A Dissertation on

A STUDY TO ESTIMATE THE PREVALENCE OF SUBCLINICAL HYPOTHYROIDISM IN NEWLY DETECTED TYPE 2 DIABETES MELLITUS AT A TERTIARY CARE HOSPITAL IN CHENNAI

Submitted to

THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY CHENNAI – 600032.

In partial fulfilment of the regulations

for the Award of the degree of

M.D. BRANCH - I

GENERAL MEDICINE

DEPARTMENT OF GENERAL MEDICINE

KILPAUK MEDICAL COLLEGE

CHENNAI – 600 010

APRIL 2017

CERTIFICATE

This is to certify that Dr.**G.SURENDHAR**, Post -Graduate Student (JULY 2014 TO JUNE 2017) in the Department of General Medicine, **KILPAUK MEDICAL COLLEGE**, Chennai- 600 010, has done this dissertation on "**A STUDY TO ESTIMATE THE PREVALENCE OF SUBCLINICAL HYPOTHYROIDISM IN NEWLY DETECTED TYPE 2 DIABETES MELLITUS AT A TERTIARY CARE HOSPITAL IN CHENNAI**" under my guidance and supervision in partial fulfilment of the regulations laid down by the Tamilnadu Dr.M.G.R. Medical University, Chennai, for M.D. (General Medicine), Degree Examination to be held in April 2017.

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DECLARATION

I, Dr.**G.SURENDHAR** declare that I carried out this work on "**A STUDY TO ESTIMATE THE PREVALENCE OF SUBCLINICAL HYPOTHYROIDISM IN NEWLY DETECTED TYPE 2 DIABETES MELLITUS AT A TERTIARY CARE HOSPITAL IN CHENNAI**" at Department of Medicine, Government Kilpauk Medical College Hospital. I also declare that this bonafide work or a part of this work was not submitted by me or any other for any award, degree, and diploma to any other university, board either in India or abroad.

This is submitted to The Tamilnadu Dr.M.G.R. Medical University, Chennai in partial fulfilment of the rules and regulation for the M. D. Degree examination in General Medicine.

DR.G.SURENDHAR

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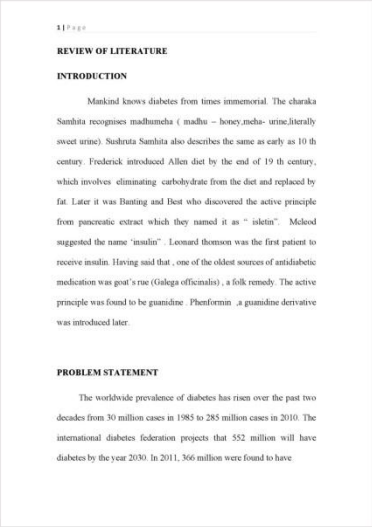

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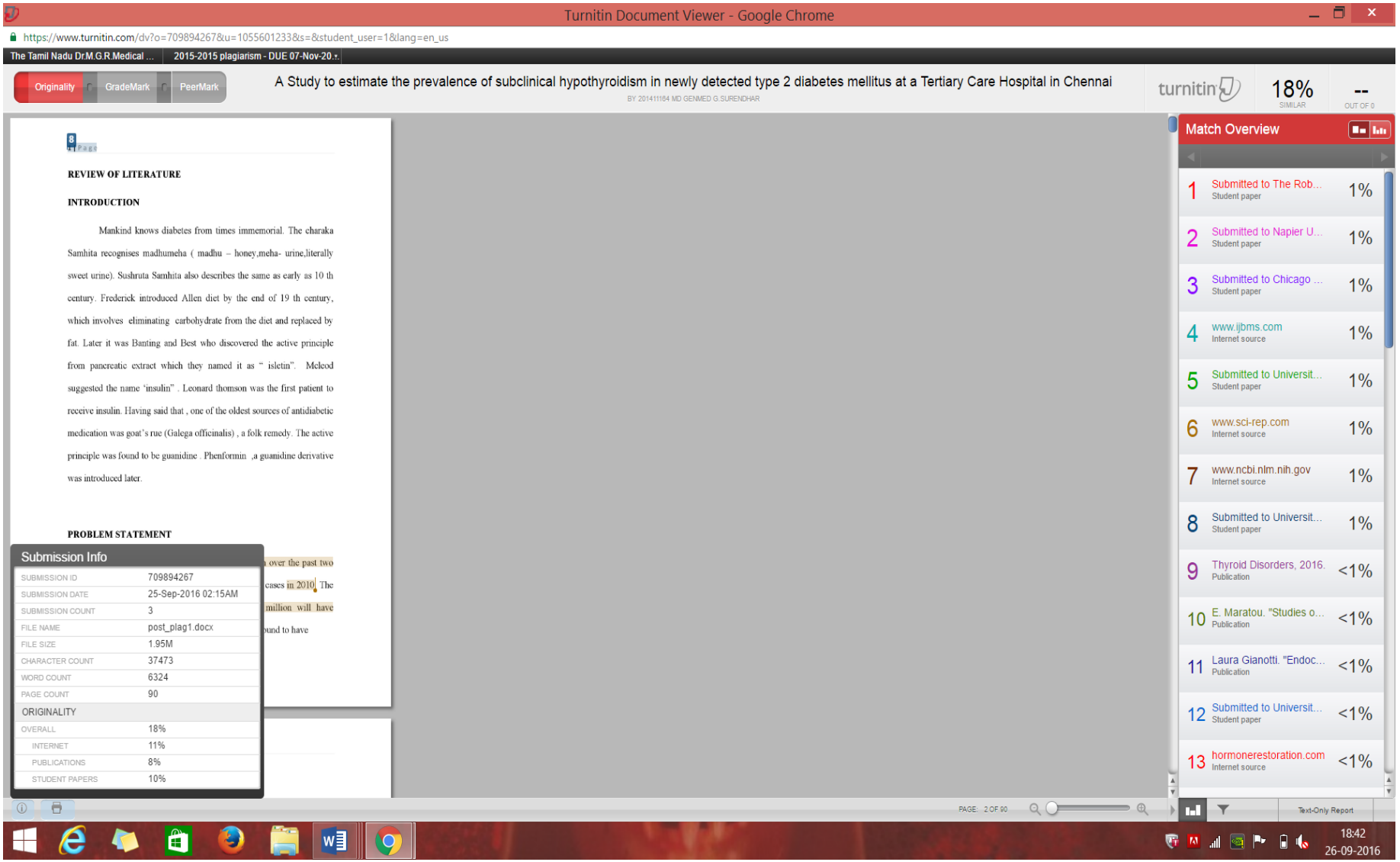
REVIEW OF LITERATURE

INTRODUCTION

Mankind knows diabetes from times immemorial. The charaka Samhita recognises madhumeha (madhu – honey,meha- urine,literally sweet urine). Sushruta Samhita also describes the same as early as 10 th century. Frederick introduced Allen diet by the end of 19 th century, which involves eliminating carbohydrate from the diet and replaced by fat. Later it was Banting and Best who discovered the active principle from pancreatic extract which they named it as " isletin". Mcleod suggested the name 'insulin" . Leonard thomson was the first patient to receive insulin. Having said that , one of the oldest sources of antidiabetic medication was goat's rue (Galega officinalis) , a folk remedy. The active principle was found to be guanidine . Phenformin ,a guanidine derivative was introduced later.

PROBLEM STATEMENT

The worldwide prevalence of diabetes has risen over the past two decades from 30 million cases in 1985 to 285 million cases in 2010. The international diabetes federation projects that 552 million will have diabetes by the year 2030. In 2011, 366 million were found to have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INTRODUCTION

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REVIEW OF LITERATURE

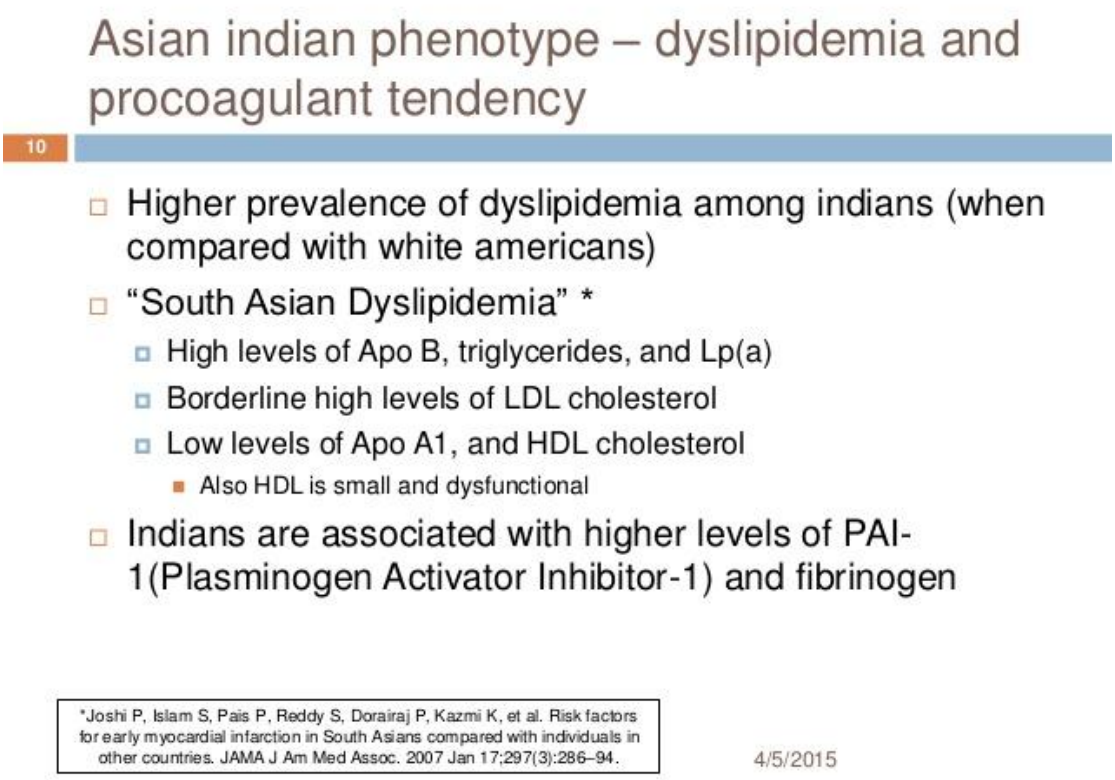
The worldwide prevalence of diabetes has risen over the past two decades from 30 million cases in 1985 to 285 million cases in 2010. The international diabetes federation projects that 552 million will have diabetes by the year 2030. In 2011, 366 million were found to have diabetes. Low and middle income countries contribute 80 % of them. The greatest number of people are found to be between 40 – 60 years of age. The prevalence of type 2 diabetes is rising due to increasing obesity,reduced activity levels as countries become more industrialised and aging of the population.

DESCRIPTION

Diabetes mellitus is a metabolic disorder characterised by the presence of chronic hyperglycemia accompanied by impairment in the metabolism of carbohydrates,lipids and proteins. Etiology of DM include defects in insulin secretion or response or both. Type 2 DM is the most common form characterised by increased glucose levels, resistance to insulin and insulin deficiency. Environmental factors ,genetic and behavioural risk factors may an important role .It can also be related to gestation and drugs.

Data from the Chennai urban population study (CUPS) and the Chennai Urban Rural Epidemiology Study provide valuable insight into the prevalence of many diabetes related complications. The prevalence of coronary artery disease was 21.4% among diabetics and 14.9% in those with impaired glucose tolerance . In another study ,retinopathy was seen in 21.2%, microalbuminemia in 41%,peripheral neuropathy in 15.3%,CAD in 7% and peripheral vascular disease in 7.4% of patients.

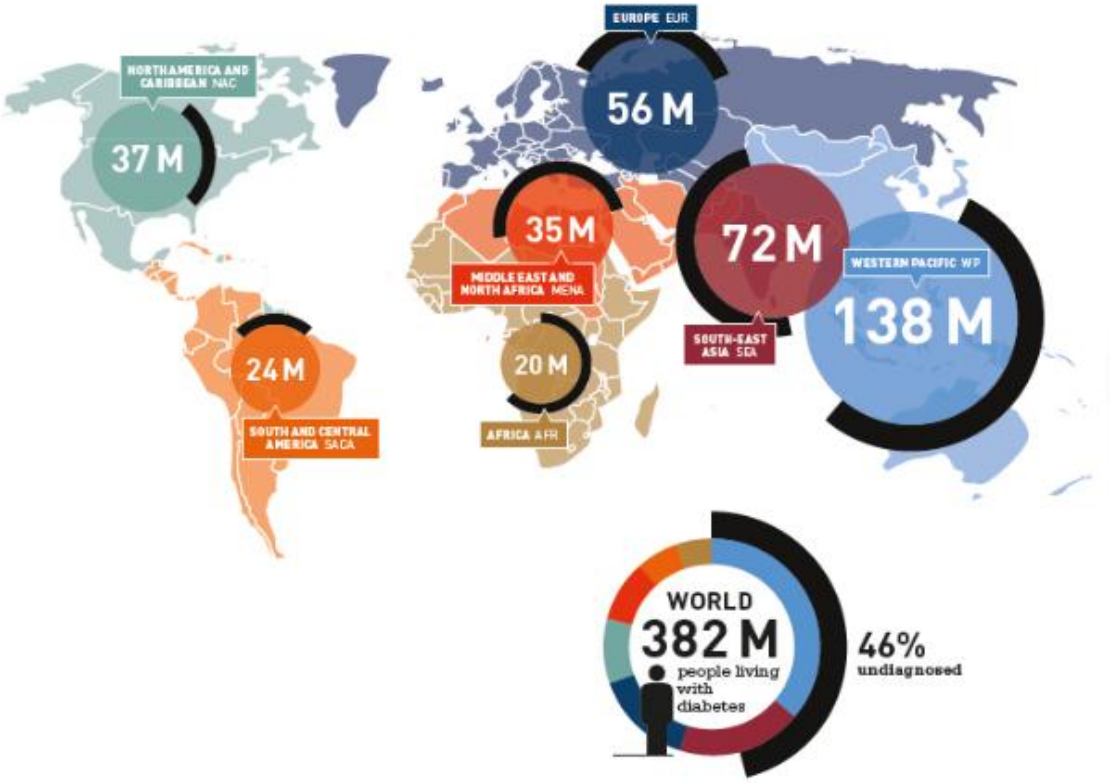
The high rate of complications could be due to variety of factors. Asian patients have higher genetic predisposition to develop type 2 diabetes. A unique combinationof clinical and biochemical parameters has been identified and labelled aas the “ASIAN INDIAN PHENOTYPE”.



EPIDEMIOLOGY

The worldwide prevalence has continued to increase dramatically. The frequency of diabetes has increased in the paediatric age group over the past two decades. Type 2 DM represents 10-40 % of all new cases of diabetes among children and adolescents which is found to be higher among girls than boys. Upto 80% of individuals with diabetes live in low income countries. The most individuals with diabetes are between the ages of 40 and 55 years in the world.

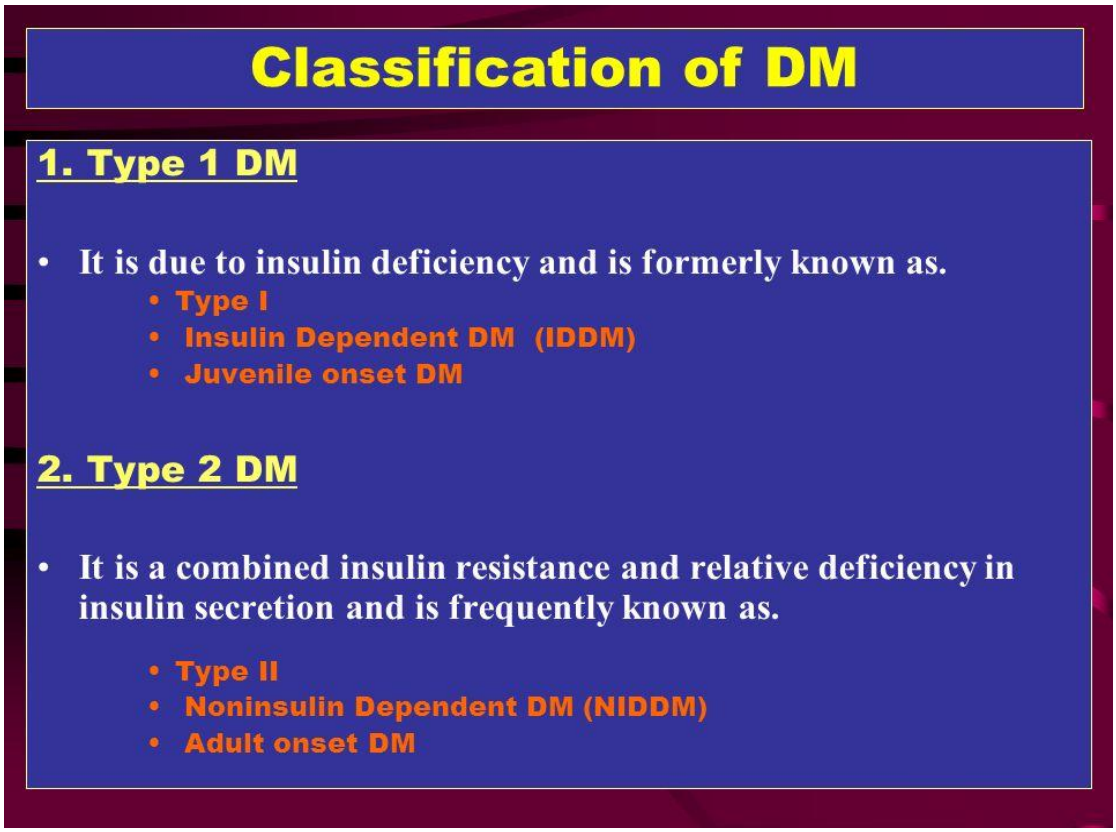
Number of people with diabetes by IDF Region, 2013



Etiological Classification of DM

i	Type 1 Diabetes	Immune mediated β cell destruction, idiopathic
ii	Type 2 Diabetes	Insulin resistance
iii	Genetic defect of β cell function	MODY
	Genetic defect in insulin processing or action	Defect in proinsulin conversion, insulin-gene & receptor mutation etc.
	Exocrine pancreatic defect	Pancreatitis, cystic fibrosis etc.
	Other endocrinopathies	Glucagonoma, hyperthyroidism, cushing syndrome etc.
	infections	CMV, Coxsackie B etc.
	Drugs	Steroids, thyroxin, β adrenergic etc.
	Genetic syndromes	Down, turner etc.
iv	Gestational Diabetes Mellitus	

Diabetic care 25, 2003



TYPE 1 DIABETES[3]

It is a multisystem disease with both biochemical and structural consequences.It is characterised by progressive inability of pancreas to secrete insulin because of autoimmune beta cell destruction. almost 85% have islet cell antibodies. It starts in children aged 4 years with peak incidence of 11-13 years.These patients are insulin dependant and unlike type 2 DM ,they are not obese.The classic symptoms are polyuria,polydipsia ,polyphagia and unexplained weight loss. They present initially with ketoacidosis. Treatment of type 1 DM requires insulin therapy lifelong.

TYPE 2 DIABETES[3]

Type 2 diabetes ,the most common form is characterised by relative insulin resistance ,insulin secretion defect,increased hepatic glucose production .We know that it is a polygenic disorder.More than 80% are obese . It usually follows a phase of impaired glucose homeostasis..Insulin Resistance syndrome (syndrome X) includes insulin resistance ,hypertension, dyslipidemia, obesity and accelerated cardiovascular disease.

Table 3. Major Diagnostic Criteria for Diabetes and Prediabetic or At-Risk States.*

Measure	American Diabetes Association		World Health Organization	
	Diabetes	Prediabetes	Diabetes	Impaired Glucose Regulation
Fasting plasma glucose	≥126 mg/dl	100–125 mg/dl (IFG)	≥126 mg/dl	110–125 mg/dl (IFG)
2-Hr plasma glucose (during an OGTT with a loading dose of 75 g)	≥200 mg/dl	140–199 mg/dl (IGT)	≥200 mg/dl	140–199 mg/dl (IGT)
Casual (or random) plasma glucose (in a patient with classic hyperglycemic symptoms)	≥200 mg/dl		≥200 mg/dl	
Glycated hemoglobin	≥6.5%	5.7–6.4%	≥6.5%	

* Data are adapted from the American Diabetes Association,[7,18] Alberti and Zimmet,[12] and the World Health Organization.[19] All listed plasma glucose levels are based on venous sampling. All tests (except for casual plasma glucose in a symptomatic patient) should be repeated and confirmed on a separate day. (The American Diabetes Association allows for glycated hemoglobin testing to be paired with fasting plasma glucose testing on the same day. If the values for both tests are in the diabetic range, the diagnosis is confirmed.) To convert the values for glucose to millimoles per liter, multiply by 0.05551. IFG denotes impaired fasting glucose, IGT impaired glucose tolerance, and OGTT oral glucose-tolerance test.

IMPAIRED GLUCOSE TOLERANCE[1]

It is a prediabetic state of hyperglycemia which precedes type 2 DM by several years. It is defined by WHO as " 2 hour glucose levels of 140-199 mg% om 75g oral glucose tolerance test. The fasting glucose may be either normal or mildly elevated. The risk of progression to diabetes is greater than for impaired fasting glucose.

IMPAIRED FASTING GLUCOSE[1]

It is also a state of prediabetes , in which the blood sugar level during fasting is higher than normal levels. ADA criteria defines it as fasting plasma glucose level from 100 mg/dL to 125 mg/dL.It is associated with insulin resistance and increased risk of cardiovascular pathology, although of lesser risk than impaired glucose tolerance . The average time for progression to frank diabetes is less than three years if not treated.

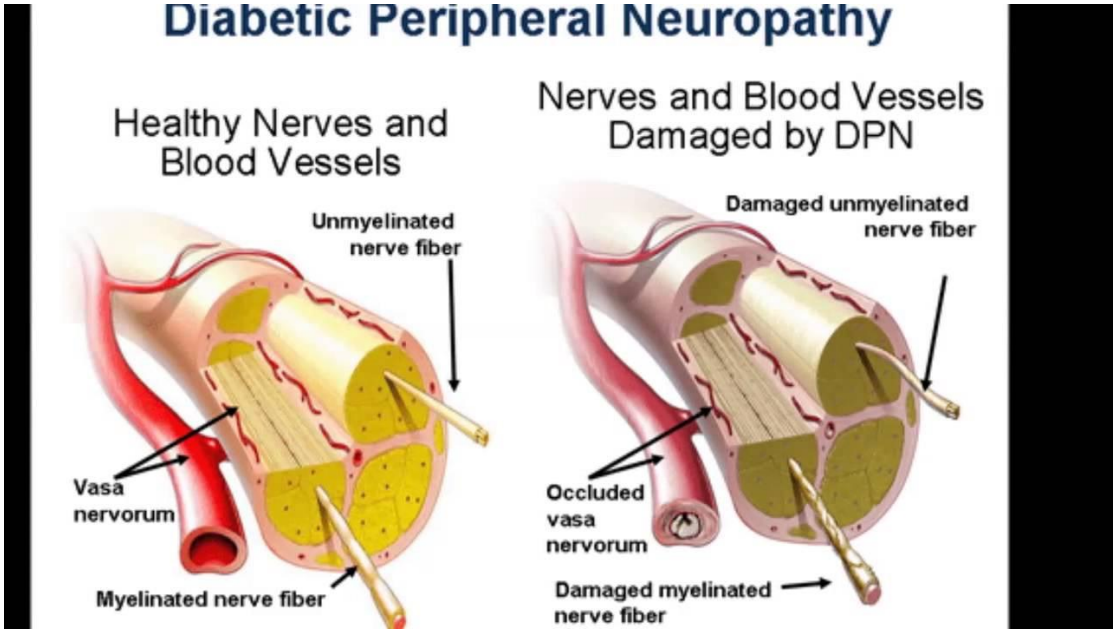
ACUTE COMPLICATIONS OF DM[2]

Diabetic Ketoacidosis (DKA)	Hyperglycemic Hyperosmolar State (HHS)
Absolute (or near-absolute) insulin deficiency, resulting in • Severe hyperglycemia • Ketone body production • Systemic acidosis	Severe relative insulin deficiency, resulting in • Profound hyperglycemia and hyperosmolality (from urinary free water losses) • No significant ketone production or acidosis
Develops over hours to 1-2 days	Develops over days to weeks
Most common in type 1 diabetes, but increasingly seen in type 2 diabetes	Typically presents in type 2 or previously unrecognized diabetes
	Higher mortality rate

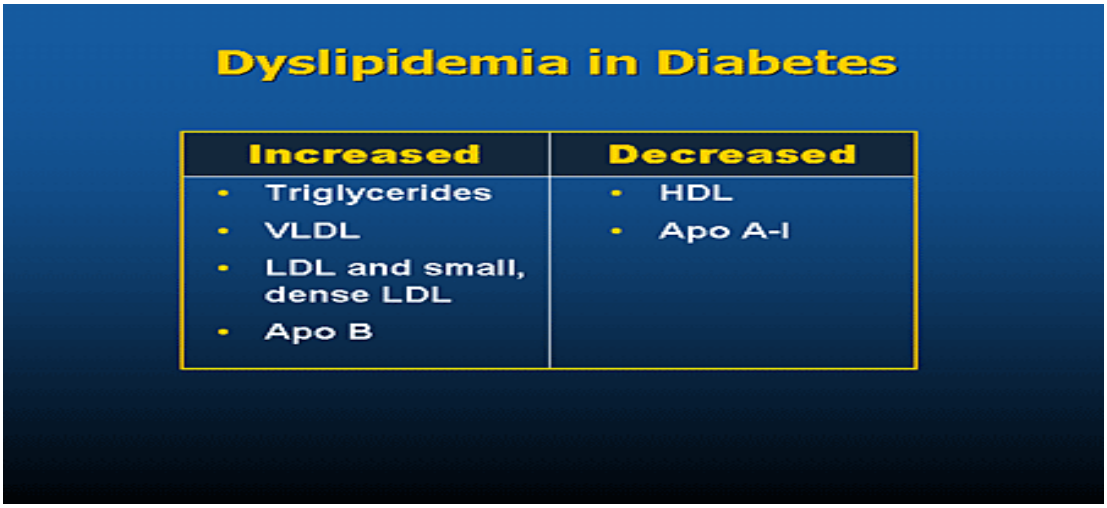
CHRONIC COMPLICATIONS OF DM[2]

1. microvascular – retinopathy
   Macular edema
   Sensory and motor neuropathy
   Autonomic neuropathy
   Nephropathy
2. macrovascular – coronary artery disease
   Peripheral arterial disease
   Cerebro vascular disease

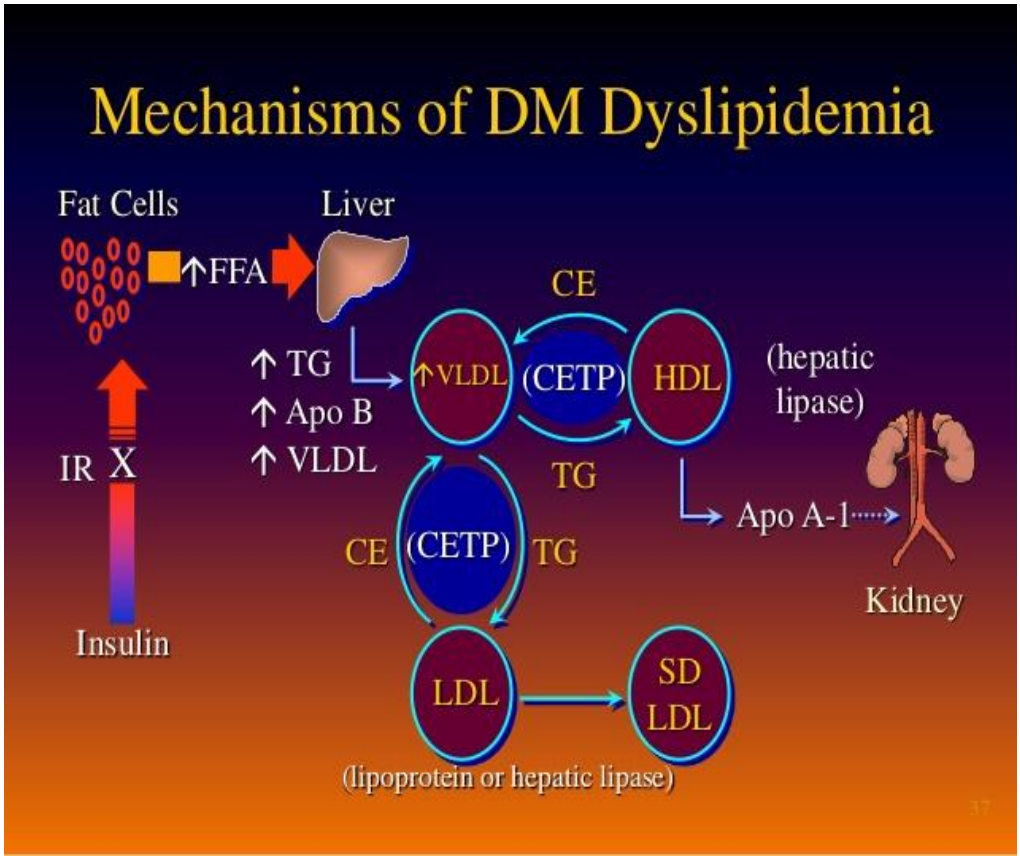
3. Gastroparesis, infections, cataracts, glaucoma and skin changes are other complications



DYSLIPIDEMIA IN DIABETES[5,6,7,8]



METABOLIC SYNDROME AND OBESITY[9]

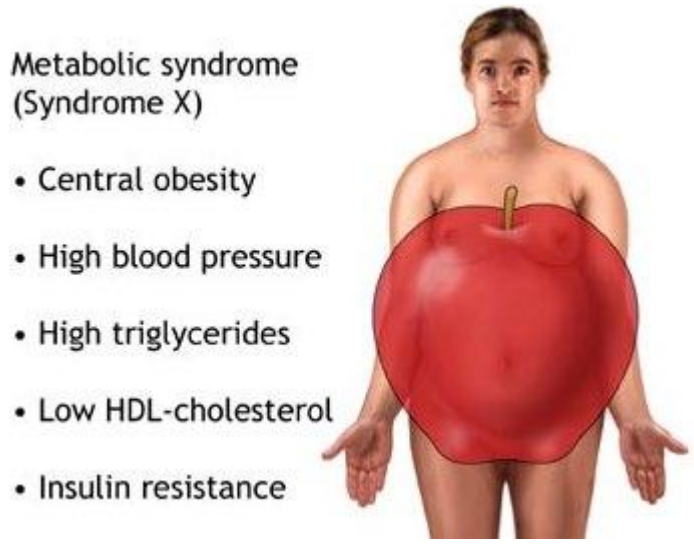


Diagnosis of the metabolic syndrome requires the presence of at least three of the following five criteria:

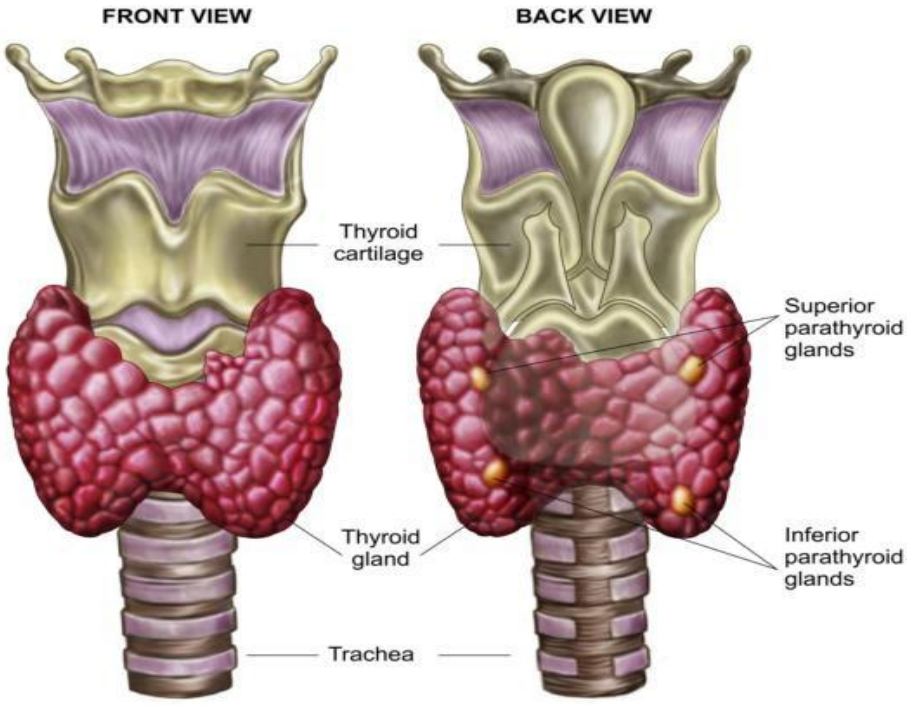
Table 2 Modified NCEP-ATP III diagnostic criteria

Criteria	Level
1: Body mass index*	> 25 kg/m²
2: HDL cholesterol	40 mg/dL
3: Triglycerides	> 150 mg/dL
4: Blood pressure	SBP > 130 mm Hg or DBP > 85 mm Hg
5: Fasting plasma glucose	> 100 mg/dL

NCEP-ATP III, National Cholesterol Education Program Adult Treatment Panel III; HDL, high-density lipoprotein; SBP, systolic blood pressure; DBP, diastolic blood pressure.
*The NCEP-ATP III diagnostic criteria require a waist circumference of greater than 40 inches in men and greater than 35 inches in women. At least 3 of the 5 listed diagnostic criteria are required for a diagnosis of metabolic syndrome.

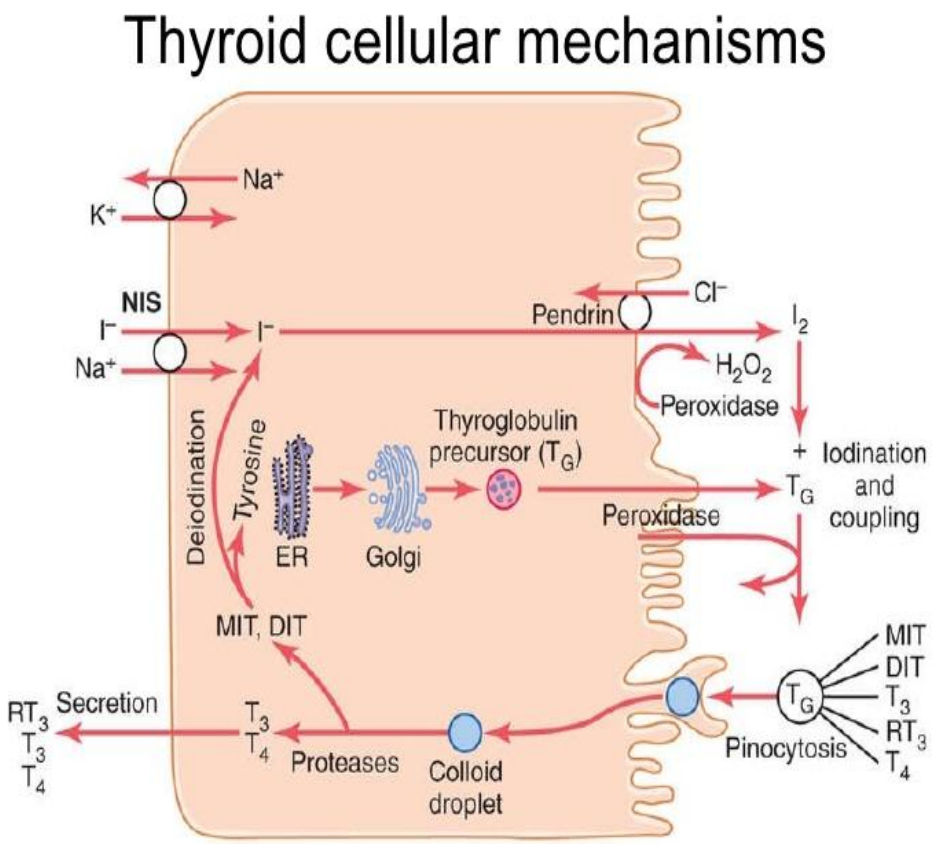

Metabolic syndrome
(Syndrome X)
• Central obesity
• High blood pressure
• High triglycerides
• Low HDL-cholesterol
• Insulin resistance

THYROID


FRONT VIEW
BACK VIEW
Thyroid cartilage
Superior parathyroid glands
Thyroid gland
Inferior parathyroid glands
Trachea

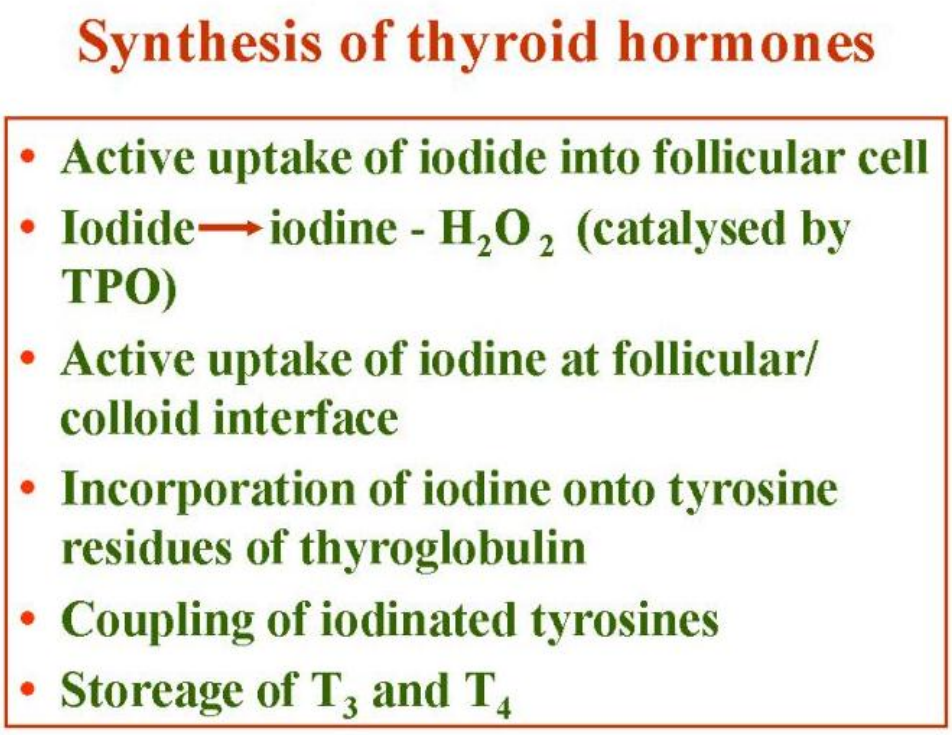
The thyroid is an endocrine gland responsible for the maintenance of a normal basal metabolic rate of the body. Anatomically it has two lobes which are connected together by an isthmus. Histologically it is made up of follicular cells which secrete thyroid hormones and parafollicular C cells which secrete calcitonin .It predominantly produces,thyroxine T4 and only small amount of triiodothyronine T3 which is stimulated by thyroid stimulating hormone(TSH).

BIOSYNTHESIS OF THYROID HORMONES

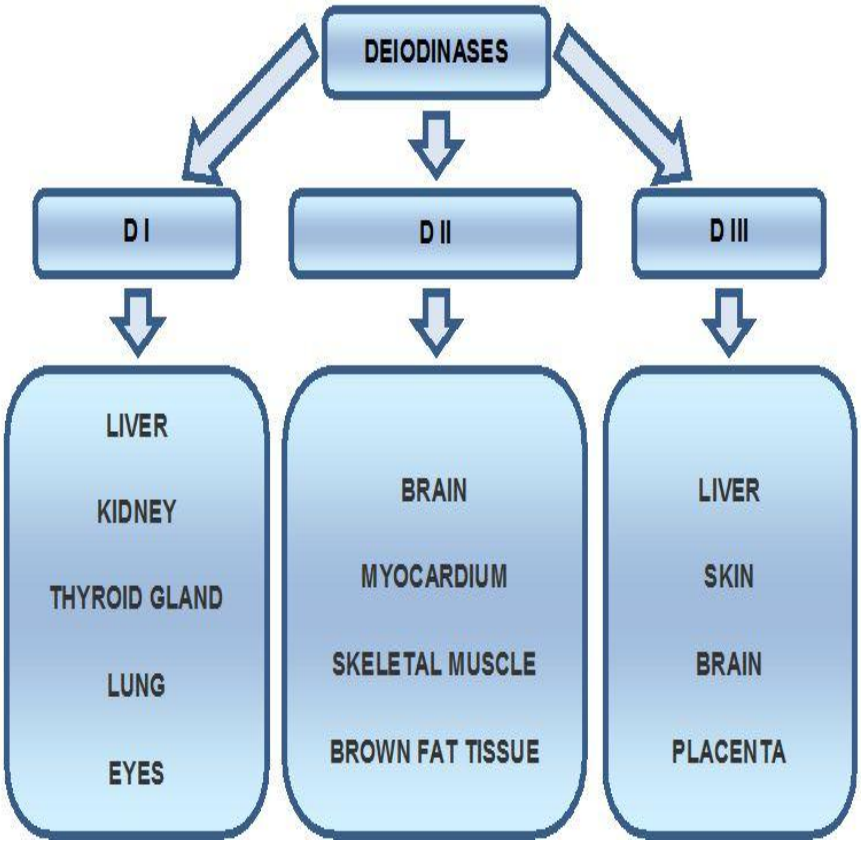


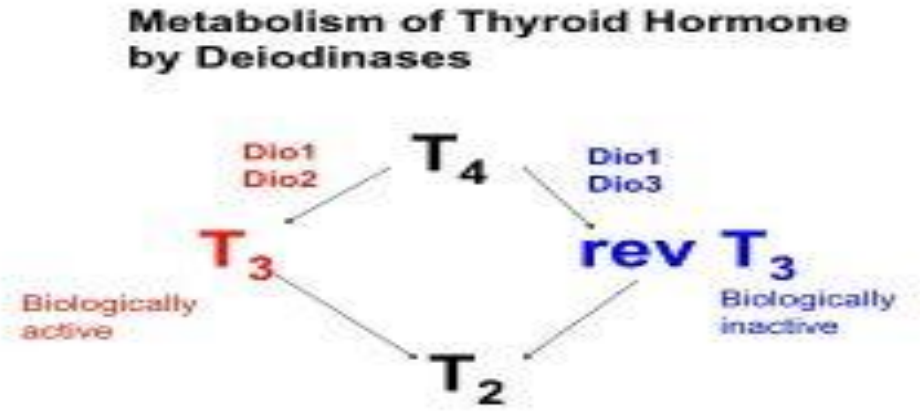
Organification, is a coupling reaction. In this reaction, iodotyrosine molecules are coupled together. Thyroxin (T4)is formed by coupling of two di-iodotyrosine molecules. Formation of tri-iodothyronine (T3) is by coupling of a di-iodotyrosine and a mono-iodotyrosine.

Tri-iodothyronine is biologically more active than T4 but the main production of T3 occurs outside the thyroid gland. The majority of T3 is produced peripherally by conversion of T4 to T3 by de-iodinaes.

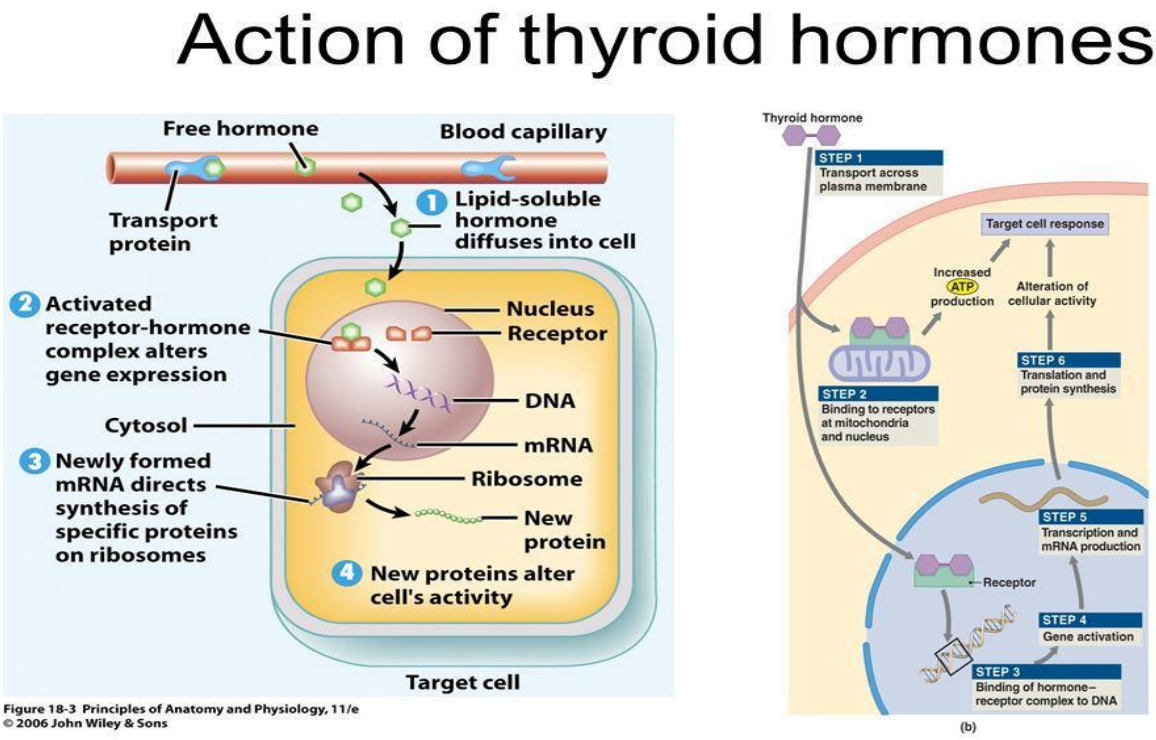


DEIODINASES



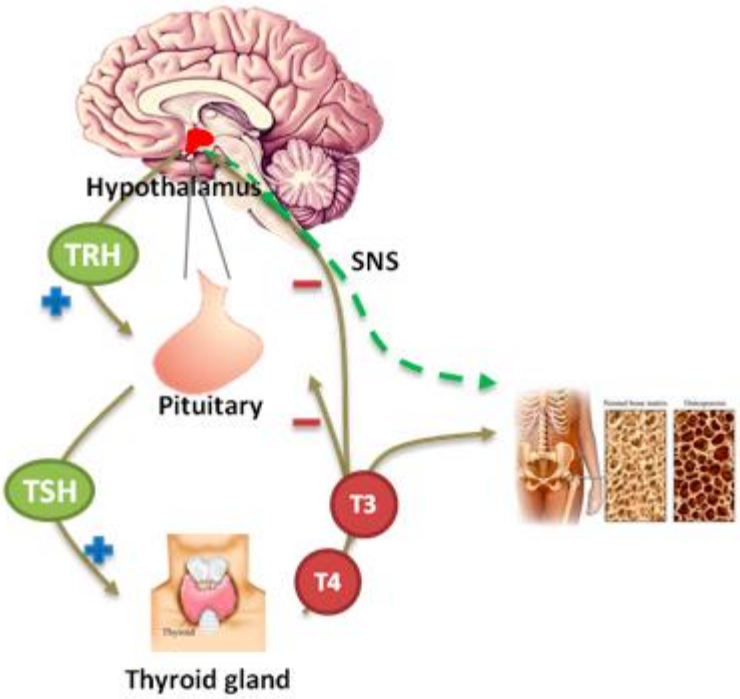


PHYSIOLOGICAL EFFECTS OF THYROID HORMONES[10]



Physiologic Effects of Thyroid Hormones.		
Target Tissue	**Effect**	**Mechanism**
Heart	Chronotropic Inotropic	Increased number of -adrenergic receptors
		Enhanced responses to circulating catecholamines
		Increased proportion of -myosin heavy chain (with higher ATPase activity)
Adipose tissue	Catabolic	Stimulated lipolysis
Muscle	Catabolic	Increased protein breakdown
Bone	Developmental	Promote normal growth and skeletal development
Nervous system	Developmental	Promote normal brain development
Gut	Metabolic	Increased rate of carbohydrate absorption
Lipoprotein	Metabolic	Formation of LDL receptors
Other	Calorigenic	Stimulated oxygen consumption by metabolically active tissues (exceptions: testes, uterus, lymph nodes, spleen, anterior pituitary)
		Increased metabolic rate

REGULATION OF THYROID AXIS[10]



Thyroid function is primarily regulated by circulating levels of pituitary TSH which in turn is increased by the hypothalamic hormone TRH and inhibited by free T4 and T3 in a negative feedback mechanism. TSH secretion is also inhibited by stress.

EXOGENOUS AND ENDOGENOUS FACTORS SUPPRESSING TSH SECRETION[11,12]

Inhibition of T4/T3 synthesis

Propylthiouracil

Methimazole

Inhibition of T4/T3 secretion

Lithium

Iodide

Amiadarone

Thyroiditis

Interferon

Interleukin 2

Sunitinib

Jod –basedow phenomenon

Iodide

Amiadarone

TSH suppression

Glucocorticoids

Dopamine agonists

Somatostatin analogs

Carbamazepine

FACTORS ASSOCIATED WITH ALTERED BINDING OF THYROXINE BY THYROXINE-BINDING GLOBULIN[11,12]

Familial excess of TBG which is a X linked inherited disorder.

Acquired : 1.increased binding:

Medications like estrogen, pregnancy ,cirrhosis,hepatitis etc

2.Decreased binding :

Androgens, Large doses of glucocorticoids, acromegaly, Nephrotic syndrome , Major systemic illness and Psychiatric illness.

HYPOTHYROIDISM[13,14]

Reduced production of thyroid hormone is the central feature of the clinical state called hypothyroidism. Primary hypothyroidism refers to permanent loss or destructionof the gland through autoimmune process or radiation injury.Secondary hypothyroidismis caused by insufficient stimulation of the gland by pituitary or hypothalamus. Primary hypothyroidism accountsfor 99% of cases.

Causes of hypothyroidism

Primary	Transient
Autoimmune hypothyroidism: Hashimoto's thyroiditis, atrophic thyroiditis	Silent thyroiditis, including postpartum thyroiditis
Iatrogenic: Treatment, subtotal or total thyroidectomy, external irradiation of neck for lymphoma or cancer	Subacute thyroiditis
Drugs: iodine excess (including iodine-containing contrast media and amiodarone), lithium, antithyroid drugs, *p*-aminosalicylic acid, interferon- and other cytokines, aminoglutethimide, sunitinib	Withdrawal of thyroxine treatment in individuals with an intact thyroid
Congenital hypothyroidism: absent or ectopic thyroid gland, dyshormonogenesis, TSH-R mutation	After ^{131}I treatment or subtotal thyroidectomy for Graves' disease
Iodine deficiency	**Secondary**
Infiltrative disorders: amyloidosis, sarcoidosis, hemochromatosis, scleroderma, cystinosis, Riedel's thyroiditis	Hypopituitarism: tumors, pituitary surgery or irradiation, infiltrative disorders, Sheehan's syndrome, trauma, genetic forms of combined pituitary hormone deficiencies
Overexpression of type 3 deoiodinase in infantile hemangioma	Isolated TSH deficiency or inactivity
	Bexarotene treatment
	Hypothalamic disease: tumors, trauma, infiltrative disorders, idiopathic

SYMPTOMS:

Tiredness

Dry skin

Hair loss

Poor memory

Feeling cold

Weight gain

Hoarse voice

Menorrhagia

Impaired healing

Paresthesia

Signs

Drycoarse skin

Puffy face,hands and feet

Alopecia

Bradycardia

Peripheral edema

Carpal tunnel syndrome

Delayed tendon reflexes

METABOLIC ABNORMALITIES IN HYPOTHYROIDISM[13,14]

Hypothyroidism causes low energy expenditure in metabolism and low heat production which results in basal metabolic rate to be low and intolerance to cold . High levels of protein in effusions and csf is explained by increased permeability of capillaries.

Effect on carbohydrates:

1. Decreased expression of GLUT4 transporter resulting in reduced disposition of glucose to skeletal muscle and adipose tissue.

2. Reduced gluconeogenesis

Effect on lipid:

1. Both synthesis and degradation are decreased with latter being relatively greater resulting in a net effect of accumulation of LDL and TGL.

2. Plasma free fatty acids are decreased and mobilisation of free fatty acids in response to fasting,catecholamines and growth hormone is impaired.

Effect on proteins :

1. Both the synthesisand degradation ofprotein are decreased, the latter especially so, with the result that nitrogen balance is positive.

2. The albumin pool is increased owing to decreased degradation of albumin.

SUBCLINICAL HYPOTHYROIDISM[15,16,17]

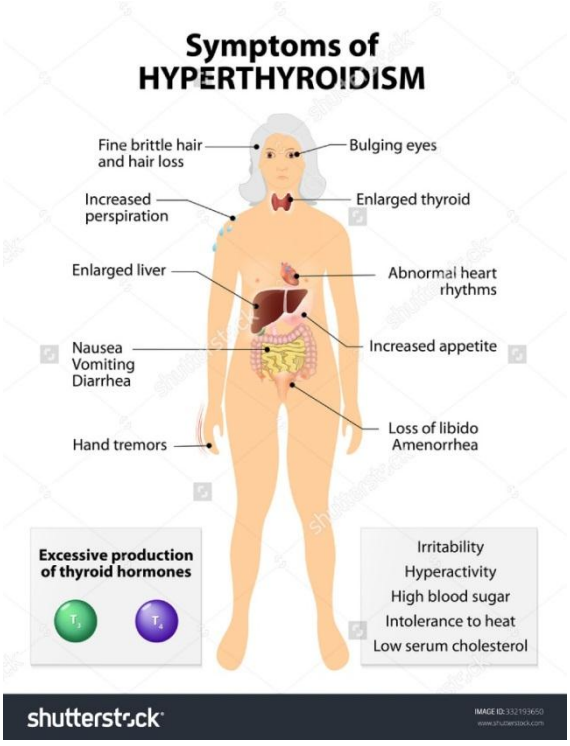
It is described as low normal ft4 and slightly elevated serum TSH level. The TSH elevation in such patients is modest ,with values between 4 and 15 mU/L ,although these patients with TSH greater than 10mU/L often have reduced ft4 and develop symptoms. the syndrome is seen most often in patients with early Hashimoto's disease and in 7-10 % of older woman.The risk of progression to overt hypothyroidism is related to magnitude of serum TSH levels and the presence of anti-TPO AB.The rate ranges from 3% to 8% per year. Factors which

predispose to rapid progression are elderly age, higher levels of TPO-AB,intercurrent infections, iodinated contrast agents and medications.

HYPERTHYROIDISM[15,16]

Hyperthyroidism is the condition that results from sustained overproduction and release of hormone by thyroid gland. **Thyrotoxicosis** refers to the classic physiologic manifestations of excessive thyroid hormones. Thyroiditis isnthe inflammation of the thyroid gland usually due to viral infections or autoimmunity.

Hyperthyroidism and thyroiditis must be differentiated from thyrotoxicosis caused by exogenous thyroid hormone whether iatrogenic or self administered. In thyrotoxicosis, the symptomsare due to excess hormones regardless of the source.



METABOLIC ABNORMALITIES IN HYPERTHYROIDISM[15,16]

1. The stimulation of metabolism and heat production is relected in increased basal metabolic rate, increased appetite and heat intolerance.
2. A state of chronic caloric and nutritional inadequacy
3. Synthesis and degradation of proteins are increased with latter to greater extent resulting in loss of weight,muscle wasting,proximal
4. muscle weakness.
5. Accelerated turn over of insulin aggravates pre-existing diabetes mellitus.
6. Both lipogenesis and lipolysis are increased with latter being to greater extent resulting in increased levels of free fatty acidsand glycerol and decrease in serum cholesterol.
7. Triglycerides are slightly increased.

SUBCLINICAL HYPERTHYROIDISM[15,16]

There are no signs of thyrotoxicosis but the serum TSH is subnormal despite normal serum free T4 concentration. Subclinical hyperthyroidism has most significant adverse effect on heart resulting in atrial premature beats and atrial fibrillation. It causes increased bone resorption in elderly women .

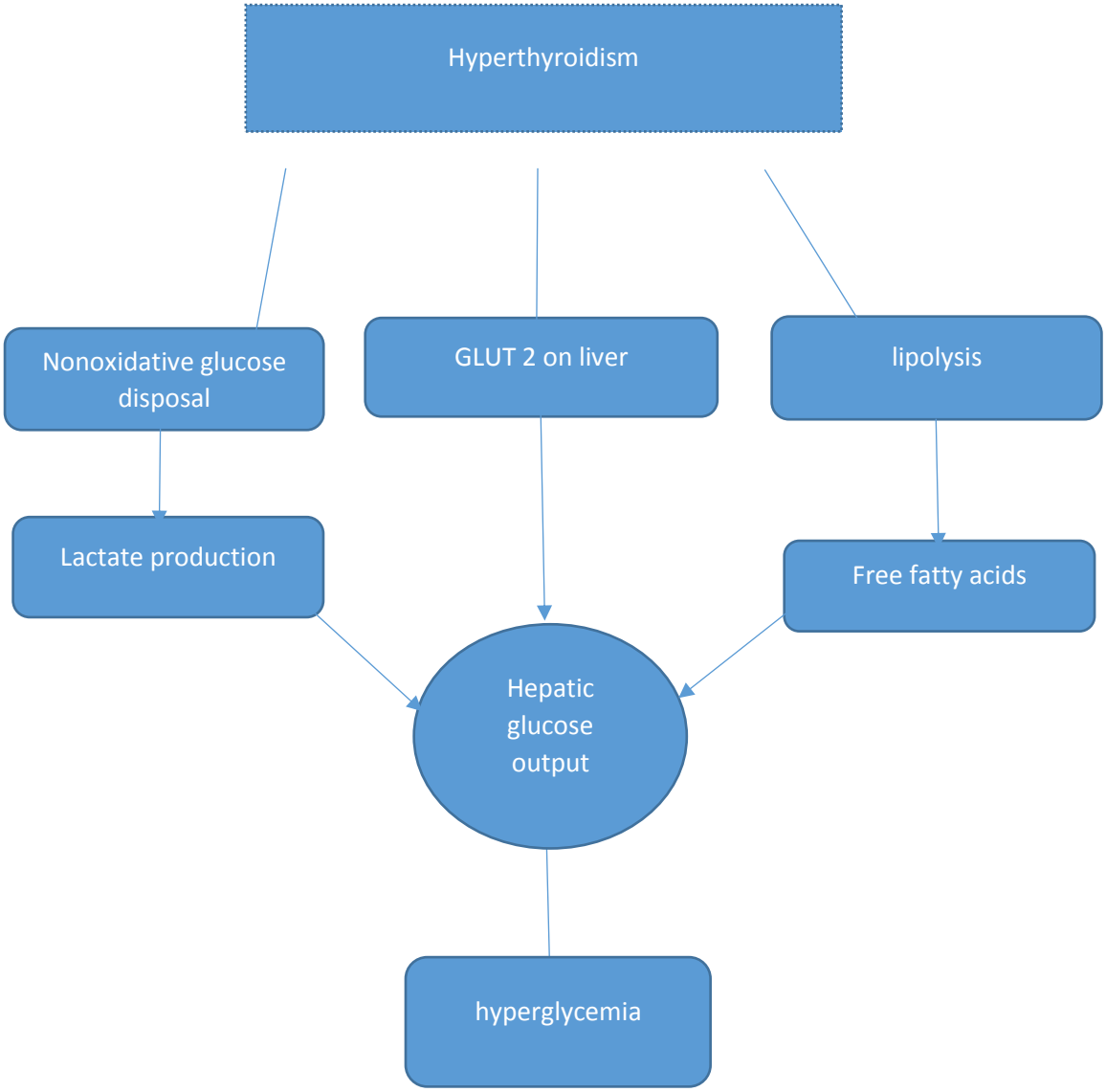
DIABETES AND THYROID DISEASES

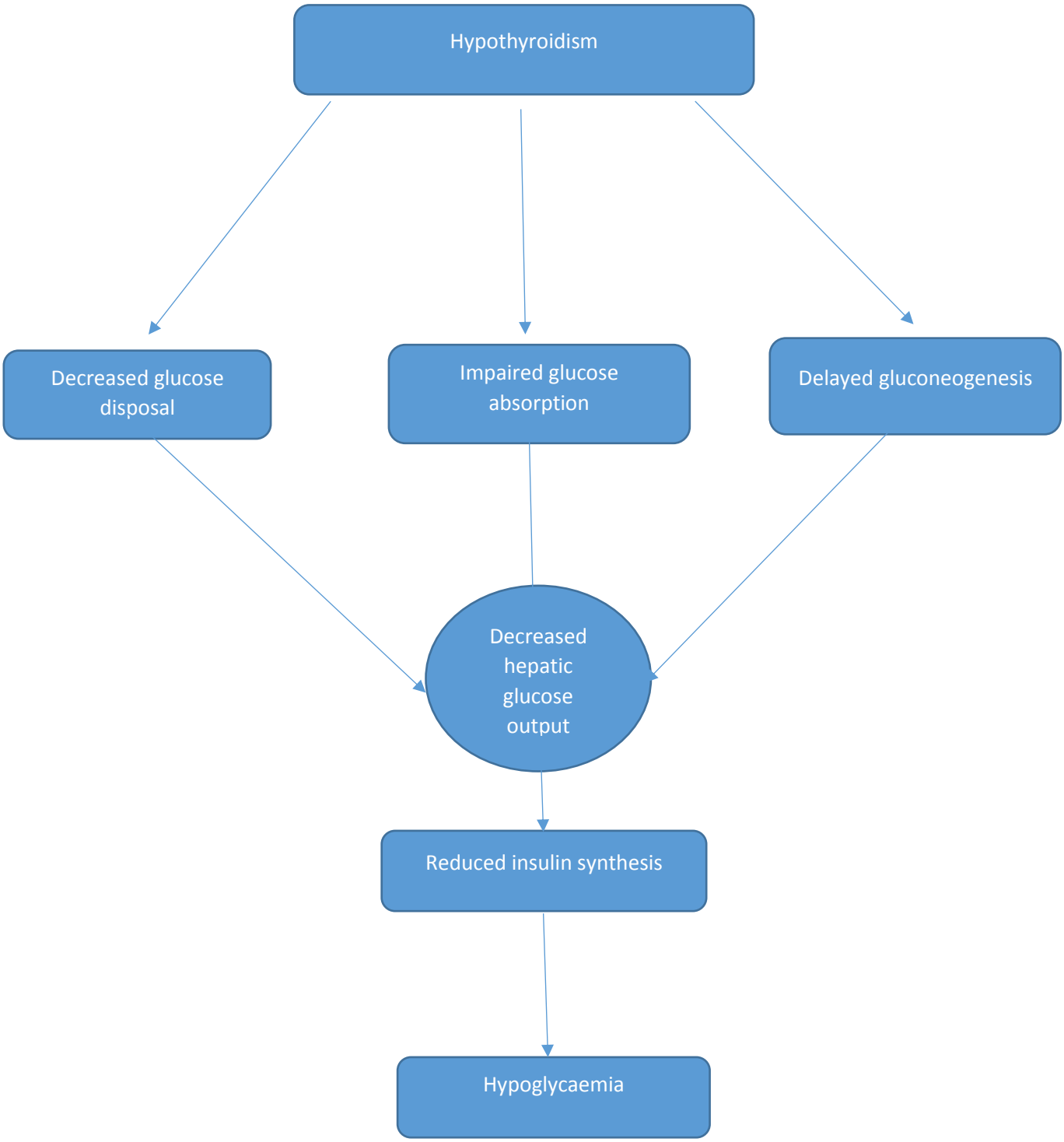
The underlying pathology of thyroid dysfunction intersects with that of diabetes. Thyroid problems are seen frequently in diabetics compared to general population.Patients who have one autoimmune disease are more susceptible to contract another autoimmune disease. Postpartum thyroiditis is more commonly seen in diabetic women than non diabetics. Thyroid dysfunction also leads to insulin resistance. In hyperthyroidism ,glucose control becomes very difficult and even insulin requirements become higher.

EFFECT OF DIABETES ON THYROID STATUS

In diabetic patients with normal thyroid profile ,the glycemic status influences the T3 response,basal TSH levels and TSH response to TRH. It is characterised by a state called “low T3 syndrome’’ ,where we have decreased total as well as free T3 levels,increased rT3,and T4 and TSH within normal limits. This is usually seen in diabetics owing to decreased peripheral conversion of T4 to T3. This state usually gets reverted with glycemic control though c-peptide negative patients may not show normal nocturnal TSH peak response.

EFFECT OF THYROID DYSFUNCTION ON GLYCEMIC STATUS




Hypothyroidism
Decreased glucose disposal
Impaired glucose absorption
Delayed gluconeogenesis
Decreased hepatic glucose output
Reduced insulin synthesis
Hypoglycaemia

ASSOCIATION BETWEEN DIABETES MELLITUS AND THYROID DISORDERS:

Abdel Rahman et al found that overall prevalence of thyroid diseases was 12.5% in type 2 diabetes mellitus group. The study suggested that diabetic patients should be screened for asymptomatic thyroid dysfunction.

Proces S et al found that in diabetic patients TSH was lower than in non diabetic subjects. They concluded that besides age and drugs, thyroid function tests can also be altered in diabetes mellitus and obesity.

Hage M, Zantout MS, Azar ST found that the two disorders diabetes and thyroid tend to coexist in patients. Both of them involve dysfunction of the endocrine system .

A. Handisurya, G. Pacini, A. Tura, A. Gessl, and A. KautzkyWiller, "Effects of T4 replacement therapy on glucose metabolism in subjects with subclinical (SH) and overt hypothyroidism (OH)," concluded that in both of them ,the basal levels of insulin is decreased whereas glucose stimulated insulin secretion is increased. [19]

G. Dimitriadis, P. Mitrou, V. Lambadiari et al., "Insulin action in adipose tissue and muscle in hypothyroidism," concluded that In hypothyroidism: 1) glucose intake in both muscle and adipose tissue becomes resistant to insulin; 2) inhibition of lipolysis by insulin is maintained; and 3) increased triglyceride levels is due to decreased clearance by the adipose tissue [20].

E. Maratou, D. J. Hadjidakis, M. Peppa et al., "Studies of insulin resistance in patients with clinical and subclinical hyperthyroidism,", concluded that In patients with HO and SHO: i) a comparable levels of resistance to insulin ii) insulin-induced rates of glucose transport in isolated monocytes were suppressed iii) these findings project the increased risk of cardiovascular disease, observed in patients with HO or SHO.[21]

R. Kadiyala, R. Peter, and O. E. Okosieme, "Thyroid dysfunction in patients with diabetes: clinical implications and screening strategies," International Journal of Clinical Practice,2010 concluded that the prevalence of thyroid disorders has increased in diabetic patients and exerts hazardous effect on the vital metabolic and cardiovascular functions. Hence is high time for a need to screen diabetics for thyroid disorders.

V. Lambadiari, P. Mitrou, E. Maratou et al., “Thyroid hormones are positively associated with insulin resistance early in the development of type 2 diabetes,” Endocrine, in 2011 suggested that

thyroid hormones may be part of the pathogenetic mechanism to explain metabolic derangement early in the development of type 2 diabetes.

AI M AND OBJECTIVES OF THE STUDY

A) To find out the prevalence of subclinical hypothyroidism in newly detected type 2 diabetes mellitus.

MATERIALS AND METHODS

- The present study titled **" A Study to estimate the prevalence of subclinical hypothyroidism in newly detected type 2 diabetes mellitus at a Tertiary Care Hospital in Chennai "** is carried out in the Department of Medicine and in the Department of Diabetology, kilpauk medical college and hospital (Chennai).
- **Study design :** Cross sectional study.
- **Period of study:** 6 months
- **Study area**: Govt.Kilpauk Medical College

Materials :

Questionnaire, BMI calculation, Blood pressure, FBS,PPBS, Blood Urea, Serum creatinine,, Urinalysis, ECG, Fasting lipid profile, Thyroid profile(FT3, FT4 and TSH).

Study group :

The study group includes persons who are newly detected diabetes mellitus without known thyroid disorders attending the outpatient departments of medicine who meet the inclusion criteria.

Sample size :

The prevalence of subclinical hypothyroidism in diabetes is 15%. With a absolute accuracy of 6 , the sample size calculated as per the formula is **140.**

N= z2 x p x q/c2 = 2x2x15x85/6x6 = 141

Inclusion criteria:

Newly detected type 2 diabetes mellitus subjects of age > 25 years who gave informed consent to participate in the study.

Exclusion criteria:

- Patients not willing for study
- Known diabetics
- Patients with known thyroid disease
- Patients with chronic renal failure and Diabetic nephropathy.
- Patients with acute illness(sepsis, acute MI, severe heart failure, recent admission in intensive care unit)

- Patients with hepatic dysfunction.
- Pregnancy
- Patients on treatment with drugs interfering with thyroid function (amiodarone, propranolol, corticosteroids and oral contraceptives)

All patients in the study group were selected without any bias for sex,duration. A thorough history was recorded with particular emphasis on symptoms of diabetes , hypothyroidism and hyperthyroidism. The presence of associated illness like coronary artery disease, hypertension and cerebrovascular accident were noted. Family history regarding diabetes mellitus was also included.

METHODOLOGY

All patients who are newly diagnosed as diabetic will be taken for study. After getting consent ,under aseptic precautions ,10 ml of venous blood will be collected from each patient and sent to the department of biochemistry,KMCH.

a.4ml – thyroid function kit

b.2ml - fbs,renal function test

c.2ml - liver function test

d.2ml – lipid profile

BMI calculation

Body mass index (BMI) is calculated with height and weight of the subject using the following formula.

BMI= weight (kg) / height (m)2

Blood sugar

Both fasting and postprandial blood sugar are estimated by Glucose oxidase method and read at 505/670 nm.

Renal function test

The Blood Urea in this study was estimated using DAM method (Diacetyl Monoxime). Serum creatinine was estimated using Modified Jaffe's method.

Urinalysis

Urine sample is collected for urine routine analysis which includes sugar, protein, cytology and urinary sediments.

Lipid Profile

Total cholesterol,Triglyceride (TGL), levels will be analysed in the early morning fasting Blood Sample. Methods used:

1. Total cholesterol- CHOD POD METHOD

2. Triglycerides - Enzymatic calorimetric method

Thyroid Profile

Estimation done in fasting serum sample.

Methods used:

1.TSH - ELISA

2. FT3 & FT4 - ELISA

DEFINITIONS

Diabetes Mellitus:

Symptoms of diabetes plus **random plasma glucose concentration - 200** mg/dl.Random is defined as any time of day without regard to time since last meal. The classic symptoms of diabetes include polyuria, polydipsia and unexplained weight loss (or)**FPG -126 mg/dl** .

Fasting is defined as no caloric intake for at least 8 hours. (or) **2 hours post load glucose -200 mg/dl** during an OGTT. The test should be performed as described by WHO, using a glucose load containing the equivalent of 75 gm anhydrous glucose dissolved in water.

In the absence of unequivocal hyperglycaemia these criteria should be confirmed by repeat testing on a different day.

Systemic Hypertension (As per the JNC VII Guidelines):

Subjects on medications for hypertension and those who had a systolic blood pressure of 140 mmHg and / or diastolic blood pressure mmHg are considered to have hypertension.

Dyslipidemia:

ATP IV guidelines developed by the National Cholesterol Education Program have been used to detect dyslipidemia in the study subjects.

THYROID PROFILE

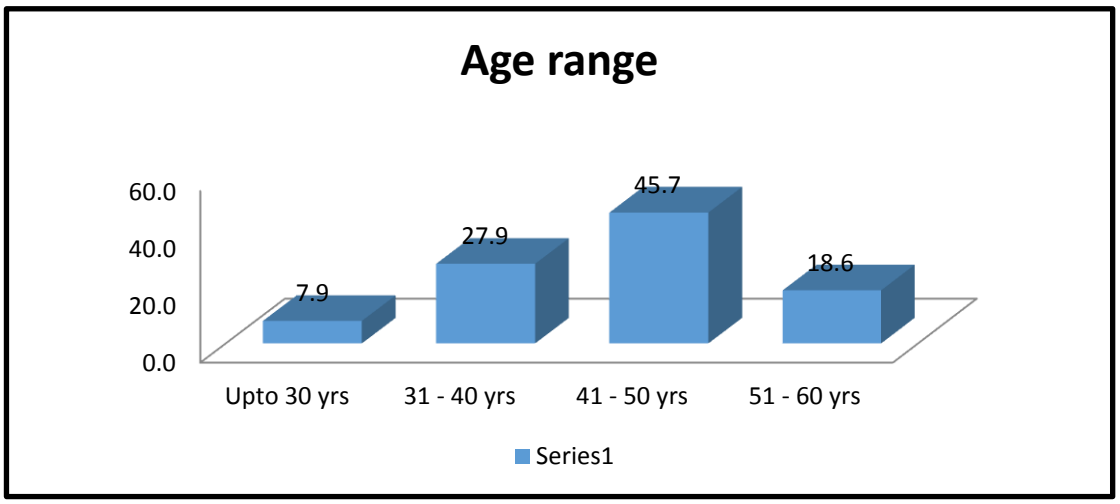
- Reference values: FT3 : 2.4-4.2 pg/ml TSH : 0.34-4.25mIU/ml
- FT4 : 0.7- 1.24 ng/dl
- **Overt** hypothyroidism is defined as TSH >5.5 mIU/ml with FT4 < 0.7 ng/dl.
- **Subclinical hypothyroidism** is defined as TSH between 5 - 15mIU/ml with normal FT3 and FT4 levels with or without symptoms.

RESULTS AND ANALYSIS

The collected data were analysed with IBM.SPSS statistics software 23.0 Version. To describe about the data descriptive statistics frequency analysis, percentage analysis were used for categorical variables and the mean & S.D were used for continuous variables. To find the significance in categorical data Chi-Square test was used. In the above statistical tool the probability value .05 is considered as significant level.

DISTRIBUTION OF CASES ACCORDING TO AGE RANGE

Valid	Frequency	Percent	Valid Percent	Cumulative Percent
Upto 30 yrs	11	7.9	7.9	7.9
31 - 40 yrs	39	27.9	27.9	35.7
41 - 50 yrs	64	45.7	45.7	81.4
51 - 60 yrs	26	18.6	18.6	100.0
Total	140	100.0	100.0	



Among the study population, 7.9 % belong to age group of less than 30 years, 27.9% belong to age group 31-40 years, 45.7% belong to 41-50 years and 18.6% belong to 51-60 years.

MEAN AGE OF STUDY POPULATION

Descriptive Statistics

	N	Minimum	Maximum	Mean	Std. Deviation
AGE	140	26	58	43.63	7.644
Valid N	140				

The table shows ,among the study population, the minimum age was 26 years and the maximum age was 58 years with the mean being 43.63 years.

MEAN AGE OF FEMALE

Descriptive Statistics FEMALE					
	N	Minimum	Maximum	Mean	Std. Deviation
AGE	78	26	56	44.96	7.430
Valid N (listwise)	78				

From the table ,we see that the minimum age of the female in the study is 26 years and maximum age is 56 years.

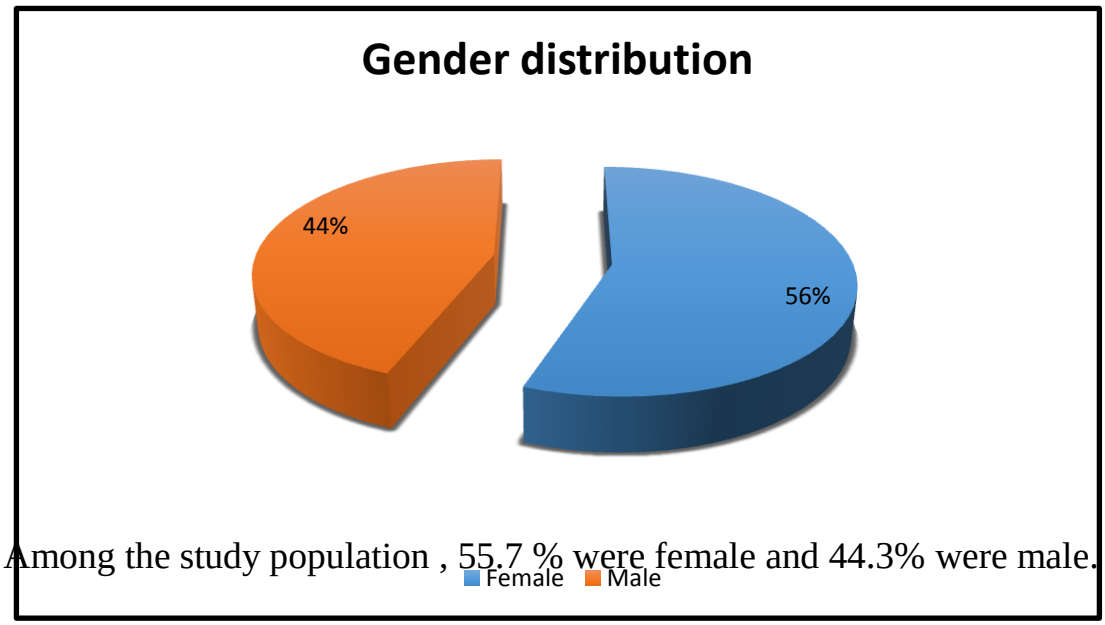
Descriptive Statistics MALE

	N	Minimum	Maximum	Mean	Std. Deviation
AGE	62	28	58	41.95	7.638
Valid N (listwise)	62				

From the table , we see that minimum age of the male among the study group is 28 and the maximum is 58 years with the mean being 41.95.

DISTRIBUTION OF CASES ACCORDING TO SEX

SEX					
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Female	78	55.7	55.7	55.7
	Male	62	44.3	44.3	100.0
	Total	140	100.0	100.0	

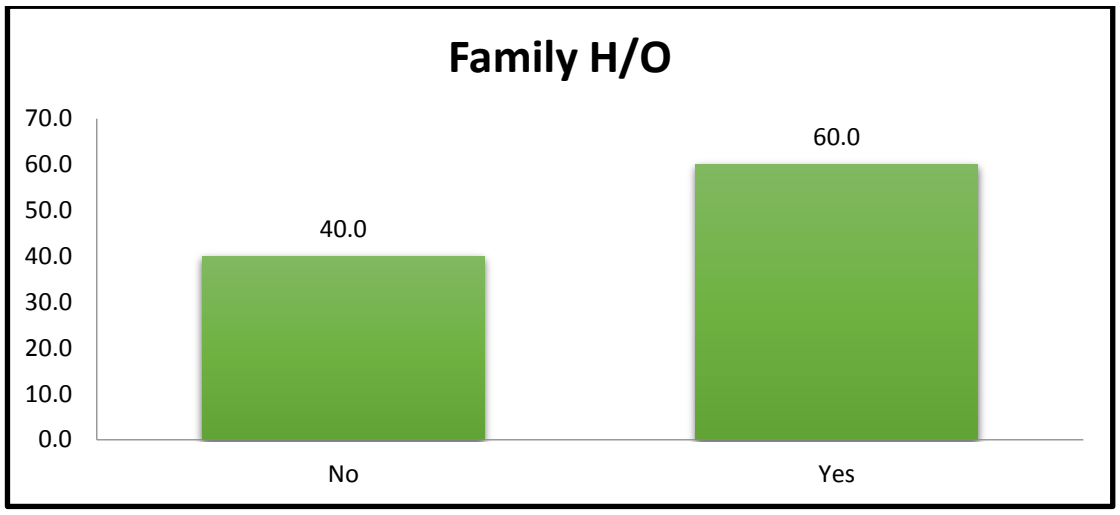


Among the study population , 55.7 % were female and 44.3% were male.

DISTRIBUTION OF CASES ACCORDING TO FAMILY HISTORY OF DIABETES

FAMILY H/O

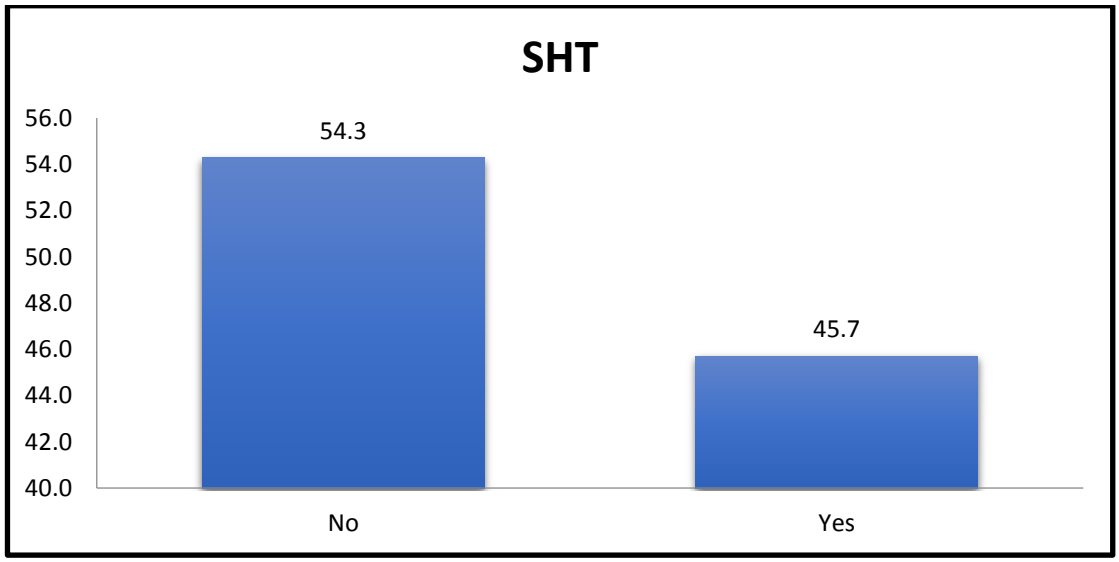
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	No	56	40.0	40.0	40.0
	Yes	84	60.0	60.0	100.0
	Total	140	100.0	100.0	



From the table and bar diagram, we see that among the study population with recently detected diabetes, 84% had family history and 56% did not have family history of diabetes.

DISTRIBUTION OF CASES ACCORDING TO SYSTEMIC HYPERTENSION

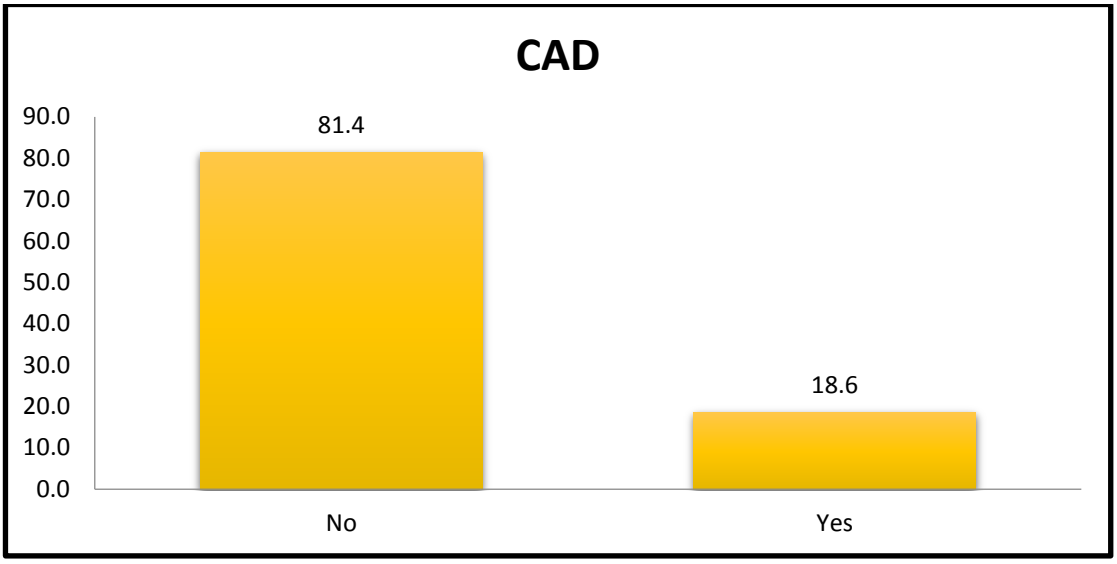
SHT					
		Frequency	**Percent**	**Valid Percent**	**Cumulative Percent**
Valid	No	76	54.3	54.3	54.3
	Yes	64	45.7	45.7	100.0
	Total	140	100.0	100.0	



The above bar diagram shows that 54.3% among the study population had systemic hypertension and 45.7% did not have hypertension.

DISTRIBUTION OF CASES ACCORDING TO CORONARY ARTERY DISEASE(CAD)

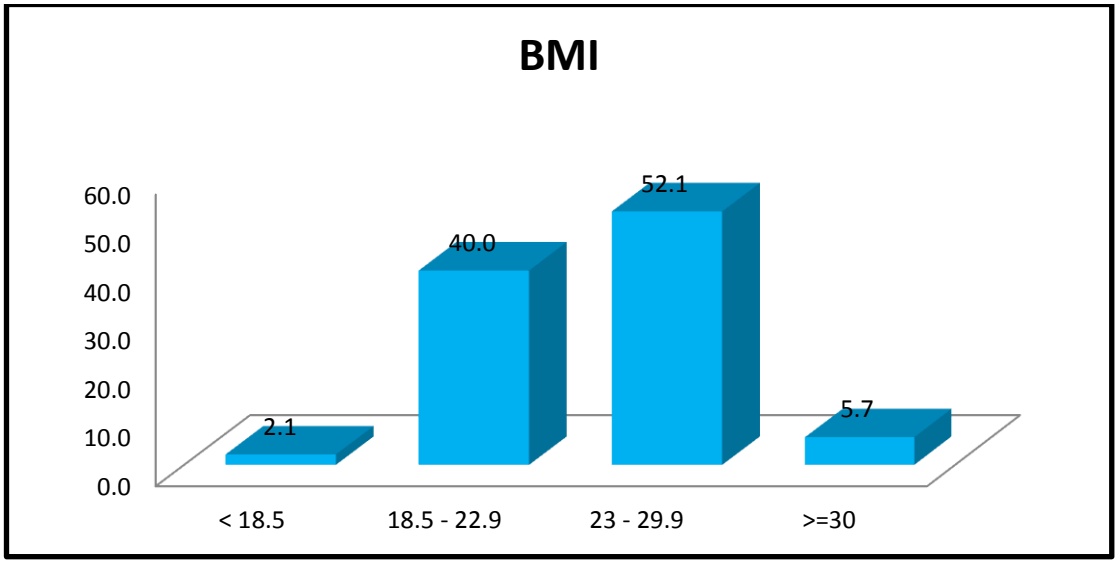
CAD					
		Frequency	**Percent**	**Valid Percent**	**Cumulative Percent**
Valid	No	114	81.4	81.4	81.4
	Yes	26	18.6	18.6	100.0
	Total	140	100.0	100.0	



From the bar diagram , we see that 18.6% among the study population had coronary artery disease and 81.4% did not have CAD.

DISTRIBUTION OF CASES ACCORDING TO BODY MASS INDEX(BMI)

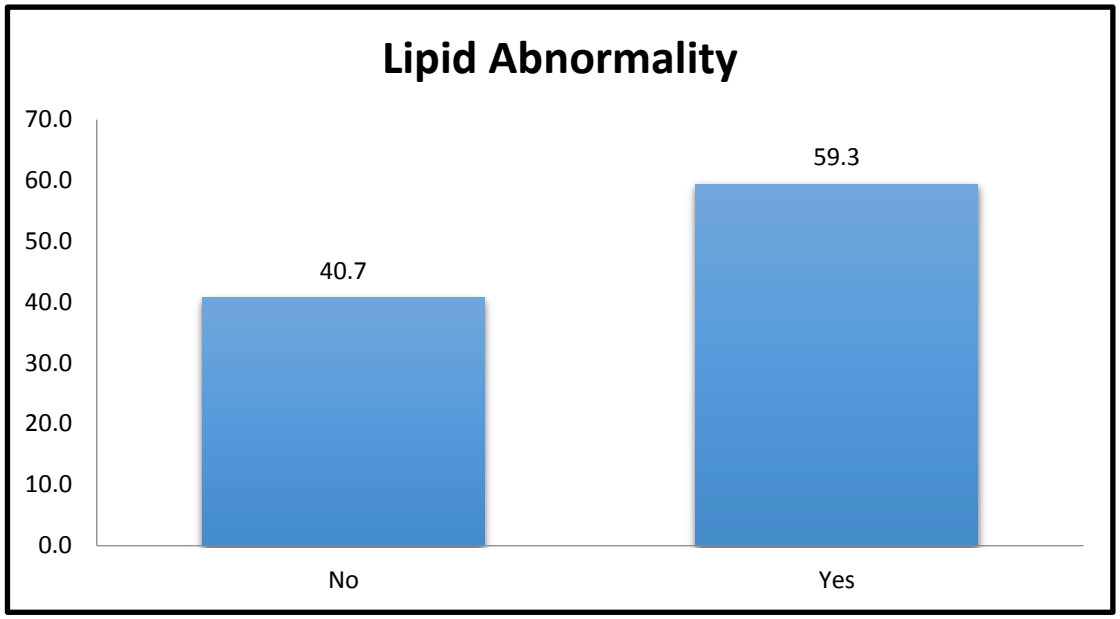
BMI		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	< 18.5	3	2.1	2.1	2.1
	18.5 - 22.9	56	40.0	40.0	42.1
	23 - 29.9	73	52.1	52.1	94.3
	>=30	8	5.7	5.7	100.0
	Total	140	100.0	100.0	



The above bar diagram shows that 2.1% belong to BMI <18.5,40%belong to BMI 18.5-23, 52.1% have BMI 23-30 and 5.7 % have BMI >30. The major portion of strudy population have BMI in the range of 23-30.

DISTRIBUTION OF CASES CCORDING TO LIPID ABNORMALITY

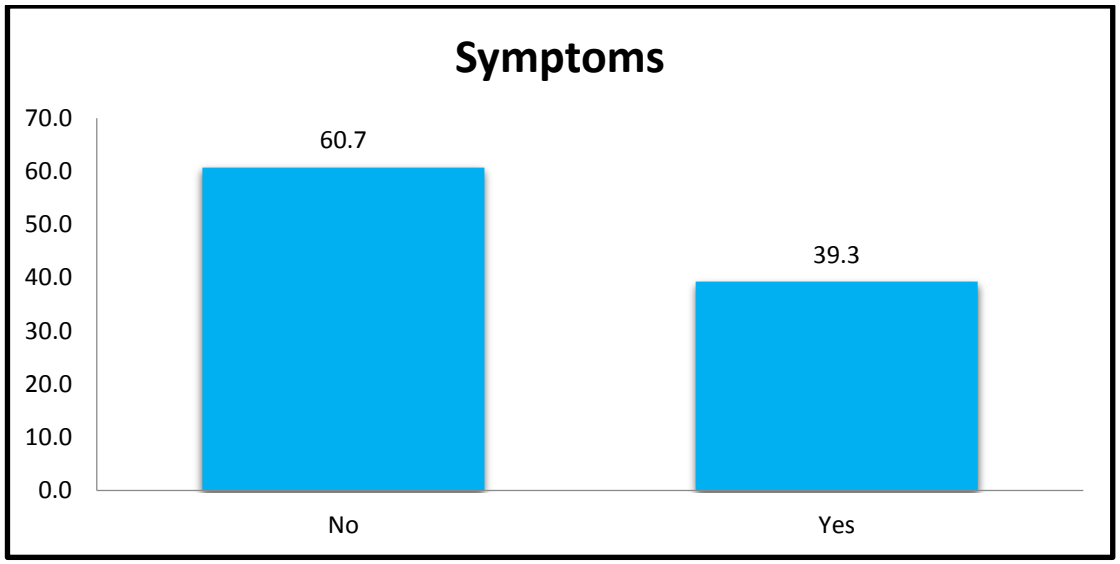
LIPID ABNORMALITY					
		Frequency	**Percent**	**Valid Percent**	**Cumulative Percent**
Valid	No	57	40.7	40.7	40.7
	Yes	83	59.3	59.3	100.0
	Total	140	100.0	100.0	



The above bar diagram shows 59.3% of the study population had abnormality in their lipid profile and 40.7% had normal profile.

DISTRIBUTION OF CASES ACCORDING TO SYMPTOMS

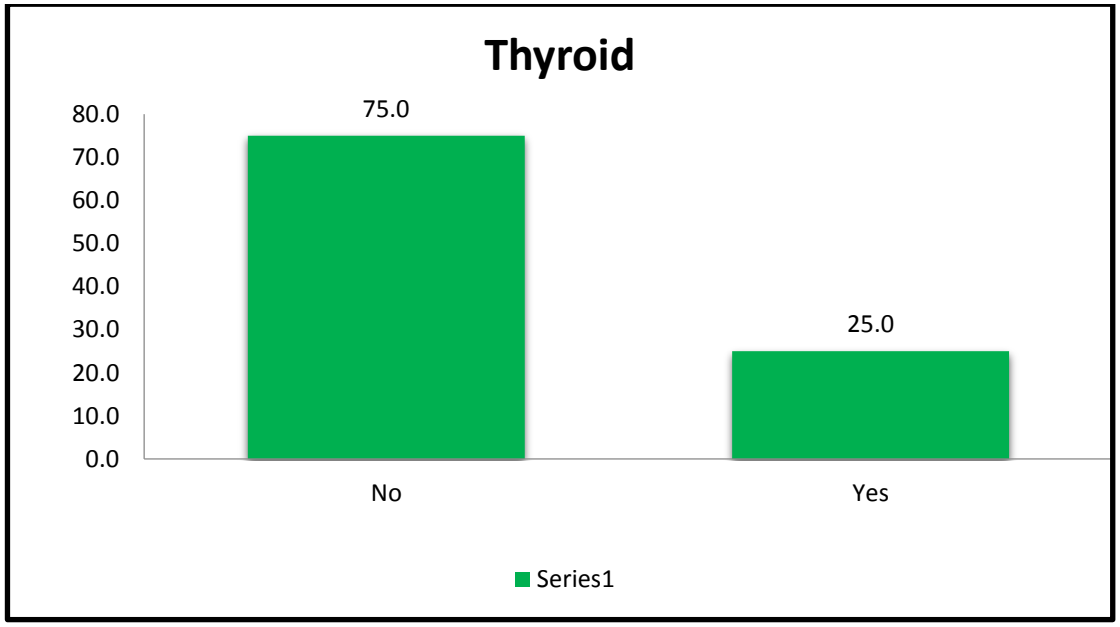
SYMPTOMS					
		Frequency	**Percent**	**Valid Percent**	**Cumulative Percent**
Valid	No	85	60.7	60.7	60.7
	Yes	55	39.3	39.3	100.0
	Total	140	100.0	100.0	



From the bar diagram and the table given above ,we can see 60.7% of the study population did not have symptoms of thyroid sysfunction whereas only 39.3% had symptoms.

DISTRIBUTION OF CASES ACCORDING TO THYROID ABNORMALITY

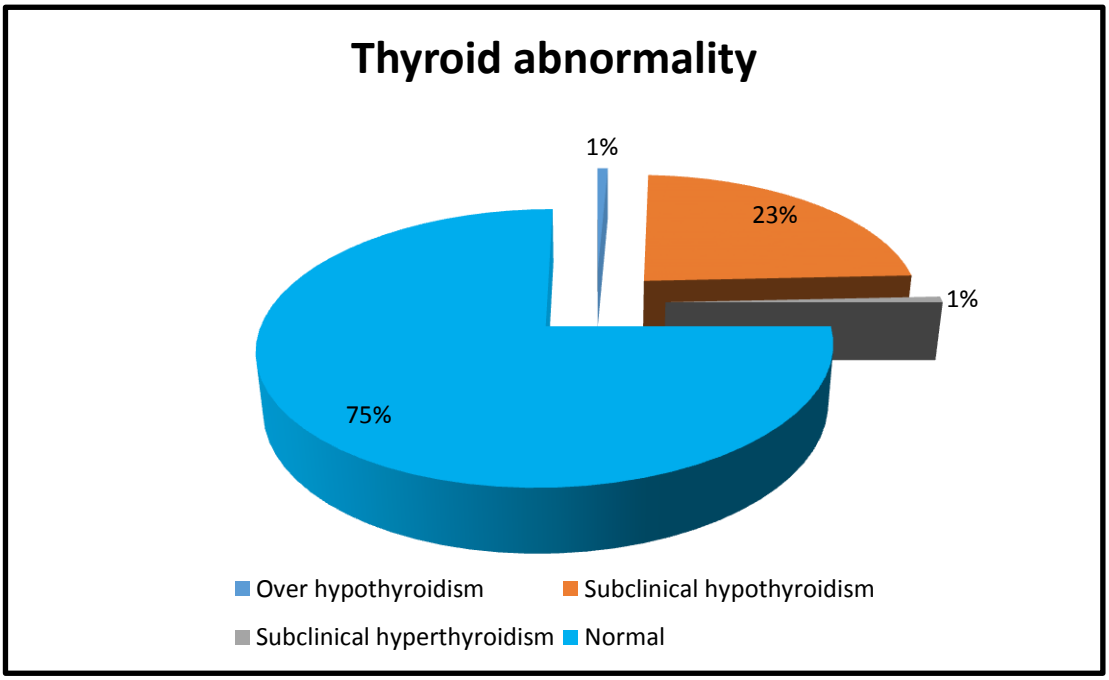
THYROID ABNORMALITY					
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	No	105	75.0	75.0	75.0
	Yes	35	25.0	25.0	100.0
	Total	140	100.0	100.0	



The bar diagram and the table above tells that 25% of study population(newly detected type 2 diabetics) had thyroid dysfunction in some form and the remaining 75% were in euthyroid state.

DISTRIBUTION OF CASES ACCORDING TO THYROID ABNORMALITY

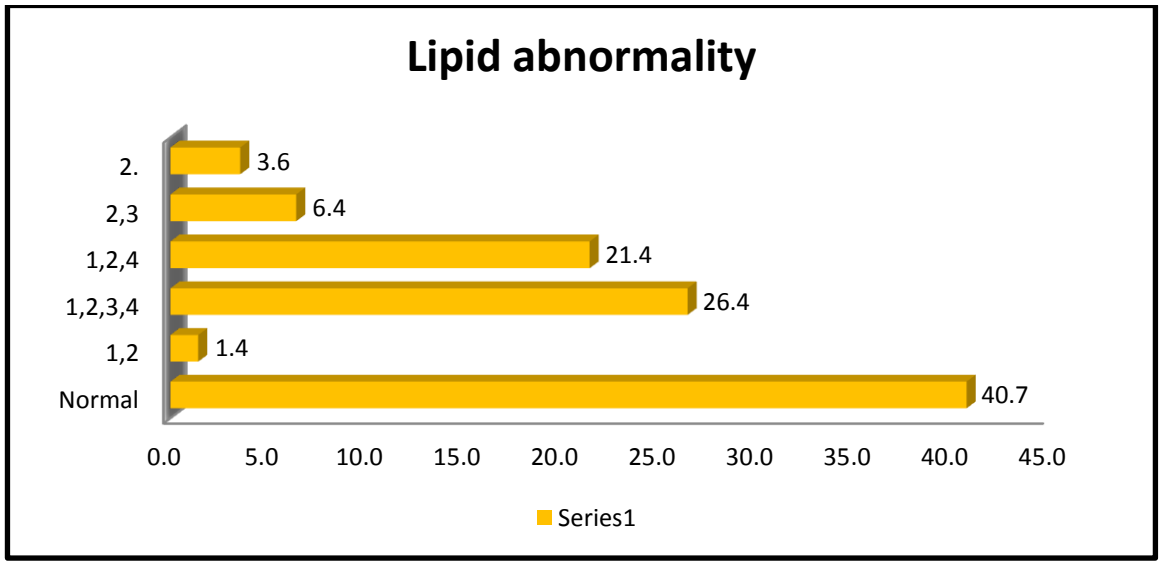
THYROID ABNORMALITY		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Over hypothyroidism	1	.7	2.9	2.9
	Subclinical hypothyroidism	33	23.6	94.3	97.1
	Subclinical hyperthyroidism	1	.7	2.9	100.0
	Total	35	25.0	100.0	
Missing	System	105	75.0		
Total		140	100.0		



From the table and the pie chart given above, 75% of study population had normal thyroid profile ,23% had subclinical variety ,1% had overt variety and the 1% had overt hyperthyroidism.

DISTRIBUTION OF CASES ACCORDING TO SPECIFIC LIPID ABNORMALITY

LIPID ABNORMALITY					
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Normal	57	40.7	40.7	40.7
	1,2	2	1.4	1.4	42.1
	1,2,3,4	37	26.4	26.4	68.6
	1,2,4	30	21.4	21.4	90.0
	2,3	9	6.4	6.4	96.4
	2.	5	3.6	3.6	100.0
	Total	140	100.0	100.0	



DYSLIPIDEMIA

1. Increased total cholesterol(>200mg%)

2. Increased LDL cholesterol(>mg%)

3. Decreased HDL cholesterol(< 50 in

4. Increased triglycerides(> 150mg%)

From the bar diagram and the table ,we see that

a. 60% had abnormal lipid profile and 40% had normal lipid profile.

b. 26.4% had abnormality in all the four parameters .

c. 21.4% had abnormal TC,LDL-C and TGL.

d. 6.4% had abnormality in LDL-C and HDL.

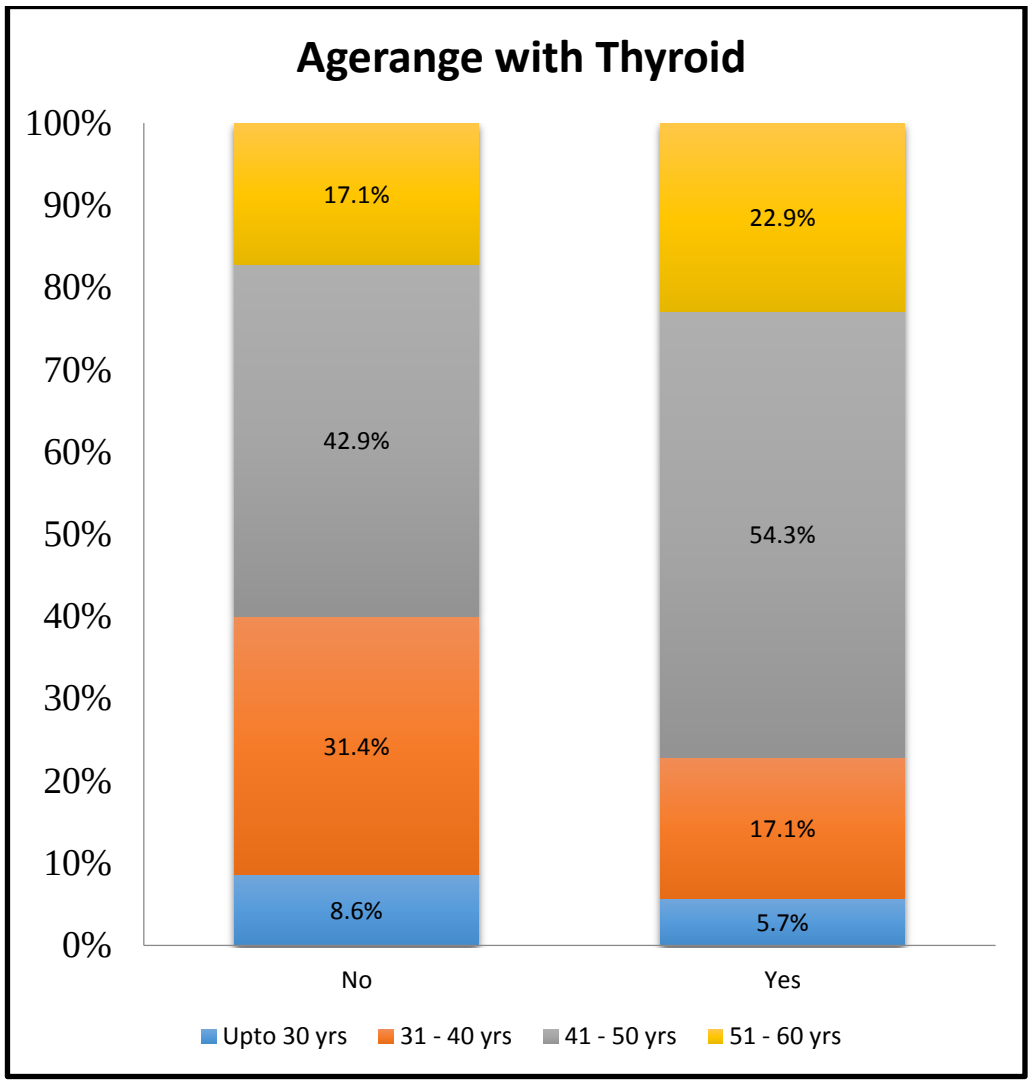
e. 3.6% had abnormality in LDL-C alone .

f. 1.4% had abnormality in TC and LDL-C.

COMPARISON OF THYROID DYSFUNCTION WITH AGE

AGERANGE VS THYROID

Crosstab					
			THYROID		Total
			N	Y	
AGE RANGE	Upto 30 yrs	Count	9	2	11
		% within THYROID	8.6%	5.7%	7.9%
	31 - 40 yrs	Count	33	6	39
		% within THYROID	31.4%	17.1%	27.9%
	41 - 50 yrs	Count	45	19	64
		% within THYROID	42.9%	54.3%	45.7%
	51 - 60 yrs	Count	18	8	26
		% within THYROID	17.1%	22.9%	18.6%
Total		Count	105	35	140
		% within THYROID	100.0%	100.0%	100.0%



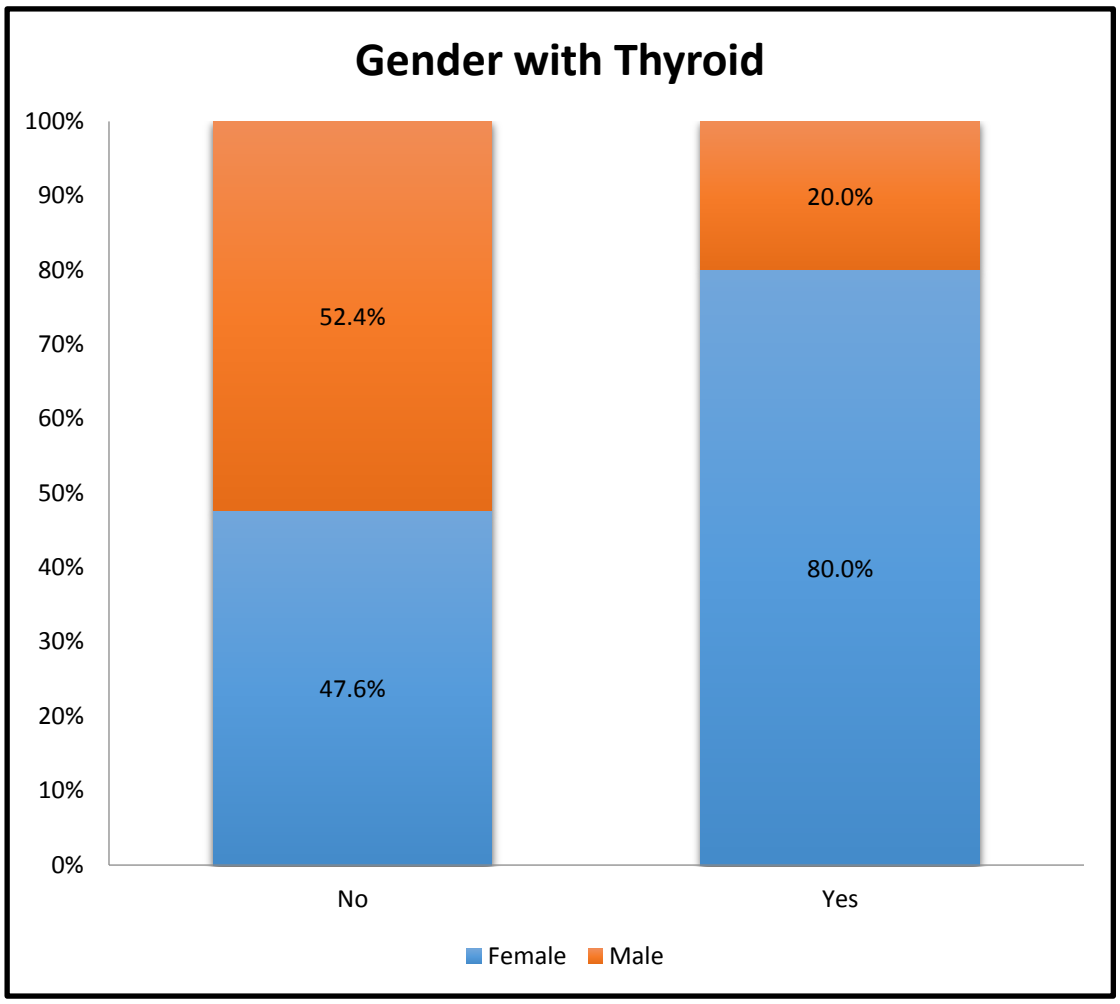
P = 0.333 NOT SIGNIFICANT

Out of 35 patients with abnormal thyroid profile, 8 patients(22.9%) were found to be of age more than 50 years , 19 (54.3%) were found to be of age between 41-50 years and 6(17.1%%) were found to be 30-40 years and 2(5.7%) were less than 30 years. Compared with normal thyroid profile group it has no statistical significance.

COMPARISON OF THYROID DYSFUNCTION WITH GENDER

SEX VS THYROID

Crosstab			THYROID		Total
			N	Y	
SEX	F	Count	50	28	78
		% within THYROID	47.6%	80.0%	55.7%
	M	Count	55	7	62
		% within THYROID	52.4%	20.0%	44.3%
Total		Count	105	35	140
		% within THYROID	100.0%	100.0%	100.0%

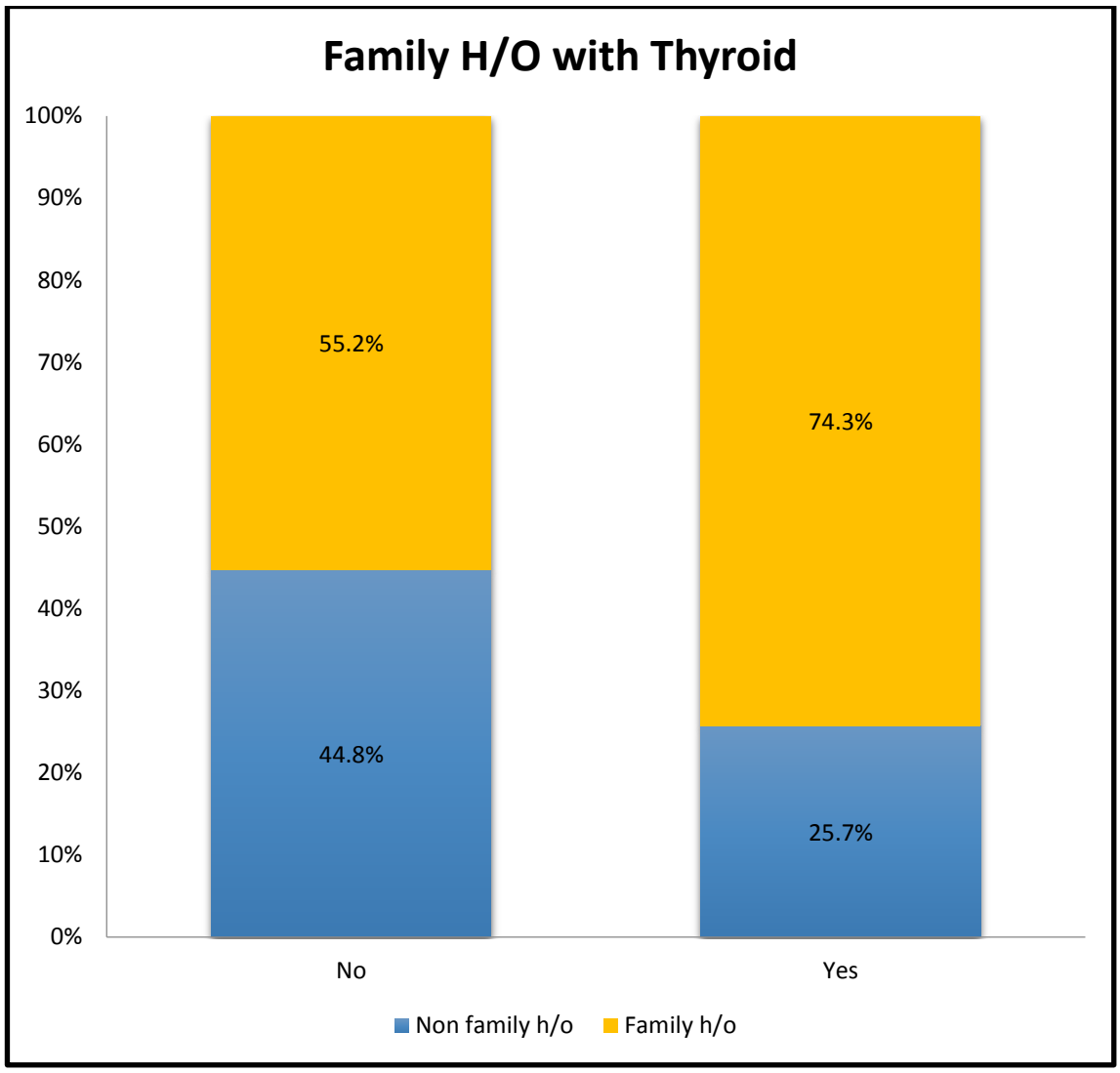


P = 0.001 STATISTICALLY SIGNIFICANT

Out of 35 patients with abnormal thyroid profile, 28 patients(80%) were found to be female and 07(20%) were found to be male. Compared with normal thyroid profile group it has statistical significance.

COMPARISON OF THYROID DYSFUNCTION WITH FAMILY HISTORY OF DIABETES

FAMILY H/O VS THYROID			THYROID		Total
			N	Y	
FAMILY H/O	N	Count	47	9	56
		% within THYROID	44.8%	25.7%	40.0%
	Y	Count	58	26	84
		% within THYROID	55.2%	74.3%	60.0%
Total		Count	105	35	140
		% within THYROID	100.0%	100.0%	100.0%

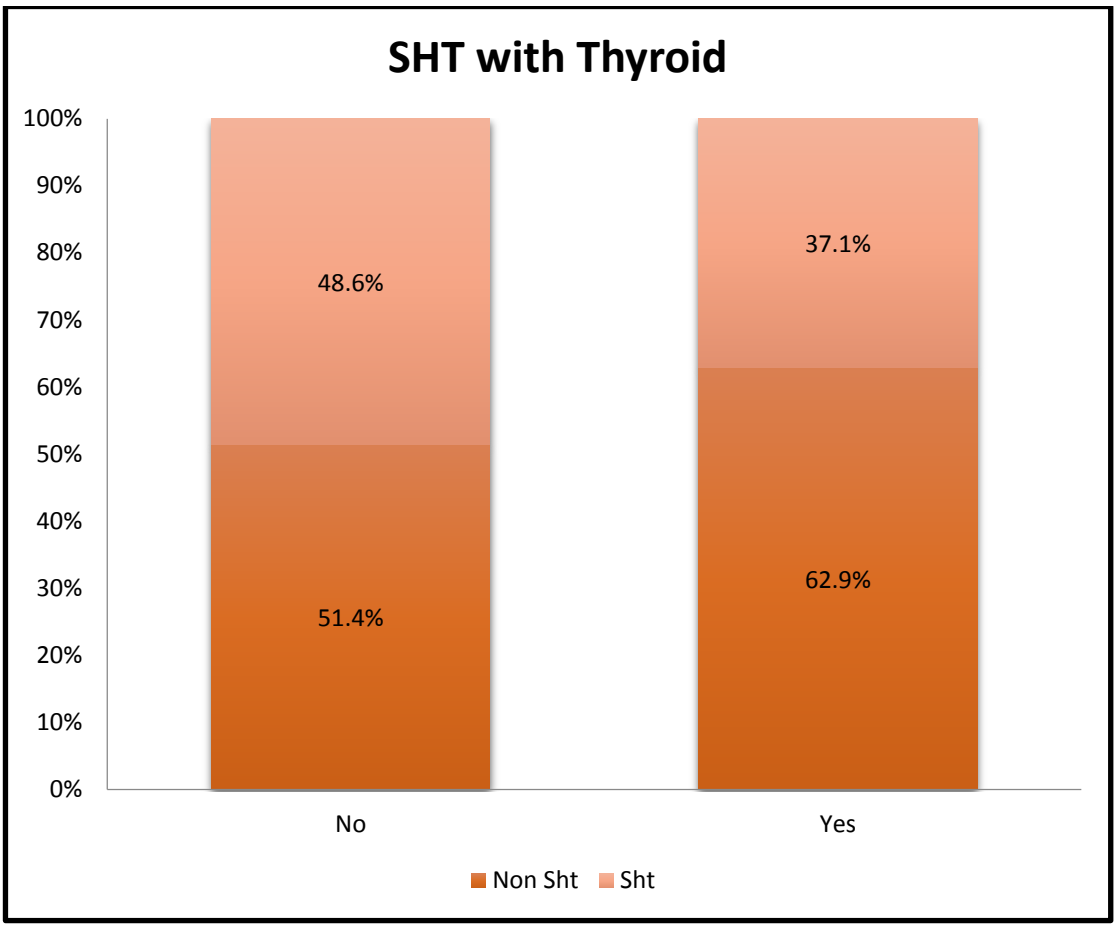


P = 0.046 STATISTICALLY SIGNIFICANT

Out of 35 patients with abnormal thyroid profile,26(74.3%) had positive family history and 9 (25.7%) had negative family history.

COMPARISON OF THYROID DYSFUNCTION WITH SYSTEMIC HYPERTENSION

SHT VS THYROID					
Crosstab			THYROID		Total
			N	Y	
SHT	N	Count	54	22	76
		% within THYROID	51.4%	62.9%	54.3%
	Y	Count	51	13	64
		% within THYROID	48.6%	37.1%	45.7%
Total		Count	105	35	140
		% within THYROID	100.0%	100.0%	100.0%



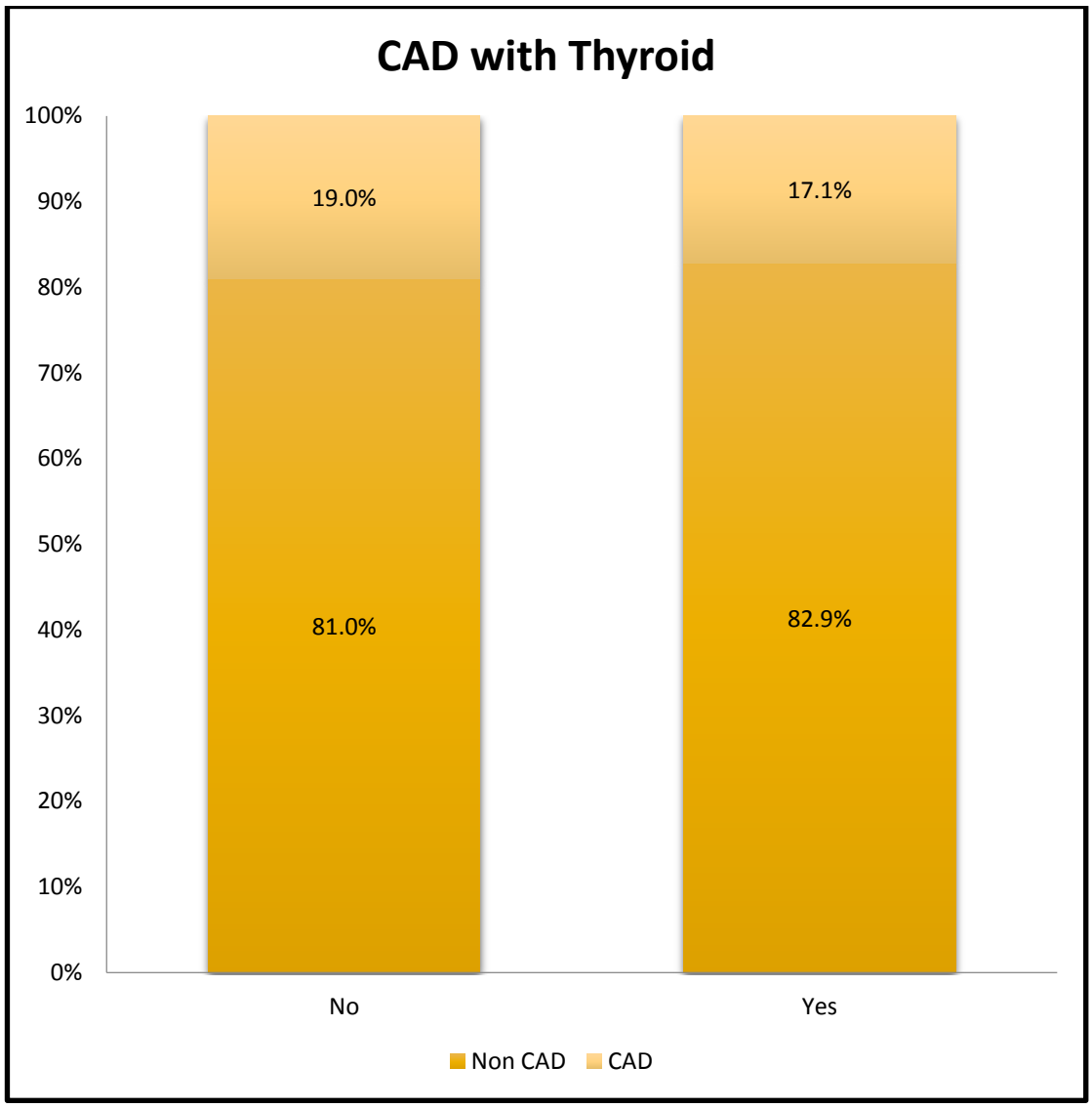
P = 0.24 NOT SIGNIFICANT

Out of 35 patients with abnormal thyroid profile, 13(37.1%) had SHT and 22(62.7%) did not have SHT.

COMPARISON OF THYROID DYSFUNCTION WITH CORONARY ARTERY DISEASE

CAD VS THYROID

Crosstab			THYROID		Total
			N	Y	
CAD	N	Count	85	29	114
		% within THYROID	81.0%	82.9%	81.4%
	Y	Count	20	6	26
		% within THYROID	19.0%	17.1%	18.6%
Total		Count	105	35	140
		% within THYROID	100.0%	100.0%	100.0%



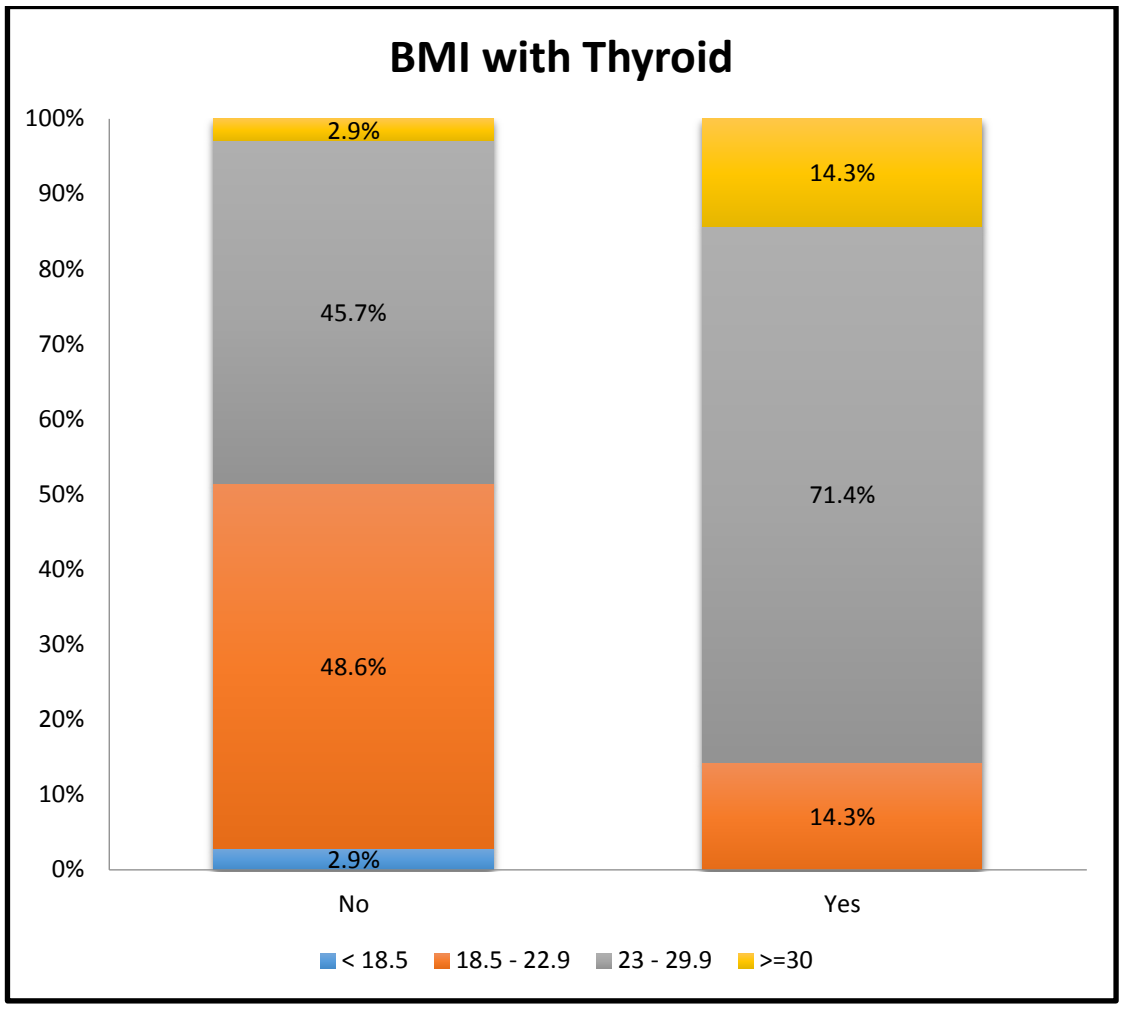
P = 0.802 NOT SIGNIFICANT

Out of 35 patients with abnormal thyroid profile, 6 (17.1%) had CAD and 29 (82.9%) did not have CAD.

COMPARISON OF THYROID DYSFUNCTION WITH BODY MASS INDEX

BMI VS THYROID

Crosstab			THYROID		Total
			N	Y	
BMI	< 18.5	Count	3	0	3
		% within THYROID	2.9%	0.0%	2.1%
	18.5 - 22.9	Count	51	5	56
		% within THYROID	48.6%	14.3%	40.0%
	23 - 29.9	Count	48	25	73
		% within THYROID	45.7%	71.4%	52.1%
	>=30	Count	3	5	8
		% within THYROID	2.9%	14.3%	5.7%
Total		Count	105	35	140
		% within THYROID	100.0%	100.0%	100.0%



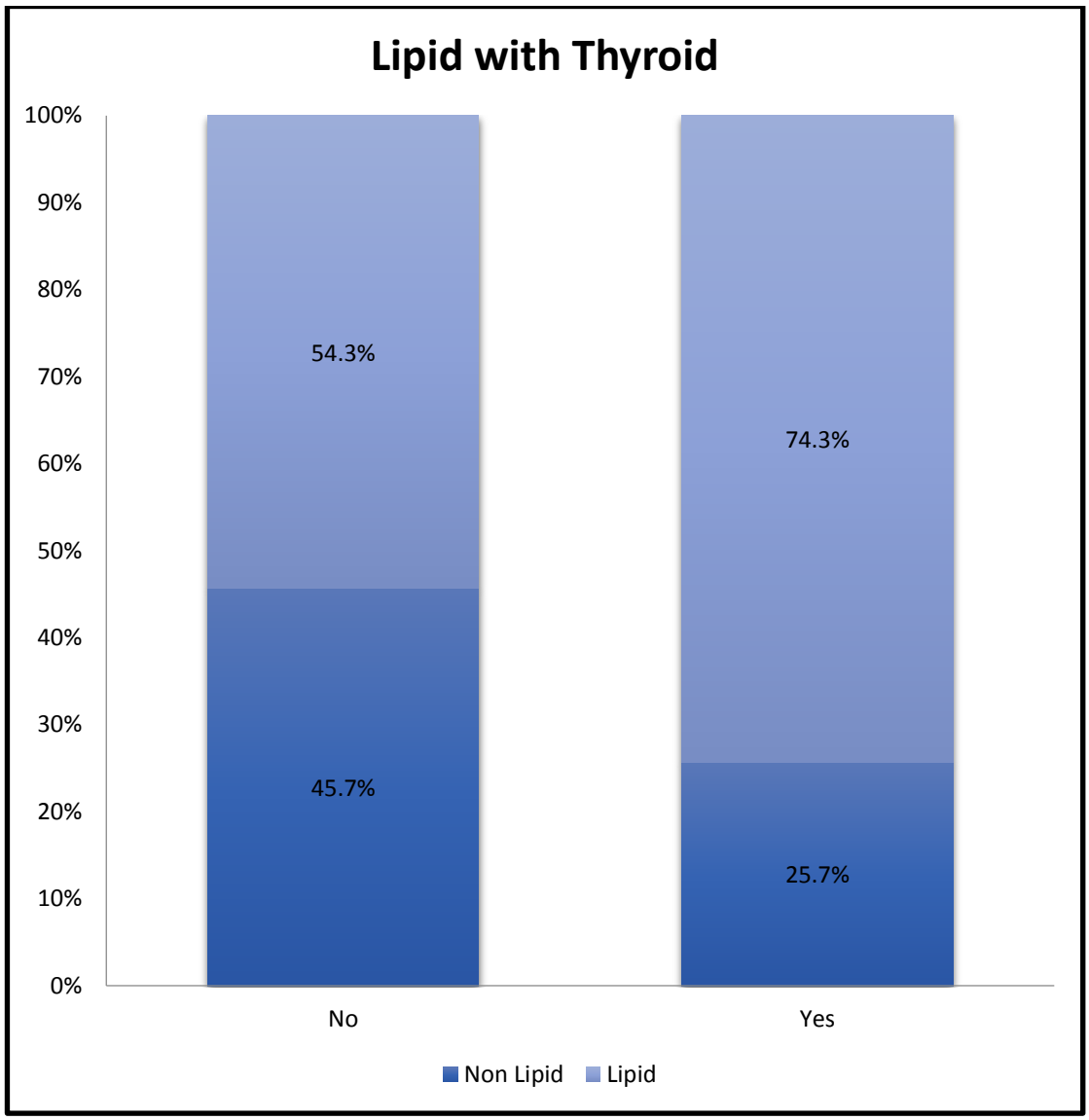
P = 0.000 HIGHLY SIGNIFICANT

Out of 35 patients with abnormal thyroid profile, 25(71.4%) had BMI of 23-30, 5(14.3%) had BMI of 18.5-23 and 5(14.3%) had BMI of > 30

COMPARISON OF THYROID DYSFUNCTION WITH LIPID ABNORMALITY

LIPID VS THYROID

Crosstab			THYROID		Total
			N	Y	
LIPID	N	Count	48	9	57
		% within THYROID	45.7%	25.7%	40.7%
	Y	Count	57	26	83
		% within THYROID	54.3%	74.3%	59.3%
Total		Count	105	35	140
		% within THYROID	100.0%	100.0%	100.0%



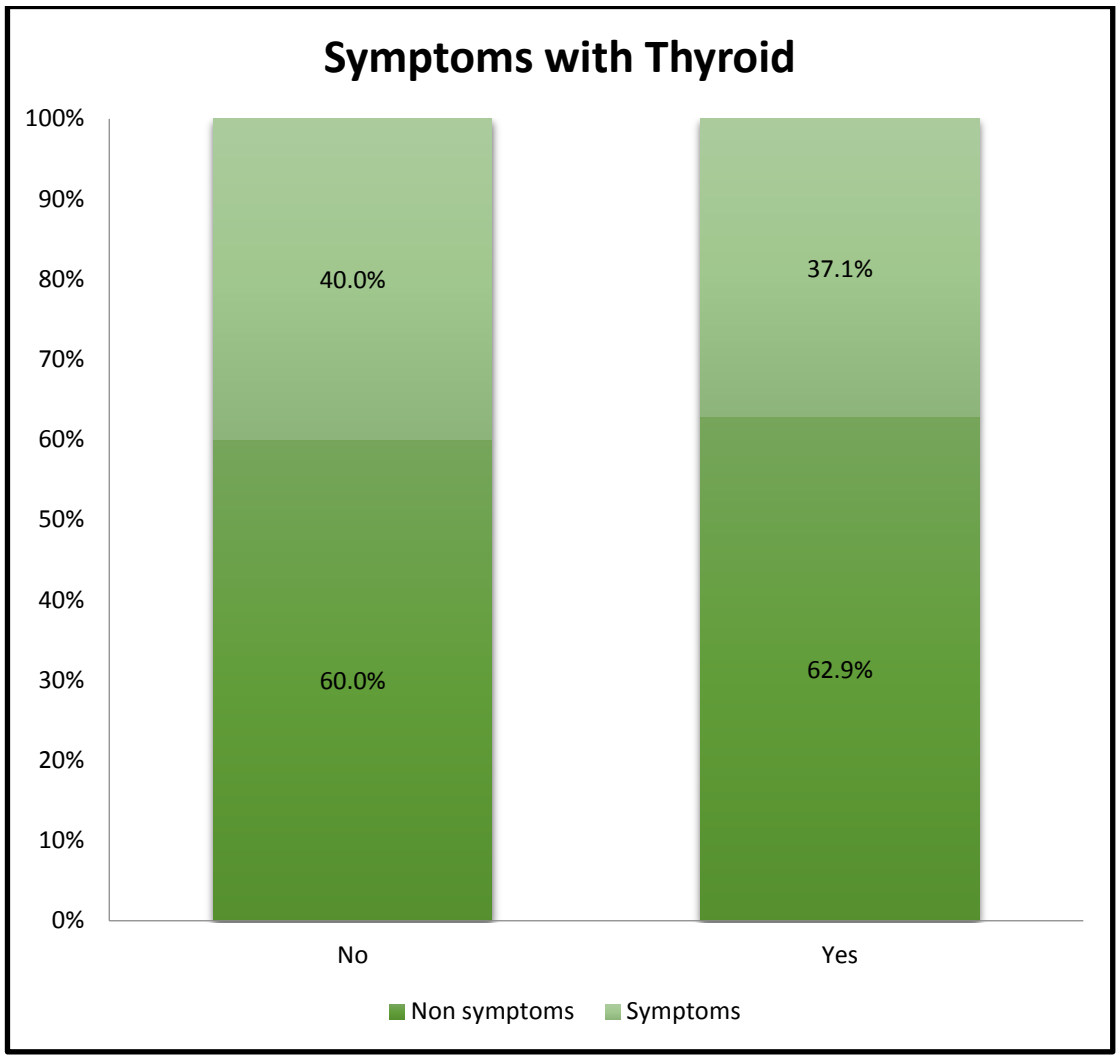
P = 0.037 **STATISTICALLY SIGNIFICANT**

Out of 35 patients with abnormal thyroid profile, 26(74.3%) had abnormal lipid profile and 9(25.7%) had normal lipid profile.

COMPARISON OF THYROID DYSFUNCTION WITH ITS SYMPTOMS

SYMPTOMS VS THYROID

Crosstab			THYROID		Total
			N	Y	
SYMPTOMS	N	Count	63	22	85
		% within THYROID	60.0%	62.9%	60.7%
	Y	Count	42	13	55
		% within THYROID	40.0%	37.1%	39.3%
Total		Count	105	35	140
		% within THYROID	100.0%	100.0%	100.0%



P = 0.76 NOT SIGNIFICANT

Out of 35 patients with abnormal thyroid profile,only 13(37.1%) had symptoms suggestive of thyroid dysfunction whereas 22(62.9%) did not have any symptoms.

BINARY LOGISTIC REGRESSION

- Binary logistic regression model was used to identify the risk factors
- associated with abnormal thyroid profile in diabetic population.
- The dependent variable is Abnormal thyroid profile.
- • The independent variables tested are Sex, Duration of diabetes mellitus
- and Family history of diabetes mellitus.The analysis report showed significant correlation between altered thyroid profile and the female gender.

DISCUSSION

Diabetes mellitus refers to group of metabolic disorders those have the state of hyperglycemia.Many types of DM are caused by a interaction of genetics and environmental factors. Factors contributing to hyperglycemia are decreased insulin secretion,impaired glucose utilisation and inappropriate excess glucose production.

The metabolic chaos causes secondary changes in multiple other organ systems that increases the morbidity of the diabetics.Thyroid diseases are also one of the most common endocrinopathies seen in general popuation whose prevalence is more common in diabetics. Thyroid hormones play a vital role in metabolism at cellular level..So any state of increase or decrease in both the hormones will affect cellular metabolism.

In the current study , recently diagnosed type 2 diabetes mellitus patients were selected from the outpatient departments of internal medicine and diabetology ,kilpauk medical college and hospital. They were studied over a period of 6 months and evaluated for thyroid dysfunction.

AGE DISTRIBUTION

In the present study of 140 type 2 diabetic patients, , 11 patients (7.9%) were up to 30 years, , 39patients (27.9%) were between 31-40

years and 64 patients (45.7%) were 41-50 years and 26(18.6%) were more than 50 years. This shows that the disease was more prevalent between 41-50 years of age.

GENDER DISTRIBUTION

In the present study 56%(78 nos) of the studied population were females and 44%(62 nos) were males. Female to male ratio was 1.25:1.

CO-MORBID DISEASES

In the present study, 45.7%(64/140) of the studied population had hypertension. L Tanow observed that 78% of IDDM patients and 50% of NIDDM had hypertension.[22] Fuller H et al observed that the frequency of WHO defined hypertension was highest in NIDDM patients older than 53 years, being 43% of male and 52% of females. Both these studies support our findings.Prevalence of CAD in general population in urban areas in India is 6.4%72. In the present study, 18% (26/140) of patients had Coronary Artery Disease almost thrice that of in general population. This is supported by two studies which concluded that Type 2 diabetes increases relative risk of cardiovascular disease two- to fourfold compared with the risk in the general population.[24,25]

FAMILY HISTORY OF DIABETES MELLITUS

In the present study, 60% (84nos) of patients had family history of Diabetes and the remaining 40% (56nos) had no family history. This study is similar to that of Tattersal and Fojans[26] and Vishwanthan[27] et al conducted a study among 107 subjects. Out of 73 subjects who gave positive family history diabetes, 19 subjects (26%) later developed diabetes.

BMI

Among the study population, 52%(73/140) were overweight and 6%(8/140) were obese. 40%(56/140) had normal BMI. Mc Larty et al reported that prevalence of IGT in subjects of all age group increased with rising BMI.[28] Yon Gik et al reported that the prevalence of diabetes mellitus and IGT increased with rising BMI and with increase in WHR[29.] Both the studies support our findings.

DYSLIPIDEMIA

In the present study, 49% (69/140) of the study group had raised total cholesterol level; 59%(83/140) had raised LDL-C level; 32% (46/140) had decreased HDL-C level and 47% (67/140) had hypertriglyceridemia. This shows that the incidence of dyslipidemia is high in diabetics.

Liao et al reported that patients who had diabetic glycaemic tolerance had more of intra-abdominal fat , higher triglyceride levels, lower HDL cholesterol levels and higher blood pressure than those with Normal glucose tolerance[30] .A.Southwell et al in their study found that 40% of the diabetics had hypercholesterolemia.[31]

ABNORMAL THYROID PROFILE

In the present study, 25% (35) of the total 140 patients with newly detected diabetes mellitus had abnormal thyroid profile. The present study is slightly different from other previous studies. Abdel-Rahman et al who in his study of 908 type 2 diabetic patients found that the prevalence of thyroid disease was 12.5%, 6.6% of whom were newly diagnosed and 5.9% had known thyroid dysfunction[32]. Chubb et al in a cross-sectional study of 420 patients with type 2 diabetes mellitus found that 8.6% of patients had subclinical hypothyroidism[33] ,whereas it is 25% in our present study which indicates that the prevalence of thyroid dysfunction has been increasing in the diabetics.

DISTRIBUTION OF THYROID ABNORMALITIES

In the present study, 23.6% (33) of the patients had report suggestive of sub clinical hypothyroidism ,0.7% (1) of the patients had report suggestive of overt hypothyroidism and 0.7%(1) had sub clinical hyperthyroidism.

Celani MF et al in their study of 290 type 2 diabetes mellitus patients found that 91 patients(31.4%) had abnormal TSH concentrations out of which 48.3% had subclinical hypothyroidism, 24.2% had subclinical hyperthyroidism, 23.1% had overt hypothyroidism and 4.4% had overt hyperthyroidism.[34]

In another study, diabetic patients, when compared with the control group of normal patients in Whickham Study[35] and a 20 years follow-up of whickham survey by Vanderpump MP et al[36] shows that the prevalence of altered thyroid profile in the study group is significant (p=0.0064).

The presence of thyroid profile dysfunction in diabetic patients may be due to the fact that:

- In euthyroid individuals with diabetes mellitus, the serum T3 levels, basal
- TSH levels and TSH response to thyrotropin releasing hormone (TRH)
- may all be strongly influenced by the glycemic status.[37]
- Poorly controlled diabetes may also result in impaired TSH response to
- TRH or loss of normal nocturnal TSH peak.[38]

SIGNIFICANCE OF ASSOCIATION OF SHT AND CAD IN PATIENTS WITH ABNORMAL THYROID PROFILE

In the present study, 37% (13/35) of patients had hypertension in the group of 35 patients with abnormal thyroid profile whereas 63% (22 /35) of patients had no hypertension. This finding has no statistical significance (p=0.240).

17% (6/35) were found to have CAD compared to 83% (29/35) without CAD in patients with abnormal thyroid profile. Compared between patients with normal and abnormal thyroid profile this finding was found to be insignificant (p=0.802).

ANALYSIS OF SERUM LIPID PROFILE IN CASES WITH NORMAL AND ABNORMAL THYROID PROFILE

74.3% (26/35) were found to have abnormal lipid profile compared to 25.7% (09/35) without dyslipidemia in patients with abnormal thyroid profile. Compared between patients with normal and abnormal thyroid profile this finding was found to be highly significant (p=0.037).

S.A.P.Chubb et al in their substudy of Fremantle diabetes study found that there were good association between Thyroid Stimulating Hormone levels and lipid abnormality with significant cardiac risks.[39]

Bakker SJL et al also concluded the same in their study in non diabetic individuals with insulin resistance.[40] Both these studies contradict our findings.

SUMMARY

This study aimed at estimating the prevalence of subclinical hypothyroidism in newly detected type 2 Diabetes mellitus patients.Hereby i extend my results to find out it's correlation with various risk factors.

The study included 140 newly detected type 2 diabetics taken from outpatient department of medicine and diabetology. All of them were assessed clinically and biochemically as well.

OBSERVATIONS FROM THE STUDY

1. In the study, 35 patients (25%) of newly detected diabetics had thyroid dysfunction .

2. In patients with abnormal thyroid function, 33(23.6%) had subclinical hypothyroidism,1 (0.7%) had overt hypothyroidism and remaining 1(0.7%) had subclinical hyperthyroidism.

3. In the study ,it was found there is significant correlation between thyroid dysfunction and female gender , BMI ,family history of diabetes and dyslipidemia.

4. In persons with abnormal thyroid profile, 80% were female and 20% were male. This is statistically highly significant. Many studies , have shown that the prevalance of hypothyroidism is more in female.

5. No significant correlation was found between thyroid dysfunction and age,systemic hypertension ,coronary artery disease.

6. In the present study, patients age group ranged from 26 years to 56 years. Majority of the patients were in the age group between 40 -50 years.

7. In the study population,60% had positive family history of diabetes and 40 % did not have the family history.

8. Majority of the patients around 52% were overweight and 5.6% were obese.

9. Nearly 60% of the diabetics were found to have dyslipidemia in one form or the other and 40% had normal lipid profile. The correlation between dyslipidemia and thyroid dysfunction in diabetics is significant.

10. The prevalence of subclinical hypothyroidism in newly detected diabetics is found to be 23.6%.

CONCLUSION

1. **The prevalence of subclinical hypothyroidism in newly detected diabetics is found to be 23.6%.**

2. Prevalence of thyroid dysfunction is more common among newly detected type 2 diabetes mellitus patients 2. Prevalence of thyroid dysfunction in patients with type 2 diabetes mellitus is higher in females than in males.

3. There is no significant correlation between Age, SHT, CAD.

4. Routine screening for thyroid dysfunction in type 2 diabetes mellitus patients may be justified especially in females because the progression to overt thyroid dysfunction is associated with significant morbidity including the adverse effects on glycemic control, lipid

LIMITATIONS

- Study population was small.
- Thyroid autoimmunity was not evaluated due to constraints. So it was not able to refine the spectrum of thyroid dysfunction in type 2 diabetics.
- The natural history of subclinical thyroid dysfunction could not be assessed since follow up of patients was not done and it's effect on various parameters could not be assessed.

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ANNEXURES

INSTITUTIONAL ETHICS COMMITTEE
GOVT.KILPAUK MEDICAL COLLEGE,
CHENNAI-10
Protocol ID. No. 05/2016 Dt: 20.06.2016
CERTIFICATE OF APPROVAL

The Institutional Ethical Committee of Govt. Kilpauk Medical College, Chennai reviewed and discussed the application for approval " **A STUDY TO ESTIMATE THE PREVALENCE OF SUBCLINICAL HYPOTHYROIDISM IN NEWLY DETECTED TYPE 2 DIABETES MELLITUS**"- For Project Work submitted by Dr.Surendhar, Post Graduate in MD (General Medicine), Govt. Kilpauk Medical College, Chennai-10.

The Proposal is APPROVED.

The Institutional Ethical Committee expects to be informed about the progress of the study any Adverse Drug Reaction Occurring in the Course of the study any change in the protocol and patient information /informed consent and asks to be provided a copy of the final report

DEAN
Govt.Kilpauk Medical College,
Chennai – 10.

SC 2k/VE : Section/Ethics Committee :

PROFORMA

DEPARTMENT OF MEDICINE

Kilpauk medical college and hospital,Chennai

"A Study to estimate the prevalence of subclinical hypothyroidism in newly detected type 2 diabetes mellitus at a Tertiary Care Hospital in Chennai"

S.No. Reg. No. (OPD)

Name: Age/Sex

Address:

Occupation Religion

Presenting Complaints:

Polyuria	polydipsia	polyphagia
Tiredness	Dry Skin	muscle cramps
Decreased sweating	Insomnia	Somnolence
Poor Appetite	Myalgia/Arthralgia	
Weight Gain	Weight Loss	Breathlessness
Cold Intolerance	Swollen Limb	
Constipation	Paresthesia	Change in Voice
Impaired Hearing	Menstrual Irregularities	Infertility/Abortion
Libido	Poor Memory	Behavioral Changes
Tremors	Palpitation	irritability

Numbness/pins and needles sensation

PAST HISTORY

HT Others

IHD

FAMILY HISTORY

Hypertension Diabetes Mellitus IHD

Hypothyroidism Goiter

PERSONAL HISTORY

Diet Menstrual History

Addiction: Tobacco Chewing/Smoking/Both

Alcohol-Occasional/Daily/Moderate/Heavy

TREATMENT HISTORY

GENERAL EXAMINATION

Height Weight BMI

Pallor Icterus Xanthelasma

Pulse B. P: Peripheral Pulsation

Skin : Cold/Coarse/Moist/Dry/Yellowish Discoloration Madarosis

Pedal Edema Facial Puffiness Alopecia Tongue

Thyroid Gland : Normal/Enlarged peripheral sensations

SYSTEMIC EXAMINATION:

C. V. S.

R. S.

P/A

C. N. S.

INVESTIGATIONS:

Hb (gm%) TLC DLC P L E M

ESR

FBS

PPBS

B. Urea S. Creatinine

ECG

Thyroid Profile: FT3 FT4 TSH

Lipid Profile

TC TG

REMARK:

PATIENT CONSENT FORM

Study detail: **"A Study to estimate the prevalence of subclinical hypothyroidism in newly detected type 2 diabetes mellitus at a Tertiary Care Hospital in Chennai"**

Study centre : KILPAUK MEDICAL COLLEGE, CHENNAI

Patients Name :

Patients Age :

Identification Number :

Patient may check (✓) these boxes

I confirm that I have understood the purpose of procedure for the above study. I have the opportunity to ask question and all my questions and doubts have been answered to my complete satisfaction. ☐

I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving reason, without my legal rights being affected. ☐

I understand that sponsor of the clinical study, others working on the sponsor's behalf, the ethical committee and the regulatory authorities will not need my permission to look at my health records, both in respect of current study and any further research that may be conducted in relation to it, even if I withdraw from the study I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from this study. ☐

I agree to take part in the above study and to comply with the instructions given during the study and faithfully cooperate with the study team and to immediately inform the study staff if I suffer from any deterioration in my health or well-being or any unexpected or unusual symptoms. ☐

I hereby consent to participate in this study. ☐

I hereby give permission to undergo complete clinical examination and diagnostic tests including hematological, biochemical, radiological tests. ☐

Signature/thumb impression:

Patients Name and Address: place date

சுயஒப்புதல் படிவம்

ஆய்வு செய்யப்படும் தலைப்பு: சென்னை கீழ்ப்பாக்கம் அரசு பொதுமருத்துவமனையில் ஆராய்ச்சி ஒன்று நடைபெற்று வருகிறது. ” **புதிதாக கண்டறிந்த** இரண்டாம் வகை நீரிழிவு நோய் உள்ளவர்களுக்கு நோய்குறி தோன்றா தைராய்டு சுரப்பிகுறைவு நோய் பரவியுள்ளமை பற்றிய ஒரு ஆய்வு” என்பதே இதன் தலைப்பாகும்.

இடம்: பொது மருத்துவத் துரை
அரசு கீழ்பாக்கம் மருத்துவ கல்லூரி மருத்துவமனை
சென்னை

பங்குபெறுபவரின் பெயர் :

பங்குபெறுபவரின் வயது : **பங்குபெறுபவரின் எண் :**

மேலே குறிப்பிட்டுள்ள மருத்துவ ஆய்வின் விவரங்கள் எனக்கு விளக்கப்பட்டது. நான் இவ்வாய்வில் தன்னிச்சையாக பங்கேற்கிறேன். எந்த காரணத்தினாலோ எந்த சட்டசிக்கலுக்கும் உட்படாமல் நான் இவ்வாய்வில் இருந்து விலகிக்கொள்ளல்லாம் என்றும் அறிந்து கொண்டேன்.

இந்த ஆய்வு சம்பந்தமாகவோ, இதை சார்ந்து மேலும் ஆய்வு மேற்கொள்ளும்போதும் இந்த ஆய்வில்பங்கு பெறும் மருத்துவர் என்னுடைய மருத்துவ அறிக்கைகளை பார்ப்பதற்கு என் அனுமதி தேவையில்லை என அறிந்து கொள்கிறேன். இந்த ஆய்வின் மூலம் கிடைக்கும் தகவலையோ, முடிவையோ பயன்படுத்திக்கொள்ள மறுக்க மாட்டேன்.

இந்த ஆய்வில் பங்கு கொள்ள ஒப்புக்கொள்கிறேன். இந்த ஆய்வை மேற்கொள்ளும் மருத்துவ அணிக்கு உண்மையுடன் இருப்பேன் என்றும் உறுதியளிக்கிறேன்.

பங்கேற்பவரின் கையொப்பம் ஆய்வாளரின் கையொப்பம்

இடம் : தேதி :

KEY TO MASTER SHEET

BMI SCORE

1.< 18.5

2.18.5 – 22.9

3.23 – 29.9

4.> 30

LIPID ABNORMALITY

1. TOTAL CHOLESTEROL > 200 MG%
2. LDL CHOL >130 MG%
3. HDL < 40 MG% IN MEN ,< 50 % IN WOMEN
4. TGL> 150 MG%

SYMPTOMS

YES- EASY FATIGABILITY, WEIGHT GAIN,COLD INTOLERANCE,CONSTIPATION,INCREASED SLEEP,ANXIETY,WEIGHT LOSS,DIARRHOEA

NO – NO SPECIFIC COMPLAINTS

THYROID ABNORMALITY

1.OVERT HYPOTHYROIDISM

2.SUBCLINICAL HYPOTHYROIDISM

3.OVERT HYPERTHYROIDISM

4.SUBCLINICAL HYPERTHYROIDISM

ABBREVIATIONS USED

BMI - BODY MASS INDEX

M - MALE

F - FEMALE

Y - YES

N - NO

VLDL - VERY LOW DENSITY PROTEIN

LDL - LOW DENSITY PROTEIN

TG - TRIGLYCERIDES

FFA - FREE FATTY ACID

TSH - THYROID STIMULATING HORMONE

AB - ANTIBODY

DM - DIABETES MELLITUS

SHT - SYSTEMIC HYPERTENSION

CAD - CORONARY ARTERY DISEASE

OH - OVERT HYPOTHYROIDISM

SH - SUBCLINICAL HYPOTHYROISM

IFG - IMPAIRED FASTING GLUCOSE

IGT - IMPAIRED GLUCOSE TOLREANCE

S.NO	AGE	SEX	FAMILY H/O	SHT	CAD	BMI	LIPID	ABNORMALITY	SYMPTOMS	THYROID	ABNORMAILTY
1	28	M	Y	N	N	2	N		N	N	
2	27	F	Y	N	N	1	N		N	N	
3	30	M	N	N	N	2	N		N	N	
4	33	M	Y	N	N	2	N		N	N	
5	29	F	Y	N	N	2	N		Y	N	
6	33	M	N	N	N	2	N		N	N	
7	30	M	N	N	N	2	N		N	N	
8	35	F	Y	Y	N	2	Y	1,2	N	Y	2
9	29	M	Y	N	N	3	N		Y	Y	4
10	31	F	Y	N	N	2	N		N	N	
11	32	F	Y	N	N	2	N		Y	N	
12	35	M	N	Y	N	2	Y	1,2	Y	N	
13	30	M	N	N	N	3	N		N	N	
14	28	F	N	N	N	1	N		N	N	
15	26	F	N	N	N	1	N		N	N	
16	33	M	Y	N	N	2	N		N	N	
17	34	M	N	N	N	2	N		N	N	
18	29	M	N	N	N	2	N		N	N	
19	34	M	Y	Y	N	2	N		N	N	
20	28	F	N	N	N	3	N		N	Y	2
21	34	F	N	N	N	2	N		Y	N	
22	36	M	N	N	N	3	N		N	N	
23	38	M	Y	N	N	2	Y	1,2,4	N	N	
24	40	F	Y	Y	N	3	Y	1,2,3,4	Y	Y	2
25	39	F	Y	N	N	2	Y	1,2,4	N	N	
26	42	M	N	Y	N	3	Y	1,2,3,4	N	Y	2
27	38	F	Y	N	N	3	Y	2,3	Y	N	
28	39	M	N	N	N	2	Y	1,2,4	N	N	

S.NO	AGE	SEX	FAMILY H/O	SHT	CAD	BMI	LIPID	ABNORMALITY	SYMPTOMS	THYROID	ABNORMAILTY
29	44	M	Y	Y	N	2	Y	2,3	N	N	
30	45	F	Y	Y	y	3	Y	1,2,4	N	N	
31	44	F	Y	Y	N	2	Y	1,2,4	Y	N	
32	37	F	N	N	N	3	Y	1,2,3,4	Y	Y	2
33	40	F	N	N	N	4	N		N	Y	2
34	45	M	N	Y	N	2	Y	1,2,4	N	N	
35	43	M	Y	Y	y	3	N		Y	N	
36	42	M	Y	N	N	2	N		N	N	
37	41	F	Y	N	N	3	Y	1,2,3,4	N	Y	1
38	41	F	N	N	N	2	Y	1,2,4	Y	N	
39	37	F	N	N	N	3	Y	2,3	Y	N	
40	38	M	Y	Y	N	3	N		N	N	
41	38	M	Y	Y	N	2	Y	1,2,3,4	N	N	
42	39	M	Y	N	N	4	Y	1,2,4	N	N	
43	40	M	Y	N	N	2	Y	1,2,3,4	N	N	
44	45	M	N	Y	N	3	Y	1,2,4	N	N	
45	43	F	Y	Y	N	4	Y	1,2,3,4	Y	Y	2
46	39	M	N	N	N	3	Y	2	N	N	
47	45	M	Y	Y	N	2	Y	2,3	N	N	
48	44	F	N	Y	N	3	Y	1,2,3,4	N	Y	2
49	44	F	Y	Y	N	3	N		N	N	
50	39	F	Y	N	N	2	Y	1,2,3,4	Y	N	
51	38	M	Y	N	N	2	Y	1,2,4	N	N	
52	40	M	Y	Y	N	3	Y	2,3	N	N	
53	40	M	Y	N	N	2	Y	1,2,4	N	N	
54	37	F	Y	Y	N	3	Y	1,2,3,4	N	Y	2
55	39	M	N	Y	N	2	Y	2	N	N	
56	40	F	N	Y	N	3	Y	1,2,3,4	Y	N	

S.NO	AGE	SEX	FAMILY H/O	SHT	CAD	BMI	LIPID	ABNORMALITY	SYMPTOMS	THYROID	ABNORMAILTY
57	41	F	Y	N	N	2	Y	1,2,4	Y	Y	2
58	43	M	N	Y	N	3	Y	1,2,3,4	N	N	
59	44	F	Y	Y	N	2	Y	1,2,4	Y	N	
60	42	F	Y	N	N	3	Y	1,2,3,4	Y	Y	2
61	39	M	N	Y	N	4	Y	1,2,3,4	N	N	
62	37	M	Y	N	N	2	Y	1,2,4	N	N	
63	41	F	Y	N	N	3	Y	1,2,3,4	Y	Y	2
64	42	M	Y	N	Y	3	Y	1,2,4	N	N	
65	45	F	N	Y	N	3	Y	1,2,3,4	Y	N	
66	44	F	Y	Y	N	4	Y	1,2,4	Y	Y	2
67	36	M	Y	N	N	2	Y	1,2,3,4	Y	Y	2
68	38	M	Y	Y	N	3	Y	2	N	N	
69	39	M	N	N	N	3	Y	1,2,4	N	N	
70	39	F	N	Y	N	2	Y	1,2,3,4	Y	N	
71	41	M	Y	N	N	3	N		N	Y	2
72	42	F	Y	N	N	2	N		Y	N	
73	41	F	Y	N	N	3	Y	1,2,4	Y	Y	2
74	45	F	Y	Y	y	2	Y	1,2,4	Y	N	
75	40	M	N	N	N	3	N		N	N	
76	38	M	N	N	N	2	Y	1,2,4	N	N	
77	45	F	Y	N	y	3	Y	1,2,3,4	Y	Y	2
78	46	M	Y	Y	y	3	N		Y	N	
79	47	M	Y	N	N	2	Y	1,2,3,4	N	N	
80	48	M	Y	N	y	3	Y	1,2,3,4	Y	N	
81	46	M	Y	N	N	2	Y	1,2,4	N	N	
82	49	M	Y	Y	N	3	N		N	N	
83	48	F	Y	Y	N	4	Y	1,2,3,4	N	Y	2
84	50	F	N	N	y	2	Y	1,2,3,4	Y	Y	2

S.NO	AGE	SEX	FAMILY H/O	SHT	CAD	BMI	LIPID	ABNORMALITY	SYMPTOMS	THYROID	ABNORMAILTY
85	49	M	N	Y	N	3	N		Y	N	
86	48	M	Y	N	N	3	Y	1,2,4	N	Y	2
87	47	F	N	Y	N	3	Y	1,2,3,4	Y	N	
88	52	F	Y	Y	N	2	Y	1,2,3,4	Y	N	
89	55	M	N	Y	y	3	Y	1,2,4	N	N	
90	47	F	N	N	N	3	Y	1,2,3,4	Y	N	
91	49	F	Y	Y	N	2	N		Y	N	
92	50	M	N	N	N	3	Y	1,2,3,4	N	Y	2
93	48	M	Y	Y	N	3	N		Y	N	
94	51	M	N	N	y	2	Y	1,2,4	N	N	
95	53	F	Y	Y	N	3	Y	1,2,3,4	Y	Y	2
96	49	M	Y	Y	N	4	N		Y	N	
97	52	F	Y	N	N	3	Y	1,2,3,4	N	Y	2
98	58	M	N	Y	y	3	Y	1,2,4	N	N	
99	55	M	N	Y	y	2	N		N	N	
100	46	F	Y	N	N	3	Y	1,2,3,4	N	Y	2
101	47	F	Y	N	N	2	Y	1,2,4	Y	N	
102	42	M	Y	N	N	3	N		N	N	
103	56	M	Y	Y	y	2	Y	1,2,3,4	N	N	
104	51	F	Y	N	y	3	Y	1,2,3,4	N	Y	2
105	49	M	Y	N	y	2	N		N	N	
106	55	F	Y	Y	y	3	Y	1,2,3,4	Y	N	
107	56	F	Y	Y	N	3	Y	1,2,4	N	Y	2
108	49	F	N	N	N	2	Y	1,2,3,4	Y	N	
109	47	F	Y	Y	N	3	Y	1,2,4	Y	N	
110	48	F	N	Y	N	3	N		Y	N	
111	52	F	Y	N	y	3	Y	1,2,3,4	N	Y	2
112	51	F	N	N	N	3	N		Y	N	

S.NO	AGE	SEX	FAMILY H/O	SHT	CAD	BMI	LIPID	ABNORMALITY	SYMPTOMS	THYROID	ABNORMAILTY
113	47	F	Y	Y	N	3	Y	1,2,4	N	N	
114	49	F	Y	N	Y	2	N		Y	N	
115	53	F	Y	Y	N	3	Y	1,2,3,4	N	Y	2
116	56	M	Y	Y	y	3	N		Y	N	
117	51	F	N	N	N	2	Y	1,2,4	Y	N	
118	50	M	N	Y	y	3	N		N	Y	2
119	46	F	N	N	N	3	Y	1,2,3,4	N	N	
120	47	F	N	N	N	2	N		Y	N	
121	48	F	Y	N	N	3	N		N	Y	2
122	50	F	N	Y	y	3	N		Y	N	
123	52	F	Y	Y	N	3	Y	2,3	N	N	
124	55	F	Y	Y	N	2	N		N	Y	2
125	54	F	N	Y	N	3	Y	2,3	Y	N	
126	56	F	Y	Y	y	3	N		Y	N	
127	50	M	Y	N	N	3	N		Y	N	
128	55	F	N	Y	y	3	Y	2,3	Y	N	
129	58	M	N	Y	y	2	Y	2	Y	N	
130	49	F	Y	N	N	3	N		N	Y	2
131	50	F	N	Y	N	3	Y	2,3	N	N	
132	47	F	N	N	N	2	N		Y	N	
133	49	F	Y	Y	N	3	N		N	N	
134	51	F	Y	Y	y	3	N		N	N	
135	55	F	Y	Y	N	2	Y	2	N	N	
136	54	F	N	Y	N	3	N		N	N	
137	54	F	N	N	y	4	N		N	Y	2
138	48	F	Y	Y	N	3	N		N	N	
139	49	F	Y	N	N	3	N		N	N	
140	50	F	N	N	N	3	N		N	N	