A DISSERTATION ON DYSLIPIDEMIA IN SUBCLINICAL HYPOTHYROIDISM

A Dissertation Submitted to

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BONAFIDE CERTIFICATE

This is to certify that this dissertation title **DYSLIPIDEMIA IN SUBCLINICAL HYPOTHYROIDISM** submitted by **Dr.SARANYA MASILAMANI** to the faculty of General Medicine, **The Tamil Nadu Dr. M.G.R. Medical University, Chennai** in partial fulfillment of the requirement for the award of MD degree branch I General Medicine, is a bonafide research work carried out by him under our direct supervision and guidance

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INTRODUCTION

The diagnosis of subclinical hypothyroidism is mostly biochemical as most of the patients have a serum thyroid stimulating hormone above the normal reference range and serum free and total thyroxine T4 and T3 are normal. Most of the patients with subclinical hypothyroidism have few or no signs of thyroid dysfunction. The normal reference range of TSH was 0.45 – 4.5mU/l.(2,10)The overall percentage range from 5 to 10% in large screening population. The prevalence is 7 to 26% in studies conducted in elderly. Since the hormone levels are normal there comes a confusion between compensated hypothyroidism and euthyroid state.(3,14)

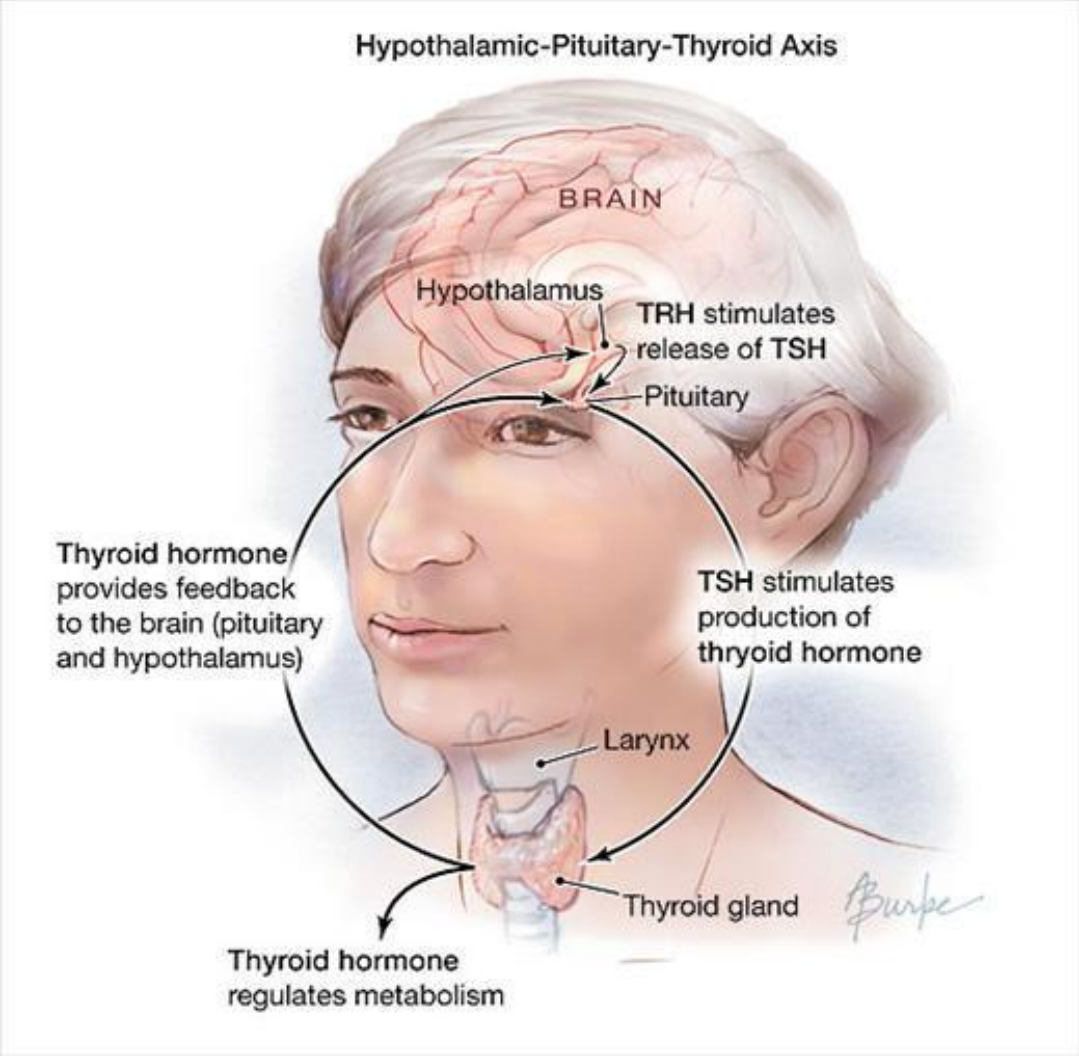
Subclinical hypothyroidism is more common in women. Among patients with subclinical hypothyroidism 80% have TSH of less than 10mIU/l. The most notable consequence of subclinical hypothyroidism is its high chance of transformation to true hypothyroidism. It is also associated with dyslipidemia and adverse cardiovascular risk profile. Now the recent practical approach of treatment of subclinical hypothyroidism is levothyroxine therapy for persons with serum TSH of more than 10mIU/L and the therapy is individualised for patients with a TSH value of less than

10mIU/L. (2,10)

Subclinical hypothyroidism is a common endocrine problem with 3 to 8% prevalence among general population. Antithyroid antibodies are positive in 80% of patients with SCH. Prior radioiodine therapy, external neck and head irradiation may cause mild form of thyroid dysfunction.(2,10) Transient elevation of TSH VALUES may occur after episodes of postpartum thyroiditis. Due to recent increasing prevalence of SCH and metabolic risk factors such as adverse cardiac function and hyperlipidemia, the AMERICAN THYROID ASSOCIATION has recommended the importance of screening by assessment of serum TSH values above the age of 35 years and followed up every 5 years later. Because of high likelihood of SCH to cause complications during pregnancy and brain development of fetus, screening of pregnant women for subclinical hypothyroidism is suggested. (2,10)

"In the conclusions of Whickham survey, the risk of acquiring hypothyroidism was 4.3% per year in women in a year, if both the levels serum TSH and anti-thyroid antibodies were found to be elevated, 2.6% chance in patients with elevated TSH alone, and 2.1% chance per year with positive anti-thyroid antibodies alone."On follow up of the course of patients with subclinical hypothyroidism, a recent prospective study by Gerold Huber and team concluded that high risk factors for progression to

overt hypothyroidism were base line TSH >12uIU/mL, reduced thyroid reserve and positive for thyroid peroxidise antibody .So treatment of subclinical hypothyroidism holds good in various situations and in prevention of conversion to overt hypothyroidism.(14)



AIM OF THE STUDY

- TO ASSESS LIPID PROFILE ABNORMALITIES IN PATIENTS DIAGNOSED WITH SUBCLINICAL HYPOTHYROIDISM

REVIEW OF LITERATURE

SUBCLINICAL HYPOTHYROIDISM

Subclinical hypothyroidism denotes mild thyroid dysfunction. Its prevalence in general population is around 5 to15 % of patients. Risk of transformation to true hypothyroidism is 2 to 5 % per year. The best screening test for any thyroid disorder is measurement of TSH. It is highly a sensitive and specific test. Serum TSH has log relationship with hormone serum thyroxine, so if serum thyroxine levels doubles there is a hundredfold change in seum TSH levels. (2,10)

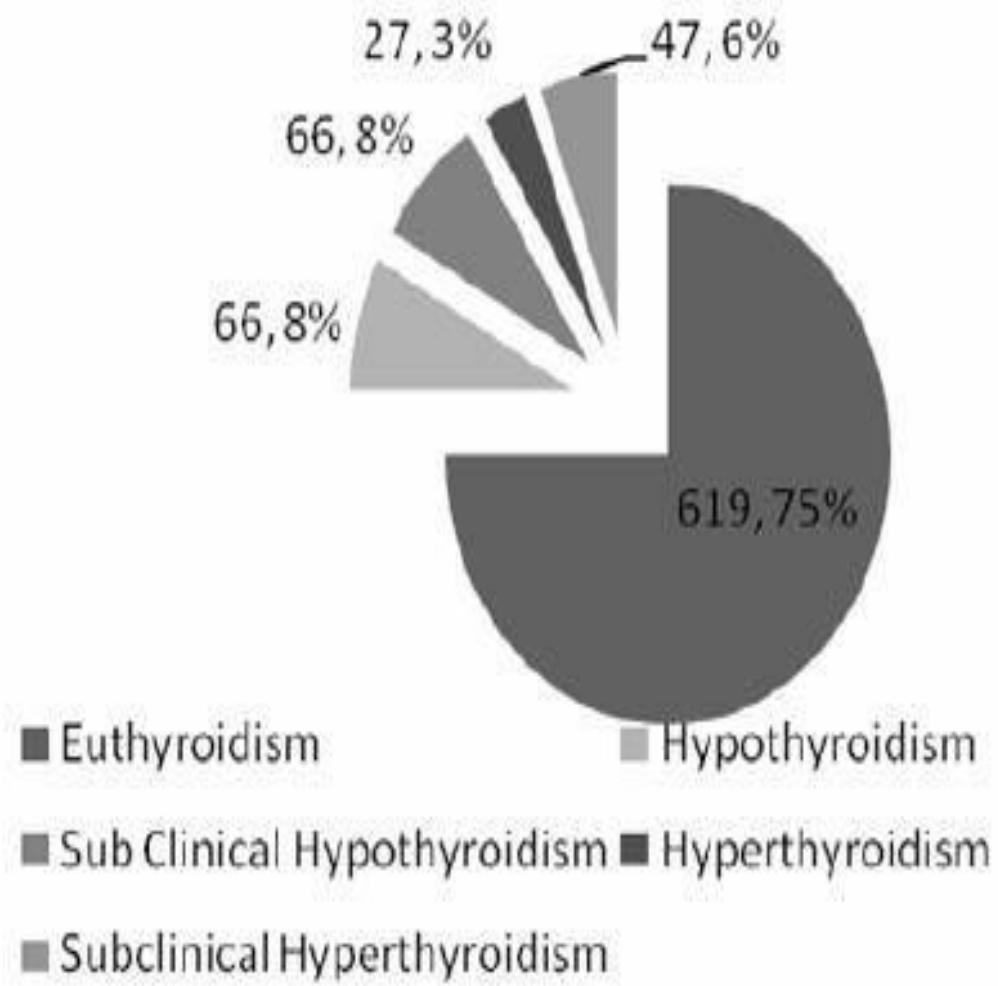
Serum TSH levels show variation with respect to race, age and iodine intake. “Most of the circulating t3 is formed by peripheral conversion of t4 by enzymatic removal of an iodine atom from t4. Very little t3 is produced by the thyroid gland itself. T3 is the active form of hormone and binds to thyroid hormone receptors in target cell nuclei to initiate various physiological functions.”(2,10). Data on health related quality of life and symptoms did not show significant differences between intervention groups. Some evidence indicates that levothyroxine improves some parameters of lipid profile and left ventricular function.

EPIDEMIOLOGY;

Prevalence of subclinical hypothyroidism is around 10 to 15 % in different studies. It is said to have increased prevalence among female gender, caucasians and iodine sufficient areas. The levels of TSH is also higher in obese patients, the level being directly proportional to the BMI. It is seen more commonly in females. After the sixth decade men and women has equal prevalence. The total prevalence of subclinical hypothyroidism in general population is 10 to 15%. Higher prevalence is seen in white than black(10,13,14). The whickham survey in the north east of england reported that 7.5% 0f women and 2.5% of men have TSH levels have > 6.0mIU/l. The NHANES III study of united states reported serum TSH levels more than 4.6mu/l in 4.5% of the population. The colorado study showed raised TSH ranging between 5.0 to 10 mu/l in 9.5% of population. The prevalence of subclinical hypothyroidism in elderly women over 65 years was 17.4% among general population.(3,14)

The framingham study and dutch study analysis has confirmed that subclinical hypothyroidism has got higher prevalence among elderly population over 60 years. The prevalence was 8.2% in men and 16.9% among women. The iodine intake has no relation to the prevalence of subclinical hypothyroidism and its prevalence seems to be little higher in areas of high iodine intake rather than low salt intake areas. (3,14)

It has got higher prevalence in patients with down syndrome, type 1 diabetes mellitus and other autoimmune diseases. Pregnant women in US had 2% prevalence of subclinical hypothyroidism of which 58% had positive anti TPO antibodies. One study with 1250 populations aged over 60 years showed the prevalence of subclinical hypothyroidism in 11.6% of women and 3% of men. Antithyroid antibodies were positive in significant titres in 46% of those with serum TSH levels between 5 and 10 mIU/l and 81% of those with serum TSH greater than 10mIU/l.(2,10)


27,3%
47,6%
66,8%
66,8%
619,75%
Euthyroidism
Hypothyroidism
Sub Clinical Hypothyroidism
Hyperthyroidism
Subclinical Hyperthyroidism

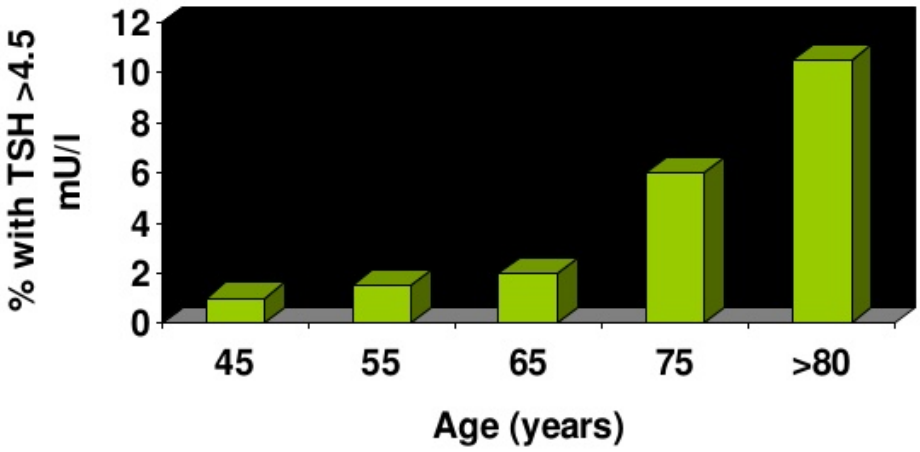
Classifying hypothyroidism by laboratory values

Type	TSH level	Free T_4 level
Primary hypothyroidism	Elevated	Low
Subclinical hypothyroidism	Elevated	Normal
Secondary hypothyroidism	Normal or low	Low

TSH, thyroid-stimulating hormone; T_4, thyroxine.

Prevalence of Subclinical Hypothyroidism in NHANES 1988-1994 (TSH>4.5)

Hollowell et al. JCEM 2002



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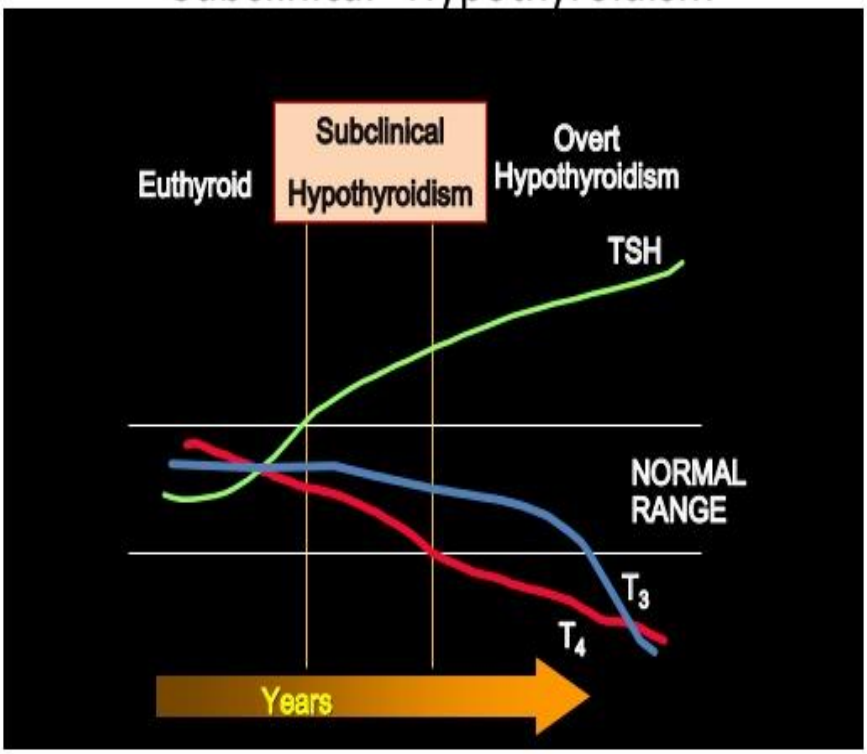
NATURAL HISTORY

Subclinical form of hypothyroidism represents mild thyroid dysfunction which has high likelihood of transformation to true hypothyroidism. In a year, transformation to true hypothyroidism is reported to be 3 to 18 %. In a follow up study consisting of 154 female patients , over a longer period of 10 years duration 57% of them retained to be SCH patients and 34% showed transformation to true hypothyroidism and only 9% of patients reverted back to normal TSH levels The strongest predictors for progression are the presence of antithyroid antibodies, serum TSH values greater than 20mIU/L, history of radioiodine ablation for graves, history of external irradiation for nonthyroidal illness and chronic lithium treatment.(3,14)

In a New Mexico study of asymptomatic ambulatory subjects with subclinical hypothyroidism older than 60 years, one third developed overt hypothyroidism during 4 years of follow-up; among them were all those whose initial serum TSH concentrations were higher than 20 uIU/mL .In a study where patients with subclinical hypothyroidism where followed for 8 years, showed that 53% of them turned out to overt hypothyroidism and 47% continued to be in subclinical range. Most of them who turned out to be overt hypothyroidism had autoimmune etiology and exposure to prior external radiotherapy and radioiodine therapy.(2,10)

Development and Progression of Mild or "Subclinical" Hypothyroidism



Subclinical is misnomer : only if found with Health check ups,
Rest all is "suspected "due to suspected and found lower range.

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IMPORTANCE;

It is necessary to treat patients with subclinical hypothyroidism if the biochemistry is sustained in patients with a past history of radioiodine treatment and positive for antithyroid antibodies. Treatment is essential in these patients because risk of progression to hypothyroidism is inevitable. Except in pregnancy where there is an immediate need for initiation, in most of the circumstances the disorder should be reconfirmed after 2 to 3 months. It has high risk for progression to heart failure and CAD. The initiation of treatment depends on age of the patient, level of TSH, and the presence of autoantibodies.(2,10,14)

ETIOLOGY:

"HASHIMOTO THYROIDITIS, an autoimmune form of thyroiditis is the commonest etiology of the disease subclinical hypothyroidism." In patients with prior history of radioiodine therapy for hyperthyroidism, subclinical hypothyroidism precedes overt thyroid failure. Subclinical hypothyroidism precedes overt hypothyroidism in patients who have undergone partial thyroidectomy for hyperthyroidism or nodular goitre. Other form of autoimmune diseases like type1 diabetes mellitus, Addison disease, down syndrome and turner syndrome are associated with increased probability of transformation to both subclinical and overt hypothyroidism of autoimmune etiology.(3,14)

Subclinical hypothyroidism is also identified during first trimester of pregnancy with positive anithyroid antibodies. The risk of developing postpartum thyroiditis or overt hypothyroidism depends largely on antibody status and titre. Subclinical hypothyroidism is also seen in patients with prior external radiotherapy to head and neck.(3,14) Nonthyroidal illness is associated with transient increase in levels of serum TSH especially in the recovery phase of critical illness. Drugs like lithium and amiodarone and radiocontrast agents are associated with increased risk of subclinical hypothyroidism.(2,10)

EFFECTS OF SUBCLICAL HYPOTHYROIDISM:

Several randomised control trials have observed rise in serum total cholesterol, serum LDL levels and serum triglceride levels in patients with subclinical hypothyroidism. It has got strong association with females ,increasing age, and those with baseline TSH >12mu/l . trials also showed correction of dyslipidemia on treatment of hypothyroidism.(2,10)

While intima and media thickness, endothelial dysfunction decreased systolic and diastolic dysfunction and dyslipidemia are all associated with subclinical hypothyroidism, this association and impact of treatment on cardiovascular outcome is limited and not constant. Variable

association is seen with prevalence of heart failure and progression to subclinical hypothyroidism. Cardiovascular morbidity and mortality is higher with TSH levels more than 10 mIU/l.(2,3,10)

Myocardial structure and contractility largely varies in relation to subclinical TSH level. Increased peripheral vascular resistance and diastolic dysfunction is seen in some patients with subclinical hypothyroidism. The cardiac function which means increased cardiac output and decreased peripheral resistance is seen after treatment with thyroxine. Few studies showed improvement in right ventricular systolic and diastolic function with thyroxine. (15,16)

The cardiovascular morbidity and mortality in subclinical hypothyroidism was illustrated by a flow mediated dilatation .This is a measure of vascular endothelial response and an early marker of atherosclerosis. It was impaired in patients with subclinical hypothyroidism against euthyroid controls. The branchial-ankle pulse velocity was significantly increased in patients with subclinical hypothyroidism. Also it was seen in some studies, patient with subclinical hypothyroidism had increased central aortic pressure and arterial stiffness. serum C reactive protein was increased in patient with subclinical

hypothyroidism which normalised with treatment. Treatment with thyroxine also seem to increase the HDL associated PAF-AH activity (platelet activating factor acetyl hydrolase) in patients with subclinical hypothyroidism.(5,15,16)

Many studies has shown increased prevalence of cardiovascular morbidity with subclinical hypothyroidism. In contrast to the above mentioned studies, the cardiovascular health study of population aged above 60 years illustrated no specific association of cardiovascular morbidity with subclinical hypothyroidism.(4,17)

LIPID ABNORMALITIES IN SUBCLINICAL HYPOTHYROIDISM.

" In patients with subclinical hypothyroidism , large cross sectional studies showed that modest elevations of serum TSH (between 5.1 and 10mIU/l) had significantly elevated total cholesterol values compared with euthyroid individuals. Consistent changes in other lipid parameters like serum LDL, serum HDL, serum triglyceride level was not appreciated. Some studies with subclinical hypothyroidism showed abnormal lipid profile with elevated LDL levels and decreased serum HDL levels."

Some studies showed higher levels of serum apoprotein A1and serum lipoprotein A levels. “In a randomised control trial, patients with subclinical hypothyroidism treated with thyroxine showed significant lowering of total cholesterol and serum LDL levels (18,19)”. A metaanalysis in patients with subclinical hypothyroidism showed significant reduction in total cholesterol levels, without much significant change in serum HDL and triglyceride levels. The lowering of serum cholesterol was noticed in patients with levels more than 240mg/dl .(21)

NEUROPSYCHIATRIC MANIFESTATIONS:

Analysis of reports has showed increased prevalence of depression and bipolar affective disorder in patients with subclinical hypothyroidism. But the study is limited because of inadequate control groups, lithium therapy, patients with increased response to serum TSH ,administration of TRH or high levels serum antithyroid antibodies.(22) Some studies revealed the prevalence of 14.8% of hypothyroidism in patients with neurotic depression. Higher prevalence of panic disorder and poor response to antidepressant therapy was seen in patients with subclinical hypothyroidism and depression. Those diagnosed with subclinical hypothyroidism has increased risk of developing anxiety, somatic complaints, depressive features, and hysteria in comparison to euthyroid

women. Improvements in neuropsychiatric manifestations are seen with appropriate treatment with thyroxine.(8,21,22)

Evaluation of patients with euthyroid, hypothyroidism, and hyperthyroidism to measure brain function using BRAIN MRI with widely used “digit -n-back working memory task.” Same functions were carried out after treatment with thyroxine. Significantly low score of brain function was seen with hypothyroidism and subclinical hypothyroidism compared to euthyroid state. Evaluation was done in areas like “common frontoparietal network, bilateral dorsolateral prefrontal cortex, bilateral premotor areas, supplementary motor area, anterior cingulate cortex and bilateral parietal areas.” The load effect of BOLD response(blood oxygen level dependant)was found only in bilateral parietal and premotor cortex. The same patients exhibited some load effects in all five areas after treatment with thyroxine. These analysis concluded impairment of working memory in subclinical hypothyroidism. Also treatment with l-thyroxine showed improvement in memory performance and frontal executive functions.(23,24)

IMPACT ON PREGNANCY AND FERTILITY:

"Subclinical hypothyroidism undetected during pregnancy adversely affect the survival and neuropsychological development of fetus Normally the requirement of thyroxine in pregnancy increases by 45% as the levels of thyroid binding globulin increases. In children of subclinical hypothyroidism aged 7 to 9 years showed a 7 point reduction in intelligent quotient compared with euthyroid mothers. So this suggest the importance of screening of pregnant women for hypothyroidism and treatment of subclinical hypothyroidism."(24)

NEUROMUSCULAR DYSFUNCTION:

Patients with subclinical hypothyroidism may develop significant neuromuscular dysfunction. This is seen with TSH levels usually greater than 10mIU/l. The neuromuscular dysfunction reverses on treatment with treatment with thyroxine.(10)

Infertility and ovulatory dysfunction has higher association with subclinical hypothyroidism. Hypothyroidism is associated with higher prevalence of infertility from anovulation. Increased risk of abortion are seen with pregnant women with overt hypothyroidism. Spontaneous abortion of 10% was seen in pregnant females with subclinical

hypothyroidism with elevated antithyroid peroxidise and antithyroglobulin antibodies. Luteal phase dysfunction, anovulatory cycles and menorrhagia are seen with subclinical hypothyroidism which results in infertility. The outcome of pregnancy in patients with hypothyroidism on adequate treatment and inadequate therapy was compared. Those who received adequate therapy, the complications during pregnancy was minimal.(22)

SPECIAL SITUATIONS:

- Transient elevation in levels of serum TSH levels was seen in patients with critical illness during recovery phase and these patients should be revaluated as subclinical hypothyroidism in hospitalised patients with elevated TSH leves may be invalid.
- Assay variability seen with diurnal variation shows elevated serum TSH levels due to robust pulse of TSH secretion especially at night.
- Heterophile antibodies might interfere with TSH measurement.
- Adrenal insufficiency is associated with elevated with TSH levels.
- TSH secreting pituitary adenomas
- Resistance to thyroid hormone
- Metoclopramide or domperidone therapy.(1,7,9)

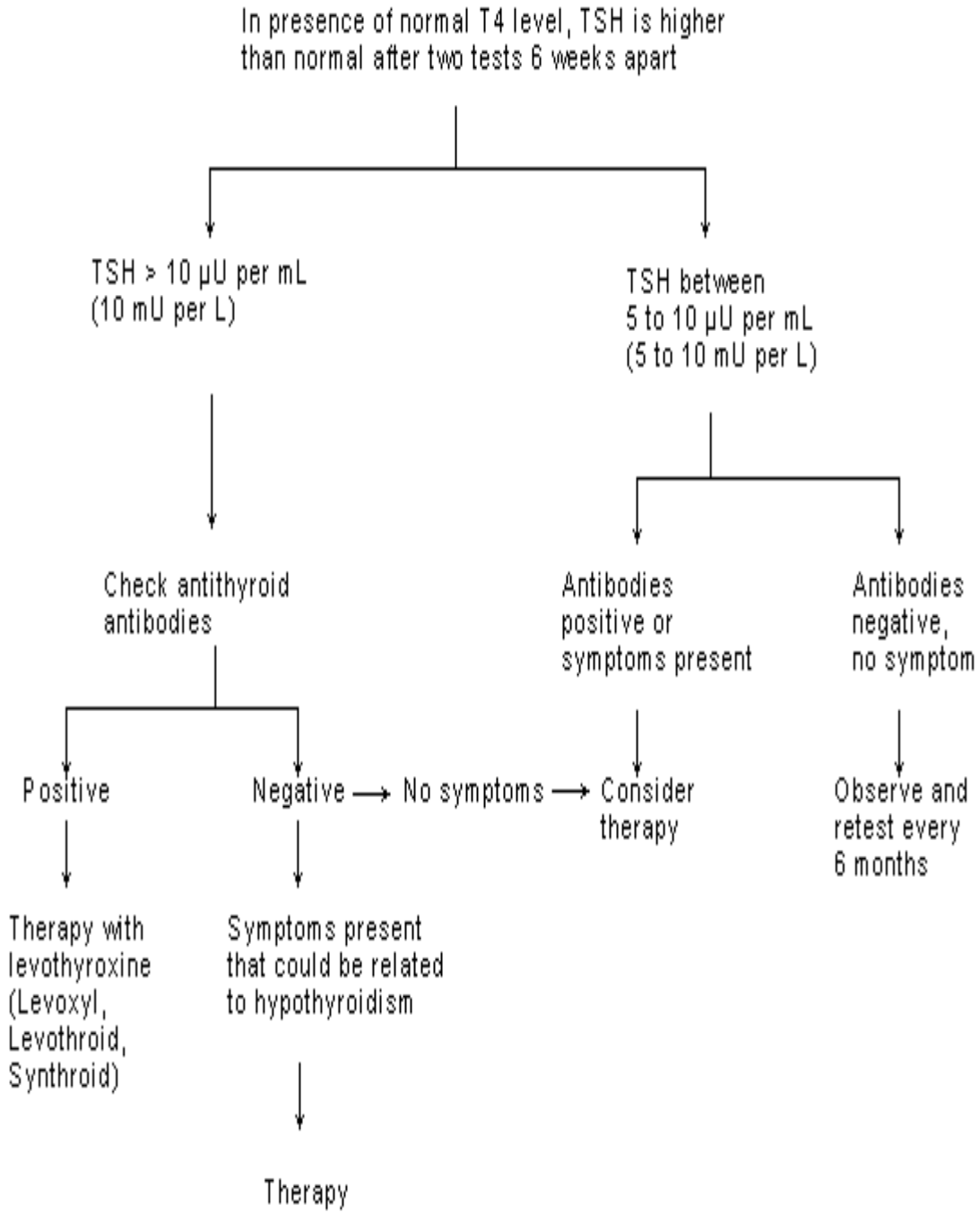
SCREENING OF THYROID DISEASE:

"The following categories of patients should be screened for thyroid disease.

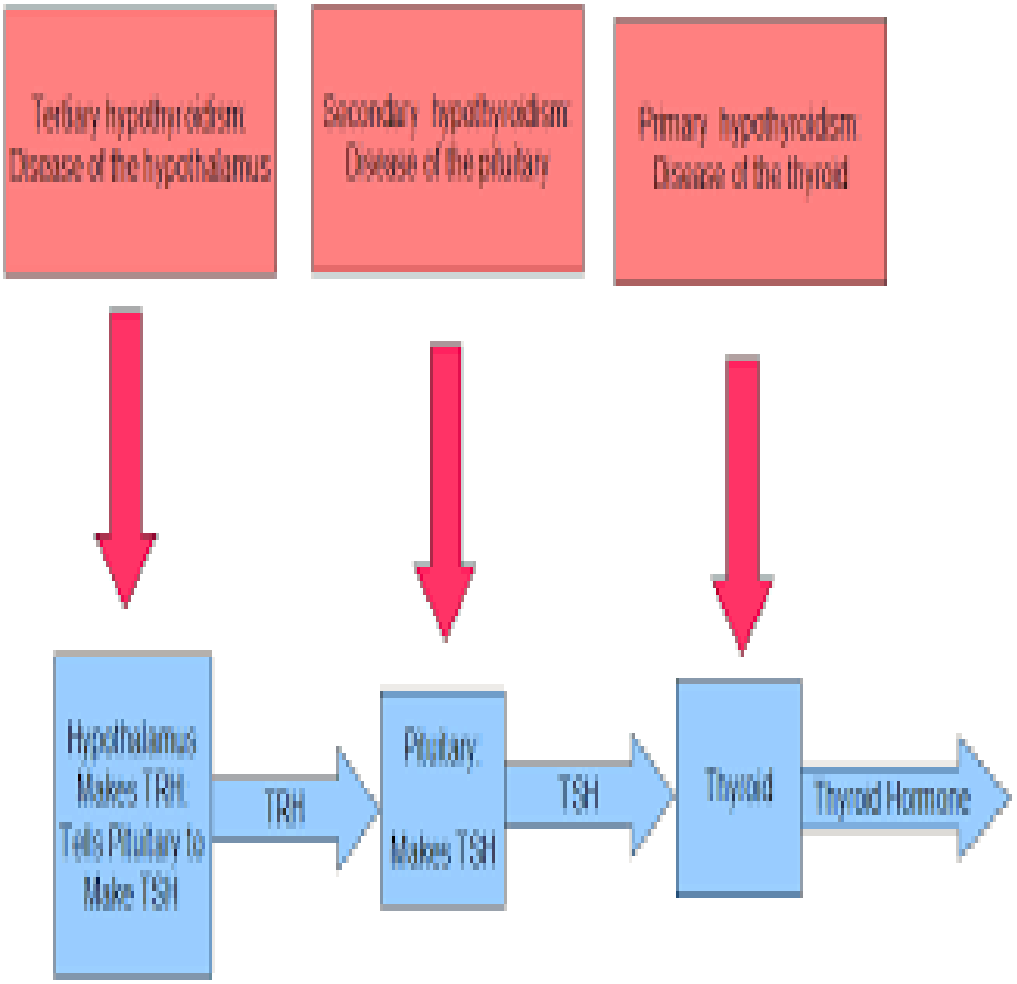
- Patients with atrial fibrillation or hyperlipidemia
- Periodic assessment in patients receiving amiodarone and lithium
- Annual check of TFT in diabetic patients
- Females with type 1 diabetes in first trimester of pregnancy and post delivery (because of 3 fold increase in incidence of postpartum thyroid dysfunction)
- Females with past history of postpartum thyroiditis.
- Annual check of thyroid function in patients with down syndrome, turner syndrome and Addison disease.
- Females with thyroid autoantibodies
- Maternal thyroid antibodies associated with miscarriage and preterm delivery. "(1,2,3,4)

Causes of Subclinical Hypothyroidism

PRIMARY (thyroid dysfunction)	SECONDARY (pituitary dysfunction)
• Hashimoto thyroiditis • Endemic iodine deficiency • History of ablative radioiodine therapy or thyroidectomy.	• Sheehan's syndrome • Lymphocytic hypophysitis • history of a hypophysectomy.


In presence of normal T4 level, TSH is higher than normal after two tests 6 weeks apart
TSH > 10 µU per mL (10 mU per L)
TSH between 5 to 10 µU per mL (5 to 10 mU per L)
Check antithyroid antibodies
Antibodies positive or symptoms present
Antibodies negative, no symptom
Positive
Negative
No symptoms
Consider therapy
Observe and retest every 6 months
Therapy with levothyroxine (Levoxyl, Levothroid, Synthroid)
Symptoms present that could be related to hypothyroidism
Therapy

Primary, Secondary and Tertiary Hypothyroidism



HYPOTHYROIDISM:

Hypothyroidism results from varied abnormalities that cause insufficient secretion of thyroid hormones. The most common cause is autoimmune thyroiditis. Myxoedema is called a severe form of thyroid disorder in which there is accumulation of hydrophilic mucopolys accharides in the ground substance of dermis and other connective tissue . It leads to thickening of facial features and a induration of skin. (1,6,4) .Other hormones like somatostatin glucocorticoids, cytokines like interleukin 1and TNF alpha, drugs like phenytoin and dopamine suppress the TSH secretion . TSH and TRH secretion is inhibited by T4, forming a negative feedback loop that maintains free T4 within the normal reference range. While T4 is exclusively secreted by the thyroid gland, about 80% of T3, which is the active hormone, is generated by 5'monoiodination of T4.(1,2)

THYROID HORMONE TRANSPORT AND ACTION

Thyroid hormone exists in both free and bound form in circulation. About 80% of the hormone is bound to thyroxine binding globulin .Other proteins to which thyroid hormone is bound are transthyretin (TTR), and albumin. Only the free form of thyroxine enters cells and produces biological effect.

After binding to a nuclear DNA bound thyroid hormone receptor (TR), for which hormone T3 has a 15-fold high binding affinity compared to T4.There are two TR genes, TRα and TRβ. The coded protein has three major functional domains, one to bind ligand, one to bind DNA, and the other for transcriptional activation.(1.3)

Iodide present in the plasma is taken up via active transport into the thyroid follicular cells, a process which becomes more evident in the iodine deficiency state. Iodine deficiency results in enlargement of the thyroid to enhance the ability of the glands to trap iodine. The term endemic goitre is used to define goitre seen in a population with iodine deficiency. An area is defined to be endemic if more than 5% of children, in the age group between 6 to 12 years , are found to have goitre. (1,2,3,4)

The stages of goitre formation include an initial diffuse parenchymatous goitre, followed by diffuse colloid goitre, hyperplastic nodular goitre, nodular parenchymatous goitre and nodular colloid goitre. The first two stages of autoimmune are found to disappear after making region iodine replete, while later stages of thyroiditis are unlikely to involute. Other manifestations of iodine deficiency depend on these verity and age at exposure. Endemic cretinism is a state of severe congenital

hypothyroidism occurring in an endemic area. Two clinical types are recognised: (1,2)neurological cretinism, characterised by mental retardation, abnormal speech and hearing, diplegia, and strabismus; myxoedematous type. It is further characterised by prominent features of hypothyroidism, mental retardation and short stature. Learning disability has been described even in euthyroid children living in endemic areas. During pregnancy exposure to iodine deficiency is also highly associated with complications like abortions, stillbirths, increased foetal anomalies and perinatal mortality. It is necessary to create awareness to people by health education for consumption of iodated salt .**(1)**

AUTOIMMUNE THYROIDITIS

"Autoimmune form of thyroid disease evolves in a stepwise manner first presenting as hashimoto's type of thyroiditis and ultimately transforming at later stages to atrophic form of thyroiditisue to damage to the thyroid tissue. This causes a compensatory increase in the level of thyroid stimulating hormone to maintain normal thyroid hormone levels .This state of condition at which at which patients are asymptomatic, but still the TSH levels are quite high is called subclinical hypothyroidism. As the disease progresses, T4 level decreases and TSH level increases further. At this stage of disease, symptoms suggestive of hypothyroidism

becomes evident especially with TSH levels more than 10 mIU/l. this clearly, marks transition from subclinical to overt hypothyroidism."(1,2,4,5)

Prevalence:

Autoimmune form of hypothyroidism has an annual incidence of 4 per 1000 among female population and 3 per 1000 among male population. It is found to be more commonly prevalent in japan, most likely relating to dietary exposure to high iodine intake and certain genetic correlation. The prevalence of hypothyroidism increases as age increases. The statistically analysed mean age group for prevalence is 60 years.(1,5,6)

The incidence of subclinical hypothyroidism is roughly around 8 to 10 % among women and 3% among males. The risk of progression from subclinical hypothyroidism to overt hypothyroidism is 4% annually. This transformation is more common when subclinical hypothyroidism is associated with positive antithyroid antibodies.

"Hashimoto's thyroiditis is characterized by marked lymphocytic infiltration of the thyroid, germinal center formation , thyroid follicles

atropy, oxyphil metaplasia, absence of colloid, and mild to moderate fibrosis. In atrophic thyroiditis, there is much more extensive fibrosis, lymphocyte infiltration is less pronounced, and thyroid follicles are almost completely absent. A weak association also exists between polymorphisms in *CTLA-4*, a T cell–regulatory gene, and autoimmune hypothyroidism. Both of these genetic associations are shared by other autoimmune diseases, which may explain the relationship between autoimmune hypothyroidism and other autoimmune diseases, especially type 1 diabetes mellitus, Addison's disease, pernicious anemia, and vitiligo."(1,2,4,11)

There is association between autoimmune form of hypothyroidism and down' syndrome relating to a gene on the chromosome 21. The association of autoimmune hypothyroidism with turner syndrome is related to X chromosome related genetic factor. High dietary iodine intake and decreased exposure of children to infection and microorganism has high risk of developing autoimmune hypothyroidism.(2,3,6,13)

Clinically significant markers of autoimmune hypothyroidism are antibodies to thyroid peroxidase and thyroglobulin .Autoimmune hypothyroidism is characterised by complement mediated attack complex

by the fixation of complement by TPO antibodies. Transplacental transfer of these antibodies TPO and thyroglobulin have no role in fetal hypothyroidism. Among autoimmune hypothyroidism, TSH-R antibodies are found to be positive in 20%. This results in hypothyroidism especially among Asian population. In this case, the transplacental transfer of antibodies causes transient neonatal hypothyroidism. (2,4,12)

PRESENTATION OF SUBCLINICAL HYPOTHYROIDISM

SYMPTOMS:

- Dry course skin
- Decreased perspiration
- Puffiness of face
- Skin thickening without obvious pitting
- Pallor
- Yellowish discoloration of skin due to hypercarotenemia
- Brittle and dry hair
- Alopecia
- Madarosis
- Constipation
- Weight gain despite of poor appetite

- Cold intolerance
- Loss of libido
- Amenorrhoea and oligomenorrhoea
- Infertility and miscarriages

SIGNS:

- Bradycardia
- Increased distolic BP
- Cool extremities
- Sleep apnoea
- Serous cavity effusions like pleural and pericardial effusions
- Carpal tunnel syndromes
- Delayed relaxation of tendon reflexes
- Memory disturbances.(4,3,6)

TREATMENT OF HYPOTHYROIDISM:

The standard daily replacement doseof oral levothyroxine is usually around 1.6 μg/kg body weight (typically 100–150 μg), to be ideally taken at least 30 min before breakfast.(2,3,4).“Adult hypothyroid patients under 60 years old, with no evidence of heart disease may be started on 50–100 μg of oral levothyroxine (T4) daily. The dose is

adjusted accordingly on the basis of TSH levels, with the treatment goal of achieving normal TSH. The treatment responses are gradual and should be measured about 2 months following treatment or after any subsequent dosage change in levothyroxine dosage. The clinical effects of replacement of levothyroxine are slow to appear. Patients might not experience full relief from symptoms till 3–6 months after the normal TSH levels are restored. Adjustment of levothyroxine dosage should be made in 12.5- or 25-µg increments if the TSH is still found to be high; Decrements of the same magnitude has to be made if the TSH level is further suppressed. (2,4)

Serum T4 has a half life of 7 days . On missing a dose of tablet , patients are advised to take 2 tablets at a time .sometimes patients require high doses of thyroxine;

- Malabsorption
- Estrogen or hormone replacement therapy
- Heavy meals
- Drugs interfering with its metabolism like anticon vulasants {carbamezepina and phenytoin}, calcium and iron supplements, Proton pump inhibitors, lovastatin, amiodarone and rifampicin etc. (1,2,3)

“Treatment of subclinical hypothyroidism is indicated to prevent progression of disease to overt hypothyroidism in patients with elevated serum TSH levels more than 10mIU/l and presence of high titres of serum anti TPO antibodies. Only 5 % of subclinical levels of TSH return to normal without treatment. Presence of obvious goiter also warrants treatment. The major practical benefit of initiation of treatment in subclinical hypothyroidism is improvement of symptoms, cognitive function like memory, lowering of levels of serum total cholesterol and serum LDL levels. Also treatment significantly improves cardiac function like myocardial contractility.”(1,2,25)

There is no universally accepted recommendations for the management of subclinical hypothyroidism. Treatment with levothyroxine is recommended when the patient is a woman and if she wishes to conceive or is already pregnant, or when TSH levels are above 10 mIU/L. When serum TSH levels are below10 mIU/L, treatment with thyroxine should be considered when patients have symptoms suggestive of hypothyroidism, presence of positive TPO antibodies, or evidence of heart disease. It is important to confirm that any elevation of TSH is sustained over a 3-month period before treatment is given. Treatment is initiated with a starting low dose of levothyroxine (25–50 μg/d) with the

goal of normalizing TSH. If levothyroxine is not given, thyroid function should be evaluated and followed up annually.(2,10,25)

TREATMENT GUIDELINES:

TSH BETWEEN 4.5 AND 10 mIU/l ;

Although there is no conclusive evidence to show reduction in symptoms and lipid profile abnormalities in any randomised control trials with levothyroxine therapy, it might prevent transformation to true disease. There is no proper analysis to show the benefits of early therapy of subclinical disease compared with treatment of patients after the development of symptoms.(2,4,25)

So therapy of this group of patients with levothyroxine has to be individualised and it largely depends on the following issues;

- Degree of TSH elevation
- Age of the patient
- Associated medical illness
- Persistent and gradual increase in TSH on follow up.
- Presence of goitre
- Presence of antithyroid antibodies
- Symptoms suggestive with hypothyroidism

So for patients with TSH levels between 4.5 and 10 mIU/l , routine treatment with levothyroxine is not advisable. It is essential to follow up such patients with thyroid function testing at 6 to 12 months interval for evaluating the progression of the disease.(25)

Considering the intelligent quotient of women with subclinical hypothyroidism during pregnancy and the effect of thyroxine on the neuropsychiatric development and growth of the patient, treatment of children and adolescent children and pregnant females with elevated TSH has become a prime indication. Some patients with subclinical hypothyroidism present with symptoms compatible with hypothyroidism and therapy may be initiated and continued for several months trial with monitoring of symptomatic improvement. Further continuation of treatment with thyroxine depend on symptomatic benefits.(25,4,2,3)

TSH LEVELS MORE THAN 10mIL/l;

This group of patients benefit much from levothyroxine therapy. The factors that determine the response of lipid profile abnormalities to thyroxine therapy are higher levels of TSH and high levels of total cholesterol and hypertriglyceridemia. Evidence based study proves worsening of bipolar disorder and depression with mild thyroid failure. It

may also alter the pattern of nerve conduction, muscle function and cardiac contractility. Treatment with levothyroxine might cause symptomatic improvement in these patients.(4,25)

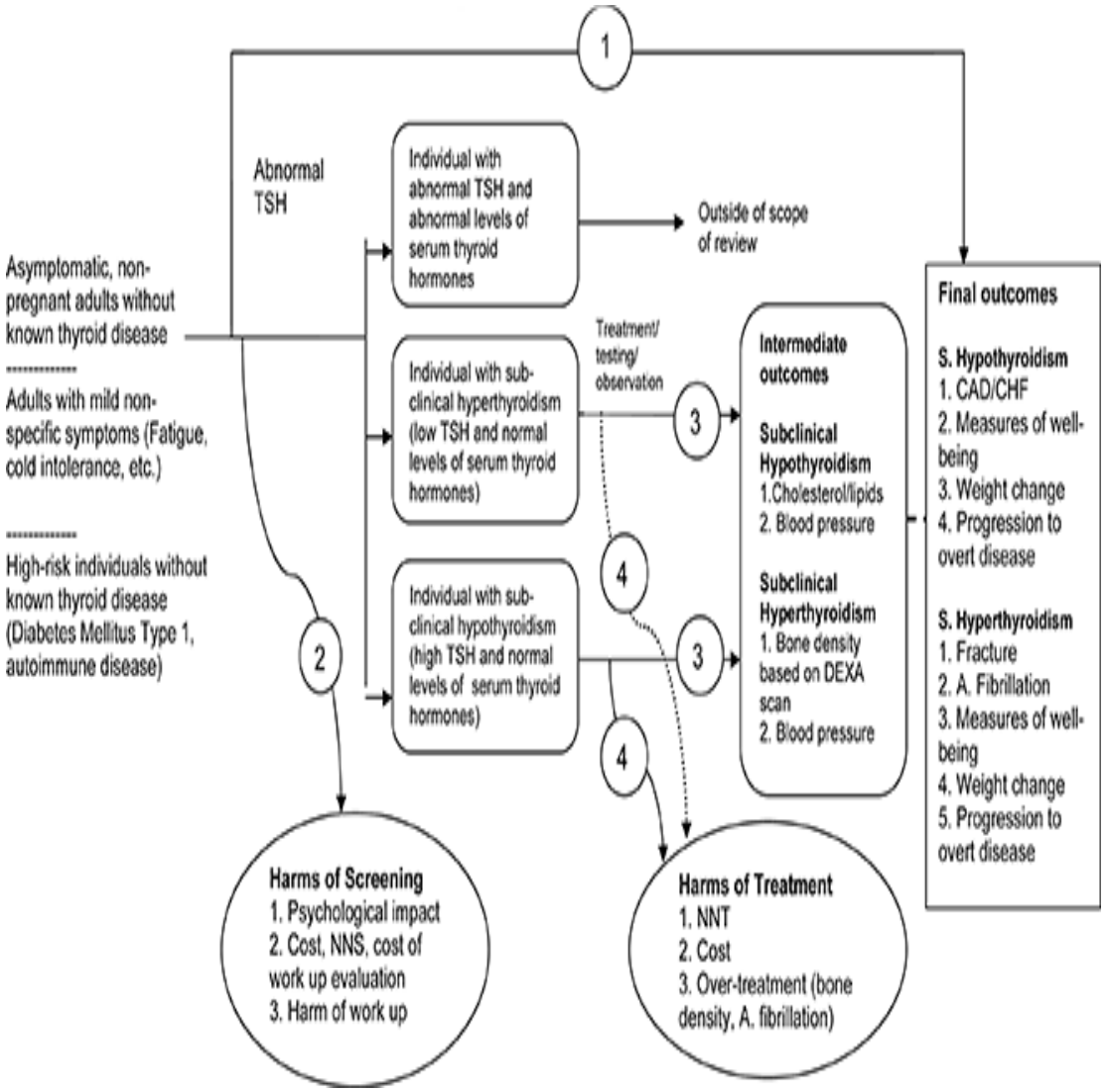
Treatment is initiated if TSH is more than 10 mIU/L in following situations:

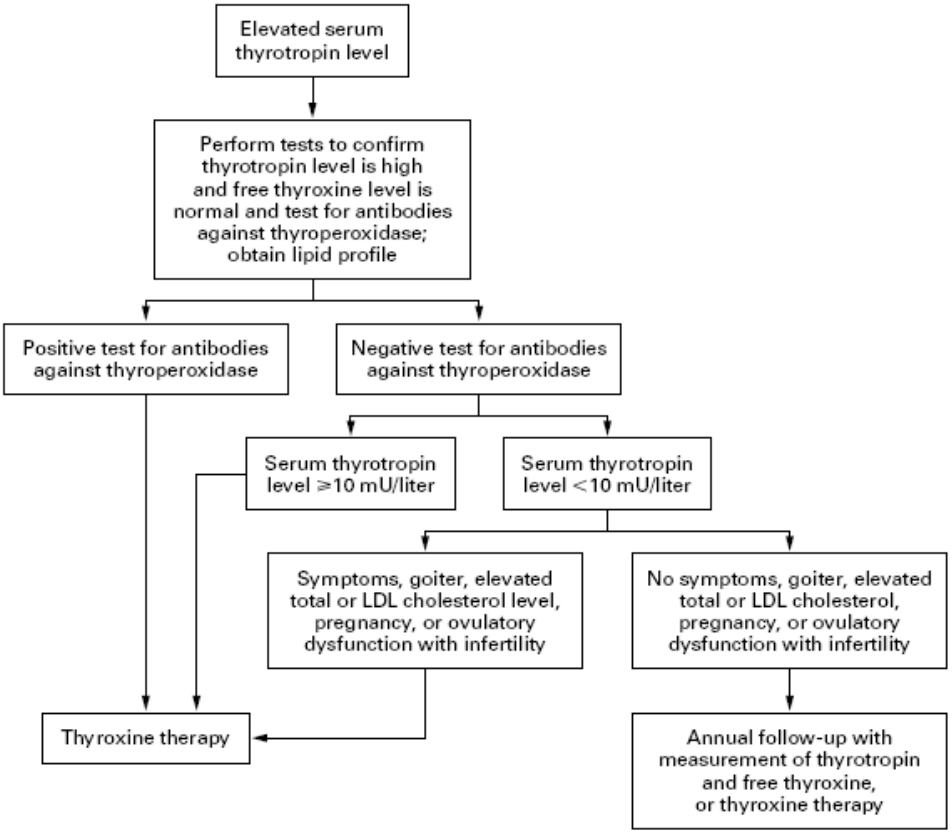
- Higher TSH levels on repeated measurements
- Presence of signs and symptoms
- Family history of thyroid disorder
- Pregnant females
- Severe hyperlipidemia
- Infertility
- Insulin resistance
- Tobacco usage
- Morbid obesity(2,3)

Start therapy with low dose of 50 to 75microgram per day .Lower doses of 12.5 to 25 microgram per day should be used in patients with coronary artery disease. Patient should be followed up 4 to 6 weeks following therapy with serum TSH levels and the dosage can be changed accordingly and then followed up yearly to achieve appropriate serum TSH level (2,3,7)

Controversies regarding treatment of subclinical hypothyroidism:

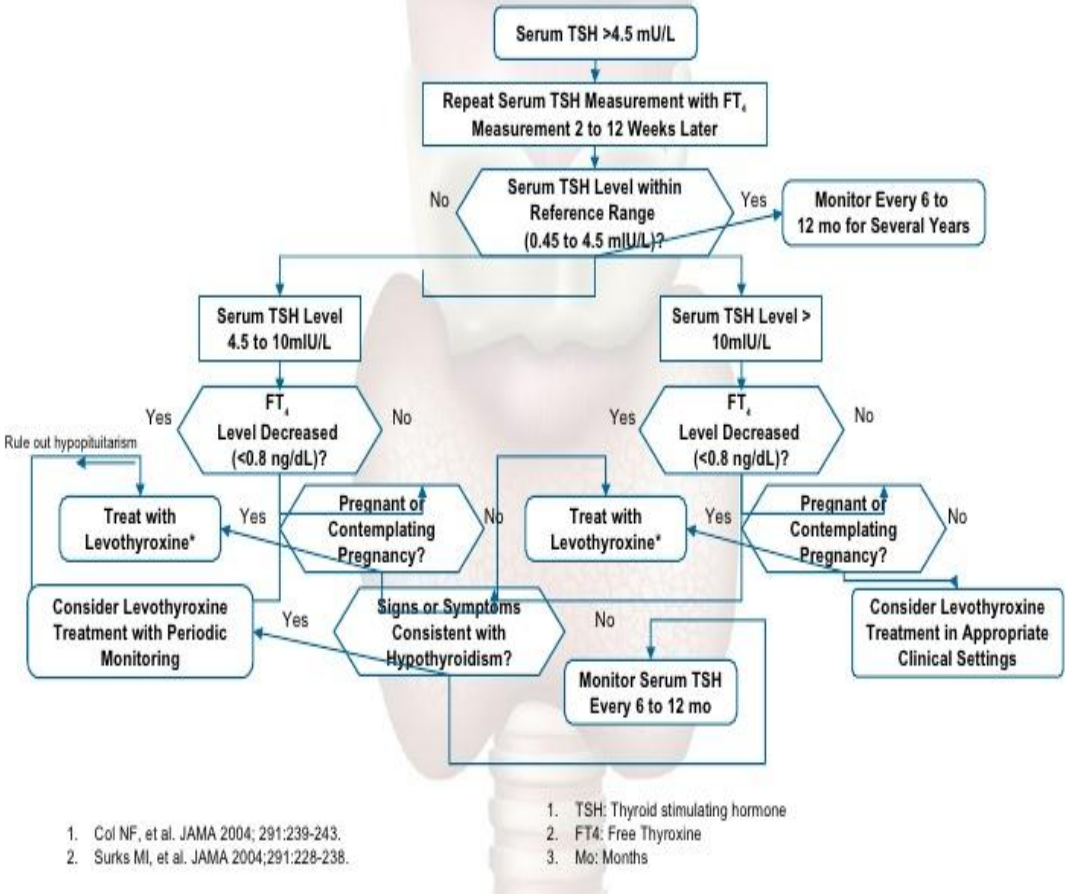
- Cost of therapy
- Cost of monitoring with TFT
- Lifelong compliance to daily therapy especially in asymptomatic patients
- Exacerbation of angina and arrhythmias(2,10,14)


1
Abnormal TSH
Individual with abnormal TSH and abnormal levels of serum thyroid hormones
Outside of scope of review
Asymptomatic, non-pregnant adults without known thyroid disease
Adults with mild non-specific symptoms (Fatigue, cold intolerance, etc.)
High-risk individuals without known thyroid disease (Diabetes Mellitus Type 1, autoimmune disease)
Individual with sub-clinical hyperthyroidism (low TSH and normal levels of serum thyroid hormones)
Treatment/ testing/ observation
3
Intermediate outcomes
Subclinical Hypothyroidism
1.Cholesterol/lipids
2. Blood pressure
Subclinical Hyperthyroidism
1. Bone density based on DEXA scan
2. Blood pressure
Final outcomes
S. Hypothyroidism
1. CAD/CHF
2. Measures of well-being
3. Weight change
4. Progression to overt disease
S. Hyperthyroidism
1. Fracture
2. A. Fibrillation
3. Measures of well-being
4. Weight change
5. Progression to overt disease
4
2
Individual with sub-clinical hypothyroidism (high TSH and normal levels of serum thyroid hormones)
3
4
Harms of Screening
1. Psychological impact
2. Cost, NNS, cost of work up evaluation
3. Harm of work up
Harms of Treatment
1. NNT
2. Cost
3. Over-treatment (bone density, A. fibrillation)


Elevated serum thyrotropin level
Perform tests to confirm thyrotropin level is high and free thyroxine level is normal and test for antibodies against thyroperoxidase; obtain lipid profile
Positive test for antibodies against thyroperoxidase
Negative test for antibodies against thyroperoxidase
Serum thyrotropin level ≥10 mU/liter
Serum thyrotropin level <10 mU/liter
Symptoms, goiter, elevated total or LDL cholesterol level, pregnancy, or ovulatory dysfunction with infertility
No symptoms, goiter, elevated total or LDL cholesterol, pregnancy, or ovulatory dysfunction with infertility
Thyroxine therapy
Annual follow-up with measurement of thyrotropin and free thyroxine, or thyroxine therapy

Subclinical Hypothyroidism: Management Algorithm

Algorithm for the management of subclinical hypothyroidism (T_4 = thyroxine: TSH = thyrotropin-stimulating hormone)



1. Col NF, et al. JAMA 2004; 291:239-243.
2. Surks MI, et al. JAMA 2004;291:228-238.

1. TSH: Thyroid stimulating hormone
2. FT4: Free Thyroxine
3. Mo: Months

AIMS AND OBJECTIVES

- To assess the lipid profile abnormalities in patients with subclinical hypothyroidism.

MATERIALS AND METHODS

Source of the data

This study is a hospital based cross sectional study performed in Government kilpauk medical Hospital. All patients who fitted the biochemical evidence for subclinical hypothyroidism and the inclusion, exclusion criteria were included in the study. None of the patients were part of a routine screening programme.

Design of study

Cross sectional, comparative study

Period of study

8 months

Sample size

96

Ethical committee approval :obtained

Consent : Informed consent obtained

Financial support : Nil

Conflict of interest : Nil

Collaborating department:

Department of endocrinology

Department of general surgery and ostretics & gynaecology.

Selection of study subjects

- **Inclusion criteria**

All newly detected cases of subclinical hypothyroidism { normal t3, t4 , free t4 and TSH > 5.5 mU/L}

- **Exclusion criteria**

1. Patients aged twelve or less.
2. Patients on thyroxine
3. Known case of diabetes and hypertension
4. Chronic renal failure
5. Chronic liver disease
6. Primary adrenal failure
7. On drugs like beta blockers ,diuretics, steroids, OCP,
8. Patients already on hypolipidemic drugs.

Applying the sample size formula :

$$N=Z^2\{P*Q\}/ l^2$$

- Z; with 95% confidence interval
- P: prevalence of subclinical hypothyroidism
- Q: 100-p
- L: relative precision is 50%

So on applying this formula my sample size was around 96

JUSTIFICATION OF STUDY

The prevalence of subclinical hypothyroidism is on increasing trend especially among females and pregnant women. It also has close association with the metabolic syndrome. The two most important complications of ignoring subclinical hypothyroidism with treatment might result in dyslipidemia and adverse cardiac function. So early diagnosis of dyslipidemia in subclinical hypothyroidism and its treatment with thyroxine helps to reduce cardiovascular complications and morbidity.

METHOD OF THE STUDY:

Cases were selected from patients presenting to general medicine op, general surgery op, endocrinology op and obstretics and gynaecology op. Patients presenting to these op with vague complaints of obesity, recent gain of weight, tiredness, coarse facial features, hair loss, dry skin, infertility, voice changes, memory disturbance, cognitive dysfunction, mood disorders, swelling of neck, menstrual irregularities are selected. They are screened for subclinical hypothyroidism by doing fasting TFT comprising freeT4, freeT3 and TSH and fasting lipid profile is also done for the patient. Among the 620 patients screened for subclincal hypothyroidism, 96 turned out to have the disease.

All pregnant females are screened with TFT. Patients are selected after they fit into the inclusion and exclusion criteria. Clinical data comprises of thorough symptomatic analysis and physical examination and detailed history regarding past illness and drug intake. Laboratory analysis of blood urea, serum creatinine, TFT comprising of free T3, free T4, and TSH. And fasting lipid profile. In our college, thyroid function test was done using ELISA and lipid profile using enzymatic kit method.

SAFETY:

- No harm done to the patient
- No extra expenses for the patient
- Informed consent was obtained

LIMITATIONS OF THE STUDY

Sample size was achieved with less absolute precision, hence the results of the study will have wide variability. Due to limited resources and practical constraints this study is being carried out with a small sample size. Thus the appropriate representation of the population and better outcomes could be attained by increasing the sample size

RESULTS

STATISTICAL TOOLS:

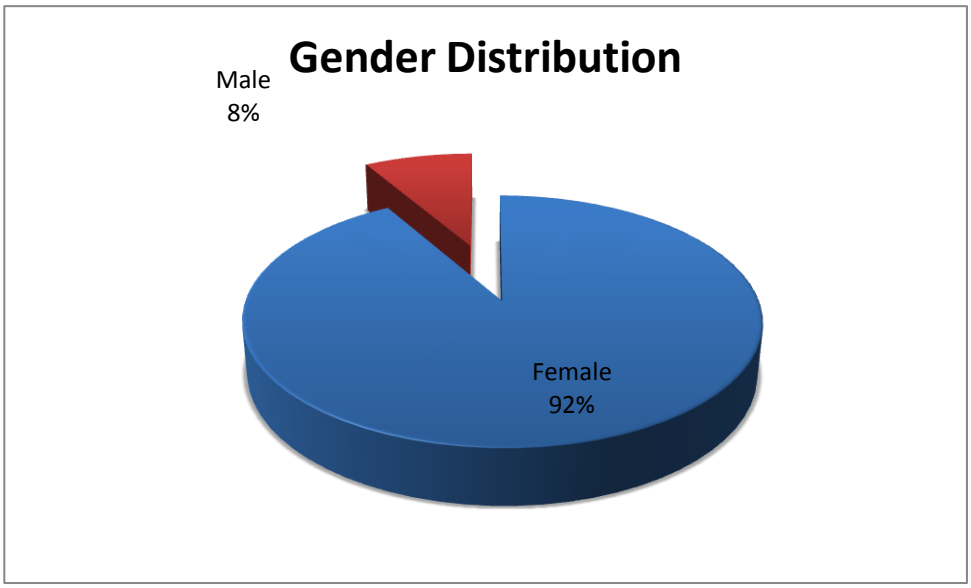
The collected data was analysed with SPSS 16.0 version. To describe about the data descriptive statistics, frequency analysis, percentage analysis were used for categorical variables and the mean & S.D were used for continuous variables. To assess the relationship between the variables Pearson's Correlation was used. To find the significance in categorical data Chi-Square test was used. In both the above statistical tools the probability value .05 is considered as significant level.

Using this computer software, multiple variables like mean range percentages, standard deviation, chi square and p value etc are used to test for the statistical significance of the study. A p value of less than 0.05 denotes significant relationship.

PROFILE OF THE STUDY CASES:

TABLE 1 : SEX DISTRIBUTION.

SEX	Frequency	Percent
Female	88	91.7
Male	8	8.3
Total	96	100.0

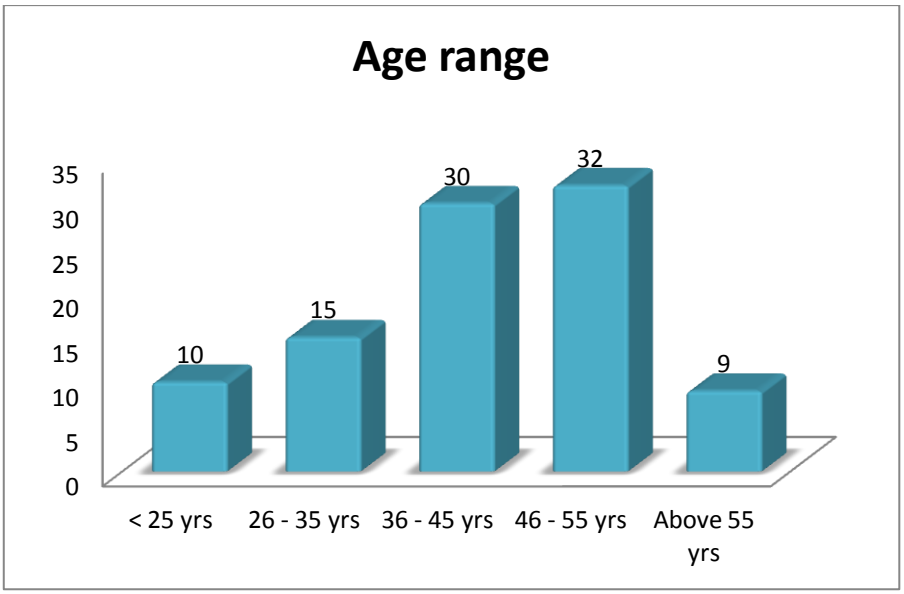


Of the 96 cases, 88 cases(91.7%) were females and 8 cases (8.3%) were males

TABLE 2:

AGE DISTRIBUTION:

AGE	Frequency	Percent
< 25 yrs	10	10.4
26 - 35 yrs	15	15.6
36 - 45 yrs	30	31.3
46 - 55 yrs	32	33.3
Above 55 yrs	9	9.4
Total	96	100.0



Among the 96 patients ranging from 11 years to 60 years with maximum 33% were between 46 to 55 years. The mean age was 41.3 years.

TABLE 3:

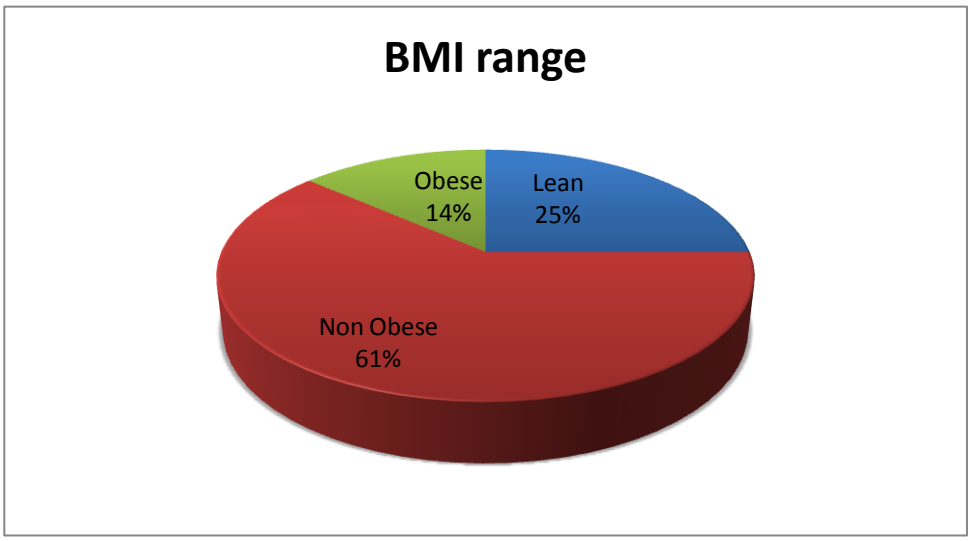
BMI DISTRIBUTION:

BMI	Frequency	Percent
Lean	24	25.0
Normal	59	61.5
Obese	13	13.5
Total	96	100.0

Lean - <20 kg/m^2

Normal -20 to 25 kg/m^2

Obese- >25 kg/m^2

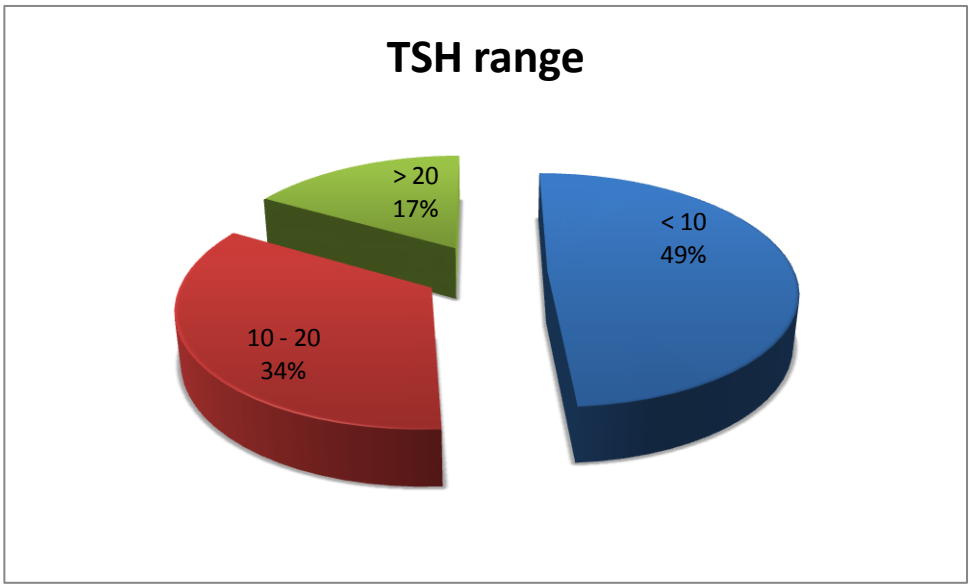


Majority of cases around 61% were having normal BMI ranging from 20 to 25 kg/m^2.

TABLE 4;

TSH DISTRIBUTION:

TSH	Frequency	Percent
< 10	47	49.0
10 - 20	33	34.4
> 20	16	16.7
Total	96	100.0



Among the 96 cases the mean TSH value was 12.3 mIU/l ranging between 5.8 and 25 mIU/l. 49% of cases were having TSH between 5.5 and 10mIU/l and 34% were having TSH between 10 to 20 mIU/l.

TABLE 5:

TOTAL CHOLESTEROL DISTRIBUTION:

TOTAL CHOLESTEROL	Frequency	Percent
Normal	39	40.6
Borderline	18	18.8
High	39	40.6
Total	96	100.0

***Normal*: < 200mg/dl**

Borderline:201 to 239 mg/dl

High: > 240mg/dl

TABLE 6:

LDL DISTRIBUTION:

LDL	Frequency	Percent
Normal	41	42.7
Borderline	14	14.6
High	41	42.7
Total	96	100.0

Ldl values

Normal: < 130mg/dl

Borderline: 131 to 159 mg/dl

High: >160 mg/dl

TABLE 7:
TRIGLYCERIDE DISTRIBUTION:

Triglyceride	Frequency	Percent
Normal	70	72.9
Borderline	16	16.7
High	10	10.4
Total	96	100.0

Normal: <150 mg/dl
Borderline: 151 -199 mg/dl
High: > 200 mg/dl

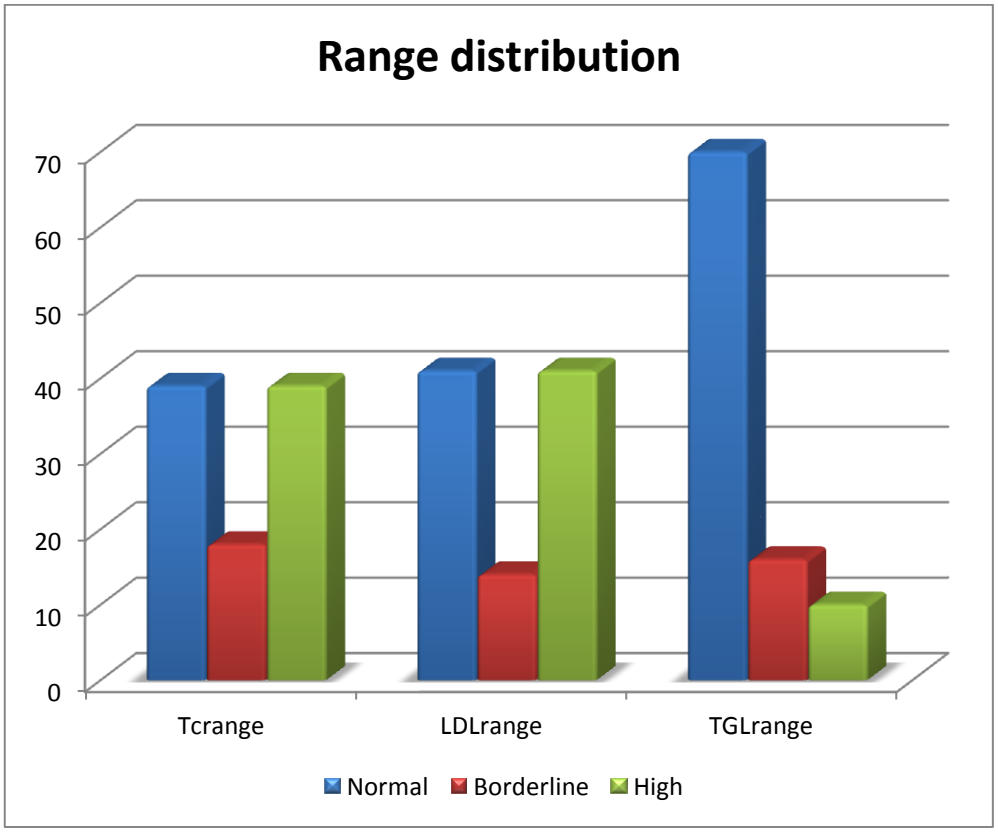
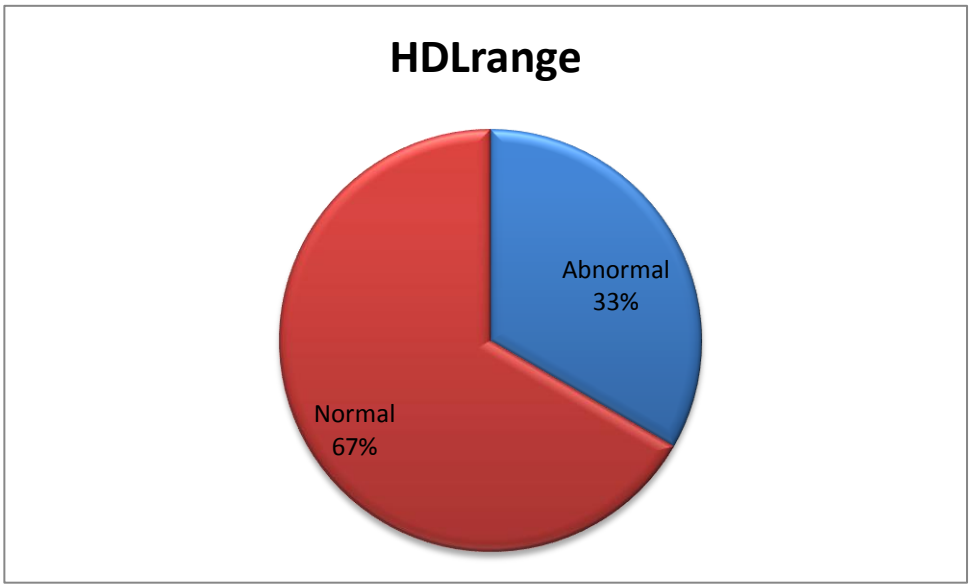


TABLE 8:

HDL DISTRIBUTION:

HDL	Frequency	Percent
Abnormal	32	33.3
Normal	64	66.7
Total	96	100.0



Normal :> 50

Hypercholesterolemia was found in 40.6% of patients . Among 96% patients, 39 cases had high total cholesterol values. Borderline high values were found in 18.8 % of patients. Mean cholesterol value of 213 mg/dl ranging from minimum of 119 to 310 mg/dl.

LDL was elevated in 42.7% of cases. Among 96 cases ,41 patients had elevated LDL levels more than 160 mg/dl. Borderline high LDL values were found in 14.6%. The mean LDL value was 139 mg/dl ranging from minimum of 76 to 290 mg/dl.

Triglyceride was elevated in only 27.1% . Among 96 cases, only 26 cases had high triglyceride values. Mean triglyceride value of 121.3 mg/dl ranging from minimum of 76 to 222 mg/dl

HDL values were found to be normal in 66.7% of cases .the mean HDL was 51.9 mg/dl ranging from minimum of 33 to 70 mg/dl.

DESCRIPTIVE STATISTICS:

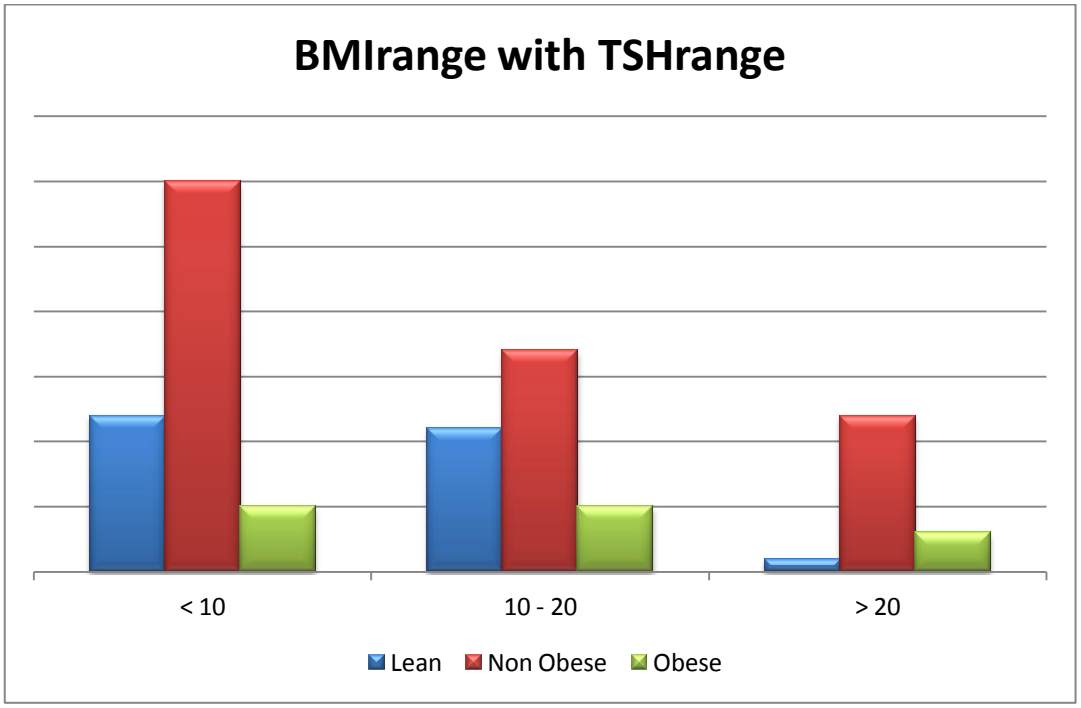
	N	Minimum	Maximum	Mean	Std. Deviation
AGE	96	11	60	41.33	10.945
TSH	96	0.0	25.0	12.356	5.7581
BMI	96	17	29	21.84	2.785
TOTAL CHOLESTEROL	96	119	310	213.81	47.692
LDL	96	76	290	139.00	41.884
TRIGLYCERIDES	96	76	222	121.39	42.650
HDL	96	3	70	51.99	10.368

CORRELATION TABLES

TABLE 1:

CORRELATION BETWEEN TSH AND BMI

			TSH range			Total
			< 10	10 - 20	> 20	
BMI range	Lean	Count	12	11	1	24
		% within TSH range	25.5%	33.3%	6.3%	25.0%
	Non Obese	Count	30	17	12	59
		% within TSH range	63.8%	51.5%	75.0%	61.5%
	Obese	Count	5	5	3	13
		% within TSH range	10.6%	15.2%	18.8%	13.5%
Total		Count	47	33	16	96
		% within TSH range	100.0%	100.0%	100.0%	100.0%

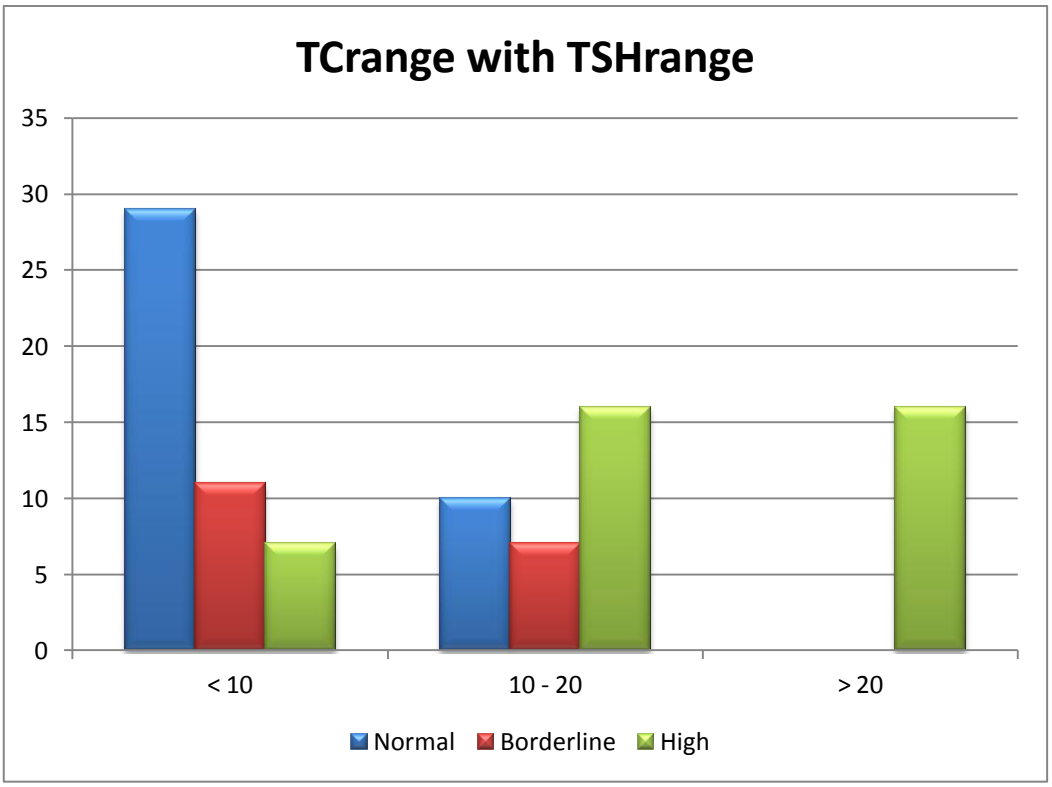


There exists a statistical correlation between rising TSH levels and increased BMI status. The correlation is not statistically significant with p value > 0.05 and x^2 value of 0.298.

TABLE 2:

CORRELATION BETWEEN TSH AND TOTAL CHOLESTEROL

TOTAL CHOLESTEROL			TSH range			Total
			< 10	10 - 20	> 20	
TC range	Normal	Count	29	10	0	39
		% within TSH range	61.7%	30.3%	0.0%	40.6%
	Borderline	Count	11	7	0	18
		% within TSH range	23.4%	21.2%	0.0%	18.8%
	High	Count	7	16	16	39
		% within TSH range	14.9%	48.5%	100.0%	40.6%
Total		Count	47	33	16	96
		% within TSH range	100.0%	100.0%	100.0%	100.0%



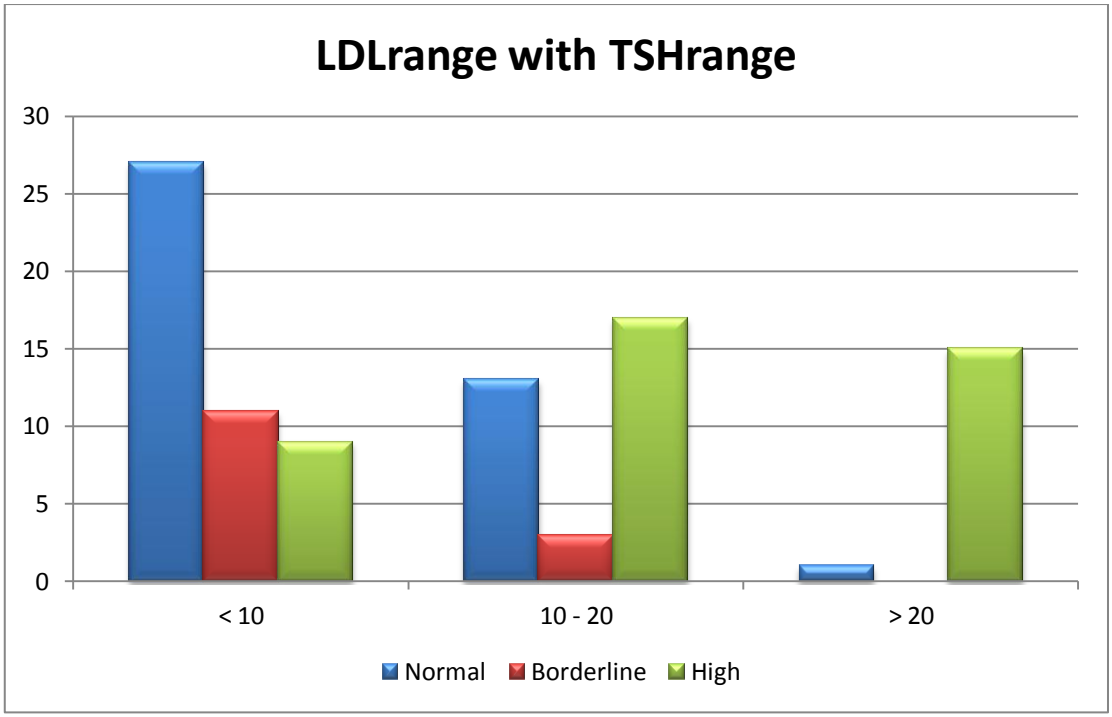
P value : 0.000 x^ 2 : 0.000

There exists correlation between rising TSH levels and total cholesterol in patients with subclinical hypothyroidism. The relation is statistically significant with a p value of 0.001

TABLE 3:

CORRELATION BETWEEN TSH AND LDL :

LDL RANGE			TSHrange			Total
			< 10	10 - 20	> 20	
LDLrange	Normal	Count	27	13	1	41
		% within TSHrange	57.4%	39.4%	6.3%	42.7%
	Borderline	Count	11	3	0	14
		% within TSHrange	23.4%	9.1%	0.0%	14.6%
	High	Count	9	17	15	41
		% within TSHrange	19.1%	51.5%	93.8%	42.7%
Total		Count	47	33	16	96
		% within TSHrange	100.0%	100.0%	100.0%	100.0%



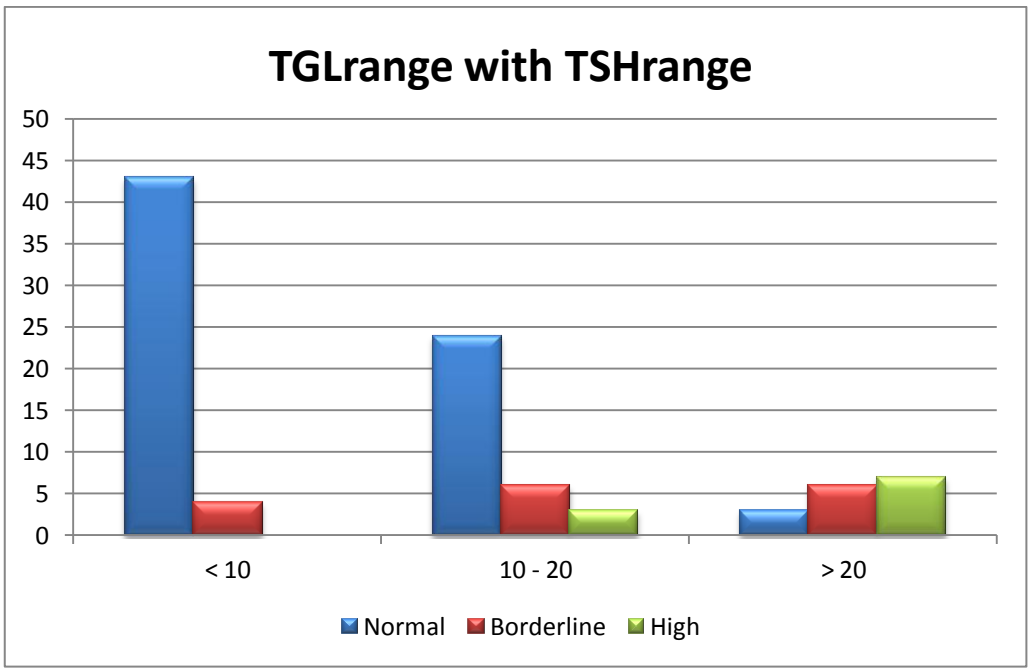
P value 0.000 x^2 0.000

There exists a relation between rising TSH and LDL levels .the correlation is statistically significant with a p value of 0.000

TABLE 4:

CORRELATION BETWEEN TSH AND TRIGLYCERIDE:

TSH RANGE			TSHrange			Total
			< 10	10 - 20	> 20	
	Normal	Count	43	24	3	70
		% within TSHrange	91.5%	72.7%	18.8%	72.9%
	Borderline	Count	4	6	6	16
		% within TSHrange	8.5%	18.2%	37.5%	16.7%
	High	Count	0	3	7	10
		% within TSHrange	0.0%	9.1%	43.8%	10.4%
Total		Count	47	33	16	96
		% within TSHrange	100.0%	100.0%	100.0%	100.0%

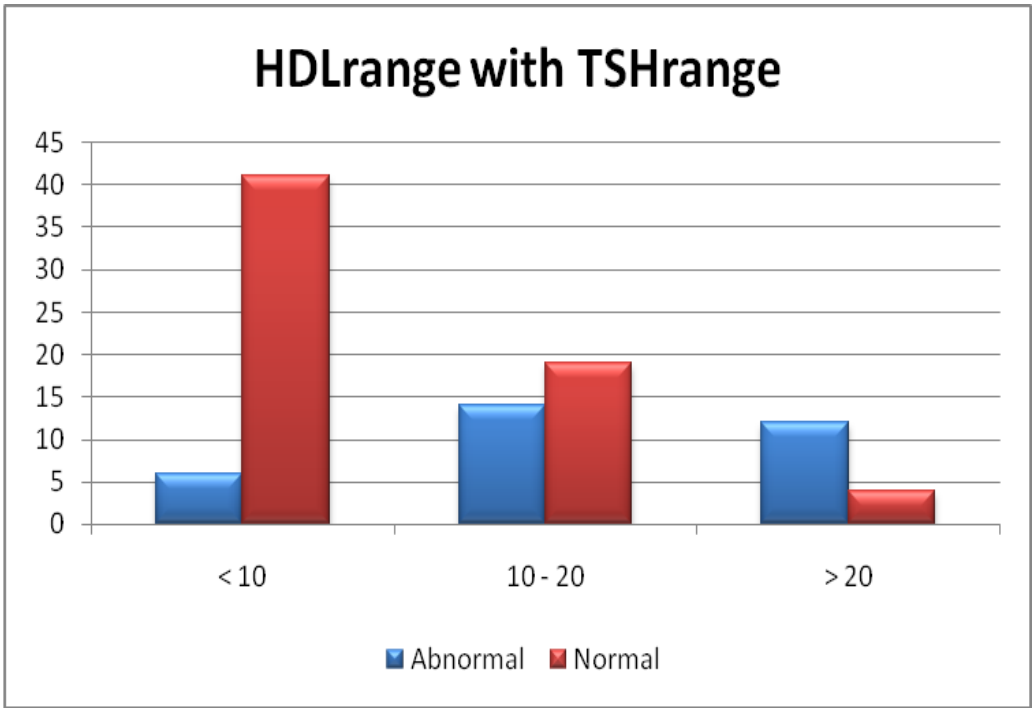


There exists correlation between rising TSH values and rise in serum triglyceride levels. The correlation is statistically significant with a p value of 0.000 and x^2 value of 0.000

TABLE 5:

CORRELATION BETWEEN TSH AND HDL:

			TSHrange			Total
			< 10	10 - 20	> 20	
HDLrange	Abnormal	Count	6	14	12	32
		% within TSHrange	12.8%	42.4%	75.0%	33.3%
	Normal	Count	41	19	4	64
		% within TSHrange	87.2%	57.6%	25.0%	66.7%
Total		Count	47	33	16	96
		% within TSHrange	100.0%	100.0%	100.0%	100.0%



There seems to exists some correlation between rising TSH and serum HDL levels.

DISCUSSION

Subclinical hypothyroidism is an endocrine disorder, where the patients mostly has no or only few symptoms and signs for diagnosis, and the diagnosis is made from elevated serum THYROID STIMULATING HORMONE and the serum free T4 and free T3 levels are within the reference range.

The diagnosis of subclinical hypothyroidism is important in the society, as the patients does not display any signs and symptoms consistent with thyroid dysfunction. So this necessitates, early dignosis and management of subclinical hypothyroidism as they may transform to true hypothyroidism

The rate of conversion of subclinical hypothyroidism to overt is around 2 to 5% per year. Though subclinical hypothyroidism is asymptomatic,the consequences of subclinical hypothyroidism warrants further evaluation and treatment. It includes

- Insulin resistance
- Obesity
- Increase in total cholesterol and LDL levels

- Increase in vascular intima and media thickness
- Endothelial dysfunction
- Increase in peripheral resistance
- Decreased myocardial contractility
- Neuropsychiatric manifestation
- Infertility

“In this study I screened patients for subclinical hypothyroidism and evaluation of dyslipidemia in these patients. Among 96 cases of subclinical hypothyroidism, 33% of them were found to be between age group of 46 to 55 years.” The mean age of presentation was found to be 41.3 years, ranging from minimum of 11 years to maximum of 60 years. This prevalence rate increases as age increases.

The BMI distribution among subclinical hypothyroidism has no correlation to serum TSH levels. Among 96 patients with subclinical hypothyroidism, 61.5% of patients had a normal BMI between 20 and 25 kg/m^2 and 13.5% of patients had BMI beyond 25 kg/m^2.

In regard to the sex distribution of patients, it was clearly evident that the prevalence of subclinical hypothyroidism is more common among women. Among 96 cases of subclinical hypothyroidism, only 8 cases were men.

On analyzing TSH distribution, it was found that among 96 cases, the mean TSH value was 12.3 mIU/l. The TSH values range from minimum of 5.8 mIU/l to maximum of 25mIU/l. 34% of the cases had TSH values between 10 and 20 mIU/l.(14 15 16,83)

On analysing the lipid profile abnormalities , patients were subjected to fasting lipid profile comprising serum total cholesterol, serum triglyceride, serum HDL and serum LDL. The reference range of serum lipid profile;(1)

Total cholesterol:

- Normal : < 200 mg/dl
- Borderline : 201 to 239 mg/dl
- High : > 240 mg/dl

LDL :

- Normal ; <130 mg/dl
- Borderline; 131 to 159 mg/dl
- High : >160 mg/dl

Triglcerides:

- Normal : < 150 mg/dl
- Borderline : 151 to 199 mg/dl
- High ; > 200 mg/dl

HDL:

- Normal : > 50 mg/dl
- Abnormal > 50 mg/dl

Hypercholesterolemia was found in 40.6% of patients. Among 96% patients, 39 cases had high total cholesterol values. Borderline high values were found in 18.8% of patients. Mean cholesterol value of 213 mg/dl ranging from minimum of 119 to 310 mg/dl.

LDL was elevated in 42.7% of cases. Among 96 cases, 41 patients had elevated LDL levels more than 160 mg/dl. Borderline high LDL values were found in 14.6%. The mean LDL value was 139 mg/dl ranging from minimum of 76 to 290 mg/dl.

Triglyceride was elevated in only 27.1%. Among 96 cases, only 26 cases had high triglyceride values. Mean triglyceride value of 121.3 mg/dl ranging from minimum of 76 to 222 mg/dl.

HDL values were found to be normal in 66.7% of cases. The mean HDL was 51.9 mg/dl ranging from minimum of 33 to 70 mg/dl.

Statistical analysis of Colorado thyroid prevalence study showed significant elevation of total cholesterol and LDL in subclinical hypothyroidism compared to euthyroid controls. A meta-analysis conducted to evaluate the effect of thyroxine treatment on the lipid profile in subclinical hypothyroidism has shown significant reduction in total cholesterol level and LDL levels. A study conducted in north India comprising 100 patients, in the age group of 15 to 60 years having

subclinical hypothyroidism were screened for lipid abnormalities. They were found to have significant elevations in triglyceride and VLDL levels and nominal increases in cholesterol and LDL levels. (73,74)

There is no established evidence for lowering of serum lipid profile with replacement therapy. The meta-analysis conducted comprising 13 studies showed a significant reduction in total cholesterol by 8 to 15 mg/dl and LDL by 10 mg/dl with thyroxine therapy. The triglyceride and HDL showed no significant changes.(77)

The changes noted in lipid abnormalities depends on multiple variables like age, race, sex and pretreatment lipid values. In view of lipid abnormalities and its association with cardiovascular abnormalities it is important to investigate the effect of hormone on lipid profile in hypothyroidism.

Among 96 patients, 39 patients had high total cholesterol values and 18 cases were having borderline high total cholesterol values. It is important to note that among the 39 cases with high cholesterol values, 16

patients were having TSH between 10 to 20 mIU/l and other 16 of them were having TSH >20 mIU/l .

Similarly among the 96 cases, 41 patients had high serum LDL levels and 14 had borderline high LDL levels .among those 41 patients 17 of them were having TSH between 10 to 20 mIU/l and 15 of them were having TSH > 20 mIU/l. so TSH levels has significant correlation with total cholesterol and LDL levels . As the TSH level increases , the serum total cholesterol and LDL also increases.

CONCLUSIONS

1. Increased prevalence of subclinical hypothyroidism among females.

2. Increased prevalence of subclinical hypothyroidism beyond the age group of 50 years.

3. 34 % of patients has TSH levels between 10 to 20 mIU/l.

4. Significant elevations in total cholesterol and serum LDL in subclinical hypothyroidism

5. Association of TSH with total cholesterol and LDL elevations

6. No much significant changes in triglycerides and HDL levels.

SUMMARY

Subclinical hypothyroidism is a condition where the thyroid gland is still producing adequate thyroid hormones and the early thyroid dysfunction is diagnosed with elevated serum thyroid stimulating hormone. On conversion to overt hypothyroidism , thyroid gland no longer produces adequate thyroid hormones. Thyroxine is a vital hormone that regulates body metabolism and balance. As single TSH value may be misguiding due to fluctuating levels over 24 hours, two TSH values in 2 to 3 months interval is taken for diagnosis.(2,14)

The risk of transformation to true hypothyroidism in is seen with the following(10,3)

- Females
- Symptomatic patients
- Presence of antithyroid antibodies
- Presence of goiter

Consensus on the treatment of subclinical hypothyroidism varies among different physicians on keeping in mind the adverse lipid abnormalities and the cardiovascular abnormalities .So it is advisable to initiate treatment in subclinical hypothyroidism patient with long term TSH more than 10 mIU/l.

After getting the institutional clearance and informed consent from the patient I selected 96 cases of subclinical hypothyroidism applying the inclusion and exclusion criteria in the study and evaluated there lipid abnormalities. Subclinical hypothyroidism is more common among females. Being a hospital based cross sectional study, most of the patients who attended the op departments were having symptoms .only few patients were screened randomly .

High risk population Screening was most useful part of the study including;

- Obesity
- Infertility
- Menstrual irregularities
- Pregnancy

- Presence of goiter
- Mood disorders
- Coarse hypothyroid facial features

Those with lipid abnormalities, mostly benefits from treatment with thyroxine. So this study holds good in evaluating cases of lipid abnormalities in subclinical hypothyroidism. Appropriate follow of patients annually in untreated cases of subclinical hypothyroidism is essential for preventing the progression of the disease.(2,3,4)

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ABBREVIATIONS

BMI	-	Body mass index
BP	-	Blood pressure
CHD	-	Coronary heart disease
FBS	–	Fasting blood sugar
HDL	-	High density lipoprotein
I Q	-	Intelligence quotient
LDL	-	Low density lipoprotein
PAF	-	Platelet activating factor
PAF- AH	-	Platelet activating factor acetyl hydrolase
RAI	-	Radio active iodine
T3	-	Total triiodothyronine
T4	–	Total thyroxine
fT4	-	Free thyroxine
TSH	–	Thyroid stimulating hormone
TRH	–	Thyrotropin releasing hormone
TPO	–	Thyroid peroxidase
TC	–	Total cholesterol
TG	-	Triglycerides

APPENDIX I

PROFORMA

STUDY OF DYSLIPIDEMIA IN SUBCLINICAL

HYPOTHYROIDISM

Name Age Sex

Address Occupation

Phone

DIAGNOSTIC CRITERIA

Elevated TSH level(>4.5uIU/mL) with normal total or free T4 & T3

Values

SYMPTOMS

Asymptomatic Tiredness

Weightgain Neck swelling

Muscle weakness Depression

Muscle cramps Cold intolerance

Myalgia, arthralgia

Anorexia

Constipation Infertility

PAST HISTORY

CAD Dyslipidemia DM

Hypertension Autoimmune diseases CRF

TB Thyroidectomy Asthma

Severe nonthyroidal Illness Adrenal Failure

Menstrual History: Menorrhagia Menopause

Obstetric History : Infertility, miscarriages

Treatment history: H/o: Drugs (Thyroxin / Lithium /

Amiadarone,antithyroid,Interferon), Radio iodine ,H/o neck Radiation .

Salt intake : Iodised / non iodised

GENERAL EXAMINATION

Built& Nourishment BMI Pallor

Icterus/ Cyanosis /Clubbing /Edema/Lymphadenopathy/

Pulse rate BP RR

Temperature Peripheral pulses

THYROID

Diffuse/ Nodular //Thyroidectomy scar

RESPIRATORY SYSTEM

Pleural Effusion Other findings

CVS

Cardiomegaly/ Murmur

MUSCULO SKELETAL

Arthralgia-

Myalgia

Stiffness /Carpel tunnel syndrome /Muscle weakness

NERVOUS SYSTEM

Neuropathy /Seizures

Cerebellar signs /Delayed Relaxation of DTR

ALIMENTARY SYSTEM

OTHERS

Periorbital Puffiness Dry, CoarseSkin

Ichthyosis

Macroglossia Loss of Hair

INVESTIGATIONS

Urine - Albumin , Sugar , Casts , RBC

FBS, PPBS, Blood Urea , Serum Creatinine

TFT- T3 T4,fT4,Ft3,TSH

TOTAL CHOLESTEROL, LDL, HDL ,TG.

MASTER CHART

NAME	AGE	SEX	TSH	BMI	TOTAL CHOLESTEROL	LDL	TRIGLYCERIDES
ANJALAI	42	F	21.2	230	100	96	52
SEKAR	46	M	6.8	27	210	133	98
RANI	41	F	15.4	23.6	245	162	110
MEERA	19	F	13.5	18	242	166	152
BHAVANI	22	F	5.9	22	150	96	88
VASANTHA	46	F	21.6	24.6	256	168	210
MARIYAMMAL	36	F	6.9	21.1	206	108	92
PUSHPA	42	F	21	23.6	261	170	160
SHIVAMANI	33	F	12.5	19.4	210	110	94
VADANI	34	F	8.9	21.6	192	114	96
KAVERI	42	F	12.4	26	196	116	92
RANI	53	F	22.5	22.4	272	166	140
SAVITHRI	39	F	12.8	18.2	172	96	116
KALYANI	48	F	12	21.2	142	98	136
KANCHANA	31	F	7.8	19	167	88	112
PRIYA	46	F	23.5	25	300	172	216
FATHIMA	11	F	9	22.2	156	86	99
MANGAI	38	F	22	25.6	310	190	220
DEVI	26	F	17	18.5	216	124	96
PARVATHAM	53	F	11	20	180	110	88
SAROJA	42	F	10.5	24	146	99	90
GAYATHRI	28	F	11.6	21.6	132	104	80
PUNITHA	35	F	15.8	21.4	247	166	82
RAVI	29	M	6.9	17	138	110	96
SANGAVI	31	F	15.7	28	248	160	158
KALYANI	46	F	7.8	21.1	169	114	90
NANDHANAM	55	F	24.5	24.2	280	168	208
LINSY	29	F	12.1	16.6	182	116	88
KUTTIYAMAL	54	F	12.7	23.6	246	156	106
ANANDHI	36	F	8.7	20.6	193	120	102
SASIKALA	43	F	13.2	28	252	162	112
DHARANI	24	F	15	21.2	234	166	112
RANGAMA	56	F	15.4	19.8	181	106	109
DEVI	25	F	20.1	20.3	260	106	160
KALYANI	48	F	25	28.5	271	176	216
SAROJA	60	F	9.6	26	190	110	110
MUNIYAMMA	59	F	16.5	20.1	246	168	112
MALLIGA	52	F	12.5	18.2	129	86	90

ARUNA	49	F	20.6	20.5	278	162	116
SRIDEVI	37	F	6	20.9	119	80	86
REVATHY	42	F	12.5	16.9	182	89	96
KALA	43	F	20.8	22.1	256	165	166
RANI	48	F	7.8	20.2	180	90	86
THANGAMANI	49	F	18.4	21.3	262	174	168
KALAIVANI	42	F	8.7	19.6	230	135	104
KONDAMA	44	F	8.9	23.2	122	90	84
RAJU	46	M	9.6	22.4	212	136	82
SALIMA	14	F	14.4	26	248	169	98
DEVI	46	F	6.6	20	146	86	76
SELVAM	52	M	17.5	24.6	232	160	92
GAYATHRI	36	M	7.6	26.2	154	92	82
ROJA	42	F	9	20.9	141	96	76
ROSY	21	F	5.8	17.6	171	102	98
MALLIGA	58	F	11.5	23.2	211	140	101
MADHAVI	34	F	19.3	18.6	260	178	218
MANJU	24	F	8.7	26.1	167	140	140
MUTHU	36	M	21.4	22.1	276	192	171
KUPPAMAL	58	F	6.7	21.2	146	76	99
SAROJA	56	F	16.5	20.3	260	166	172
VALLI	46	F	8.7	20.8	170	99	101
KOMALA	42	F	16.8	21.2	242	158	104
KAVITHA	32	F	7.8	23.3	186	101	108
NALINI	42	F	7.6	17.5	248	160	162
USHA	46	F	14.3	24.2	252	162	166
PIARREBEE	43	F	8.7	28	248	158	111
AMULU	55	F	9.8	19.2	162	112	99
AKILA	16	F	8.8	20.2	243	163	105
DEVIKA	48	F	6.9	19.8	215	155	112
ASWINI	27	F	6.4	25	259	171	170
SETTU	42	M	13.4	27.3	262	179	216
THULASI	44	F	5.8	20.1	154	102	112
SHYAMALA	46	F	22.5	24.3	310	290	222
ANDAL	59	F	21.9	20	248	276	167
SAROJA	53	F	8.7	20.2	182	110	94
KALYANI	42	F	8.6	20.6	217	165	101
NAGAMMA	46	F	14.4	21.3	260	170	176
PUNITHA	41	F	24	28.2	271	276	180
DHIVYA	23	F	6.8	21.4	190	138	93
SEETHA	41	F	22.1	21.2	279	174	219
MEENA	35	F	8.7	21.1	222	140	101
SURESH	46	M	5.9	20.4	234	136	90
SATHYA	42	F	7.9	19.4	242	160	162

MALA	48	F	7.6	21.6	181	96	90
RANI	52	F	5.9	22.3	239	162	101
BHAVANI	42	F	18.6	19.8	260	180	109
SASIKALA	46	F	6.9	21.2	136	78	86
PUVI	26	F	6.9	21.5	234	169	94
SHEELA	42	F	11.3	23.1	210	131	76
MAHALAKSHMI	46	F	17.6	20.6	260	171	210
RUPA	29	F	7	20	142	76	78
SAROJA	42	F	8.9	20.4	220	169	98
MUNIYAMMA	58	F	7.8	23.6	168	96	86
MARI	48	F	8.7	18.6	248	167	160
MALLIGA	49	F	24.7	24.2	256	162	76
SAVITHA	56	F	8.6	22.4	180	100	90
SAROJA	50	F	6.9	18.2	186	148	85

INSTITUTIONAL ETHICAL COMMITTEE
GOVT.KILPAUK MEDICAL COLLEGE,
CHENNAI-10
Protocol ID No.07/01/2015 Dt.20. 01.2015
CERTIFICATE OF APPROVAL

The Institutional Ethical Committee of Govt. Kilpauk Medical College, Chennai reviewed and discussed the application for approval "Dyslipidemia in subclinical Hypothyroidism in Kilpauk Medical College." -For Project Work-submitted by Dr. Saranya Masilamani, PG in General Medicine, KMC, 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.

GOVT. KILPAUK MEDICAL COLLEGE * 20 JAN 2015 * Kilpauk, Chennai-10.

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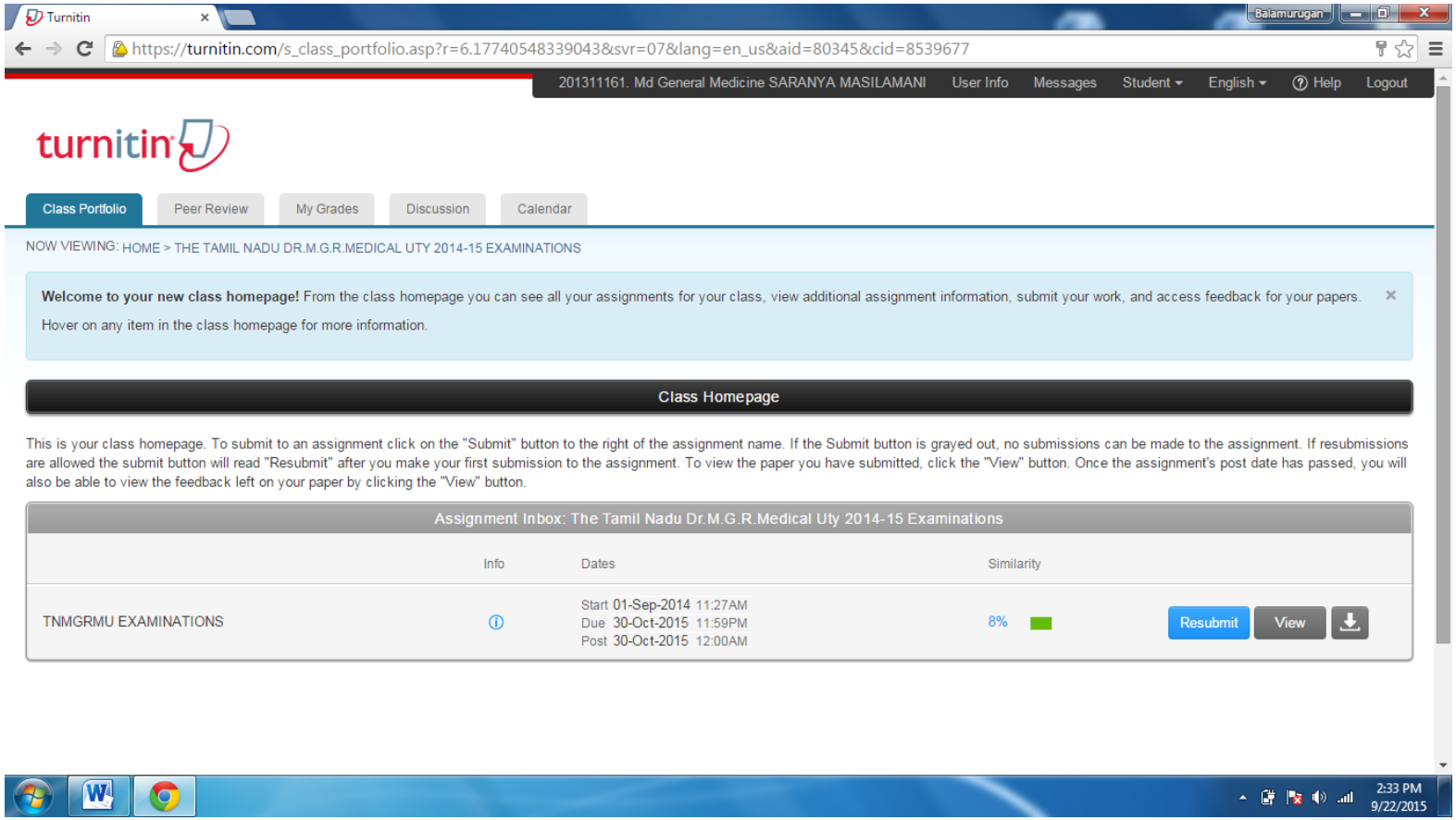
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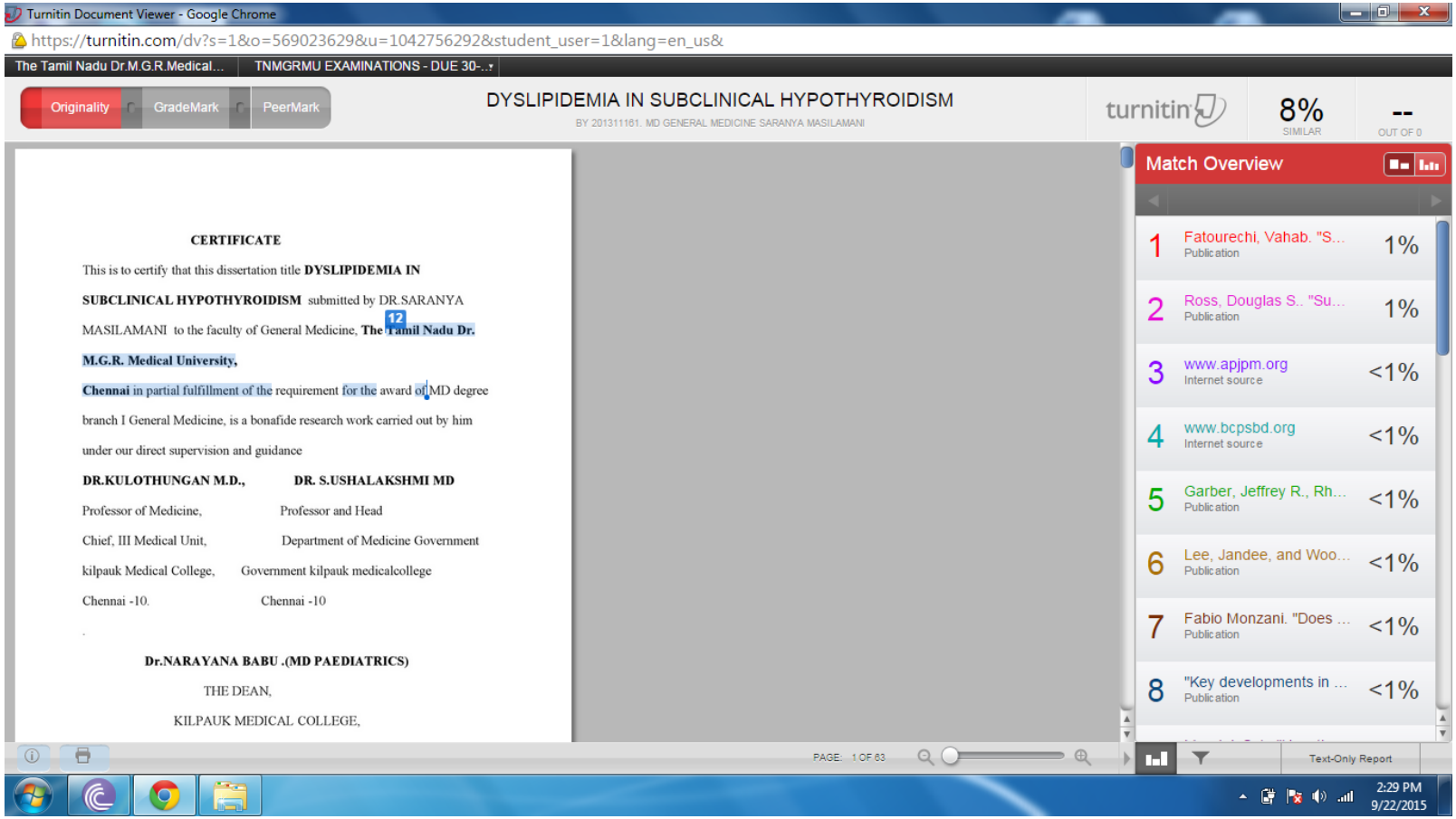
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