Dissertation on

A STUDY OF THYROID DYSFUNCTION AND ITS ASSOCIATED RISK FACTORS AMONG TYPE 2 DIABETES MELLITUS PATIENTS

Submitted to

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

Chennai – 600032

In partial fulfilment of the requirement

for the award of degree of

DOCTOR OF MEDICINE IN BIOCHEMISTRY

BRANCH –XIII

Submitted by

Register number : 201523352

KARPAGA VINAYAGA INSTITUTE OF MEDICAL SCIENCES

AND RESEARCH CENTRE

MADHURANTHAGAM

TAMILNADU

MAY 2018

CERTIFICATION

This is to certify that **"A Study of Thyroid Dysfunction and its associated risk factors among Type 2 Diabetes Mellitus patients"** is a bonafide work of **Dr.C.Sathishkumar** in partial fulfilment of the requirements for the **M.D Biochemistry** (Branch XIII) examination of **The Tamilnadu Dr.M.G.R Medical University** to be held on May 2018.

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DECLARATION

I, **Dr.C.Sathishkumar** hereby declare that this dissertation "**A Study of Thyroid Dysfunction and its associated risk factors among Type 2 Diabetes Mellitus patients"** is a presentation of my own work and that it has not been submitted anywhere for any award.

Wherever contributions of others are involved, every effort is made to indicate this clearly, with due reference to literature and discussions.

This work was done under the guidance of Professor **Dr.Aruna kumari.R MD**, at Karpaga Vinayaga Institute of Medical Sciences, Madhuranthagam.

Candidate's Name: Dr. C. Sathishkumar

Candidate's signature:

Date:

In the capacity as guide for the candidate's dissertation work, I certified that the above statements are true to the best of my knowledge.

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ACKNOWLEDGEMENT

I bow myself in front of the **Almighty** expressing my thankfulness for all his blessings throughout my life.

I express my sincere and heartfelt gratitude to our respected Managing Director, **Professor Dr.R.Annamalai., M.S.,** for permitting and for extending his valuable support in conducting this study.

I humbly respect and thank our former **Dean, Professor Dr.A.R.Chakaravarthy., M.S.,** and **Principal Dr.Sufala Sunil Viswas Rao., M.D.,** for permitting and supporting me to conduct this study.

"There are two kinds of teachers; the kind that fill you with so much quail shot that you can't move, and the kind that just gives you a little prod behind and you jump to the skies." - Robert Frost

By God's grace, I am blessed to be a student of a great teacher, who is always there to direct her students in the right direction, who does not put undue pressure and She is the one who taught the virtue of simplification and understanding in learning. She always greets us with a beautiful smile and shows that Knowledge is her power. She is none other than our esteemed and beloved, Head of Department of Biochemistry and my guide, **Professor Dr.Aruna Kumari. R. MD.** The word **"Gratitude"** falls short for her. I express my deep, heartfelt and sincere thanks to her for her guidance in every process of this study.

I would like to thanks my **Professor Dr.Subiman Saha** for his wisdom filled words. I would like to thank **Dr.Khadeja Bi** my Assistant Professor for her kind support and timely guidance for my study.

I would like to express my sincere gratitude to **Dr.Siva, Ph.D.,** Associate Professor for his unflinching support and encouragement throughout this study.

I would like to thank **Dr.Firoz Pathan.,** Assistant Professor for his kind support and encouraging words during the dissertation work.

I would like to thank **Dr.Amar Nakeshkumar.,Ph.D.,** for his unbounded support and suggestions during the dissertation work.

I express my sincere thanks to **Mr.Saravanan.,M.Sc.,Ph.D.,** Assistant Professor for his concern, affection, priceless support and willingness to help at all times.

I extend my immense thanks and gratitude to **Dr.Selvakumar Kandaswamy, Ph.D.,** Clinical Biochemist, Kauvery Hospital, Chennai for his tremendous support and boundless guidance for the completion of dissertation work and for being constant source of inspiration.

I also wish to thank **Mr.R.Radhakrishnan.,** Non-Medical Demonstrator for his kind support and guidance during the dissertation work and I would like to thank our Laboratory Technicians of Undergraduate Laboratory and Central Research Laboratory for their help and Co-operation

I would like to thanks **Mrs.Gladius Jennifer** for her guidance towards statistical analysis techniques.

I immensely thank my Co-PG's for their help and great support during the course of the study.

Many thanks to all patients and volunteers who participated in the study.

Last but not the least; I am grateful to my beloved parents **Mr.S.Chakravarthy & Mrs.N.Kanchana and all my family members** for their unbounded, unconditional love, trust and support throughout my life and especially during my post graduation period. Because without their support this would not have been possible.

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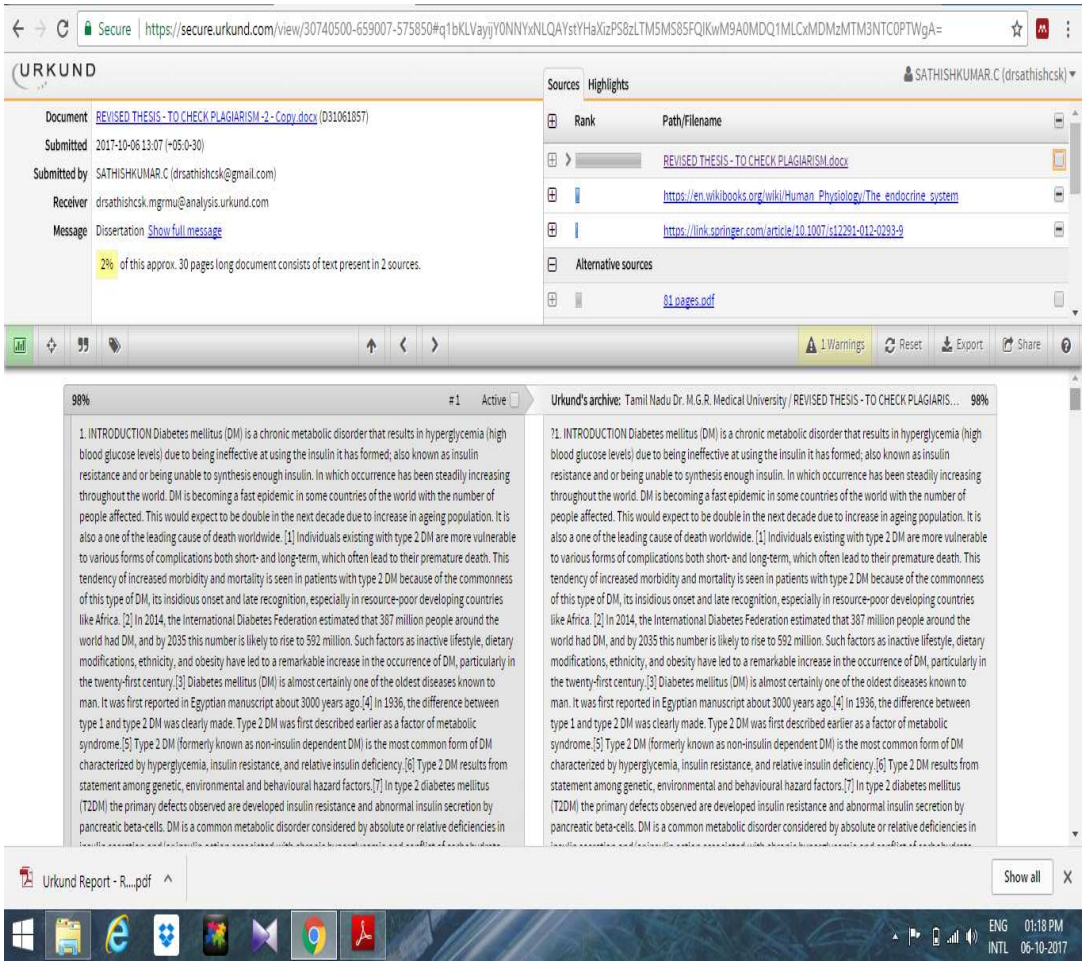
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1. INTRODUCTION Diabetes mellitus (DM) is a chronic metabolic disorder that results in hyperglycemia (high blood glucose levels) due to being ineffective at using the insulin it has formed; also known as insulin resistance and or being unable to synthesis enough insulin. In which occurrence has been steadily increasing throughout the world. DM is becoming a fast epidemic in some countries of the world with the number of people affected. This would expect to be double in the next decade due to increase in ageing population. It is also a one of the leading cause of death worldwide. [1] Individuals existing with type 2 DM are more vulnerable to various forms of complications both short- and long-term, which often lead to their premature death. This tendency of increased morbidity and mortality is seen in patients with type 2 DM because of the commonness of this type of DM, its insidious onset and late recognition, especially in resource-poor developing countries like Africa. [2] In 2014, the International Diabetes Federation estimated that 387 million people around the world had DM, and by 2035 this number is likely to rise to 592 million. Such factors as inactive lifestyle, dietary modifications, ethnicity, and obesity have led to a remarkable increase in the occurrence of DM, particularly in the twenty-first century.[3] Diabetes mellitus (DM) is almost certainly one of the oldest diseases known to man. It was first reported in Egyptian manuscript about 3000 years ago.[4] In 1936, the difference between type 1 and type 2 DM was clearly made. Type 2 DM was first described earlier as a factor of metabolic syndrome.[5] Type 2 DM (formerly known as non-insulin dependent DM) is the most common form of DM characterized by hyperglycemia, insulin resistance, and relative insulin deficiency.[6] Type 2 DM results from statement among genetic, environmental and behavioural hazard factors.[7] In type 2 diabetes mellitus (T2DM) the primary defects observed are developed insulin resistance and abnormal insulin secretion by pancreatic beta-cells. DM is a common metabolic disorder considered by absolute or relative deficiencies in
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ABBREVIATIONS

LIST OF ABBREVIATIONS

ACh	Acetyl Choline
ADA	American Diabetes Association
ATP	Adenosine Tri Phosphate
BMI	Body Mass Index
CHOD POD	Cholesterol Oxidase Peroxidase
Cyclic AMP	Cyclic Adenosine Mono Phosphate
GLUT-4	Glucose Transporter
HbA1C	Glycosylated Hemoglobin
HDL	High Density Lipoprotein
IGF-1	Insulin Growth Factor-1
IL-6	Interleukin-6
IR	Insulin Receptor
IRS-1 gene	Insulin Receptor Substrate – 1 gene
LDL	Low Density Lipoprotein
NHANES III Study	National Health And Nutrition Examination Survey III Study
TC	Total Cholesterol
TD	Thyroid Dysfunction
TGL	Triglycerides
TNF-α	Tumor Necrosis Factor-α
TRH	Thyrotropin Releasing Hormone
TSH	Thyroid Stimulating Hormone
VLDL	Very Low Density Lipoprotein
WHO	World Health Organization

INTRODUCTION

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In type 2 diabetes mellitus (T2DM) the primary defects observed are developed insulin resistance and abnormal insulin secretion by pancreatic beta-cells. DM is a common metabolic disorder considered by absolute or relative deficiencies in insulin secretion and/or insulin action associated with chronic hyperglycemia and conflict of carbohydrate, lipid and protein metabolism.

The thyroid gland is significantly concerned in metabolism of lipid and carbohydrate, role in metabolism of adipogenesis and thermogenesis, regulation of body weight.[8] Thyroid dysfunction may also affect and interfere in control of diabetes. Hyperthyroidism is characteristically associated with deteriorating glycemic control and amplified insulin requirements. There is primary increased hepatic gluconeogenesis, rapid gastrointestinal glucose absorption, and probably increased insulin resistance. Indeed, thyrotoxicosis may unmask latent diabetes[8]. The most common thyroid disorder is hypothyroidism. The association of thyroid disorder with diabetes is more frequent in diabetics who have deranged metabolic control. Thyroid also influences the glycosylated haemoglobin levels.[9]

In practice, there are several implications for patients with both diabetes and hyperthyroidism. First, in hyperthyroid patients, the diagnosis of glucose intolerance needs to be considered cautiously, since the hyperglycemia may improve with treatment of thyrotoxicosis. Second, underlying hyperthyroidism must be considered in diabetic patients with unexplained worsening hyperglycemia. Third, clinician need to anticipate potential deterioration in glycemic control and amend the treatment accordingly in patients with diabetic and hyperthyroidism, lower the blood glucose level will found in euthyroidism restoration.[10]

Although wide-ranging changes in carbohydrate metabolism are seen in hypothyroidism, clinical manifestation of these abnormalities is seldom conspicuous. However, the condensed rate of insulin degradation may inferior the exogenous insulin condition. The presence of hypoglycemia is uncommon in isolated thyroid hormone deficiency and should elevate the opportunity of hypopituitarism in a hypothyroid patient. More importantly, hypothyroidism is accompanied by a variety of abnormalities in plasma lipid metabolism, including elevated triglyceride and low-density lipoprotein (LDL) cholesterol concentrations.[11] Even subclinical hypothyroidism can exacerbate the coexisting dyslipidemia commonly found in type 2 diabetes and further increase the risk of cardiovascular diseases. Lipid abnormalities can reverse by replacement of sufficient thyroxine.

Prevalence of thyroid dysfunction is higher in type 2 diabetes population compared to normal population. Diabetes mellitus and thyroid dysfunction are

the most common endocrine diseases seen among the adult population[11] while insulin or thyroid hormones metabolism can result in functional abnormalities of one another. The strong link between diabetes and thyroid diseases encouraged the American Diabetes Association (ADA) to propose that people with diabetes must be checked periodically for thyroid dysfunction.[12]

Thyroid hormones may influence glucose manage through a variety of actions on intermediary metabolism. One of these effects becomes clinically appropriate in patients with co-existent diabetes and hyperthyroidism. Excess thyroid hormones promote hyperglycaemia by facilitating increasing insulin clearance, glucose intestinal absorption, and glycogenolysis and gluconeogenesis enhancement. Also, hyperthyroidism is associated with increased hepatic glucose output, reduced insulin action and increased lipolysis[13] (Potenza et al., 2009). Accordingly, diabetic patients with overt hyperthyroidism may experience poor glycaemic control and indeed hyperthyroidism has been known to impulsive diabetic ketoacidosis in patients with diabetes.[14] Thyroid disease must be screened every year in diabetic patients to detect asymptomatic thyroid dysfunction.[15] At the same time, patients with thyroid dysfunction may require to be tested for the prospect of abnormal glucose metabolism, since extreme thyroid hormones cause increased glucose production in the liver, rapid absorption of glucose through the intestine and increased insulin resistance.[16] There are many risk factors known to be associated with thyroid dysfunction in the general population, including age, gender, BMI, family history of thyroid disease, smoking, and pregnancy.

Incidence of hyperthyroidism and hypothyroidism increases with age, especially beyond 30 years, and it has been established that female gender is 10–20 times more likely to have this medical problem than males.[17]

Morbidly accounting for 19.5% obese individuals show a high prevalence of overt and subclinical hypothyroidism.[8] Risk factors for thyroid dysfunction among diabetic patients are similar to what have been reported in non-diabetics, although they will vary with the type of thyroid dysfunction., while hypothyroidism among diabetic patients is more prevalent among women[18] and the older population.[19]

Thus, the present study was intended to explore a study of thyroid dysfunction and associated risk factors among type 2 diabetes mellitus patients in Tamil Nadu.

AIMS AND OBJECTIVES

AIM AND OBJECTIVES

Aim

- To evaluate thyroid profile, lipid profile, and renal parameters in type 2 Diabetes mellitus

Objectives

- To assess the risk factors like thyroid profile, lipid profile and renal parameters for cardiovascular disease and renal disease in type 2 diabetes Mellitus among male and female patients
- To compare the serum levels of thyroid profile, lipid profile and renal parameters between controlled and uncontrolled diabetes patients

REVIEW OF LITERATURE

REVIEW OF LITERATURE

THYROID GLAND

The thyroid gland is among the most significant organs of the endocrine system and has a weight of 15-20g. It is soft and its colour is red. This organ is located between the C5-T1 vertebrae of columna vertebralis, in front of the trachea and below the larynx. It is comprised of two lobes (lobus dexter and lobus sinister) and the isthmus that binds them together. Capsule glandular which is internal and external folium of thyroid gland is wrapped up by a fibrosis capsule named thyroid. The thyroid gland is nourished by a thyroidea superior that is the branch of a. carotis external and a. thyroid inferior that is the branch of a subclavia.[20-27]

THYROID HORMONES AND ITS FUNCTIONS

The thyroid hormones, triiodothyronine (T3) and its prohormone, thyroxine (T4), are tyrosine-based hormones produced by the thyroid gland that are primarily responsible for regulation of metabolism. T3 and T4 are partially composed of iodine (see molecular model). A deficiency of iodine leads to decreased production of T3 and T4, enlarges the thyroid tissue and will cause the disease known as simple goitre. T4 increase the spectacular apoptosis (programmed cell death) of the cells of the larval gills, tail and fins. Contrary to amphibian metamorphosis, hypothyroidism and thyroidectomy in mammals may be considered a sort of phylogenetic and metabolic regression to a forestage of reptilian life. Indeed, many disorders that seem to afflict hypothyroid humans have reptilian-like features, such as scaly , dry, hairless,

cold skin and a general slowing of metabolism, heart rate , digestion, and nervous reflexes, with lethargic cerebration, hyperuricemia and hypothermia. [28]

IODINE

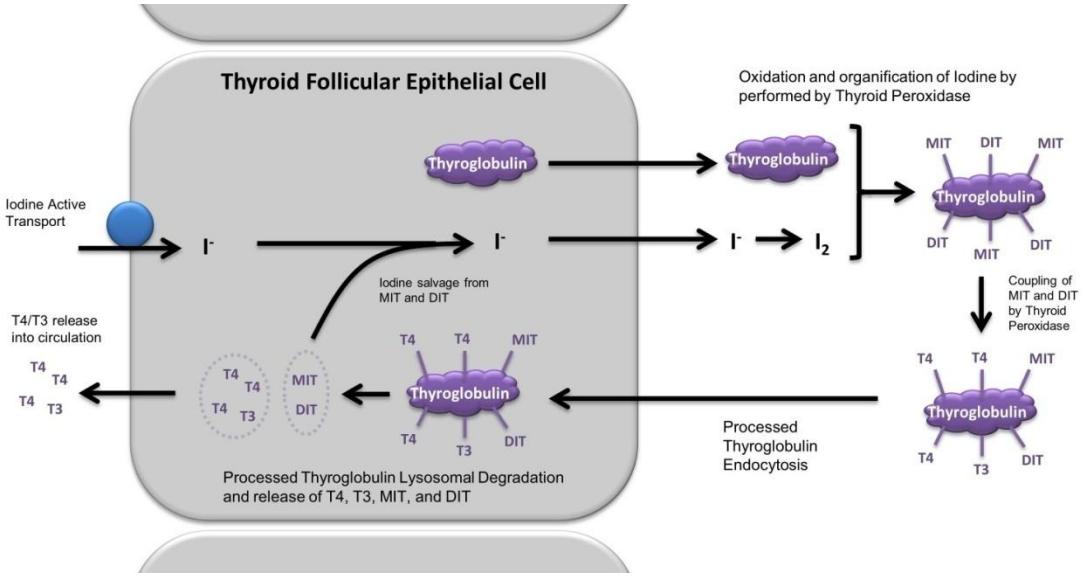
Iodine is taken into the body oral. Among the foods that contain iodine are seafood, iodine-rich vegetables grown in soil, and iodized salt. For this reason, iodine intake geographically differs in the world. Places that are seen predominantly to have iodine deficiency are icy mountainous areas and daily iodine intake in these places is less than 25 µg. Hence, diseases due to iodine deficiency are more common in these geographies. Cretinism in which mental retardation is significant was first identified in the Western Alps. [27, 29]

Iodine absorbed from the gastrointestinal system immediately diffuses in extra cellular fluid. T3 and T4 hormones are fundamentally formed by the addition of iodine to tyrosine amino acids. While the most synthesized hormone in thyroid gland is T4, the most efficient hormone is T3. [22, 24]

THYROGLOBULIN

The synthesized thyroglobulin is transported to the apical section of the cell and passes to the follicular lumen through exocytose, and then joins thyroid hormone synthesis [27, 29]. Through this deiodinization, about 50% of iodine in the thyroglobulin structure is taken back and can be reused. Iodine deficiency in individuals lacking this enzyme, and correspondingly,

hypothyroid goiter is observed. Such patients are given iodine replacement treatment. [26, 31]



ALBUMIN

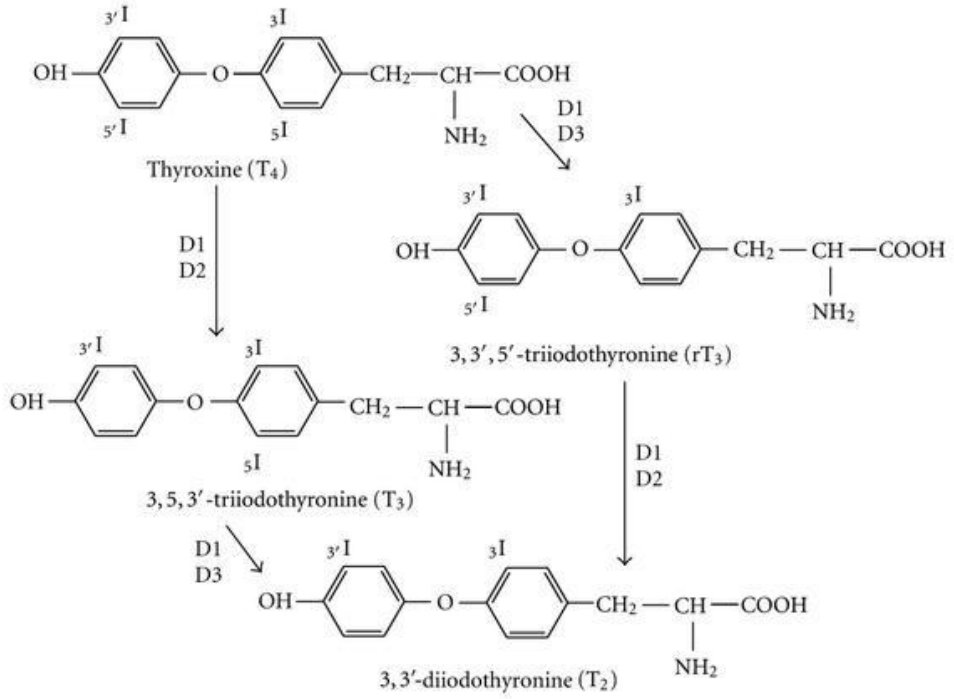
Serum albumin is a protein with a molecule weight of 65kDa and has a lower rate of binding even though its plasma concentration is the highest. [22] Synthesis and secretions need to be kept at a certain level in order for the liveliness of thyroid hormones to be maintained. In this respect, the most important mechanism in controlling the synthesis and secretion of thyroid hormones is the hypothalamus-hypophysis-thyroid axis. Another one is the auto control mechanism that is dependent on iodine concentration as noted earlier [26]

HORMONES

TRH also increases the secretions of growth hormone (GH), follicle stimulating hormone (FSH), and prolactin (PRL). While the TRH secretion is increased by noradrenaline, somatostatin and serotonin inhibits it. [26]

METABOLISM

Thyroid hormones carry out their metabolic effects by carbohydrates, fat and protein metabolisms, vitamins, basal metabolic rate and its effect on body weight. When the effects of thyroid hormones on carbohydrate metabolism are observed, it is established that it is both anabolic and catabolic. As a result of thyroid hormones increasing the enzyme synthesis due to protein synthesis in cells, enzymes in carbohydrate metabolism also increase their activities. Thus, thyroid hormones increase the entrance of glucose into the cell, absorption of glucose from the gastrointestinal system, both glycolysis and gluconeogenesis, and secondarily, insulin secretion [26, 29]



THYROID HORMONE METABOLISM

In addition, as metabolism products also increase due to an increase in oxygen consumption when thyroid hormones are over secreted, vasodilation occurs in periphery. Thus, blood flow increases, and cardiac output can be observed to be 60% more than normal. The thyroid hormone also raises the heart rate due to its direct increasing effect on heart stimulation.[21] Thyroid hormones increase the contraction of heart muscles only when they raise it in small amounts. When thyroid hormones are over secreted, a significant decrease occurs in muscle strength, and even myocardial infarction is observed in severely thyrotoxic patients. [26, 31]

TYPES OF GLAND

Endocrine Glands are the glands which contain no duct and release their secretions into the intercellular fluid or directly into the blood. The compilation of endocrine glands makes up the endocrine system.

1. The important endocrine glands are the pituitary (anterior and posterior lobes), thyroid, parathyroid, pancreas , adrenal (cortex and medulla), and gonads.
2. The thyroid gland comprises of two lateral masses, held by a cross bridge, that are fixed to the trachea. They are slightly lower in position to the larynx.
3. The parathyroid glands are four masses of tissue, two lodged posterior in each lateral mass of the thyroid gland.
4. One adrenal gland is situated on top of each kidney. The cortex is the outer most layer of the adrenal gland. The medulla is the inner core.
5. The pancreas is situated along the lower curvature of the stomach, close to where it meets the first part of the small intestine, the duodenum.
6. The ovaries and testes are found in the pelvic cavity.

HORMONES AND TYPES

The endocrine system secretes hormones that are important in maintaining regulation of reproduction , homeostasis and development. A hormone is a chemical messenger secreted by a cell that effects specific change in the cellular activity of the target cells. But exocrine glands which secrete

substances such as milk, saliva , stomach acid and digestive enzymes. Endocrine glands do not secrete substances into ducts (tubes). Instead, they secrete their hormones directly into the surrounding extra cellular space. The hormones then enter into the nearby capillaries and then they are transported throughout the body in the blood.

Classification of Hormones based on chemical nature :

Amino acid-derived, Polypeptide and proteins, Steroids, Eicosanoids [22].

Lipid-soluble hormones (steroid hormones and hormones of the thyroid gland) enter through the cell membranes of target cells. The lipid-soluble hormone then attach to a protein receptor that, in turn, promotes a DNA segment which turns on specific genes. The proteins transcription in the genes and results in subsequent translation of mRNA which acts as enzymes that will regulate specific physiological actions of the cell.

Water-soluble hormones like polypeptide, protein, and most amino acid hormones , attach to a receptor protein on the plasma membrane of the cell [22]. The receptor protein, in turn, activates the production of second messengers which results in the synthesis and secretion of hormones to that specific tissue.

DIABETES

Diabetes Mellitus is a disorder caused by the total or relative absence of insulin, with or without insulin resistance that leads to dysregulation of carbohydrate , fat and protein metabolism which manifests clinically as an elevated blood glucose. Diabetes mellitus becoming the epidemic of the

twenty first century with more than 1.5 million deaths worldwide directly attribute to this disease in 2012 (WHO). Despite advances in medical treatment, cardiovascular disease (CVD) remains the important cause of morbidity and mortality in individuals with diabetes. The risk of vascular complications is double in diabetes mellitus resulting in significant reduction in life expectancy. **[32]**

After a vascular event occurred, the outcome in patients with diabetes mellitus is worse when compared with individuals with normal glucose metabolism, regardless of the therapeutic strategy used in the acute stage**[33, 34, 35, 36, 37]**.

There are two important reasons for the adverse vascular outcome in patients with diabetes mellitus. The first one is related to more extensive vascular pathology and the second one involves an enhanced thrombotic environment. **[38]**

STRUCTURE OF INSULIN AND PROPERTIES

Insulin a polypeptide found in 1928 and sequence of amino acid identified in 1952. It is a dipeptide, containing A and B chains linked by disulphide bridges, and containing 51 amino acids, contains molecular weight of 5802. The isoelectric point is pH 5.5. [39] A chain consists of 21 amino acids and the B chain 30 amino acids. A chain has an N-terminal helix related to an anti-parallel C-terminal helix; the B chain has a central helical segment. These two chains are connected by 2 disulphide bonds, which link the N- and C-terminal helices of the A chain to the central helix of the B chain.[40]

SYNTHESIS AND RELEASE OF INSULIN

The short arm of chromosome 11[41]7 is coded for Insulin and synthesised in the β cells of the pancreatic islets of Langherhans as its precursor, proinsulin (PI). PI is synthesised in the Ribosomes of the rough endoplasmic reticulum from mRNA as pre-proinsulin (PPI). This PPI is produced by sequential synthesis of a signal peptide, B chain, the linking peptide and then the A chain comprising a single chain of 100 amino acids. Secretory vesicles transfer proinsulin from the rough endoplasmic reticulum to the Golgi apparatus, which favours formation of soluble zinc-containing proinsulin hexamers using aqueous zinc and calcium rich environment.[40] As immature storage vesicles form from the Golgi, enzymes acting outside the Golgi convert proinsulin to insulin and C-peptide.[42] Insulin forms zinc-containing hexamers which are insoluble, precipitating as chemically stable crystals at pH 5.5. Granules are get matured and secreted into the blood stream by exocytosis, insulin, and an equal concentration ratio of C-peptide were also released. Proinsulin and zinc usually comprise no more than 6% of the islet cell secretion. [40]

Insulin secretion from the islet cells into the portal veins is pulsatile. An ultradian oscillatory mould of insulin discharge, in addition to post meal deviation, has been reported. [43] In response to a stimulus such as glucose, insulin secretion is characteristically biphasic, with an initial rapid phase of

insulin secretion, followed by a less intense but more sustained release of the hormone. [44]

FACTORS INFLUENCING BIOSYNTHESIS OF INSULIN AND ITS RELEASE

Insulin secretion may be subjective by alterations in production at the level of gene transcription, translation, and post-translational modification in the Golgi as well as by factors influencing insulin release from secretory granules. Longer-term modification may occur via influences on β cell mass and differentiation. [45] Insulin plays a pivotal role in glucose consumption and metabolism, it is not unanticipated that glucose has numerous influences on insulin biosynthesis and secretion. However, other factors such as fatty acids, amino acids, Ach, glucagon-like peptide-1 (GLP-1), and several other agonists, together in arrangement, also influence this processes. [44]

MOLECULAR MECHANISMS OF SECRETION OF INSULIN

Increased levels of glucose provoke the initial phase of glucose-mediated insulin secretion by release of insulin from β cell. Glucose entry into the β cell is sensed by glucokinase, which phosphorylates glucose to glucose-6-phosphate (G6P), generating ATP.[12] Closure of K+-ATP-dependent channels results in membrane depolarization and commencement of voltage dependent calcium channels leading to an raise in intracellular calcium concentration; which triggers insulin secretion in a pulsatile manner. [46] Escalation of this

reaction occurs by both a potassium-ATP channel-independent Calcium dependent pathway and potassium ATP channel-independent calcium self-directed pathways of glucose action. [44] Other intermediaries are activation of phospholipases and protein kinase C (i.e., acetycholine) and by stimulus of adenylyl cyclase action and commencement of β cell protein kinase A, which potentiates insulin secretion. This latter mechanism may be activated by hormones and appear to partake an important role in the second part of glucose mediated insulin secretion, granules are translocated from reserve pools which is responsible for the refilling of insulin. [44]

REGULATION OF INSULIN SECRETION

Nutrient and non-nutrient secretagogues play a vital role in regulation of synthesis and secretion of insulin, in the context of stimuli from environmental and the interaction of other hormones. [42] Nutrient secretagogues such as glucose appear to generate insulin secretion from the β cell by increasing intracellular ATP and closing of potassium ATP channels as described above. Generation of cyclic AMP and other cellular energy intermediates are also amplified, further enhancing insulin release. Glucose does not require insulin action to enter the β cell [42] Non-nutrient secretagogues might act via neural stimuli such as cholinergic and adrenergic pathways, or through peptide hormones.

INSULIN SECRETION AND ITS PHYSIOLOGY

Glucose is the principal stimulus for insulin secretion, although other hormones, macronutrients and neural input may adjust this response. Insulin, together with its principal counter-regulatory hormone glucagon, regulates blood glucose concentrations. [47] β cells secreted from pancreas is 0.25–1.5 units of insulin/ hour during the basal (or fasting) state, enough to allow glucose insulin-dependent access into cells. This concentration prevents unconstrained hydrolysis of triglycerides and controlled gluconeogenesis, thus maintaining normal fasting glucose levels. Insulin basal state secretion accounts above for 50% of total 24 hour insulin secretion. Successive insulin secretion into the portal venous system, 60% is consequently separated by the liver; so portal vein insulin concentrations attain the liver approach triple that of the peripheral circulation. Circulating fasting insulin concentrations in healthy individuals are about 3–15 mIU/L [47]

INSULIN SECRETION IN RESPONSES TO GLUCOSE

An individual in healthy condition, glucose activates biphasic pancreatic secretion. Intravenous administration of glucose is related with a instantaneous "primary phase" of insulin release within 1 minute, peaking at 3–5 minutes, and lasting about 10 minutes; the slower beginning "second phase" of insulin secretion begins soon after the glucose bolus but is not obvious until 10 minutes later, lasts the period of the hyperglycaemia and is comparative to the glucose absorption immediately prior to the glucose administration. [47]

The primary phase of insulin secretion represents release of insulin previously synthesised and stored in secretory granules; the second phase represents newly synthesised insulin and insulin secretion stored. On the whole insulin secretion relates to the entire dose of glucose and its pace of administration; occurs with 20 g of glucose given intravenously over 3 minutes in humans is the maximal pancreatic response. [48]

In compare to the reproducible pattern of insulin secretion in response to intravenous glucose, insulin secretion following oral glucose is greatly more variable. With an oral glucose load, gastric emptying and gastrointestinal motility affect glucose absorption, gastro-intestinal hormones and neural input linked with glucose ingestion adjust the insulin response, and insulin secretion continues some time after glucose intake. [47]

MECHANISMS OF INSULIN RESISTANCE

Physiologically, the entire body levels, the actions of insulin are prejudiced by the interaction of other hormones. Insulin, even if the dominant hormone driving metabolic processes in the fed state, acts in performance with growth hormone and Insulin growth factor-1; growth hormone is secreted in reaction to insulin, among other stimuli, preventing insulin-induced hypoglycaemia. Other counter-regulatory hormones comprise glucagon, glucocorticoids and catecholamines. These hormones drive metabolic processes in the fasting state. Glucagon promotes ketogenesis gluconeogenesis and glycogenolysis. The relative amount of insulin to glucagons determines the

quantity of phosphorylation or dephosphorylation of the relevant enzymes.[49] Catecholamines promotes glucocorticoids, lipolysis and glycogenolysis; promote catabolism of the muscle, gluconeogenesis and lipolysis. Surplus secretion of these hormones may donate to insulin resistance in meticulous settings, but does not description for the vast mainstream of insulin resistant states.

Post-receptor defects in insulin signalling initiate the insulin resistance in most cases which is believed to be manifest at the cellular level. Even though promising result in experimental animals with respect to a variety of insulin signalling defects, their significance to human insulin resistance is currently unclear. Potential mechanisms consist of down-regulation, deficiencies or genetic polymorphisms of tyrosine phosphorylation of the IR, IRS proteins or PIP-3 kinase, or may involve abnormality of GLUT 4 utility. [50]

INSULIN RESISTANCE AND THE SITES OF INSULIN ACTION

Insulin, insulin deficiency and insulin resistance effects may vary according to the physiological role of the organs and tissues concerned, and their dependence on metabolic processes of insulin. Those tissues definite as insulin dependent, based on glucose transport in intracellular, are predominantly adipose tissue and muscle. However, actions of insulin are pleotropic and extensive, as are the manifestations of insulin resistance and the hyperinsulinaemia as associated compensatory. [51]

Adipose Tissue

Glucose transport into intracellular adipocytes in the postprandial state is insulin-dependent GLUT 4; it is estimated that accounts for about 10% of insulin stimulated among whole body glucose uptake is adipose tissue.[34] Insulin stimulates glucose uptake, promotes lipogenesis while suppressing lipolysis, and consequently free fatty acid fluctuation into the bloodstream. As adipocytes are not reliant on glucose in the basal state, intracellular energy may be supplied by fatty acid oxidation takes place in insulin-deficient states, whereas liberating free fatty acids into the circulation for undeviating utilization by other organs e.g. heart, or liver where they are transformed to ketone bodies. During prolonged starvation these ketone bodies provide an alternative energy substrate for the brain. **[52]**

Muscle

GLUT 4 is essential for insulin dependent glucose uptake into muscle is, and 60–70% of whole-body insulin mediated uptake is take part in muscle. **[53]** In the fed condition insulin promotes glycogen synthesis via glycogen synthase activation. This enables energy to be unconfined anaerobically via glycolysis, e.g. during intense muscular action. Muscle cells do not depend on glycogen (or glucose) for energy during the fasting state, when insulin levels are low. Insulin releases amino acids for gluconeogenesis and suppresses protein catabolism while insulin deficiency promotes it. In starvation, 50% protein synthesis is reduced **[54]** In experimental studies, proved that the protein

synthesis is considerably superior than the dose necessary to suppress proteolysis is depend on insulin dose promoting. Anabolic effect of insulin is conjunction with IGF-1, growth hormone, and enough amino acids. [54] Muscle glycogen synthesis is impaired in insulin resistance; this appears mainly mediated by condensed intracellular glucose translocation. [49]

Liver increased free fatty acid flux tends to support hepatic very low density lipoprotein (VLDL) assembly whilst ketogenesis typically remains suppressed by the compensatory hyperinsulinaemia. In insulin resistance the effects on adipose tissue are similar. Furthermore, insulin resistance impairment and lipoprotein lipase action is insulin-dependent, peripheral uptake of triglycerides from VLDL is also diminished. These mechanisms may contribute to the observed hypertriglyceridaemia of insulin resistance.38 In addition to free fatty acids, adipose tissue secretes a amount of cytokines which have systemic effects on insulin resistance such as IL-6, TNFα, angiotensinogen and leptin which are associated with increased insulin resistance, and adiponectin with insulin resistance reduction. [55] TNFα and IL-6 impairs insulin signalling, endothelial function and lipolysis. IL-6 assembly is improved by sympathetic nervous system activation, e.g. stress. [55] Adipose tissue depots differ in insulin response. [54] GLUT 4 translocation reduced in adipocytes from diabetic and insulin resistant individuals, impaired intracellular signalling via reduced IRS-1 gene and protein expression. [53]

Liver

Liver glucose uptake is not insulin-dependent, it accounts for about 30% of whole body insulin-mediated glucose removal, [53] with insulin being needed to facilitate key metabolic processes., glycogen synthesis is stimulated while protein synthesis and lipoprotein metabolism are modulated through intracellular signalling which was described above.[30] Gluconeogenesis and ketone body production are inhibited. Hepatic production of insulin-like growth factors and potentially mediated by mitogenic effects of insulin (and growth hormone) via suppression of sex-hormone binding globulin (SHBG) production. [49]

While in deficiency of insulin, e.g. starvation, these processes are more consistently affected; this is not unavoidably the case with insulin resistance. Compensatory hyperinsulinaemia, discrepancy insulin resistance and differential tissue needs may dissociate these processes. [51] Insulin's resistance metabolic effects results in increased output of glucose via increased gluconeogenesis (as in starvation), however, unlike starvation, compensatory hyperinsulinaemia depresses sex hormone binding globulin production and promotes mitogenic effects of insulin. Alterations in lipoprotein metabolism correspond to a major hepatic demonstration of insulin resistance. Increased free fatty acid liberation, and reduced catabolism of very low density lipoprotein by adipocytes of insulin resistant, results in increased hepatic triglyceride content and secretion of very low density lipoprotein. [56] Hepatic synthesis of C-reactive protein and fibrinogen is induced in response to

adipocyte-derived pro-inflammatory cytokines such as TNFα and IL-6. Gene expression of factor VII may also increased by insulin. [55]

SYNDROME OF INSULIN RESISTANCE

The syndrome of insulin resistance describes the cluster of abnormalities which occur more frequently in individuals in insulin resistant. These include glucose intolerance, endothelial dysfunction, dyslipidaemia, and increased pro-coagulant factors, changes in haemodynamics, enhanced inflammatory markers, abnormal metabolism of uric acid, elevated ovarian testosterone secretion and sleep-disordered. [51] Type 2 diabetes is the major clinical syndromes associated with insulin resistance include, cardiovascular disease, hypertension, syndrome of polycystic ovary, fatty liver disease of non-alcoholics, certain forms of cancer and sleep apnoea. [51]

INSULIN RESISTANCE ASSOCIATED CONDITION

Type 2 Diabetes

Bornstein[57] and the Nobel Prize-winning effort of Yalow and Berson, [58] the first insulin assays became extensively available in the late 1960s; [49] it was later confirmed that diabetic patients with so-called or adulthood onset or type 2 diabetes had normal or elevated plasma insulin levels. Insulin resistance was reported to be a characteristic feature of T2DM in the early 1970s. [51] A progressive inability of the β cells to recompense for the widespread insulin resistance by enough hyperinsulinaemia, heralds the clinical beginning of this disorder. [51] While two studies and linkage analyses are reliable with a tough

genetic constituent in the improvement of type 2 diabetes, numerous decades of research have unsuccessful to recognize a predominant genetic deformity in the majority of cases. [59] The aetiology of T2DM is consideration to be polygenic, with ecological factors being superimposed upon this basic inclination.

Insulin resistance characteristically predates the augmentation of diabetes and is usually found in unchanged first-degree relatives. [49] The morbidity of the disorder relates both to the severity of hyperglycaemia and the metabolic penalty of insulin resistance itself. The primary defects in insulin action become visible to be in muscle cells and adipocytes, with impaired GLUT 4 translocation ensuing in impaired insulin-mediated glucose transport. [49]

Compensatory hyperinsulinaemia develops primarily, but the first phase of insulin secretion is vanished early in the disorder. Additional environmental and physiological stresses such as weight gain, pregnancy, physical inactivity and medications may get worse in the insulin resistance. β cells fail to reimburse for the existing insulin resistance, impaired glucose tolerance and diabetes develops. As glucose levels rises, β cell function got deteriorates additionally, with diminishing sensitivity to glucose and decline hyperglycaemia. The pancreatic islet cell mass is reported to be condensed in size in diabetic patients; humoral and endocrine factors may be imperative in maintaining islet cell mass. [45] In contrast to large forms of type 2 diabetes, the genetic basis of Maturity Onset diabetes of the Young (MODY) has been fine characterised and relates to defects in glucokinase. [59]

INSULIN AND ITS RESISTANCE MEASUREMENT

There are a variety of approaches to the laboratory assessment of insulin resistance. Over the lifetime the partial specificity of older radio-immunoassays that cross-react with pro insulin has reduced the trustworthiness of measuring insulin resistance in medical settings. Present assays have enhanced specificity and precision. Insulin resistance may be calculated by looking directly at insulin mediated glucose uptake in the basal or post-stimulated condition, by inference from the relative concentrations of glucose and insulin, or by looking at surrogate markers of insulin action.

TYPES OF DM

There are two important types of diabetes, one is characterised by insulin deficiency, termed type 1 diabetes (T1DM), and the another one is, type 2 diabetes (T2DM), arises mainly due to insulin resistance secondary to increased prevalence of obesity. However, the two conditions may overlap as a significant proportion of individuals with T1DM develop a phenotype seen in T2DM, makes them fall into a new category termed as double diabetes. [39] Equally, longer duration of T2DM can lead to insulin deficiency, making T2DM individuals similar to T1DM patients

FREQUENCY OF THYROID DISORDERS

Thyroid disorders are more common with variable prevalence among the different populations. Data from the Whickham survey, a study conducted in the late 1970s in the north of England showed a prevalence of 6.6% of

thyroid dysfunction in the adult general population. In the Colorado Thyroid Disease Prevalence study involving 25,862 participants attending a state health fair, 9.5% of the studied population were found to have an increased level of TSH, while 2.2% had a decreased level of TSH [60]. In the NHANES III study, a survey of 17,353 subjects representing the US population, hypothyroidism was seen in 4.6% and hyperthyroidism in 1.3% of subjects. Latter further observed an greater frequency of thyroid dysfunction with advancing age and a higher prevalence of thyroid disease in women when compared to men and in diabetic subjects compared to non-diabetic individuals . Many reports documented a higher prevalence of thyroid dysfunction in the diabetic population. Particularly, Perros et al. [60] demonstrated an overall prevalence of 13.4% of thyroid diseases seen in diabetics with the highest prevalence in type 1 female diabetic patients (31.4%) and lowest prevalence in type 2 male diabetic patients (6.9%).

Recently, a prevalence of 12.3% was reported that among Greek diabetic patients and 16% of Saudi patients with type 2 diabetes mellitus were found to have thyroid dysfunction. In Jordan a study described that thyroid dysfunction was present in 12.5% of type 2 diabetes mellitus patients. However, thyroid disorders were found to be more commonly seen in subjects with type 1 diabetes compared to those with type 2 diabetes mellitus.

THYROID HORMONES ON GLUCOSE HOMEOSTASIS

Thyroid hormones have an effect on glucose metabolism via several mechanisms. Hyperthyroidism has long been recognized to encourage

increased blood glucose. During hyperthyroidism, the half-life of insulin is decreased most likely secondary to an increased rate of degradation and an intensified release of biologically inactive insulin precursors.

In elevated proinsulin levels in response to a meal were observed in a study by Bech et al. [61] In addition, untreated hyperthyroidism was affiliated with a reduced C-peptide to proinsulin ratio suggesting an fundamental defect in proinsulin processing. Another mechanism explaining that the relationship between hyperglycemia and hyperthyroidism is the increase in glucose gut absorption intervened by the surplus thyroid hormones.

Endogenous production of glucose is also increased in hyperthyroidism via several mechanisms. Thyroid hormones secretes an increase in the hepatocyte plasma membrane concentrations of GLUT2 which is the main glucose transporter in the liver, and accordingly, the increased levels of GLUT-2 contribute to the increased hepatic glucose output and unusual glucose metabolism.

Furthermore, an increased lipolysis is noticed in hyperthyroidism resulting in an elevation in FFA that trigger the hepatic gluconeogenesis. The increased release of FFA could relatively be explained by an strengthened catecholamine-stimulated lipolysis induced by the excess thyroid hormones [62]. Moreover, the nonoxidative glucose disposal in hyperthyroidism is enhanced resulting in an increased production of lactate that enters the Cori cycle and stimulates further hepatic gluconeogenesis. The increase in glucagon, growth

hormone, and catecholamine levels integrated with hyperthyroidism further contributes to the impaired glucose tolerance.

It is well known that diabetes mellitus patients with hyperthyroidism experience worsening of their glycemic control in blood and thyrotoxicosis has been prone to diabetic ketoacidosis in subjects with diabetes. In hypothyroidism, glucose metabolism is affected via several mechanisms [63, 64]. A inreased rate of liver glucose production is observed in hypothyroidism and it is a cause for the decrease in insulin requirement in hypothyroid diabetic patients.

MATERIALS AND METHODS

MATERIAL AND METHODS

A cross-sectional study was carried out during the period of February 2016 to June 2017 among all types were used for the investigation. Type 2 diabetes individuals on treatment for 3 years with age group of more than 30 to 50 years and the total number of subjects were taken for the study 100 samples attending the outpatient Department of Karpaga Vinayaga Institute of Medical Science for regular health checkup who have no known significant medical illness which can affect the outcome of the study.

This study was ethically approved by the institutional ethical committee. Age and Body mass index was quantified by bioelectrical impedance analysis. TSH, T4, T3, total cholesterol (TC), triglycerides (TGL), HDL-C, LDL-C, levels along with a written consent was taken from every patient. Fasting Serum sample from cases as well as control group was obtained to determine the following investigations. Thyroid function tests were measured by (Avantor Performance Materials, India) kit using enzyme linked Immunosorbent assay (ELISA). Normal range of thyroid tests was

- TSH: 0.39–6.16 (µIU/ml)
- Free T4: 0.8-2.0 (ng/dl) and FT3: 1.4 - 4.2 (pg/ml)

AVANTOR Kits were used for the investigation. Patients with TSH levels > 6.2 (µIU /ml) with normal FT4 & FT3 values were accepted to have SCH. Total cholesterol (130-250 mg/dl)triglycerides (60-170 mg/dl), HDL – cholesterol (male:35-80mg/dl;female:42-88mg/dl)VLDL (20-40mg/dl), LDL (80-150 mg/dl). Blood sugar fasting (70-110 mg/dl) and post prandial (upto

130 mg/dl) and renal function test such as urea (15- 40 mg/dl), creatinine (male: 0.9-1.4 mg/dl; female 0.8-1.2 mg/dl) was investigated by GOD/POD method, enzymatic method respectively. Beacon kit were used for the investigation.HBA1C (5-7%) Quantia kit was used for investigation.

The subjects were studied in terms of their thyroid dysfunction and its risk factors among type 2 diabetes. The study parameter used was:

Assessment parameters: Lifestyle factors

- Age (30-50 years)
- Gender (males and females)
- Physical activity and exercise wise: low, moderate, high
- Socio ecnomic condition
- Body mass index (BMI)
- Alcohol intake
- Blood pressure

Exclusion criteria:

- Type I diabetes mellitus individuals
- Patients on medications affecting thyroid function
- Total and hemi thyroidectomy individuals
- Gestational diabetes mellitus
- Cortico steroid therapy.
- Diabetic keto acidosis.
- Neurodegenerative diseases
- Cerebrovascular diseases

- Tuberculosis
- Cancer.
- Test for thyroid profile

HISTORY

History was elicited according to Pro forma enclosed in the annexure. Importance was given to their family history to look for history of drug history and menstrual history was taken while drug affecting thyroid function. History was the first level for the selection process of individuals to include them in the study.

GENERAL AND SYSTEMATIC EXAMINATION:

General examination including anthropometric measurements and systematic examination was done according to the proforma attached in the annexures.

BODY MASS INDEX CALCULATION:

Body mass index (BMI) was calculated by dividing weight (Kg) by height squared (m2)5.They were classified in terms of table

Table: WHO recommended BMI table for Asians

NORMAL	18.50-22.99
UNDER WEIGHT	< 18.50
OVERWEIGHT	23-24.99
PRE OBESE	25-29.99
EXTREME OBESITY	>30

ESTIMATION OF GLUCOSE

METHOD

GOD- POD (Glucose oxidase /peroxidise) Method (Trinder 1969)[65]

PRINCIPLE

Glucose is oxidised to gluconic acid and hydrogen peroxide in the presence of glucose oxidase. Hydrogen peroxide further reacts with phenol and 4- amino antipyrine by the catalytic action of peroxidises to form a red coloured quinineamine dye. Intensity of colour is directly proportional to the concentration of glucose present in the sample.

REACTIONS

Glucose + O_2 + H_2O Glucose oxidase → Gluconic acid + H_2O_2

H_2O_2 + 4-amino antipyrine + phenol peroxidise → Red quinine imine dye + H_2O

SAMPLES PREPARATION

Blood is collected in a tube containing heparin / sodium fluoride, mixed well and centrifuged . The separated plasma is used for analysis.

REAGENTS

Standard Glucose: 100 mg/dl

Glucose reagent enzyme

PROCEDURE

Addition Sequence	Blank	Standard	Test
Glucose Enzyme reagent	1 ml	1 ml	1 ml
Standard	-	10µl	-
Sample	-	-	10µl

Mix well and incubate at room temperature for 10 mins .

Measure Absorbance of the standard (Abs. S) and Absorbance of the test (Abs.T) against reagent blank at 505 nm

CALCULATION

Glucose conc. mg/dl = (Abs. T) / (Abs.S) × 100

NORMAL VALUE

Fasting Blood Glucose: 70-110mg/dl

Post Prandial Blood Glucose : Upto 130mg/dl

ESTIMATION OF UREA

METHOD

Urease / Berthelot Method (Tietz 1986)[66]

PRINCIPLE

Urease breaks down urea into ammonia and carbon dioxide in alkaline medium, Ammonia liberated from the breakdown of Urea reacts with hypochlorite and salicylate to form dicarboxylindophenol. This reaction is catalysed by the presence of Nitropruside. The intensity of the colour produced

by the reaction is directly proportional to the concentration of urea present in the sample and it is measured photometrically at 600 nm (600-630 nm) .

$$\text{Urea} + H_2O \xrightarrow{\text{Urease}} 2NH_3 + CO_2$$

$$NH_3 + \text{Salicylate} + \text{CIO} \xrightarrow{\text{Sodium nitropruside}} \text{2, 2 dicarboxylindophenol}$$

REAGENTS

Reagent 1 : Enzyme reagent

Reagent 2 : Chromogen reagent

Reagent 3 : Standard 40 mg/ dl

SAMPLES

Unhemolysed serum/ Heparinised plasma

REAGENT PREPARATION AND STABILITY

Step 1: Bring all the reagents to Room temperature

Step 2: Working reagent 1 (W1) – Dissolve the enzyme reagent 1 in deionised water

Step 3 : Working reagent 2 (W2) – ready for use

Step 4 : Allow the reagents to stand for 5 minutes at R.T for equilibration

Working reagents and Urea standard with value 40 mg/dl were provided in the kit and were ready for the assay and stable till their expiry date when stored at 2- 8°C

PROCEDURE

Reagent	Blank	Standard	Test
Working reagent	1ml	1ml	1ml
Standard	-	10µl	-
Sample	-	-	10µl
Mix well and incubate at 37 □ C for 5 minutes			
Reagent 2	1 ml	1ml	1ml

Mix well and incubate at 37°C for 5 minutes . Measure the absorbance of standard and sample at 600nm (580-630 nm)

CALCULATION

Urea .Conc.(mg/dl) = Abs (Sample) / Abs (Standard) × 40

REFERENCE VALUE

Adults : 15- 40 mg/dl

ESTIMATION OF CREATININE [100-101]

METHOD

Alkaline picrate Method

PRINCIPLE

Picric acid in an alkaline medium reacts with creatinine to form an orange coloured complex with the alkaline picrate. Intensity of the colour formed is directly proportional to the amount of creatinine present in the sample.

Creatinine + Picric acid $\xrightarrow{\text{Alkaline medium}}$ Orange Coloured Complex

REAGENTS

Reagent 1 ; Creatinine Buffer reagent

Reagent 2 : Creatinine Picrate reagent

Reagent 3 : Creatinine Standard 2 mg/dl

SAMPLES

Unhemolysed serum

REAGENT PREPARATION AND STABILITY

Step 1 : Working reagent 1 is prepared by combining equal volumes of Reagent 1 and Reagent 2

Step 2 : Mix by gentle swirling

Step 3 : Allow the reagent mixture to stand at R.T for 5 minutes for equilibration

Working reagents and Creatinine standard with value 2mg/dl were provided in the kit and were ready for the assay and stable till the expiry date when stored at 2- 8°C

PROCEDURE

Addition Sequence	Standard	Test
Working Reagent	1.0 ml	1.0ml
Standard	50µl	-
Sample	-	50µl

Mix well and read the initial absorbance (A) for the standard and Test after exactly 30 seconds. Read another absorbance (A) of standard and Test exactly 120 seconds later. Calculate the change in absorbance A for both the standard and Test

Determine for Standard $\triangle$ AS = $A_2S - A_1S$

For Test $\triangle$ AT = $A_2T - A_1T$

CALCULATION

Creatinine Conc. mg/dl = $\triangle$ AT /$\triangle$ AS $\times$ 2

REFERENCE VALUE

Serum :

Male : 0.9 – 1.4 mg/dl

Female : 0.8 – 1.2 mg/dl

LIPID PROFILE

CHOLESTEROL (CHOD / POD METHOD) [102-104]

AIM

Quantitative estimation of Total Cholesterol in human serum by CHOD/POD method.

PRINCIPLE

Cholesterol esterase hydrolyses esterified cholesterols to free cholesterol. The free cholesterol is oxidised to form hydrogen peroxide which further reacts with phenol and 4-amino antipiyrine by the catalytic action of

peroxidise to form a red coloured quinine imine dye complex. Intensity of colour is directly proportional to the amount of cholesterol present in the sample.

REACTIONS

Cholesterol esters +H2o $\xrightarrow{\text{Cholesterol esterase}}$ Cholesterol + fatty acids

Cholesterol + O_2 $\xrightarrow{\text{Cholesterol oxidase}}$ Cholestenone + H_2O_2

H_2O_2 + Phenol + 4- amino antipyrine $\xrightarrow{\text{peroxidise}}$ Red quinineimine dye + H_2O

REAGENTS

Reagent 1: Cholesterol enzyme reagent

Reagent 2: Cholesterol standard 200 mg/dl

Reagent 3: Cholesterol precipitating reagent

SAMPLES

Serum, Heparinised /EDTA plasma

REAGENT PREPARATION AND STABILITY

All reagents are ready to use and are stable till the expiry date , when stored at 2-8°C

PROCEDURE

Addition sequence	**Blank**	**Standard**	**Test**
Enzyme reagent	1 ml	1 ml	1 ml
Standard	-	10µl	-
Sample	-	-	10µl

Mix well and incubate at 37°C for 5 mins.

Measure Absorbance of the standard (Abs . S) and Absorbance of the test(Abs.T) against reagent blank at 505 nm

CALCULATION

Cholesterol mg/dl = Abs.T / Abs.S ×200

NORMAL VALUE

Serum : 130- 250 mg/dl

Interpretation of Results:

Increased Serum levels are seen in the following conditions:

- Familial hypercholesteremia
- Nephrotic syndrome
- Biliary obstruction
- Hypothyroidism
- Pregnancy

Decreased Serum levels are seen in the following conditions:

- Hyperthyroidism
- Malnutrition
- Chronic anemia
- Thyroiditis
- Severe liver insufficiency

TRIGLYCERIDES (GPO/POD METHOD) [105-107]

AIM

Quantitative estimation of triglycerides by enzymatic GPO - POD (glycerol phosphate oxidase – peroxidase) end point method. Screening the lipids of an individual is an important diagnostic feature to detect artherosclerotic risks. Triglycerides values are increased in primary and secondary hyperlipoproteinemias. It is also increased in conditions like Diabetes mellitus, nephrosis, biliary obstruction, and various metabolic abnormalities due to endocrine disturbances.

PRINCIPLE

Glycerol released from hydrolysis of triglycerides by lipoprotein lipase is converted by glycerol kinase into glycerol-3-phosphate which is oxidised by glycerol phosphate oxidase to dihydroxy acetone phosphate and hydrogen peroxide. In presence of peroxidise, hydrogen peroxide oxidises phenolic chromogen to a red coloured compound.

REACTIONS

Triglycerides $\xrightarrow{\text{LPG lipase}}$ Glycerol+ fatty acids

Triglycerides + ATP $\xrightarrow{\text{Glycerol kinase}}$ Glycerol- 3-P + ADP

Glycerol-3-P +O_2 $\xrightarrow{\text{Gly- 3- P oxidise}}$ DHAP+H_2O_2

H_2O_2 + Phenolic chromogen $\xrightarrow{\text{POD}}$ Red colour compound

REAGENTS

Reagent1: Triglycerides enzyme reagent

Reagent 2: Triglycerides standard 200mg/dl

SAMPLES

Unhemolysed serum, heparinised plasma , EDTA Plasma

REAGENT PREPARATION AND STABILITY

All reagents are ready to use and are stable till the expiry date , when stored at 2-8°C

PROCEDURE

Addition sequence	Blank	Standard	Test
Enzyme reagent	1 ml	1 ml	1 ml
Standard	-	10µl	-
Sample	-	-	10µl

Mix well and incubate at 37°C for 10 mins.

Measure Absorbance of the standard (Abs. S) and Absorbance of the test (Abs.T) against reagent blank at 505 nm

CALCULATION

Triglycerides mg/dl = (Abs.T) / (Abs.s)) × 200

NORMAL VALUE

Serum : 60-170mg/dl

Interferences:

- The criteria for no significant interference is recovery within 10% of the initial value.
- Bilirubin: No significant interference up to 40 mg/dLBilirubin.
- Hemolysis: No significant interference up to 500 mg/dLHemolysate.
- Ascorbate: No significant interference up to 20 mg/dLAscorbate.

Calculation: Not Applicable.

Interpretation of Results:

- Increased Serum levels are seen in the following conditions like Diabetes mellitus, Nephrotic syndrome, Pregnancy, Excessive alcohol intake, Familial hyper triglyceridemia, etc.,
- Decreased Serum levels were seen in the following conditions like Malnutrition, Congenetial abetalipoprotenimia, etc.,

Potential Sources of Variability:

- Presence of fibrin in the sample may lead to erroneous results and hence centrifuge the sample only after complete clot formation.
- Lysed serum specimens may give falsely elevated values.

HDL CHOLESTEROL DIRECT REAGENT KIT [108-110]

AIM

Quantitative estimation of HDL – Cholesterol in human serum by Enzymatic colour test. Measurement of serum HDL – cholesterol is useful in the screening of the lipid status of the individual to detect atherosclerotic risks

& in monitoring the response to lipid lowering measures and also in the diagnosis and classification of hyperlipoprotienimias. An inverse relationship exists between serum HDL- Cholesterol and the risk of coronary heart disease. An HDL –C value below 30 mg/dL is considered as a risk factor for coronary and cerebral vascular disease.

PRINCIPLE

The reaction between cholesterol other thean HDL & Enyme for cholesterol assay is suppressed by the electrostatic interaction between polyanions and cationic substances. Hydrogen peroxide is formed by the free cholesterol in HDL by cholesterol oxidase . Oxidative condensation of EMSE and 4- AA is caused by hydrogen peroxide in the presence of peroxidise, and the absorbance of the resulting red-purple quinine is measured to obtain the cholesterol value in HDL.

REACTIONS

Other lipoprotein than HDL $\xrightarrow{\text{polyanions}}$ suppress reaction with enzyme

HDL + H_20_2 $\xrightarrow{\text{cholesterol esterase}}$ HDL (Free cholesterol) + free fatty acids

HDL (free cholesterol) + O_2 +H $\xrightarrow{\text{cholesterol oxidase}}$ cholestenone + H_20_2

$2H_2O_2$ +4- AA/EMSE +H_3 +O $\xrightarrow{\text{peroxidise}}$ Red-purple quinine +$5H_2O$

REAGENTS

Reagent 1 : R1 Reagent

Reagent 2 : R2 Reagent

Reagent 3 : Direct HDL Calibrator

SAMPLES

Fresh serum (Free of hemolysis)

Performance Specifications:

- **Linearity:** The method is linear up to 150 mg/dL of serum.

Primary Sample:

- Use only serum as specimen for the test.
- Collect 2 ml of venous blood in a plain Red topped vacutainer tube. Separate the serum by centrifugation at 2500- 3000 rpm for 5 – 10 minutes.
- Do not use lysed serum for testing as it may give very high results.
- Do not use contaminated / turbid samples for testing.
- Process the sample on the same day.
- If analysis is not done on the same day, separate the serum and store it at 2 to 8°C for up to 7 days.

Patient Preparation: Preferable in fasting

REAGENT PREPARATION AND STABILITY

Reagent 1 & Reagent 2 are ready to use.

All reagents are ready to use and were stable till the expiry date, when stored at 2-8°C

PROCEDURE

Addition sequence	Blank	Standard	Test
R1Reagent	450µl	450µl	450µl
Calibrator	-	5µl	-
Sample	-	-	5µl
Mix well and incubate for 5 minutes at 37 □ C			
R2Reagent	150 µl	150 µl	150 µl

Mix and incubate for 5 min at 37 °C . Measure Absorbance of the calibrator and test against reagent blank at 578 nm .

CALCULATION

HDL – D concentration = (Abs.T) / (Abs.Calibrator) × Calibrator concentration

NORMAL VALUE

Males : 35 – 80 mg/dl

Females : 42 – 88 mg/dl

Interferences:

- The criteria for no significant interference is recovery within 10% of the initial value.
- Ascorbate: No significant interference up to 20 mg/dL Ascorbate.
- Bilirubin: No significant interference up to 40 mg/dL Conjugated Bilirubin.
- Globulin: No significant interference up to 5 g/dLadded Gamma Globulin.

- Hemolysis: No significant interference up to 500 mg/dLHemolysate.
- Lipemia: No significant interference up to 1500 mg/dLIntralipid.
- Triglycerides: No significant interference up to 900 mg/dL Triglycerides.

Interpretation of Results:

- **Increased Serum levels are seen in the following conditions:**
- Congenital hyper lipoproteinimia
- **Decreased Serum levels are seen in the following conditions:**
- Lipid metabolism disorders
- **Potential Sources of Variability:**
- Presence of fibrin in the sample may lead to erroneous results and hence centrifuge the sample only after complete clot formation.
- Lysed serum specimens may give falsely elevated values.

VERY LOW DENSITY LIPOPROTEIN (VLDL)

Based on the Friedewald equation :

$$VLDL = \frac{\text{Triglycerides}}{5}$$

Reference range : 20 – 40 mg/dl

LOW DENSITY LIPOPROTEIN (LDL)

Based on Friedewald equation :

LDL = Total cholesterol – HDL – (triglycerides / 5)

Reference range:

80 – 150 mg/dl

ESTIMATION OF HbA1c

METHOD

Quantia – HbA1c is a turbidimetric immunoassay for the direct determination of HbA1c in human blood without the need to estimate total haemoglobin [47].

REAGENTS

Latex reagent (R1) : ready to use uniform suspension of latex particles

Antibody reagent (R2) : ready to use solution of mouse anti human HbA1c monoclonal antibody

Antibody reagent (R3) : ready to use solution of goat anti mouse human IgG antibody

Hemolysing solution : ready to use solution

REAGENT STABILITY

R1 , R2 and Hemolysing solution were stable till the expiry date ,when stored at 2-8°C

PRINCIPLE

Based on the principle of agglutination reaction. The test specimen after treatment with hemolysing solution is allowed to react with latex reagent (R1). Total Hb and HbA1c bind with same affinity to latex particles. The amount of

binding is proportional to the relative concentration of both substances in blood. The reaction mixture is then allowed to react with mouse anti human HbA1 c monoclonal antibody(R2) where in the mouse anti human HbA 1c antibody bind to the HbA1c on the latex. Goat anti-mouse human IgG (R3) is then allowed to interact with above reaction mixture which interacts with the HbA 1c – mouse anti human HbA1c complex resulting in agglutination reaction that is measured at 630nm. The increase in turbidity corresponds to the concentration of HbA1c in the test specimen.

SAMPLE COLLECTION

Collect venous blood in EDTA using aseptic techniques.

SPECIMEN PREPARATION

Mix the specimen (sample or reconstituted calibrator or reconstituted control) thoroughly to obtain uniform distribution of erythrocytes. Avoid bubble formation.

Take 500µl HbA1c Hemolysing solution in a test tube.

Add 100µl of homogenised specimen. Mix well and allow to stand for 15 mins or until complete hemolysis. This hemolysed specimen is referred as **Lysate** .

Additional material required :

Quantia HbA1c lyophilised calibrator set , Quantia – HbA1c lyophohilsed control

PROCEDURE

1. Zero the instrument with distilled water
2. Pipette 400µl of latex reagent in a measuring cuvette
3. Add 10µl of **Lysate** prepared from specimen (sample/calibrator/control) as described in the **" specimen preparation''** , to the measuring cuvette, mix well and incubate at 37°c for 5 mins
4. Add 100 µl of mouse anti human HbA1c monoclonal antibody , mix well and incubate at 37°c for 4 mins
5. Add 20 µl of goat anti mouse human IgG antibody reagent , mix gently and to start the stopwatch simultaneously
6. Read absorbance A1 exactly at 10 seconds, and absorbance A2 at the end of 2 minutes exactly.

REFERENCE INTERVAL

Non –diabetics <6%

For Glycemic control in diabetics <7%. A level of >7 % indicates persistent glycemia over previous 6-8 weeks indicating poor diabetes management.

ESTIMATION OF FT3 (AVANTOR KIT) – Microwell ELISA (Lundberg 1982) [106-110]

AIM

An enzyme immune assay for the quantitative determination of Free T3 hormone concentration in human serum or plasma

PRINCIPLE

Competitive EIA (Quantitative)

In a competitive EIA, there exist a competitive reaction between native antigen and enzyme – antigen conjugate for limited number of insolubilized binding sites. The essential reagents required for a solid phase immuno assay include immobilized T3 antibody, enzyme conjugate and native Free T3 antigen. The enzyme T3 conjugate should have no measurable binding to serum proteins especially TBG and albumin. This method achieves this goal. The fraction of the enzyme bound antigen or native antigen from the sample that does not bind to the coated well is washed away. The enzymatic activity in the antibody bound fraction, which inversely proportional to the native antigen concentration, is measured by addition of the substrate. By utilizing calibrators of known antigen values, a dose response curve can be generated from which the antigen concentration in a sample can be found out.

REAGENTS

1. **Antibody coated micro plate :** Microplate coated with sheep anti triiodothyronine serum and packaged in an aluminum bag with a drying agent. Stored at 2 - 8°C

2. **Free T3 enzyme reagent :** One vial of triiodothyronine-horse radish peroxidase (HRP) conjugates in a bovine albumin stabilizing matrix. A preservative has been added. Stored at 2 - 8°C

3. **Human serum references :** 6 vials of serum reference for free triiodothyronine. Stored at 2 - 8°C

4. **Substrate A :** One bottle containing tetra methyl benzidine (TMB) in buffer. Stored at 2 - 8°C

5. **Substrate B :** One bottle containing hydrogenperoxide in buffer. Stored at 2 - 8°C

6**. Wash solution concentrate :** One vial containing a surfactant in buffered saline. A preservative has been added stored at 2 - 30°C

7. **Stop solution** - One bottle containing a strong acid (1N Hcl) stored at 2 - 30°C

PROCEDURE

1. Format the microplate wells for each calibrator and patient specimen to be assayed.
2. Add 50 µl of calibrator and the patient specimen to assigned well
3. Add 100 µl of FT3 enzyme conjugate to each well
4. Shake the microplate gentle for 20 – 30 sec to mix and cover
5. Incubate for 60 min at RT
6. Aspirate the content of the wells and fill them completely (approximately 300 µl) with diluted washing solution. Repeat the washing procedure for 2 -3 times. After last wash blot the micro plate on absorbent tissue to remove excess liquid from wells
7. Add 100 µl of working substrate solution to all the wells.
8. Incubate at RT for 15 mins
9. Add 50 µl of stop solution to each well and mix well for 15 – 20 secs
10. Read the absorbance of each well at 450 nm in micro plate reader

NORMAL VALUES

Adult (pg/ml) – 1.4 – 4.2

Pregnancy (pg/ml) – 1.8 -4.2

ESTIMATION OF FT4 (AVANTOR KIT) – Microwell ELISA [101-104]

AIM

An enzyme immune assay for the quantitative determination of Free T4 hormone concentration in human serum or plasma

PRINCIPLE

Competitive EIA (Quantitative)

In a competitive EIA, there exist a competitive reaction between native antigen and enzyme – antigen conjugate for limited number of insolubilized binding sites on the antibody coated on the micro well. After the antigen antibody reaction has taken place, the fraction of the antigen in the conjugate or native antigen from the sample, which does not bind to the coated well, is washed away. The enzymatic activity in the antibody bound fraction, which is inversely proportional to the native antigen concentration is measured by addition of the substrate. By utilizing calibrators of known antigen values, a dose response curve can be generated from which the antigen concentration in a sample can be found out.

REAGENTS

1. **Antibody coated micro plate** (96 wells) : Microplate coated with sheep anti thyroxine serum and packaged in an aluminum bag with a drying agent. Stored at 2 - 8°C

2. **Free T4 enzyme reagent:** One vial of thyroxine-horse radish peroxidase (HRP) conjugates in a protein stabilizing matrix. A preservative has been added. Stored at 2 - 8°C

3**. Free T4 calibrators** (1ml per vial): 6 vials of human serum reference for free thyroxine. Stored at 2 - 8°C

4. **Substrate A :** One bottle containing tetra methyl benzidine (TMB) in buffer. Stored at 2 - 8°C

5. **Substrate B :** One bottle containing hydrogenperoxide in buffer. Stored at 2 - 8°C

6. **Wash solution concentrate :** One vial containing a surfactant in buffered saline. A preservative has been added stored at 2 - 30°C

7. **Stop solution** - One bottle containing a strong acid (1N Hcl) stored at 2 - 30°C

PROCEDURE

1. Format the microplate wells for each calibrator and patient specimen to be assayed.
2. Add 50 µl of calibrator and the patient specimen to assigned well
3. Add 100 µl of FT4 enzyme conjugate to each well
4. Shake the microplate gentle for 20 – 30 sec to mix and cover

5. Incubate for 60 min at RT
6. Aspirate the content of the wells and fill them completely (approximately 300 µl) with diluted washing solution. Repeat the washing procedure for 2 -3 times. After last wash blot the micro plate on absorbent tissue to remove excess liquid from wells
7. Add 100 µl of working substrate solution to all the wells.
8. Incubate at RT for 15 mins
9. Add 50 µl of stop solution to each well and mix well for 15 – 20 secs
10. Read the absorbance of each well at 450 nm in micro plate reader

NORMAL VALUES

Adult (ng/dl) – 0.8 – 2.0

Pregnancy (ng/dl) – 0.76 -2.24

ESTIMATION OF TSH (AVANTOR KIT) - Microwell ELISA [105-109]

AIM

An enzyme immune assay for the quantitative determination of TSH hormone concentration in human serum or plasma

PRINCIPLE

Competitive EIA (Quantitative)

In a competitive EIA, high affinity antibodies react with antigen to form an insoluble sandwich complex on the surface of a coated microplate. The antigen from the specimen gets linked at the surface of the well through interaction of reacting IgG coated on the well and affinity purified x-antigen

IgG conjugated wit HRP. The fraction of the X-antigen IgG conjugated with enzyme that does not bind to the coated well is washed away. The enzymatic activity, which is proportional to the antigen concentration, is measured by addition of the substrate. By utilizing calibrators of known antigen values, a dose response curve can be generated from which the antigen concentration in a sample can be found out.

REAGENTS

1. TSH reactive coated micro plate (96 wells)

Microplate coated with reactive IgG and packaged in an aluminum bag with a drying agent. Stored at 2 - 8°C

2. **TSH enzyme reagent**

One vial of Horse radish peroxidase (HRP) conjugates, reactive X-TSH IgG in buffer.

A preservative has been added. Stored at 2 - 8°C

3. **Thyrotropin calibrators**(1ml per vial) - 7 vials of TSH antigen.. Stored at 2 - 8°C

4**. Substrate A** - One bottle containing tetra methyl benzidine (TMB) in buffer. Stored at 2 - 8°C

5. **Substrate B** - One bottle containing hydrogenperoxide in buffer. Stored at 2 - 8°C

6. **Wash solution concentrate** - One vial containing a surfactant in buffered saline. A preservative has been added stored at 2 - 30°C

7. **Stop solution** - One bottle containing a strong acid (1N Hcl) stored at 2 - 30°C

PROCEDURE

1. Format the microplate wells for each calibrator and patient specimen to be assayed.
2. Add 50 µl of calibrator and the patient specimen to assigned well
3. Add 100 µl of enzyme TSH reagent to each well
4. Shake the microplate gentle for 20 – 30 sec to mix and cover
5. Incubate for 60 min at RT
6. Aspirate the content of the wells and fill them completely (approximately 300 µl) with diluted washing solution. Repeat the washing procedure for 2 -3 times. After last wash blot the micro plate on absorbent tissue to remove excess liquid from wells
7. Add 100 µl of working substrate solution to all the wells.
8. Incubate at RT for 15 mins
9. Add 50 µl of stop solution to each well and mix well for 15 – 20 secs
10. Read the absorbance of each well at 450 nm in micro plate reader

NORMAL VALUES

Low normal range - 0.39µIU/ml

High normal range - 6.16µIU/ml

STATISTICAL ANALYSIS

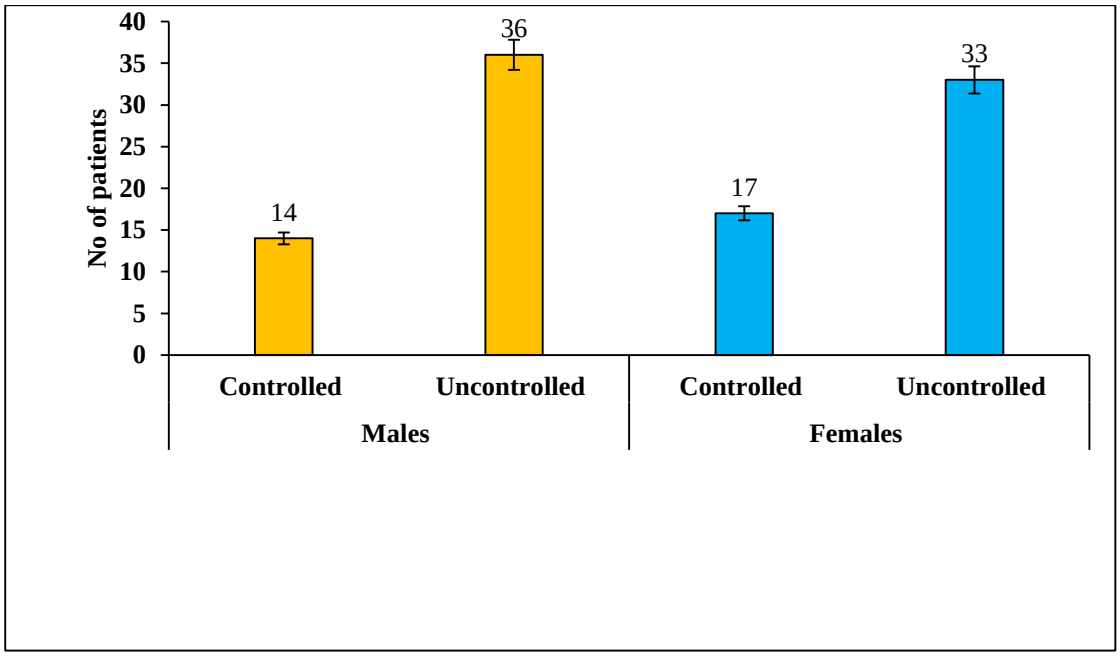
This study done to evaluate serum thyroid profile, lipid profile and renal parameters in type 2 diabetes mellitus patients and was done in total number of 100 subjects of which 50 patients were males and 50 patients were females. The data were analyzed by using standard Mean deviation, student's T test, % graph to compare the levels of various biochemical parameters in age-categorized male and female patients. Univariate analysis was performed to evaluate the gender, age and Thyroid dysfunction with glycemic control. p-value of <0.05 was considered as statistically significant.

RESULTS

RESULTS

The results obtained in the study as represented in figure 1-8 revealed significance in thyroid dysfunction and its risk factors among type 2 diabetes mellitus patients. Comparison assesment of males and females thyroid dysfunction and its associated risk factors.

FIG. 1. ASSESSMENT OF STATUS OF DIABETES MELLITUS IN STUDYGROUP



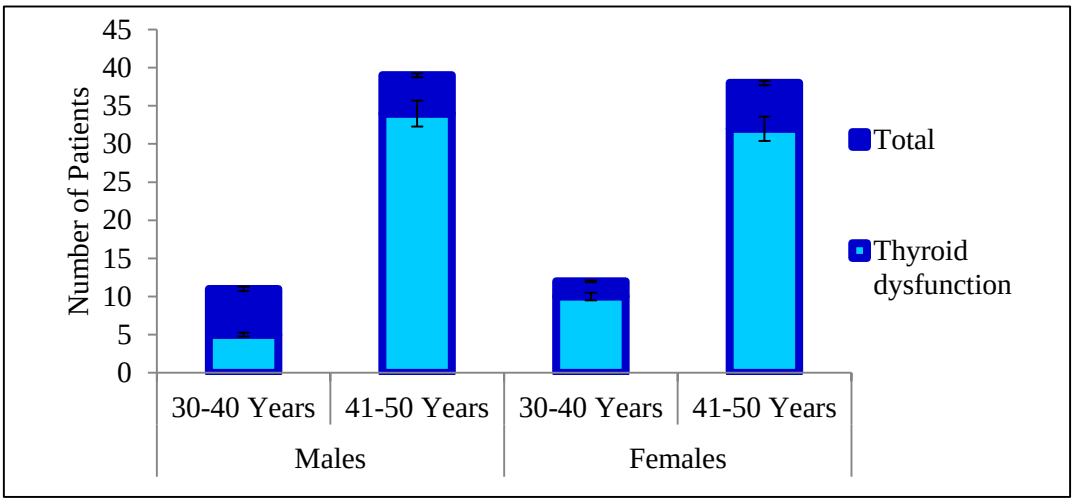
	Status	Number of Patients
Males	**Controlled**	**14**
	Uncontrolled	**36**
Females	**Controlled**	**17**
	Uncontrolled	**33**

First column bar: Males with HbA1c 6.0 – 7.0; Second column bar: Males with HbA1c >7.0; Third column bar: Third column bar: Females with HbA1c 6.0 – 7.0; Fourth column bar: Females with HbA1c >7.0 Cases. Total number of individuals: 50 (Males), 50 (Females). Each bar represents the assessment of status of diabetes in males and females among various age groups. P value is <0.05 and it is statistically significant.

FIG. 1. ASSESSMENT OF STATUS OF DIABETES MELLITUS IN STUDYGROUP

Figure : 1 Represents the assessment of status of diabetes in males and females among various age groups. P value <0.05 is considered as statistically significant. Each bar represents controlled and uncontrolled diabetes among male and female through HbA1c levels. First column bar: Males with HbA1c 6.0 – 7.0; Second column bar: Males with HbA1c >7.0; Third column bar: Females with HbA1c 6.0 – 7.0; Fourth column bar: Females with HbA1c >7.0 Cases. Total number of individuals: 50 (Males), 50 (Females). Each bar represents the assessment of status of diabetes in males and females among various age groups. P value is <0.05 and it is statistically significant. Total number of individuals: 50 (Males), 50 (Females). From this assessment visualize the males have uncontrolled diabetes when compared to females.

FIG. 2. ASSESSMENT OF THYROID DYSFUNCTION DIABETIC PATIENTS AMONG VARIOUS AGE GROUP



	Age	Number of Patients with thyroid dysfunction	Total
Males	**30-40 Years**	**5**	**11**
	41-50 Years	**34**	**39**
Females	**30-40 Years**	**10**	**12**
	41-50 Years	**32**	**38**

Total number of individuals: 50 (Males), 50 (Females).

Each stacked bar represents the assessment of status of diabetes in males and females among various age groups. P value is <0.05 and it is statistically significant.

FIG. 2. ASSESSMENT OF THYROID DYSFUNCTION IN DIABETIC PATIENTS

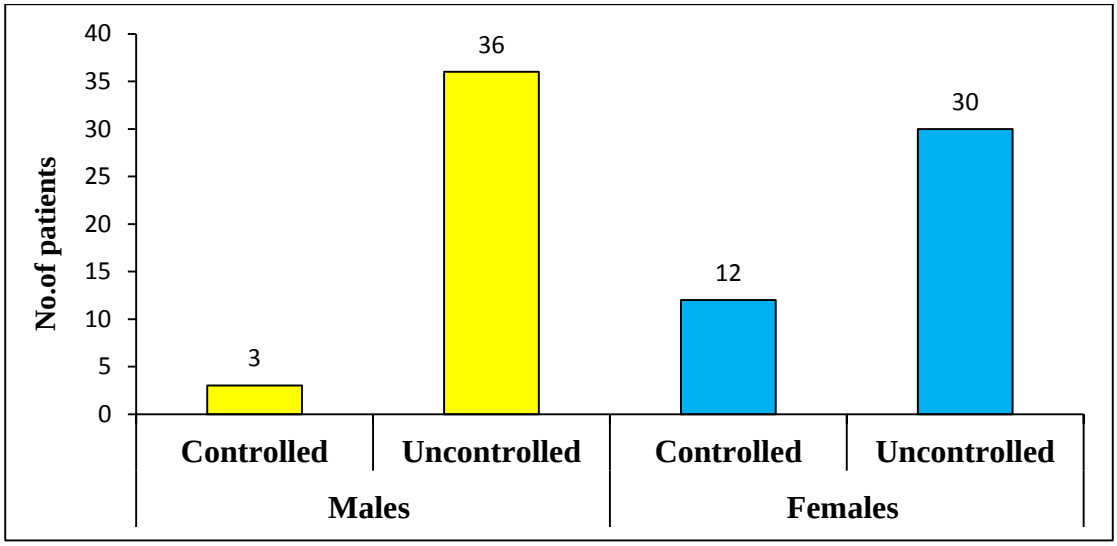
Figure : 2 Represents the assessment of thyroid dysfunction in diabetic males and females among various age groups. P value is <0.05 and it is statistically significant. Total number of individuals: 50 (males), 50 (females)**.**

Each stacked bar represents thyroid dysfunction in diabetic individual. From this assessment, the number of males with thyroid dysfunction at the age of 30-40 years are less when compared to females in the same age group.

P value is <0.05 and is statistically significant.

The second stacked bar of this assessment shows that there is no much difference in both genders at the age group of 41-50 years with thyroid dysfunction in diabetic patients. But there is higher incidence of thyroid dysfunction in type 2 DM in the age group of 41-50 years in both genders when compared to age group of 30-40 years.

FIG. 3. CORRELATION BETWEEN THYROID DYSFUNCTION AND DIABETES BASED ON HBA1c



	Status	*DM+Thyroid dysfunction*
Males	***Controlled***	***3***
	Uncontrolled	***36***
Females	***Controlled***	***12***
	Uncontrolled	***30***

Total number of individuals: 50 (Males), 50 (Females).

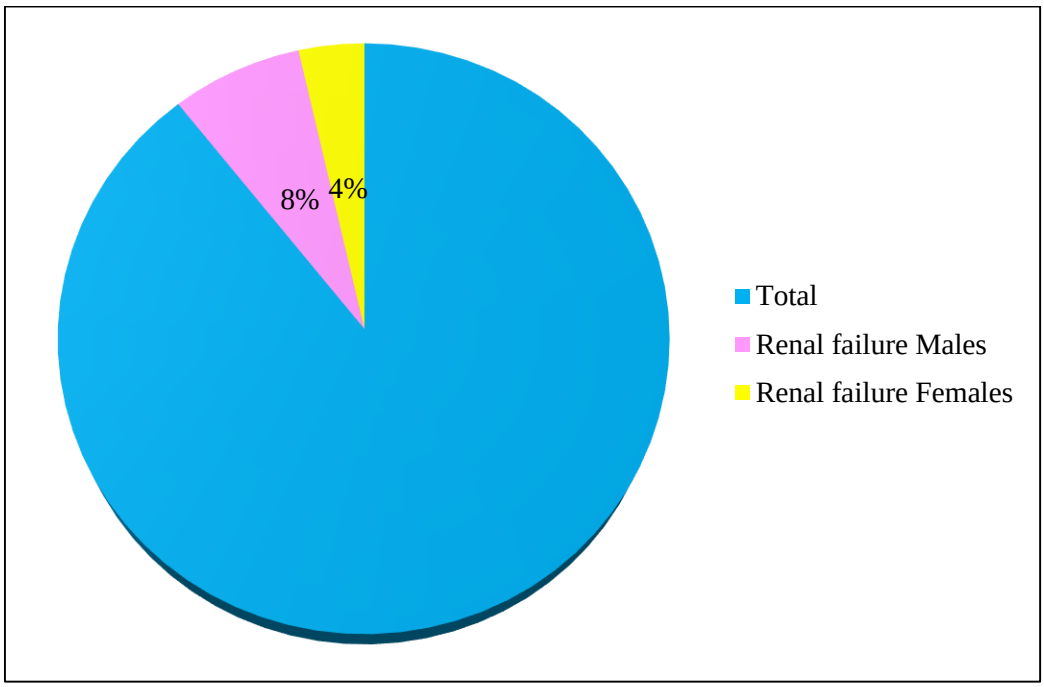
This bar diagram is a representative of the relationship between thyroid dysfunction and diabetes. P value is <0.05and it is statistically significant.

FIG. 3. CORRELATION BETWEEN THYROID DYSFUNCTION AND DIABETES BASED ON HBA1c

Figure : 3 Represents correlation between thyroid dysfunction and diabetes in males and females among various age groups. P value is <0.05 and it is statistically significant. Each bar represents controlled and uncontrolled diabetes among thyroid dysfunction in males and females. First column bar: Males have with thyroid dysfunction among controlled diabetes. Second column bar : Males with thyroid dysfunction among uncontrolled diabetes.

Third column bar : Represents Females with thyroid dysfunction among controlled diabetes. Forth column bar : Shows Females with thyroid dysfunction among uncontrolled diabetes .Total number of individuals: 50 (Males), 50 (Females). From this assessment, it is observed that thyroid dysfunction in females is greater even if they have controlled diabetes when compared to males. But thyroid dysfunction in males with uncontrolled diabetes is higher than females with uncontrolled diabetes. There is more incidence of thyroid dysfunction in females even if they have controlled diabetes.. This may be linked with their reproductive age.

FIG. 4. INCIDENCE OF RENAL FAILURE IN DIABETIC PATIENTS



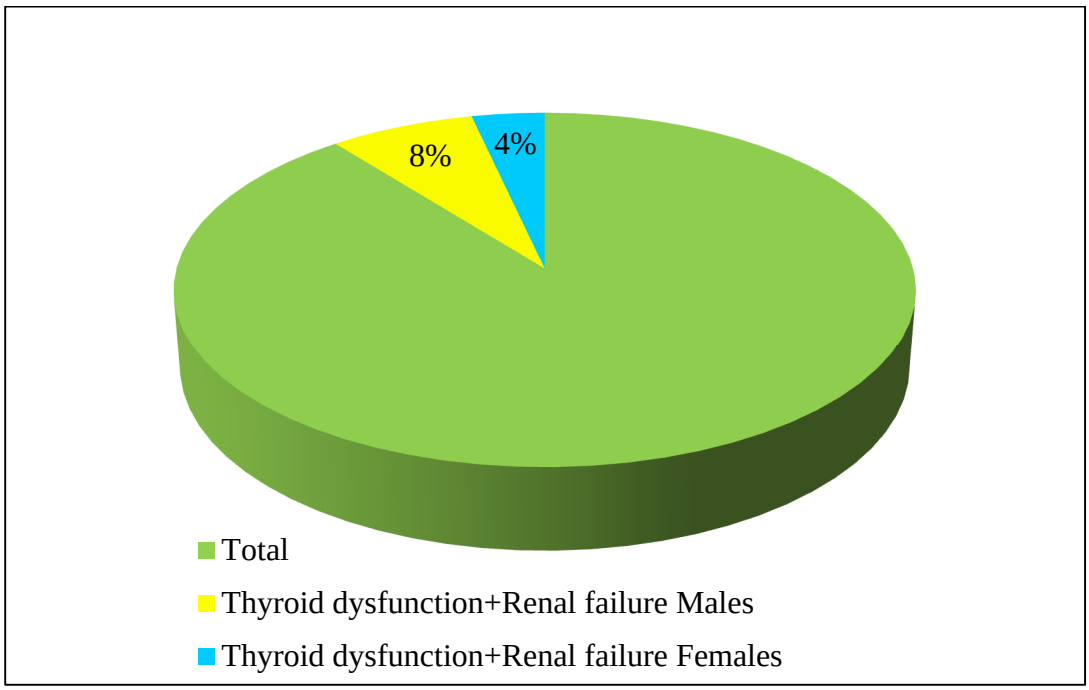
	Age	Renal Failure	Total
Males	30-50 Years	4	50
Females		2	50

Total number of individuals: 50 (Males), 50 (Females). This Pie chart is a representative of the incidence of renal failure in both diabetic males and females among 30-50 years age group (Data given as percentage)

FIG. 4. INCIDENCE OF RENAL FAILURE IN DIABETIC PATIENTS

Figure. 4. Incidence of renal failure in diabetic patients. Total number of individuals: 50 (Males), 50 (Females). Pie chart is a representative of the incidence of renal failure in both diabetic males and females among 30-50 years age group. Comparison of incidence of renal failure in diabetic patients shows 8% of the males have renal failure and 4% of females have renal failure, indicates greater incidence of renal failure among males .

FIG. 5. Co-INCIDENCE OF THYROID DYSFUNCTION AND RENAL FAILURE IN DIABETIC PATIENTS



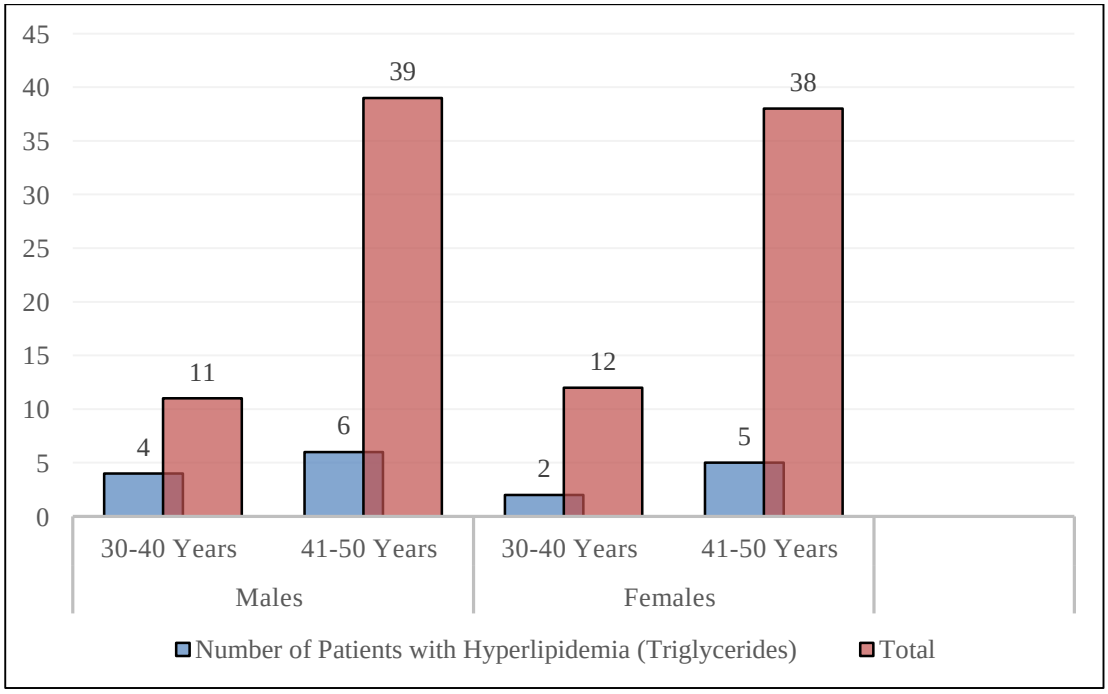
	Age	Thyroid dysfunction and Renal Failure	Total
Males	30-50 Years	4	50
Females		2	50

Total number of individuals: 50 (Males), 50 (Females). This Pie chart is a representative of the incidence of thyroid dysfunction and renal failure in both diabetic males and females among 30-50 years age group (Data given as percentage)

FIG. 5. Co-INCIDENCE OF THYROID DYSFUNCTION AND RENAL FAILURE IN DIABETIC PATIENTS

Figure. 5. Incidence of thyroid dysfunction and renal failure in diabetic individuals 50 (Males), 50 (Females). Pie chart is a representative of the incidence of thyroid dysfunction and renal failure in diabetic males and females among 30-50 years age group. Comparison of co-incidence of thyroid dysfunction and renal failure is about 8% in males which is greater than females .

FIG. 6. INCIDENCE OF HYPERLIPIDEMIA (TRIGLYCERIDES) IN DIABETIC PATIENTS



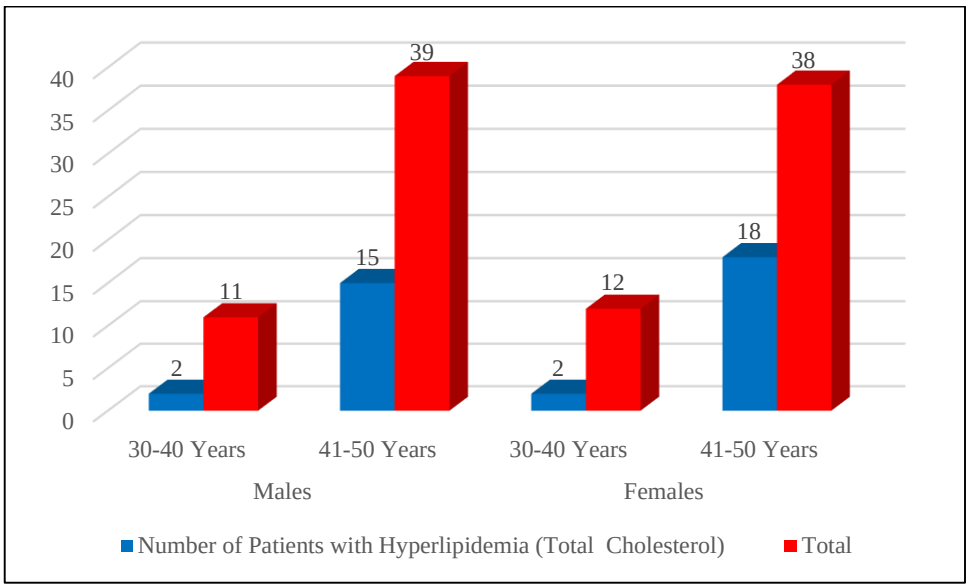
	Age	Number of Patients with Hyperlipidemia (Triglycerides)	Total
Males	**30-40 Years**	**4**	**11**
	41-50 Years	**6**	**39**
Females	**30-40 Years**	**2**	**12**
	41-50 Years	**5**	**38**

Total number of individuals: 50 (Males), 50 (Females). This stacked bar diagram is a representative of the incidence of hyperlipidemia (triglycerides) in both diabetic males and females. P value is <0.05and it is statistically significant

FIG. 6. INCIDENCE OF HYPERLIPIDEMIA (TRIGLYCERIDES) IN DIABETIC PATIENTS

Figure 6 . Incidence of hypertriglyceridemia (triglycerides) in diabetic patients. Total number of individuals: 50 (Males), 50 (Females). This stacked bar diagram is a representative of the incidence of hypertriglyceridemia (triglycerides) in both diabetic males and females. P value is <0.05and it is statistically significant. Each bar represents incidence of hypertriglyceridemia (triglycerides) in both diabetic males and females. First column bar: Represents 4 Males at the age of 30-40 years are having hypertriglyceridemia (triglycerides). Second column bar: Represents 6 Males at the age of 41-50 years are with hypertriglyceridemia. Third column bar shows 2 Females at the age of 30-40 years having hypertriglyceridemia . Fourth column bar shows 5 Females at the age of 41-50 years are having hypertriglyceridemia . From this assesment it is observed that incidence of hypertriglyceridemia is higher in males when compared to females.

FIG. 7. INCIDENCE OF HYPERLIPIDEMIA (TOTAL CHOLESTEROL) IN DIABETIC INDIVIDUALS



	Age	Number of Patients with Hyper-lipidemia (Total cholesterol)	Total
Males	**30-40 Years**	**2**	**11**
	41-50 Years	**15**	**39**
Females	**30-40 Years**	**2**	**12**
	41-50 Years	**18**	**38**

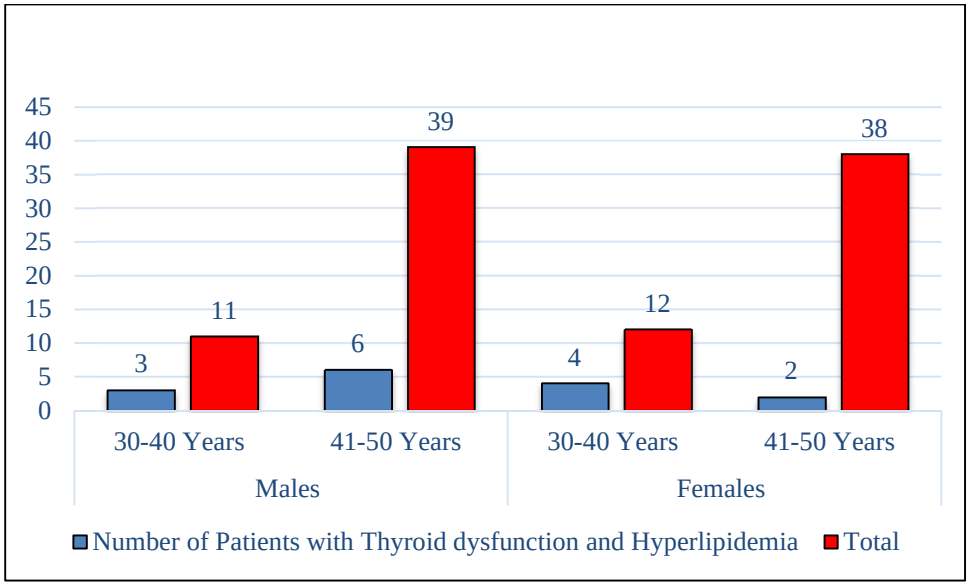
Total number of individuals: 50 (Males), 50 (Females).

This stacked bar diagram is a representative of the incidence of hyperlipidemia (total cholesterol) in diabetic individuals. P value is <0.05 and it is statistically significant.

FIG. 7. INCIDENCE OF HYPERLIPIDEMIA (TOTAL CHOLESTEROL) IN DIABETIC INDIVIDUALS

Figure: 7. Incidence of hypercholesterolemia (total cholesterol) in diabetic individuals. Total number of individuals: 50 (Males), 50 (Females). This stacked bar diagram is a representative of the incidence of hypercholesterolemia (total cholesterol) in both diabetic males and females. P value is <0.05 and it is statistically significant. Each bar represents incidence of hypercholesterolemia (total cholesterol) in both diabetic males and females. First column bar: Represents 2 Males at the age of 30-40 years having hypercholesterolemia (total cholesterol). Second column bar represents 15 males at the age of 41-50 years are with hypercholesterolemia Third column bar shows 2 females with hypercholesterolemia . Fourth column bar: Represents 18 females at the age of 41-50 years are with hypercholesterolemia. So it is observed that incidence of hypercholesterolemia is higher in females than males in the age group of 41-50 years

FIG. 8. CO-INCIDENCE OF THYROID DYSFUNCTION WITH HYPERLIPIDEMIA IN DIABETIC PATIENTS



	Age	Number of Patients with Thyroid dysfunction and Hyperlipidemia	Total
Males	**30-40 Years**	**3**	**11**
	41-50 Years	**6**	**39**
Females	**30-40 Years**	**4**	**12**
	41-50 Years	**2**	**38**

Total number of individuals: 50 (Males), 50 (Females).

This stacked bar diagram is a representative of the co-incidence of thyroid dysfunction and hyperlipidemia in diabetic individuals. P value is <0.05and it is statistically significant.

FIG. 8. CO-INCIDENCE OF THYROID DYSFUNCTION WITH HYPERLIPIDEMIA IN DIABETIC INDIVIDUALS

Figure : 8 Co-incidence of thyroid dysfunction with hyperlipidemia in diabetic individuals. Total number of individuals: 50 (Males), 50 (Females). This stacked bar diagram is a representative of the co-incidence of thyroid dysfunction with hyperlipidemia in both diabetic males and females. $p<0.05$ is considered as statistically significant. Each bar represents co-incidence of thyroid dysfunction with hyperlipidemia in diabetic males and females. It is observed that the Co-incidence of thyroid dysfunction with hyperlipedemia is higher in male diabetic patients when compared to female diabetics.

DISCUSSION

DISCUSSION

In our study, we reported a higher prevalence of thyroid dysfunction among both gender of diabetic patients. In a study by Perros et al.[60] the prevalence of thyroid dysfunction was 10.9% in females and 6.9% in males [60]. NHANES III study reported that the prevalence of subclinical hypothyroidism was 3.4% in males and 5.8% in females.[69] In addition, a study in 420 adult females with T2D randomly selected from participants in the community-based Fremantle Diabetes Study showed that the prevalence of subclinical hypothyroidism was 8.6%. [70] Finally, a recent study revealed that the prevalence of subclinical hypothyroidism was 5.2% in males and 8.4% in females with T2D [71]

Our study results showed that male diabetic patients had poorer glycemic control with higher HbA1c level when compared to females. The FBS levels were slightly higher in males when compared to females. The levels of TGs were higher in males than females. Total cholesterol was slightly higher in females than males .

Also the levels of renal parameters like urea and creatinine were increased in diabetic males when compared to diabetic females since there is poor glycemic control in males.

In the present study we also observed that thyroid dysfunction in females is greater even if they had controlled diabetes when compared to males. But thyroid dysfunction in males with uncontrolled diabetes is higher than females with uncontrolled diabetes. There is more incidence of thyroid

dysfunction in females even if they had controlled diabetes.. This may be linked with their reproductive age. It is observed that the Co-incidence of thyroid dysfunction with hyperlipedemia and renal failure is higher in male diabetic patients when compared to female diabetics.

Higher levels of FBS, TG , TD, similar to other studies. [72,73] However these patients had a higher level of TGL cholesterol when compared to patients with poor glycemic control. It has been reported that TGL cholesterol is inversely associated with CAD risk in diabetes patients. [74] The cause of dyslipidaemia in type 2 diabetes mellitus may be due to impaired liver apolipoprotein production which in turn regulates the enzymatic activity of lipoprotein lipase and cholesterol ester transport protein.[75]

In the present study we found that diabetic patients with thyroid disorders had derangement in lipid profile, regarding TGL and total cholesterol levels. The existing literature data regarding the association between hyperlipidemia and thyroid dysfunction supports the present study. While dyslipidemia is a reported complication of overt hypothyroidism in diabetic [76, 77] subclinical hypothyroidism does not seem to be associated with dyslipidemia. A study by Chubb et al. did not find any significant relationship between subclinical hypothyroidism and the presence of dyslipidemia. Also, in large studies of subclinical hypothyroidism and coronary heart disease. [78,79] there was no association with raised serum cholesterol. The levels of HbA1c were higher in male patients when compared to females. Diabetes confers markedly increased risk of cardiovascular complications among both males and

females. [80] However, women with diabetes are more susceptible to increased cardiovascular mortality. [81] They are subject to more adverse changes in coagulation, vascular function and cardiovascular risk factors than diabetic men. Serum TGL increased with poor glycemic control among males unlike females. The results of lipid profile showed that male diabetic patients had higher levels of TGL cholesterol, which is in agreement with earlier reports. [82,83] This may be attributed to the effects of sex hormones on body fat distribution, leading to differences in altered lipoproteins.[84]

Glucose lowering is essential for the prevention of micro vascular complication, and improvement in cholesterol is central to reducing cardiovascular disease in these patients. [73] A significant correlation between dyslipidemia (increased TGL) has been observed in type 2 diabetics, suggesting their increased susceptibility to vascular disease. [85] It is likely that the combination of thyroid dysfunction, hyperglycemia, dyslipidemia, insulin resistance and hypertension as in metabolic syndrome produces an enhanced atherogenic environment within the circulation.

CONCLUSION

CONCLUSION

In the presence study the serum levels of FBS, PPBS , HbA1c, Thyroid profile, urea, Creatinine and lipid profile were evaluated in type 2 Diabetes mellitus patients of both gender in the age group of 30-50 years .

Our study results showed poor glycemic control with higher HbA1c levels in male diabetic patients when compared to females.

Assesment of Thyroid profile showed thyroid dysfunction is greater in females even if they had controlled diabetes when compared to males. Thyroid dysfunction is higher in males with uncontrolled diabetes is higher when compared to females with uncontrolled diabetes. It seems that more incidence of thyroid dysfunction in females even if they had controlled diabetes.. This may be associated with their reproductive age. The present study showed that the prevalence of thyroid dysfunction among Indian diabetic patients attending an outpatient clinic was 12.3%.

The levels of urea and creatinine were raised in diabetic males when compared to diabetic females since there is poor glycemic control in males indicating higher incidence of renal failure in diabetic males.

The levels of TGL were higher in diabetic males when compared to females. It is observed that the Co-incidence of thyroid dysfunction with hyperlipidemia and renal failure is higher in male uncontrolled diabetic patients when compared to female diabetics. Hence, it is concluded that thyroid dysfunction is positively associated with hyperlipidemia and renal dysfunction

in type 2 diabetes mellitus. So the estimation of serum thyroid profile , lipid profile and renal parameters is highly beneficial in type 2 diabetes mellitus patients to assess the cardiovascular and renal complications.

Regular treatment and follow up of thyroid dysfunction with hyperlipidemia may prevent or decrease the development of cardiovascular and renal complications in type 2 diabetes mellitus. . Further research is needed to elucidate the exact molecular mechanism behind the link between hyperlipidemia and thyroid hormone dysfunction in type2 DM and the life style modification also to be assessed.

BIBLIOGRAPHY

BIBLIOGRAPHY

1. Faghilimnai S, Hashemipour M, Kelishadi B. Lipid profile of children with type 1 diabetes compared to controls. ARYA J. 2006;2(1):36–38.
2. Azevedo M, Alla S. Diabetes in sub-saharan Africa: kenya, mali, mozambique, Nigeria, South Africa and zambia. Int J Diabetes Dev Ctries 2008 Oct;28(4):101-108.
3. Zimmet P, Alberti KG, Shaw J. Global and societal implications of the diabetes epidemic. Nature. 2001;414 (6865):782–787.
4. Ahmed AM. History of diabetes mellitus. Saudi Med J 2002 Apr;23(4):373-378.
5. Patlak M. New weapons to combat an ancient disease: treating diabetes.FASEB J 2002 Dec;16(14):1853.
6. Maitra A, Abbas AK. Endocrine system. In: Kumar V, Fausto N, Abbas AK (eds). Robbins and Cotran Pathologic basis of disease (7th ed) 2005. Philadelphia, Saunders; 1156-1226
7. Chen L, Magliano DJ, Zimmet PZ. The worldwide epidemiology of type 2 diabetes mellitus--present and future perspectives. Nat Rev Endocrinol. 2011 Nov 8;8(4):228-36.
8. Michalaki MA, Vagenakis AG, Leonardou AS, Argentou MN, Habeos IG, Makri MG, et al. Thyroid function in humans with morbid obesity. Thyroid. 2006;16((1)):73–8. 10.1089/ thy. 2006. 16.73 [PubMed]

9. Vibha Uppal, Chittranjan Vij, Gurdeep Kaur Bedi, Anil Vij, Basu Dev Banerjee, Thyroid Disorders in Patients of Type 2 Diabetes Mellitus Indian J Clin Biochem. 2013 Oct; 28(4): 336–341.

10. Patricia Wu, MD Feb 2000, Thyroid Disease and Diabetes, original article.

11. L. H. Duntas, J. Orgiazzi, and G. Brabant, "The interface between thyroid and diabetes mellitus," Clinical Endocrinology, vol. 75, no. 1, pp. 1–9, 2011.

12. American Diabetes Association, "Standards of medical care in diabetes—2013," Diabetes Care, vol. 36, no. 1, pp. S11–S66, 2013.

13. Potenza M, Via MA, Yanagisawa RT. Excess thyroid hormone and carbohydrate metabolism. EndocrPract 2009; 15: 254–62.

14. Naeije R, Golstein J, Clumeck N, Meinhold H, Wenzel KW, Vanhaelst L. A low T3 syndrome in diabetic ketoacidosis. ClinEndocrinol (Oxf). 1978; 8: 467-472

15. R. S. Gray, W. J. Irvine, and B. F. Clarke, "Screening for thyroid dysfunction in diabetics," British Medical Journal, vol. 2, no. 6202, p. 1439, 1979

16. J. L. Johnson, "Diabetes control in thyroid disease," Diabetes Spectrum, vol. 19, no. 3, pp. 148–153, 2006.

17. R. W. V. Flynn, T. M. MacDonald, A. D. Morris, R. T. Jung, and G. P. Leese, "The thyroid epidemiology, audit, and research study: thyroid

dysfunction in the general population," Journal of Clinical Endocrinology and Metabolism, vol. 89, no. 8, pp. 3879– 3884, 2004.

18. G. E. Umpierrez, K. A. Latif, M. B. Murphy et al., "Thyroid dysfunction in patients with type 1 diabetes: a longitudinal study," Diabetes Care, vol. 26, no. 4, pp. 1181–1185, 2003.
19. S. A. P. Chubb, W. A. Davis, and T. M. E. Davis, "Interactions among thyroid function, insulin sensitivity, and serum lipid concentrations: the Fremantle diabetes study," Journal of Clinical Endocrinology and Metabolism, vol. 90, no. 9, pp. 5317–5320, 2005.
20. Snell, R.S. (1995). Clinical Anatomy for my students (fifth edition), Little, Brown and Company, 0-316-80135-6, Boston.
21. Ganong, W.F. (1997). Review of Medical Physiology (eighteenth edition), Appleton&Lange, 0-8385-8443-8,
22. Guyton, A.C. & Hall, JE. (2006) .Textbook of Medical Physiology (eleventh edition), Elsevier Sanders, 0-7216-0240-1, Philadelphia
23. Mc Gregor, A.M. (1996). The thyroid gland and disorders of thyroid function, In: OxfordFextbook of Medicine, Weatherall, DJ., Ledingham, JGG. & Warrell, DA, pp. (1603–1621), Oxford University Press, 0-19-262707-4, Oxford, Vol. 2.Lo Presti & Singer, 1997;
24. Utiger, R.D. (1997). Disorders of the thyroid gland, In: Textbook of Intecnal Medrane, Kelley, WN., pp. (2204–2219), Lippincott – Raven Publishers, 0-397-51540-5, Philadelphia.

25. Di Lauro, R. & De Felice, M. (2001). Basic Physiology anatomy development, In: Endocrinology, DeGroot, LJ.&Jameson, JL., pp. (1268-1275), W.B. Saunders Company, 0-7216-7840-8, Philadelphia.

26. Dillmann, W.H. (2004). The thyroid, In: Cecil Textbook of Medicine, Goldman, L.&Ausrello, D., pp. (1391-1411), Saunders, Philadelphia.

27. Jameson, J.L. & Weetman, A.P. (2010) .Disorders of the thyroid gland, In: Harrison'sEndocrinology, Jameson, JL., pp. (62-69), The McGraw-Hill Companies, Inc., 978-0-07-174147-7, New York.

28. Venturi, S.; Donati, F.M.; Venturi, A.; Venturi, M. (2000). "Environ-mental Iodine Deficiency: A Challenge to the Evolution of Terrestrial Life?". Thyroid 10 (8): 727–9. doi:10.1089/10507250050137851. PMID 11014322.

29. Larsen, P.R., Davies, T.F., Schlumberger, M.J. & Hay, I.D. (2003). Thyroid physiology and diagnostic evaluation of patients with thyroid disorders, In: Williams Textbook ofEndocrinology,

30. Larsen, PR., Kronenberg, HM., Melmed, S.&Polonsky, KS., pp. (331-353), Saunders, 0-7216-9184-6, Philadelphia.Guyton & Hall, 1997; Utiger, 1997

31. Dunn, J.T. (2001). Biosynthesis and secretion of thyroid hormones, In: Endocrinology, DeGroort, LJ.,&Jameson, JL., pp. (1290-1298), W.B. Saunders Company, 0-7216-7840-8, Philadelphia.Benvenga, 2005;

32. Booth GL, Kapral MK, Fung K, Tu JV. Relation between age and cardiovascular disease in men and women with diabetes compared with

non-diabetic people: a population-based retrospective cohort study. Lancet. 2006;368(9529):29–36.

33. Cubbon RM, Wheatcroft SB, Grant PJ, Gale CP, Barth JH, Sapsford RJ, Ajjan R, Kearney MT, Hall AS, et al. Evaluation of M et al. temporal trends in mortality of patients with diabetes mellitus suffering acute myocardial infarction: a comparison of over 3000 patients between 1995 and 2003. Eur Heart J. 2007;28(5):540–5

34. van Straten AH, Soliman Hamad MA, van Zundert AA, Martens EJ, Schonberger JP, ter Woorst JF, de Wolf AM. Diabetes and survival after coronary artery bypass grafting: comparison with an age- and sexmatched population. Eur J Cardiothorac Surg. 2010;37(5):1068–74

35. James S, Angiolillo DJ, Cornel JH, Erlinge D, Husted S, Kontny F, Maya J, Nicolau JC, Spinar J, Storey RF, et al. Ticagrelor vs. clopidogrel in patients with acute coronary syndromes and diabetes: a substudy from the PLATelet inhibition and patient Outcomes (PLATO) trial. Eur Heart J. 2010;31(24):3006–16

36. Kahn MB, Cubbon RM, Mercer B, Wheatcroft AC, Gherardi G, Aziz A, Baliga V, Blaxill JM, McLenachan JM, Blackman DJ, et al. Association of diabetes with increased all-cause mortality following primary percutaneous coronary intervention for ST-segment elevation myocardial infarction in the contemporary era. Diabetes Vasc Dis Res. 2012;9(1):3–9.

37. Kohli P, Wallentin L, Reyes E, Horrow J, Husted S, Angiolillo DJ, Ardissino D, Maurer G, Morais J, Nicolau JC, et al. Reduction in first and recurrent cardiovascular events with ticagrelor compared with clopidogrel in the PLATO Study. Circulation. 2013;127(6):673–80.

38. Ryden L, Grant PJ, Anker SD, Berne C, Cosentino F, Danchin N, Deaton C, Escaned J, Hammes HP, Huikuri H, et al. ESC Guidelines on diabetes pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD: the Task Force on diabetes, pre-diabetes, and cardiovascular diseases of the European Society of Cardiology (ESC) and developed in collaboration with the European Association for the Study of Diabetes (EASD). Eur Heart J. 2013;34(39):3035–87

39. Home PD. Insulin therapy. In: Alberti KGMM, Zimmet P, Defronzo RA editors & Keen H (Hon) editor International Textbook of Diabetes Mellitus (2nd ed) John Wiley & Sons, New York; 1997 p. 899–928.

40. Dodson G, Steiner D. The role of assembly in insulin's biosynthesis. Curr Opin Struct Biol. 1998;8:189–94. [PubMed]

41. Schroder D, Zuhlke H. Genetechnology, characterization of insulin gene and the relationship to diabetes research. Endokrinologie. 1982;79: 197–209. [PubMed]

42. Malaisse WJ. Insulin biosynthesis and secretion *in vitro*. In: Alberti KGMM, Zimmet P, Defronzo RA & Keen H (Hon) editors. International Textbook of Diabetes Mellitus (2nd ed) John Wiley & Sons, New York; 1997 p. 315–36.

43. Porksen N, Hollingdal M, Juhl C, Butler P, Veldhuis JD, Schmitz O. Pulsatile insulin secretion: detection, regulation, and role in diabetes. Diabetes. 2002;51 (Suppl 1):S245–54. [PubMed]

44. Bratanova-Tochkova TK, Cheng H, Daniel S, et al. Triggering and augmentation mechanisms, granule pools, and biphasic insulin secretion. Diabetes. 2002;51 (Suppl. 1):S83–90. [PubMed]

45. Nielsen JH, Galsgaard ED, Moldrup A, et al. Regulation of beta-cell mass by hormones and growth factors. Diabetes. 2001;50 (Suppl 1):S25–9. [PubMed]

46. Soria B, Quesada I, Ropero AB, Pertusa JA, Martin F, Nadal A. Novel players in pancreatic islet signaling: from membrane receptors to nuclear channels. Diabetes. 2004;53 (Suppl 1):S86–91. [PubMed]

47. Kahn SE, McCulloch DK, Porte D. Insulin secretion in the normal and diabetic human. In: Alberti KGMM, Zimmet P, Defronzo RA, editors & Keen H, (hon) editor. International Textbook of Diabetes Mellitus. (2nd ed) John Wiley & Sons, New York; 1997 p. 337–54.

48. Chen M, Porte D., Jr The effect of rate and dose of glucose infusion on the acute insulin response in man. J Clin Endocrinol Metab. 1976; 42:1168–75. [PubMed]

49. Hunter SJ, Garvey WT. Insulin action and insulin resistance: diseases involving defects in insulin receptors, signal transduction, and the glucose transport effector system. Am J Med. 1998;105: 331–45.[PubMed]

50. Wheatcroft SB, Williams IL, Shah AM, Kearney MT. Pathophysiological implications of insulin resistance on vascular endothelial function. Diabet Med. 2003;20:255–68. [PubMed]

51. Reaven G. The metabolic syndrome or the insulin resistance syndrome? Different names, different concepts, and different goals. Endocrinol Metab Clin North Am. 2004;33:283–303. [PubMed]

52. Denton RM, Tavaré JM. Molecular basis of insulin action on intracellular metabolism. In: Alberti KGMM, Zimmet P, Defronzo RA, Keen H (Hon), editors. International Textbook of Diabetes Mellitus (2nded) John Wiley & Sons, New York; 1997 p. 469–88.

53. Smith U. Impaired (‘diabetic’) insulin signaling and action occur in fat cells long before glucose intolerance--is insulin resistance initiated in the adipose tissue? Int J Obes Relat Metab Disord. 2002;26: 897–904. [PubMed]

54. Giorgino F, Laviola L, Eriksson JW. Regional differences of insulin action in adipose tissue: insights from in vivo and in vitro studies. Acta Physiol Scand. 2005;183:13–30. [PubMed]

55. Devaraj S, Rosenson RS, Jialal I. Metabolic syndrome: an appraisal of the pro-inflammatory and procoagulant status. Endocrinol Metab Clin North Am. 2004;33:431–53. [PubMed]

56. Krauss RM, Siri PW. Metabolic abnormalities: triglyceride and low-density lipoprotein. Endocrinol Metab Clin North Am. 2004;33: 405–15. [PubMed]

57. Bornstein J. A technique for the assay of small quantities of insulin using alloxan diabetic, hypophysectomized, adrenalectomized rats. Aust J Exp Biol Med Sci. 1950;28:87–91. [PubMed]

58. Yalow, RS, Berson SA. Immunoassay of endogenous plasma insulin in man. J Clin Invest. 1960;39:1157–75. [PMC free article] [PubMed]

59. Withers DJ, White M. Perspective: The insulin signaling system--a common link in the pathogenesis of type 2 diabetes. Endocrinology. 2000;141:1917–21. [PubMed]

60. Cleland SJ, Fisher BM, Colhoun HM, Sattar N, Petrie JR. Insulin resistance in type 1 diabetes: what is 'double diabetes' and what are the risks? Diabetologia. 2013;56(7):1462–70

61. P. Perros, R. J. McCrimmon, G. Shaw, and B. M. Frier, "Frequency of thyroid dysfunction in diabetic patients: value of annual screening," Diabetic Medicine, vol. 12, no. 7, pp. 622–627, 1995

62. Bech K, Damsbo P, Eldrup E, et al. β-Cell function and glucose and lipid oxidation in Graves' disease. Clinical Endocrinology. 1996;44(1):59–66

63. Vaughan M. An in vitro effect of triiodothyronine on rat adipose tissue. Journal of Clinical Investigation. 1967;46(9):1482–1491.

64. E. Solá, C. Morillas, S. Garzón, M. Gómez-Balaguer, and A. Hernández-Mijares, "Association between diabetic ketoacidosis and thyrotoxicosis," Acta Diabetologica, vol. 39, no. 4, pp. 235–237, 2002.

View at Publisher · View at Google Scholar · View at PubMed · View at Scopus

65. A. Bhattacharyya and P. G. Wiles, “Diabetic ketoacidosis precipitated by thyrotoxicosis,” Postgraduate Medical Journal, vol. 75, no. 883, pp. 291–292, 1999. View at Google Scholar · View at Scopus

66. Trinder, P. (1969). Determination of blood glucose using an oxidase-peroxidase system with a non-carcinogenic chromogen. J. Clin. Pathol., 22, 2, 158-161.

67. Tietz, N.W., textbook of Clinical Chemistry, W.B. Saunders Co., Philadelphia, p.1270-1271 (1986).

68. IFCC reference system for measurement of hemoglobin A1c in human blood and the National Standardization Schemes in the United states, Japan and Sweden: a method comparison study, Clinical chemistry (2004) 50:1,pg: 166-174.

69. Lundberg PR et al Clin Chem 28, 1241 (1982

70. J. G. Hollowell, N. W. Staehling, W. Dana Flanders et al., “Serum TSH, T4, and thyroid antibodies in the United States population (1988 to 1994): National Health and Nutrition Examination Survey (NHANES III),” Journal of Clinical Endocrinology and Metabolism, vol. 87, no. 2, pp. 489–499, 2002

71. S. A. P. Chubb, W. A. Davis, and T. M. E. Davis, “Interactions among thyroid function, insulin sensitivity, and serum lipid concentrations: the

Fremantle diabetes study," Journal of Clinical Endocrinology and Metabolism, vol. 90, no. 9, pp. 5317–5320, 2005

72. Chen HS, Wu TE, Jap TS, Lu RA, Wang ML, Chen RL, Lin HD. Subclinical hypothyroidism is a risk factor for nephropathy and cardiovascular diseases in Type 2 diabetic patients. Diabet Med 2007;24(12):
1336-1344.

73. Ladeia AM, Adan L, Couto-Silva AC, Hiltner A, Guimaraes AC. Lipid profile correlates with glycemic control in young patients with type 1 diabetes mellitus. Prev Cardiol. 2006;9(2):82-8.

74. Huang ES, Meigs JB, Singer DE. The effect of interventions to prevent cardiovascular diseases in patients with type-2 diabetes mellitus. Am J Med. 2001;111(8):633-42.

75. Eshaghian S, Horwich TB, Fonarow GC. An unexpected inverse relationshipbetween HbA1c levels and mortality in patients with diabetes and advanced systolic heart failure. Am Heart J. 2006;151(1):91.

76. Goldberg IJ. Lipoprotein lipase and lipolysis: central roles in lipoprotein metabolism and atherogenesis. J Lipid Res. 1996;37(4):693-707.

77. Staub JJ, Althaus BU, Engler H, Ryff AS, Trabucco P, Marquardt K, Burckhardt D, et al. Spectrum of subclinical and overt hypothyroidism:

effect on thyrotropin, prolactin, and thyroid reserve, and metabolic impact on peripheraltarget tissues. Am J Med 1992;92(6):631-642

78. Johnston J, McLelland A, O'Reilly DS. The relationship between serum cholesterol and serum thyroid hormones in male patients with suspected hypothyroidism. Ann Clin Biochem 1993;30 (Pt 3)(256-259.

79. Tunbridge WM, Evered DC, Hall R, Appleton D, Brewis M, Clark F, Evans JG, et al. Lipid profiles and cardiovascular disease in the Whickham area with particular reference to thyroid failure. Clin Endocrinol (Oxf)1977;7(6):495-508.

80. Imaizumi M, Akahoshi M, Ichimaru S, Nakashima E, Hida A, Soda M, Usa T, et al. Risk for ischemic heart disease and all-cause mortality in subclinical hypothyroidism. J Clin Endocrinol Metab 2004;89(7):3365-3370.

81. Haffner SM, Lehto S, Ronnemaa T, Pyorala K, Laakso M. Mortality from coronary heart disease in subjects with type 2 diabetes and in nondiabetic subjects with and without prior myocardial infarction. N Engl J Med. 1998;339(4):229-34.

82. Gu K, Cowie CC, Harris MI. Diabetes and decline in heart disease mortality in US adults. JAMA. 1999;281(14):1291-7.

83. Hanefeld M, Fischer S, Julius U, Schulze J, Schwanebeck U, Schmechel H, et al. Risk Factors for myocardial infarction and death in newly detected NIDDM: the Diabetes intervention study, 11-year follow-up. Diabetologia. 1996;39(12):1577-83.

84. Esteghamati A, Abbasi M, Nakhjavani M, Yousefizadeh A, Basa AP, Afshar H. Prevalence of diabetes and other cardiovascular risk factors in an Iranian population with acute coronary syndrome. Cardiovasc Diabetol. 2006;5:15.

85. Sibley SD, Thomas W, de Boer I, Brunzell JD, Steffes MW. Gender and elevated albumin excretion in the Diabetes Control and Complications trial/Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC) cohort: role of central obesity. Am J Kidney

Dis. 2006;47(2):223-32.

86. Nasri H, Yazdani M. The relationship between serum LDL-cholesterol, HDLcholesterol and systolic blood pressure in patients with type 2 diabetes. Kardiol Pol. 2006;64(12):1364–8; discussion. 1369-71.

87. Pederson, K.O, Scand, J.Clin.Lab Invest, 34 , 247(1974).

88. Wild, D., Immunoassay Handbook, Stockton Press, p339 (1994).

89. Wenzel, K.W., Metabolism, 30, 717 (1981).

90. Bhagat, C., et.al, Clin chem., 29 ,1324(1983).

91. Lalloz m.r., et.al. Clin Endocrinol, 18 , 11 (1983).

92. Barker, S.B., " Determination of Protein Bound iodine''., Jouma / Biological chemistry, 173,175, (1948).

93. Chopra , I.J., Solomon, D.H ., and Ho , R.S ., " A Radioimmunoassay of Thyroxine" , J.Clinical Endocrinol, 33,865 (1971).

94. Young, D.S ., Pestaner, L.C., and Gilberman, U., “Effects of Drugs on Clinical Laborotary , Tests’’ , Clinical chemistry,3660(1975).

95. Stjernholm, MR, Alsever, RN and Rudolph , MC. “ Thyroid function tests in diphenylhydantoin-treated patients ”. Clin chem.. vol 21 1388-1392(1977).

96. Beck-pacozz P., Persani,l: “Variable biological activity of Thyroid stimulating hormone”. European journal of Endocrinol; 131:331-340, 1994.

97. Young, D.S ., Pestaner, L.C., and Gilberman, U., “Effects of Drugs on Clinical Laborotary , Tests’’ , Clinical chemistry 21, 3660(1975).

98. Caldwell Get.al. “A new strategy for thyroid function testing” Lancet 1,1117 (1985).

99. Fisher D : “Physiological variations in thyroid hormones’’ . Physiological and pathophysiological considerations, Clin chem.. 42; 135-139, 1996 .

100. Spencer CA , et.al., “Interlaboratory / Inter method differences in functional sensitivity of immunometric assays of thyrotrophin (TSH) on “Reliability of measurement of subnormal concentration of TSH’’ Clin chem. , 41,367(1995).

101. Fawcett, J.K., Scott, J.E., J.Clin Path ; 2960;13: 156-159

102. Patton , C.J., Crouch, S.R ., Anal chem. ., 1977; 49: 464-469

103. Richmond, N.Clin chem. . 1973: 1350-356.

104. Overview and recommendations : current status of blood cholesterol measurement clin chem. ., 34/1, 193-201 (1988).

105. Allain C.Cand al., Clin.chem .,20(1974) , 470 .

106. Jacobs N.J., Van Denmark, P.J., Arch . Biochem biophys .1960; 88 250-255.

107. Koditscheck L.K., Umbriet, W.W.,J.Bacteriol 1969;1063-1068.

108. Trinder.P., Ann .clin biochem., 1969;6;24-27.

109. Williams Pet.al., High density lipoprotein and coronary risk factor , Lancet.1: 72(1979).

110. Gordon, T.Castelli., W.P Hjo tjand, M.C.et.al.Am. J.Med.62, 707-174(1977).

111. Rifai, N.and warnick, G.R., Ed.Laboratory measurement of lipids , lipo-proteins and Apolipoproteins AACC Press Washington, DC,USA., 1994.

ANNEXURES

ANNEXURES

SL.NO	CONTENT
1	Information Sheet (English)
2	Patient Consent Form (English)
3	Patient Consent Form (Tamil)
4	PROFORMA
5	Institutional Ethical Committee Approval Certificate
6	Master Chart

INFORMATION SHEET

- Your blood sample has been accepted.
- We are conducting a study on all type 2 diabetes individuals on treatment for 3 years attending Karpaga Vinayaga Institute of Medical Sciences,Kanchipuram District-603308 and for that your blood sample may be valuable to us.
- The purpose of this study is to identify " **A study of thyroid dysfunction and associated risk factors among type 2 Diabetes mellitus patients** " with the help of certain special tests.
- We are selecting certain cases and if your blood sample is found eligible, we may be using your blood sample to perform extra tests and special studies which in any way do not affect your final report or management.
- The privacy of the patients in the research will be maintained throughout the study. In the event of any publication or presentation resulting from the

  research, no personally identifiable information will be shared.
- Taking part in this study is voluntary. You are free to decide whether to participate in this study or to withdraw at any time; your decision will not result in any loss of benefits to which you are otherwise entitled.
- The results of the special study may be intimated to you at the end of the study period or during the study if anything is found abnormal which may aid in the management or treatment.

Signature of investigator Signature of participant

Date:

PATIENT CONSENT FORM

“A study of thyroid dysfunction and its associated risk factors among type 2 Diabetes mellitus patients ’’

Name	:	Date	:
Age	:	OP No	:
Sex	:	Individual ID No:	:

The details of the study have been provided to me in writing and explained to me in my own language.

I confirm that I have understood the above study and had the opportunity to ask questions.

I understand that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason, without the medical care that will normally be provided by the hospital being affected.

I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s).

I have been given an information sheet giving details of the study.

I fully consent to participate in the above study.

Signature

ஆய்வு ஒப்புதல் படிவம்

பங்கு பெறுபவரின் பெயர் ..... பங்கு பெறுபவரின் வயது .....
ங்கு பெறுபவரின் எண்..... ஆண் / பெண் .....

ஆய்வு மேற்கொள்ளப்படும் இடம் : கற்பக விநாயகா மருத்துவக் கல்லூரி மற்றும்
ஆராய்ச்சி மையம்,
சின்னகோளம்பாக்கம்,
காஞ்சிபுரம் மாவட்டம்-603 308.

பங்குபெறுபவர் இதனை குறிக்கவும் [√]

1. மேலே குறிப்பிட்டுள்ள மருத்துவ ஆய்வின் விபரங்கள் எனக்கு விளக்கப்பட்டுள்ளது. என்னுடைய சந்தேகங்களை கேட்கவும் அதற்கான தகுந்த விளக்கங்களை பெறவும் வாய்ப்பளிக்கப்பட்டுள்ளது என நான் புரிந்து கொண்டுள்ளேன். [ ]

2. இந்த ஆராய்ச்சியில் என் பங்கேற்பு தன்னிச்சையானது மற்றும் என் மருத்துவப் பாதுகாப்பு மற்றும் சட்ட உரிமைகள் பாதிக்கப்படாமல் எந்த நேரத்திலும் எந்த காரணமுமின்றி நான் இதிலிருந்து விலகி கொள்ள தடையேதும் இல்லை எனவும் நான் புரிந்து கொண்டுள்ளேன். [ ]

3. நான் ஆய்விலிருந்து விலகினாலும் கூட மருத்துவ ஆய்வு மேற்கொள்ளும் மருத்துவமனை அவர்களின் சார்பாக பணியாற்றும் மருத்துவர்கள், நன்நடத்தை நெறிமுறைகள் குழு மற்றும் ஒழுங்குமுறை ஆணையங்கள் தற்போதைய ஆய்வு மற்றும் இதற்கு தொடர்பாக நடத்தப் பெறக்கூடிய மேலும் ஏதேனும் வருங்கால ஆய்வு இரண்டும் குறித்த என் உடல்நல பதிவுகளை ஆராய என் அனுமதிப் பெற வேண்டிய அவசியமில்லை எனவும் நான் புரிந்து கொண்டுள்ளேன். இவைகளை அணுகிப் பெற நான் ஒப்புக் கொள்கிறேன். ஆயினும் மூன்றாம் நபர்களுக்கு தரப்படும் அல்லது பிரசுரிக்கப்படும் ஏதேனும் தகவல்களில் என் தனிப்பட்ட அடையாளம் வெளிப்படுத்தபடமாட்டாது எனவும் நான் புரிந்து கொண்டுள்ளேன். [ ]

4. ஆய்வின் போது மேற்கொள்ளப்படும் பரிசோதனைகளுக்காக என் உடலிலிருந்து இரத்தம் மற்றும் சிறுநீர் எடுப்பதற்கு சம்மதிக்கிறேன். ☐

5. இந்த ஆராய்ச்சியிலிருந்து வெளிப்படும் ஏதேனும் தகவல்கள் அல்லது முடிவுகளை பயன்படுத்த அத்தகைய பயன்பாடு அறிவியல் சார்ந்த தேவைகளுக்காக மட்டும் எனும் பட்சத்தில் நான் அதற்கு நிபந்தனை ஏதும் விதிக்கமாட்டேன் என ஒப்புக் கொள்கிறேன். மேலே குறிப்பிட்ட ஆய்வில் பங்கு கொள்ள சம்மதிக்கிறேன். ☐

6. எனக்கு கொடுக்கப்பட்ட அறிவுரைகளின் படி நடந்து கொள்வதுடன் இந்த ஆய்வை மேற்கொள்ளும் மருத்துவ அணிக்கு உண்மையுடன் இருப்பேன் என்றும் உறுதியளிக்கிறேன். என் உடல் நலம் பாதிக்கப்பட்டாலோ, எதிர்பாராத வழக்கத்திற்கு மாறான நோய்அறிகுறி தென்பட்டாலோ உடனே இதை மருத்துவ அணியிடம் தெரிவிப்பேன் என உறுதி அளிக்கிறேன். ☐

பங்கேற்பவரின் கையொப்பம் ..... இடம் ..... தேதி.....
/ கட்டை விரல் ரேகை

பங்கேற்பவரின் பெயர் மற்றும் விலாசம் : .....

.....

ஆய்வாளரின் கையொப்பம் ..... இடம் ..... தேதி .....

ஆய்வாளரின் பெயர் .....

PROFORMA

NAME:

AGE:

GENDER:

OP.NO.:

INDIVIDUAL ID. NO:

ADDRESS:

HISTORY:

Lifestyle Factors:

Physical activity :

Socioeconomic conditions :

Body mass index, smoking (pack years) :

Alcohol(criteria) :

Blood pressure :

FAMILY HISTORY :

MENSTRUAL HISTORY :

DRUG HISTORY :

GENERAL EXAMINATION:

HEIGHT : **WEIGHT :**

BMI :

BLOOD PRESSURE : **PULSE :**

SYSTEMIC EXAMINATION :

CARDIOVASCULAR SYSTEM :

RESPIRATORY SYSTEM :

ABDOMEN :

NERVOUS SYSTEM :

INVESTIGATION:

Fasting serum glucose/Post prandial glucose – GOD / POD method/Enzymatic method, HbA1C

Lipid profile

- **Total Cholesterol**
- **Triglycerides**
- **HDL**
- **LDL**
- **VLDL**

Renal function test

- **Urea**
- **Creatinine**

Thyroid profile (ELISA)

- **TSH**
- **Free T3**
- **Free T4**

DIAGNOSIS:

INSTITUTIONAL ETHICAL COMMITTEE

KARPAGA VINAYAGA INSTITUTE OF MEDICAL SCIENCES & RESEARCH CENTRE

MADURANTHAGAM - 603 308.

EC Ref. No: 18/2016

CERTIFICATE FOR APPROVAL

The Institutional Ethical Committee of Karpaga Vinayaga Institute of Medical Sciences & Research Centre, Maduranthagam reviewed and discussed the application for approval **"A study of thyroid dysfunction and its risk factors among type 2 diabetes mellitus patients "** by **Dr.C. Sathish kumar ,** Post graduate, guided by **Dr. Arunakumari, Professor, Department of Bio Chemistry**, Karpaga Vinayaga Institute of Medical Sciences & Research Centre, Maduranthagam.

The proposal is **APPROVED**

The Institutional Ethics Committee expects to be informed about the progress of the study, and Adverse Drug Reaction occurring in the course of the study, any changes in the protocol and patients information / informed consent and asks to be provided a copy of the final report.

23/01/16

Chairperson, Ethics Committee

Date: 23.01.2016

A STUDY OF THYROID DYSFUNCTION ITS ASSOCIATED RISK FACTORS AMONG TYPE 2 DIABETES MELLITUS PATIENTS

Sl. No.	NAME	AGE	SEX	OP/IP No.	FT3 PG/ML	FT4 NG/DL	TSH IU/ML	LIPID PROFILE MG/DL					UREA MG/DL	CREATINE MG/DL	FBS MG/DL	PPBS MG/DL	HBA1C %
								TC	TGL	HDL	VLDL	LDL					
1	DHANAPAL	50	M	201609010059	0.342	5.378	0.124	210	158	41	32	137	31	0.8	119	227	8%
2	KARTHIK	38	M	201608260037	3.239	3.053	5.543	133	150	59	30	44	28	0.7	117	168	8%
3	RAMALINGAM	50	M	20160711342	0.634	2.963	6.852	143	83	23	29	91	32	0.9	76	174	6%
4	GANGATHARAN	38	M	201608290018	1.120	2.930	0.135	219	217	32	43	144	25	0.8	153	287	9%
5	SELVARAJ	49	M	201609010080	2.910	5.257	1.362	171	208	40	42	89	28	0.9	134	221	9%
6	RANI	34	F	20161122038	0.357	0.714	0.268	185	97	58	19	108	26	0.7	116	210	8%
7	SHANTHI	50	F	1111160022	1.205	2.091	0.065	248	175	50	35	163	29	0.9	147	234	9%
8	RAMESH	50	M	2211160051	0.974	2.117	0.849	194	89	46	18	130	31	1.0	227	280	9%
9	RATHINAVEL	50	M	1104160036	0.765	2.750	0.327	210	92	50	18	142	30	0.9	138	193	8%
10	PAULINMARY	49	F	201611190052	0.375	0.721	0.278	193	124	41	31	121	24	0.7	198	241	9%
11	ALAMELU	50	F	130212093	5.348	2.670	0.052	305	150	64	30	211	29	0.9	113	167	7%
12	ABDUL MANNAN	50	M	20160106084	0.593	2.293	1.463	114	92	45	18	51	24	0.7	117	208	7%
13	MEENA	37	F	201609060047	0.404	0.933	0.949	219	150	55	30	134	27	0.8	102	182	7%
14	NAINABI	50	F	1009160293	0.584	1.981	4.775	200	183	55	37	108	31	0.9	104	239	9%
15	IRUSAN	50	M	1607160036	2.159	1.923	0.447	286	92	64	18	204	28	0.7	81	170	6%
16	MANGALAKSHMI	50	F	1305160034	0.860	0.723	0.352	219	150	55	30	134	29	0.8	109	181	6%
17	MALLIGA	50	F	20161080050	1.208	2.530	1.185	229	100	50	20	159	27	0.7	86	147	6%
18	KANNAN	49	M	270160039	1.069	1.350	1.497	267	175	64	35	168	31	0.9	150	212	8%

Sl. No.	NAME	AGE	SEX	OP/IP No.	FT3 PG/ML	FT4 NG/DL	TSH IU/ML	LIPID PROFILE MG/DL					UREA MG/DL	CREATINE MG/DL	FBS MG/DL	PPBS MG/DL	HBA1C %
								TC	TGL	HDL	VLDL	LDL					
19	KRISHNAVENI	48	F	201610200050	0.630	1.337	3.342	286	142	72	28	186	34	1.0	220	345	9%
20	GOPI	40	M	201609070055	1.164	1.521	3.430	248	83	36	17	195	26	0.7	112	204	8%
21	PIYARI	45	F	2610160040	2.475	2.128	4.194	352	150	50	30	272	29	0.8	247	338	9%
22	SELVIYAMMAL	40	F	1411160049	3.386	3.019	2.068	361	183	68	37	256	29	0.8	159	236	8%
23	ARJUNAN	50	M	201611160078	0.356	2.992	1.207	342	167	77	33	232	34	0.9	254	447	9%
24	PARVATHY	49	F	2608160028	0.162	2.218	1.357	361	117	64	23	274	29	0.6	116	211	8%
25	PONNUDASS	47	M	201611120038	0.504	2.858	0.480	343	183	82	37	224	45	1.7	150	242	9%
26	SIVA	50	M	201610240069	0.097	1.790	4.252	210	108	45	22	143	35	1.2	105	182	6%
27	SHANTHI	48	F	201611120050	1.668	3.021	0.447	175	137	55	27	93	31	0.9	225	311	9%
28	SAYEETHA FAHEE	36	F	20160907052	0.103	3.488	0.473	295	183	55	37	203	34	0.9	114	210	8%
29	KALAIVANI	42	F	1608160263	3.348	1.830	1.915	343	192	64	38	241	28	0.9	162	294	8%
30	KESAVAN	42	M	3110160026	0.440	2.611	0.929	295	150	55	30	210	29	0.8	157	224	8%
31	SUNDARAMUTHI	50	M	20161109062	0.967	2.924	2.208	286	125	50	25	211	43	1.6	224	286	9%
32	KALATHINATHAN	47	M	201610170643	0.226	2.230	0.687	276	133	45	27	204	29	0.9	103	190	7%
33	SARALA	46	F	2610160063	0.884	3.244	2.226	295	100	55	20	220	28	0.6	116	184	7%
34	SUBRAMANI	49	M	201610250043	0.775	0.102	1.415	257	125	68	25	164	39	1.2	124	208	8%
35	SAMSATH BEGAM	50	F	201611120057	1.503	0.911	5.479	257	150	45	30	182	30	0.8	186	201	8%
36	LOOSIYAMARY	48	F	201611170059	1.819	1.055	2.638	224	103	65	21	138	21	0.6	201	264	9%

Sl. No.	NAME	AGE	SEX	OP/IP No.	FT3 PG/ML	FT4 NG/DL	TSH IU/ML	LIPID PROFILE MG/DL					UREA MG/DL	CREATINE MG/DL	FBS MG/DL	PPBS MG/DL	HBA1C %
								TC	TGL	HDL	VLDL	LDL					
37	ELUMALAI	42	M	1382160031	1.347	0.293	3.297	333	157	64	31	238	30	1.0	149	265	8%
38	INDIRANI	50	F	1408160035	0.943	2.368	1.537	305	164	59	33	213	50	2.0	177	235	9%
39	RAJESHWARI	50	F	201610130049	0.717	1.197	3.171	177	114	45	23	109	26	0.7	89	186	7%
40	BASKAR	40	M	201611040044	0.655	1.454	4.597	147	98	50	20	77	28	0.8	171	196	8%
41	SELVI	50	F	201610180046	0.412	0.697	7.828	144	192	59	38	47	26	0.7	115	159	5%
42	NALLATHAMBI	40	M	201611010037	1.164	1.074	0.748	167	200	82	40	45	29	0.8	121	168	8%
43	KUPPAMMAL	49	F	201611150080	0.918	0.552	4.119	150	79	45	16	89	26	0.7	250	291	9%
44	MANI	41	M	20161030012	0.314	1.481	2.068	128	83	50	17	61	29	0.9	118	204	7%
45	THANGAVEL	50	M	201611210064	0.770	1.059	3.097	161	93	41	19	101	34	1.3	87	155	7%
46	THARA	50	F	201610240050	0.751	1.182	4.324	144	150	68	30	46	26	0.7	143	188	9%
47	NAGARANI	40	F	20160826056	0.421	2.483	0.488	156	207	55	41	60	28	0.8	114	201	8%
48	GNANASEKAR	47	M	201611020060	1.298	1.520	2.810	146	96	52	19	75	27	0.9	219	298	9%
49	KUPPUSAMY	48	M	201611020057	0.304	0.314	3.489	167	107	82	21	64	28	0.8	108	206	7%
50	BHUVANA	50	F	1710160391	0.605	1.195	1.695	144	114	45	23	76	29	0.9	109	169	5%
51	ANTHONY	45	M	201610210045	0.358	0.578	1.763	150	150	68	30	52	25	0.7	112	216	7%
52	KANNIYAMMAL	35	F	2016140062	0.211	1.645	2.590	178	200	59	40	79	24	0.8	75	186	5%
53	RAJ	35	M	201611090059	2.234	1.561	3.419	189	192	59	38	92	29	0.7	157	163	7%
54	SHAHITHA BEGAM	50	F	2710160033	1.099	2.004	4.624	133	93	45	19	69	31	0.8	115	148	7%

Sl. No.	NAME	AGE	SEX	OP/IP No.	FT3 PG/ML	FT4 NG/DL	TSH IU/ML	LIPID PROFILE MG/DL					UREA MG/DL	CREATINE MG/DL	FBS MG/DL	PPBS MG/DL	HBA1C %
								TC	TGL	HDL	VLDL	LDL					
55	PONNUSAMI	50	M	2405100029	0.699	2.707	2.667	161	150	45	30	86	26	0.7	79	164	7%
56	DASS	50	M	201610240041	0.728	1.294	8.242	138	120	31	24	83	37	1.3	111	186	7%
57	KATHAVARAYAN	49	M	20161119042	0.559	1.961	1.212	194	193	80	39	75	36	1.4	118	301	8%
58	JOSEPH	50	M	1811160026	0.125	2.157	5.900	146	79	48	16	82	31	1.0	150	312	9%
59	MOHAN	45	M	0609160927	0.730	0.304	1.026	133	79	65	27	41	34	0.9	248	308	9%
60	SUDHAKAR	36	M	20161070542	0.472	2.520	2.391	115	100	50	20	45	31	1.0	129	253	8%
61	VENKADAPERUMA	50	M	201611140056	0.129	2.795	2.767	123	71	45	14	64	28	0.8	217	291	9%
62	GOVINDAMMAL	47	F	2706160234	0.612	1.199	4.964	261	79	50	16	195	31	0.9	190	267	9%
63	RAJ	49	M	201610250044	0.921	1.238	3.746	123	143	65	29	29	28	0.8	128	304	9%
64	SANTHI	50	F	201611120050	0.800	1.659	0.481	200	114	75	23	102	29	0.9	230	374	9%
65	SRINIVASAN	50	M	20161110077	0.671	0.023	13.26	123	193	40	39	44	89	2.0	160	211	8%
66	AAMINA	48	F	2610160043	1.466	1.277	3.500	131	64	80	13	38	28	0.8	86	183	8%
67	GOWRI	40	F	1306160213	0.595	0.441	3.293	277	193	85	39	153	26	0.6	94	168	7%
68	VALLI	39	F	2001100024	0.740	1.287	3.445	123	186	50	37	36	31	0.9	164	352	9%
69	SUGUMAR	50	M	201611040049	0.362	1.789	2.161	177	136	35	27	115	24	0.8	162	210	8%
70	GABRIEL	49	M	201610070052	1.993	1.564	2.586	123	86	25	17	81	27	0.9	69	223	7%
71	SULOKSHANA	46	F	1205150027	1.576	1.917	2.146	238	186	70	37	131	28	0.7	108	206	7%
72	VASANTHA	49	F	201610260058	0.905	1.766	2.985	138	86	45	17	76	39	1.0	209	264	9%

Sl. No.	NAME	AGE	SEX	OP/IP No.	FT3 PG/ML	FT4 NG/DL	TSH IU/ML	LIPID PROFILE MG/DL					UREA MG/DL	CREATINE MG/DL	FBS MG/DL	PPBS MG/DL	HBA1C %
								TC	TGL	HDL	VLDL	LDL					
73	RANI	47	F	20160960063	0.435	0.705	8.995	223	186	45	37	141	26	0.8	110	201	7%
74	CHINNAPONNU	50	F	07101600378	0.045	0.337	7.720	146	157	40	31	75	28	0.6	97	168	7%
75	KURUVAMMAL	50	F	20168090042	0.578	0.445	1.051	131	207	37	41	55	31	1.0	306	364	9%
76	KAMAL	35	M	201610280041	0.344	0.243	44.17	123	86	30	17	76	75	6.5	109	168	7%
77	MAHADEVI	48	F	201612170037	0.196	3.391	1.311	194	214	43	43	108	28	0.9	194	221	8%
78	MUTHU	45	M	20162160044	0.305	3.451	1.720	165	200	43	40	82	20	1.1	191	276	9%
79	JAHIRHUSSAIN	38	M	0501170053	1.151	2.841	1.668	159	214	29	43	87	17	1.3	173	272	9%
80	JANAKIYAMMAL	50	F	2209160090	1.146	3.953	1.033	141	186	39	37	65	41	1.6	124	203	8%
81	SENTHILKUMAR	34	M	201701050008	1.677	3.189	0.721	194	214	43	43	108	34	0.9	155	224	9%
82	BALACHANDRAN	50	M	201612190090	0.390	2.524	0.271	135	200	57	40	38	33	1.1	139	215	8%
83	ANNAL	50	F	201612290055	0.798	2.564	1.208	153	200	54	40	59	62	2.1	208	264	9%
84	RAJAMMAL	47	F	2507160091	0.652	2.839	3.013	159	186	50	37	72	24	0.9	118	231	8%
85	MUNUSAMY	48	M	2209160037	3.972	2.699	5.280	112	171	46	34	32	22	1.4	117	260	8%
86	MAHALAKSHMI	37	F	0501170050	1.152	1.796	5.476	153	143	71	29	53	19	1.1	126	225	8%
87	MUNIYAMMAL	40	F	201612150064	0.941	2.841	1.757	176	157	32	31	113	29	0.8	110	210	8%
88	SUNDARI	50	F	201612110017	0.881	2.371	1.709	153	200	61	40	52	34	1.2	180	235	9%
89	PACHAIYAPPAN	49	M	20170180047	0.228	1.645	4.470	212	200	68	40	104	160	10.0	110	189	8%
90	RAMESHKUMAR	39	M	201701020065	1.150	3.247	0.263	176	171	71	34	71	41	1.2	123	210	8%

Sl. No.	NAME	AGE	SEX	OP/IP No.	FT3 PG/ML	FT4 NG/DL	TSH IU/ML	LIPID PROFILE MG/DL					UREA MG/DL	CREATINE MG/DL	FBS MG/DL	PPBS MG/DL	HBA1C %
								TC	TGL	HDL	VLDL	LDL					
91	PANJAVARNAM	50	F	201701020043	0.881	1.848	4.211	153	186	79	37	37	42	1.2	246	294	9%
92	POONGODI	25	F	201612160012	0.932	1.674	2.657	165	171	79	34	52	28	1.0	107	198	7%
93	KILIYAMMAL	50	F	201612300065	0.864	2.354	4.102	194	143	71	29	94	29	0.7	110	192	7%
94	DHANASINGH	49	M	1412160220	0.911	2.611	2.070	188	171	75	34	79	31	1.2	346	446	9%
95	SHAMALA	50	F	2811160019	0.692	2.633	2.013	135	214	68	43	24	33	1.0	92	187	7%
96	ARUMUGAM	49	M	1211160034	0.921	2.957	2.102	129	157	75	31	23	32	0.8	116	202	8%
97	ELUMALAI	50	M	201612240056	1.121	3.243	2.441	218	214	71	43	104	94	2.7	130	194	8%
98	VASUGI	50	F	1712160029	0.861	3.498	5.643	218	229	68	46	104	29	1.0	317	374	9%
99	GAJENDRAN	48	M	201612060038	0.867	2.245	3.490	147	143	36	29	82	42	1.3	139	263	9%
100	PARIPURNAM	47	F	1902160035	0.871	0.708	0.263	216	142	65	28	123	31	0.8	173	276	9%