Evaluation of Cardiac Functions in Hypothyroidism and Subclinical Hypothyroidism

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Abbreviations: HR-Heart Rate; SBP-Systolic Blood Pressure; DBP-Diastolic Blood Pressure; TSH-Thyroid Stimulating Hormone; ECG- Electrocardiogram ; LVEDD-Left Ventricular End Diastolic Diameter; LVESD-Left Ventricular End Systolic Diameter; dIVST - Inter Ventricular Thickness In Systole; dLVPWT – Left Ventricular Posterior Wall Thickness In Systole; EF%-Ejection Fraction; FS-Fractional Shortening; IRT-Isovolumic Relaxation Time; WNL-With In Normal Limit; AB- Anti Thyroid Antibodies; LAHB- Left Anterior Hemi Block; RBBB- Right Bundle Branch Block; LVC-Low Voltage Complexes

Introduction

Cardiovascular features are sum of most profound and reproducible clinical findings associated with thyroid disease.

Many of the clinical manifestations of hypo and subclinical hypothyroidism are due to ability of thyroid hormones to alter cardiovascular structural and hemodynamic characters.

The characteristic dilated cardiac silhouette, pericardial effusion, low electrocardiographic voltage and slow indolent heart action are well recognized in overt hypothyroidism.

Subclinical hypothyroidism characterized by variably increased serum TSH and normal serum free T4 and T3 levels occurs in 10 to 15% of the general population.

Though the clinical presentation of subclinical hypothyroidism is nonspecific, and the symptoms are usually subtle, as compared with those of overt hypothyroidism, it is well proved to alter several metabolic and organ function indices which become clinically relevant over a period of time. Heart is one of many important organs to be affected.

With the advent of newer echocardiographic techniques, mechanism of altered myocardial contractile function in both clinical and subclinical thyroid dysfunction has been well delineated.

Anatomy

The thyroid gland is a highly vascular organ, situated at the front and sides of the neck; it consists of right and left lobes connected across the middle line by a narrow portion, the isthmus. Each lobe is about 5 cm long, width 3 cm. A third lobe, of conical shape, called the pyramidal lobe, frequently arises from the upper part of the isthmus. Its weight is about 30 gms [1].

Structure

The microscopic structure of the thyroid is quite distinctive. Thyroid epithelial cells responsible for synthesis of thyroid hormones are arranged in spheres called thyroid follicles. Follicles are filled with colloid, proteinaceous depot of thyroid hormone precursor. When active colloid is minimum and cells become columnar and during rest colloid is minimum and cells are cubic (Figure 1-3).
Synthesis of Thyroid Hormones

The entire synthetic process occurs in three major steps,

1. Production and accumulation of the raw material.
   - Tyrosines are provided from a large glycoprotein scaffold called thyroglobulin, synthesized by thyroid epithelial cells and secreted into the lumen of the follicle – colloid is essentially a pool of thyroglobulin.
   - Iodine, or more accurately iodide (I-), is avidly taken up by thyroid epithelial cells, through sodium iodide symporter or “iodine trap”.

2. Fabrication or synthesis of thyroid hormones is conducted by enzyme thyroid peroxidase, in two sequential reactions:
   - Iodination of tyrosines on thyroglobulin (a.k.a. “organification of idode”) (Figure 4).
   - Synthesis of thyroxine or triiodothyronine from two iodothyrosines. Through the action of thyroid peroxidase, thyroid hormones accumulate in colloid, on the surface of thyroid epithelial cells.

2. Thyroid hormones are released from thyroglobulin in the following steps:
   - Thyroid epithelial cells ingest colloid by endocytosis.
   - Hydrolytic enzymes in epithelial cells digest thyroglobulin, and liberate free thyroid hormones.
   - Finally, free thyroid hormones apparently diffuse out into the blood where they quickly bind to carrier proteins for transport to target cells.

Normally the thyroid releases 100-125 mcg of thyroxine (T4) daily and only small amounts of triiodothyronine (T3). The half-life of T4 is approximately 7 to 10 days. T4, a prohormone, is converted to T3, the active of thyroid hormone, in the peripheral tissues.

Control of the Thyroid Gland Activity

The concentration of thyroid hormones in the circulation is regulated by a homeostatic feedback loop involving the hypothalamo-pituitary axis. The synthesis and secretion of TSH from the thyrotrophs is stimulated by the tripeptide, thyrotrophin-releasing hormone (TRH). It is secreted in a pulsatile fashion with a diurnal variation, peaking around midnight. SH secretion is inhibited by other hormones (including somatostatin and dopamine) and also cytokines, particularly IL-1β, IL-6 and TNF-α. Cold environment, estrogens increase thyroid hormone secretions by affecting the TSH secretory response to TRH and pharmacological doses of glucocorticoids inhibit release of TSH. TSH stimulates release of thyroid hormones from thyroid gland. Thyroid hormones in turn control rate of TSH secretion by altering response of the pituitary thyrotrophs to TRH [2-5] (Figure 5).

Effect of Thyroid Hormones on the Heart

Thyroid hormone has relevant effects on the cardiovascular system. Many symptoms and signs recognized in patients

Figure 2: thyroid hormone precursor.

Figure 3: Chemistry of Thyroid Hormones.

Figure 4: Fabrication or synthesis of thyroid hormones is conducted by enzyme thyroid peroxidase, in two sequential reactions.
with overt hyperthyroidism and hypothyroidism are due to the increased or reduced action of thyroid hormone on the heart and the vascular system respectively, and the related hemodynamic derangements. A significant effect of thyroid hormones on the heart results from an interaction with specific nuclear receptors in cardiac myocytes.

Overall, changes in thyroid hormone status influence cardiac action by three different routes.

1. The biologically relevant TH, T3, exerts a direct effect on cardiac myocytes by binding to nuclear T3 receptors influencing cardiac gene expression.
2. T3 may influence the sensitivity of the sympathetic system.
3. T3 leads to hemodynamic alteration in periphery those results in increased cardiac filling and modification of cardiac contraction (Table-1) (Figure-6).

Sites of action Triiodothyronine on cardiac myocytes

Triiodothyronine enters the cell, possibly by a specific transport mechanism, and binds to nuclear triiodothyronine receptors. The complex then binds to, thyroid hormone response elements of genes for several cell constituents and regulates transcription of these genes, including those for Ca2+-ATPase and phospholamban in the sarcoplasmic reticulum, myosin, β-adrenergic receptors, adenylyl cyclase, guanine-nucleotide-binding proteins, Na+/Ca2+ exchanger, Na+/K+/ATPase, and voltage-gated potassium channels. Nonnuclear triiodothyronine actions on ion channels for Na+, K+ and Ca2+ ions are indicated at the cell membrane. Dashed arrows indicate pathways with multiple steps, and mRNA denotes messenger RNA.

**Cellular Effects of Thyroid Hormone on the Cardiovascular System**

Most of the molecular and cellular mechanisms responsible for the cardiovascular effects of thyroid hormone have been clarified. Thyroid hormone may result both genomic and nongenomic effects on cardiac myocytes.

**Genomic Effects of Thyroid Hormone (T3) on Cardiomyocytes**

The genomic effects of thyroid hormone are mediated by the transcriptional activation or repression of specific target genes that encode both structural and functional proteins.

This process begins with the entry of triiodothyronine (T3), the biologically active thyroid hormone, into the cardiomyocyte through specific transport proteins located within the cell membrane.

Once in the cardiomyocyte, T3 enters the nucleus and interacts with specific transcriptional activators (nuclear receptor – 1) or repressors (nuclear receptor -2). Occupancy of these receptors by the T3, in combination with recruited cofactors, allows the

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Hypothyroidism</th>
<th>Normal</th>
<th>Hypothyroidism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood volume (% of normal value)</td>
<td>100</td>
<td>105.5</td>
<td>84.5</td>
</tr>
<tr>
<td>Heart rate (bpm)</td>
<td>72-84</td>
<td>88-130</td>
<td>60-80</td>
</tr>
<tr>
<td>Cardiac output (L / min)</td>
<td>4.0-6.0</td>
<td>&gt;7.0</td>
<td>&lt;4.5</td>
</tr>
<tr>
<td>Systemic resistance (dyn. sec / cm_5)</td>
<td>1500-1700</td>
<td>700-1200</td>
<td>2100-2700</td>
</tr>
<tr>
<td>Left ventricular EF (%)</td>
<td>&gt;50</td>
<td>&gt;65</td>
<td>&lt;60</td>
</tr>
<tr>
<td>Isovolumic relaxation time (msec)</td>
<td>60-80</td>
<td>25-40</td>
<td>80</td>
</tr>
</tbody>
</table>

**Table 1: Hemodynamics and Cardiac Function in Overt Thyroid Dysfunction.**
thyroid hormone-receptor complex to bind (nuclear receptor -1) or release (nuclear receptor -2) specific sequences of DNA (thyroid responsive elements) that, in turn, by acting as cis- or trans-regulators, modify the rate of transcription of specific target genes [9].

**TH regulation of genes coding for cardiac proteins**

**Positive regulation**
- Sarcoplasmic reticulum calcium adenosine triphosphatase
- Myosin heavy chain α
- α1-Adrenergic receptor
- Guanine-nucleotide-regulatory proteins
- Na+/K+ adenosine triphosphatase
- Voltage-gated K+ channels

**Negative regulation**
- T3 nuclear receptors α
- Myosin heavy chain β
- Phospholamban
- Na+/Ca2+ exchanger
- Adenyl cyclase types V and VI

Among various above proteins whose expression is modulated at transcriptional level, the most extensively characterized are myosin heavy chains and the sarcoplasmic reticular protein involved in the regulation of intracellular calcium handling, calcium activated ATPase and its inhibitory cofactor.

Thyroid hormone up regulates the expression of the α-isofrom of the myosin heavy chain in cardiomyocytes, while it down regulates the β isoform [10-13].

Cardiac functions in patients with thyroid dysfunction directly reflect the effect of thyroid hormone on calcium-activated ATPase and phospholamban, which are involved primarily in the regulation of systodiastolic calcium concentration in cardiomyocytes.

Sarcoplasmic reticular calcium-activated ATPase is responsible for the rate of calcium reuptake into the lumen of sarcoplasmic reticulum during diastole that, in turn is a major determinant of the velocity of myocardial relaxation after contraction. However, the performance sarcoplasmic reticular calcium-activated ATPase is influenced by the level of expression of phospholamban. The higher the phospholamban expression, the lower the sarcoplasmic reticular calcium-activated ATPase activity. In this regard, it has been extensively demonstrated that thyroid hormone up regulates expression of the sarcoplasmic reticular calcium-activated ATPase and down regulation expression of phospholamban, their by enhancing myocardial relaxation.

Indeed, the improved calcium reuptake during diastole may favorably affect myocardial contractility. In fact, the greater reduction in cytoplasmic concentration of calcium at end-diastole increases the magnitude of the systolic transient of calcium that, in turn, augments its availability for activation of tropo-myosin units. In fact, in phospholamban deficient mice, cardiac contractility was found to be increased, with no further increase after thyroid hormone treatment. This finding strongly supports the key role of sarcoplasmic reticulum proteins and their effects on intracellular calcium handling in thyroid hormone-mediated changes in systodiastolic cardiac function in patients with thyroid dysfunction [14].

In this context, it is important to recognize that thyroid hormone also modified the expression other ion channels, such as Na+/K+ activated ATPase, Na+/Ca2+ exchanger, and some voltage-rated K+ channels (Kv1.5, Kv4.2, Kv4.3) thereby coordinating the electrochemical and mechanical responses of the myocardium. In addition to these genomic effects, thyroid hormone produces changes in cardiac ionotropism and chronotropism more rapidly than would be expected from regulation of gene expression, which usually take minutes to hours to be phenotypically and functionally appreciable.

This process is mediated in part by the activation of intracellular kinase pathways involved in signal transduction of the adrenergic stimulus and this explain functional and analogous between cardiovascular effects of the thyroid hormone and those promoted by the adrenergic system.

Indeed, although most of the cardiovascular manifestation associated with hyperthyroidism and hypothyroidism mimic a condition of increased and reduced adrenergic activity respectively, the sensitivity of cardiovascular system to adrenergic stimulus does not seem to be substantially altered in these conditions.

Thyroid hormone also exerts an important effect on the vascular system. It acutely reduces peripheral vascular resistance by promoting relaxation in vascular smooth muscle.

**Hypothyroidism**

Hypothyroidism is the most common pathologic hormone deficiency. It results from failure of gland to produce adequate amounts of hormone. Patients may be largely asymptomatic or may rarely present with coma and multisystem organ failure (myxedema coma). The frequency of hypothyroidism, goiters, and thyroid nodules increases with age. Hypothyroidism is most prevalent in elderly population. Thyroid disease is much more common in females than in males, with reports of prevalence 2-8 times higher in females [15-16].

**Causes of Hypothyroidism**

A variety of functional or structural disorders may lead to hypothyroidism, the severity of which depends on the degree and duration of thyroid hormone deprivation.

1. Central (hypothalamic/pituitary) hypothyroidism
   a. Loss of functional tissue.
   i. Tumors (pitutary adenoma, craniopharyngioma, meningioma, dysgerminoma, glioma, metastases).
   ii. Trauma (surgery, irradiation, head injury).
iii. Vascular (ischemic necrosis, hemorrhage, stalk interruption, aneurysm of internal carotid artery).

iv. Infections (abcess, tuberculosis, syphilis, toxoplasmosis).

v. Infiltrative (sarcoidosis, histiocytosis, hemochromatosis).

vi. Chronic lymphocytic hypophysitis.

vii. Congenital (pituitary hypoplasia, septooptic dysplasia, basel encephalcoele).

b. Functional defects in TSH biosynthesis and release
   i. Mutations in genes encoding for TRH receptors, TSHY, or Pit-1
   ii. Drugs: dopamine, glucocorticoids, L-thyroxine withdrawal.

2. Primary (thyroidal) hypothyroidism
   a) Loss of functional thyroid tissue
   i. Chronic autoimmune thyroiditis.
   ii. Reversible autoimmune hypothyroidism (silent and postpartum thyroiditis, cytokine-induced thyroiditis).
   iii. Surgery and irradiation (I131 or external irradiation).
   iv. Infiltrative and infectious diseases, sub acute thyroiditis.
   v. Thyroid dysgenesis.
   b) Functional defects in thyroid hormone biosynthesis and release
   i. Congenital defects in thyroid hormone biosynthesis.
   ii. Iodine deficiency and Iodine excess.
   iii. Drugs: antithyroid agents, lithium, natural and synthetic goitrogenic chemicals.

3. “Peripheral” (extra thyroidal) hypothyroidism.
   a) Thyroid hormone resistance.
   b) Massive infantile hemangioma.

Systemic Manifestations of Hypothyroidism
The clinical expression of thyroid hormone deficiency varies considerably between individuals, depending on the cause, duration and severity of the hypothyroid state. Characteristically, there is a slowing of physical and mental activity, and of many organ functions. System-wide effects due to derangements in metabolic processes or direct effect by myxedematous infiltration of the tissues.

Energy and Nutrient Metabolism
Thyroid hormone deficiency slows metabolism, resulting in a decrease of resting energy expenditure, oxygen consumption, and utilization of substrates. BMR may fall between 35 and 45 percent below normal.

1. Protein metabolism

In general, both the synthesis and the degradation of protein are reduced.

2. Carbohydrate metabolism
Glucose is absorbed from the intestine at a slower rate than normal. Fasting plasma glucose values are on average lower than normal. The oral glucose tolerance test usually produces a low peak value that remains elevated at 2 hours. The insulin response to intravenous glucose is blunted and slightly delayed [17].

3. Lipid Metabolism

<table>
<thead>
<tr>
<th>Metabolite</th>
<th>Hypothyroidism</th>
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<tbody>
<tr>
<td>Serum LDL – cholesterol</td>
<td>---- increased</td>
</tr>
<tr>
<td>Serum HDL – cholesterol</td>
<td>---- decreased</td>
</tr>
<tr>
<td>Serum triglycerides</td>
<td>---- increased</td>
</tr>
<tr>
<td>Lipoprotein (a)</td>
<td>---- increased</td>
</tr>
</tbody>
</table>

Taken together, the changes in plasma lipids in hypothyroidism results in an atherogenic lipid profile.

Facies
Following features are noted
Dry skin, Jaundice, Pallor, Coarse, brittle, strawlike hair loss of scalp hair, dull facial expression, coarse facial features, Periorbital puffiness, Macroglossia

Neurologic and Psychiatric Manifestations

Symptoms or signs:
Headache, Parasthesias, carpel tunnel syndrome, Cerebellar ataxia, Deafness: nerve or conduction type, Vertigo or tinnitus, sleep apnea, Myxedema coma.
Delayed relaxation of deep tendon reflexes
Prolonged evoked potentials
Elevated CSF protein concentration
Cognitive deficits: calculation, memory, reduced attention span
Low-amplitude theta and delta waves on EEG
Psychiatric syndromes: Depression, akinetic or agitated Schizoid or affective, Psychoses, Bipolar disorders

Gastrointestinal Manifestation of Hypothyroidism
Symptoms: anorexia, gaseous distention, constipation
Signs:-prolonged gastric emptying, prolonged intestinal transit time, slowed intestinal absorption, ileus, ascites, elevated liver enzymes and CEA, gallbladder hypotonia

Respiratory System
Dyspnea, decreased ventilator drive, decreased maximal breathing capacity, decreased diffusion capacity, and decreased ventilator response to carbon dioxide are found. Patients with myxedema may develop carbon dioxide retention, and carbon dioxide narcosis may be a cause of myxedema coma.

Musculoskeletal System
Clinical symptoms and signs
Myalgia, muscle weakness, stiffness, cramps, fatigue
arthralgias joint stiffness
Joint effusion and pseudo gout, carpal tunnel syndrome,
Delayed linear bone growth in children

Laboratory Findings
Normal ionized calcium, phosphate, 25-OH vitamin D3 and
bone density.
Increased serum PTH, 1,25(OH)2_vitamin D3,
Reduce urine calcium, hydroxyproline.
Serum alkaline phosphatase, osteocalcin, and IGF-1 Epiphyseal
dysgenesis or delayed ossification in children

The Cardiovascular Effects of Overt Hypothyroidism
HYPOTHYROIDISM has many structural and effects on the
cardiovascular system which includes pericardial effusion,
hypertension, hyperlipidemia, increased risk of coronary
artery disease, congestive heart failure and primary pulmonary
hypertension along with electrocardiographic and echocardiographic
manifestations [18-20].

Pathophysiology
The heart may be pale, flabby, dilated and hypertrophied.
Interstitial edema and an increase in fibrous tissue are present.
Myxedema is associated with increased capillary permeability
and subsequent leakage of protein into the interstitial space,
resulting in pericardial effusion. Rarely, the presenting
symptoms is complicated by tamponade
The blood vessels often show prominent atherosclerosis.

Clinical Symptoms
Tiredness, fatigue
Dyspnea on exertion
Ankle edema (pitting and non pitting)

Clinical Signs
In addition to typical hypothyroid facies, skin changes and
delayed reflexes patient with hypothyroid have following
cardiovascular Significant bradycardia,
Weak arterial pulses (narrow pulse pressure)
Increased mean arterial pressure (hypotension in late stages)
Faint heart sounds
Cardiac enlargement, dilatation
Distant heart sounds
Non pitting edema and
Evidence of congestive heart failure.

Electrocardiographic finding in hypothyroidism include
1-sinus bradycardia
2-Qt prolongation
3- Decreased amplitude of P wave
4-ventricular tachycardia, because of bradycardia and
hypothermia
5-Low voltage P, ORS, T (pericardial effusion finding)
6-Atrioventricular and interventricular block
7-Incomplete or complete right bundle branch block
8-Atrial fibrillation

Hypertension: Overt hypothyroidism is associated with
higher blood pressure Two factors contribute to systemic
hypertension in overt hypothyroidism are
1. The remarkable increase in peripheral vascular
resistance.
2. Increase in arterial stiffness, which likely results from
Myxedema of the arterial wall.
In general, systemic hypertension associated with overt
hypothyroidism is poorly controlled by conventional
treatments, where as it promptly improves with achievement
of euthyroidism. This finding would encourage the
routine assessment of thyroid function in all patients with
preexisting systemic hypertension that becomes resistant to
pharmacological treatment

Cardiac Function in Hypothyroidism
The most-consistent cardiac abnormality recognized in
patients with overt
Hypothyroidism is impairment of LV diastolic function which
is characterized by slow myocardial relaxation and impaired
early ventricular filling Lvsystolic function usually is only
marginally sub normal, as demonstrated by slightly reduced
values of ejection fraction and stroke volume. On the one hand,
the reduced cardiac preload, in combination with bradycardia
and slightly depressed myocardial contractility, accounts for a
subnormal cardiac output in overt hypothyroidism. On the other
hand, the lower cardiac performance and the abnormalities in
peripheral and proximal vascular function may contribute to
the poor exercise tolerance in overt hypothyroidism. Cardiac
function may be further compromised by the development of
pericardial effusion, which occurs with severe, long standing
over hypothyroidism. In addition, overt hypothyroidism may
be associated with some increase in LV mass that does not
correspond to myocardial hypertrophy but rather to interstitial
myxedema. By increasing wall stiffness, cardiac myxedema
may further compromise LV mechanics, contributing to
reduced cardiac output.

Although overt hypothyroidism is associated with a lower
myocardial oxygen demand, myocardial mechanical work
efficiency is worse than in euthyroid controls, because the
increase in peripheral vascular resistance and arterial stiffness
in overt hypothyroidism contributes increased cardiac
after load, one of the major factors determining myocardial
oxygen consumption. The disproportionate increase in myocardial oxygen uptake with respect to the level of cardiac performance may, therefore, explain at least in part why overt hypothyroidism may precipitate or worsen angina in patients with suspected or known ischemic heart disease and why some of these patients have an improvement in angina symptoms after thyroid hormone replacement is initiated.

Overt Hypothyroidism in Elders

Overt hypothyroidism may be particularly hazardous in the elderly, independent of the presence of underlying cardiovascular disease. Again, it is accompanied by the development of cardiac hypertrophy and interstitial fibrosis, which may be responsible for some diastolic dysfunction and reduced cardiovascular performance. Therefore, the onset of overt hypothyroidism in this vulnerable population occasionally may precipitate cardiac decomposition and CHF.

Noteworthy, diastolic heart failure was strongly associated with hypothyroidism and was more prevalent in women. Therefore, thyroid function should be routinely assessed in older patients with newly diagnosed or worsening heart failure [21].

Management

The treatment goals for hypothyroidism are the reversal of clinical progression and the correction of metabolic derangements as evidenced by normal blood levels of TSH and free T4 thyroid hormone (LT4) replacement is treatment of choice. Dose of LT4 is titrated every 4-6 weeks to achieve TSH levels within reference range.

In elderly patients or those with known ischemic heart disease, treatment should begin with one fourth to one half the expected dose, and the dose should be adjusted in small increments every y-6 weeks.

After dose stabilization, patients can be monitored with annual clinical evaluations and TSH monitoring. Patients should be monitored for symptoms and signs of overtreatment.

Subclinical Hypothyroidism

Definition:

The state of an elevated TSH level with a normal free T3 and T4 levels referred to as subclinical hypothyroidism.

It is also referred to as mild thyroid failure some individual patients may present with symptoms and signs of hypothyroidism.

Incidence

Worldwide in adults it is 1-10% increases to 7-27% in over 60 years (men 16%, women 26%)

Risk increase with female gender, advanced age.

Screening

Considering increasing of subclinical hypothyroidism in elderly recommendations have been made for thyroid screening. But definite guidelines are not present.

In the absence of the guidelines, some clinicians may elect to perform routine screening with serum TSH measurement or to measure TSH in patients with persistent nonspecific complaints, especially women, the elderly and persons with risk factors for thyroid failure.

Risk Factors for Thyroid Failure

1) Family history of thyroid disease.
2) Personal history of thyroid disease.
3) Radiation treatment.
4) Drugs e.g. amiodarone, lithium, iodine, anti-thyroid drugs.
5) Presence of thyroid antibodies.
6) Other autoimmune disease.

Characteristics

Up to 75% of patients with subclinical hypothyroid have mildly elevated serum TSH (5-10mIU)

50-80% of patients test positive for anti-thyroid peroxidase goiter is seen twice common as compared to general population.

Clinical Manifestations

Subclinical hypothyroidism is not simple biochemical abnormality, instead variety of metabolic, neuromuscular and neurobehavioral alterations have been described about 30% of patients are symptomatic. Followign findings are more common in patients with subclinical hypothyroidism.

- Dry skin
- Easy fatigability
- Cold intolerance
- Poor memory
- Slow thinking
- Constipation
- Neurobehavioral abnormalities and neuromuscular dysfunction
- Lipid abnormalities

Cardiovascular Manifestations OD Subclinical Hypothyroidism

There is no evidence to date that subclinical hypothyroidism cause’s clinical heart disease. Impaired LV function and cardio respiratory adaptation to effort become unmasked during exercise. Cardiovascular abnormalities have been detected echocardiographically. Subclinical hypothyroidism does not produce structural abnormalities. But it does manifest functional disturbances. More specifically, these patients have resting LV diastolic dysfunction, evidenced by delayed relaxation and impaired systolic dysfunction on effort that results in poor exercise capacity. These changes are reversible when euthyroidism is restored.
Flow-mediated vasodilatation, a marker of endothelial function is significantly impaired in subclinical hypothyroidism and decreased heart rate variability a marker of autonomic activity suggests hypo functional abnormalities in the parasympathetic nervous system. Subclinical hypothyroidism does result in a small increase in LDL cholesterol and a decrease in high-density lipoprotein cholesterol, changes that enhance the risk for development of atherosclerosis and coronary artery disease. It has been established that subclinical that subclinical hypothyroidism is an independent risk factor for atherosclerosis and myocardial infarction.

**Course of Diseases**

About 5% of patients with raised TSH levels and detectable antithyroid antibodies progress to overt hypothyroidism. In selected cases (e.g. elderly patients with high titers of antithyroid antibodies), the risk of progression to overt disease may be closer to 20% year.

**Management**

Indications for treatment in subclinical hypothyroidism are not established but general guidelines can be offered Features that increases the potential benefit of treatment include:

1. Greater magnitude and duration of TSH elevation
2. Presence and higher titers of anti-thyroid anti-bodies
3. Symptoms that might be related to mild hypothyroidism

Potential benefit of therapy must be balanced against risk of harms to that patient. In patients with coronary artery disease and minimal elevation of TSH, however, it may be advisable to follow the TSH level rather than subject the patient to the small risk of levothyroxine therapy (Figure 7).

**Treatment**

The goal is to maintain the TSH level within normal limits.

Levothyroxine is treatment of choice Initial dose is 25 micro grams per day. This should be titrated to maintain normal levels of TSH. Dose titration should be made after 6-8 weeks of staring therapy. Once the correct dosage of thyroxin is established, the frequency of TSH measurement may be decreased to every six to 12 months.

**Objectives of the Study**

Clinical electrocardiographic and echocardiographic evaluation of cardiovascular system in hypothyroid and subclinical hypothyroid patients.

**Materials and Methods**

**Inclusion Criteria**

1. 18 patients with diagnosis of untreated, overt hypothyroidism and 18 patients with newly diagnosed and untreated primary subclinical hypothyroidism attending medical and endocrine clinics of Gandhi general hospital are included in the study.
2. Age ranged from 15-60 years.

**Exclusion Criteria**

1. Patients with known cardiac disorder.
2. Patients who had hypertension, diabetes mellitus, renal failure, pregnancy.
3. Patients with non-reproducible TSH, T3 and T4 values are excluded from study

All subjects gave informed consent before participating in the study.

In every patient following parameters are assessed.

1) Clinical assessment
2) Thyroid profile
3) 12 lead ECG
4) Standard m-mode 2D echo and Doppler echocardiography

**Assessment of Thyroid Status**

The blood samples were collected in the morning time after overnight fast Normal levels in GGH laboratory are

<table>
<thead>
<tr>
<th>TSH (0.3-5.5mcIU/L), FT4(5-12.5mcg/dL), FT3(230-619pg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnosis of hypothyroidism was confirmed by</td>
</tr>
<tr>
<td>1. FT3&lt;70pg/dl,</td>
</tr>
<tr>
<td>2. FT4&lt;3mcg/dl,</td>
</tr>
<tr>
<td>3. TSH &gt;15mcIU/ml</td>
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</tbody>
</table>

Diagnosis of subclinical hypothyroidism was confirmed by

1. TSH>5mcIU/ml and
2. Normal T3, T4 levels.

**Echocardiographic Techniques and Measurements M-Mode Echocardiography**

Following parameters were assessed using standard m-mode...
echocardiography LVEDD (mm):-The distance between left side of IVS and posterior left ventricular endocardium at the level of chorda at end diastole.

LEVSE D (mm):-Above distance at end systole

Diastolic IVST (mm):-Measured as distance between anterior edge of right and left ventricular septal endocardial surface at diastole

Diastolic LVPWT (mm):-measured as vertical distance from anterior edge of endocardial surface to anterior edge of epicardial surface of left ventricular posteriobasal wall at end diastole and at end systole

**Doppler Echocardiography**

**Systolic Function**

Fractional shortening (FS%): calculated by the formula

\[ FS\% = \frac{LVIDd - LVIDs}{LVIDd} \]

Ejection fraction (EF%): 

**Diastolic function**

Peak E (cm/sec):-early transmittal flow velocity
Peak A (cm/sec):-Late transmittal flow velocity

E/A ratio:-

IRT(msec):-Isovolumic relaxation time

**Case Proforma**

- Name
- Age
- Sex
- Occupation
- Address
- Social Status
- HISTORY
- Dry skin
- Weight gain
- Decreased appetite
- Constipation
- Hair loss
- Fatigue, loss of energy, lethargy
- Forgetfulness, impaired memory, inability to concentration
- Cold intolerance
- H/O swelling, pain in the neck
- H/O fever
- H/O drug intake
- H/O neck surgeries, neck irradiation
- H/O headache, visual symptoms

**Past History**

- Diabetes mellitus
- Hypertension
- Coronary artery disease
- History of thyroid illness

**Personal History**

- Diet (goitrogens)
- Addictions
- Menstrual history (females)
- H/O any auto immune disease

**Physical Examination**

Ht: Wt:  
BMI:  
Pallor / icterus / cyanosis / clubbing / lymphadenopathy / pedal edema  
Facies  
Goiter  
Skin / hair changes  
PR: BP: RR:  
Heart:  
Lungs:  
CNS: ankle jerks

**Diagnosis**

**Investigations**

Blood counts

Hb%:  
RBC:  
WBC:  
DC:  
ESR:  

**Complete urine examination:**

Albumin:  
sugar:  
microscopy:  

Random Blood sugar/Blood urea/Serum Creatinine Thyroid hormone assays

ECG/Chest X-ray

2D Echocardiography

Thyroid antibodies

**Master charts**

**Overt Hypothyroidism**

At the time of diagnosis all the patient were biochemically
hypothyroid All the patients have varying clinical feature of hypothyroidism of which general weakness, fatigue, weight gain, dry skin, are most common features. The mean heart rate was 65±5 at diagnosis Pulmonary Hypertension was documented in 1 out of 18 cases and 1 patient had hypertension. (Figure 8) (Table 2).

Above Table reveals low voltage complexes in seven Patients. Generalized T-waves inversion was seen in 2 patients who became upright.

Nonspecific T-waves changes, left anterior hemi block was seen in 2 and 1 case respectively.

Table 3 demonstrates Mild to moderate pericardial effusion was seen in 11 patients.

Sever pericardial effusion was seen in 1 patients of whom one had evidence of tamponade and required pericardiocentesis. M-mode echocardiographic parameters of left ventricular function in overt hypothyroid patients at diagnosis (Figure 9, 10) (Table 4, 5).

E/A was significantly reduced in overt hypothyroid patients.

<table>
<thead>
<tr>
<th>Pericardial Effusion</th>
<th>No of patients</th>
</tr>
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<tbody>
<tr>
<td>ABSENT</td>
<td>5</td>
</tr>
<tr>
<td>MILD</td>
<td>5</td>
</tr>
<tr>
<td>MODERATE</td>
<td>6</td>
</tr>
<tr>
<td>SEVERE</td>
<td>2</td>
</tr>
<tr>
<td>TOTAL</td>
<td>18</td>
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</table>

Table 3: pericardial effusion in overt hypothyroidism.

<table>
<thead>
<tr>
<th>Overt hypothyroidism</th>
<th>Normal values</th>
<th>Achieved values</th>
</tr>
</thead>
<tbody>
<tr>
<td>LEEDD(mm)</td>
<td>41.5 -56</td>
<td>47.1±1.8</td>
</tr>
<tr>
<td>LVESD(mm)</td>
<td>26-38</td>
<td>30.2±1.6</td>
</tr>
<tr>
<td>dIVST(mm)</td>
<td>6- 10.5</td>
<td>12.0±1</td>
</tr>
<tr>
<td>DLVPWT(mm)</td>
<td>6-10.5</td>
<td>11.9±1</td>
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</table>

Table 4: M-mode echocardiographic parameters of left ventricular function in overt hypothyroid patients at diagnosis.

<table>
<thead>
<tr>
<th>ECE changes</th>
<th>No of patients</th>
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<tr>
<td>WNL</td>
<td>5</td>
</tr>
<tr>
<td>low voltage complexes</td>
<td>7</td>
</tr>
<tr>
<td>Generalized T ↓</td>
<td>2</td>
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<tr>
<td>Non specific T wave changes</td>
<td>2</td>
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<tr>
<td>LAHB</td>
<td>2</td>
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<tr>
<td>AV blocks</td>
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</table>

Table 2: Electrocardiographic changes in Overt Hypothyroidism.
Isovolumetric relaxation (IRT) time was significantly prolonged in overt hypothyroid patient. Above two parameters directly reflect impaired diastolic function in overt hypothyroidism (Figure 11).

**Subclinical Hypothyroidism**

Patients with subclinical hypothyroidism do have clinical features of which easy fatigue, weight gain and inability to lose weight are commonly found. Mean heart rate was 76±5 at diagnosis, 3 patients had blood pressure on upper range. And all these patients were on higher age side. (Table 6,7) (Figure 12, 13). Isovolumetric relaxation time was significantly prolonged in subclinical hypothyroidism patients.

**Discussion**

In patients with primary hypothyroidism cardiovascular manifestations such as bradycardia, pericardial effusion and abnormal ECG findings are frequently observed. Of these findings reduced heart rate was common finding of this the abnormal ECG changes low voltage QRS complex is common findings. It is caused by multiple factors which include severity and duration of hypothyroidism, large pericardial effusion and aging of the 8 patients exhibiting low voltage complexes all were severely hypothyroid, 7 had associated pericardial effusion. Saritha et.al reported similar findings in study of 33 patients with hypothyroidism. 10 patients who were overtly hypothyroid had low voltage complexes. Similar findings were observed in study conducted by saritha bajaj et.al at department of medicine MLN medical college Allahabad. Pericardial effusion was found in 13 of 18 patients. Hypothyroidism has long been known to produce abnormalities of cardiac structure and performance. Systolic and diastolic myocardial functions

<table>
<thead>
<tr>
<th>PARAMETER</th>
<th>Normal values</th>
<th>Achieved values</th>
</tr>
</thead>
<tbody>
<tr>
<td>EF(%)</td>
<td>55%</td>
<td>64±4</td>
</tr>
<tr>
<td>FS(%)</td>
<td>26-44%</td>
<td>35±3</td>
</tr>
<tr>
<td>Peak E</td>
<td>50-90mm</td>
<td>77±5</td>
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<tr>
<td>Peak A</td>
<td>40-90mm</td>
<td>54±4</td>
</tr>
<tr>
<td>E/A</td>
<td>1-2mm</td>
<td>1.4±0.2</td>
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<tr>
<td>iRT</td>
<td>60-90mm</td>
<td>89±6.3</td>
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Table 5: Doppler-echocardiographic parameters of left ventricular function in overt patients hypothyroid patients.

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<th>PARAMETER</th>
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<td>T4</td>
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<tr>
<td>T3</td>
<td>6.8±1.4</td>
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Table 6: Achieved values.

<table>
<thead>
<tr>
<th>PARAMETER</th>
<th>Normal values</th>
<th>Achieved values</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVEDD(mm)</td>
<td>41.5 -56</td>
<td>47.4±1.7</td>
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<tr>
<td>LVESD(mm)</td>
<td>26-38</td>
<td>29.6±1.4</td>
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<tr>
<td>dVIST(mm)</td>
<td>6- 10.5</td>
<td>8.7±0.5</td>
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<tr>
<td>dLVPWT(mm)</td>
<td>6-10.5</td>
<td>8.5±0.7</td>
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</tbody>
</table>

Table 7: M-mode echocardiographic parameters of left ventricular function in subclinical hypothyroidism patients.

![M-mode echocardiographic parameters of left ventricular function in overt hypothyroid patients at diagnosis.](image-url)
are a sensitive index of myocardial abnormality. It is observed that IVS and posterior wall show disproportionate thickness in long standing untreated hypothyroidism. It is independent of age and presence or absence of pericardial effusion (Santos Ad, Miller et.al). Fazio, Biondi et.al reported decreased fractional shortening in overtly hypothyroid patients. Saritha Bajaj, PC Saxena et.al found no changes in FS%. In our study we did not find any changes in FS%. Diastolic dysfunction as suggested by reduced E/A and increased IRT was noted in all patients [22-23] (Table 8,9).
Figure 12: M-mode echocardiographic parameters of left ventricular function in subclinical hypothyroidism.

Figure 13: Doppler-echocardiographic parameters of left ventricular function in subclinical hypothyroid patient.
Subash kumar CH (2018) Evaluation of Cardiac Functions in Hypothyroidism and Subclinical Hypothyroidism

<table>
<thead>
<tr>
<th>S.NO</th>
<th>NAME</th>
<th>SEX</th>
<th>AGE</th>
<th>CLINICAL FEATURES</th>
<th>HR</th>
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<th>DBP</th>
<th>TSH</th>
<th>T4</th>
<th>T3 ab</th>
<th>ECG</th>
<th>Pericardial effusion</th>
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<td>-</td>
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<td>-</td>
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<td>-</td>
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<td>110</td>
<td>70</td>
<td>90</td>
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<td>-</td>
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<td>120</td>
<td>80</td>
<td>50</td>
<td>-</td>
<td>-</td>
<td>Non specific T wave changes</td>
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<tr>
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</table>

Table 8: Case Profile of Overt Hypothyroidism.

Subclinical Hypothyroidism

Cardiac function has been previously investigated by non-invasive techniques in patients with subclinical hypothyroidism. Earlier, systolic time intervals were measured to give an insight into the myocardial function. Recent reports suggest abnormalities in both systolic and diastolic function of the LV in patients with SH. However, Arem et al found normal cardiac function in patients with SH both at rest and during exercise. In this study also we did not found any abnormality in LV systolic function. Coming to diastolic dysfunction this study demonstrated a wide range of LV relaxation abnormality with prolong DT, IVRT and reduced E/A ratio. Similar finding have been reported by Biondi et al Vital et al studied LV diastolic function both by conventional Doppler and tissue Doppler echocardiography. By both methods, they demonstrated significant abnormalities in LV diastolic function though tissue Doppler echocardiography was more valuable in finding subtle abnormalities. The diastolic parameters depend upon cytosolic calcium concentration modulated by sarcoplasmic reticulum, ATP dependent calcium. Calcium transport is controlled by thyroid hormones. Hence, diastolic dysfunction can occur in patients with SH. This diastolic impairment may be a prelude to systolic dysfunction (Table 10,11).

Limitations of Study

1. Small study group with difference in age and sex distribution.
Table 9: Case Profile of Sub Clinical Hypothyroidism.

<table>
<thead>
<tr>
<th>S.NO</th>
<th>NAME</th>
<th>SEX</th>
<th>AGE</th>
<th>WEIGHT GAIN</th>
<th>HR</th>
<th>SBP</th>
<th>DBP</th>
<th>TSH</th>
<th>T4</th>
<th>T3</th>
<th>Anti bodies</th>
<th>ECG</th>
<th>PERICARDIAL EFFUSION</th>
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<td>124</td>
<td>86</td>
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<td>7.4</td>
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Table 10: Echocardiographic Measurements of Overt Hypothyroidism.

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2. There is no comparison in cardiac functions before and after thyroxine hormonal replacement

Conclusions

This study indicates that

1. Hypothyroidism is associated with intrinsic myocardial changes reflected by alterations in contractility and relaxation.

2. Overt hypothyroidism in addition to common findings like bradycardia, ECG abnormalities produces structural and functional abnormalities (systolic and diastolic) in cardiovascular system.

3. Subclinical hypothyroidism though asymptomatic, can cause diastolic dysfunction of heart.

4. Doppler echocardiography technique is simple, reliable and reproducible

Echocardiographic Measurements of Sub Clinical Hypothyroidism.

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References

1. Arem R, Rokey R, Kiefe C, Escalante DA, Rodriguez A. (1996) cardiac systolic and diastolic function at rest and exercise in subclinical hypothyroidism: effects or thyroid hormone therapy. Thyroid 6:397-402. [View Article]
21. Santos AD, Miller RP, Mathew PK, Wallace WA, Cave WT Jr,
