concentrations, which in turn leads to an abnormal generation of inflammatory molecules. Given that inflammation is a recognized inducer of oxidative stress, a synergistic interaction occurs between the two processes after a heavy meal, with consequent amplification of harmful postprandial effects (Hummasti et al., 2010) . The sustained and marked increase in steady-state levels of ROS contributes significantly to the pathogenesis of T2DM and IR. Therefore, a pro-oxidant environment leads to mitochondrial dysfunction, ER stress, activation of NADPH oxidase (NOX) and superoxide (O_2^-) production. The increase in O_2^- production activates the five major pathways involved in the pathogenesis of diabetes complications: enhancement of the polyol pathway, increased formation of advanced glycation end products (AGEs), increased expression of AGEs receptor and its activating ligands, activation of protein kinase C (PKC) isoforms, and overactivity of the hexosamine pathway (Roca et al., 2013). Through these pathways, increased intracellular ROS causes defective angiogenesis in response to ischemia, activates a number of proinflammatory pathways, and cause long-lasting epigenetic changes which drive persistent expression of proinflammatory genes even after glycemia is normalized (Giacco et al., 2010). Additionally, increased blood levels of FFAs also lead to mitochondrial dysfunction through two different mechanisms: (1) FFA metabolism by-products disturb the electron flow throughout the mitochondrial respiratory chain and (2) through the incorporation of FFAs into the mitochondrial membranes, thus likely favoring electron leakage (Graciano et al., 2011).

Physical Activity

Reduced physical activity and exercise training, and increased sedentary behaviors constitute a link between obesity and T2DM and are associated with increased markers of chronic low-grade systemic inflammation (Esser et al., 2014). In this condition, proinflammatory molecules are released into the bloodstream and within specific tissues such as interleukin 6 (IL-6), C-Reactive Protein (CRP), tumor necrosis factor-alpha (TNF-α) or IL-1 induces an inflammatory state known as metabolic inflammation (Bunney et al., 2017). Indeed, IL-1 is involved in the autoimmune response to β-cells in the pancreas, inhibition of β-cell function and activation of the nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) transcription factor, thus inhibiting β-cell function and promoting apoptosis (Venkataswamy et al., 2013). Preclinical data suggest that inflammation resolution could prevent the development of T2DM in obesity and prediabetes, which was substantiated by preclinical animal data showing that deletion of the macromolecular complex NLRP3 inflammasome, responsible for the production of IL-1β and IL-18, resulted in improved insulin sensitivity (Vandanmagsar et al., 2011)

Intentional weight loss remains the cornerstone therapy to improve insulin sensitivity and, in some circumstances, to prevent the incidence of T2DM in individuals with obesity and prediabetes (Diabetes care, 2019). Regular exercise and increased physical activity enhance the production of anti-inflammatory cytokines such as IL-1 Receptor antagonist (IL-1Ra) and soluble TNF receptor (s-TNF-R) that are antagonists of IL-1 and TNF-α, respectively. Individuals with increased physical activity also show reduced circulating levels of IL-6, IL-18 and CRP, together with lower levels of leptin, a molecule associated with CRP. Physical exercise can improve T2DM-inducing oxidative stress by inducing the synthesis of antioxidants such as glutathione (GSH), a major non-enzymatic antioxidant and other antioxidant enzymes which lead to a long-term reduction in free radical levels (Venkataswamy et al., 2013).

Finally, irisin is an exercise-regulated myokine, which improves glucose tolerance (Pulak et al., 2017) secreted by skeletal muscle (Bostrom et al., 2012) and adipose tissue (Roca-Rivada et al., 2013) in response to exercise. T2DM patients have been found to have lower circulating levels of irisin compared to control subjects. Additionally, diabetic patients with CVD had significantly lower serum irisin than non-CVD patients (Park et al., 2013) Low levels of serum irisin have been associated with 1.6 times increased risk of CVD incidence in T2DM patients (El – Lebedy et al., 2018).

Gut dysbiosis

Gut microbiota is composed of many microbial species that impact human physiology and participate in different biological processes (Lynch et al., 2016). They can modulate the immune system and inflammatory response, regulate gut barrier integrity and human metabolism, take part in the synthesis of metabolites (Ochoa – Reparaz et al., 2014). Gut resident microorganisms produce many metabolites that contribute to physiology in healthy individuals (Scarpellini et al., 2012). However, changes due to both inherited and acquired factors such as age, nutrition, lifestyle, genetic predisposition, or underlying diseases can affect the gut microbiota produced metabolite proportion leading to metabolic disturbances that can culminate in disease (Biagi et al., 2012). The better understating of gut microbiota has evidenced its important role in the development of diabetes and recent studies indicate that changes in dysbiosis can promote IR and T2DM (Sircana et al., 2018). A high-fat diet can induce up to threefold lipopolysaccharide (from Gram-negative bacteria) production in mice models, thereby contributing to low-grade inflammation and insulin resistance (Li. X et al., 2017). Furthermore, intestinal dysbiosis can reduce short-chain fatty acid synthesis that promotes gut barrier integrity, pancreatic β-cell proliferation and insulin biosynthesis (Tang, C et al., 2015) . Dysbiosis can also compromise the production of other metabolites such as branched aminoacids and trimethylamine thus disrupting glucose homeostasis and triggering T2DM development (Neis et al., 2015). Understanding the clinical implications of the gut

microbiome is a relatively new field, and requires further research to better elucidate the connection between gut microbiota and T2DM (Shan, Z et al., 2017)

Metabolic memory

Metabolic memory refers to the persistence of diabetic complications even after maintained glycemic control. This concept arose from the results of multiple large-scale clinical trials, which showed that after diabetes onset, diabetes complications persist and progress even when glycemic control is restored through pharmaceutical intervention. Among them, the UKPDS post-trial study and Steno-2 trial showed that specifically early glycemic interventions prevent diabetic complication and has a marked decrease in CVD endpoints in patients that received either standard or intensive treatment following their diagnosis. Later on, animal models of diabetes and in vitro cell cultures demonstrated that the initial hyperglycemic period results in permanent abnormalities (including aberrant gene expression) of target organs/cells (Olsen et al., 2012). Metabolic memory involves four mechanisms: epigenetics, oxidative stress, non-enzymatic glycation of proteins and chronic inflammation.

Epigenetics involves genetic modulation by factors other than individuals' DNA sequence, and can regulate gene expression and determine which proteins are transcribed. There are different epigenetic regulation mechanisms: direct methylation of cytosine or adenine residues, covalent modifications of histone proteins, higher-order chromatin structure and non-coding RNAs. Disruptions or imbalances in epigenetic mechanisms can lead to the development of diabetic pathophysiology (Rosen et al., 2018).

MicroRNAs (miRNAs) are small non-coding RNA sequences synthesized as non-mature molecules that undergo several processing steps both in the nucleus and in the cytoplasm to become fully matured miRNAs. Once matured, miRNAs bind to their target gene's mRNA, leading to mRNA silencing or degradation (Wahed et al., 2010). Increasing evidence highlights the importance of miRNA mediated post-transcriptional regulation in different aspects of β-cell biology such as cell differentiation, cytokine and growth factor-mediated signaling, glucose metabolism and insulin synthesis and secretion (Lapierre et al., 2017). Deregulation of miRNA expression can directly impair β-cell function leading to the development of T2DM (Esguerra et al., 2018) . To date, more than 2600 miRNAs have been described within the human genome (miRBase, v.22.1), and multiple miRNAs have been shown to be involved in the pathogenesis of T2DM, including miR-200, miR-7, miR-184, miR-212/miR132 and miR-130a/b/miR-152 (Ofori et al., 2017). For instance, overexpression of miR-7 results in reduced insulin secretion via inhibition of genes involved in vesicle fusion and SNARE activity such as Snca, Cspa and Cplx1 (Latreille et al., 2014). In the case of

miR-375, over-expression results in impaired exocytosis and thereby reduced insulin secretion. Conversely, it is the down regulation of miR-375 expression that causes a reduction in β-cell mass (Latreille et al.,2015).

(Reddy et al., 2015) Several studies have evidenced that deregulation of the microRNA (miRNA) profile (post-translational histone methylation and non-canonical histone variant inclusion in octomers) may persist even after normoglycemia restoration (Mosammaporast et al., 2010). MiRNAs participate in metabolic memory by targeting the mRNA of genes encoding enzymes involved in DNA methylation and those tightly regulated at the level of promoter methylation, transcription, and processing (Breving et al., 2010). (Bravsacchi et al., 2019) It has been shown that high glucose levels can alter post-translational histone modifications (PTHMs) and the activity of DNA methyltransferases generating irreversible changes that explain the long-term harmful effects of metabolic memory (Al – Haddad et al., 2016).

Hyperglycemia induces an excess of ROS generation by mitochondria, which gives rise to diabetes complications that may persist even when hyperglycemia is controlled. The damage following hyperglycemia-induced oxidative stress can be prevented when good glycemic control is initiated very early, but is not easily reversed if poor control is maintained for a longer duration. At the early stages of T2DM, there is a relationship between hyperglycemia, increased oxidative stress, and excessive AGE formation. As the disease progresses, there is persistent protein glycation of the components of the respiratory chain that together with mitochondrial DNA damage can generate a hyperglycemia-independent concatenation of events leading to a synergy between oxidative stress and AGEs. The effects of this metabolic imbalance activate inflammatory processes through receptor binding of AGEs or ROS which can modify the composition and structure of the extracellular matrix. These structural changes may cause endothelial dysfunction and then atherosclerosis.

(Reddy et al., 2011) Finally, low-grade inflammation, which is involved in T2DM development and its vascular complications, has been shown to mediate metabolic memory. (Thompson et al., 2013) Many environmental factors (age, obesity, sedentarism and diet) that promote T2DM development trigger an inflammatory response leading to IR and endothelial dysfunction (Guarner et al., 2015). Obesity leads to NF-κB activation, which mediates the expression of inflammatory genes, which enhances monocyte binding to endothelial and vascular smooth muscle cells, subsequently promoting monocyte-to-macrophage differentiation (Reddy et al., 2011). In addition, NF-κB activation induces expression of inflammatory cytokines that are involved in vascular inflammation, with subsequent generation of endothelial adhesion molecules, proteases, and other mediators (Guarner et al.,

2015). Another important factor that links inflammation and oxidative stress in obesity conditions is the Toll-like receptor, which contributes to hypertension, insulin resistance, and obesity (Reddy et al., 2011).

In summary, T2DM is a heterogeneous and progressive disorder that represents a series of metabolic conditions associated with hyperglycemia and caused by defects in insulin secretion and/or insulin action due to a complex network of pathological conditions. There are many different paths, driven by various genetic and environmental factors, that interact and mutually reinforce each other leading to an increased risk of other diseases including heart, peripheral arterial and cerebrovascular disease, obesity and nonalcoholic fatty liver disease, among others. The complex network of pathological conditions leading to T2DM.

2.2.5. Insulin resistance

IR refers to a decrease in the metabolic response of insulin-responsive cells to insulin or, at a systemic level, an impaired/lower response to circulating insulin by blood glucose levels (C zech, 2017) There are three broad categories of IR or insulin-deficient conditions: (1) diminished insulin secretion by β-cells; (2) insulin antagonists in the plasma, due either to counter-regulatory hormones or non-hormonal bodies that impair insulin receptors or signaling; and (3) impaired insulin response in target tissues (Pearson et al., 2016). The action of insulin is influenced by the interplay of additional molecules including growth hormone and IGF-1 in the fed state. While fasting, the insulin response is mitigated by glucagon, glucocorticoids and catecholamine in order to prevent insulin-induced hypoglycemia. The ratio of insulin/glucagon plays a major role in this regulation, since it determines the relative degree of phosphorylation of downstream enzymes in the regulatory signaling pathways. While catecholamine promotes lipolysis and glycogenolysis, glucocorticoids promote muscle catabolism, gluconeogenesis and lipolysis. Hence, excessive secretion of these hormones may be responsible for inducing IR. Regarding the last category, there are three main extra-pancreatic insulin-sensitive organs that play major roles in the aforementioned processes: skeletal muscle, adipose tissue and liver. A defective action of insulin in these tissues often precedes the development of systemic IR, thus progressively leading T2DM.

2.5.1. Skeletal Muscle

Skeletal muscle IR is considered to be the most important extra-pancreatic factor in the development of T2DM. Under physiological conditions, insulin stimulates muscle glycogen synthesis by enhancing glucose uptake from plasma. There are three primary rate-limiting

factors implicated in glucose uptake and glycogen synthesis: glycogen synthase, hexokinase and the glucose transporter GLUT4. Upon insulin binding to insulin receptor (INSR) in muscle cells, GLUT4 translocates from intracellular compartments (early endosomes (EE), endosomal recycling compartment (ERC) and trans-Golgi network (TGN)) to the plasma membrane. This process allows glucose uptake and reduces circulating glucose levels (Satoh, T et al., 2014).

Mutations that reduce the expression of insulin receptor or GLUT4, as well as any defect in either upstream or downstream signaling pathway would reduce glucose intake into the muscle resulting in a hyperglycaemic state. The activation of INSR tyrosine kinase activity is essential for the action of insulin on glucose metabolism. Insulin binding to the α-subunit of the INSR causes phosphorylation of the β-subunit on multiple tyrosine residues and allows insulin-mediated signaling. Thus, mutations in any of the main phosphorylation sites can impair INSR tyrosine kinase activity, thereby impairing insulin action on skeletal muscle (Abdul – Ghani et al., 2010) . As mentioned above, mutations in key proteins of the downstream signaling pathway such as IRS-1 and IRS-2 or phosphoinositide 3-kinase (PI3K) also impair insulin action on the muscle. Apart from mutations or defective epigenetic regulation, environmental factors can also play an important role in glucose uptake by muscle. Physical activity increases blood flow into skeletal muscle cells and thereby enhances glucose utilization (Venkataswamy et al., 2015) . Obesity, which is associated with chronic inflammation, contributes to IR and T2DM. Increasing evidence suggests that as a consequence of obesity, increased immune cell infiltration and secretion of proinflammatory molecules in intermyocellular and perimuscular adipose tissue leads to skeletal muscle inflammation. This ultimately leads to myocyte inflammation, impaired myocyte metabolism, and contributes to IR via paracrine effects (Wu, H et al., 2017).

2.5.2. Adipose Tissue

Adipose tissue is a metabolically dynamic tissue capable of synthesizing a wide range of biologically active compounds that regulate metabolic homeostasis at a systemic level (Coelho, M et al.,2013). Indeed, adipose tissue participates in a broad range of biological processes involving, among others, immunity, coagulation, angiogenesis, fibrinolysis, reproduction, vascular tone control, appetite regulation, body weight homeostasis and glucose and lipid metabolism (Rosen, E. D et al., 2006).

Insulin acts on adipose tissue in two different ways: (1) stimulating glucose uptake and triglyceride synthesis; and (2) suppressing triglyceride hydrolysis and inducing the uptake of FFA and glycerol from circulation (Gastaldelli, A et al., 2017). In the fed state, GLUT4 allows uptake of glucose from the bloodstream into adipocytes, activating glycolysis in which

glycerol-3-phospate (glycerol-3-P) is produced and incorporated into lipogenic pathways. Glycerol-3-P, along with the fatty acids coming from VLDLs, are esterified, forming triacylglycerol (TGA) that is stored in lipid droplets. During metabolic stress, TGA droplets the adipocyte is depleted, in order to provide FFA to be used as an energy source in other tissues.

An impaired response to insulin stimulation by adipose tissue is known as adipose IR (Adipose-IR). Adipose-IR can lead to impaired suppression of lipolysis, impaired glucose uptake, and enhanced FFA release into plasma even in the presence of high insulin levels (C zech et al., 2020) . Among the signaling elements affected by adipose-IR, we found that defective AKT activation impairs GLUT4 translocation to the membrane and promotes the activation of lipolytic enzymes that aggravate hyperglycemia (C zech et al., 2017). Adipose-IR, as mentioned before, is associated with glucose intolerance and elevated release of FFA into a plasma that accumulates in other tissues such as muscle or liver. In the case of the liver, FFA accumulation results in impaired insulin signaling that promotes hepatic gluconeogenesis and impairs the glucose-stimulated insulin response, inducing T2DM development.

It has been shown that abnormally increased adipose tissue mass and adipocyte size correlate with pathologic vascularisation, hypoxia, fibrosis and macrophage-mediated inflammation (Scherer, P. E et al., 2019) . A high-fat diet and obesity can activate saturated FFA-stimulated adenine nucleotide translocase 2 (ANT2), an inner mitochondrial protein that results in adipocyte hypoxia and triggers the transcription factor hypoxia-inducible factor-1α (HIF-1α). This culminates in adipose tissue dysfunction and inflammation (Roden, M et al., 2019) . Hypertrophied adipocytes as well as adipose tissue-resident immune cells contribute to increased circulating levels of proinflammatory cytokines. This increase in circulating proinflammatory molecules, together with an increase in local cytokine releases such as TNF and IL-1β and IL-6 facilitates the emergence of a chronic state of low-grade systemic inflammation, also known as metabolic inflammation (Roden, M et al., 2019) . This chronic inflammatory state is considered to be a key part in the pathogenesis of IR and T2DM (Maki, K et al., 2011). The insulin stimulation effects on healthy and hypertrophic adipose tissue.

2.5.3. Liver

In the liver, insulin does not only regulate glucose production/utilization but also affects lipid metabolism more broadly. When circulating glucose levels increase and insulin is secreted by pancreatic β-cells, insulin binding to liver INSR induces autophosphorylation of the receptor. Consequently, insulin receptor substrates (IRSs) are recruited and phosphorylated. In turn, IRSs activate PI3K, which phosphorylates phosphatidylinositol (4,5)-bisphosphate (PIP2), generating phosphatidylinositol (3,4,5)-triphosphate (PIP3). PIP3 then activates PDK1, which

phosphorylates AKT. In addition, AKT is phosphorylated by mTORC2. Once AKT is fully activated, it participates in several downstream pathways that regulate multiple metabolic processes including glycogen synthesis, gluconeogenesis, glycolysis and lipid synthesis (Titchenell, P. M et al., 2017).

In physiological states, the combined action of glucagon and insulin allows the precise regulation of hepatic glucose output. While glucagon induces hepatic glucose production, insulin acts as a potent inhibitor of glucose production when its concentration in the blood is elevated. The effect of insulin on hepatic glucose production is due to both direct and indirect mechanisms. However, the relative importance of each of these mechanisms remains unclear.

In addition to inducing glycogen synthesis, insulin also inhibits hepatic glucose production by activating FOXO1, resulting in a reduction of hepatic glucose release. FOXO1 is a transcription factor that belongs to a subclass of the forkhead family of transcription factors that possess a forkhead box-type DNA binding domain (Oh, K. J et al., 2013). FOXO1 recognizes a specific regulatory element termed the insulin response element (IRE) on the promoters of glucose-6-phosphatase (G6Pase) and phosphoenolpyruvate carboxykinase (PEPCK) genes, both of which play important roles in maintaining glucose level in states of starvation (Montal et al., 2015). Thus, through inhibition of FOXO1, insulin promotes glucose storage as glycogen and inhibits glucose synthesis and hepatic glucose output.

Similar to the case in insulin-sensitive tissues, in states of IR, physiologic levels of circulating insulin are insufficient to elicit the appropriate insulin response in hepatic cells (Gast, K. B et al., 2012) . In the liver, IR impairs glycogen synthesis, fails to suppress glucose production, enhances lipogenesis, and increases the synthesis of proteins such as the proinflammatory CRP. In fact, the abnormal production of proinflammatory proteins such as adipocytokines and cytokines, combined with conditions such as oxidative stress, can lead to an inflammatory state responsible for altered insulin response by the liver.

2.2.6. T2DM Outcomes / Complications: Cardiovascular Risk

As described in the previous sections, T2DM is a multisystem disease with a strong correlation with CVD development (Gast KB et al., 2012). T2DM leads to a two- to four-fold increase in the mortality rate of adults from heart disease and stroke and is associated with both micro- and macro-vascular complications, the latter consisting of accelerated atherosclerosis leading to severe peripheral vascular disease, premature coronary artery disease (CAD) and increased risk of cerebrovascular diseases. These factors lead to T2DM

being considered a significant risk factor for CVD, likely through the involvement of several molecular mechanisms and pathological pathways. (Reaven G et al., 2012) These include the role of IR in atherosclerosis, vascular function, oxidative stress, hypertension, macrophage accumulation and inflammation (Laakso M et al.,2014). The following sections describe in detail the main factors implicated in cardiovascular risk outcomes from T2DM and the interactions between them (Bornfeldt KE et al., 2011).

2.2.7. Diabetes Projection Worldwide

Type 2 diabetes is a major health threat and a rising public health burden to millions of people worldwide. The number of people with diabetes will rise. It is expected that type 2 diabetes' prevalence in developing nations will rise 69 percent, and there could be a 20% increase in developed countries (Kaiser et al.,2012). This chronic metabolic disorder has become an epidemic in some countries, further exacerbating the existing burden for public health and healthcare providers in many locations (Olokoba et al., 2012). Population growth, increasing urbanization in developing countries, obesity, and increasing sedentary lifestyle are different risk factors contributing to the rise in diabetes around the globe (Acee, 2012).

2.2.8. Dietary Non-adherence

While it is common that physical activity and dietary adjustments are significant throughout the course of the disease, many type 2 diabetics may not follow the instructions from physicians, health educators, and dieticians about dietary change. Non-compliant behavior is likely to persist, even for many people who are on dietary plans (Sevick et al., 2010). For many type 2 diabetics, altering their dietary behaviors has proven to be beyond their reach (Vijan et al., 2011). Therefore, many of these patients fail to maintain good glycemic outcomes. In most cases, patients with diabetes have similar dietary practices compared to the general public (Kohinor et al., 2011). However, according to the National Institutes of Health (NIH, 2011) patients with diabetes need to make the following food choices:

- Eat smaller portions
- Eat less fat
- Eat more fiber by eating more whole-grain foods
- Eat variety of fruits and vegetables everyday
- Eat fewer foods that are high in sugar
- Eat fewer foods that are high in salts
- Never skip meals
- Limit the amount of alcohol you drink
- And make changes slowly

2.2.9. Physical Activity Non-adherence

Physical activity is important for diabetics along with proper meal planning and taking medications as prescribed by physicians (ADA, 2013b). However, people with diabetes are believed to be less ready to improve their physical activity than people without the diseases (Vähäsarja et al., 2012). According to the CDC (2012a), diabetic individuals need at least 30 minutes of moderate-intensity physical activity on five or more days each week. According to the World Health Organization (WHO, 2014), moderate- intensity physical activity involves a reasonable amount of energy and noticeably increases the heart rate. Moderate-intensity includes brisk walking, dancing, gardening, housework and domestic chores, traditional hunting and gathering, general building tasks, and carrying or moving moderate loads (< 20kg; WHO, 2014). On the other hand, WHO (2014) defines vigorous-intensity physical activity any exercise that requires an enormous amount of energy and causes rapid breathing and a significant rise in heart rate. According to WHO (2014), vigorous- intensity physical activity includes running, fast cycling, aerobics, fast swimming, competitive sports (e.g., football and basketball), heavy shoveling or digging ditches, and carrying or moving heavy loads (> 20kg). The ADA recommends the following types of physical activity for diabetics to manage their diabetes: aerobic exercise and strength training. The aerobic exercise (e.g., swimming, cycling, walking, and rowing) helps the body use insulin better, improves blood circulation, and lowers heart disease risks (ADA, 2013c). The ADA endorses the CDC's recommendation that type 2 diabetics need to perform at least 30 minutes of moderate to vigorous aerobic exercise five days a week, with no more than two consecutive days between exercising (ADA, 2013c). Also, the strength training (e.g., lifting light weights, resistance bands, heavy gardening, and free weight) lowers blood glucose in the body, helps to maintain strong muscles, and minimizes the risks for developing osteoporosis and bone fractures (ADA, 2013d) and ADA recommends twice a week. Sites serving as recruitment venues for the current study (i.e., Terre Haute Regional Hospital and Diabetes Endocrinology Clinic) confirmed that they instruct patients to follow the ADA's physical activity procedure.

2.2.10. Medication Non-adherence

According to CDC (2013a), medication adherence is "the patient's conformance with the provider's recommendation with respect to timing, dosage, and frequency of medication-taking during the prescribed length of time. Although dietary and exercise behavior change are essential to control blood glucose levels, adherence to physicians' guidelines about medication is equally important. While it is common that diabetics are advised about lifestyle changes and adherence to medications (as prescribed by physicians), medication non-compliance is prevalent among diabetics for example, in the Netherlands, type 2 diabetics'

adherence rate with oral glucose-reducing medications was between 61 percent and 85 percent (Wabe, Agoma, & Hussein, 2011).

2.2.11. Factors that Influence Patients' Adherence

Asche, LaFleur, and Conner (2011) reported that better compliance among type 2 diabetics leads to improved glycemic outcomes. However, several factors influence diabetic patients' adherence to physicians and health educators' instructions to improve their blood glucose levels. These factors include socioeconomic status (SES), education level of the patient, and the patient's self-efficacy. Also, the factors may include gender and race.

2.2.12. Socioeconomic Status

There is an inverse relationship between SES and the prevalence of type 2 diabetes among people and SES may influence the adherence rate of the type 2 diabetics with regards to medication and exercise. For instance, low-income families usually have "less access to both healthy food choices and opportunities for physical activity" (CDC, 2013b). (Peeters et al.,2010) reported that socioeconomic status may prevent some diabetic patients from getting access to medications and the materials needed for blood glucose control. In other words, diabetic patients from low-income families with a low education background may have difficulties enrolling in exercise practices, and buying diabetes medications on a regular basis. All these challenges may influence type 2 diabetics' adherence to treatment regimens prescribed by physicians and health educators. Work by (Borgsteede et al.,2011) indicated that patients' compliance is influenced by their experience with the disease, their past medications, and their friends and family members. Furthermore, patients' socioeconomic status may influence their beliefs about the disease as(Piette et al.,(2010) suggest in the following statement:

Many low-income patients with diabetes hold negative beliefs about their treatments, and that these beliefs are particularly prominent among African Americans. A trusting relationship with a primary care provider may mitigate these patient concerns but did not explain the consistent disparities in beliefs across racial groups, nor racial disparities in cost-related medication underuse. Clinicians should consider identifying ways to provide patients with more information about their treatments, and in particular should consider raising some of the specific areas of concern identified in this study during outpatient encounters.

2.2.13. Education Level

Many type 2 diabetics may not follow physicians and health educator's instructions about medication, exercise, and diet treatment to maintain optimum blood glucose levels (Al-Qazaz et al.,2011) argue that patients' level of education and their compliance to medication are two

variable factors that affect glycemic outcomes. The researchers concluded that “knowledge enhancement of patients with diabetes may improve their self-management activity and increase their awareness about the control of the disease” (Al-Qazaz et al., 2011). Patients can manage to control their blood glucose levels when they understand their disease better. However, some of the type 2 diabetics may have difficulties understanding the disease in the first several years after the diagnosis. It was found that long term diabetic patients understand the disease better than recently-diagnosed diabetics who do not realize that diabetes is a silent illness that may not show its effects long after the diagnosis.On the other hand, researchers differ on some of the factors that may influence type 2 diabetics’ adherence to recommendations. They reported that “education, income, health insurance coverage, number of physician visits per year, and other variables were not predictive of poor glycemic control”.

2.2.14. Self-efficacy

Self-efficacy may also have direct association with diabetes glycemic control and diabetics’ medication and exercise adherence. Self-efficacy is a key factor for the diabetics in managing active self-care (Gao et al., 2013). (Gao et al.,2013) argued that self- efficacy has a strong and direct link to better glycemic control. People are more likely to engage in a health behavior when they view it as beneficial and likely to reduce a health risk that would have serious consequences if left unchecked. Therefore, some diabetics may comprehend the health complications from uncontrolled blood sugars, such as kidney failure and heart diseases, then other diabetics. As a result, they regularly take their diabetes medications, eat healthy diets, and perform exercise routines as instructed by their doctors and health educators. Diabetics’ self-efficacy in adhering to physicians and health educators recommendations can be based on the benefits and the consequences of performing or ignoring certain activities.

2.2.15. Prevention / Delay of Type II Diabetes

Before people develop Type II diabetes, they almost always have "prediabetes" – blood glucose levels that are higher than normal but not yet high enough to be diagnosed as diabetes. Prediabetes is a serious medical condition that can be treated. A recently completed study carried out by scientists in the United States conclusively showed that people with prediabetes can prevent the development of Type II diabetes by making changes in their diet and by increasing their level of physical activity. They may even be able to bring their blood glucose levels back to the normal range. physical activity. They may even be able to bring their blood glucose levels back to the normal range.

Lifestyle changes are of outmost importance. A balanced diet and an increase of the level of physical activity can help maintain a healthy weight, stay healthier for longer and reduce the risk of diabetes. The results of the Diabetes Prevention Program (DPP) proved that weight loss through moderate diet changes and physical activity can delay or prevent Type II diabetes (Haus, 2010). The Diabetes Prevention Program (DPP) was a major multicenter

clinical research study aimed at discovering whether modest weight loss through dietary changes and increased physical activity or treatment with the oral diabetes drug metformin (Glucophage) could prevent or delay the onset of type II diabetes in study participants.

2.3. Vitamin D and type 2 diabetes mellitus

Vitamin D deficiency is associated with a decreased insulin release, insulin resistance and type 2 diabetes in experimental and epidemiological studies. Animal studies show that 1α,25–dihydroxy vitamin D_3($1,25(OH)_2D_3$) stimulates the pancreatic β-cell to secrete insulin. The relationship between vitamin D deficiency and insulin resistance could develop through inflammation, as vitamin D deficiency is associated with increased inflammatory markers. In addition, genetic polymorphisms of vitamin D −related genes may predispose to impaired glycemic control and type 2 diabetes. Epidemiologic studies showed an association between low serum 25-hydroxyvitamin D_3 ($25(OH)D_3$) concentration and an increased risk for the metabolic syndrome and type 2 diabetes. This may be partly explained by an increased fat mass. A possible causal relationship between vitamin D deficiency and type 2 diabetes should be proven by randomized clinical trials showing that either type 2 diabetes can be prevented or insulin release and insulin sensitivity can be improved by vitamin D supplements. The results of randomized clinical trials on the effect of vitamin D versus placebo, sometimes combined with calcium, in patients with impaired glucose tolerance (“prediabetes”) or type 2 diabetes are inconsistent. Some studies showed a slight decrease of fasting plasma glucose or improvement of insulin resistance, but often only in posthoc analyses. These effects are mainly visible in patients with vitamin D deficiency and impaired glucose tolerance at baseline. Meta-analyses of randomized clinical trials in general did not show significant effects of vitamin D supplementation on glycemic control. Currently, several large scales randomized clinical trials with vitamin D supplementation in doses of 1600–4000 IU/d are ongoing with glycemic control or incidence of diabetes mellitus as outcome. Vitamin D deficiency needs to be prevented or cured, but until the results of these trials are published, high-dose vitamin D supplementation cannot be recommended for prevention or amelioration of type 2 diabetes. (Paul Lips et al.,2017).

2.4. Association between vitamin D status and type 2 diabetes

2.4.1. Vitamin D

Vitamin D is a secosteroid hormone and it is critically important for the development,

growth, and maintenance of a healthy skeleton from birth until death (Andersen et al., 2007). Vitamin D has other roles in human health; it can play a role in decreasing the risk of many chronic illnesses, including cardiovascular disease, diabetes, autoimmune diseases, infectious diseases, and cancer (Zhang and Naughton, 2010 and Grober et al, 2013). Vitamin D exists in two common forms: cholecalciferol (vitamin D3) and ergocalciferol (vitamin D2). The primary route of vitamin D for most people is casual exposure to exposure to ultraviolet B

(UVB) sunlight at wavelengths between 290-315 nm. Vitamin D3 is also found in certain foods, including fish, egg yolk, offal such as Liver (Godar, D.E et al, 2011).

2.4.2. Regulation

Vitamin D through feedback inhibitory loop regulates its own synthesis (auto-regulation). Whereas, the activity of renal 1α-hydroxylase (rate limiting enzyme) is tightly regulated by numerous factors namely calcium, parathyroid hormone (PTH), calcitonin, Insulin like growth factor (IGF-I), fibroblast growth factor 23 (FGF23) and growth hormone (GH).(Girgis CM et al., 2013) PTH enhances1,25(OH)2D synthesis. Phosphate depletion enhances and hyperphosphatemia suppresses 1,25(OH)2D production. Furthermore, hypercalcemia reduces 1,25(OH)2D synthesis. The identification of fibroblast growth factor 23, a secretory protein expressed in osteoblasts and osteocytes, demonstrated a complex feedback loop along a bone-kidney axis, with pivotal roles in phosphate and vitamin D metabolism (Al Mheid I et al., 2017).

2.4.3. Mechanism of Vitamin D

The conjugated vitamin D with its receptor forms a heterodimer complex with retinoid X receptor and with other factors, attaches to vitamin D responsive elements on deoxyribonucleic acid, and alters gene expression. It has been estimated that vitamin D regulates more than 200 genes, directly or indirectly, thereby influencing a wide variety of physiological processes (Vanga et al., 2010; Stivelman and Retnakaran, 2012 and Wang et al., 2013).

2.4.4. Causes

Exposure to sunlight (UV-B radiation) is the limiting factor for the dermal synthesis of vitamin D. Even at optimal sunlight exposure, dark-skinned individuals (high melanin) synthesize less vit D compared to the whites. Decreased bioavailability mainly occurs due to malabsorption syndromes and obesity (sequestration of vit D in adipose tissue results

in low plasma concentration). Increased catabolism occurs through the induction of hepatic cytochrome p450 enzymes. Certain classes of drugs like anti-epileptics, anti-retrovirals, immune-suppressants increase hepatic degradation of vit D. Decreased conversion of 25(OH)D to 1,25(OH)D due to renal dysfunction and chronic kidney disease limiting the renal 1-alpha-hydroxylase activity and excess urinary loss of vitamin D binding protein. Thyroid disorders namely hyperthyroidism and primary hyperparathyroidism enhance the metabolism of vit D. (Holick MF et al., 2011) Besides all the above-mentioned factors, with increasing age the ability of skin to convert 7-dehydrocholesterol into vitamin D decreases

thus predisposing individuals to VDD associated skeletal and non-skeletal diseases (Chakhtoura M et al., 2013).

Over the years, vitamin D has been implicated in various non-skeletal diseases. The extraskeletal phenomenon can be attributed to the presence of vitamin D receptors (VDRs) and identification of 1 - α hydroxylase in extrarenal tissues. The identification of VDRs in almost all tissues in the body (Adam JS et al., 2010) linked vitamin D (1,25(OH)2D) with a wide array of biological functions such as, pancreatic insulin production, inhibition of renin release, suppression of angiogenesis cellular proliferation inhibition, induction of terminal differentiation, and stimulation of macrophage cathelicidin production. (Adam JS et al., 2010) The presence of 1 α - OHase in almost all tissues [150, 174, 175] coupled with the local production of 1,25(OH)2D may be involved in the regulation of nearly 200 genes [177] which in turn facilitate various health benefits of vitamin D. (Holick MF et al., 2007) Moreover, VDD has been linked to the increased rates of T2DM and CAD. (Young KA et al., 2011). Mere association does not essentially mean causation, the effect of restoration of normal vitamin D status on T2DM and CAD prevention is still debatable (Kunadian V et al., 2014).

There is no unanimity on the additional health benefits credited with the maintenance of serum 25(OH)D levels of 30 ng/mL or higher compared to 20 ng/mL in the general population. The higher levels proposed by the Endocrine Society guidelines were opposed by the Institute of Medicine owing to the lack of substantial evidence to establish the basis for these recommendations. The two bodies however, agreed that vitamin D is vital for bone health and there is no convincing evidence regarding the benefits of vitamin D on CVD or overall mortality. Other major points of disagreement are the cost involved in screening (limiting the routine use of the test) and the definition of “at-risk” population. However, both bodies were consistent over the dietary reference intakes and also said that routine screening of general population for VDD is not necessary (Al Mheid I et al., 2017).

2.4.5. Vitamin D status assessment and normal values:

25-hydroxyvitamin D is the major circulating form of vitamin D and the concentrations are under homeostatic control. Serum concentrations are closely reflecting the amount of vitamin D synthesized either from cutaneous synthesis or from dietary intake. For this reason, the blood concentration of 25OHD is widely accepted and used by clinicians as a biomarker to determine vitamin D status (Hill TR et al, 2013).

VITAMIN D NORMAL AND ABNORMAL LEVELS (Holick et al, 2011)

25(OH) Level (ng/ML)	25 (OH) D Level (n mol/L)	Laboratory Diagnosis
<20	<50	Deficiency
20 – 32	50 - 80	Insufficiency
54 – 90	135 - 225	Normal in sunny countries
>100	>250	Excess
>150	>325	Intoxication

2.4.6. Vitamin D and Diabetic complications:

Vitamin D has got various pleiotropic effects such as suppression of cell-mediated immunity, regulation of cell proliferation, stimulation of neurotrophic factors like nerve growth factor, neurotropin, suppression of RAAS, reduction of albuminuria, immunomodulatory, anti-inflammatory and antiangiogenic effects (Zhang Y et al,2009; Chabas JF et al, 2008). Thus, vitamin D levels may play a significant role in the pathogenesis of type 2 diabetes. The researchers concluded that low vitamin D levels might play a significant role in the pathogenesis of diabetic complications.

Robinson JG et al, 2011 in his study among older women found that vitamin D levels were significantly lower in those diabetics who had microvascular complications. In another study Aksoy H et al, 2000 also found that mean vitamin D3 concentrations negatively significant with increasing severity of diabetic retinopathy.

Payne JF et al, 2012 in his cross-sectional study showed that patients with diabetes, especially those with PDR, have lower 25(OH) D levels than those without diabetes. In earlier study Suzuki. A et al, 2006 found that the existence of PDR was significantly associated with a decrease in serum vitamin D concentrations.

Soderstorm LH et al, 2012 noticed vitamin D insufficiency is associated with the adjusted composite measure of neuropathy. Similar results noticed in another study where Chaychi et

al, 2012 found that severity of diabetic polyneuropathy significantly associated lower mean serum vitamin D level.

Diaz et al, 2009 in their cross-sectional analysis found that there is a high prevalence of vitamin D deficiency (48.9%) and insufficiency (36.6%) in individuals with diabetic nephropathy. Lee P et al, 2009 conducted a cross-study to evaluate the impact of vitamin D repletion on neuropathic pain in patients with type 2 diabetes and found that all patients were vitamin D insufficient.

Recently Balaji S et al, 2014 conducted a cross-sectional study (Philadelphia) to study the correlation of vitamin D levels with microvascular complications in type 2 diabetes. Where they demonstrated mean vitamin D was lower in type 2 diabetics than healthy subjects (19.046 vs. 27.186 ng/ml). Prevalence of vitamin D deficiency and insufficiency was found to be significantly higher in diabetics when compared to healthy subjects. Lower levels of vitamin D were found to be associated with increasing prevalence of combinations of microvascular complications namely neuropathy with retinopathy, neuropathy with nephropathy, retinopathy with nephropathy and neuropathy with retinopathy with nephropathy.

METHODOLOGY

CHAPTER-3

METHODOLOGY

The methodology for the study entitled "**INCIDENCE OF DIABETES AMONG SEDENTARY WOMEN AND ASSESSMENT OF VITAMIN D STATUS**" is described

3.1. SELECTION OF AREA

3.2. SELECTION OF SAMPLES

3. 3. TOOLS AND TECHNIQUES OF DATA COLLECTION

3.4 ASSESSMENT OF NUTRITIONAL STATUS

3.4.1 ANTHROPOMETRIC MEASUREMENTS

3.4.2 BIOCHEMICAL ASSESSMENT

3.4.3 CLINICAL ASSESSMENT

3.4.4 DIETARY ASSESSMENT

3.5 ORAL INVESTIGATION

3.5.1 LIFESTYLE PATTERN

3.5.2 DIETARY PATTERN

3.6 DEVELOPMENT OF AN EDUCATIONAL TOOL TO CREATE AWARENESS AMONG SELECTED SUBJECTS

3.1 SELECTION OF AREA

More than one- fourth of adults, both men and women, in Ernakulam have diabetes and high blood pressure or hypertension. This is the population that is so vulnerable to complications. Diabetes and hypertension are the two most common comorbidities in sedentary women.

Almost 26% of men and women have high or very high sugar levels and are taking medication for it, while it is 30% each for hypertension.

As per the Ministry of health and family welfare's district health fact-sheet for 2019 to 2020 most of the people born in South Asian ethnicity are genetically predisposed with two or three times are at a high risk of developing coronary heart disease and diabetes mellitus.

Higher prevalence of hypertension and diabetes has been known to occur in states with greater urbanization. It may be related to unhealthy lifestyle, food habits, lack of exercise, alcohol consumption. Ernakulam district of Kerala state was selected as the locale for the study. This area was selected because of the availability of samples as well as our accessibility for the project.

3.2 SELECTION OF SAMPLES

Random sampling is the basic sampling technique where we select a group of subjects (a sample) for study from a larger group (a population). Each individual is chosen entirely by chance and each member of the population has an equal chance of being included in the sample. Every possible sample of a given size has the same chance of selection (Definition taken from Valerie J. Easton and John H. McColl's).

Technique of sampling for the survey used was purposive sampling method. About 150 samples were selected from the general population by random sampling. The samples included at the age of above 30 years of sedentary women since it was seen that the samples at this age group were more prone to diabetes.

Inclusion criteria:

Sedentary women above 30 years

Exclusion criteria:

Pregnant women
Lactating women
Geriatric
population

3.3. TOOLS AND TECHNIQUES OF DATA COLLECTION

The data collected for the study was collected through a well-structured questionnaire. From the subjects, an interview schedule was formulated. The interview schedule included: personal details, medical history, nutritional assessment and lifestyle pattern. The data was collected through an interview with the subjects. They were assessed anthropometrically, biochemically and clinically, whereas, self-reported data was collected for the dietary analysis. The questions included in the questionnaire were divided into various section; personal details, dietary details, anthropometric measures, medical history, dietary assessment. The dietary assessment was done through, 24-hour recall section and certain general questions which included mainly open-end questions.

3.3.1 Interview Schedule

A pretested interview schedule was developed for the study. According to Kothari (2004), the interview method of collecting data involves presentation of oral-verbal stimuli and reply in terms of oral verbal responses. The interview schedule was administered to each of the subjects to elicit information on socio-demographic profile, genetic predisposition, physical activity pattern, dietary intake and medical profile. Frequency of food intake and twenty-four-hour dietary recall were determined. Physical activity pattern was recorded using the 24-hour activity record.

3.3.2 Questionnaire

Questionnaire was used to collect the information required for the study. A questionnaire is simply a list of mimeographed or printed questions that is completed by or for a respondent to give his opinion (S Roopa et al., 2012). Appropriate data gathering tool is devised with the due reference to the objectives of the present study an interview schedule which is defined as an oral questionnaire that permits an exchange of ideas and information is used for data collection it is unique as it involves gathering data through direct verbal interaction between the interview and interview that he feels free to express himself fully and truthfully (Kothari 2004).

Various questions useful in the field of study were included in the schedule, mainly covered were information gathering socioeconomic status, knowledge, attitude, medical history, biochemical values, anthropometric measurements, clinical assessments and dietary pattern.

3.4 ASSESSMENT OF NUTRITIONAL STATUS

Nutritional status is a global term that encompasses a number of specific components (August et al., 2002). Nutritional assessment of groups and individuals is a prerequisite to planning for the prevention or solution of nutrition related health problems (Judith,2011). To assess the nutritional status of selected samples Anthropometric measurements, Biochemical analysis and Dietary assessment were done.

3.4.1 Anthropometric Measurements

The term anthropometry refers to comparative measurements of the body. Anthropometric measurements are used in nutritional assessments. Those that are used to assess growth and development in children, and adolescents include height and weight. Individual measurements are usually compared to reference standards on a growth chart. Anthropometric measurements used for adults usually include height, weight, BMI, waist-to-hip ratio These measures are then compared to reference standards to assess weight status and the risk for various disease.

3.4.1.1 Measurement of height

Height is useful in determining the nutritional status. The height of an individual is influenced by both genetic (hereditary) and environmental factors. It is affected only by long term nutritional deprivation and is considered as an index of chronic long duration malnutrition (Bamji, 2007). A measuring tape was used to measure the height. The subject was made to stand erect looking straight (Frankforts plane) on a leveled surface without shoes toes apart, with heels together touching the wall. The point of contact of the head was then marked with a scale held perpendicular and the reading noted with an accuracy of 0.1cm graduation.

PLATE NO. 1

3.4.1.2 Measurement of weight

Body weight is the most widely used and the simplest reproducible anthropometric measurement for the evaluation of nutritional status. Weight is a most important factor for identifying obesity. Weight is measured in kilograms (kg). Weight can be assessed using a weighing machine. The subjects should have minimal clothing and the weighing scale should be tared to zero. Weight that is higher than what is considered as a healthy weight for a given height is described as overweight or obese. Weight that is lower than what is considered as healthy for a given height is described as underweight (Centre for disease control and prevention,2020). The weight measurements were taken using a weighing machine.

PLATE NO. 2

3.4.1.3 Body Mass Index

BMI is one of the most popular measures used to assess overweight and obesity. BMI does not separate fat mass from muscle mass, but is highly correlated with both adipose tissue and muscle mass. BMI tends to increase with age in young adults. This increasing trend is reversed at older ages which differ in different ethnicities (Stevens et al., 2010).

The Body Mass Index (BMI) is defined as the weight in kilograms divided by the square of the height in meters (kg/m2). BMI was calculated from the following equation:

BMI (kg/m^2) = Weight (kg) / Height (m^2)

Thus, BMI was computed from the height and weight measurements recorded.

Nutritional status based on the WHO and Asian criteria value

Nutritional status	**WHO criteria** **BMI cut-off**	**"Asian criteria "** **BMI cut – off**
Underweight	<18.5	<18.5
Normal	18.5 – 24.9	18.5 – 22.9
Overweight	25 – 29.9	23 – 24.9
Pre-Obese	-	25 – 29.9
Obese	>30	>30
Obese Type 1(obese)	30 – 40	30 – 40
Obese Type 2 (morbid obese)	40.1 – 50	40.1 – 50
Obese Type 3 (super obese)	>50	>50

3.4.1.4 Measurement of waist circumference (WC)

The measuring tape was made of leather, which provided soft tactile sensation for the participants and was not stretched. The participants were asked to stand upright, with both feet touching and arms hanging freely. The tape was placed at the midpoint between the lowest rib and iliac crest, and measurement made with sufficient tension after individuals purposefully exhaled (Klein et al., 2007). The WC measurements were taken three times and recorded to the nearest 0.1cm. The mean values were used for statistical analysis.

3.4.1.5 Measurement of hip circumference (HC)

Hip circumferences are measured to the nearest 0.1 cm using a flexible narrow non stretch tape in adults wearing minimal clothing, standing straight but not pulling in their stomachs. It is measured at the largest circumference around the buttocks. Measurement error occurs if the tape is pulled too tight or loose, or if subjects wear clothes with belts and/or full pockets (J. Eaton–Evans, 2005).

3.4.2 Biochemical Assessment

I had measured the serum 25-hydroxyvitamin D and HBA1C for the test and also noted down their values.

PLATE NO. 3

3.4.2.1 HBA1C

HbA1c reflects average plasma glucose over the previous eight to 12 weeks. It can be performed at any time of the day and does not require any special preparation such as fasting. These properties have made it the preferred test for assessing glycemic control in people with diabetes. More recently, there has been substantial interest in using it as a diagnostic test for diabetes and as a screening test for persons at high risk of diabetes (WHO, 2011).

A report published in 2009 by an International Expert Committee on the role of HbA1c in the diagnosis of diabetes recommended that HbA1c can be used to diagnose diabetes and that the diagnosis can be made if the HbA1c level is ≥6.5% (16). Diagnosis should be confirmed with a repeat HbA1c test, unless clinical symptoms and plasma glucose levels >11.1mmol/l (200 mg/dl) are present in which case further testing is not required. Levels of HbA1c just below 6.5% may indicate the presence of intermediate hyperglycemia. The precise lower cut-off point for this has yet to be defined, although the ADA has suggested 5.7 – 6.4% as the high-risk range.

Diagnostics criteria for diabetes and prediabetes, (ICMR,2018)

Parameter	**Normoglycemia (mg/dl)**		**Prediabetes (mg/dl)**		**Diabetes (mg/dl)**
	WHO	ADA	WHO	ADA	
FPG	<110	<100	110-125(IFG)	110-125(IFG)	≥ 126
2-h PG	<140		140-199(IGT)		≥ 2000
Hba1c	<5.7%		5.7-6.4%		≥ 6.5%
Random Plasma glucose*					≥ 200 (with symptoms of diabetes)

3.4.2.2 Serum 1, 25 – hydroxy vitamin D test

According to Bc Guidelines (2019)

25(OH)D Levels and Health	
<30 nmol/L	Risk of Vitamin D deficiency (rickets or oseteomalacia)
30-50 nmol/L	Clinical features of inadequacy in some individuals
≥50 nmol/L	Adequate for bone health in practically all individuals
> 125 nmol/L	Concern for vitamin D toxicity

3.4.3 Clinical Assessment

It includes medical history, health history and physical examination on the day of appointment, the clinical procedures were done as follows:

a. Completion of the focused history section of the study protocol
b. Physical measurements which included:

- Weight Measurement – Weight was measured with an electronic weighing scale without shoes and with the subject on light clothing to the nearest 0.1kg
- Height Measurement – Height was measured with a portable stadiometer to the nearest 0.1cm
- Waist circumference – Using a non-stretch tape, the waist circumference was taken midway between the inferior margin of the last rib and the iliac crest in a horizontal plane to the nearest 0.1cm at the end of normal expiration
- Hip circumference – using a non-stretch tape, the hip circumference was taken around the widest portion of the buttocks, to the nearest 0.1cm

3.4.4 Dietary Assessment

Dietary assessment is conducted with the help of interview schedule. When a systematic enquiry into the food supplies and food consumption of individual and population group is made, we call it a diet survey. Dietary assessment provides information about the dietary intake of individuals. Several methods are used to collect dietary assessment. In my

study it was done by using 24-hour recall method for 3 days food intake was not holidays or days of celebration by asking some questions about their dietary intake.

3.4.4.1 24 Hour Recall

According to NIH, a 24-hour dietary recall is a structured interview intended to capture detailed information about all the foods and beverages consumed by the respondent in the past 24 hours. In addition to other detailed descriptors, such as time of day and source of food, the portion of size of each food and beverage is captured. The food intake of all samples was recorded by 24hour diet recall method. The subjects were asked to recall for 3 days food intake were not holidays or days of celebration in terms of simple household measures.

3.4.4.2 Food Frequency Questionnaire (FFQ)

Food frequency was determined using the Food Frequency Questionnaire (FFQ). It is the most commonly used method in epidemiological studies to assess the diet in relation to chronic diseases. The goals of diet assessment are to obtain a measure of usual rather than current diet.

The consumption of a particular food by an individual is estimated using FFQ wherein frequency of intake of food items in major food groups like cereals

(Wheat and rice), pulses and legumes, vegetables, roots and tubers, fruits, milk and milk products, flesh foods by the subject is noted, to assess dietary consumption pattern.

3.5 Oral Investigation

3.5.1 Lifestyle Pattern

The lifestyle patterns of the 200 samples were assessed. I had also included yes or no questions to know their lifestyle patterns. Questions about exercise, sleeping hours, daily activity etc. was asked to the samples.

3.6 Dietary Pattern

The dietary patterns of 200 samples were assessed. some general questions and objective type questions were included in the interview schedule such as details on meal consumption, skipping meals, intake of supplements and tablets, binging junk foods, vegetarianism or non-vegetarianism for more specific data.

5.Development of educational tool to create awareness among selected subjects

The studies show that interventions should be aimed at increasing physical activity along with healthier food patterns and health education. Successful community-based intervention programs have been reported in developed countries and a similar approach is required in developing countries.

Nutritional Awareness class was conducted among selected diabetic sedentary women with vitamin d deficiency using educational tools such as PowerPoint. This imparted knowledge on causes, risk factors leading to vitamin d deficiency. The selected diabetic sedentary women given awareness about the management techniques through the practice of healthy food habits increasing consumption of vitamin d rich food, exposure of sunlight and other sources through which vitamin d can be achieved. It was circulated among the selected subjects.

RESULT AND DISCUSSION

Chapter-4

RESULT AND DISCUSSION

The result and discussion of the study entitled "**INCIDENCE OF DIABETES AMONG SEDENTARY WOMEN AND ASSESSMENT OF VITAMIN D STATUS**" are discussed under the following headings:

4.1 SOCIOECONOMIC DETAILS

4.1.1 AGE

4.1.2 RELIGION

4.1.3 MARITAL STATUS

4.1.4 MONTHLY INCOME

4.1.5 TYPE OF FAMILY

4.1.6 NATURE OF WORK

4.2 DIABETES

4.2.1 SUBJECT WITH DIABETES MELLITUS

4.2.2 MEDICATION FOR DIABETES

4.3 CLINICAL SIGNS PERTAINING TO DETERMINE VITAMIN D DEFICIENCY

4.3.1 LETHARGY EXPERIENCED BY THE SUBJECTS

4.3.2 BODY ACHE EXPERIENCED BY THE SUBJECTS

4.3.3 BACK ACGE EXPERIENCED BY THE SUBJECTS

4.3.4 DEPRESSION EXPERIENCED BY THE SUBJECTS

4.3.5 INFECTIONS EXPERIENCED BY THE SUBJECTS

4.3.6 MUSCLE PAIN EXPERIENCED BY THE SUBJECTS

4.3.7 CONSTIPATION EXPERIENCED BY THE SUBJECTS

4.3.8 DEHYDRATION EXPERIENCED BY THE SUBJECTS

4.3.9 TREATMENT FOR INFERTILITY

4.4 COVID-19 AFFECTED BY THE SUBJECTS

4.4.1 SYMPTOMS DURING COVID-19

4.4.2 POST COVID PROBLEMS EXPERIENCED BY THE SUBJECTS

4.5 POSSIBLE CAUSES OF VITAMIN D DEFICIENCY

4.5.1 USE OF SUNSCREEN

4.5.1.1 FREQUENCY OF USING SUNSCREEN

4.5.1.2 SPF OF SUNSCREEN Use

4.5.2 PREFERENCE OF SHADES WHEN OUTDOOR

4.5.3 PREFERENCE TO STAY INDOOR DURING THE DAY

4.5.4 PHYSICAL ACTIVITY AMONG THE SUBJECTS

4.5.5 DETAILS ON SUN EXPOSURE

4.5.5.1 DURATION OF SUN EXPOSURE

4.5.5.2 PREFERENCE OF DRESS

4.6 NUTRITIONAL STATUS

4.6.1 ANTHROPOMETRIC ASSESSMENT

4.6.1.1 HEIGHT

4.6.1.2 WEIGHT

4.6.1.3 WAIST HIP RATIO

4.6.1.4 BMI

4.6.2 BIOCHEMICAL ASSESSMENT

4.6.2.1 HBA1C

4.6.2.2 SERUM VITAMIN D (1,25-HYDROXY VITAMIN D)

4.6.3 DIETARY ASSESSMENT

4.6.3.1 DIETARY HABIT

4.6.3.2 FOOD INTAKE AT REGULAR TIME

4.6.3.3 MEAL PATTERN PER DAY

4.6.3.4 SKIPPING OF MEALS

4.6.3.5 COMPENSATE FOR SKIPPED MEALS

4.6.4.6 GOOD APPETITE

4.6.3.7 PLACE OF FOOD CONSUMPTION

4.6.3.8 EATING JUNK FOODS

4.6.3.8.1 FREQUENCY OF EATING FAST FOOD

4.6.3.9 CONSUMPTION OF VITAMIN D SUPPLEMENTS

4.6.3.10 24 HOUR RECALL METHOD

4.6.3.10.1 ENERGY (kcal)

4.6.3.10.2 CARBOHYDRATE (gm)

4.6.3.10.3 PROTEIN (gm)

4.6.3.10.4 FAT (gm)

4.6.3.10.5 FIBRE (gm)

4.6.3.10.6 CALCIUM (mg)

4.6.3.10.7 VITAMIN D (IU/day)

4.6.3.10.8 PHOSPHORUS (mg)

4.6.3.10.9 MAGNESIUM (mg)

4.6.3.11 FOOD FREQUENCY TABLE

4.6.3.11.1 FOOD FREQUENCY OF VITAMIN D RICH FOODS

4.6.3.11.2 FOOD FREQUENCY OF CARBOHYDRATE RICH FOODS

4.7 STATISTICAL DATA

4.7.1 T-TEST 24 HOUR RECALL

4.7.2 SERUM VITAMIN D

4.7.3 ASSOCIAION BETWEEN DAIBETES MELLITUS AND SERUM VITAMIN D

4.1 SOCIOECONOMIC DETAILS

TABLE NO. 4.1.1: AGE

Age (years)	**No: of Subjects (n=150)**	**% of subjects**
30 - 35	39	26%
36- 40	12	8%
41 - 45	26	17%
46 - 50	25	17%
51 - 55	48	32%

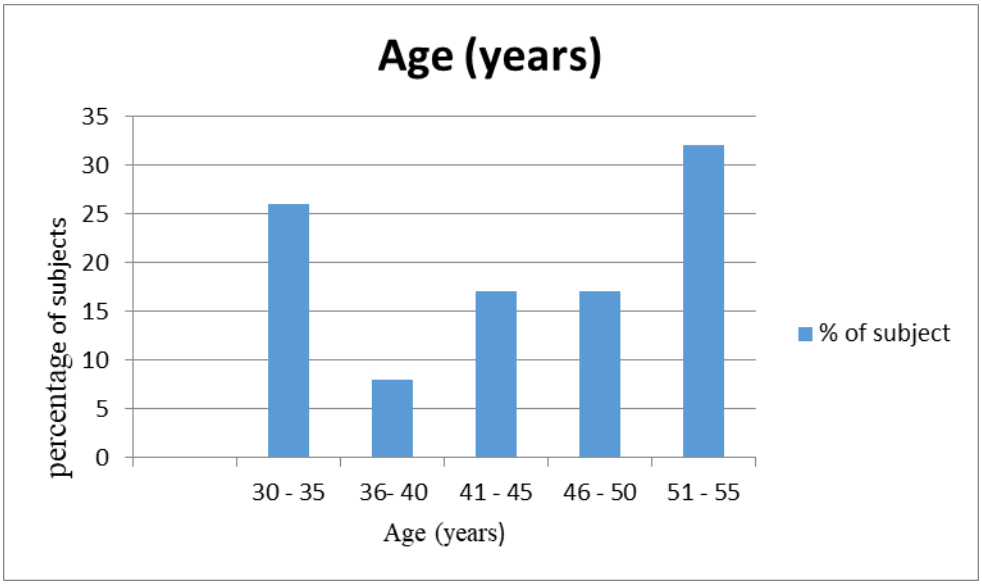

FIGURE NO. 4.1.1

From the graph it is clear that more than 30% of the subjects were in the range of 51-55 years and 8% of the subject fall under the range of 36-40 years. The age range 41-45 and 46-50 showed a same distribution of 13%.

TABLE NO. 4.1.2: RELIGION

Religion	**No: of subjects (n=150)**	**% of subjects**
Christian	26	17%
Muslim	51	34%
Hindu	73	49%

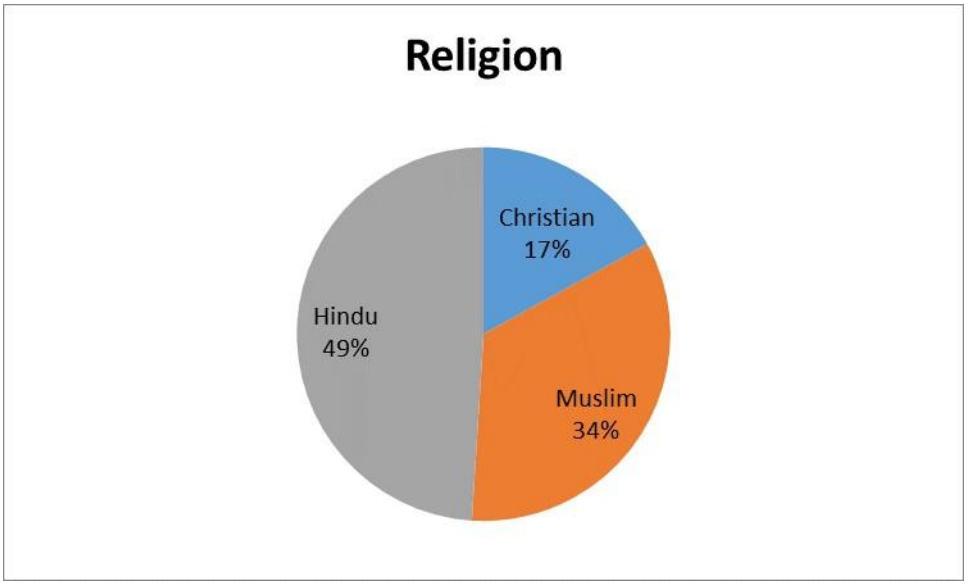

FIGURE NO. 4.1.2

Among the subjects 49% of the subjects were Hindus, 34% were Muslims and 17% were Christians.

TABLE NO.4.1.3: MARITAL STATUS

Marital Status	**No: of subjects (n=150)**	**% of subjects**
Single	2	2%
Married	134	89%
Widow	14	9%

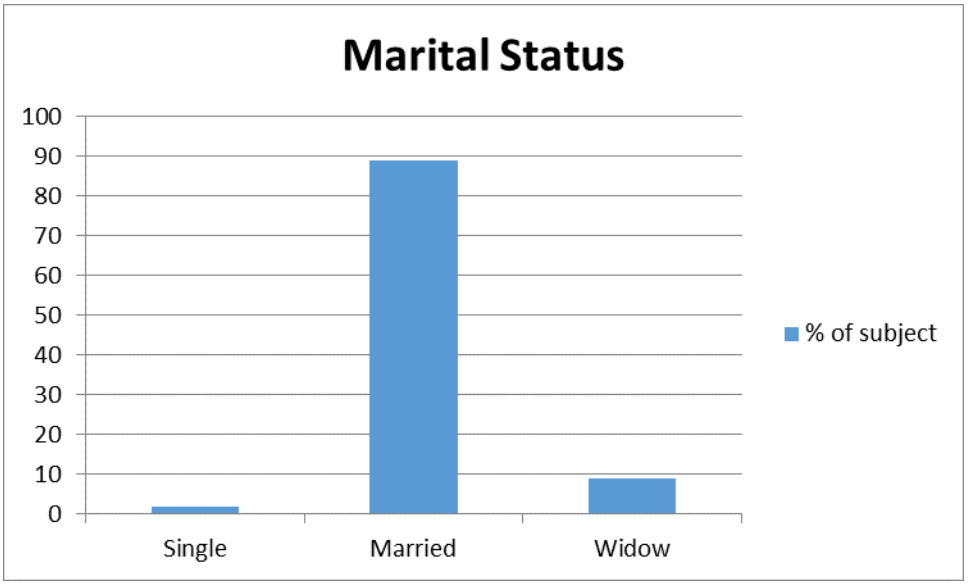

FIGURE NO. 4.1.3

Out 150 participants 89% were married, 9% were Widow and 2% were single.

TABLE NO.4.1.4: MONTHLY INCOME

Monthly Income (Rs)	**No: of subjects (n=150)**	**% of subjects**
10 - 20,000	9	6%
20– 30,000	33	22%
Above 40,000	108	72%

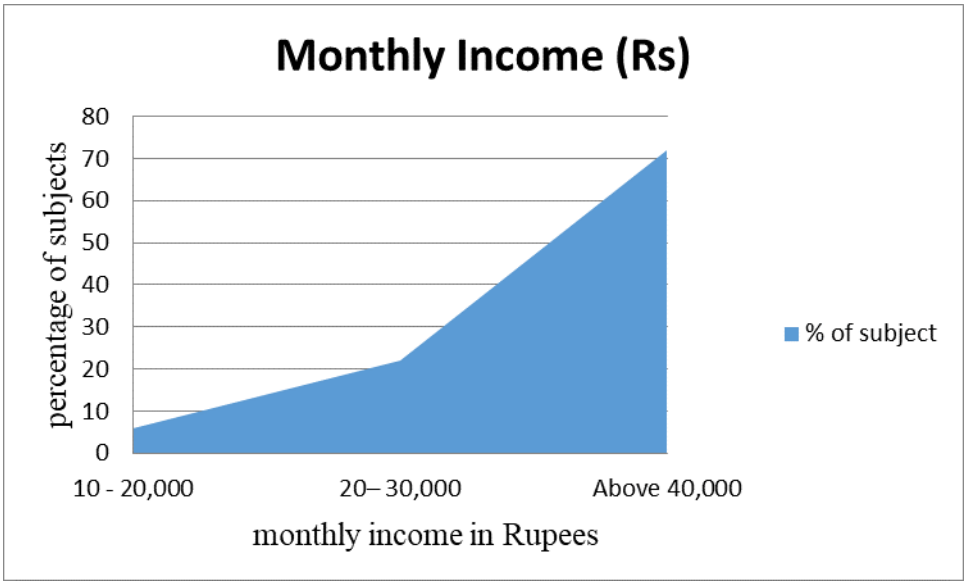

FIGURE NO. 4.1.4

Among the subject 72% have an income ranging above Rs 40,000, 22% have an income ranging from 20 to 30 thousand and 6% have an income ranging from 10 to 20 thousand.

TABLE NO. 4.1.5: TYPE OF FAMILY

Type Of Family	**No: of subjects (n=150)**	**% of subjects**
Joint family	19	13%
Nuclear family	131	87%

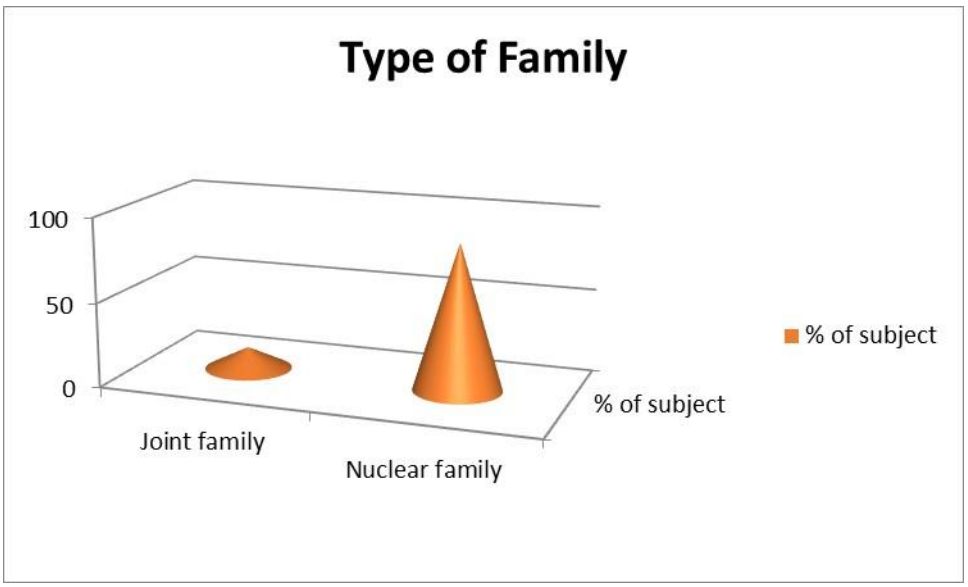

FIGURE NO. 4.1.5

Among the 150 subjects 87% of the subjects were from the nuclear family and 13% of the subjects from the joint family.

TABLE NO. 4.1.6: NATURE OF WORK

Nature of work	**No: of subjects (n=150)**	**% of subjects**
Academician	6	4%
Bank professional	10	7%
Health professional	7	5%
Other	127	84%

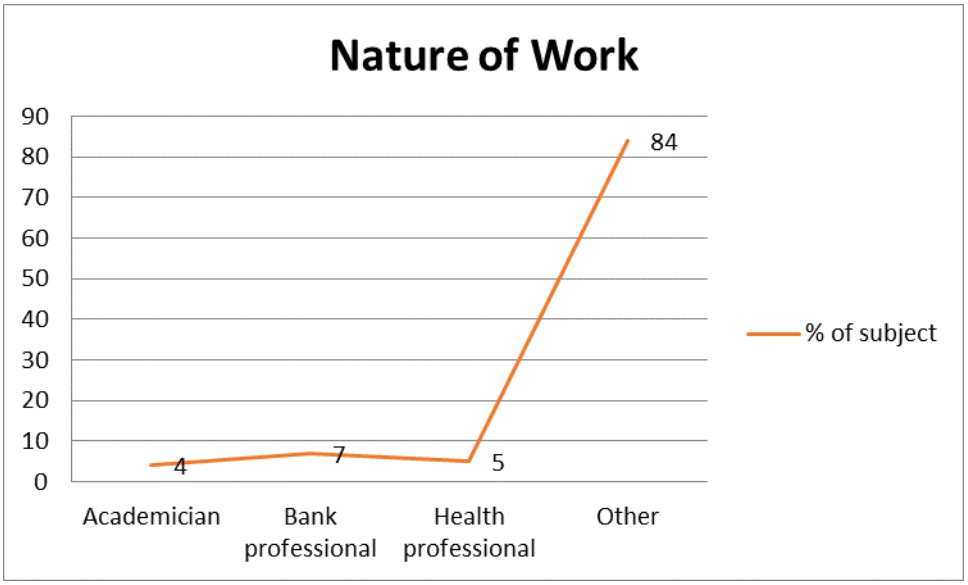

FIGURE NO. 4.1.6

The above data represents the nature of work, among them the least 4% of subjects were found to be working as academician and highest 84% of them were having other nature of work.

4.2 DIABETES

TABLE NO. 4.2.1: SUBJECTS WITH DIABETES MELLITUS

No: of subjects with diabetes mellitus	**No: of subjects (n=150)**	**% of subjects**
Yes	120	80%
No	30	20%

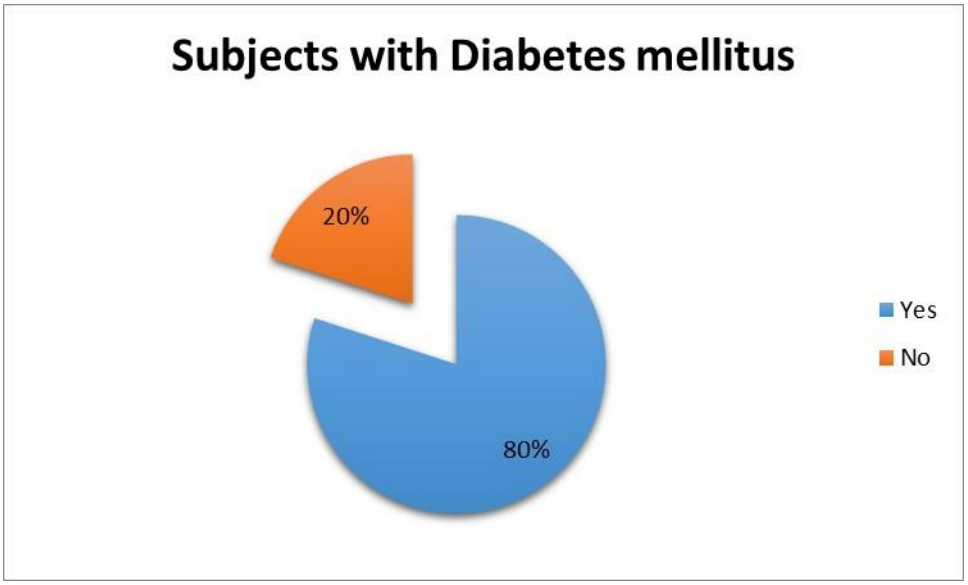

FIGURE NO. 4.2.1

Among the total subjects 80% of subjects suffer from diabetes and 20% are not diabetic.

TABLE NO. 4.2.2: MEDICATION FOR DIABETES

Medication	**No: of subjects(n=150)**	**% of subjects**
Yes	135	90%
No	15	10%

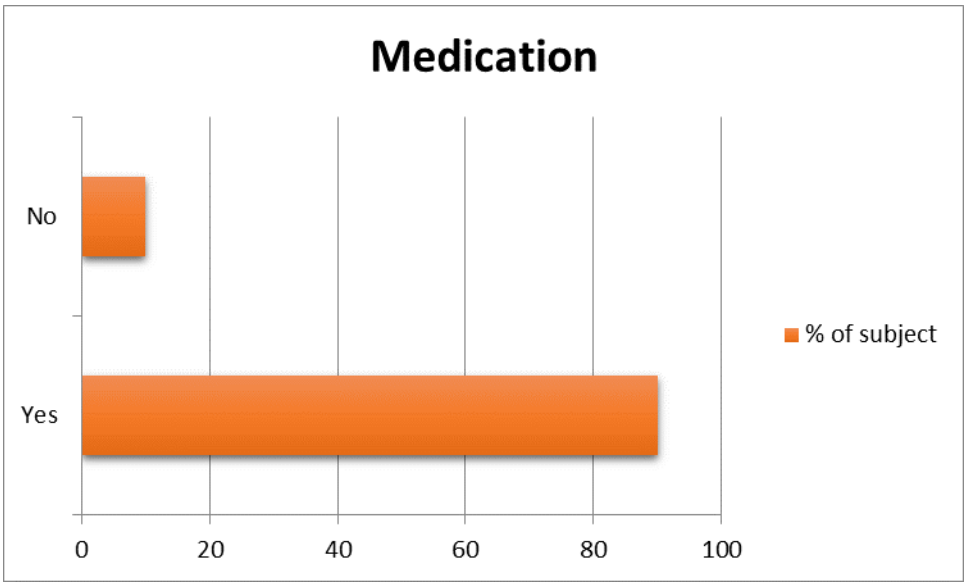

FIGURE NO. 4.2.2

From the graph it is clear that around 90% of the total subjects are on medication and 10% of the subjects are not taking medication

4.3 CLINICAL SIGNS PERTAINING TO DETERMINE VITAMIN D DEFICIENCY

TABLE NO. 4.3.1: LETHARGY EXPERIENCED BY THE SUBJECTS

Lethargy	**No: of subjects (n=150)**	**% of subjects**
Yes	54	36%
No	96	64%

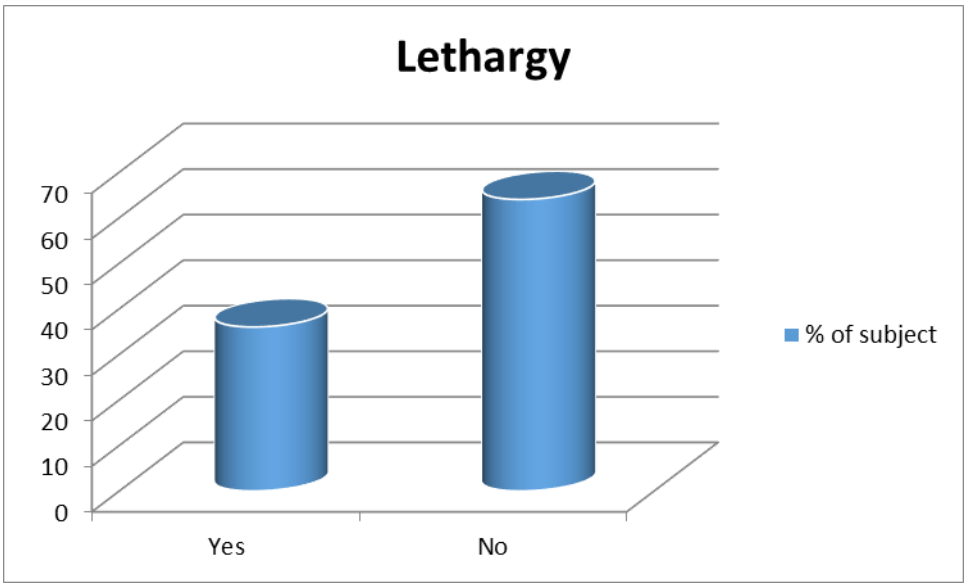

FIGURE NO. 4.3.1

From the above table and graph, it was found that lethargy was reported by 64% of the subjects and about 36% did not experience lethargy.

TABLE NO. 4.3.2: BODY ACHE EXPERIENCED BY THE SUBJECTS

Body ache	**No: of subjects (n=150)**	**% of subjects**
Yes	35	23%
No	115	77%

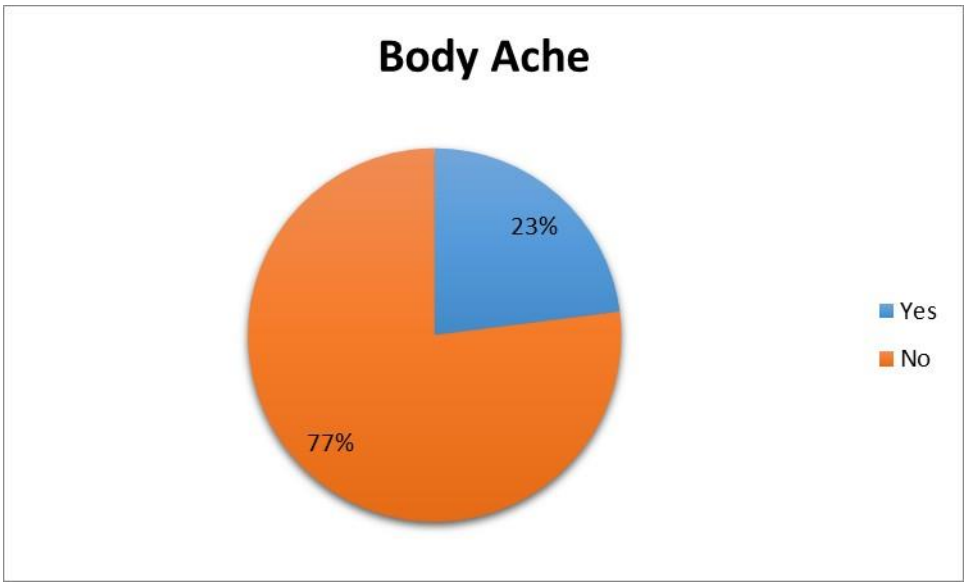

FIGURE NO. 4.3.2

From the above graph and table, it is clear that 77% of the subjects experienced body ache and 23% of subjects did not have persistent body ache.

TABLE NO. 4.3.3: BACK ACHE EXPERIENCED BY THE SUBJECTS

Back ache	**No: of subjects (n=150)**	**% of subjects**
Yes	9	6%
No	141	94%

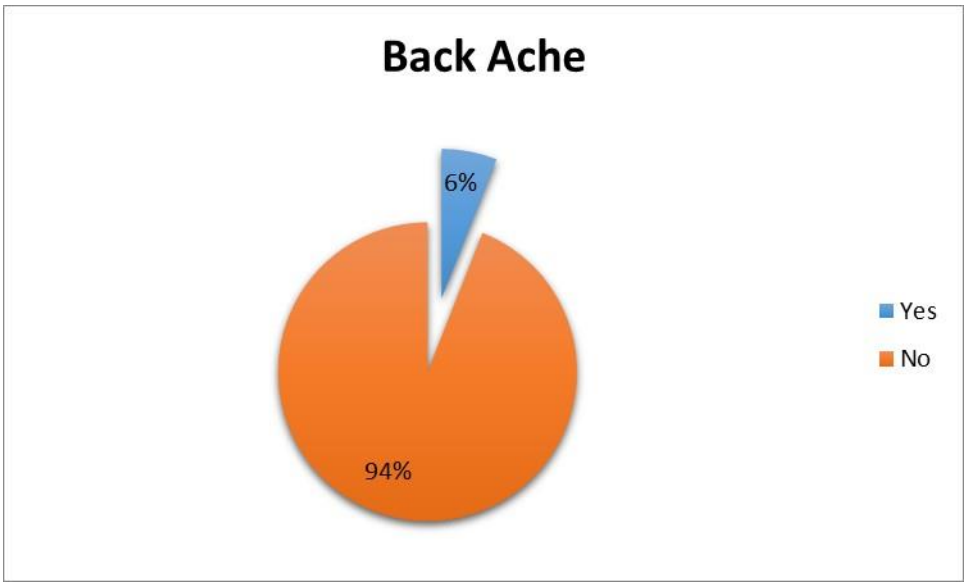

FIGURE NO. 4.3.3

From the above table and graph 6% subjects experience back ache while remaining 94% of subjects doesn't experience back ache.

TABLE NO. 4.3.4: DEPRESSION EXPERIENCED BY THE SUBJECTS

Depression	**No: of subjects (n=150)**	**% of subjects**
Yes	2	1%
No	148	99%

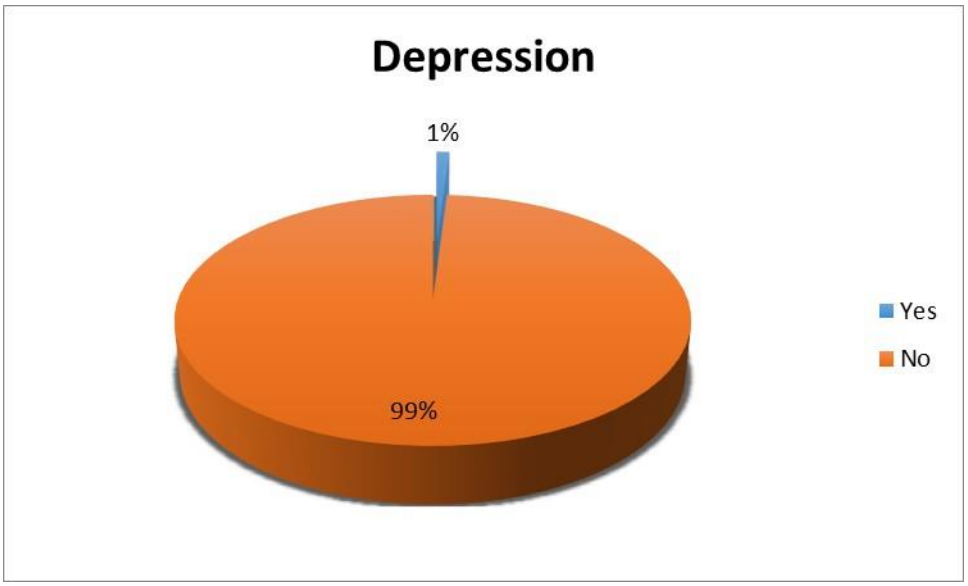

FIGURE NO. 4.3.4

From the above table and graph, it is clear that only 1% of subjects experience depression and majority about 99% of subjects not experience depression.

TABLE NO. 4.3.5: INFECTIONS EXPERIENCED BY THE SUBJECTS

Infections	**No: of subjects (n=150)**	**% of subjects**
Yes	3	2%
No	147	98%

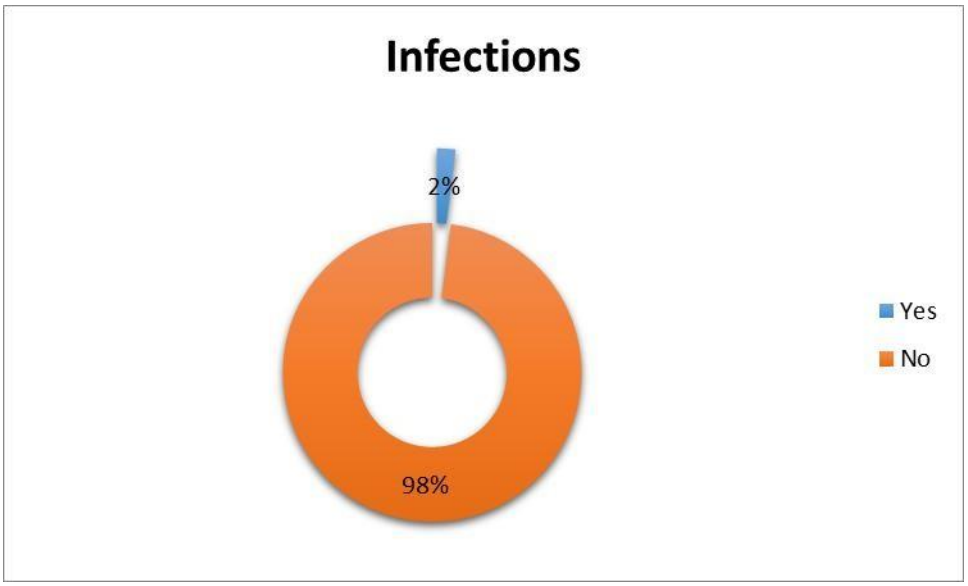

FIGURE NO. 4.3.5

From the graph it is clear that about 2% of subjects were reported to have infections and about 98% has not had infections.

TABLE NO. 4.3.6: MUSCLE PAIN EXPERIENCED BY THE SUBJECTS

Muscle pain	**No: of subjects (n=150)**	**% of subjects**
Yes	22	15%
No	128	85%

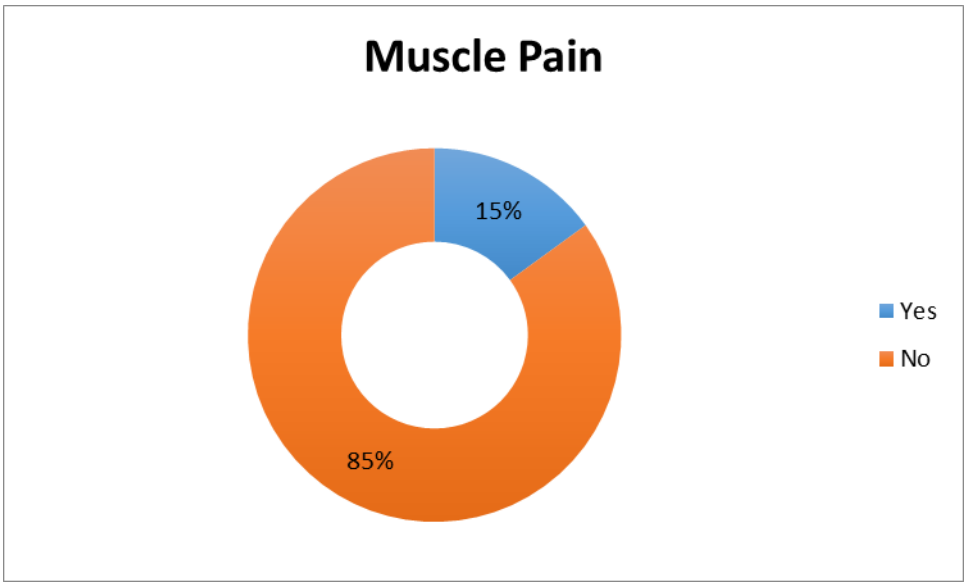

FIGURE NO. 4.3.6

From the graph it was found that about 15% of subjects experience muscle pain and 85% of subjects did not experience muscle pain.

TABLE NO. 4.3.7: CONSTIPATION EXPERIENCED BY THE SUBJECTS

Constipation	**No: of subjects (n=150)**	**% of subjects**
Yes	3	2%
No	147	98%

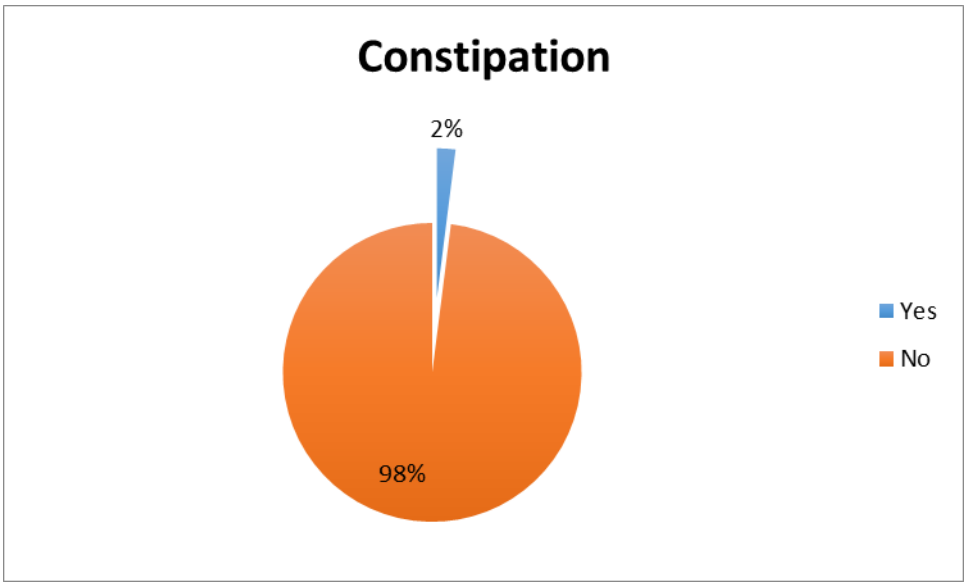

FIGURE NO. 4.3.7

From the above pie diagram, it is clear that 2% of the subjects having constipation and about 98% of subjects were not having constipation.

TABLE NO. 4.3.8: DEHYDRATION EXPERIENCED BY THE SUBJECTS

Dehydration	**No: of subjects (n=150)**	**% of subjects**
Yes	4	3%
No	146	97%

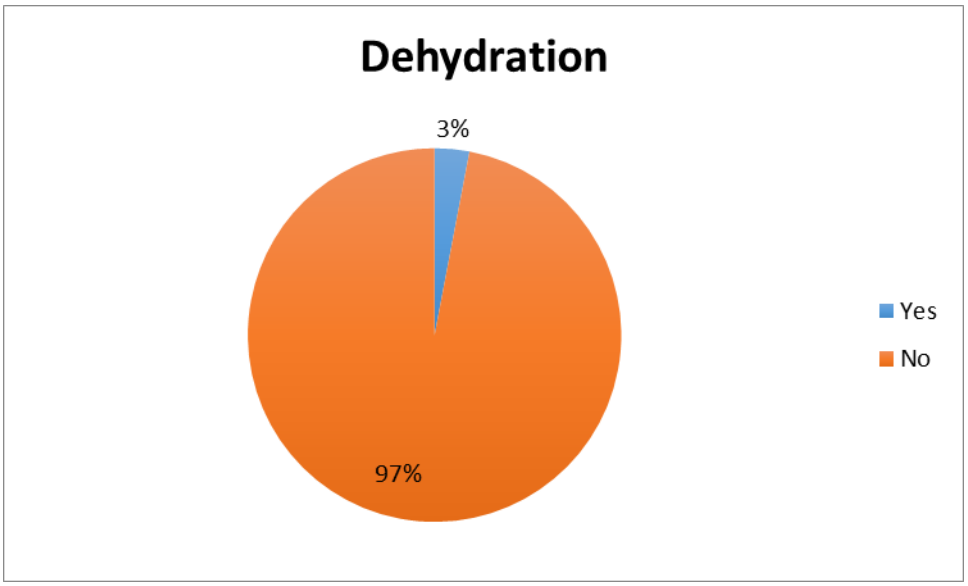

FIGURE NO. 4.3.8

From the pie diagram it is clear that around 3% of the total subjects have dehydration and 97% of the subjects does not have dehydration.

TABLE NO. 4.3.9: TREATMENT FOR INFERTILITY

Infertility	**No: of subjects (n=150)**	**% of subjects**
Yes	8	5%
No	142	95%

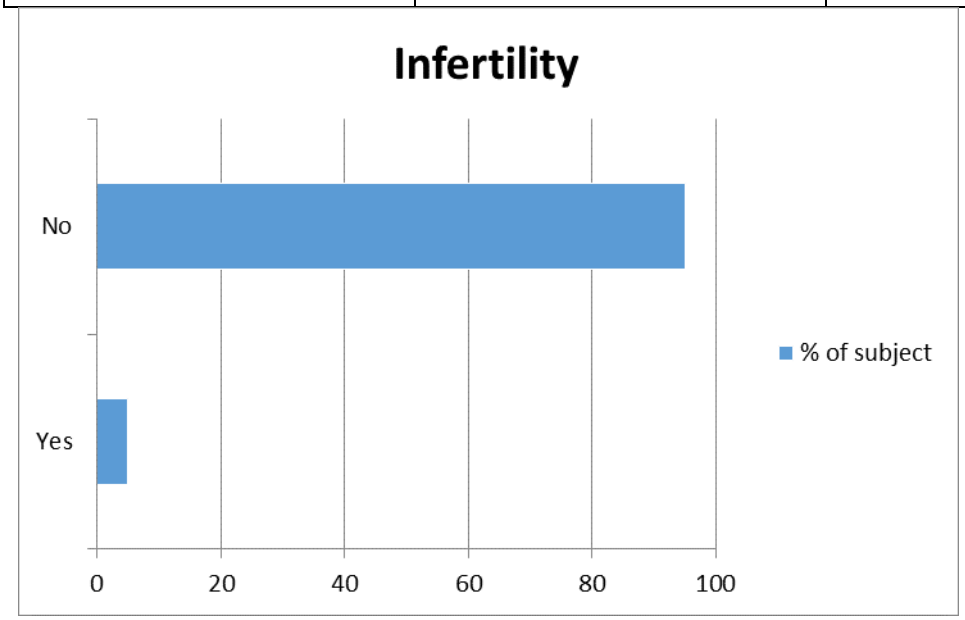

FIGURE NO. 4.3.9

From the above graphical representation, it is understood that 5% of women are found to be infertile and 95% of them are found to be fertile.

4.4 COVID-19 AFFECTED BY THE SUBJECTS

COVID – 19	**No: of subjects (n=150)**	**% of subjects**
Yes	72	48%
No	78	52%

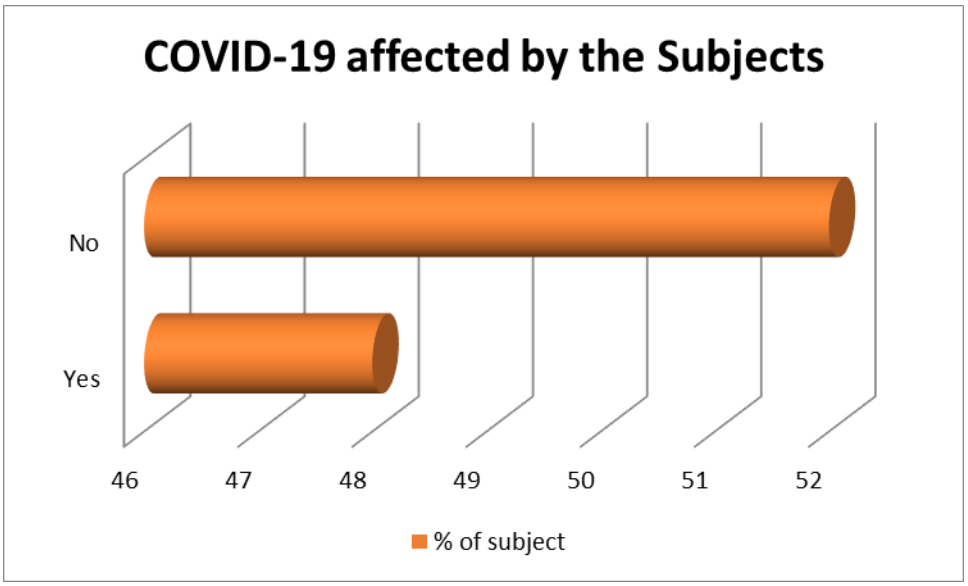

FIGURE NO. 4.4

The graph shows that 48% of the subjects had been affected with the COVID-19 and 52% of the SUBJECTS were not affected by COVID.

TABLE NO. 4.4.1: SYMPTOMS DURING COVID-19

Symptoms	**No: of subjects (n=150)**	**% of subjects**
Fever	66	44%
Body pain	26	17%
Hand pain	1	0.6%
Throat pain	3	2%
Cough	9	6%
Headache	3	2%
Cold	2	1%
Lethargy	1	0.6%

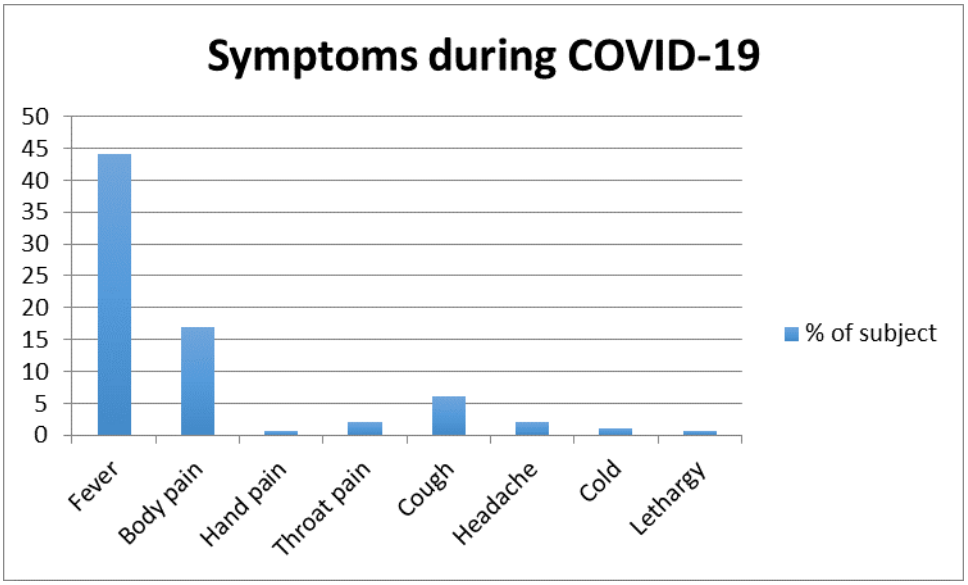

FIGURE NO. 4.4.1

The graph shows that majority of the subjects have been diagnosed with fever as a symptom with a percentage of 44 and among them the least popular symptom was lethargy and hand pain with a percentage of 0.6.

TABLE NO. 4.4.2: POST COVID PROBLEMS EXPERIENCED BY THE SUBJECTS

Post COVID problem	**No: of subjects (n=150)**	**% of subjects**
Memory problem	1	0.6%
Fatigue	7	5%
Depression	1	0.6%
Breathing problem	8	5%
Hair fall	1	0.6%
Headache	7	5%
Body pain	9	6%

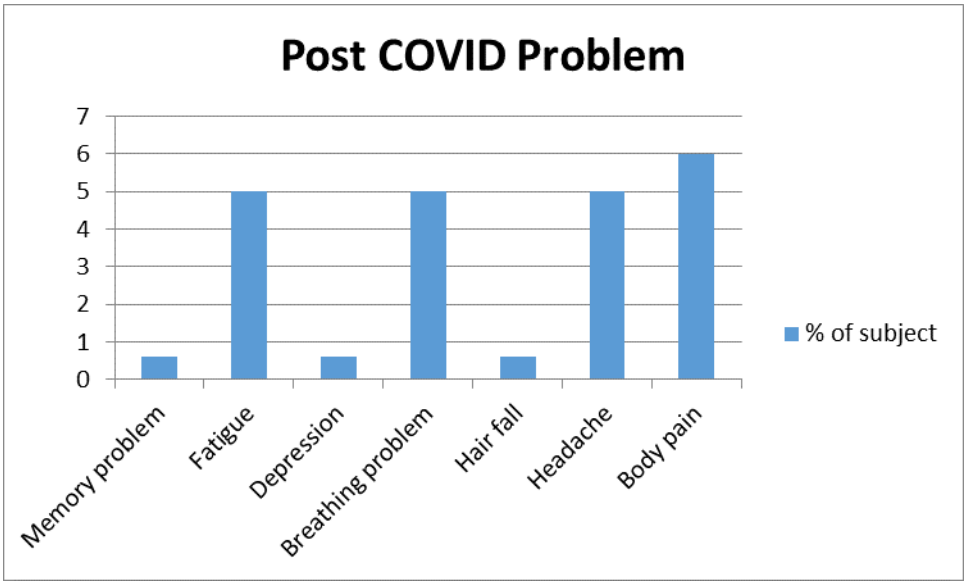

FIGURE NO. 4.4.2

The above figure represents the post covid problems among the subjects. 0.6% of them were found to be having memory problem and hair fall and depression .5% of them were found to have problems like fatigue, breathing problem and headache. 6% of them were found to have body pain.

4.5 POSSIBLE CAUSES OF VITAMIN D DEFICIENCY

TABLE NO. 4.5.1: USE OF SUNSCREEN

Sunscreen	**No: of subjects (n=150)**	**% of subjects**
Yes	63	42%
No	87	58%

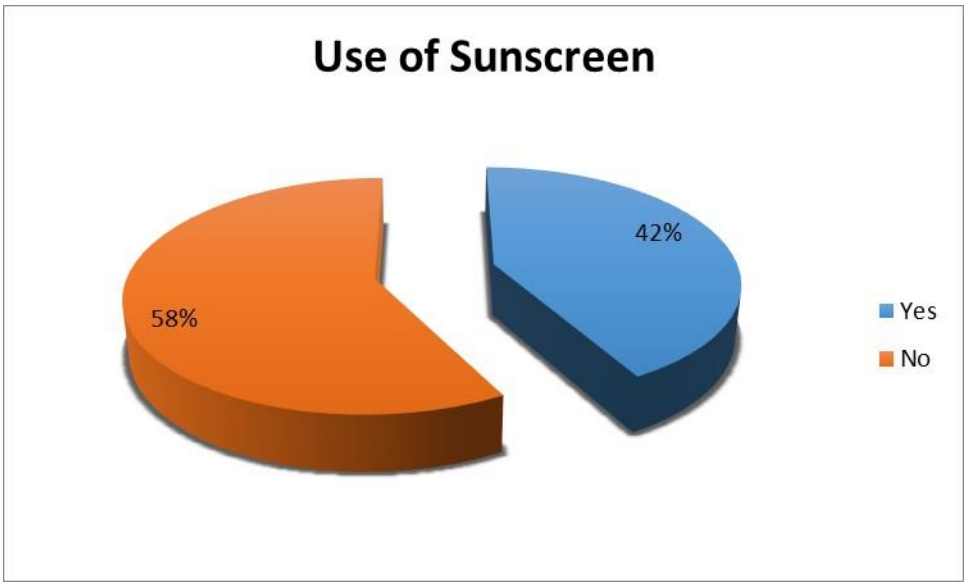

FIGURE NO.4.5.1

The figure shows that 42% of the total subjects were using sunscreen and 58% of the total subjects were not using sunscreen.

TABLE NO. 4.5.1.1: FREQUENCY OF USING SUNSCREEN

Frequency	**No: of subjects (n=63)**	**% of subjects**
Regularly/Always	22	15%
Mostly/Some times	27	18%
Rarely	14	9%

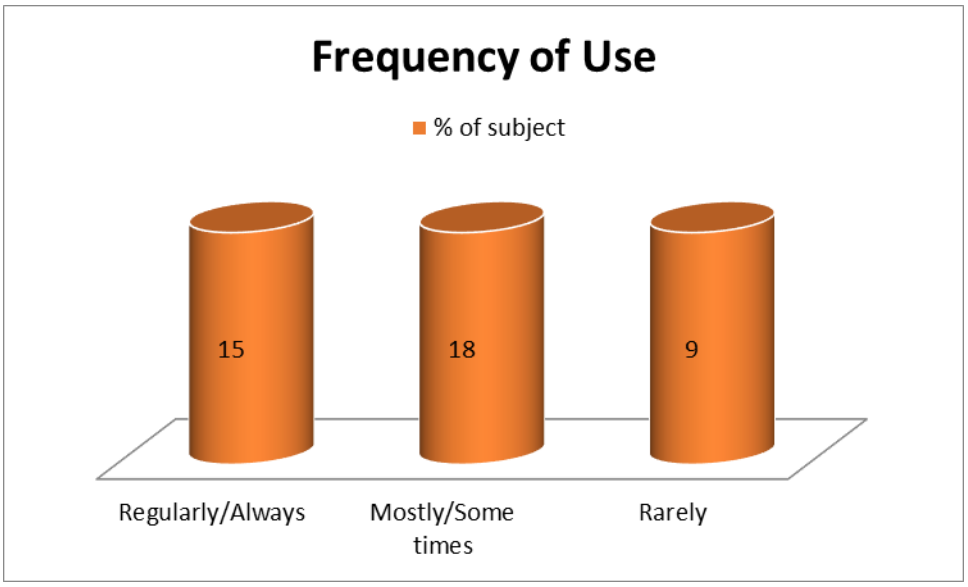

FIGURE NO. 4.5.1.1

The above data represents that about 15% of the subjects are seen to be using sunscreen regularly and 18% of them uses it mostly and about 9% of them uses it very rarely.

TABLE NO. 4.5.1.2: SPF OF SUNSCREEN USE

SPF	No: of subjects (n=63)	% of subjects
SPF<15	23	36%
SPF<30	7	12%
SPF<50	33	52%

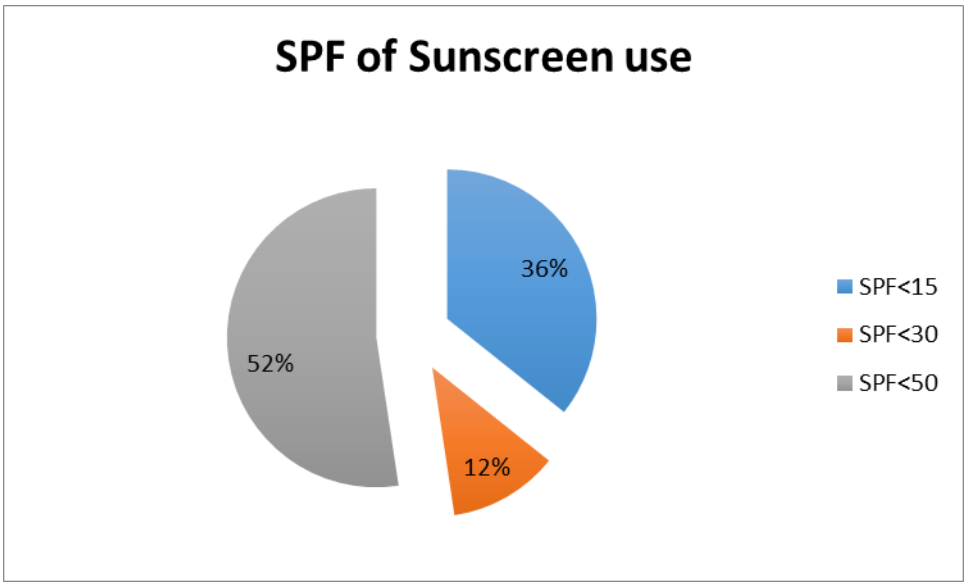

FIGURE NO. 4.5.1.2

The above figure represents the SPF of sunscreen use. The highest data obtained was the use of SPF <50 which was about 52%. The least data obtained was the use of SPF <30 which was about 12%.

TABLE NO. 4.5: PREFERENCE OF SHADES WHEN OUTDOOR

Preference	**No: of subjects (n=150)**	**% of subjects**
Yes	72	48%
No	78	52%

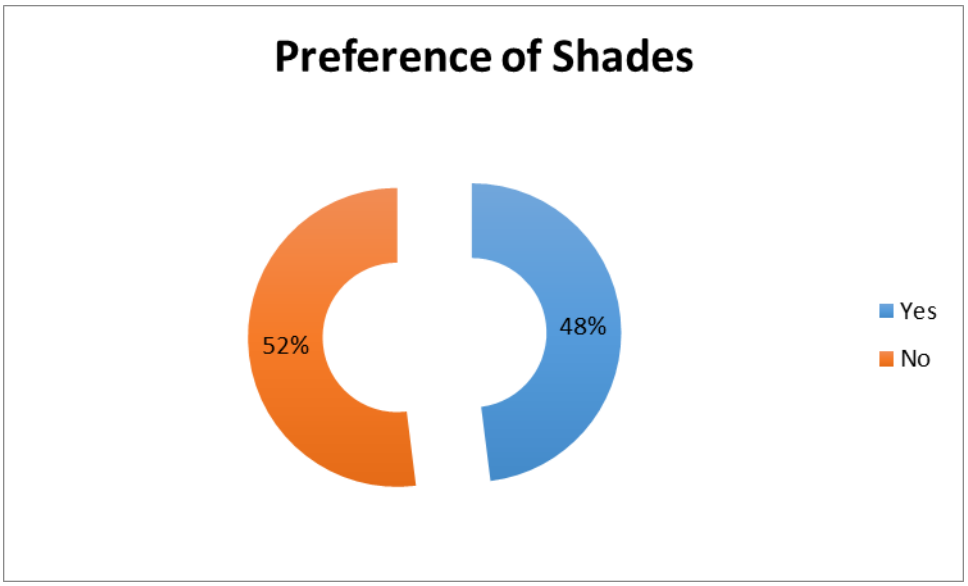

FIGURE NO. 4.5.2

The above data represents the preference of shades. Among them 48% of them preferred to wear shades whereas the other 52% of them did not prefer to wear shades.

TABLE NO. 4.5.3: PREFERENCE TO STAY INDOOR DURING THE DAY

Preference	**No: of subjects (n=150)**	**% of subjects**
Yes	86	57%
No	64	43%

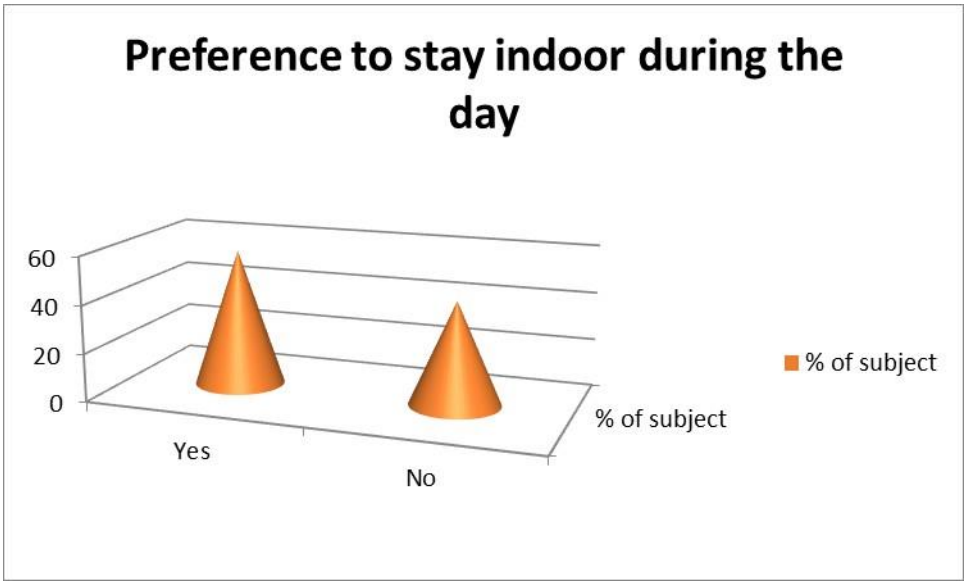

FIGURE NO. 4.5.3

The above data represents the number of subjects who preferred to stay indoor during the day time. 57% of them preferred to stay indoors while 43% of them preferred to stay outside.

TABLE NO. 4.5.4: PHYSICAL ACTIVITY AMONG THE SUBJECTS

Physical activity	**No: of subjects (n=150)**	**% of subjects**
Yes	74	49%
No	74	49%

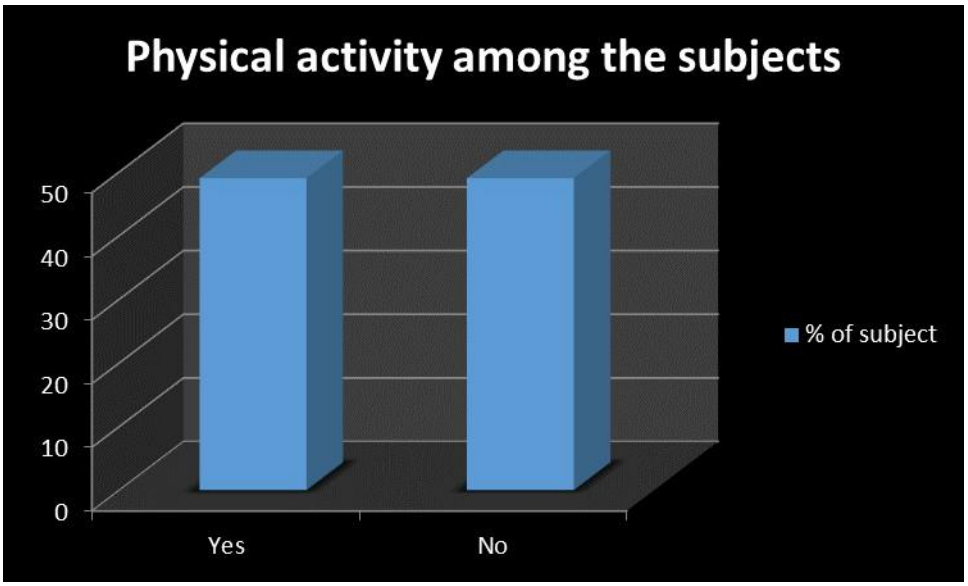

FIGURE NO. 4.5.4

The above figure represents the physical activity among the subject and it was found out to be equal among the two.

TABLE NO. 4.5.5: DETAILS ON SUN EXPOSURE

Time	**No: of subjects (n=150)**	**% of subjects**
5.00 Am – 9.59 Am	77	52%
10.00 Am – 3.59 PM	11	7%
4.00 PM – 5.59 PM	61	41%

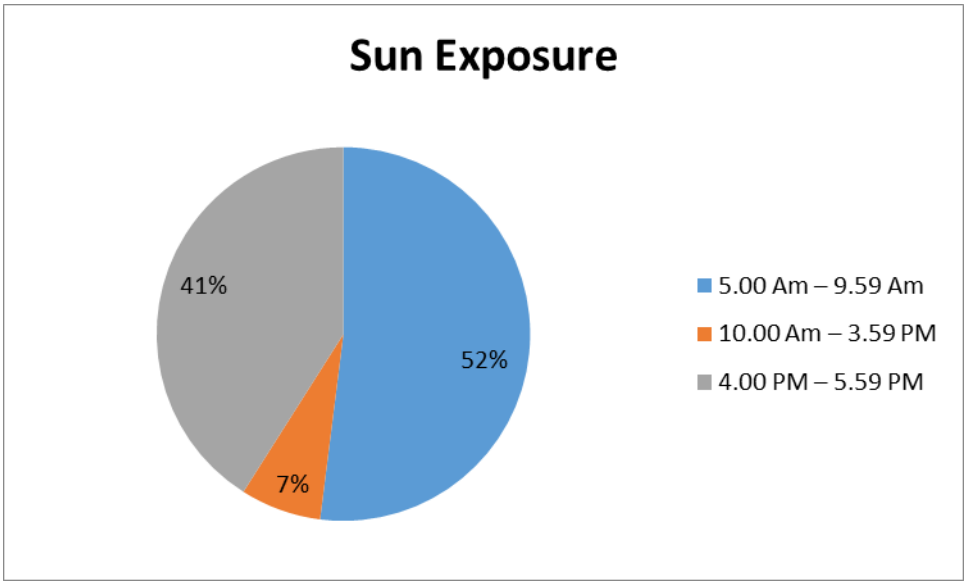

FIGURE NO.4.5.5

From the above table and figure it was found that majority of subjects that is about 52% are exposed to sun between 5.00 AM to 9.59 AM and least percentage about 7% are exposed to sun between 10.00 Am to 3.59 PM.

TABLE NO. 4.5.5.1: DURATION OF SUN EXPOSURE

Duration	**No: of subjects (n=150)**	**% of subjects**
>15 Minutes	38	25%
15 – 30 Minutes	41	27%
30 – 45 Minutes	9	6%
>45 Minutes	63	42%

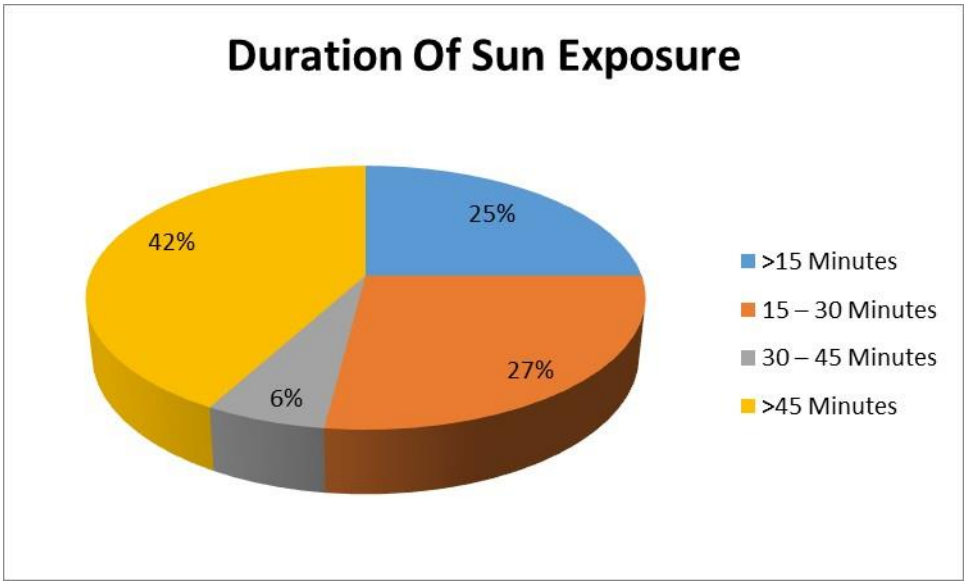

FIGURE NO. 4.5.5.1

From the above pie chart, it is clear that 42% of subjects are exposed to sun more than 45 minutes and 25% of subjects are exposed to sun more than 15 minutes.

TABLE NO. 4.5.5.2: PREFERENCE OF DRESS

Type of dress	**No: of subjects (n=150)**	**% of subjects**
Saree blouse without collar	34	23
Saree blouse with collar	3	2
Full sleeve kameez deep back neck	1	0.6
Full sleeve kameez with collar	4	3
Fully covered religious attire	27	18
Half sleeve kameez or blouse	81	53.4

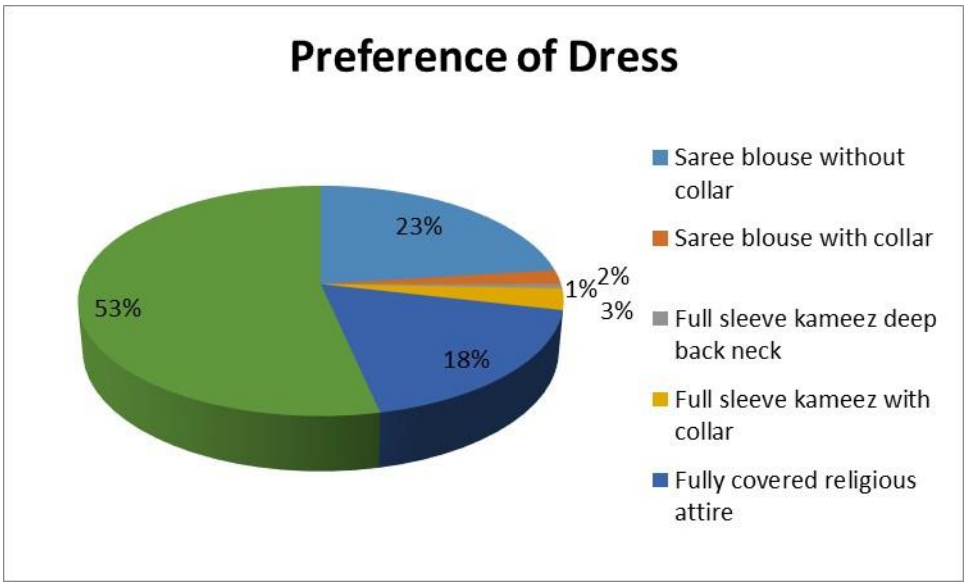

FIGURE NO. 4.5.5.2

From the above pie chart, it was found that majority of subject that is 53.4% of subjects prefer to wear half sleeve kameez or blouse and only a small percentage that is about 0.6% of subjects prefer to wear full sleeve kameez deep back neck.

4.6 NUTRITIONAL STATUS

4.6.1 ANTHROPOMETRIC ASSESSMENT

TABLE NO. 4.6.1.1: HEIGHT

Height (cm)	**No: of subjects (n=150)**	**% of subjects**
140 – 150	31	21%
151 – 160	84	56%
161 – 170	29	19%
Above 170	6	4%

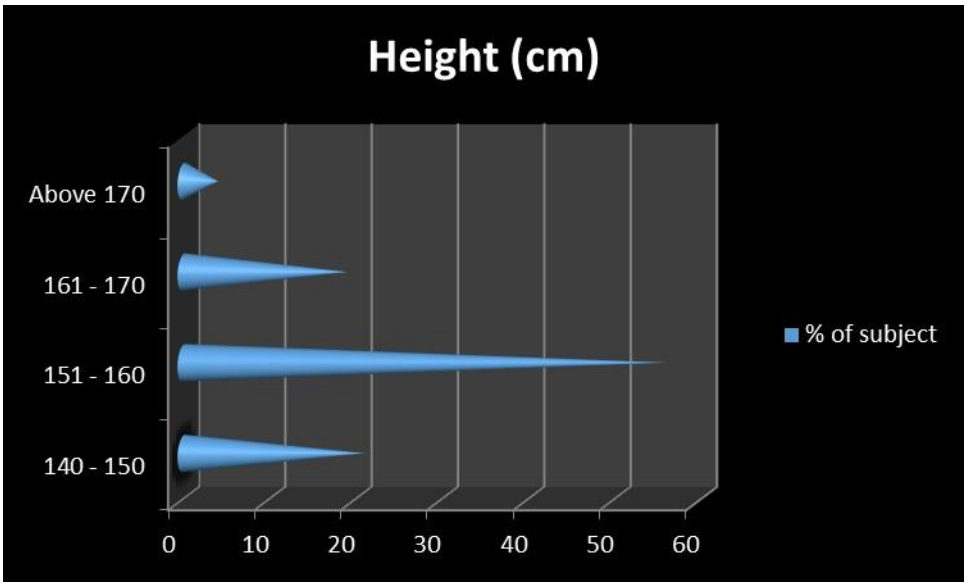

FIGURE NO. 4.6.1.1

From the above table and figure it is clear that 56% of the subjects have a height in between 151 to 160 cm and 4% of them had a height above 170 cm. Height measurement were taken manually.

TABLE NO. 4.6.1.2: WEIGHT

Weight (kg)	**No: of subjects (n=150)**	**% of subjects**
40 – 60	68	45%
61 – 80	72	48%
81 – 90	10	7%

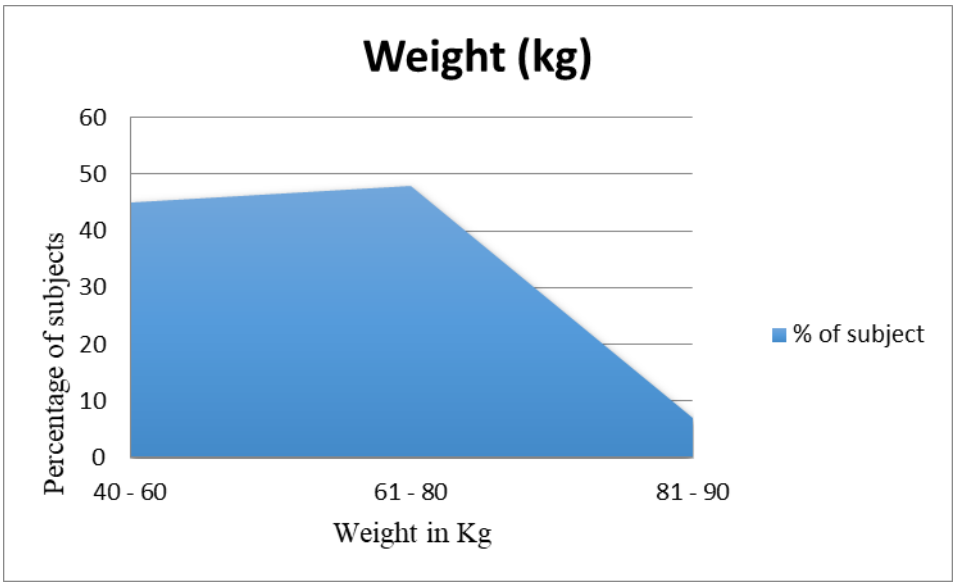

FIGURE NO. 4.6.1.2

Weight is the most important factor for identifying obesity here the measurement was taken using a weighing machine. From the above table and figure, it was found that 48% of the subjects had weight between 61 to 80 kg, and 7% of them had a weight between 81 to 90 kg respectively.

TABLE NO. 4.6.1.3: WAIST HIP RATIO

Waist Hip Ratio	**No: of subjects (n=150)**	**% of subjects**
0.8 – 1	62	41%
>1	88	59%

FIGURE NO. 4.6.1.3

Waist Hip Ratio is an important factor for the determination of central obesity. Here from the above table and figure, it was found that most of the subjects had a waist Hip Ratio greater than 1 and the least number of them had ratio between 0.8 to 1.

TABLE NO. 4.6.1.4: BMI (Kg/M²)

BMI (Kg/M²)	**No: of subjects (n=150)**	**% of subjects**
Below 18	3	2%
18 – 24.9	60	40%
25 –29.9	48	32%
30 – 39.9	39	26%

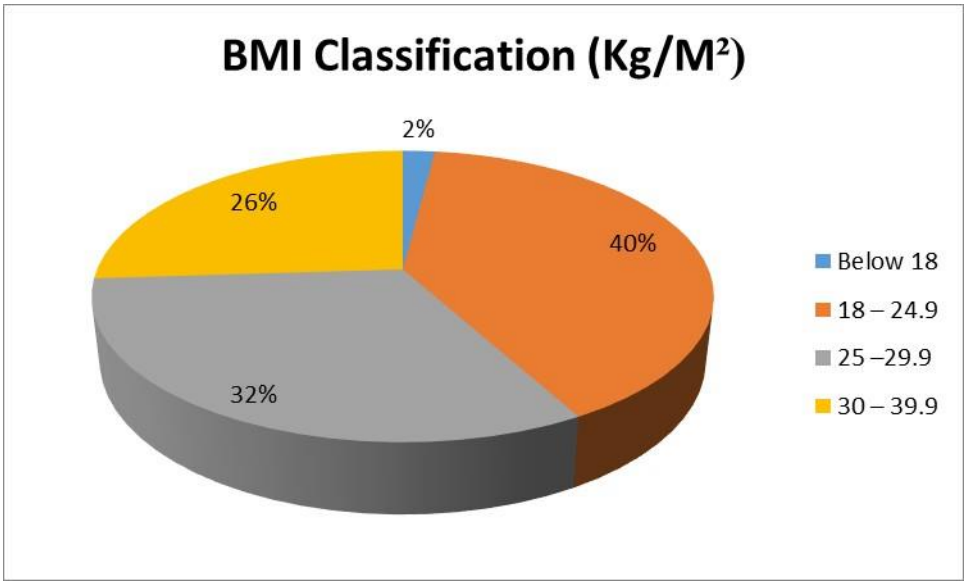

FIGURE NO. 4.6.1.4

BMI is a measure for indicating nutritional status in adults.

From the above figure, it was found that 40% of the subjects were normal and about 2% of subjects were found to be underweight.

4.6.2 BIOCHEMICAL ASSESSMENT

TABLE NO. 4.6.2.1: HbA1c

Values (%)	**No: of subjects(n=150)**	**% of subjects**
< 5.7 %	10	7%
5.7 – 6.4%	9	6%
>6.5 %	130	87%

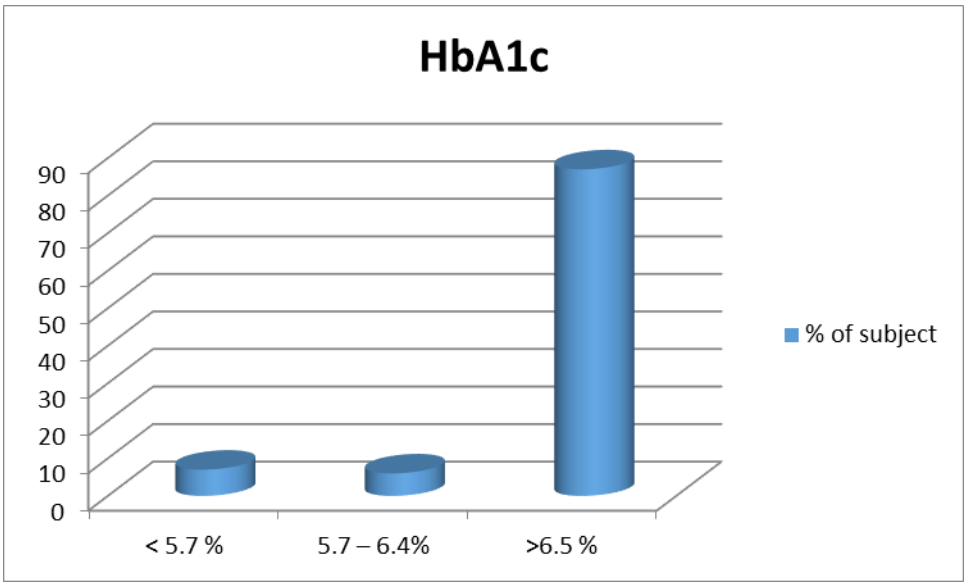

FIGURE NO. 4.6.2.1

The HbA1c value of the subjects were collected and tabulated. From the above table and figure, it was found that a large number of the subjects (130) had HbA1c >6.5%, 10 subjects had HbA1c value <5.7% and 9 subjects have the range between 5.7 to 6.4%.

TABLE NO. 4.6.2.2: SERUM VITAMIN D (1,25-hydroxy vitamin D)

Values (ng/ml)	**No: of subjects (n=150)**	**% Of subjects**
<10	24	16%
10 - 20	45	30%
20 - 30	58	39%
>30	22	15%

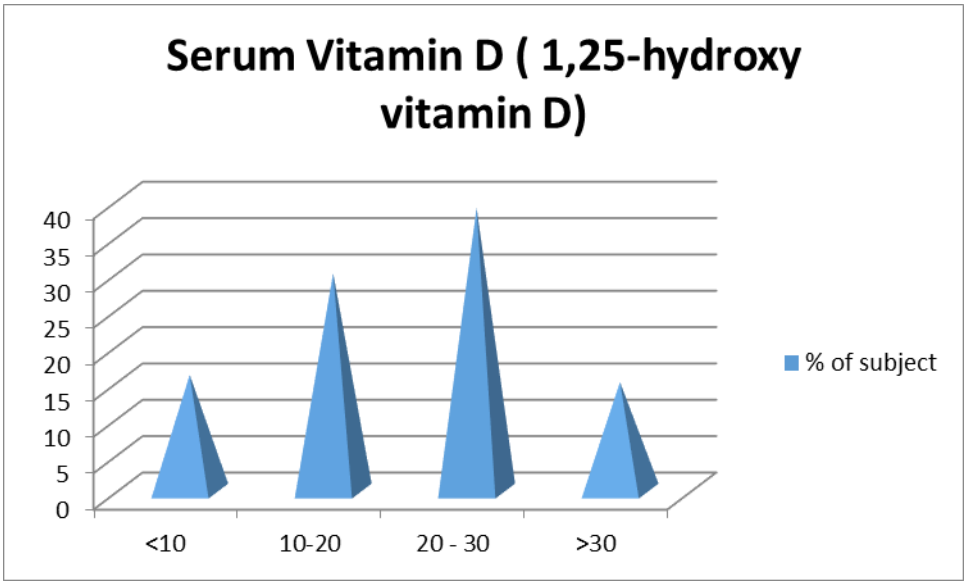

FIGURE NO. 4.6.2.2

From the above table and figure it was found that 58 subjects had vitamin D insufficiency and 22 subjects are found to be accurate.

4.6.3 DIETARY ASSESSMENT

Table NO. 4.6.3.1: DIETARY HABIT

Dietary habit	**No: of subjects (n=150)**	**% of subjects**
Vegetarian	10	7%
Non vegetarian	140	93%

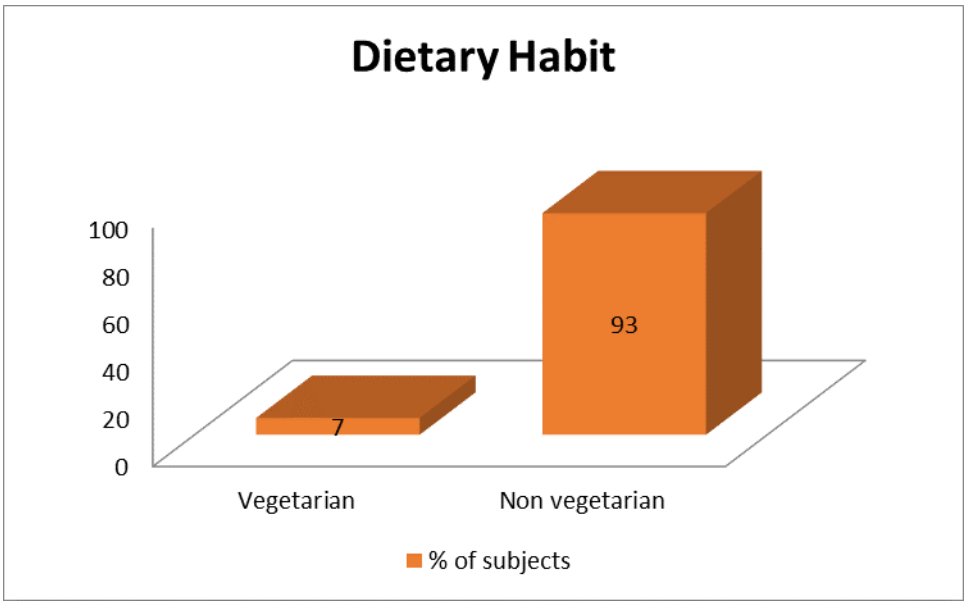

FIGURE NO. 4.6.3.1

From the above table and figure it is clear that majority of subjects that is around 93% are consuming non vegetarian and remaining 7% of subjects are consuming vegetarian.

TABLE NO. 4.6.3.2: FOOD INTAKE AT REGULAR TIME

Regular time	**No: of subjects (n=150)**	**% of subjects**
Yes	115	77%
No	35	23%

FIGURE NO. 4.6.3.2

From the above table and figure it was found that 77% of subjects consume their food at regular time and 23% of subjects do not consume their food at regular time.

TABLE NO. 4.6.3.3: MEAL PATTERN PER DAY

Meal pattern	**No: of subjects (n=150)**	**% of subjects**
3 meals	56	37%
4 meals	92	61%
5 meals	2	1%

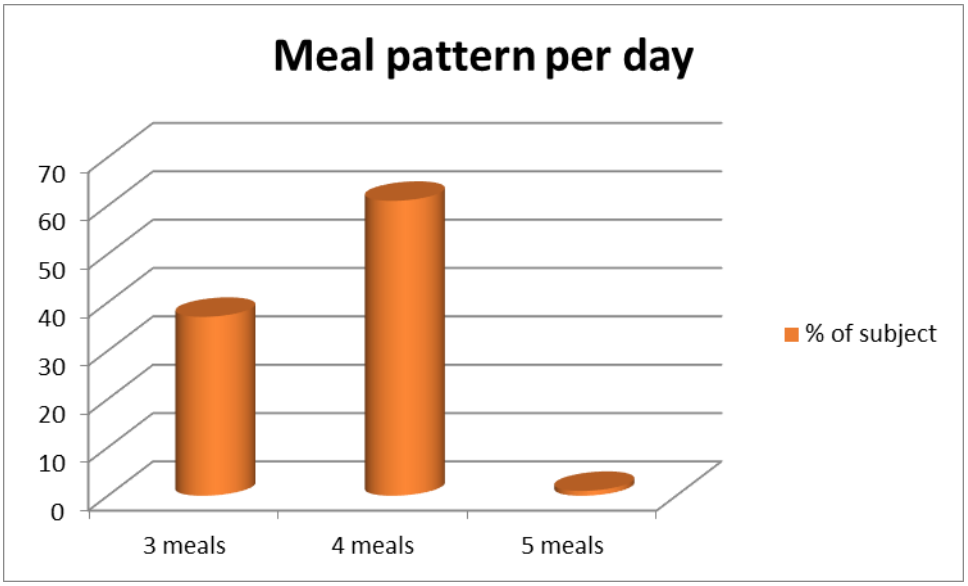

FIGURE NO. 4.6.3.3

The above data represents about 61% of subjects follow 4 meals per day and only 1% of subjects follows 5 meals per day.

TABLE NO. 4.6.3.4: SKIPPING OF MEALS

Skipping of meals	**No: of subjects (n=150)**	**% of subjects**
Yes	47	31%
No	103	67%

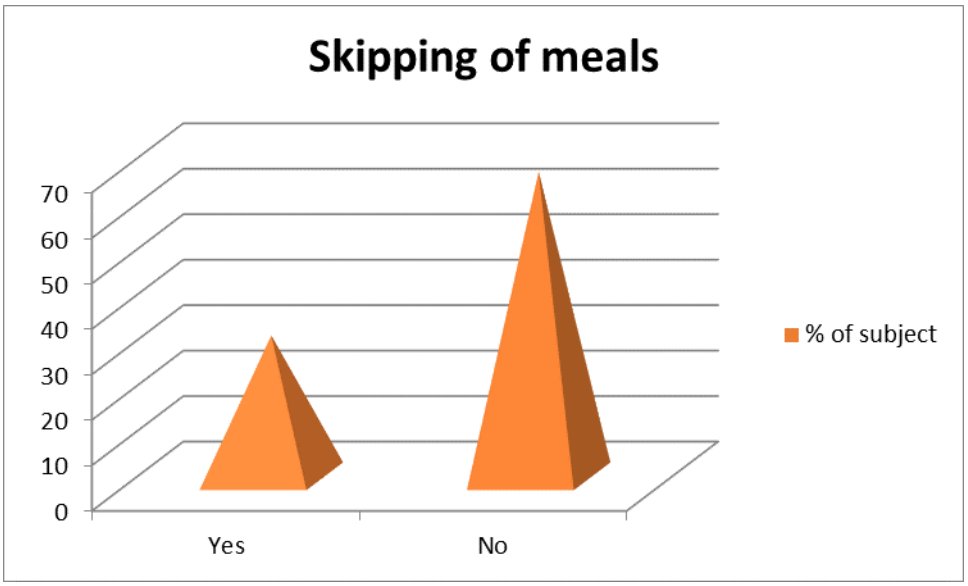

FIGURE NO. 4.6.3.4

From the above table and graph, it is clear that 31% of subjects are skipping their meals and about 67% of subjects do not skip their meals.

TABLE NO. 4.6.3.5: COMPENSATE FOR SKIPPED MEALS

Compensation	**No: of subjects (n=150)**	**% of subjects**
Coffee	14	9%
Tea	9	6%
Vegetable salad	6	4%
Snacks	7	5%
Fruit juices	5	3%
Any other	6	4%

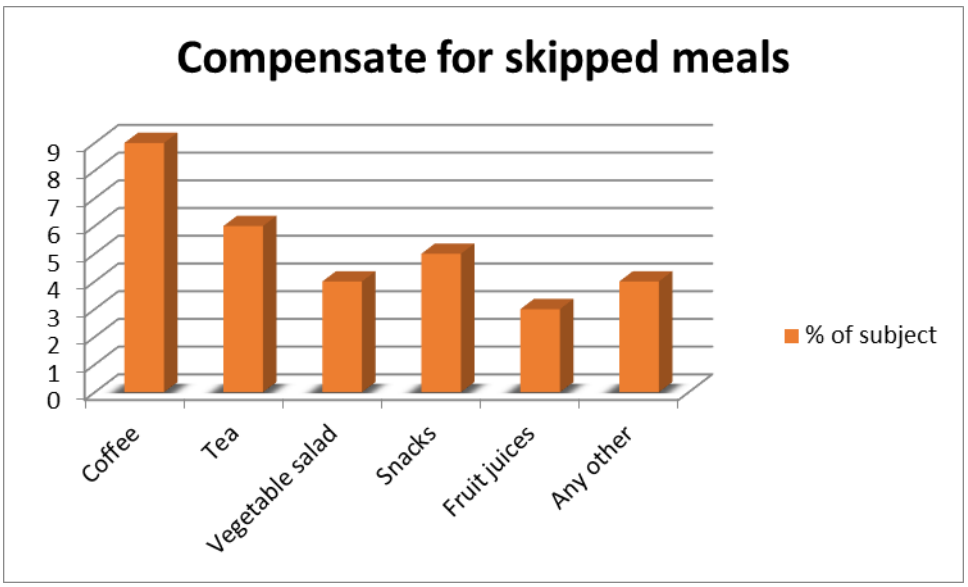

FIGURE NO. 4.6.3.5

From the above table and figure it was found that about 9% of subjects Compensate their meal with coffee and 3% of subjects are consuming fruit juices to Compensate their meals.

TABLE NO. 4.6.3.6: GOOD APPETITE

Good appetite	**No: of subjects (n=150)**	**% of subjects**
Yes	124	83%
No	26	17%

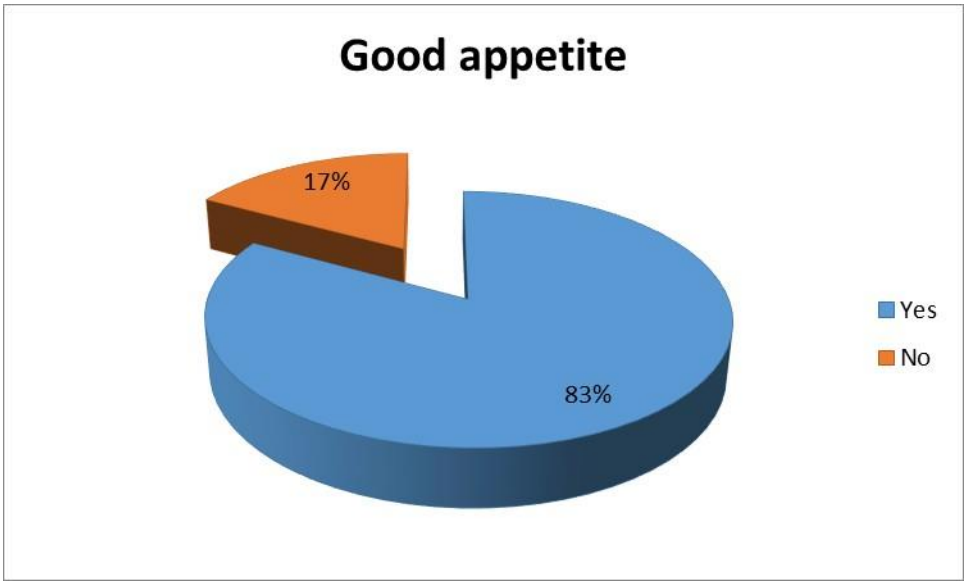

FIGURE NO. 4.6.3.6

From the above table and figure it is clearly represents that majority of subject that is about 83% have good appetite and 17% of subjects does not have appetite.

TABLE NO. 4.6.3.7: PLACE OF FOOD CONSUMPTION

Place	**No: of subjects (n=150)**	**% of subjects**
Home	144	64%
Canteen	6	36%

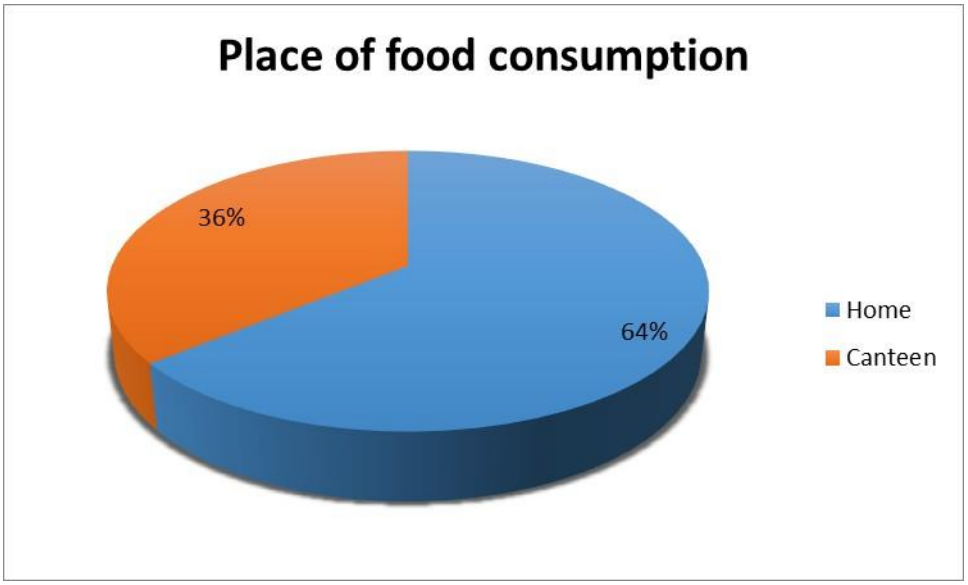

FIGURE NO. 4.6.3.7

From the above table and figure it was found that more number of subjects that is around 64% are consuming food at home and 36% of subjects are consuming food from the canteen.

TABLE NO. 4.6.3.8: EATING JUNK FOODS

Junk food	**No: of subjects (n=150)**	**% of subjects**
Yes	115	77%
No	35	23%

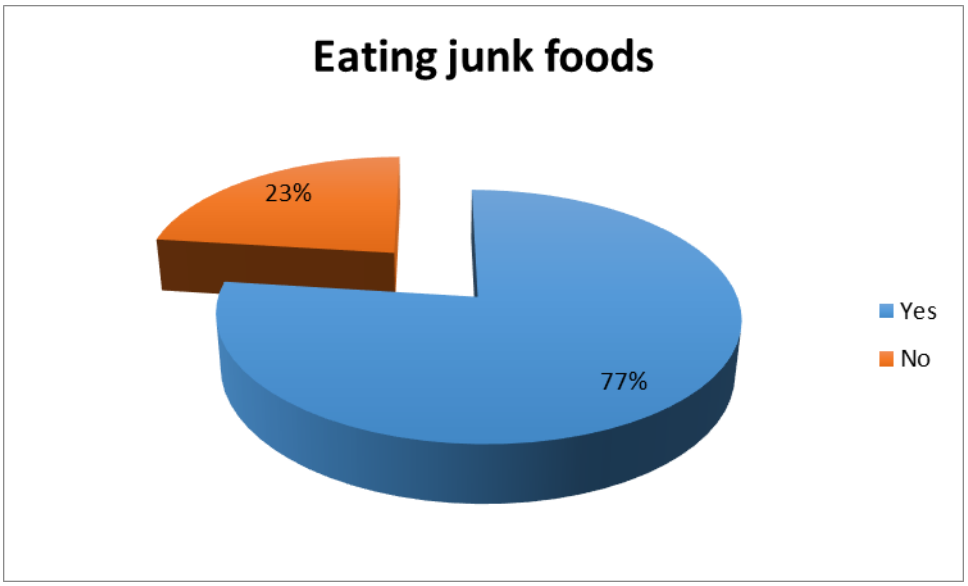

FIGURE NO. 4.6.3.8

From the above table and figure it is clear that about 77% of subjects consume junk foods and 23% of the subjects are not consuming junk foods.

TABLE NO. 4.6.3.8.1: FREQUENCY OF EATING FAST FOOD

Frequency	**No: of subjects(n=150)**	**% of subjects**
2 times per day	14	9%
2 times per week	71	47%
2 times per month	29	19%
2 times per year	2	1%

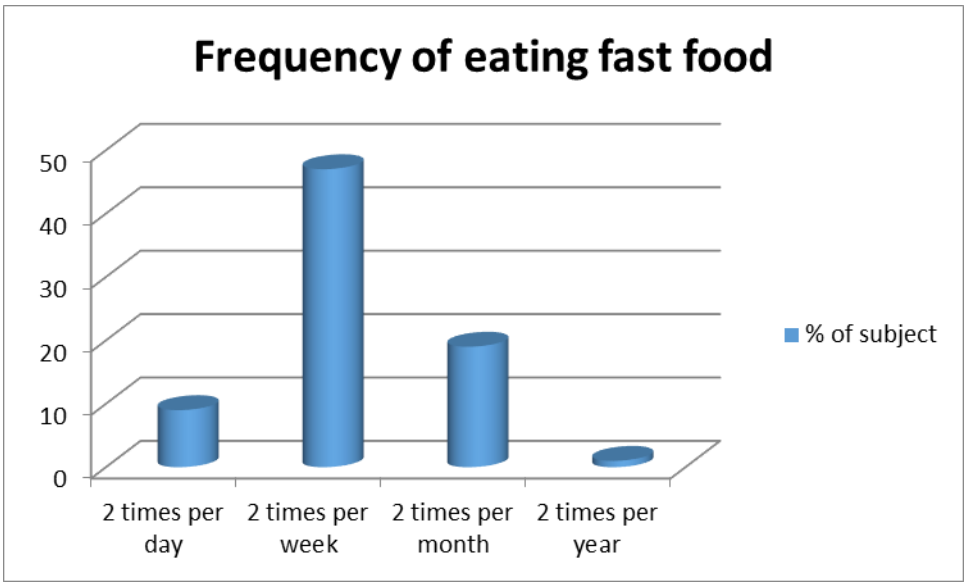

FIGURE NO. 4.6.3.8.1

From the above table and figure it was found that about 47% of subjects are consuming fast food 2 times per week and least percentage that is about 1% of subjects are consuming fast food 2 times per year.

TABLE NO. 4. 6.3.9: CONSUMPTION OF VITAMIN D SUPPLEMENTS

Consumption	**No: of subjects(n=150)**	**% of subjects**
Yes	67	45%
No	83	55%

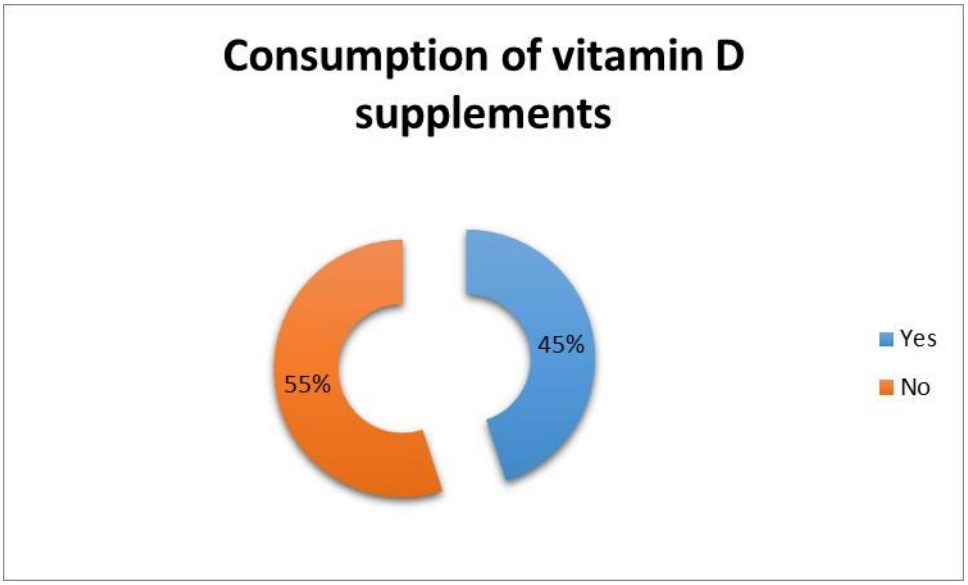

FIGURE NO. 4.6.3.9

From the above table and figure it was found that 55% out of total subjects do not consume vitamin D supplements and 45% out of total subjects are consuming vitamin D supplements.

4.6.3.10 24 HOUR RECALL METHOD

The 24-hour dietary recall method consists of precisely recalling, describing and quantifying the intake of food and beverages consumed in the 24-hour period prior to, or during the day before the interview, from the first intake in the morning until the last food or beverages consumed at night.

In this study, 150 subjects 3 days 24-hour recall is analyzed and the result are discussed below:

TABLE NO. 4.6.3.10.1: ENERGY IN KCAL

Energy(kcal)	**No: of subjects (n=150)**	**% of subjects**
Above >1660	147	98%
Below <1660	3	2%

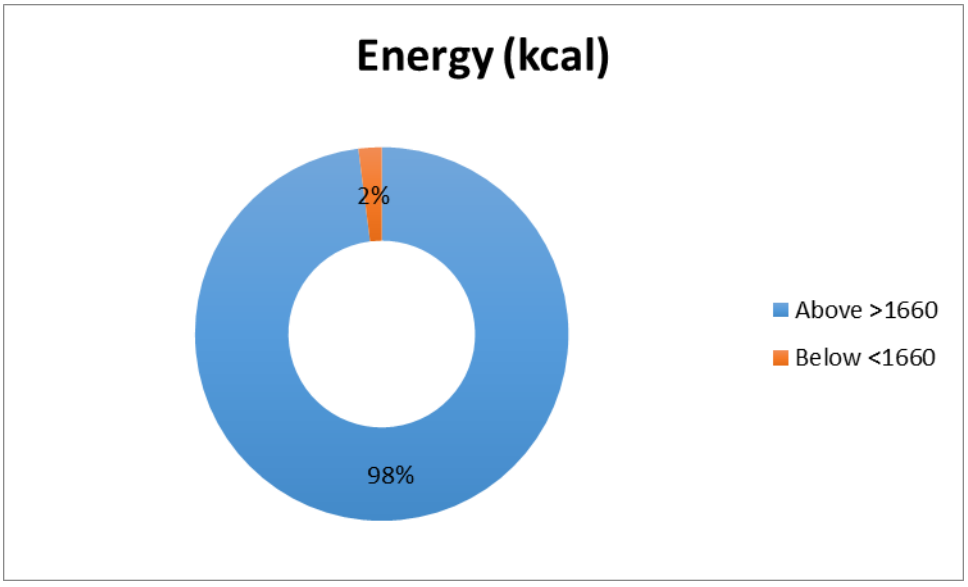

FIGURE NO. 4.6.3.10.1

Table no. 4.6.3.10.1 depicts the total calorie intake of the selected subjects was calculated using the Nutritive app. About 147 subjects had a calorie intake of >1660 kcal per day and 3 subjects had a core intake of <1660 kcal.

TABLE NO.4.6.3.10.2: Carbohydrate (gm)

Carbohydrate (gm)	**No: of subjects (n=150)**	**% of subjects**
Above >130	148	99
Below <130	2	1

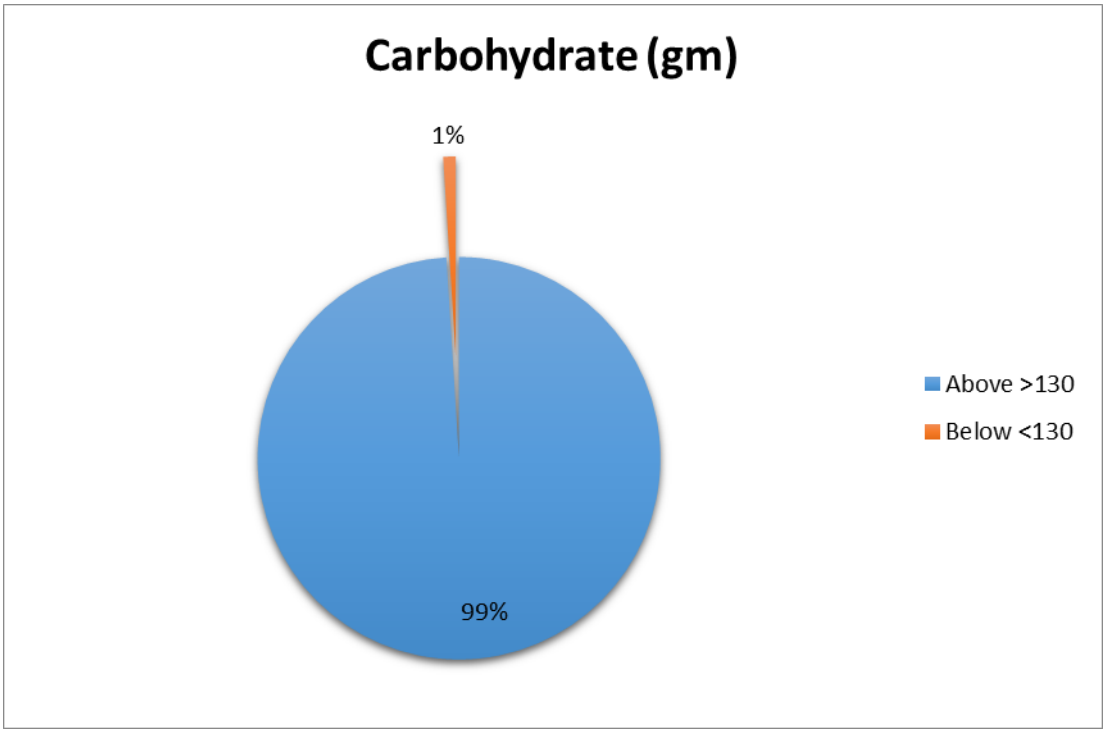

FIGURE NO. 4.6.3.10.2

Table No. 4.6.3.10.2 depicts the total Carbohydrate intake of selected subjects. It was found that 148 subjects are consuming more than 130 gm of carbohydrate per day and only 2 subjects are consuming carbohydrate below 130 gm per day.

TABLE NO. 4.6.3.10.3: PROTEIN (gm)

Protein (gm)	**No: of subjects (n=150)**	**% of subjects**
>46	147	98%
<46	3	2%

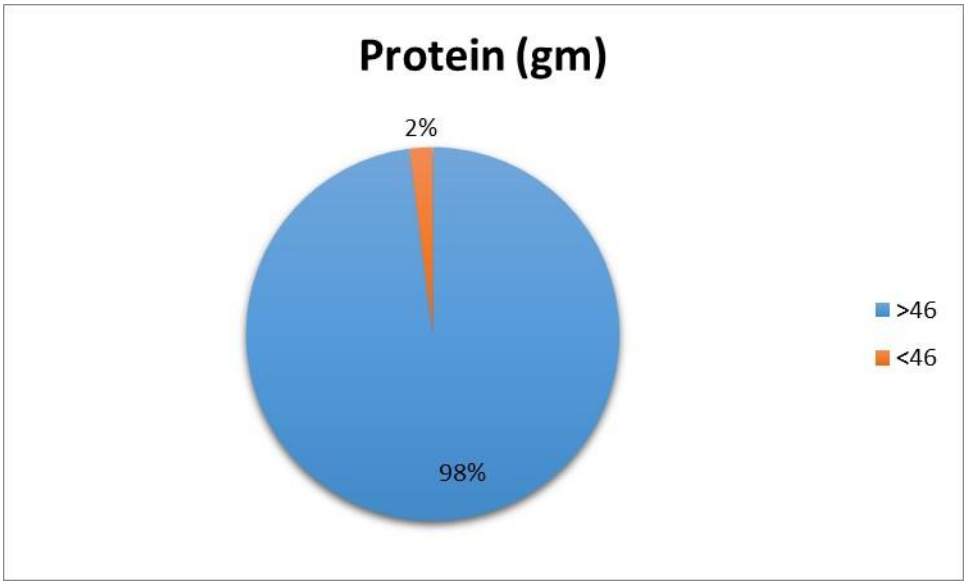

FIGURE NO. 4.6.3.10.3

Table No. 4.6.3.10.3 depicts the total protein intake of selected subjects. About 147 subjects had a protein intake of >46 gm per day and about only 3 subjects had a protein intake <46 gm per day.

TABLE NO. 4.6.3.10.4: Fat (g)

Fat (gm)	**No: of subjects (n=150)**	**% of subjects**
>20	146	97%
<20	4	3%

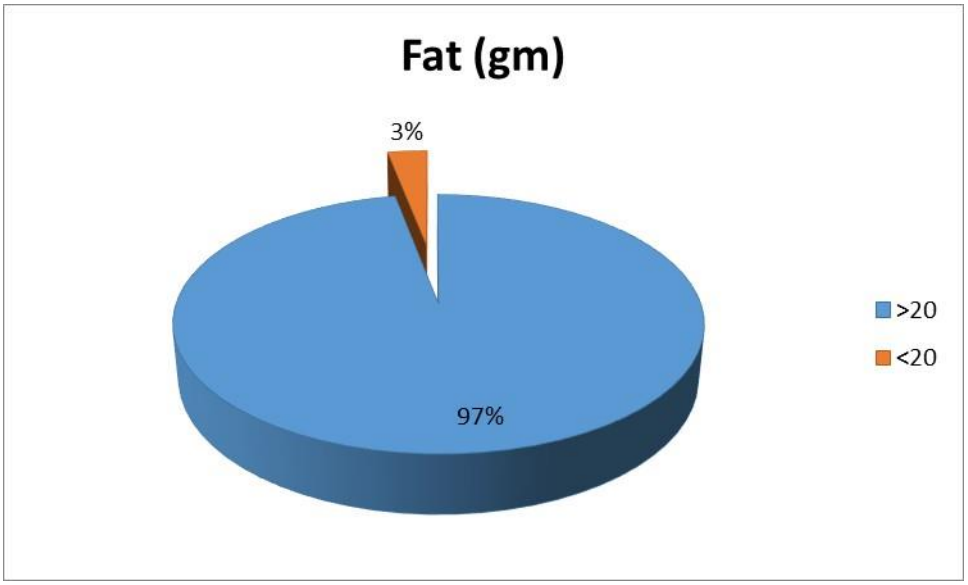

FIGURE NO. 4.6.3.10.4

Table No. 4.6.3.10.4 depicts the total fat intake of the selected subjects. About 146 subjects had a fat intake >20 gm per day and 4 subjects had a fat intake <20 gm per day.

4.6.3.10.5: Fibre (gm)

Fibre (gm)	No: of subjects (n=150)	% of subjects
>25	41	27%
<25	109	73%

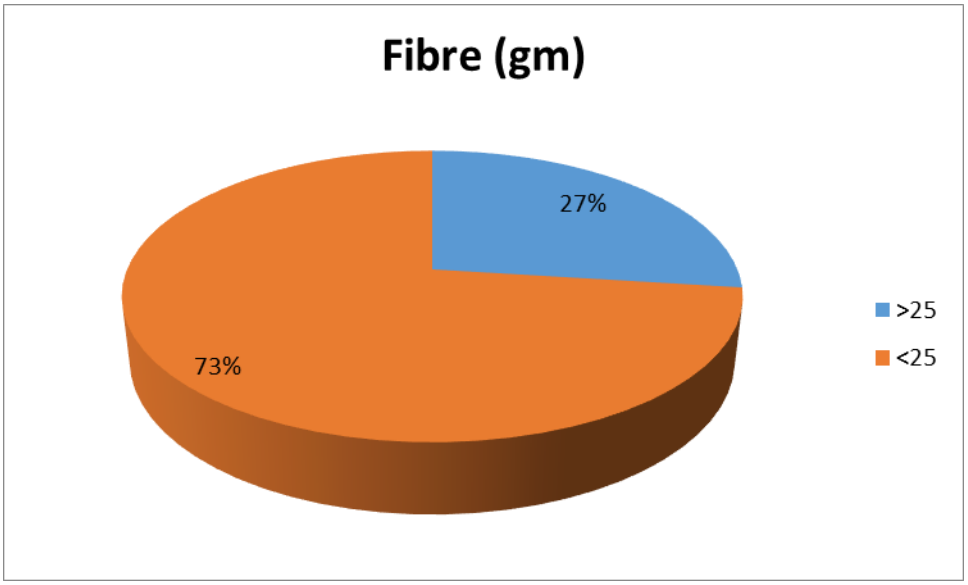

FIGURE NO. 4.6.3.10.5

Table No. 4.6.3.10.5 depicts the total fibre intake of selected subjects. It was found that 27% of subjects are consuming >25 gm per day and 73% of subjects are consuming <25 gm per day.

TABLE NO. 4.6.3.10.6: Calcium (mg)

Calcium (mg)	**No: of subjects (n=150)**	**% of subjects**
>1000	6	4%
<1000	144	96%

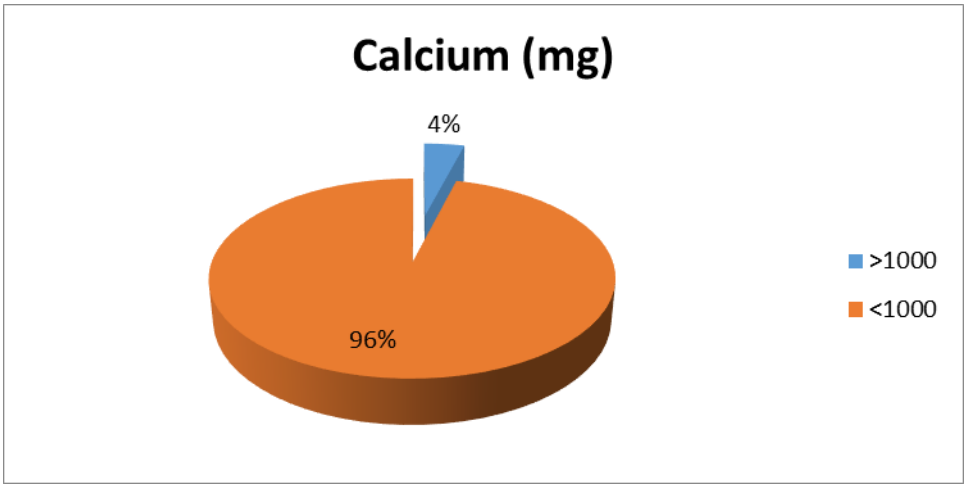

FIGURE NO. 4.6.3.10.6

Tae No. 4.6.3.10.6 depicts the total calcium intake of selected subjects. It was found that 6 subjects are consuming calcium >1000 mg per day and majority of the subjects that is about 144 subjects are consuming calcium <1000 mg per day.

TABLE NO.4.6.3.10.7: VITAMIN D (IU/day)

Vitamin D (IU/day)	**No: of subjects (n=150)**	**% of subjects**
<600	150	100%

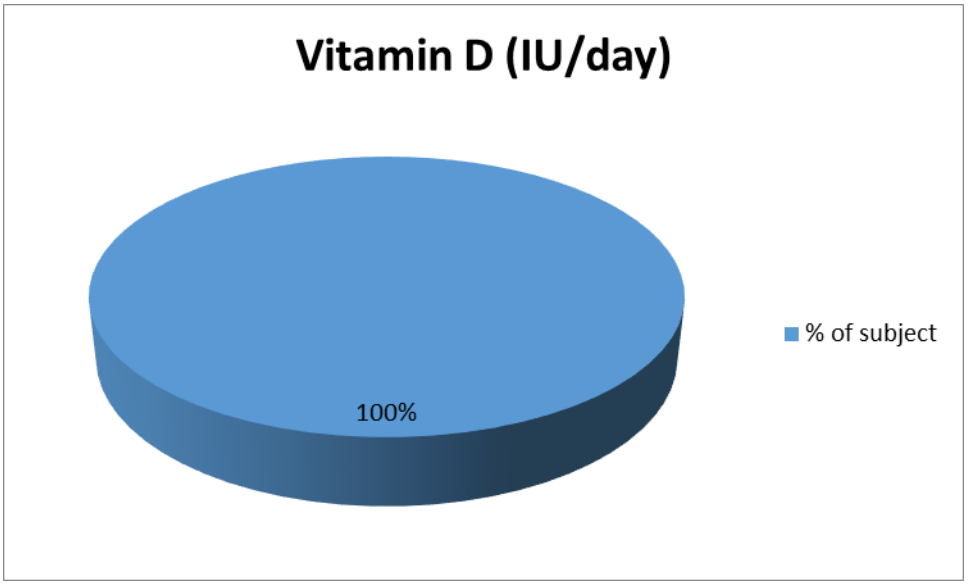

FIGURE NO. 4.6.3.10.7

Table No. 4.6.3.10.7 depicts the total vitamin D intake of selected subjects. Majority of the subjects are consuming vitamin D <600 IU/day.

TABLE NO. 4.6.3.10.8: PHOSPHORUS (mg)

Phosphorus (mg)	**No: of subjects (n=150)**	**% of subjects**
>1000	2	1%
<1000	148	99%

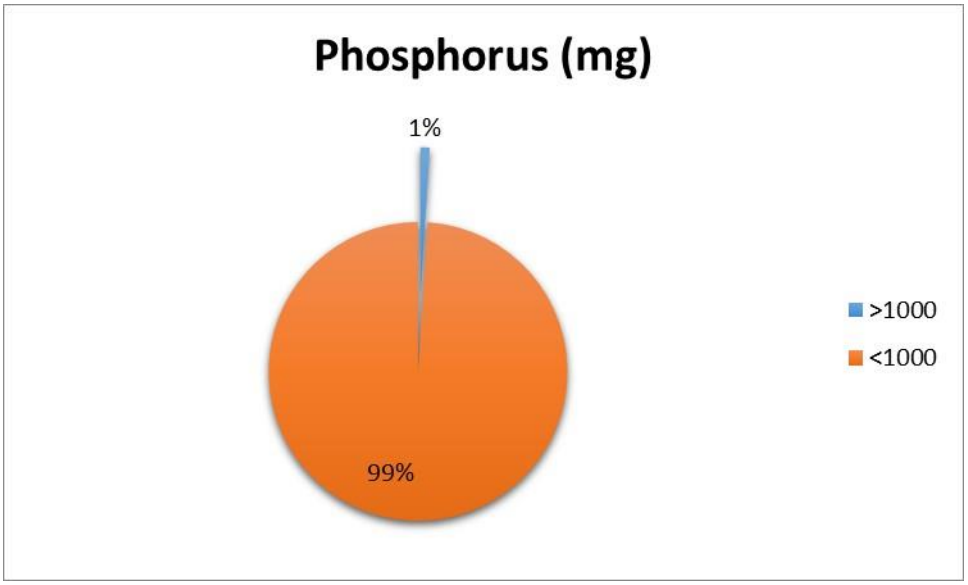

FIGURE NO. 4.6.3.10.8

Table No. 4.6.3.10.8 depicts the total intake of phosphorus among selected subjects. It was found that majority of the subjects are consuming phosphorus <1000 mg/day that is 99% while only 1% of subjects are consuming phosphorus >1000 mg/day.

TABLE NO. 4.6.3.10.9: Magnesium (mg /day)

Magnesium (mg/day)	**No: of subjects (n=150)**	**% of subjects**
>325	42	28%
<325	108	72%

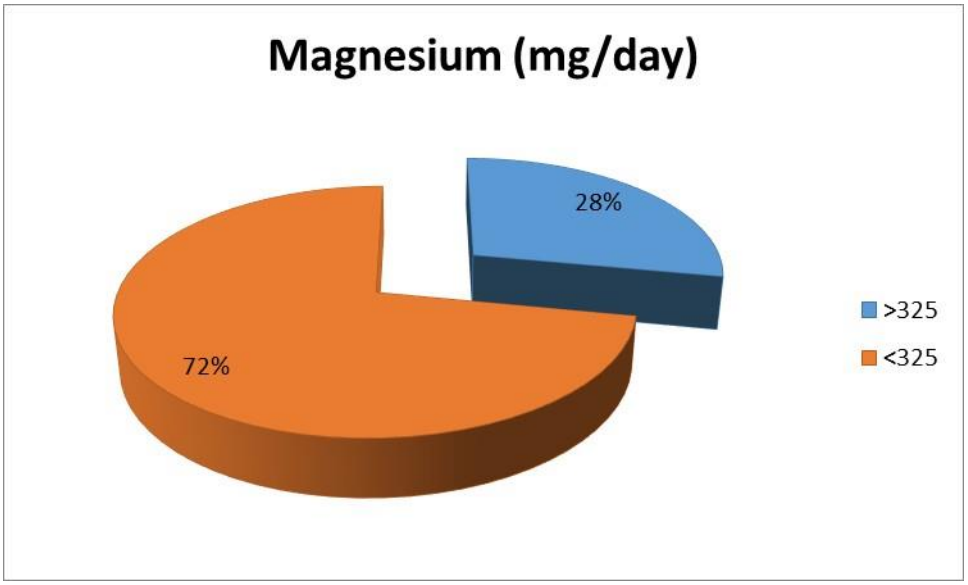

FIGURE NO. 4.6.3.10.9

Table No. 4.6.3.10.9 depicts the total intake of magnesium among selected subjects. It was found that 72% of subjects are consuming magnesium <325 mg/day and about 28% of subjects are consuming magnesium >325 mg/day.

4.6.3.11 FOOD FREQUENCY TABLE

TABLE NO. 4.6.3.11.1: FOOD FREQUENCY OF VITAMIN D RICH FOODS

Food items	Daily		Once in a week		Twice in a week		Once in a month		Never	
	No: of subjects (n=150)	% of subjects	No: of subjects (n=150)	% of subjects	No: of subjects (n=150)	% of subjects	No: of subjects (n=150)	% of subjects	No: of subjects (n=150)	% of subjects
Milk	61	41	35	23	14	9	36	24	4	3
Vitamin D fortified milk products	1	0.6	36	24	2	1	24	16	88	59
Vitamin D fortified oil			6	4			18	12	126	84
Egg			98	65	36	24	3	2	13	9
Fish	109	73	9	6	23	15			10	7
Fresh water Oily Fish	8 48	5 32	86 25	57 17	43 59	29 39	3 8	2 1	10 10	7 7

Consumption of vitamin D supplements (from above table) among the selected subjects is about 45% and the vitamin D from foods are discussed here. Majority of subjects are consuming fish daily especially oily fish. Milk and egg are consumed moderately and vitamin D fortified milk and oil are consumed by very few subjects.

TABLE NO. 4.6.3.11.2: FOOD FREQUENCY OF CARBOHYDRATE RICH FOODS

Food items	Daily		Once in a week		Twice in a week		Once in a month		Never	
	No: of subjects (n=150)	% of subjects	No: of subjects (n=150)	% of subjects	No: of subjects (n=150)	% of subjects	No: of subjects (n=150)	% of subjects	No: of subjects (n=150)	% of subjects
Cereals	150	100%								
Legumes and pulses	9	6%	103	69%	38	25%				
Fruits	22	15%	67	45%	53	35%	8	5%		
Vegetables	148	99%	2	1%						
Milk and milk products	61	41%	38	25%	13	9%	34	23%	4	3%
Roots and tubers	2	1%	126	84%	22	15%				
Carbonated beverages			10	7%	2	1%	32	21%	105	70 %
Sugars	45	30%	11	7.3%	2	1%	2	1%	91	61 %

Food Frequency Questionnaire was used to assess the dietary assessment of the subjects. The consumption rate of Cereals and legumes are high among the subjects. Milk and milk products, vegetables and Sugars were taken daily by majority of the subjects. Fruits and Carbonated beverages were taken rarely or mostly sometimes.

4.7 **STATISTICAL DATA**

TABLE NO.4.7.1: T-TEST

24 HOUR RECALL

NUTRIENT	**MEAN**	**RDA (ICMR-2020)**	**P VALUE**
ENERGY (Kcal)	2688.834	1660	< .00001
CARBOHYDRATE(g/d)	186.0273	130	< .00001
PROTEIN(g/d)	68.77727	45	< .00001
FAT(g/d)	30.60467	20	< .00001
FIBRE(g/d)	21.33207	25	< .00001
CALCIUM (mg/d)	747.6455		< .00001
VITAMIN D(IU/d)	232.0104	600	< .00001
PHOSPHORUS (mg)	737.1423	1000	< .00001
MAGNESIUM (mg/d)	288.0051	325	< .00001

One sample T test of the 24-hour recall was calculated and it was found that the p value of nutrients is significant at P value <0.05. For this analysis, the significance level is< 0.05, and alternative hypothesis accepted. Thus, there is a difference between the mean intakes of selected subject to RDA.

The null hypothesis states that there is no difference between the mean intakes of selected subject to RDA. The alternative hypothesis state that there is a difference between the mean intakes of selected subject to RDA.

4.7.2 SERUM VITAMIN D

KOLMOGORORV –SMIRNOV TEST OF NORMALITY

	N	**MEAN**	**df**	**SKEWNESS**	**KURTOSIS**	**P VALUE**
SERUM VITAMIN D	150	20.2	9.48	0.15	0.393	.24882

The value of the K-S test statistic (D) is 0.0822. The p value is 0.24882. It can be concluded that the values are normally distributed.

4.7.3 ASSOCIATION BETWEEN DIABETES (HBA1C) AND SERUM VITAMIN D

SPEARMAN CORRELATION

		SERUM VITAMIN D
DIABETES (HbA1C)	**CORRELATION COEFFICIENT**	0.216
	SIG. (2 TAILED)	0.0078
	N	150

By normal standards, the association between the diabetes (HbA1C) and serum vitamin D could be considered statistically significant. Therefore, there is a relationship between diabetes (HbA1C) and serum vitamin D

4.7.4 DIABETES

KOLMOGORORV –SMIRNOV TEST OF NORMALITY

	N	**MEAN**	**Df**	**SKEWNESS**	**KURTOSIS**	**P VALUE**
HbA1C	150	9.024	4.35	8.49	91.59	<0.00001

The value of the K-S test statistic (D) is 0.2079. The p value is <0.00001. It can be concluded that the values are not normally distributed

SUMMARY AND CONCLUSION

CHAPTER-5

SUMMARY AND CONCLUSION

The study entitled "**Incidence of diabetes among sedentary women and assessment of vitamin D status**" was carried out among 150 subjects aged between 30-55 years, all subjects were sedentary women of Ernakulam district. The result of the current study summarizes as follows:

Socio economic details reveal that out of 150 subjects the highest number of subjects (72%) have above Rs 40,000 income per month. Majority of the subjects are belong to Hindu community and only 17% of subjects from Christian. Most of the selected subjects are married and only 2% of selected subjects are single. Out of 150 subjects around 87% of subjects belong to nuclear family. The nature of work of selected subjects are mainly other type of work like home makers and only 4% are academicians.

Among the total subjects 80% of subjects suffer from diabetes. A major portion of subjects i.e. 90% of the subjects are on medication for diabetes mellitus. By analyzing the history of diabetes among subjects the highest proportion of subjects show lethargy, 23% of the subjects show body ache, however depression, constipation and dehydration were less observed. Minor proportion of subjects undergo treatment for infertility. 40% of subjects were affect by COVID-19 with fever. The major post COVID problems among selected subjects observed was body pain and fatigue.

Out of 150 subjects majority of the subjects suffer from vitamin D deficiency one of the reasons being the use of sunscreen (42%) and frequency of using sunscreen among the selected sample was 18%. Other possible causes of hypovitaminosis D include SPF of sunscreen use, preference of Shades when Outdoor and preference to stay indoor during the day 52%,48% and 57% respectively. Majority of the subjects that is about 52% are exposed to sun between 5.00 Am to 9.00 Am and least percentage is about 7% are exposed to sun between 10.00 Am to 3.59 PM. The duration of sun exposure among selected subjects are mostly >45 Minutes as well as the preference of dress among the selected subjects are half sleeve kameez or blouse is about 53.4% all favoring the synthesis of vitamin D cutaneosly.

Majority of subjects (59%) had WHR in the range between >1. According to Who, in females' obesity is indicate as the range of >0.85.

Through biochemical analysis 87% of subjects had HbA1c value above 6.5% and only 7% of subjects have the HbA1c value below 5.7%. About 16% of subjects have severe vitamin D

deficiency, 30% have vitamin D deficiency, 39% have vitamin D insufficiency and only about 15% have normal vitamin D status.

It was found that majority of the subjects out of 150 subjects are consuming non vegetarian and remaining 7% of subjects are consuming vegetarian foods. About 77% of subjects are consuming food at regular time and 61% of subjects follows 4 meals per day. Minority of the subjects are skipping their meals and it was compensated with mainly coffee. Among the subjects 115 subjects are consuming junk foods mostly 2 times per week. Among the selected subjects only 45% of subjects are consuming vitamin D supplements.

The average intake of 24-hour recall of 3 continues days show that only 2% of subjects consumed calorie insufficient diet and 98% of subjects consume more than recommended RDA. Majority of the selected subjects consume fat more than 20 gm. About 73% of subjects consume fibre <25 gm and only 27% subjects consume >25 gm of fibre. According to RDA the daily requirement of vitamin D is 600 IU/day. Majority of the subjects (100%) had vitamin D <600 IU/day. So the consumption of vitamin D is insufficient in selected subjects.

Nutrition education was imparted to all the selected subjects by creating video and sharing them among the selected subjects. The topics covered were about the importance, function and risk factors of vitamin D and its rich sources.

The correlation coefficient was 0. 216.By normal standards, the association between the diabetes mellitus (HbA1c) and serum Vitamin D could be considered statistically considered significant. Therefore, there is a relationship between diabetes mellitus (HbA1c) and serum Vitamin D.

CONCLUSION

The present study was conducted to assess the incidence of diabetes mellitus among sedentary women and assessment of vitamin D status. The main finding of the study was that majority of the selected subjects affected with diabetes mellitus had food habits, physical inactivity and their sedentary lifestyle leading to the condition. The majority of the selected subjects were vitamin D deficient, one of the reasons being sunscreen and frequency of using sunscreen. Other possible causes of hypovitaminosis D include SPF of sunscreen use, preference of Shades when and preference to stay indoor during the day time.

According to parameters of diabetes mellitus based on ICMR criteria 80% of selected subjects were affected with diabetes mellitus condition and 85% were deficient in vitamin D. The relationship between vitamin D status and diabetes mellitus are considered statistically significant.

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APPENDIX

APPENDIX-1

QUESTIONNAIRE TO ELICIT INFORMATION ON INCIDENCE OF DIABETES AMONG SEDENTARY WOMEN AND ASSESSMENT OF VITAMIN D STATUS

1. GENERAL INFORMATION
   - 1.1 Name of the Respondent
   - 1.2 Age
   - 1.3 Address
   - 1.4 Mobile No:
   - 1.5 Educational level
     a. up to X^{th}
     b. XII^{th}
     c. Undergraduate
     d. Post Graduate and above
     e. Occupation
   - 1.6 Religion, Caste
   - 1.7 Marital status
     a. Single
     b. Married
     c. Widow
   - 1.8 Details of Family

Sl.No	Family Member	Relation to respondent	Age	Monthly Income

2. Health Status

2.1 Do you have any of the following Cardiovascular/kidney diseases/ diabetes mellitus/ cirrhosis of liver/ inflammatory bowel disease/ epilepsy/ gastroduodenal ulcers/Celiac disease

a. Yes b. No

2.2 Do you take any vitamin D supplements or medications containing Cholecalciferol or any supplement with 25, hydroxy cholecalciferol?

a. Yes b. No

2.3. Do you take any medication or insulin for diabetes?

a. Yes b. No

If yes, mention it?

_____

2. 4 Do you experience any of the following conditions, if so mention frequency?

a. Lethargy

b. Body aches

c. Back ache

d. Depression

e. Infections

f. Muscle pain

g. Constipation

h. Dehydration

2.5 Are you receiving treatment for infertility?

a.Yes b. No

2. 6 Were you affected by COVID -19?

a. Yes b. No

2.6.1 If yes, what symptoms did you have? _____

2.6.2 Were there post COVID problems? If yes specify

3.Life style Pattern

3.1 Nature of work

a. Academician b. Bank Professional c. Health Professional

d. Agriculture e. Other (specify)_____

3.2 Do you use sunscreen?

a. Yes b. No

If yes, frequency

a. Regularly/always b. mostly/sometimes c. rarely

If yes which do you Use:

a. SPF≤15 b. SPF≤30 c. SPF≤50

3.3 Do you prefer shades when outdoors. (use of umbrellas, hat/ or trying to remain in shades)

a. Yes b. No

3.4 Do you spent more time in Air conditioned/ indoors during the day?

a. Yes B. No

3.5 Do you engage in re creational/ sports activities/ spend time out door during the day?

a. Yes B. No

If Yes, how long:

And what kind of physical activity:

Nutritional Status

4.Anthropometric Assessment

4.1. Height (cm)
4.2. Weight (kg)
4.3. Waist Circumference
4.4. Hip Circumference

5.Dietary Assessment

5.1.1Dietary Habits

a. Vegetarian b. Non vegetarian c. Ovo Vegetarian d.any other

5.1.2. Do you have the habit to take food at regular time?

a. Yes b. No

5.1.3. Meal pattern per day

a.2 meals b. 3 meals c.4 meals d. 5 meals

5.1.4. Do you skip meals?

a.Yes b. No

If yes, which meal?

a. Breakfast b. Lunch c. Dinner

5.1.5. How do you compensate the skipped meals?

a. Tea b. Coffee c. Snacks d. Chocolates

e. Vegetable salads f. Fruit juices h. Any other foods, specify _____

5.1.6. Do you have good appetite?

a. Yes b. No

5. 1.7. Where do you take food regularly?

a. Home b. Hotel c. Canteen d. Door delivery system

5.1.8. Do you eat junk foods?

a. Yes b. No

If yes, mention it?

a. 2 Times per day b. Times per week

c. Times per month d. Times per year e. Never

5.1.9. Do you take Vitamin D Supplements?

a. Yes b. No

If yes, specify the name of tablet and in what dosage:

APPENDIX -II

24 Hour recall (The table was used to assess recall for 3 consecutive days)

Time	Menu	Serving size	Ingredients	Amount(gm/ml)

APPENDIX -III

Food Frequency of Vitamin D rich foods

Sl.No	Food Items	Daily	Once in a week	Twice in a week	Once in a month	Never
1.	Milk					
2.	Vitamin D Fortified milk products					
3.	Vitamin D fortified Oil					
4.	Egg					
5.	Fish Fresh water Oily Fish					

Food frequency of carbohydrate rich foods

Sl.No	Food Items	Daily	Once in a week	Twice in a week	Once in a month	Never
1	Cereals					
2	Legumes And Pulses					
3	Fruits					
4	Vegetables					
5	Milk and Milk products					

6	Roots and Tubers					
7	Carbonated Beverages					
8	Sugars					

APPENDIX -IV

Details on Sun exposure

Time	**Sun exposure (in minutes)**					**Activity**	**Dress**
	0	>15	15-30	30-45	>45		
5-5.59 am							
6-6.59 am							
7-7.59 am							
8-8.59 am							
9-9.59 am							
10-10.59 am							
11-11.59 am							
12-12.59 pm							
1-1.59 pm							
2-2.59 pm							
3-3.59 pm							
4-4.59 pm							
5-5.59 pm							

APPENDIX-V

Tool developed against hypovitaminosis D to create awareness among selected subjects.

Nutrition Education was imparted to all the selected subjects by creating video with the importance, functions and risk factors of vitamin D, sources and Hypovitaminosis D in sedentary women, causes, symptom, complications and management by sharing them to the selected subjects.

VIDEO LINK

https://youtu.be/h2cBvnE4gAo

PLATE No. 4