STUDY OF ANEMIA IN PATIENTS OF PRIMARY HYPOTHYROIDISM

BY

REGISTRATION NO: BG0119003

Dissertation

Submitted to

KAHER, Belagavi, Karnataka

In partial fulfilment

of the requirements for the degree of

M.D.

IN

GENERAL MEDICINE

DEPARTMENT OF GENERAL MEDICINE

J. N. MEDICAL COLLEGE

BELAGAVI- 590010. KARNATAKA

APRIL - 2022

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ABBREVIATIONS

Apo	-	Apolipoprotein
BMR	-	Bas al metabolic rate
CBC	-	Complete blood countCp - Ceruloplasmin
DIT	-	Diiodothyronine
DMT	-	Divalent metal transporter
ELISA	-	En zyme linked immune sorbent assay
EDTA	-	Ethyelene diamine tetra acetic acid
ER	-	Endop lasmic reticulum
FeOOH	-	Ferric oxyhydroxide
FSH	-	Follicle stimulating hormone
HCG	-	Human chorionic gonadotropin
HCP	-	Heme carrier protein
Hb	-	Hemoglobin
HH	-	Hereditary Hemochromatosis
HRP	-	Horse radish peroxidase
HMP	-	Hexose monophosphate
IDA	-	Iron deficiency anemia
IRE	-	Iron regulatory element
IRP	-	Iron regulatory protein
kDa	-	Kilo Dalton
LH	-	Luteinizing hormone
MIT	-	Moniodo thyronine
NADPH	-	Nicotinamide adenine dinucleotide phosphate
Na-K-ATPase	-	Sodium potassium ATPase

PAX-8	-	Paired box gene 8
PTH	-	Parathormone
RNA	-	Ribonucleic acid
RBC	-	Red blood cells
sTfR	-	Soluble transferrin receptor protein
TPO	-	Thyroid peroxidase
TBG	-	Thyroid binding globulin
T3	-	Triiodoth yronine
T4	-	Tetraiodothyronine f
T3	-	free
fT4	-	free TetraiodothyronineTR - Thyroid receptor
TRH	-	Thyrotropin releasing hormone
TSH	-	Thyroid Stimulating Hormone
TfR	-	transferrin receptor
Tf	-	Transferrin
IBC	-	Total iron binding capacity
TMB	-	Tetramethylbenzidine
UTR	-	untran slated region
WHO	-	World health organization”

ABSTRACT

Background: Hypothyroidism affects the hematopoietic system and anemia is an important feature of the same. This study aimed to assess the prevalence and pattern of anemia in patients with primary hypothyroidism.

Methodology: This cross-sectional study was conducted from January 2020 to December 2020 in KLEs DR Prabhakar Kore hospital & MRC, Belagavi. All the patients above age of 18yrs diagnosed newly for primary hypothyroidism were taken in this study after obtainingan informed consent.

Results: Total of 100 patients in accordance with the inclusion criteria were taken in present study after obtaining an informed consent from each of them. The average age in years the present study is 39.53±16.4yrs, where 73% were female patients and 27% were male patients, with female preponderance. Primary hypothyroidism patients showed the prevalence of anemia in 77% of the patients. There was significant negative strength of association betweenthe hemoglobin with serum TSH ($r= -0.352$, $p<0.05$), and significant association of severity of anemia with higher TSH value among hypothyroid patients.

Conclusion: The prevalence of anemia among the hypothyroidism patients was found higher (77%) and normochromic normocytic and microcytic hypochromic type of peripheral pictureare common among the patients. There is a significant association between the severity of anemia with the serum TSH level and T4 in hypothyroid patients.

Keyword: Hypothyroidism, TSH, Anemia, Hemoglobin, Hypochromic, Microcytic

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INTRODUCTION

Anemia is an important public health issue in India, hypothyroidism being one of the causative agents for the same. Hypothyroidism causes a slowing of metabolic activity in the body, and it can impact practically any organ system. How severe are the signs and symptoms, is determined by the age of onset and the level of hormone in sufficiency. Hypothyroidism affects the hematopoietic system and anemia is an important feature of the same.[1]

Anemia of all types can occur with hypothyroidism. Anemia in hypothyroidism can occur as a consequence of suppression of bone marrow, decrease in the production of erythropoietin, or deficiency of iron, folic acid or vitamin B12. The morphology of anemia is normocytic normochromic type, most likely due to bone marrow activity depression, reduced activity of thyroid or due to suppression of production of erythropoietin secondary to feedback inhibition due to decreased need for oxygen.

Hypothyroidism is associated with hypo-proliferative erythropoiesis. 2,3-diphosphoglycerate production is increased by thyroid hormone, which in turn alleviates the shift of oxygen to the cells. Hypothyroidism affects this particular function.[2]

Menorrhagia in females leading to blood loss and malabsorption – both of these produce microcytic hypochromic type of anemia, which may be found in hypothyroidism.[2] Autoimmune thyroiditis can also be seen. Polyglandular autoimmune syndrome can lead to pernicious anemia. There is intrinsic factor (IF) deficiency in pernicious anemia, this leads to reduction of vitamin B12 absorption. Gastric achlorhydria may be a secondary cause for the same. This is the reason why microcytic anemia occurs in hypothyroidism.[2]

So, it is important to understand the correlation between anemia and hypothyroidism in diagnosis, in order to decide the treatment course as both are interrelated and one might causethe other.

Since there is a correlation between hypothyroidism and anemia both being clinical burdens, at the time of diagnosis of thyroid disorder a simultaneous evaluation of anemia and the type of anemia will help in early diagnosis and treatment of the same.

OBJECTIVE

Aim

To assess the prevalence and pattern of anemia seen in patients with primary hypothyroidism.

Objectives

1. To assess the prevalence of anemia in patients of hypothyroidism.
2. The type of anemia.
3. To correlate severity of anemia with thyroid profile.

REVIEW OF LITERATURE

Apart from regulation of metabolism and growth, thyroid hormone has multiple other functions in the body. The hypothalamic-pituitary-thyroid axis is composed of the hypothalamus, the pituitary gland (anterior part) and the thyroid gland. Thyroxine or tetraiodothyronine (T4) and triiodothyronine (T3) are the major hormones produced by the thyroid gland (T3). Thyrotropin-releasing hormone (TRH) secreted by the hypothalamus, thyroid-stimulating hormone (TSH) secreted by the anterior pituitary gland, and T4 from the thyroid gland are responsible for the feedback and homeostasis, which is the mainstay of the hypothalamic-pituitary-thyroid axis. Patients of hypothyroidism present with features like depressed heart rate, intolerance to cold, constipation, tiredness, and increased weight gain due to an underactive thyroid gland. Hyperthyroidism, on the other hand, is characterized by heat sensitivity, diarrhea, loss of weight, fine tremors, and weakness of skeletal muscles. The trace element iodine, whose absorption is done by the small colon, is a vital constituent of T3 and T4. Rich iodine sources are iodized salt, shellfish, macroalgae, and vegetables. Shortage of iodine and reduced thyroid hormone production can result from inadequate iodine intake. Lack of iodine can causes diseases like cretinism, myxedema, goiter and hypothyroidism.[3–5]

Anatomy

The thyroid gland has two lobes and is shaped like a butterfly. The two lobes of the gland are joined by a bridge like structure, called the isthmus. Weight of the thyroid gland is 25 g. Its main blood supply is the thyrocervical arteries, and it is innervated by the autonomic nervous system.[6]

Thyroxine is produced by the follicles. Epithelial cells surround each follicle and they are filled with a substance called colloid, which is proteinaceous in nature. Thyroglobulin is an abundant glycoprotein found in colloid. The follicles expand during the dormancy of the gland and the follicular acini shrink when there's glandular activity. The colloid is then resorbed by thyrocytes during the latter. Parafollicular cells are also essential cells. They are also called C shaped cells. They are present in between the follicles. They are responsible for the secretion of the hormone calcitonin.

The form and size of the thyroid gland vary anatomically. Diseases like thyroiditis, goiter, hypothyroidism, cancer and iatrogenic interventions like past surgery, and prior exposure to radio-iodine can majorly distort, or change the size of the gland or obscure its borders. It contains the following parts:

- Thyroid lobes
- Thyroid isthmus
- Pyramidal lobe
- Tubercle of Zucker Kandl
- Ectopic thyroid tissue

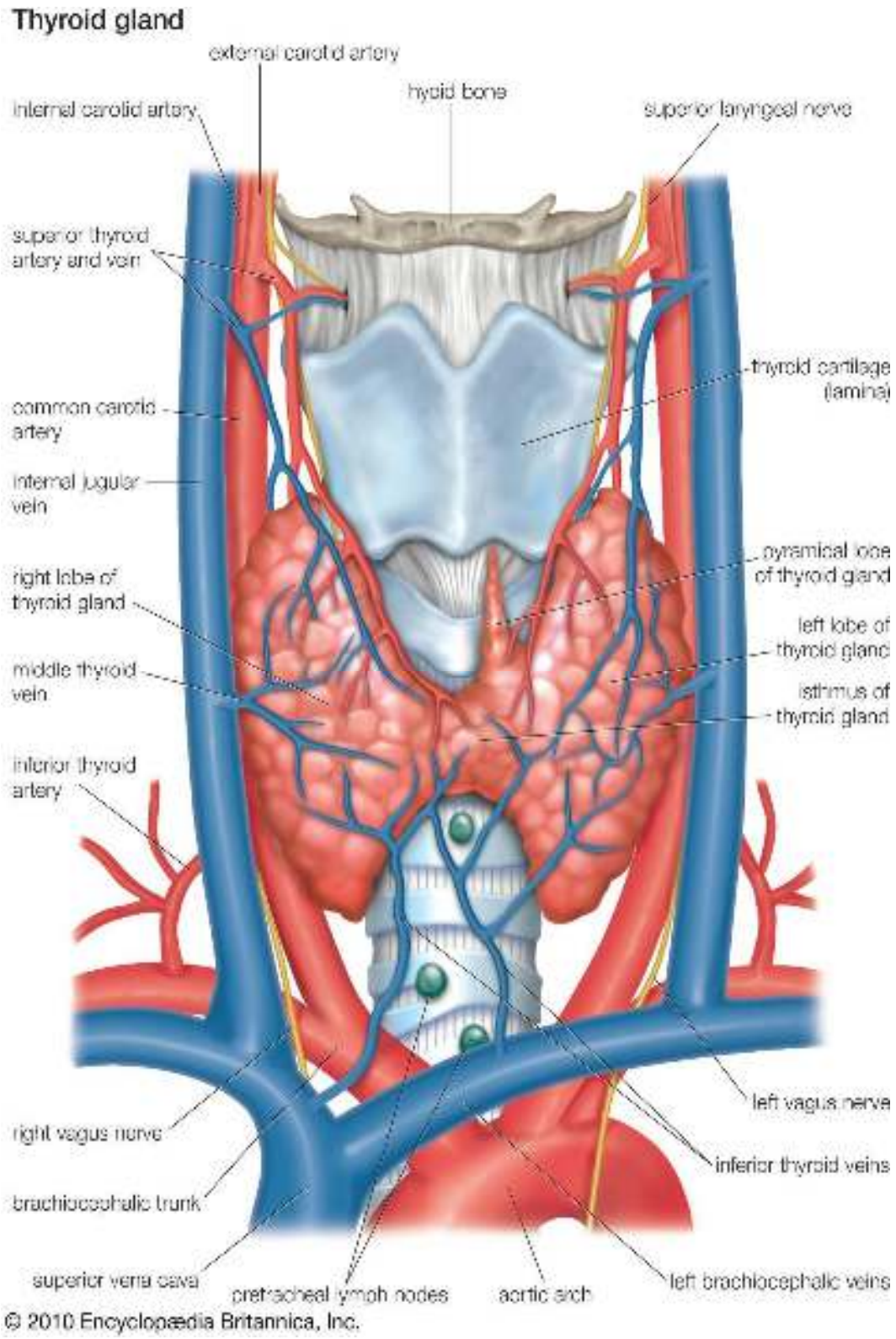

Figure 1: Thyroid gland anatomy

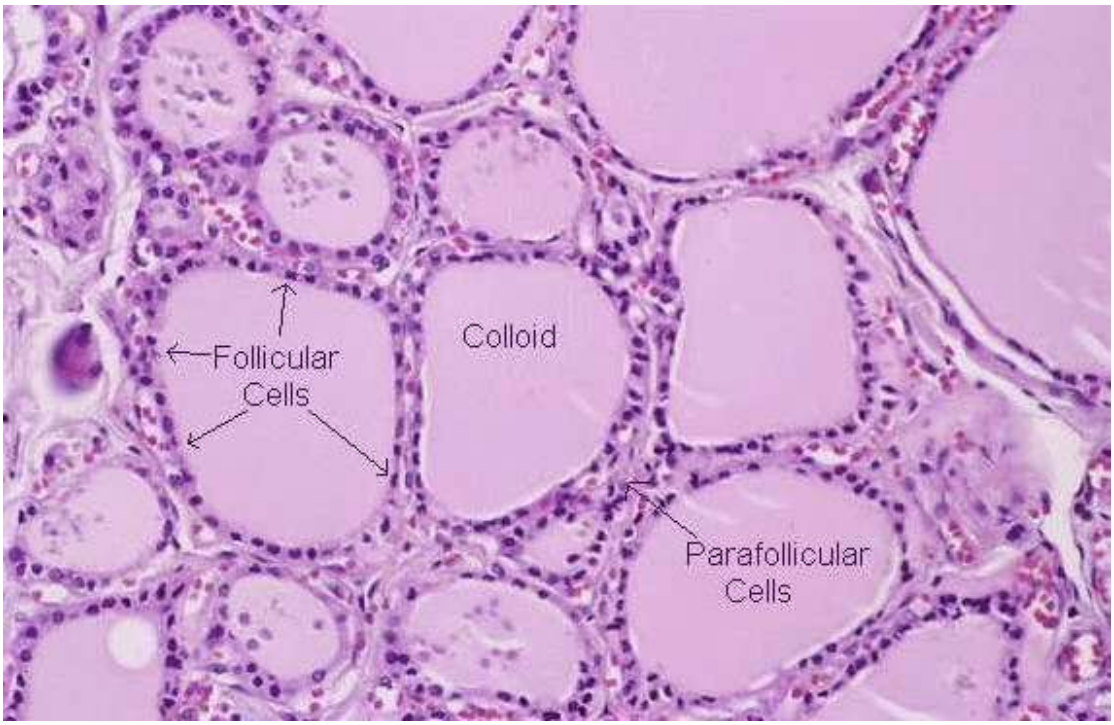

Figure 2: Thyroid gland histology

3 nuclear transcription factors help in expression of the thyroid follicle cells namely transcription factor for thyroid 1 and 2 and PAX-8.[7]

Embryology

Thyroid gland growth is seen in the 3rd gestational week, mainly originating from the endoderm. Lateral thyroid lobes are produced by the fourth pharyngeal pouch (ventral portion). The pyramidal lobe, which may or may not be present, develops from the descent ofthe thyroglossal duct that migrates from the pharyngeal organ at the tongue (foramen caecum) and later attaches itself to the thyroid isthmus. After its descent, the thyroglossal duct is obscured. The patient may develop a thyroglossal duct cyst if it remains patent.[8,9]

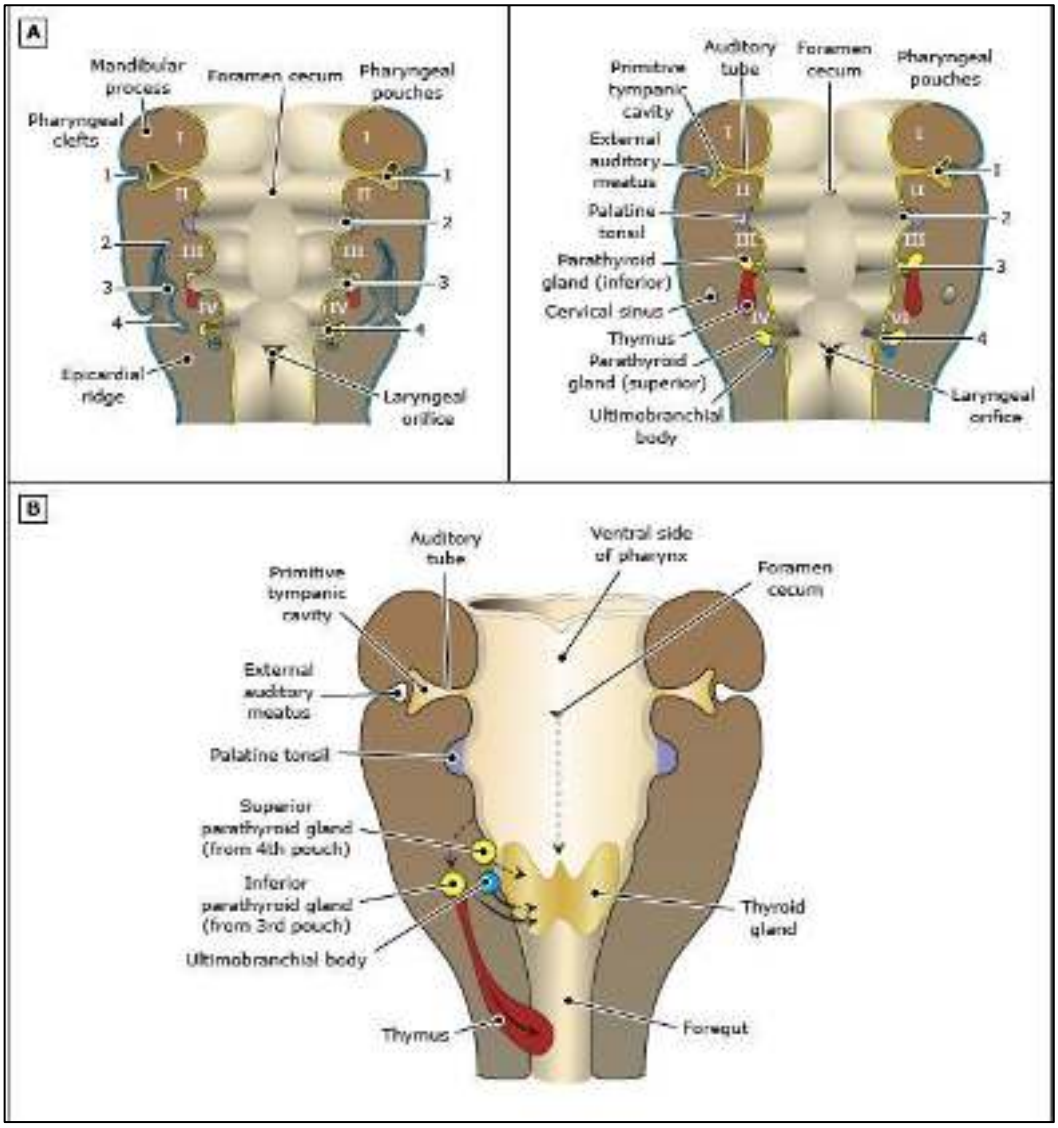

Figure 3: Pharyngeal arch - transformations (Coronal view)

The tympanic membrane of the ear persists as a thin barrier between the inner and the outer side. The auditory tube is present on the inner side while the ear canal on the outer side. The rest of the clefts smoothen out as a result of enlargement and descent of the second arch. A trapped cyst or fistula may persist in the connective tissue of the neck (B). The second pouch contains lymphatic tissue, which eventually becomes the tonsil. Third and fourth pouches give rise to the parathyroid gland and thymus gland.

Blood supply[4]

The right and left superior and inferior thyroid arteries are the main arteries supplying the endocrine thyroid. It's drained by the superior, middle, and inferior thyroid veins which eventually turn the channel into the vena jugularis interna and innominate veins.

Innervation:

The nerve supply to the gland is derived from

- Superior laryngal nerve
  - External branch
  - Internal branch
- Recurrent laryngeal nerve
  - Right Recurrent laryngeal nerve
  - Left Recurrent laryngeal nerve
- Non-recurrent laryngeal nerves

Cellular

The steps involved in the thyroid hormone synthesis are as below;

- Thyroglobulin synthesis
- Iodine uptake
- Iodination of Thyroglobulin
- Storage
- Release

1. Thyroglobulin synthesis: Thyrocytes in the thyroid follicles are responsible for the production of thyroglobulin. It is synthesised in the rough endoplasmic reticulum. The packing is done by golgi apparatus in the vesicles. Via

exocytosis, thyroglobulin entersthe follicles.

2. Uptake of iodine: Basolateral Na+-I-symporter – via protein kinase A phosphorylation, this causes Na+-K+-ATPase to shift iodine into thyrocytes from circulation. Then, via pendrin transporter, the iodine diffuses into the apex of the cell from the basolateral membrane into the colloid.
3. Thyroglobulin iodination: Protein kinase A causes phosphorylation and activation of the enzyme thyroid peroxidase (TPO). TPO gives rise to the three reactions – oxidative reaction, organification reaction, and coupling process.
   - Oxidative reaction: Hydrogen peroxide is oxidized from iodide to iodine.
   - Organification: Thyroglobulin contains tyrosine residues, which are linked with I2 by TPO. Monoiodotyrosine (MIT) and diiodotyrosine (DIT) are generated by this reaction. MIT = 1 tyrosine residue + iodine. DIT = 2 tyrosine residues + iodine.
   - Coupling process: Iodinated tyrosine compounds are combined to produce triiodothyronine and tetraiodothyronine respectively. MIT + DIT = T3; DIT + DIT = T4.
4. Storehouse: In the follicles
5. Release: Following steps:
   - Endocytosis occurs, and thyrocytes take up thyroglobulin which has been iodinated.
   - Lysosome fusion occurs with the endosome which contains iodinated thyroglobulin
   - Endolysosome cleaves thyroglobulin into the following: MIT, DIT, T3, and T4.
   - MCT8 transporter releases T3 and T4 inside capillaries which are fenestrated. Occurrence of T3 is 20% and T4 is 80%.[10]
   - Iodine molecules are removed from DIT and MIT by deiodinase enzymes. [5,11,12]

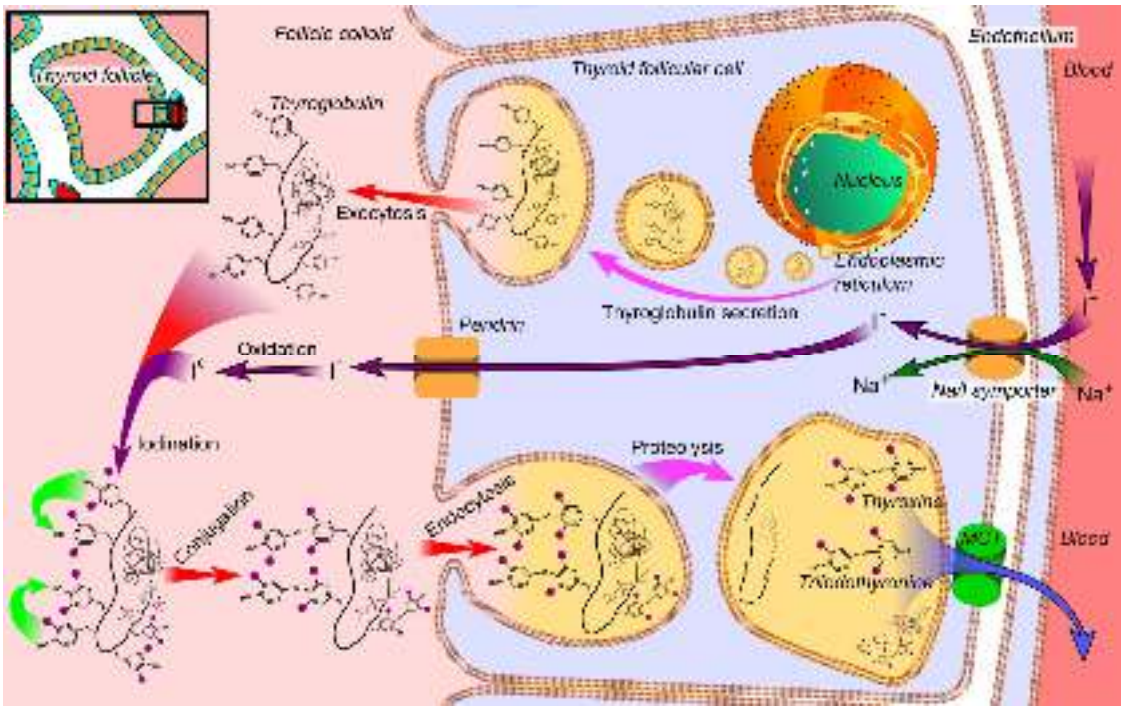

Figure 4: Thyroid hormone synthesis steps.

Transport

99% of T4 and T3 is protein bound. Remainder one percent is unbound. Active hormone isthe protein bound hormone.

Proteins involved in thyroid hormone binding are: Thyroxine binding globulin, Transthyretin and Albumin.

Importance of thyroid peroxidase

The complete bio metabolism of thyroid hormone formation is catalysed by TPO enzyme. Co-factors like iron, selenium and zinc play an important role in their functioning. The studyof iron as a cofactor is important, especially with regards to our study as we study the correlation of anemia and hypothyroidism.

Regulation of thyroid hormone

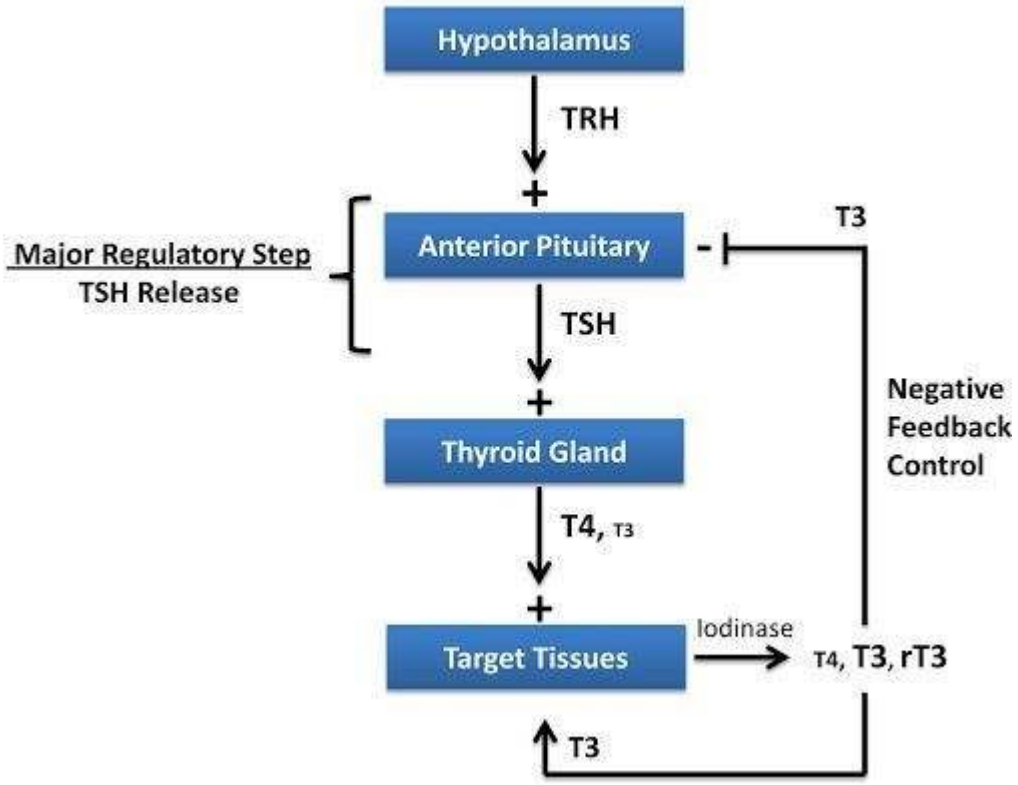

Figure 5: Thyroid hormone regulation

Feedback Effect of Endocrine Thyroid on TRH & TSH"

Thyroid hormone homeostasis is maintained on a daily basis through negative feedback on TRH and TSH. TSH secretion nearly ceases when thyroid hormone synthesis rate exceeds

1.75 times the baseline. Thyroid hormones have an effect on both the anterior pituitary and the hypothalamus. TSH and TRH are inhibited by excess thyroid hormone, and vice versa in the case of thyroid deficiency.

Purpose

The physiological effects of thyroid hormones are listed below:

- Raise the basal metabolic rate
- Reliant on the metabolic status, it can provoke lipolysis or lipid synthesis.
- Provoke the metabolism of carbohydrates
- Metabolism of proteins. Thyroid hormones can also induce catabolism of proteins in high doses.
- Permissive effect on catecholamines
- In children, thyroid hormlones act synergistically with growth hormone to provoke bone growth.
- The impact of thyroid hormone in CNS is vital. During the prenatal period, it is crucial for the development of the brain. In adults, it can affect mood. Hyperthyroidism can cause hyperexcitability and irritability. Hypothyroidism cancause dememtia, slowed speech, and sleepiness.
- Thyroid hormone affects obstetric and gynaecological functions.

Effect of thyroidal hormones

Growth	Crucial for connective tissue development
Sexual development	Deficiency of thyroxine in females:menstrual irregularities In males: Decreased Libido
Cellular metabolism	Increases mitochondria Increases glucose absorption, gluconeogenesis, glycogenolysis Increases lipolysis & protein synthesis Increases the BMR Increases O2 consumption
Cardiovascular system	Increases cardiac output Increases heart rate Increases cardiac strength Increases tissue blood flow Increases respiration
Central nervous system	Increases rapidity of cerebration promoting normal brain development
Other endocrine organs	Stimulates pancreas to secrete insulin Stimulates PTH

Thyroid hormone metabolism

There are major differences in the production and metabolism of thyroxine (T4) and triiodothyronine (T3), both quantitatively and qualitatively.

Thyroxine: T4 is created at a rate of 80 to 100 mcg (100 to 130 nmoles) per day, entirely in the thyroid. The extrathyroidal pool of T4 contains 800 to 1000 mcg (1000 to 1300 nmoles), most of which is extracellular. T4 degrades at a rate of about ten percent per day. Approximately 80% is deiodinated, 40% is converted to T3, and

40% is converted to reverse T3 (rT3). The remaining 20% is conjugated with glucuronide and sulfate, deaminated and decarboxylated to generate tetraiodothyroacetic acid, or cleaved between the two rings to form tetrac.[13] T4 deiodination to T3 results in increased biologic activity, whereas the other T4 metabolites are inert. T4 to T3 conversion in extra-thyroidal organs is controlled, hence T3 production can fluctuate independently of pituitary-thyroid function variations.

Triiodothyronine: The majority of T3 (80%) is created by extra-thyroidal deiodination of T4, with the remainder produced by the thyroid. The overall daily production rate is 30 to 40 mcg (45 to 60 nmoles). The extrathyroidal T3 pool includes about 50 mcg (75 nmoles), the vast majority of which is intracellular. T3 degrades significantly faster than T4, primarily by deiodination (approximately 75 percent per day).

Reverse triiodothyronine (rT3): is produced at a rate of 30 to 40 mcg (45 to 60 nmoles) per day, almost entirely through extrathyroidal deiodination of T4. rT3 degrades significantly faster than T3, primarily through deiodination.[13]

T4 and T3 thyronamines are inactivated by inner ring deiodination (5'-deiodination) to generate rT3 and 3,5-dioidothyronine (T2). T2 is also formed when the outer ring of rT3 is deiodinated. T2 and other iodothyronamines (e.g., 3-iodothyronamine) have been proven to be separate chemical messengers with direct effects on mitochondrial activities in the serum using immunological approaches.[14,15]

Serum binding proteins

More than 99.95% of thyroxine (T4) and 99.5% of the triiodothyronine (T3) in serum isbound to various serum proteins, like

- Thyroxine binding globulin (TBG)
- Transthyretin (TTR)
- Albumin
- Lipoproteins

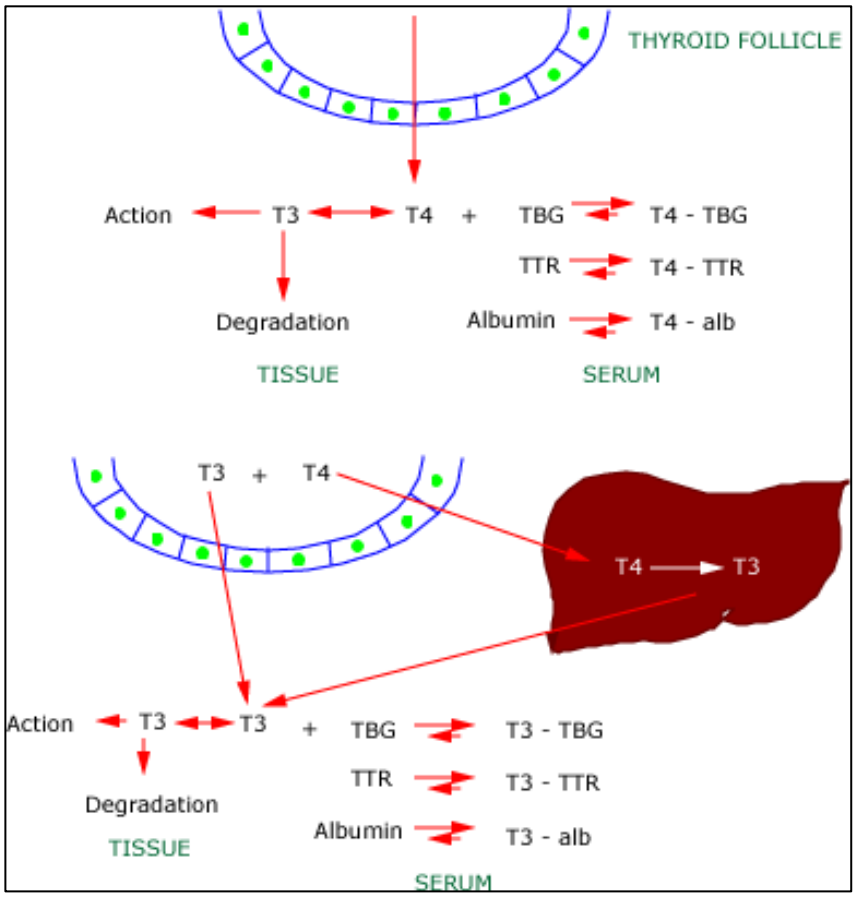

Figure 6: Transport and metabolism of thyroid hormones

Hypothyroidism

In most cases, hypothyroidism is a chronic illness that necessitates lifetime therapy. Thyroid hormone replacement therapy is used lest the hypothyroidism is transitory (as in subacute thyroiditis or painless thyroiditis) or reversible (owing to a drug that can be stopped)

Definitions

Biochemically, overt **primary hypothyroidism** is defined by an elevated serum TSH concentration and a depressed serum free thyroxine (T4) concentration. Clinical signs vary greatly depending on the age of commencement, as well as the duration and severity of thyroid hormone shortage.

Biochemically, **subclinical hypothyroidism** is defined by an elevated blood TSH concentration and a normal serum free T4 concentration. The majority of patients are asymptomatic.

Central hypothyroidism instigated by hypothalamic or pituitary illness is distinguished by a depressed serum T4 concentration and an inappropriately increased serum TSH concentration. TSH levels might be depressed, normal, or high (up to 10 mU/L). Central hypothyroidism has clinical signs that are comparable to, but occasionally milder than,primary hypothyroidism.

Classification

- Primary hypothyroidism
    - Secondary hypothyroidism
    - Subclinical hypothyroidism
    - Clinical or overt hypothyroidism
    - Congenital hypothyroidism

Table 1: Major Causes for hypothyroidism
Primary hypothyroidism
Chronic autoimmune thyroiditis
Iatrogenic
Thyroidectomy
Radioiodine therapy or external irradiation
Iodine deficiency or excess
Drugs - thionamides, lithium, amiodarone, interferon alfa, interleukin-2, tyrosine kinase inhibitors, checkpoint inhibitor immunotherapy
Infiltrative diseases - fibrous thyroiditis, hemochromatosis, sarcoidosis
Transient hypothyroidism
Painless (silent, lymphocytic) thyroiditis
Subacute granulomatous thyroiditis
Postpartum thyroiditis
Subtotal thyroidectomy
Following radioiodine therapy for Graves' hyperthyroidism
Following withdrawal of suppressive doses of thyroid hormone in euthyroid patients
Congenital thyroid agenesis, dysgenesis, or defects in hormone synthesis

Clinical manifestation of hypothyroid state

Table 2: Major symptoms and signs of hypothyroid state

Mechanism	Symptoms	Signs
Decelerating metabolic processes	Fatigue and weakness Cold intolerance	Slow movement and slow speech
	Dyspnea on exertion	Delayed relaxation of tendon reflexes
	Weight gain	
		Bradycardia
	Cognitive dysfunction	
		Carotenemia
	Mental retardation (infantile onset)	
	Constipation	
	Growth failure	
Accumulation of matrix substances	Dry skin Hoarseness	Coarse skin
		Puffy facies and loss of eyebrows
	Edema	Periorbital edema
		Enlargement of the tongue
Other	Decreased hearing	Diastolic hypertension
	Myalgia and paresthesia Depression	Pleural and pericardial effusions
	Menorrhagia Arthralgia	Ascites Galactorrhea
	Pubertal delay	

Skin: Cool and pale in patients due to reduced blood supply. The epidermal part develops cellular atrophy with hyperkeratosis that causes the skin its characteristic dry and rough nature.

- Sweating is reduced
- Skin discoloration
- Coarse hair or hair loss
- Brittle nails
- Non-pitting edema (myxedema)
- Vitiligo and alopecia areata

Eyes: periorbital edema can be commonly seen

Cardiovascular system: there is systemic hypometabolism that is associated with reduction in cardiac output which is catalysed via the reduction in heart rate and contractility.[16,17] The decrease in contractility is caused by thyroidal hormone control of genes coding for specific myocardial enzymes involved in cardiac contraction and relaxation.[18]

Other abnormalities contributing to cardiovascular disease may be

- Pericardial effusion
- Hypertension
- Hypercholesterolemia
- Hyperhomocysteinemia

Respiratory System: Tiredness, Dyspnea on exertion, rhinitis and reduced exercise limit may result from the impaired respiratory function as well as the

cardiovascular function.Sleep apnea can also occur in some of the patients.

Gastrointestinal disorders: reduced gut motility, leading to constipation. Other problems related are

- Dysgeusia
- Atrophy of gastric mucosa, due to antibodies against parietal cells
- Celiac disease
- Non-alcoholic fatty liver disease[19]
- Weight gain due to reduced metabolic rate
- Ascites

Haematological: Many systematic reviews found that there is increased risk of bleeding in hypothyroidism which is associated with hypercoagulable state.

Neurological dysfunction: The neurologic manifestations of hypothyroidism are both common and protean, affecting both the central and peripheral nervous system.

- Hashimoto encephalopathy
- Myxedema coma
- Carpal tunnel

Musculoskeletal symptoms: weakness, cramps, myalgias, joint pains, aches and stiffness areseen in the patients with hypothyroid state.

Gynaecological abnormalities: Females with hypothyroid state may be either oligo/amenorrhea or hypermenorrhea/menorrhagia. These menstrual changes result in decreased fertility. If pregnancy does occur, it may have higher propensity for early spontaneous termination. Hyperprolactinemia may arise and seldom sufficiently severe

to cause amenorrhea or galactorrhea.[20] Decreased libido, erectile dysfunction, and delayed ejaculation are found in 64 percent of hypothyroid men.[21]

Drug clearance: Many drugs, including antiseizure, anticoagulant, hypnotic, and narcotic medications, have reduced clearance in hypothyroidism. As a result, if the drug dose is not lowered, drug toxicity may occur. Furthermore, medicines that are taken at effective levels in hypothyroid patients may become less effective after T4 replacement.

Anemia: reduction in red corpuscular mass and normochromic, normocytic hypoproliferative anemia is seen. Pernicious anemia can occur in patients with hypothyroidism due to chronic autoimmune thyroiditis.

Assessment of thyroid function

Patients exhibiting symptoms or clinical signs of hypothyroid state, the serum TSH should bethe mandatory first investigation. In case the serum TSH level is high, the TSH estimation ought to be reevaluated combined with a serum free T4 to clinch the diagnosis of hypothyroidstate.

Thyroid function is assessed by one or more of the following tests:

- Serum TSH concentration
- Serum total T4 and T3 concentrations
- Serum free T4 and T3 concentrations

Serum TSH	Serum free T4	Serum T3	Assessment
Normal hypothalamic-pituitary function			
Normal	Normal	Normal	Euthyroid
Normal	Normal or high	Normal or high	Euthyroid hyperthyroxinemia
Normal	Normal or low	Normal or low	Euthyroid hypothyroxinema
Normal	Low	Normal or high	Euthyroid: T3 therapy
Normal	Low-normal or low	Normal or high	Euthyroid: thyroid extract therapy
High	Low	Normal or low	Primary hypothyroidism
High	Normal	Normal	Subclinical hypothyroidism
Low	High or normal	High	Hyperthyroidism
Low	Normal	Normal	Subclinical hyperthyroidism
Abnormal hypothalamic-pituitary function			
Normal or high	High	High	TSH-mediated hyperthyroidism
Normal or low*	Low or low-normal	Low or normal	Central hypothyroidism

Various articles establishing the relationship of hypothyroidism with anemia

In a study performed by Das C et al., (2012) to assess association of anemia in primary hypothyroidism. In 31 patients (51.6 percent), Normocytic, normochromic anemia was found, trailed by microcytic anemia in 26 individuals (43.3 percent). 6 patients (10%) were diagnosed with megaloblastic anemia due to deficiency of vitamin B12, with three diagnosed pernicious anemia cases. 2 individuals were iron and vitamin B12 deficient. The most prevalent type of anemia in the current study was normocytic normochromic anemia with normal bone marrow, followed by iron deficiency anemia.[22]

In a study by Rezvani MR et al., to identify the anemia among the patients with hypothroidism. In a study population of twenty-four patients diagnosed with hypothyroid state, 12 patients (50%) were diagnosed with deficiency of iron. Prevalence of deficiency of iron is fifteen percent in normal people. In twenty-six of the study population with iron deficiency anemia 8 patients (30.8%) were established to have hypothyroidism. The prevalence of hypothyroidism is five percent in normal population. This study showcased thatco-incidence of these 2 conditions in 2 groups of study samples is significantly more than normal people.[23]

In a case control study performed by Kulkarni VK et al., (2017) to investigate the prevalence, type and cause of anemia among the hypothyroid patients. It was seen the incidence of anemia was showcased to be 69% in the overt hypothyroid group and 56% inthe subclinical hypothyroid group. Normocytic normochromic (53%) was the most prevalentanemia type, trailed by microcytic (30%) and macrocytic anemia (27%). Anemia was seen in

75% of the patients, which was greater than in the euthyroid controls. Hypothyroid individuals had greater anemic symptoms than controls. The most prevalent kind of anemia in our study was normocytic normochromic anemia. Anti TPO positive state was found in sixty-nine percent of patients having anemia, indicating autoimmunity. Deficiency of iron was more prevalent in case group versus the control group. TSH and hemoglobin had a statistically significant negative connection.[24]

In an observational study by Patel RP et al., (2017) to assess the anemia and the etiology in patient group with primary hypothyroid state not treated. Anemia occurred in 18% of subclinical hypothyroid individuals and 11% of overt hypothyroid patients. Anemia due to chronic disease was discovered to be the most prevalent anemia in individuals with overt and subclinical hypothyroidism, according to a subgroup analysis of patients in hypothyroid state. Anemia is a typical outcome in overt hypothyroidism; however, it is not included as a complication of untreated subclinical hypothyroidism. The kind and etiology of anemia differs between overt and subclinical hypothyroid individuals. As a result, anemia in hypothyroidism must be adequately examined because treatment varies depending on the etiology of anemia.[25]

In the prospective observational study by Anand R et al., (2018) to investigate the incidence of anemia and pattern in primary hypothyroidism. It was seen that anemia was present in 114 out of 203 patients (56%) in the subclinical hypothyroid patients and 124 out of 180 patients (69%) in the overt hypothyroid group. Among those with anemia, normocytic normochromic (53%) was the maximally prevalent type of anemia, trailed by microcytic (30%) and macrocytic anemia (27%). The most prevalent kind of anemia in subjects of hypothyroid state is normocytic

normochromic anemia. Anemic state was showcased to be present in 69 percent of the overt hypothyroid group and 56 percent of the subclinical hypothyroid group. Anemia was equally as common in people with subclinical hypothyroidism as it was in those with overt hypothyroidism. TPO antibodies have been linked to an increased risk of developing anemia in hypothyroidism. Higher TSH levels werelinked to more severe anemia.[1]

In a study by Patil MB et al., (2018) to investigate the anemic state in patients with primary hypothyroid state. Women are more likely than men to suffer from hypothyroidism. Anemia affects a higher fraction of hypothyroid females (54%) than hypothyroid males (45 percent). The most prevalent kind of anemia was normocytic normochromic anemia (58.49 percent), trailed by MCHC (20 percent), macrocytic hypochromic anemia (12 percent), and dimorphic anemia (8.5 percent). The more frequent symptom & sign established was generalized weakness, which was seen in 49.5 percent of clinical hypothyroidism subjects, followed by gain in body mass (34.5 percent), heart rate less than 60 (27.5 percent), edematous changes (23 percent), menstruation abnormalities in women (12.5 percent), and intolerance to cold in 12 percent of the study population. Few participants had greater than 1 indication and feature. Plenty of the participants were evaluated if they exhibited any one of the signs and symptoms, putting them in clinical hypothyroid state strata (78 percent). Antibodies to TPO were found in only a handful of the study sample, with the higher fraction of them living in their 40s and 50s and incidence decreasing as age surged, most likely due tothe fact that study population's average age was around 45. When compared to men, females (17.41 percent) showcased somewhat elevated incidence of hypothyroidism due toautoimmune etiology (13.63 percent).[26]

In a prospective study by Peraka SA et al., (2019) to assess the prevalence and classification of anemia in people with hypothyroid state and associated with magnitude of TSH level. Out of 1500 hypothyroid patients that were considered in the study population, thecondition of anemia was observed to be 41.8 percent. Normocytic normochromic anemia was most prevalent 98.56%, MCHC was 0.95 percent and macrocytic anemia was 0.49 percent. Sixty percent had anemia of mild kind, forty percent had anemia of moderate kind and 1 percent had anemia of severe kind.[27]

In a cross-sectional study by Fatima Q et al., (2019) to assess the hematological changes in patients with primary hypothyroidism. The overall prevalence rate of anemia in patients with hypothyroidism was 56%, which is higher than the WHO stated data on anemia prevalence worldwide. Our findings revealed that the prevalence of normocytic normochromic anemia was much greater, microcytic anemia was second, and macrocytic anemia had the lowest prevalence rate. In terms of hematological markers and type of anemia, there was nil difference statistically when comparing subclinical hypothyroidism versus overt hypothyroidism on subgroup analysis. It is generally difficult to obtain complete anemia correction without a good diagnosis and adequate treatment of the underlying thyroid illness. Because of the high prevalence of anemia state in patients of hypothyroidism, screening for hypothyroid state ought to be included in the differential diagnosis of cases presenting with anemia.[28]

MATERIALS AND METHODS

Study design: Cross sectional study

Study period: The study was conducted from January 2020 to December 2020 in KLEs DR Prabhakar Kore Hospital & MRC, Belagavi.

Sample size: 100

Source of data: Patients on out-patient & in-patient basis in department of General Medicine & Endocrinology at KLES Dr. Prabhakar Kore Hospital, Belgaum fulfilling the inclusion criteria.

Inclusion criteria:

- All newly diagnosed patients of Primary Hypothyroidism
- >18 years of age

Exclusion criteria

- Multifactorial anemia or anemia due to other reasons like hemolytic anemias, gastrointestinal or genitourinary losses due to malignancy and/ or acute/ subacute blood losses.
- Presence of any comorbid disease like coronary heart disease, diabetes mellitus, renal failure.

Method:

Patients coming to OPD or admitted with laboratory confirmed Primary Hypothyroidism fulfilling inclusion criteria and willingness to participate were asked for consent, detailed history taken & examination was done.

Laboratory confirmation with Overt hypothyroidism with low free T4 and Serum TSH > 10mIU/L; Basic investigations to see for anemia & types–CBC, RBC indices and Peripheral smear will be done. Peripheral smears study of patients with anaemia were studied to investigate the kind of anaemia by erythrocyte morphology and to eliminate other possible diseases like leukemia.

On the foundation of red cell indices (mean corpuscular volume), patients in the anemic state were further defined as normocytic normochromic (MCV 80–96fl), microcytic hypochromic (MCV <80 fl), and microcytic (MCV >96fl). Anemia was established as hemoglobin (Hb) levels lower than 12 g/dL in females and 13 g/dL in males and was further classified as: Patients with Microcytic anemia, Ferritin, Iron & TIBC was done. Patients with Macrocytic anemia Folate & Vitamin B12 levels was done.

ANALYSIS

All the data was inserted in the Microsoft excel and computed using the SPSS v21. The demographic details of patients are presented using tables, figures, bar diagrams and summarised as frequency, percentage, mean and standard deviation. The mean difference between the continuous variable is analysed using the student's t-test and categorical variables using the chi-square test. A $p<0.05$ was considered statistically significant.

RESULTS

Total of 100 patients fulfilling inclusion criteria participated in the present study after obtaining the informed consent from all these patients. The average age of patients in the present study was 39.53± 16.4yrs, with 73% were female patients and 27% were male patients, with female preponderance.

Table 3: Mean age of the patients

	N	Minimum	Maximum	Mean	SD
Age	100	18	78	39.53	16.41

Table 4: Gender distribution of the patients

		Frequency	Perc ent
Gender	Female	73	73.0
	Male	27	27.0
	Total	100	100. 0

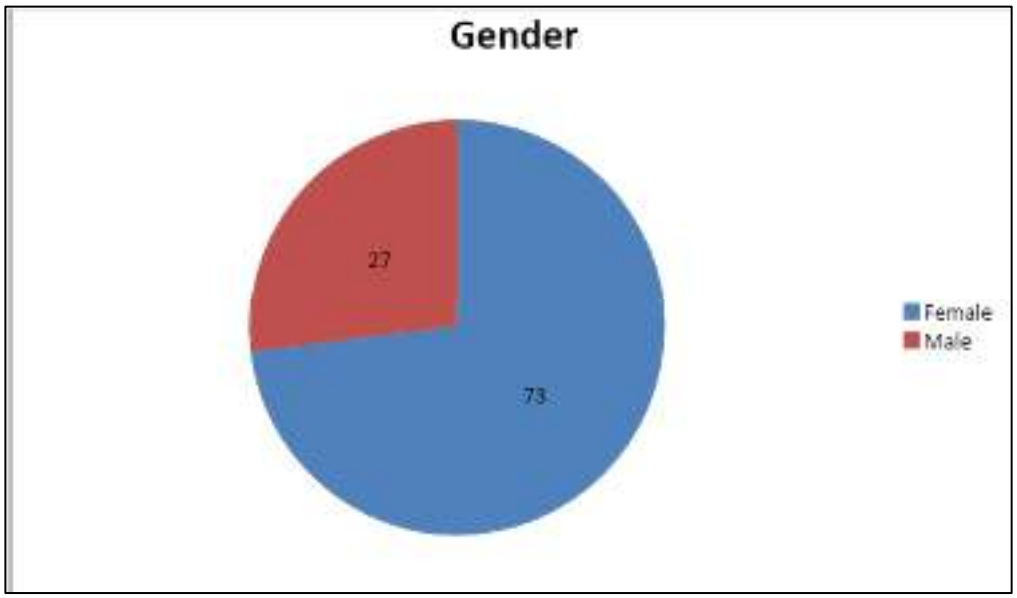

Figure 7: Gender distribution of the patients

The above image depicts gender distribution of patients, the majority being females constituting 73% & 27% males.

Table 5: Mean age difference between the genders

	Gender			
	Female		Male	
	Mean	SD	Mean	SD
Age	36.2	15.1	49.02	16.2

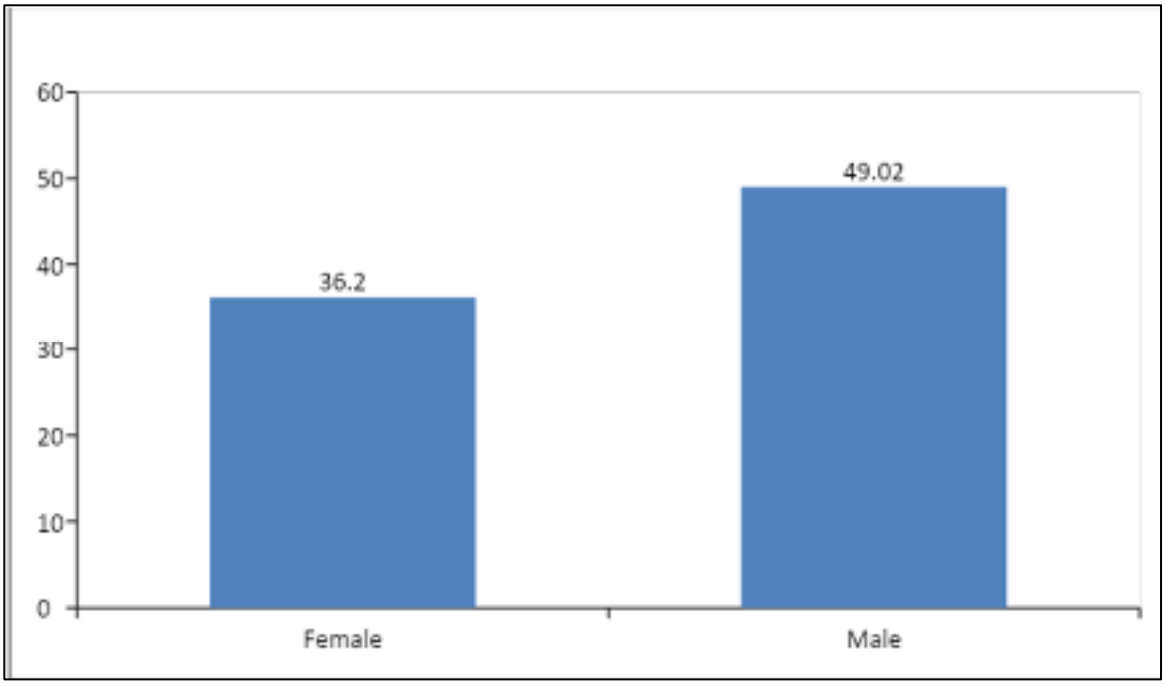

Figure 8: Mean age difference between the genders

The above image depicts the mean age difference between the genders, mean age in femalesis 36.2 yrs and males is 49.02 yrs.

Table 6: Distribution of presence of anemia among genders

		Gender			
		Female		Male	
		Count	Column N %	Count	Column N %
Anemia	Anemia Absent	12	16.4%	11	40.7%
	Anemia Present	61	83.6%	16	59.3%

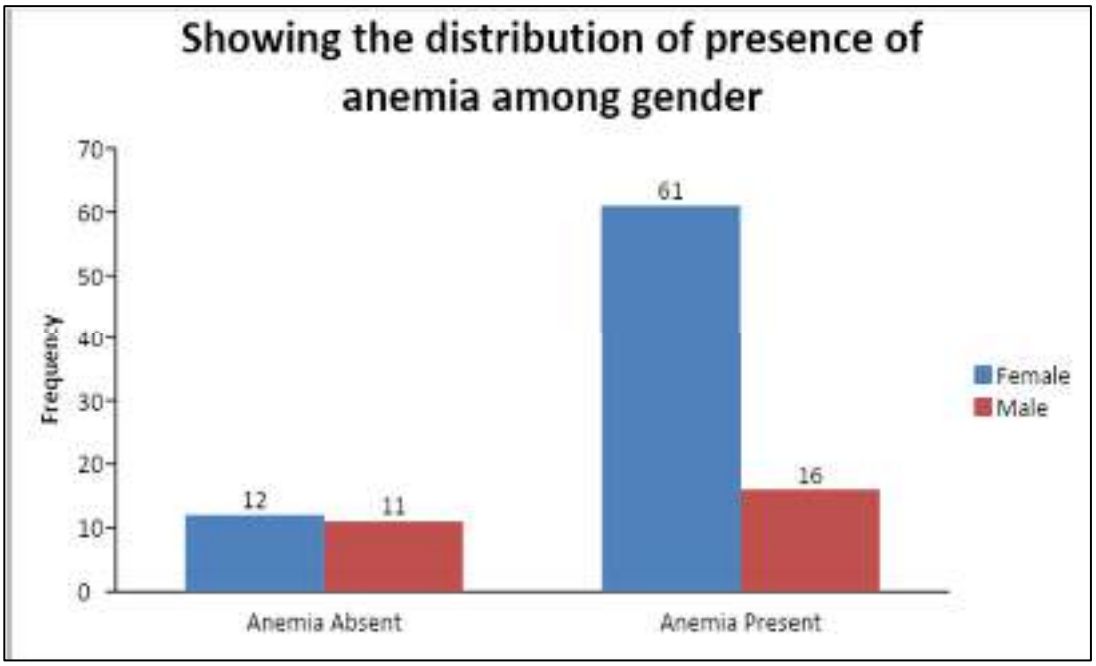

Figure 9: Distribution of presence of anemia among genders

The above images show the distribution of anemia among genders: Anemia is present in 61out of 73 females and 16 out of 27 males.

Table 7: Mean level of Hemoglobin, MCV, MCH and MCHC among thepatients

	N	Minimum	Maximum	Mean	SD
Hb	100	6.5	17.0	11.30	1.94
MCV	100	70.0	98.8	86.08	4.50
MCH	100	24.80	36.40	29.11	2.08
MCHC	100	29.1	34.8	32.35	1.00

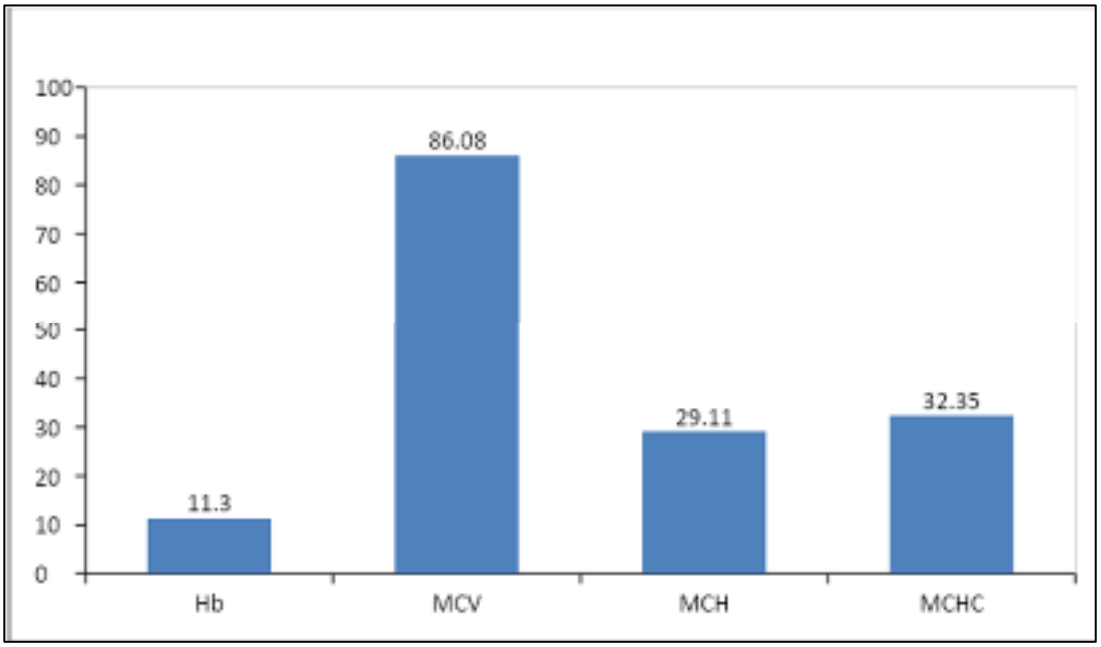

Figure 10: Mean level of Hemoglobin, MCV, MCH and MCHC among thepatients

The above images depict the mean level of Hb, MCV, MCH & MCHC among the patients. The mean Hb is 11.30, mean MCV is 86.08, mean MCH 29.11 and mean MCHC is 32.35.

Table 8: Number of patients with anemia

		Frequency	Percent
Anemia	Anemia Absent	23	23.0
	Anemia Present	77	77.0
	Total	100	100.0

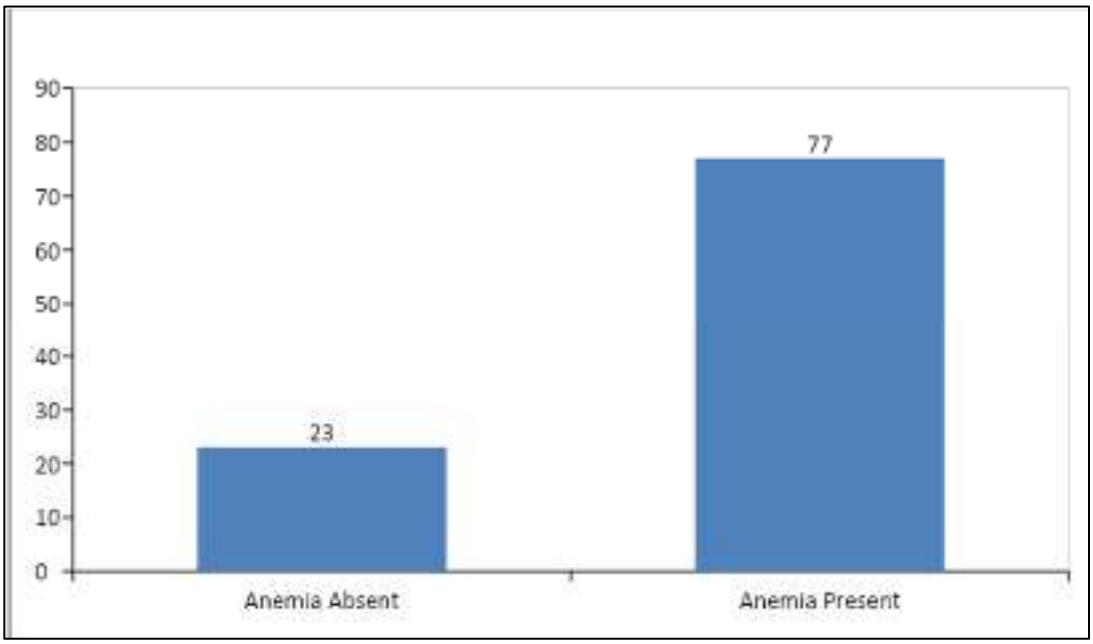

Figure 11: Number of patients with anemia

The above images show the number of patients with anemia. Anemia is present in 77 out of100 patients and absent in 23 out of 100 patients.

Table 9: Peripheral smear finding among the patients

		Frequency	Percent
Periphera lSmear	MCHC	3	3.0
	NBP	22	22.0
	NCNC	75	75.0
	Total	100	100.0

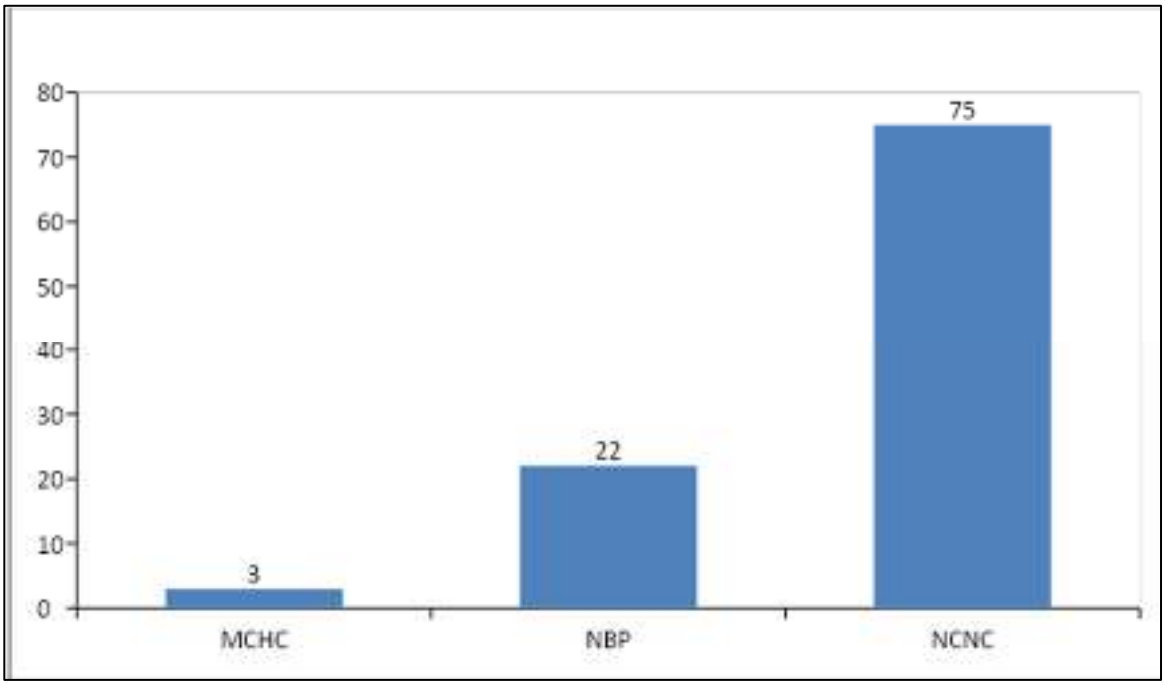

Figure 12: Peripheral smear finding among the patients

The above images depict the peripheral smear findings among the patients with the Normocytic Normochromic being the most common, seen in 75 patients followed by Normal blood picture seen in 22 patients and Microcytic Hypochromic seen in 3 patients.

Table 10: Grade of anemia among the patients

		Frequency	Percent
Anemia grade	Normal hemoglobin	31	31.0
	Mild anemia	45	45.0
	Moderate anemia	21	21.0
	Severe anemia	3	3.0
	Total	100	100.0

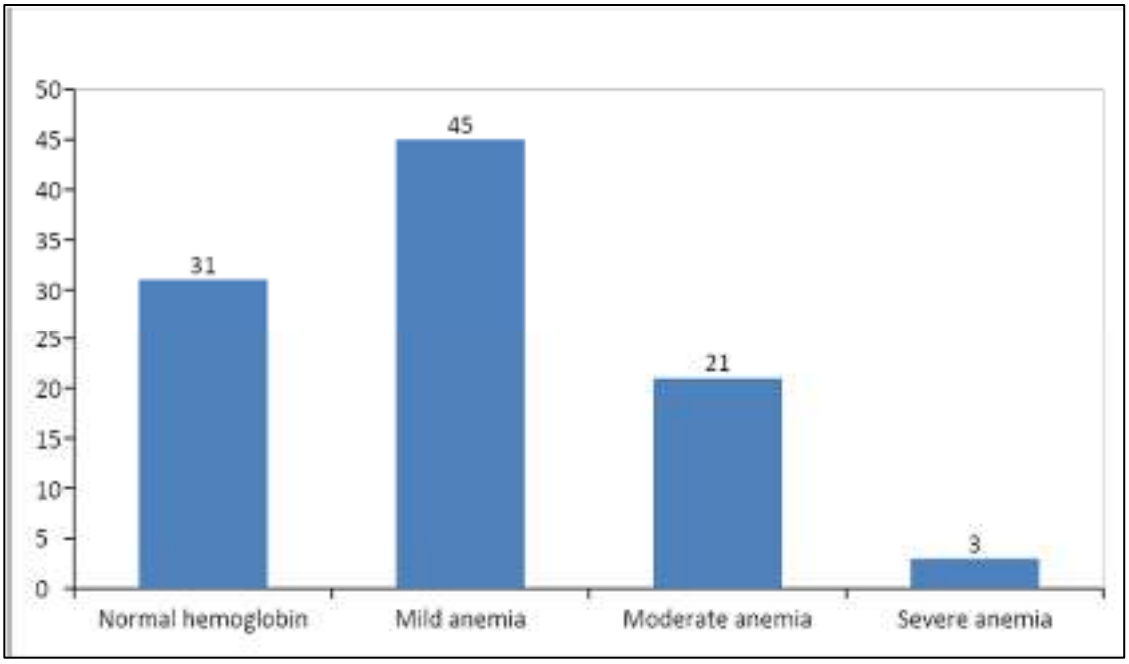

Figure 13: Grade of anemia among the patients

The above images depict the grade of anemia among patients with 45% having mild anemia,21% with moderate anemia & 3% with severe anemia.

Table 11: Thyroid profile status of the patients

	N	Minimum	Maximum	Mean	SD
TSH	100	10.00	120.00	47.51	22.88
T3	100	.20	3.79	1.25	.73
T4	100	.30	10.00	3.87	2.65

Table 12: Comparison of mean level of thyroid hormone between the group with anemiausing Mann-Whitney test

	Anemia				
	Anemia Absent		Anemia Present		Mann-Whitney test
	Mean	SD	Mean	SD	U (p-value)
TSH	25.40	18.81	37.69	24.15	770.5 (0.034)
T3	1.11	.48	1.30	.79	813.5 (0.554)
T4	4.87	1.89	3.57	2.78	599.5 (0.019)*

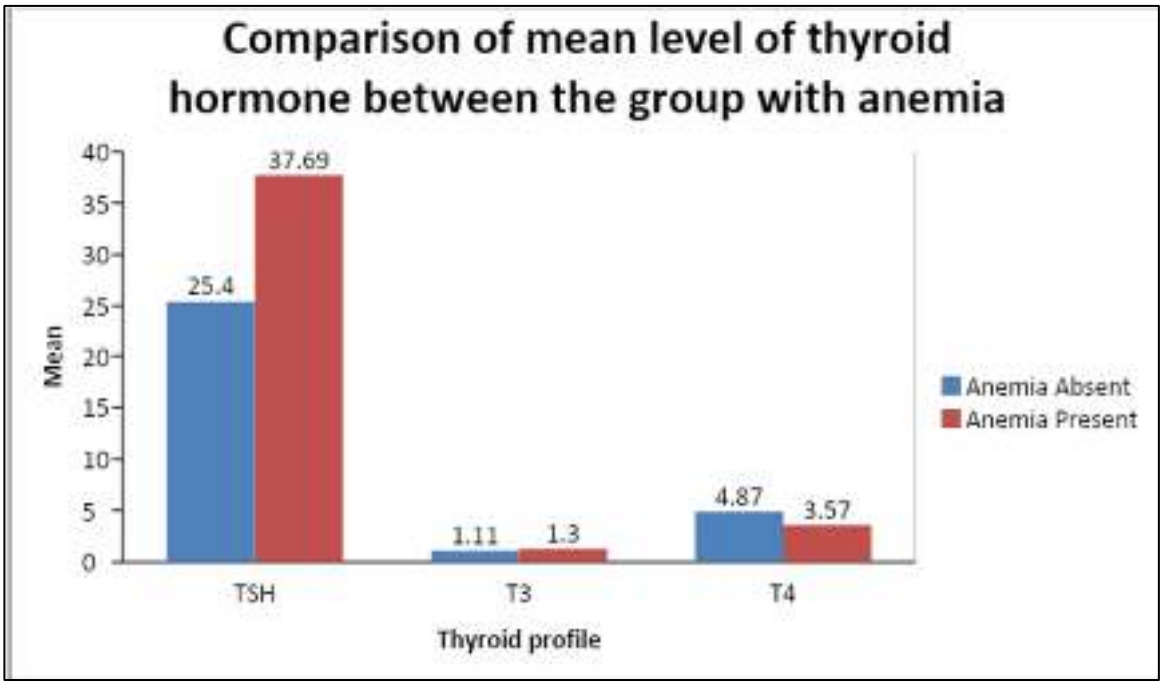

Figure 13: Comparison of mean level of thyroid hormone between the group withanemia

The above images show the comparison of mean level of thyroid hormones in patients withanemia and those without anemia. Mean TSH was 37.69, mean T4 3.57 and mean T3 1.3 inpatients having anemia and mean TSH 25.4, mean T4 4.87 and mean T3 1.11 in patients without anemia.

Table 13: Comparison of mean TSH level between the grade of anemia using ANOVAstudy

	Anemia grade								
	Normal hemoglobin		Mild anemia		Moderate anemia		Severe anemia		ANOVA
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	p-value
TSH	24.85	16.89	32.61	31.81	51.58	39.74	54.99	44.68	0.013*
Significance was seen between the TSH level in mild anemia with moderate grade of anemia using Bonferroni Post-hoc analysis. *P<0.05 is considered statistically significant.									

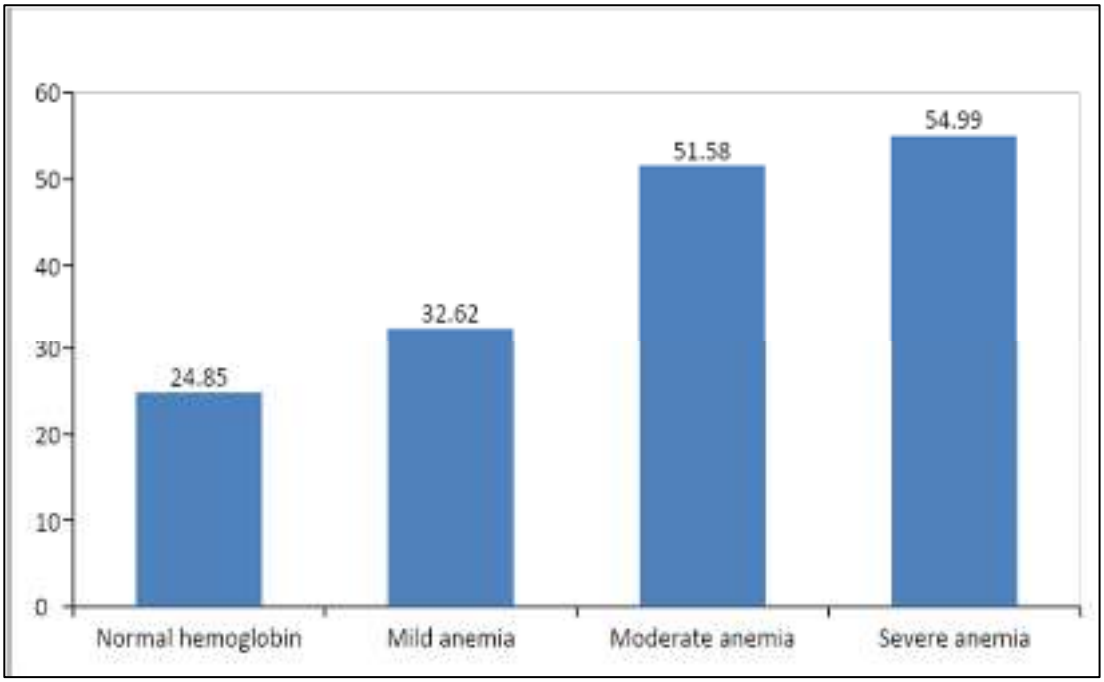

Figure 15: Comparison of mean TSH level between the grade of anemia

The above images show comparison of mean TSH level between the grade of anemia. Patients with mild anemia have a mean TSH value of 32.62, patients with moderate anemia have a mean TSH of 51.58 and those with severe anemia have a mean TSH of 54.99.

Table 14: Pearson's correlation of hemoglobin with TSH and other thyroid hormones

		TSH	T3	T4
Hemoglobin	r	-.352**	.049	.235*
	Sig	.000	.629	.018
*P<0.05 is considered statistically significant.				

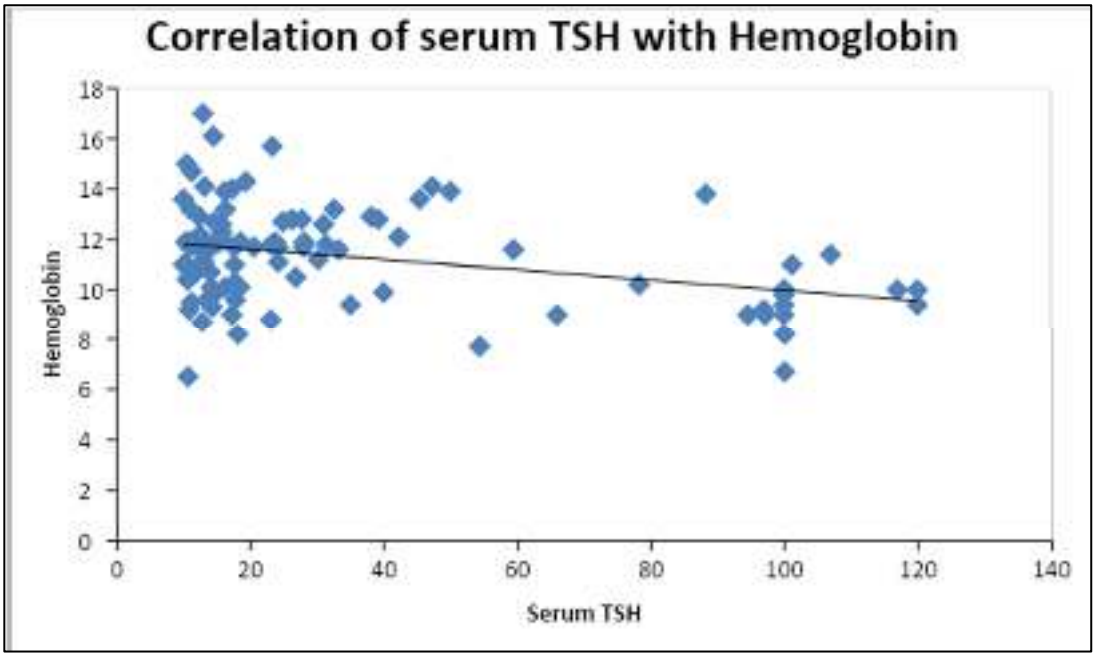

Figure 16: Correlation of serum TSH with Hemoglobin

The above image is a graphical representation showing correlation of serum TSH with hemoglobin in which significant prevalence of anemia is seen in hypothyroidism

DISCUSSION

Hypothyroid state is a common illness with different frequency between borders. As reduced thyroid hormone seriously affects erythropoiesis, anemia progresses in hypothyroidism. There are a plethora of mechanisms implicated in the pathogenesis of these anemic states which can be microcytic, macrocytic, and normocytic. Microcytic anemia is usually ascribed to malabsorption of iron and loss of iron by menorrhagia.

Total of 100 patients fulfilling inclusion criteria were involved in the current study after obtaining the informed consent from all the patients. The average age in years of patients in the present study was 39.53±16.4yrs, with 73% were female patients and 27% were male patients, with female preponderance. Similar to present study, various studies have documented the female preponderance with the anemia and hypothyroid incidence compared to men. This can be mainly due to menstruation. The chief complaints of easy fatigability, apathy, breathlessness on exercise and generalised weakness occur much more commonly in the hypothyroid versus the controls.1,24–26,28

In the present study, patients with primary hypothyroidism showed the presence of anemia in 77% of the patients and 23% were with normal hemoglobin. The distribution of the anemia among the females (83.6%) was significantly higher than in males (59.3%) ($p<0.05$). In a similar to present study Kulkarni VK et al., documented the incidence of anemia to be 69% in the overt hypothyroid group. 24 In study by Anand R et al., 124 out of 180 patients (69%) in the overt hypothyroid group. 1 Similar to present study Patil MB et al., stated that Anemia affects a bigger fraction of hypothyroid females (54%) than hypothyroid males (45 percent).

26 Peraka SA et al., found hypothyroid patients that were considered normal had anemia 41.8%.27

CONCLUSION

The prevalence of anemia among the hypothyroidism patients was found higher (77%) and the different morphologies seen on peripheral blood smear were normocytic normochromic, microcytic hypochromic and normal blood morphology. Normocytic normochromic type was seen most commonly among the patients followed by normal blood morphology and microcytic hypochromic. There is a significant association between the severity of anemia with the serum TSH level and T4 in hypothyroid patients.

SUMMARY

Hypothyroidism affects the hematopoietic system and anemia is an important feature of the same. This study aimed to assess the prevalence and pattern of anemia in patients with primary hypothyroidism. Total of 100 patients in accordance with the inclusion criteria were taken in present study after obtaining an informed consent from each of them. The average age in years in the present study was 39.53±16.4yrs, where 73% were female patients and 27% were male patients. Primary hypothyroidism patients showed the prevalence of anemia in 77% of the patients. There was significant negative strength of association between the hemoglobin with serum TSH ($r= -0.352$, $p<0.05$), and significant association of severity of anemia with higher TSH value among hypothyroid patients. Hence, the prevalence of anemia among the hypothyroidism patients was found higher (77%) and the different morphologies seen on peripheral blood smear were normocytic normochromic, microcytic hypochromic and normal blood morphology. Normocytic normochromic type was seen most commonly among the patients followed by normal blood morphology and microcytic hypochromic. There is a significant association between the severity of anemia with the serum TSH level and T4 in hypothyroid patients.

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ANNEXURE I. ETHICAL CLEARANCE.

K.L.E. ACADEMY OF HIGHER EDUCATION AND RESEARCH
(Deemed - to - be University)
Accredited 'A' Grade by NAAC (2nd Cycle) Placed in Category 'A' by MHRD (Govt.)
JAWAHARLAL NEHRU MEDICAL COLLEGE,
NEHRU NAGAR, BELAGAVI-590010 (KARNATAKA-INDIA)
Website: http://www.jnmc.edu
E-Mail : dome@jnmc.edu
Phone: [+91-0831] Office : 2472550
Principal: 2471701
Fax No. +91-0831 - 2470759

Ref: MDC/DOME/ 253

Date: 24/12/2019

To.

REG. NO: BG0119003
PG student in Medicine,
J.N.Medical College,
BELAGAVI.

Sub: Institutional Ethical Clearance for the study.

With reference to the above, we wish to inform you that your proposed research project titled **"ASSESSMENT OF ANEMIA IN PATIENTS OF PRIMARY HYPOTHYROIDISM "**, is ethical and justifiable. The proposed research project has been cleared by the JNMC Institutional Ethics Committee on Human Subjects Research.

(Dr. Anita Dalal)
Member Secretary
JNMC Institutional Ethics Committee
on Human Subjects Research,
J.N.Medical College, Belagavi.

(Dr. Roopa M Bellad)
Chairman,
JNMC Institutional Ethics Committee
on Human Subjects Research,
J.N.Medical College, Belagavi.

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ANNEXURE II
INFORMED CONSENT

Title of Research Study: STUDY OF ANEMIA IN PATIENTS OF PRIMARY HYPOTHYROIDISM

Principal Investigator:

REGISTRATION NO: BG0119003

Post Graduate Student,
Department Of General Medicine,
JNMC, Belgaum.

Guide:

Dr. _____
Professor & Head of Unit,
Department of General Medicine
JNMC,Belgaum.

Introduction and Purpose:

There is a correlation between hypothyroidism and anemia and since both are clinical burdens, at the time of diagnosis of thyroid disorder a simultaneous evaluation of anemia and the type of anemia will help in early diagnosis and treatment of the same.

Procedure:

If you agree to be part of the research study, you will be asked the relevant history and will be subjected to relevant clinical examination and investigations. You will also have to give blood samples for the necessary investigations.

Risk and Benefits:

The only risk and possible discomfort you might get is while taking blood from your arm for the investigations. It may cause swelling, pain, redness (rarely happens) at the site from where the blood is drawn.

In case anemia is detected in your investigations appropriate management can be started timely. Also you will be a part of a study that is going to be useful to others in the future.

Alternatives:

Taking part in this study is voluntary. You may choose not to take part in this study. If you decide to take part you can later change your mind and withdraw from the study. Your decision will not change the present or future healthcare or other services that you receive. The study doctor or sponsor may stop your participation in this study at anytime. If you choose not to take part in the study, you will receive the standard treatment for patients with your condition.

Privacy and Confidentiality:

All information collected about you during the course of this study will be kept confidentialto the extent permitted by law. The code numbers will identify you in this research record. Information from this study may be published but your identity will be confidential in any publication.

Institution/Sponsor's policy: Does not apply to this research

Financial incentives for participation: You will not be paid/offered any gifts/incentives forparticipating in the study.

Authorization to publish the results:

The results of the study would be forwarded to the KLE University, Belgaum as part ofrequirement towards the completion of MD degree, review and publishing.

CONSENT FORM

I voluntarily agree to take part in this study by signing below. I may withdraw at anytime. I am not giving up any of my legal rights by signing his form. My signature below indicates that I have read this consent form, or it has been read to me in my vernacular language andhave had all the questions answered.

Signature/Left Thumb print of the Participant or legally authorized representative

Participant's name: ……..

Signature/ Left thumb impression:

Of the participant …….

Name of the legally authorize: ……...

representative/guardian

Signature/ Left thumb impression: ……...

Witness' name: ……

Signature/Left thumb impression: ……...

Investigator's name and signature: ……...

Date: Place:

ತಿಳುವಳಿಕೆಯ ಸಮ್ಮತಿ

ಸಂಶೋಧನಾ ಅಧ್ಯಯನದ ಶೀರ್ಷಿಕೆ: ಪ್ರಾಥಮಿಕ ಹೈಪೋಥೈರಾಯ್ಡಿಸಮ್ ರೋಗಿಗಳಲ್ಲಿ ರಕ್ತಹೀನತೆಯ ಅಧ್ಯಯನ

ಪ್ರಧಾನ ತನಿಖಾಧಿಕಾರಿ: -

REGISTRATION NO: BG0119003

ಸ್ನಾತಕೊತ್ತರ ವಿದ್ಯಾರ್ಥಿ,
ಜನರಲ್ ಮೆಡಿಸಿನ್ ಇಲಾಖೆ,
ಜೆಎನ್ಎಂಸಿ, ಬೆಳಗಾವಿ.

ಮಾರ್ಗದರ್ಶಿ: -

ಡಾ._____

ಪ್ರೊಫೆಸರ್ ಮತ್ತು ಘಟಕದ ಮುಖ್ಯಸ್ಥ
ಜನರಲ್ ಮೆಡಿಸಿನ್ ಇಲಾಖೆ,
ಜೆಎನ್ಎಂಸಿ, ಬೆಳಗಾವಿ.

ಪರಿಚಯ ಮತ್ತು ಉದ್ದೇಶ: -

ಹೈಪೋಥೈರಾಯ್ಡಿಸಮ್ ಮತ್ತು ರಕ್ತಹೀನತೆಯ ನಡುವೆ ಪರಸ್ಪರ ಸಂಬಂಧವಿದೆ ಮತ್ತು ಎರಡೂ ಕ್ಲಿನಿಕಲ್ ಹೊರೆಗಳಾಗಿರುವುದರಿಂದ, ಥೈರಾಯ್ಡ್ ಅಸ್ವಸ್ಥತೆಯನ್ನು ಪತ್ತೆಹಚ್ಚುವ ಸಮಯದಲ್ಲಿ ರಕ್ತಹೀನತೆಯ ಏಕಕಾಲಿಕ ಮೌಲ್ಯಮಾಪನ ಮತ್ತು ರಕ್ತಹೀನತೆಯ ಪ್ರಕಾರವು ಆರಂಭಿಕ ರೋಗನಿರ್ಣಯ ಮತ್ತು ಚಿಕಿತ್ಸೆಯಲ್ಲಿ ಸಹಾಯ ಮಾಡುತ್ತದೆ.

ವಿಧಾನ:

ಸಂಶೋಧನಾ ಅಧ್ಯಯನದ ಭಾಗವಾಗಲು ನೀವು ಒಪ್ಪಿದರೆ, ನಿಮಗೆ ಸಂಬಂಧಿತ ಇತಿಹಾಸವನ್ನು ಕೇಳಲಾಗುತ್ತದೆ ಮತ್ತು ಸಂಬಂಧಿತ ಕ್ಲಿನಿಕಲ್ ಪರೀಕ್ಷೆ ಮತ್ತು ತನಿಖೆಗೆ ಒಳಪಡಿಸಲಾಗುತ್ತದೆ. ಅಗತ್ಯ ತನಿಖೆಗಾಗಿ ನೀವು ರಕ್ತದ ಮಾದರಿಗಳನ್ನು ಸಹ ನೀಡಬೇಕಾಗುತ್ತದೆ.

ಅಪಾಯ ಮತ್ತು ಪ್ರಯೋಜನಗಳು:

ತನಿಖೆಗಾಗಿ ನಿಮ್ಮ ತೋಳಿನಿಂದ ರಕ್ತವನ್ನು ತೆಗೆದುಕೊಳ್ಳುವಾಗ ನೀವು ಪಡೆಯುವ ಏಕೈಕ ಅಪಾಯ ಮತ್ತು ಸಂಭವನೀಯ ಅಸ್ವಸ್ಥತೆ. ಇದು ರಕ್ತವನ್ನು ಎಳೆಯುವ ಸ್ಥಳದಲ್ಲಿ ಬೆವರುವಿಕೆ, ನೋವು, ಕೆಂಪು (ವಿರಳವಾಗಿ ಸಂಭವಿಸುತ್ತದೆ) ಗೆ ಕಾರಣವಾಗಬಹುದು.
ನಿಮ್ಮ ತನಿಖೆಯಲ್ಲಿ ಇನ್ಕಾಸೆನೆಮಿಯಾ ಪತ್ತೆಯಾಗಿದೆ ಸೂಕ್ತ ನಿರ್ವಹಣೆಯನ್ನು ಸಮಯೋಚಿತವಾಗಿ ಪ್ರಾರಂಭಿಸಬಹುದು. ಭವಿಷ್ಯದಲ್ಲಿ ನೀವು ಇತರರಿಗೆ ಉಪಯುಕ್ತವಾಗಲಿರುವ ಅಧ್ಯಯನದ ಭಾಗವಾಗುತ್ತೀರಿ.

ಪರ್ಯಾಯಗಳು:

ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸುವುದು ಸ್ವಯಂಪ್ರೇರಿತವಾಗಿದೆ. ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸದಿರಲು ನೀವು ಆಯ್ಕೆ ಮಾಡಬಹುದು. ನೀವು ಭಾಗವಹಿಸಲು ನಿರ್ಧರಿಸಿದರೆ ನೀವು ನಂತರ ನಿಮ್ಮ ಮನಸ್ಸನ್ನು ಬದಲಾಯಿಸಬಹುದು ಮತ್ತು ಅಧ್ಯಯನದಿಂದ ಹಿಂದೆ ಸರಿಯಬಹುದು. ನಿಮ್ಮ ನಿರ್ಧಾರವು ಪ್ರಸ್ತುತ ಅಥವಾ ಭವಿಷ್ಯದ ಆರೋಗ್ಯ ರಕ್ಷಣೆ ಅಥವಾ ನೀವು ಸ್ವೀಕರಿಸುವ ಇತರ ಸೇವೆಗಳನ್ನು ಬದಲಾಯಿಸುವುದಿಲ್ಲ. ಅಧ್ಯಯನ ವೈದ್ಯರು ಅಥವಾ ಪ್ರಾಯೋಜಕರು ಈ ಅಧ್ಯಯನದಲ್ಲಿ ನಿಮ್ಮ ಭಾಗವಹಿಸುವಿಕೆಯನ್ನು ಯಾವುದೇ ಸಮಯದಲ್ಲಿ ನಿಲ್ಲಿಸಬಹುದು. ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸದಿರಲು ನೀವು ಆರಿಸಿದರೆ, ನಿಮ್ಮ ಸ್ಥಿತಿಯ ರೋಗಿಗಳಿಗೆ ನೀವು ಪ್ರಮಾಣಿತ ಚಿಕಿತ್ಸೆಯನ್ನು ಸ್ವೀಕರಿಸುತ್ತೀರಿ.

ಗೌಪ್ಯತೆ ಮತ್ತು ಗೌಪ್ಯತೆ:

ಈ ಅಧ್ಯಯನದ ಸಮಯದಲ್ಲಿ ನಿಮ್ಮ ಬಗ್ಗೆ ಸಂಗ್ರಹಿಸಲಾದ ಎಲ್ಲಾ ಮಾಹಿತಿಯನ್ನು ಕಾನೂನಿನಿಂದ ಅನುಮತಿಸುವ ಮಟ್ಟಿಗೆ ಗೌಪ್ಯವಾಗಿಡಲಾಗುತ್ತದೆ. ಈ ಸಂಶೋಧನಾ ದಾಖಲೆಯಲ್ಲಿ ಕೋಡ್ ಸಂಖ್ಯೆಗಳು ನಿಮ್ಮನ್ನು ಗುರುತಿಸುತ್ತವೆ. ಈ ಅಧ್ಯಯನದ ಮಾಹಿತಿಯನ್ನು ಪ್ರಕಟಿಸಬಹುದು ಆದರೆ ಯಾವುದೇ ಪ್ರಕಟಣೆಯಲ್ಲಿ ನಿಮ್ಮ ಗುರುತು ಗೌಪ್ಯವಾಗಿರುತ್ತದೆ.

ಸಂಸ್ಥೆ / ಪ್ರಾಯೋಜಕರ ನೀತಿ: ಈ ಸಂಶೋಧನೆಗೆ ಅನ್ವಯಿಸುವುದಿಲ್ಲ

ಭಾಗವಹಿಸುವಿಕೆಗೆ ಆರ್ಥಿಕ ಪ್ರೋತ್ಸಾಹ:

ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸಲು ನಿಮಗೆ ಯಾವುದೇ ಉಡುಗೊರೆಗಳನ್ನು / ಪ್ರೋತ್ಸಾಹಕಗಳನ್ನು ನೀಡಲಾಗುವುದಿಲ್ಲ / ನೀಡಲಾಗುವುದಿಲ್ಲ.

ಫಲಿತಾಂಶಗಳನ್ನು ಪ್ರಕಟಿಸಲು ಅಧಿಕಾರ:

ಅಧ್ಯಯನದ ಫಲಿತಾಂಶಗಳನ್ನು ಭಾಗವಾಗಿ ಬೆಳಗಾವಿಯ ಕೆಎಲ್ಇ ವಿಶ್ವವಿದ್ಯಾಲಯಕ್ಕೆ ರವಾನಿಸಲಾಗುತ್ತದೆ
ಎಂಡಿ ಪದವಿ, ವಿಮರ್ಶೆ ಮತ್ತು ಪ್ರಕಟಣೆಯ ಪೂರ್ಣಗೊಳಿಸುವಿಕೆಯ ಅವಶ್ಯಕತೆ.

ಒಪ್ಪಿಗೆ ಪತ್ರ

ಕೆಳಗೆ ಸಹಿ ಮಾಡುವ ಮೂಲಕ ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸಲು ನಾನು ಸ್ವಯಂಪ್ರೇರಣೆಯಿಂದ ಒಪ್ಪುತ್ತೇನೆ. ನಾನು ಯಾವುದೇ ಸಮಯದಲ್ಲಿ ಹಿಂತೆಗೆದುಕೊಳ್ಳಬಹುದು. ಈ ಫಾರ್ಮ್ಗೆ ಸಹಿ ಮಾಡುವ ಮೂಲಕ ನಾನು ನನ್ನ ಯಾವುದೇ ಕಾನೂನು ಹಕ್ಕುಗಳನ್ನು ಬಿಟ್ಟುಕೊಡುತ್ತಿಲ್ಲ. ಕೆಳಗಿನ ನನ್ನ ಸಹಿ ನಾನು ಈ ಒಪ್ಪಿಗೆಯ ಫಾರ್ಮ್ ಅನ್ನು ಓದಿದ್ದೇನೆ ಅಥವಾ ಅದನ್ನು ನನ್ನ ಸ್ಥಳೀಯ ಭಾಷೆಯಲ್ಲಿ ಓದಿದ್ದೇನೆ ಮತ್ತು ಹೊಂದಿದ್ದೇನೆ ಎಂದು ಸೂಚಿಸುತ್ತದೆ
ಎಲ್ಲಾ ಪ್ರಶ್ನೆಗಳಿಗೆ ಉತ್ತರಿಸಲಾಗಿದೆ.

ಭಾಗವಹಿಸುವವರ ಅಥವಾ ಕಾನೂನುಬದ್ಧವಾಗಿ ಅಧಿಕೃತ ಪ್ರತಿನಿಧಿಯ ಸಹಿ / ಎಡ ಹೆಬ್ಬೆರಳು ಮುದ್ರಣ
ಭಾಗವಹಿಸುವವರ ಹೆಸರು: …….

ಭಾಗವಹಿಸುವವರ ಸಹಿ / ಎಡ ಹೆಬ್ಬೆರಳು ಅನಿಸಿಕೆ: ……

ಕಾನೂನುಬದ್ಧವಾಗಿ ಅಧಿಕೃತ ಪ್ರತಿನಿಧಿ / ರಕ್ಷಕರ ಹೆಸರು: …… ..

ಸಹಿ / ಎಡ ಹೆಬ್ಬೆರಳು ಅನಿಸಿಕೆ: …… ..

ಸಾಕ್ಷಿಯ ಹೆಸರು: …… ..

ಸಹಿ / ಎಡ ಹೆಬ್ಬೆರಳು ಅನಿಸಿಕೆ: …… ..

ದಿನಾಂಕ:

ಸ್ಥಳ

माहितीपूर्ण संमती

संशोधन अभ्यासाचे शीर्षकः प्राथमिक हायपोथायरॉईडीझमच्या रुग्णांमध्ये अशक्तपणाचा अभ्यास

प्रधान अन्वेषक: -

REGISTRATION NO: BG0119003

पदव्युत्तर विद्यार्थी,
सामान्य औषध विभाग,
जेएनएमसी, बेळगावी.

मार्गदर्शनः-
डॉ. _____
प्राध्यापक णि युनिट हेड
जेएनएमसी, बेळगावी.

परिचय णि उद्देश: -

हायपोथायरॉईडीझम णि अशक्तपणा यांच्यात परस्परसंबंध हे णि दोन्ही क्लिनिकल ओझे असल्याने थायरॉईड डिसऑर्डरच्या निदानाच्या वेळी emनेमियाचे एकाच वेळी मूल्यांकन केले जाऊ शकते णि अशक्तपणाचा प्रकार लवकर निदान करण्यात णि उपचार करण्यास मदत करेल.

प्रक्रियाः

 पण संशोधन अभ्यासाचा भाग होण्यास सहमत असल्यास, पणास संबंधित इतिहास विचारला जाईल णि संबंधित क्लिनिकल परीक्षा णि तपासणीस पात्र केले जाईल. वश्यक तपासणीसाठी पल्याला रक्ताचे नमुने देखील द्यावे लागतील.

जोखीम णि फायदे:

तपासणीसाठी पल्या बाहेरून रक्त घेत असताना पल्याला फक्त धोका णि संभाव्य असुविधाची समस्या उद्भवू शकते. ज्या स्थानावरून रक्त ओढले हे त्या जागेवर सूज, वेदना, लालसरपणा (क्वचितच घडते) होऊ शकते.

 पल्या तपासणीत इंकसेनेमिया ढळला हे की योग्य व्यवस्थापन वेळेवर सुरू केले जाऊ शकते. तसेच पण भविष्यात इतरांना उपयुक्त ठरणाऱ्या अभ्यासाचा एक भाग व्हाल.

विकल्पः

या अभ्यासामध्ये भाग घेणे ऐच्छिक हे. पण या अभ्यासामध्ये भाग न घेणे निवडू शकता. पण भाग घेण्याचा निर्णय घेतल्यास पण नंतर पले मत बदलू णि अभ्यासापासून दूर जाऊ शकता. पल्या निर्णयामुळे पल्याला प्राप्त झालेल्या वर्तमान किंवा भविष्यातील रोग्य सेवा किंवा इतर सेवा बदलणार नाहीत. अभ्यास डॉक्टर किंवा प्रायोजक या अभ्यासात पला सहभाग कधीही थांबवू शकतात. पण अभ्यासामध्ये भाग न घेणे निवडल्यास, पल्या अट असलेल्या रूग्णांसाठी तुम्हाला प्रमाणित उपचार मिळेल.

गोपनीयता णि गोपनीयता:

या अभ्यासाच्या दरम्यान पल्याबद्दल संकलित केलेली सर्व माहिती कायद्याद्वारे परवानगी असलेल्या मर्यादेपर्यंत गोपनीय ठेवली जाईल. कोड नंबर पल्याला या संशोधन रेकॉर्डमध्ये ओळखतील. या अभ्यासाची माहिती प्रकाशित केली जाऊ शकते परंतु पली ओळख कोणत्याही प्रकाशनात गोपनीय असेल.

संस्था / प्रायोजक यांचे धोरणः

या संशोधनास लागू होत नाही

सहभागासाठी र्थिक प्रोत्साहनः

अभ्यासामध्ये भाग घेण्यासाठी पल्याला कोणत्याही भेटवस्तू / प्रोत्साहन दिले जाणार नाहीत.

परिणाम प्रकाशित करण्यासाठी अधिकृतताः

अभ्यासाचा निकाल भाग म्हणून केएलई विद्यापीठ, बेळगाव येथे पाठविला जाईल एमडी पदवी, पुनरावलोकन णि प्रकाशन पूर्ण करण्यासाठी वश्यक

संमती फॉर्म

मी खाली स्वाक्षरी करून या अभ्यासात भाग घेण्यास स्वेच्छेने सहमत □ हे. मी केव्हाही माघार घेऊ शकतो. या फॉर्मवर सही करून मी माझा कोणताही कायदेशीर हक्क सोडत नाही. खाली माझी स्वाक्षरी सूचित करते की मी हा संमती फॉर्म वाचला □ हे, किंवा तो मला माझ्या स्थानिक भाषेत वाचला गेला □ हे □ णि □ हे सर्व प्रश्नांची उत्तरे दिली होती.

सहभागी किंवा कायदेशीररित्या अधिकृत प्रतिनिधीची सही / डावा अंगठा प्रिंट

सहभागीचे नाव: ……

स्वाक्षरी / डावा अंगठा ठसा: …… ...
सहभागीचा

कायदेशीररीत्या अधिकृत नाव: ……
प्रतिनिधी / पालक

स्वाक्षरी / डावा अंगठा ठसा: ……

साक्षीचे नाव: …… ...

स्वाक्षरी / डावा अंगठा ठसा: …… ...

अन्वेषकांचे नाव □ णि स्वाक्षरीः ……

तारीख:

ठिकाणः

ANNEXURE III

PROFORMA

CASE NO:

NAME:

AGE/SEX:

IPNO:

ADDRESS:

OCCUPATION:

PRESENTING COMPLAINTS:

Past history:

Family history:

Personal history:

Dietary history:

Veg/Nonveg

Menstrual history:

Treatment history:

PHYSICAL EXAMINATION:

GENERAL CONDITION:

PALLOR- YES/NO

ICTERUS- YES/NO

LYMPHADENOPATHY- YES/NO

CYANOSIS- YES/NO

CLUBBING-YES/NO EDEMA-YES/NO

VITALS:

TEMPERATURE PULSE

RESPIRATORY RATE

BLOOD PRESSURE

SYSTEMIC EXAMINATION:

R.S.:

C.V.S.:

P.A.:

C.N.S.:

INVESTIGATIONS

1) CBC:

- HEMOGLOBIN
- RED CELL INDICES: MCV, MCH, MCHC
- PERIPHERAL SMEAR

2) THYROID PROFILE:

- S.TSH
- FREE T4

FREE T3

3) IRON PROFILE:

- S.IRON
- S.FERRITIN
- TIBC

4) S.FOLATE

5) VITAMIN B-12 LEVELS

IP NO.	Gender	Age	Hb	Anemia	PS	TSH	T3	T4	MCV	MCH	MCHC
831214	M	27	15	FALSE	NBP	10.48	2.81	1.51	87	28	32
5383245	F	37	10.4	TRUE	NCNC	10.6	2.6	1.01	88	28.5	32.5
5685878	F	25	6.5	TRUE	MCHC	10.65	0.8	1.07	70	26.04	31.5
4098883	F	32	11.9	TRUE	NCNC	10.86	2.8	1.52	85	29.5	32
1039060	M	65	10.7	TRUE	NCNC	11.08	2.8	0.9	87.2	28.5	32.6
1039369	F	78	10.8	TRUE	NCNC	11.12	0.4	6.5	88.5	28.1	31.8
1040844	F	60	9.5	TRUE	NCNC	11.2	0.7	5.2	88.6	29.1	32.8
4640768	F	55	10.7	TRUE	NCNC	11.96	0.8	1.01	80.5	27.9	32.2
2734909	F	55	11.9	TRUE	NCNC	28.11	0.7	6.2	88.2	28	31.5
4654294	F	57	11.6	TRUE	NCNC	13.84	0.8	6.6	83.7	29.1	31.5
5640174	F	39	12.2	FALSE	NBP	12.44	1.5	6.7	89.9	27.4	31.6
5181666	F	24	11.6	TRUE	NCNC	12.5	2.62	0.8	86.1	28.3	32.1
5020940	F	36	11.1	TRUE	NBP	13.06	1	4.8	84.5	29.1	32.2
3858149	F	39	11.6	TRUE	NCNC	13.43	1.2	5.2	82.1	29.2	32.1
1031240	M	72	10.1	TRUE	NCNC	14.16	0.6	5.1	85.5	29.5	32.4
5110338	F	26	9.9	TRUE	NCNC	40	1.9	0.75	87.5	27.9	32.6
4153234	F	23	12	TRUE	NCNC	15.08	0.9	7.1	82.1	29.2	32.1
4355610	F	26	11.9	TRUE	NCNC	15.34	1.4	6.6	89.7	29.1	32.4
869317	M	36	12.6	TRUE	NCNC	15.69	2.22	1.24	80	30.1	32.9
5355653	F	20	12.3	FALSE	NBP	15.76	1.2	5.04	86.2	27.1	31.1
5437857	F	49	10.1	TRUE	NCNC	16.24	0.8	3.1	86.2	27.8	31.9
988339	F	71	13.2	FALSE	NBP	16.29	0.8	2.1	88	27.9	29.8
1043829	M	45	9	TRUE	NCNC	17.27	1.2	5.9	86.1	28.3	32.8
992092	F	47	11.7	TRUE	NCNC	17.53	1.9	0.75	83.7	29	32.1
960134	F	38	10.3	TRUE	NCNC	17.73	1.8	0.78	82.1	27.4	32.9

3038230	F	26	8.2	TRUE	NCNC	18.1	0.8	2.2	87.5	29.1	32.4
1032537	F	25	10.1	TRUE	NCNC	18.46	0.4	9.1	86.3	29.1	31.8
5201970	F	21	11.9	TRUE	NCNC	18.51	2.65	0.84	86.2	27.8	31.1
827795	F	69	11	TRUE	MCHC	10.38	0.9	7.1	72.8	26.8	29.1
5814912	F	18	11.7	TRUE	NBP	20.55	0.7	5.4	85.5	27.9	32.6
5075545	F	20	8.8	TRUE	NCNC	23.1	0.9	3.01	86.4	26.8	32.9
5708923	M	64	15.7	FALSE	NBP	23.32	0.7	5.7	87.5	28.8	32.9
4700490	F	23	11.9	TRUE	NCNC	23.75	0.6	3.1	86.2	26.8	31.2
1040390	F	20	11.1	TRUE	NCNC	24.19	0.8	1.1	89.7	29.2	32.6
5542708	M	48	12.8	TRUE	NCNC	26.26	2.04	1.05	89.6	28.8	32
5648960	M	44	11.2	TRUE	NCNC	30.19	0.2	0.5	88.1	28.2	31.8
1041479	M	58	12.6	TRUE	NCNC	31.01	2.05	1.02	86.2	26.8	31.1
626261	F	39	9.4	TRUE	NCNC	35	2.62	1.29	87.4	28.6	32.8
1036880	F	65	12.9	FALSE	NCNC	38.12	1.2	6.4	87.5	28.8	32.9
1019877	F	62	12.8	FALSE	NCNC	39.16	0.7	5.5	89.7	29.1	32.4
5972782	M	54	13.6	FALSE	NCNC	45.39	1.81	1.17	88.2	28.2	31.5
5195399	M	27	14.1	FALSE	NBP	47.26	0.8	5.4	82.2	28.1	32.5
4547364	F	30	9	TRUE	NCNC	66	1.02	5.2	86.8	28.5	32.2
3942100	F	32	10.2	TRUE	NCNC	78.29	0.3	2.2	90.2	28.2	31.5
5806067	F	26	9	TRUE	NCNC	94.6	1.4	5.6	86.8	28.5	32.2
778553	M	58	9	TRUE	NCNC	97.2	1	3.2	98	33.2	30.1
763618	M	78	12.9	TRUE	NCNC	12.36	0.8	6	86.2	27.8	33.4
2682147	F	22	6.7	TRUE	MCHC	100	0.3	1.2	90.2	32.2	33.2
2615028	M	41	9.8	TRUE	NCNC	100	0.3	1.4	92.6	30.6	33
1009225	F	45	9.4	TRUE	NCNC	120	0.2	0.5	86.8	28	32.3
5456677	F	37	10	TRUE	NCNC	320	0.2	1	86.8	29	32.3
1317503	M	43	12	TRUE	NCNC	15.76	2.16	1.49	89.4	29	33.2
4364656	F	29	11.8	TRUE	NCNC	23.17	2.35	0.89	82.8	27.5	33.2

3108592	M	53	16.1	FALSE	NBP	14.47	1.2	6.4	92	30.2	34.8
912299	F	48	9.8	TRUE	NCNC	14.5	0.7	8.2	86.8	28	32.3
3137009	F	62	11.7	TRUE	NCNC	24.17	1.81	1.17	82.1	27.5	33.2
1039211	F	40	9.6	TRUE	NCNC	13.54	1.1	5.4	85	30.2	34.8
974288	M	51	12.1	TRUE	NCNC	42.26	0.7	5.5	98.8	33.2	33.6
999388	M	33	14.3	FALSE	NBP	19.35	1.4	5.6	98.8	33	33.4
1003791	M	60	14.7	FALSE	NBP	11.23	0.8	5.1	89.4	29.8	33.3
1019363	F	78	11.6	TRUE	NCNC	33.26	0.4	1.4	87	30.2	34.8
1019982	F	49	11.6	TRUE	NCNC	59.46	0.6	2.7	82.8	27.5	33.2
1033759	F	43	12.7	FALSE	NBP	14.61	0.5	6	82.2	26.3	32
4685935	F	30	13.6	FALSE	NBP	10.02	0.9	6.2	82.2	26.3	32.2
937979	F	29	11	TRUE	NCNC	12.89	1.5	8.4	84.2	29.2	32.4
981491	F	35	10.5	TRUE	NCNC	26.83	0.9	6.4	85.8	30.2	33
4736498	F	41	13.9	FALSE	NBP	49.98	1.2	3.5	86	32.2	34.8
935752	F	34	11	TRUE	NCNC	17.68	1.5	8.2	84.2	29.2	32.4
5985953	F	21	14	FALSE	NBP	17.3	0.8	3.7	84.4	30.2	32
6061752	F	23	13.8	FALSE	NBP	88.29	1.1	3.7	82.2	29.5	31.8
3991912	F	23	9	TRUE	NCNC	100	2.36	0.47	80.6	27	31.5
4126853	F	43	11.9	TRUE	NCNC	10.34	1.3	5.3	82.2	26.3	32
2615028	M	41	10	TRUE	NCNC	100	0.3	1.4	92.6	30.6	33
4324821	M	24	11	TRUE	NCNC	10	1.5	9	84.2	29.2	32
4780071	F	36	12.7	FALSE	NBP	24.88	0.8	2.7	86	34.2	32.2
5573805	F	22	11.8	TRUE	NCNC	31.41	1.1	5.5	80.2	28.2	32.2
6010979	F	27	8.2	TRUE	NCNC	100	1.92	0.3	80.2	27.2	31.2
4488706	F	21	13.2	FALSE	NBP	11	1.4	4.8	86.2	30.2	32
5069185	F	36	9.6	TRUE	NCNC	17.78	0.8	5.2	90.1	32	34.2
933228	M	67	13.2	FALSE	NBP	32.58	1.2	5.6	96.2	31.8	34.8

4038238	F	30	9.2	TRUE	NCNC	96.98	0.2	4.1	80.6	27.5	31.5
5970101	F	32	8.7	TRUE	NCNC	12.78	2.57	0.87	80	27.2	32
5653271	F	25	11.7	TRUE	NCNC	10.96	3.79	1.56	84.2	29.2	32.2
924169	F	27	10	TRUE	NCNC	100	1.9	10	81.8	28	32
3532715	F	36	9.4	TRUE	NCNC	100	1.92	0.3	88.2	29.2	33.2
4045562	M	18	12.8	TRUE	NCNC	27.72	1.2	5.1	88.4	30.2	33
4992851	F	26	11.7	TRUE	NCNC	28.01	1.4	6.2	80	24.8	31.2
1044912	F	40	9.2	TRUE	NCNC	10.87	1.1	6.6	80.6	27.5	31.5
1020971	F	21	9.3	TRUE	NCNC	14.28	0.8	1.1	82.2	28	32.5
5957014	F	38	11	TRUE	NCNC	12.34	1.2	5.5	86.6	30.2	33.5
4789157	F	22	10.5	TRUE	NCNC	11.02	2.81	0.95	88.2	32.5	33.8
4327546	F	20	10	TRUE	NCNC	100	1.71	0.46	81.8	28	32
4807158	F	22	11	TRUE	NCNC	101.2	1.3	5.3	86.8	29	32.2
940191	M	70	17	FALSE	NBP	12.93	0.9	9	88.3	29.2	33.1
3636198	M	24	14.1	FALSE	NBP	13.17	1.1	6.8	91.4	33	30.1
1155964	F	30	11.4	TRUE	NCNC	107	1.63	0.9	92.2	34	32
2998320	F	22	10	TRUE	NCNC	117	1.6	0.47	86.4	36	33.4
1057960	M	65	13.9	FALSE	NBP	16.17	0.8	3.4	91.6	33.4	30.6
856028	M	51	10.7	TRUE	NCNC	14.01	0.8	8.6	86.4	36.4	33
1055875	F	58	7.7	TRUE	NCNC	54.33	1.1	6.2	80.2	27.8	32.1