Awareness and Prevalence of Hypothyroidism in Endocrine Disordered Patients of Bangladesh

A dissertation submitted to Department of Pharmacy, East West University, in Partial fulfillment of the requirements for the Degree of Bachelor of Pharmacy (B. Pharm)

Submitted by
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Declaration by the Candidate

I hereby declare that this dissertation, entitled **"Awareness and Prevalence of Hypothyroidism in Endocrine Disordered Patients of Bangladesh''** is an authentic and genuine research work carried out by me under the guidance of **Nigar Sultana Tithi,** Senior Lecturer, Department of Pharmacy, East West University, Dhaka. No part of the thesis has been submitted for any other degree. I further certify that all sources of information in this connection are duly acknowledged.

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Certificate by the Supervisor

This is to certify that the research work on **"Awareness and Prevalence of Hypothyroidism in Endocrine Disordered Patients of Bangladesh"** submitted to the department of pharmacy, East West University, Aftabhnagar, Dhaka in partial fulfillment of the requirements for the degree of Bachelor of pharmacy (B. Pharm) was carried out by **Fariha Tasnim** (ID: 2012-1-70-018) under my guidance and supervision.

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List of Abbreviations

TH - Thyroid hormone

TRH - Thyrotropin-releasing hormone

TSH - Thyroid stimulating hormone

T_3 - Triodothyronine

T_4 - Thyroxine or Tetraiodothyronine

TGA – Thyroglobulin

NIS - Na/I symporter

TPO - Thyroid peroxidase

MIT – Monoiodotyrosine

DIT – Diiodotyrosine

cAMP - Cyclic Adenosine monophosphate

PIP2 – Phosphatidylinositol

TBG - Thyroxine binding globulin

RXR - Retinoid X receptor

GH - Growth Hormone

MPO – Myeloperoxidase

FT4 - Free Thyroxine

FT3 - Free Triidothyronine

RIA – Radioimmunoassay

IRMA - Immunoradiometric assay

Abstract

Thyroid gland is an important endocrine organ which starts functioning in early fetal life and maintains the level of metabolism in the tissues that is optimal for their normal function and related with physical and mental growth. Imbalance of thyroid function can arise many severe problems. There can be many forms of thyroid disease and Hypothyroidism is one of the major forms of it. A study was conducted and this study was aimed to find out the prevalence of Hypothyroidism, its common symptoms, diagnosis and treatment pattern, and knowledge level of patients regarding this disease in Bangladesh. For this, 273 endocrine patients from 6 different hospitals were interviewed with a questionnaire and their prescriptions and medical test reports were observed. The Obtained data are analyzed by Microsoft excel. We have found that, 223 (82%) patients had thyroid disease and among thyroid disease patients 23% had hypothyroidism. Thyroid disease is primarily predominant in women (73%) but rate of hypothyroidism is little bit higher in male (57%) than female (43%) and suffering age range is 20-60 years (83%). The most common diagnosis test is TSH test (94%) because it is very effective in determining thyroid disease. However, along with TSH test, T_4 testing is also very common in hypothyroid patients. In Bangladesh all of the hypothyroidism containing patients is treated with thyroid hormone therapy (Levothyroxine). Although knowledge level about the disease history not good enough the awareness level about the diagnostic pattern and treatment level (97%) of the respondents were quite satisfactory. However, most of the patients have misconception they will recover (94%). We have seen that the prevalence of under reactive thyroid disease among endocrine disease is high but knowledge level of patients of our country is relatively poor and needs to be improved. The most common cause of hypothyroidism worldwide is iodine deficiency and in our countries iodine deficiency is very common, especially at rural sites of the country. So Government should take adequate steps to lessen iodine deficiency as well as there should be proper steps in our country to make the hypothyroid patients and general public conscious about this disease.

Key words: *Thyroid gland, Endocrine system, Hypothyroidism, TSH test, T_4 test, Prevalence, Thyroid hormone therapy, Iodine deficiency.*

CHAPTER 1

INTRODUCTION

Introduction

1.1 Thyroid Gland

The thyroid gland is butterfly shaped and sits on the trachea, in the anterior neck. It is comprised of two lobes, which are connected in the middle by an isthmus. Inside, the gland is made up of many hollow follicles, whose epithelial cell walls (also known as follicle cells) surround a central cavity filled with a sticky, gelatinous material called colloid. Parafollicular cells are found in the follicle walls, protruding out into the surrounding connective tissues. The thyroid is the largest exclusively endocrine gland in the body. The endocrine system is the body's communication hub, controlling cell, and therefore organ, function. A primary goal of the endocrine system is to maintain homeostasis within the organism, despite external fluctuations of any sort. Hormones, which act as chemical messengers, are the mechanism for this communication. The hormones secreted by the thyroid gland are essential in this process, targeting almost every cell in the body (only the adult brain, spleen, testes, and uterus are immune to their effects.) Inside cells, thyroid hormone stimulates enzymes involved with glucose oxidation, thereby controlling cellular temperature and metabolism of proteins, carbohydrates, and lipids. Through these actions, the thyroid regulates the body's metabolic rate and heat production. Thyroid hormone also raises the number of adrenergic receptors in blood vessels, thus playing a major role in the regulation of blood pressure. In addition, it promotes tissue growth, and is particularly vital in skeletal, nervous system, and reproductive development (Steinberg, 2008).

The two major thyroid hormones (TH) are unique in that, unlike most hormones, they are neither protein nor cholesterol based. Instead, they incorporate iodine as an active constituent; the amount of iodine differentiates between thyroxine (also known as tetraiodothyronine or T_4) with four iodine molecules and triiodothyronine (T_3) with, predictably, three iodine molecules. While T_4 exists in greater abundance than T_3 in the body- thought to be at a fifty to one ratio, T_3 is considered to be ten times more active. There is much debate about the physiological difference between the two hormones. It is currently thought that T_4 may act as the reserve form, having a more direct role in the hypothalamus/pituitary negative feedback loop, while T_3 has a more dynamic physiological effect in the body. Others suggest that both have a critical part in physiological activity (Steinberg, 2008).

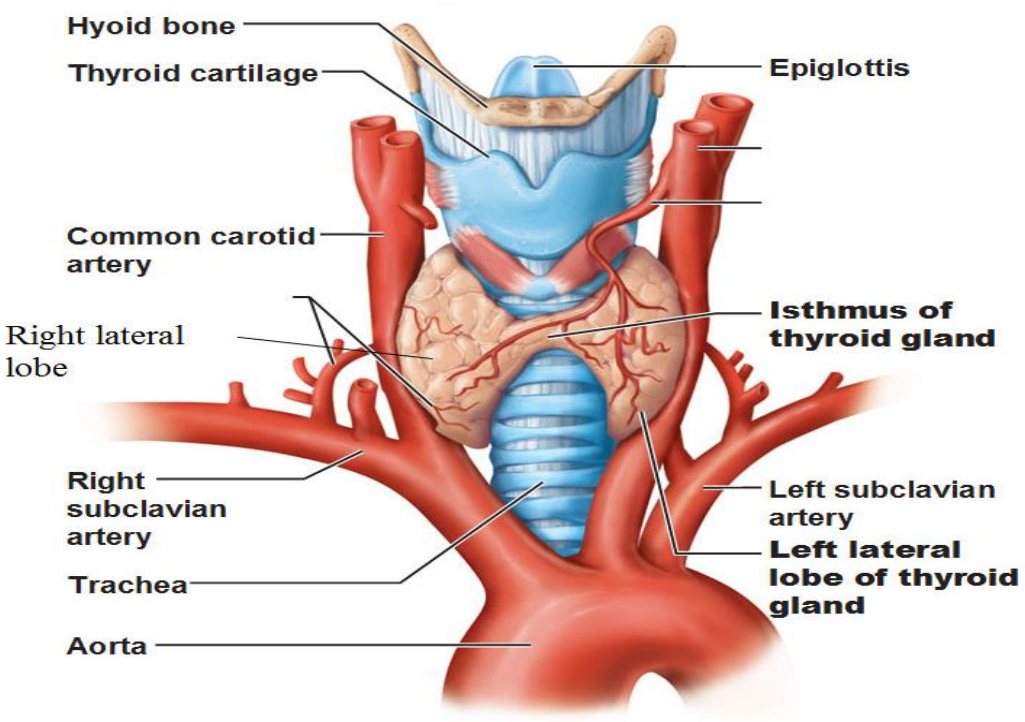

Figure 1.1: The thyroid gland

1.2 Hormones of thyroid gland

The thyroid gland produces

1. **Thyroxine (T_4):** 80% of the total thyroid hormone which is a relatively inactive prohormone.
2. **Triiodothyronine (T_3):** Lower amount of the active hormone, triiodothyronine (T_3).Collectively, T_3 and T_4 are referred to as the thyroid hormones. Twenty percent of the body's triiodothyronine is made by the thyroid gland.
3. **Calcitonin:** The thyroid gland also produces calcitonin from cells called C-cells. Calcitonin is understood to play a role in regulating calcium levels in the body, but its exact function in humans remains unclear (Society for endocrinology, 2015).

1.2.1 Thyroid hormone synthesis

TH (particularly T_4) is synthesized in the gland's colloid filled lumen from the combination of the glycoprotein thyroglobulin and stored iodine atoms. This process involves six interrelated steps that are initiated when thyroid stimulating hormone (TSH), released by the pituitary gland, binds to follicle cell receptors (yumpu.com, 2015).

1.2.1.1 Thyroglobulin synthesis

Tyrosine is converted into the glycoprotein thyroglobulin, which contains approximately 110 tyrosine residues and discharged into the lumen where it becomes part of the colloid mass (yumpu.com, 2015). The processing of iodine involves two stages as plasma iodine concentrations are very low (Steinberg, 2008).

1.2.1.2 Iodine trapping

Plasma iodide ions (I^-) are actively transported from the plasma into the follicular cells against a steep concentration gradient by the Na/I symporter (NIS). This is a rate-limiting step (yumpu.com, 2015).

1.2.1.3 Iodide oxidation

I^- is rapidly oxidized into iodine (I_2) by thyroid peroxidase (TPO) anchored on the luminal surface of the follicular cell membrane. The two components are then combined in the colloidal lumen (yumpu.com, 2015).

1.2.1.4 Iodination of thyroglobulin

Reactive iodine rapidly attaches to the tyrosine molecules within the extracellular thyroglobulin in a process that is catalysed by TPO. Monoiodotyrosine (MIT or T_1) and diiodotyrosine (DIT or T_2) are formed (yumpu.com, 2015).

1.2.1.5 Coupling

Tyrosine molecules within thyroglobulin are then coupled together. Combinations of T_1 and T_2 can form thyroid hormones (yumpu.com, 2015).

1.2.1.6 Secretion

Under the direction of thyroid stimulating hormone (TSH or thyrotrophin), iodinated thyroglobulin is taken into the follicular cells by pinocytosis and degraded by lysosomal enzymes. Coupled tyrosine molecules are released, including some T_3 and T_4. Some T_4 is converted to T_3 in the follicular cell cytoplasm by the enzyme type 1,5'deiodinase. Whilst the secreted ratio of T_4:T_3 is usually 20:1 conversion to T_3 is promoted by TSH stimulation and can result in the so-called T_3 thyrotoxicosis. MIT and DIT are also released, but they are deiodinated by iodotyrosine deholgenase to recycle iodine (yumpu.com, 2015).

1.2.2 Regulation of thyroid hormone (T_3 & T4) in the body

As well as stimulating the release of thyroid-stimulating hormone (TSH) from thyrotrophs in the anterior pituitary gland Hypothalamic thyrotrophin-releasing hormone (TRH) also causes up regulation of TSH gene transcription. TSH acts on extracellular receptors (TSH-R) on the surface of thyroid follicle cells, activating the Gprotein–adenyl-cyclase–cAMP and phosphatidylinositol (PIP2) pathways. Ultimately, TSH stimulates the following processes in the thyroid gland:

- Iodine uptake.
- Transcription of thyroglobulin and thyroid peroxidase.
- Iodination.
- Coupling.
- Type 1 5'deiodinase conversion of T_4 to T_3.
- Pinocytosis and secretion of thyroid hormones (yumpu.com, 2015).

As a result, T_3 and T_4 are synthesized and secreted more rapidly TSH also has long-term actions on the thyroid gland by increasing its size and vascularity to improve hormone synthesis. TSH forms part of a negative feedback loop, as its release is inhibited by increased serum T_3 and T_4 and also by somatostatin, glucocorticoids and chronic illness (yumpu.com, 2015).

1.2.3 Synthesis and regulation of TSH

Messages from the anterior pituitary gland are the main stimulus for the action of the thyroid gland. The pituitary gland, in turn, is triggered from above by the hypothalamus. The three organs are connected in a negative feedback loop that involves their vigilant monitoring of and response to the levels of Thyroid Hormone in the blood, as well as other internal and external stimuli; this relationship is sometimes referred to as the hypothalamic-pituitary-thyroid axis (Steinberg, 2008).

The hypothalamus secretes protein hormone thyrotropin releasing hormone (TRH), which heads directly to the pituitary gland via the hypophysial portal blood system, stimulating the release of TSH. TSH then moves through the bloodstream, binding with receptors in the thyroid gland, prompting the secretion of TH into the blood. Both T_4 and T_3 then exert a negative feedback effect on the hypothalamus and pituitary-an increase in their blood levels lowers the amount of TRH and TSH secreted and a decrease in their levels causes a rise in the TRH and TSH (Steinberg, 2008).

Stimuli to the higher brain including temperature and stress can also effect TRH production in the hypothalamus; for instance, cold temperatures can increase the body's requirements for TH as more internal heat will be need to maintain homeostasis and the hypothalamus reacts accordingly (Steinberg, 2008).

Stress affects the thyroid gland not only through the hypothalamus, but also directly via the sympathetic nervous system. There are sympathetic nerves that connect with the gland; during their stimulation in times of stress, they trigger increased TH release. In addition, it appears that epinephrine from the adrenal gland can also act directly on the thyroid Diet can effect thyroid function, as a high calorie/high carbohydrate diet can lead to increased conversion of T_4 to T_3- a mechanism that likely assists in keeping an organism's weight stable. Meanwhile, prolonged fasting can result in a decrease in T_3 production- which may be adaptive for conditions of food scarcity, slowing down the body's metabolism and energy (Steinberg, 2008).

1.2.4 Transport of thyroid hormones in the body

In its behavior, Thyroid hormone (TH) functions somewhat similarly to steroid hormones. As it is not water soluble, it requires a protein-based molecule for transport throughout the blood stream. T_3 and T_4 will generally pair with thyroxine binding globulin (TBG) for this purpose, though they can also use albumin and prealbumin (Steinberg, 2008).

70% are bound to thyroid-binding globulin (TBG), 30% are bound to albumin. While circulating in the blood in bound form, binding protein protects thyroid hormone from enzymatic attack (yumpu.com 2015).

At any given moment, the vast majority of Thyroid hormone in the body is in this bound, and essentially inactive, state, either in route or awaiting transport. The small percentage (Only 0.1% of T_4 and 1% of T_3) of unbound, physiologically active hormone is called "free" T_3 or T_4 (Steinberg, 2008).

It appears that TBG and albumin have higher affinity for T_4, which could explain T_4's higher levels in blood and its slower metabolism, and perhaps account for free T_3 being the more physiologically active substance (Steinberg, 2008).

Both T_3 and T_4 can cross cell membranes, though a carrier transport may be involved. The concentration of circulating T_4 is much higher than that of T_3 (50:1). There are two reasons for this:

- The thyroid secretes more T_4 than T_3.
- T_4 has a longer half-life (7 days vs 1 day) (yumpu.com 2015).

1.2.5 Mechanism of thyroid hormone

- The general effect of thyroid hormone is to activate nuclear transcription of large numbers of genes.
- Therefore, in virtually all cells of the body, great numbers of protein enzymes, structural proteins, transport proteins, and other substances are synthesized.
- The thyroid hormone receptor usually forms a heterodimer with retinoid X receptor (RXR) and binds at specific thyroid hormone response elements on the DNA.

- This hormone receptor complex then initiates the transcription of many genes (Nowak, 2009).

1.2.6 Physiological Effects of Thyroid Hormones

1.2.6.1 Metabolism

Thyroid hormones, especially T_3, enter tissue cells by diffusion or specific transport where they bind to two different receptors nuclear receptors designated as hTR-α1 and hTR-β1. The T_3 receptor complex then binds DNA via "zinc fingers" and this produces a change in the expression of a variety of genes that encode enzymes that control cellular metabolism and function (Torio, 2012).

T_3 and T_4 stimulate metabolic activities in most tissues in the body resulting in an increase in basal metabolic rate. This causes an increase in body heat production due to increased oxygen consumption and energy expenditure. Increased thyroid hormone levels stimulate fat mobilization, which results in increased fatty acid concentration in the plasma. Carbohydrate metabolism is also stimulated, causing enhanced activity of glucose entering the cells and increased gluconeogenesis and glyogenolysis which generate free glucose (Torio, 2012).

1.2.6.2 Growth and Development

Other hormones, including Growth Hormone (GH) and Prolactin, also depend on the presence of TH to exert their own effects on cells; the absence of TH inhibits their activity (Steinberg, 2008).

1.2.6.3 Calcium metabolism

Calcitonin is secreted by the C cells of parafollicular cells of the thyroid gland. It inhibits calcium absorption, thus lowering serum calcium levels. Secretion of calcitonin can be stimulated by increased levels of serum calcium, pentagastrin, and alcohol (Torio, 2012).

Table 1.1 : Physiological effect of thyroid hormone in different body parts (deruiter, 2001).

Target Tissue	Effect	Mechanism
Heart	Chronotropic	Increase number and affinity of beta-adrenergic receptors.
	Inotropic	Enhance responses to circulating catecholamines. Increase proportion of alpha myosin heavy chain (with higher ATPase activity).
Adipose tissue	Catabolic	Stimulate lipolysis.
Muscle	Catabolic	Increase protein breakdown.
Bone	Developmental and metabolic	Promote normal growth and skeletal development; accelerate bone turnover.
Nervous system	Developmental	Promote normal brain development.
Gut	Metabolic	Increase rate of carbohydrate absorption.
Lipoprotein	Metabolic	Stimulate formation of LDL receptors.
Other	Calorigenic	Stimulate oxygen consumption by metabolically active tissues (exceptions: adult brain, testes, uterus, lymph nodes, spleen, anterior pituitary). Increase metabolic rate.

1.2.7 Degradation of Thyroid Hormone

The main site of TH degradation is in the liver and its primary elimination is via kidneys. Thyroxine (T_4) and triiodothyronine (T_3) are rapidly degraded by a purified preparation of myeloperoxidase (MPO) and H_2O_2 with the formation of iodide. T_3 can be detected as a minor product of T_4 degradation (Seymour, Klebanoff & Green, 1973).

1.3 Thyroid diseases

A thyroid disease is a medical condition impairing the function of the thyroid creating and using energy). These diseases frequently have wide-ranging systemic effects as thyroid gland manufactures hormones that regulate the body's metabolism. Thyroid gland diseases can result in either an overproduction or underproduction of thyroid hormones (National Library of Medicine, 2014).

The main categories of disease are

- Hyperthyroidism - when thyroid gland makes more thyroid hormones than the body needs
- Hypothyroidism - when thyroid gland does not make enough thyroid hormones
- Thyroid cancer or carcinoma
- Thyroid nodules - lumps in the thyroid gland
- Thyroiditis
- Goitres (National Library of Medicine, 2014).

1.3.1 Hyperthyroidism

Hyperthyroidism is a hyper metabolic state caused by excess in the synthesis and secretion of thyroid hormone by the thyroid gland, which can be due to thyrotropic stimulus or autonomous function of thyroid tissue (Ferri, 2008).

On the other hand, thyrotoxicosis is the clinical condition which is associated with elevated levels of free T_4 and/ or free T_3. The terms hyperthyroidism and thyrotoxicosis are oftentimes used interchangeably; however, hyperthyroidism pertains to the excess synthesis and release of thyroid hormone, while thyrotoxicosis is the clinical presentation resulting from it. Its prevalence is 1 in every 2000 adults. Graves' disease is mostly account for hyperthyroidism (Weetman, 2000).

This is an autoimmune disease caused by an antibody that binds to and activates the TSH receptor and stimulates the gland to synthesize and secrete excess thyroid hormone. Autonomous production of thyroid hormone occurs when thyrocytes function independently of TSH receptor activation, which could result from a benign thyroid adenoma or nodules from a toxic multinodular goitre. Toxic adenomas are common in younger patients and in iodine-deficient areas. Toxic multinodular goitre (also known as Plummer disease) accounts for about 15 to 20 percent of hyperthyroidism cases and can be 10-fold more common in areas where there is iodine deficiency. This also occurs more commonly among elderly patients with a long-standing goitre (Reid &Wheeler, 2005).

1.3.1.1 The causes of hyperthyroidism

The thyroid is a gland in the neck that produces two thyroid hormones, thyroxine (T_4) and triiodothyronine (T_3). Thyroxine is inactive and is converted by the tissues and organs that need it into triiodothyronine. The role of thyroid hormones, put simply, is to regulate the metabolism of virtually all cells in the body. In health, the production of these thyroid hormones is tightly regulated by the secretion of thyroid stimulating hormone (TSH; also known as thyrotropin) from the pituitary gland in the brain. When the thyroid gland becomes affected by disease, sometimes the production or release of thyroxine and triiodothyronine can be abnormally high, leading to increased levels in the blood; a state of thyroid overactivity known as hyperthyroidism or thyrotoxicosis. If this happens, the body's metabolism speeds up and this can be manifest by changes in various, and seemingly unrelated tissues, that are listed below. In this state of hyperthyroidism, a blood test will show an elevated amount of these thyroid hormones circulating. Conversely, the TSH level in the blood almost always becomes suppressed, because the pituitary gland senses the abnormally high levels of thyroid hormones, which are more than is needed by the brain (Karnath and Hussain, 2006).

1.3.2 Goitre

Goitre is a swelling in the neck caused by an enlarged thyroid gland. It is a common finding, and it is usually asymptomatic; however, large goitres can compress the oesophagus and trachea. If goitre is associated with hyperthyroidism it is described as toxic. Non-toxic goitres secrete normal or reduced levels of thyroid hormones. Non-toxic goitres are usually the result of excessive TSH stimulation in the presence of hypothyroidism. Goitre is treated by correcting the underlying pathology or by surgical removal for cosmetic reasons or to prevent compression of surrounding structures (WebMD, 2015).

1.3.2.1 Causes of Goiter

Goiters can occur when the thyroid gland produces either too much thyroid hormone (hyperthyroidism) or not enough (hypothyroidism). Much more rarely, the problem may arise when the pituitary gland stimulates thyroid growth to boost production of the

hormone. Enlargement could also occur with normal production of thyroid hormone, such as a nontoxic multinodular gland (WebMD, 2015).

1.3.3 Thyroid cancer

Thyroid carcinoma is relatively rare (ca. 16,000 cases annually), but is the most common endocrine malignancy. While the causes of this form of cancer are not precisely understood, it is known that iodine deficiency, long-term use of goitrogenic drugs and exposure to ionizing radiation are risk factors for thyroid hyperplasia and ultimately malignancy. Thyroid carcinoma may be discovered as a small thyroid nodule or a metastatic tumor arising from lung, brain or bone cancer (Deruiter, 2012).

This cancer is detected by changes in the voice or swallowing due to tumor growth impinging on the trachea or esophagus. Treatment for thyroid carcinoma remains controversial but may involve partial or total thyroidectomy, TSH suppression therapy with levothyroxine, or radioactive iodine therapy (iodine concentrating tumors). Post-operative radiation therapy and chemotherapy also may be employed (Deruiter, 2012).

1.3.4 Thyroiditis

Thyroiditis is the medical term for inflammation (swelling) of the thyroid gland, which can either cause abnormally high or low levels of thyroid hormones in the blood (National Library of Medicine, 2014).

There are several different types of thyroiditis. The common types are:

1.3.4.1. Hashimoto's thyroiditis (the most common)

Hashimoto's thyroiditis is an autoimmune condition. This means immune system mistakenly attacks thyroid gland, causing it to gradually swell and become damaged (NHS, 2014).

1.3.4.2 De Quervain's or subacute thyroiditis

De Quervain's thyroiditis (sometimes called subacute thyroiditis) is a painful swelling of the thyroid gland that is thought to be triggered by a viral infection, such as mumps or the flu. It's most commonly seen in females aged 20 to 50 (NHS, 2014).

1.3.4.3 Post-partum thyroiditis (triggered after giving birth)

Like Hashimoto's thyroiditis, post-partum thyroiditis is an autoimmune condition, but it only happens in women who have recently given birth.

In post-partum thyroiditis, immune system attacks thyroid gland within around six months of giving birth, causing a temporary rise in thyroid hormone levels (thyrotoxicosis) and symptoms of an overactive thyroid gland (NHS, 2014).

Then, after a few weeks, thyroid gland becomes depleted of thyroid hormone, leading to low levels of thyroid hormone and symptoms of an underactive thyroid gland. However, not every woman with post-partum thyroiditis will go through both these phases (NHS, 2014).

1.3.4.4 Silent or painless thyroiditis

Silent thyroiditis is very similar to post-partum thyroiditis. It is also an autoimmune condition, but is not related to giving birth and can occur in both men and women.

Like postpartum thyroiditis, there may be a phase of high thyroid hormone levels (thyrotoxicosis), causing symptoms of an overactive thyroid gland. This may then be followed by a phase of symptoms of an underactive thyroid gland, before the symptoms eventually go away within around 12 to 18 months (NHS, 2014).

If low thyroid hormone levels are causing severe symptoms, patients need to take thyroid hormone replacement until the condition gets better. In a few cases, the low thyroid levels can be permanent (NHS, 2014).

1.3.4.5 Drug-induced thyroiditis

Thyroiditis can also be triggered by medications including interferon, amiodarone, lithium and a class of drugs to treat certain cancers (which include sunitinib), if these medicines damage the thyroid gland (NHS, 2014).

1.3.4.6 Radiation-induced thyroiditis

Radioactive iodine treatment for an overactive thyroid gland or radiotherapy for certain cancers can also damage the thyroid gland, leading to symptoms of an overactive thyroid gland or symptoms of an underactive thyroid gland (NHS, 2014).

1.3.4.7 Acute or infectious thyroiditis

Acute or infectious thyroiditis is usually triggered by a bacterial infection. It is rare and is associated with either a weakened immune system or, in children, with a problem in the development of the thyroid (NHS, 2014).

1.3.5 Thyroid Nodules

Thyroid disorders can also occur because of thyroid nodules, which are growths on the gland. These small growths are usually harmless and can go unnoticed for years. At times, thyroid nodules can be cancerous (Wartofsky *et al*, 2013).

1.4 Hypothyroidism

Hypothyroidism is a common endocrine disorder mainly characterized by a deficiency of thyroid hormone due to insufficient amounts produced by the thyroid gland. It could also be due to inadequate secretion of either TRH from the hypothalamus or TSH from the pituitary, affecting the feedback loop, and therefore causing hypothyroidism. Normally, the thyroid gland releases 100 to 125 nmol of T_4 and small amounts of T_3 daily. T_4, with a half-life of 7 to 10 days, is converted in the peripheral tissues to T_3, which is the active form of thyroid hormone. Early on in the disease, compensatory mechanisms are at work in order to maintain adequate T_3 levels. When there is a decreased production of T_4, the pituitary gland compensates by increasing the secretion of TSH, which stimulates thyroid hypertrophy and hyperplasia and more T_3 release (Torio, 2012).

1.4.1 Types of Hypothyroidism

1.4.1.1 Subclinical hypothyroidism

Subclinical hypothyroidism is defined biochemically as a normal serum free thyroxine (T_4) concentration in the presence of an elevated serum thyroid-stimulating hormone (TSH) concentration. Some patients with subclinical hypothyroidism may have vague, non-specific symptoms suggestive of hypothyroidism, but attempts to identify patients clinically have not been successful. Thus, this disorder can only be diagnosed on the basis of laboratory test results (Gavrila, 2012).

1.4.1.2 Overt Hypothyroidism

Overt hypothyroidism is characterized by an increased TSH and a decreased T_4 level. All patients with overt hypothyroidism are usually treated with thyroid hormone pills (Gavrila, 2012).

1.4.2 Symptoms and Signs of hypothyroidism

Table1.2: Symptoms and Signs of hyperthyroidism (Karnath and Hussain, 2006).

General	Fatigue, weight gain, anemia, cold intolerance
Dermatologic	Dry coarse skin, brittle hair, hair loss, nonpitting peripheral edema
Ears, eyes, throat	Hearing loss, hoarse voice, periorbital edema, facial puffiness
Neck	Goiter
Pulmonary	Dyspnea, pleural effusions, hypoventilation, sleep apnea
Cardiac	Bradycardia, congestive heart failure, pericardial effusions
Gastrointestinal	Anorexia, constipation

Genitourinary	Menstrual disorders, decreased libido, impotence, infertility
Neuromuscular	Muscle weakness, delayed ankle jerk relaxation phase
Psychiatric	Depression, psychomotor retardation, coma

1.4.3 Causes of hypothyroidism

There can be many reasons why the cells in the thyroid gland can't make enough thyroid hormone.

Here are the major causes, from the most to the least common.

1.4.3.1 Autoimmune disease

In some people's bodies, the immune system that protects the body from invading infections can mistake thyroid gland cells and their enzymes for invaders and can attack them. Then there aren't enough thyroid cells and enzymes left to make enough thyroid hormone. This is more common in women than men. Autoimmune thyroiditis can begin suddenly or it can develop slowly over years. The most common forms are Hashimoto's thyroiditis and atrophic thyroiditis (Karnath and Hussain, 2006).

1.4.3.2 Surgical removal of part or all of the thyroid gland

Some people with thyroid nodules, thyroid cancer, or graves' disease need to have part or all of their thyroid removed. If the whole thyroid is removed, people will definitely become hypothyroid. If part of the gland is left, it may be able to make enough thyroid hormone to keep blood levels normal (Karnath and Hussain, 2006).

1.4.3.3 Radiation treatment

Some people with graves' disease, nodular goiter, or thyroid cancer are treated with radioactive iodine (i-131) for the purpose of destroying their thyroid gland. Patients with Hodgkin's disease, lymphoma, or cancers of the head or neck are treated with radiation.

All these patients can lose part or all of their thyroid function (Karnath and Hussain, 2006).

1.4.3.4 Congenital hypothyroidism (hypothyroidism that a baby is born with)

A few babies are born without a thyroid or with only a partly formed one. A few have part or all of their thyroids in the wrong place (ectopic thyroid). In some babies, the thyroid cells or their enzymes do not work right (Karnath and Hussain, 2006).

1.4.3.5 Thyroiditis

Thyroiditis can make the thyroid dump its whole supply of stored thyroid hormone into the blood at once, causing brief hyperthyroidism (too much thyroid activity); then the thyroid becomes underactive (Karnath and Hussain, 2006).

1.4.3.6 Medicines

Medicines such as amiodarone, lithium, interferon alpha, and interleukin-2 can prevent the thyroid gland from being able to make hormone normally. These drugs are most likely to trigger hypothyroidism in patients who have a genetic tendency to autoimmune thyroid disease (Karnath and Hussain, 2006).

1.4.3.7 Too much or too little iodine

The thyroid gland must have iodine to make thyroid hormone. Iodine comes into the body in food and travels through the blood to the thyroid. Keeping thyroid hormone production in balance requires the right amount of iodine. Taking in too much iodine can cause or worsen hypothyroidism (Karnath and Hussain, 2006).

1.4.3.8 Damage to the pituitary gland

The pituitary, the “master gland,” tells the thyroid how much hormone to make. When the pituitary is damaged by a tumor, radiation, or surgery, it may no longer be able to give the thyroid instructions, and the thyroid may stop making enough hormones (Karnath and Hussain, 2006).

1.4.3.9 Rare disorders that infiltrate the thyroid

In a few people, diseases deposit abnormal substances in the thyroid and impair its ability to function, for example, amyloidosis can deposit amyloid protein, sarcoidosis can deposit granulomas, and hemochromatosis can deposit iron (British thyroid association, 2014).

1.4.4 Thyroid Function Testing for Hypothyroidism

The majority of hypothyroidism cases result from primary thyroid failure. The pituitary gland responds to that failure by secreting more TSH, raising serum TSH levels to 10 to 15 µU/mL well before there is a detectable decline in circulating thyroid hormones T_4 and tri-iodothyronine (T_3). Thus, elevated TSH level is the earliest and most definitive indicator of hypothyroidism (Deruiter, 2012).

As thyroid failure progresses, T_4 and T_3 levels eventually become very low or even undetectable, and the TSH level increases to100 µU/mL or more. If the patient has obvious thyroid dysfunction, the free T4 level should be measured in addition to the TSH level. Measuring the total T_4 level may not be necessary since its results are difficult to interpret; for example total T_4 consists largely of hormone that is bound to serum proteins or whose levels can be altered by drugs or nonthyroidal illness (Deruiter, 2012).

Table 1.3: Thyroid function tests (Deruiter, 2012).

Test	Measures	Normals	Interference	Comments
Measurements of circulating thyroid hormone levels				
FT_4	Direct measure of free T_4	0.7-1.9 ng/mL (Analog)	Altered TBG do not interfere	Most accurate measure of free T_4
FT_4I	Calculated free T_4 level	6.5-12.5 T_4 (1.3-3.9)	Euthyroid sick syndrome	Estimates direct free T_4, compensates for altered TBG
TT_4	Total free + bound T_4	5.0-12 mg/dL	Alterations of TBG	Adequate if TBG is not altered
TT_3	Total free + bound T_3	70-132 ng/dL	Alterations of TBG; Euthyroid sick syndrome	Useful to detect early, relapsing and T_3 toxicosis
RT_3U	Indirect measure of TBG saturation	26-35%	Alterations of TBG	Used to calculate FT_3I and FT_4I
Tests of Thyroid Gland Function				
RAIU	Thyroid uptake of iodine	24 hr: 15-35%	< with Excess Iodine and > with iodine deficiency	Different. of hyperthyroidism
Scan	Size, shape & activity	----------	Thyroid and antithyroid drugs	Detect "Hot" vs "cold" nodules
Test Hypothalamic-Pituitary-Thyroid Axis				
TSH	Pituitary TSH levels	0.5-4.7 U/L	DA, glucocort-coids, TH, amiodarone	Most sensitive index for hyper-thyroidism & to monitor therapy
Tests of Autoimmunity				
ATgA	Antibodies to thyroglobulin	<8%	Non-thyroidal immune disease	Present in auto-immune thyroid disease; not present in remission
TPO	Thyroperoxidase antibodies	<100IU/mL	Non-thyroidal immune disease	More sensitive test; detectable during remission
TRab (TSAb)	Thyroid receptor IgG antibody	Titers negative	----------	Confirms Graves' incl. neonatal
Thyroglobulin	Colloid protein of gland	5-25 mg/dL	Goiters, Inflam thyroid	Thyroid cancer marker

Measurements of serum T_3 levels likewise have little diagnostic value because they can be lowered by so many other conditions, including aging, other illnesses, weight loss, and a number of drugs. Low or normal TSH and free T_4 levels rule out hypothyroidism unless the patient has symptoms consistent with diminished pituitary function, in which case testing for hypopituitarism is indicated (Deruiter, 2012).

If the TSH level is elevated, free T_4 levels should be determined. A low level T_4 indicates hypothyroidism. A high TSH and normal T_4 indicate subclinical hypothyroidism and mandates testing for antithyroid antibodies; these patients may have no clinical signs of hypothyroidism. A TSH level greater than about 15 µU/mL or an antithyroid antibody

titer greater than 1:1,500 (or a recent history of exposure to radioactive iodine or thyroid surgery) points to impending overt hypothyroidism. A TSH level of less than 15 µU/mL and an antibody titer of less than 1:1,500 in an asymptomatic patient is inconclusive. The TSH level should be measured again after six months, although one can opt for treatment if the patient has begun to experience symptoms (Deruiter, 2012).

1.4.5 Test used to identify Hypothyroidism

1.4.5.1 Measurement of Serum Thyroid Hormones: T4 by RIA

T_4 by RIA (radioimmunoassay) is the most used thyroid test of all. It is frequently referred to as a T_7 which means that a resin T_3 uptake (RT_3u) has been done to correct for certain medications such as birth control pills, other hormones, seizure medication, cardiac drugs, or even aspirin that may alter the routine T_4 test. The T_4 reflects the amount of thyroxine in the blood. If the patient does not take any type of thyroid medication, this test is usually a good measure of thyroid function (Norman, 2016).

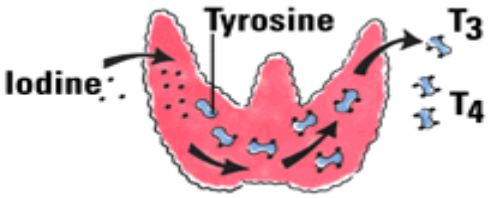

Figure 1.2: Radioimmuno assay

1.4.5.2 Measurement of Serum Thyroid Hormones: T3 by RIA

As stated on our thyroid hormone production page, thyroxine (T_4) represents 80% of the thyroid hormone produced by the normal gland and generally represents the overall function of the gland. The other 20% is triiodothyronine measured as T_3 by RIA. Sometimes the diseased thyroid gland will start producing very high levels of T_3 but still produce normal levels of T_4. Therefore measurement of both hormones provides an even more accurate evaluation of thyroid function (Norman, 2016).

1.4.5.3 Measurement of Pituitary Production of TSH

Pituitary production of TSH is measured by a method referred to as IRMA (immunoradiometric assay). Normally, low levels (less than 5 units) of TSH are sufficient to keep the normal thyroid gland functioning properly. When the thyroid gland becomes inefficient, such as in early hypothyroidism, the TSH becomes elevated even though the T_4 and T_3 may still be within the "normal" range. This rise in TSH represents the pituitary gland's response to a drop in circulating thyroid hormone; it is usually the first indication of thyroid gland failure. Since TSH is normally low when the thyroid gland is functioning properly, the failure of TSH to rise when circulating thyroid hormones are low is an indication of impaired pituitary function. The new "sensitive" TSH test will show very low levels of TSH when the thyroid is overactive (as a normal response of the pituitary to try to decrease thyroid stimulation).Interpretations of the TSH level depends upon the level of thyroid hormone; therefore, the TSH is usually used in combination with other thyroid tests such as the T_4 RIA and T_3 RIA (Norman, 2016).

1.4.5.4 Thyroid Scan

Taking a "picture" of how well the thyroid gland is functioning requires giving a radioisotope to the patient and letting the thyroid gland concentrate the isotope (just like the iodine uptake scan above). Therefore, it is usually done at the same time that the iodine uptake test is performed. Although other isotopes, such as technetium, will be concentrated by the thyroid gland; these isotopes will not measure iodine uptake which is what we really want to know because the production of thyroid hormone is dependent upon absorbing iodine. It has also been found that thyroid nodules that concentrate iodine are rarely cancerous; this is not true if the scan is done with technetium. Therefore, all scans are now done with radioactive iodine (Norman, 2016). Thyroid scan is used for following reasons:

- Identifying nodules and determining if they are "hot" or "cold"
- Measuring the size of the goiter prior to treatment
- Follow-up of thyroid cancer patients after surgery
- Locating thyroid tissue outside the neck, i.e. base of the tongue or in the chest (Norman, 2016).

1.4.5.5 Thyroid Antibodies

The body normally produces antibodies to foreign substances such as bacteria; however, some people are found to have antibodies against their own thyroid tissue. A condition known as Hashimoto's Thyroiditisis associated with a high level of these thyroid antibodies in the blood. Whether the antibodies cause the disease or whether the disease causes the antibodies is not known; however, the finding of a high level of thyroid antibodies is strong evidence of this disease. Occasionally, low levels of thyroid antibodies are found with other types of thyroid disease. When Hashimoto's thyroiditis presents as a thyroid nodule rather than a diffuse goiter, the thyroid antibodies may not be present (Norman, 2016).

1.4.6 Diagnosis of hypothyroidism

The correct diagnosis of hypothyroidism depends on the following -

1.4.6.1 Symptoms

Hypothyroidism doesn't have any characteristic symptoms. There are no symptoms that people with hypothyroidism always have and many symptoms of hypothyroidism can occur in people with other diseases. One way to help figure out whether symptoms are due to hypothyroidism or whether the symptom is a change from the way patients used to feel (hypothyroidism is more likely) (American thyroid association, 2014).

1.4.6.2 Medical and family history.

The doctor should be informed first the followings-

- About changes in health that suggest that body is slowing down
- If undergoes thyroid surgery
- If having radiation to neck to treat cancer
- If taking any of the medicines that can cause hypothyroidism- amiodarone, lithium, interleukin-2
- Whether any of family members have thyroid disease (American thyroid association, 2014).

1.4.6.3 Physical exam

The doctor will check the thyroid gland and look for changes such as dry skin, swelling, slower reflexes, and a slower heart rate (American thyroid association, 2014).

1.4.6.4 Blood tests

Basically TSH and T_4 blood test are used in the diagnosis of hypothyroidism.

1.4.7 Medications

In general, the goal of thyroid replacement therapy is to replace endogenous thyroid hormone production, avoid iatrogenic thyrotoxicosis, and treat systemic complications of severe hypothyroidism (Torio, 2012).

1.4.7.1 Levothyroxine

Levothyroxine is the treatment of choice because it is well absorbed and has a half-life of 7 days which allows daily dosing and steady levels of T_3 and T_4 being reached in approximately 6 weeks (Fish *et al*, 1987).

The starting dose should take into consideration factors such as age, preexisting coronary artery disease, and cardiac arrhythmias. A starting dose of 1.6 μg/kg/day, in one healthy patient is recommended, but in elderly patients or those with cardiac disease, it would be prudent to start at a dose of 25 μg to 50μg once daily (Fish *et al*, 1987).

1.4.7.2 Liothyronine

Liothyronine (L-triiodothyronine) is rarely used alone as thyroid hormone replacement because it can cause rapid increases in its concentration, which could be detrimental in elderly patients and those with cardiac disease. It can be used along with levothyroxine when levothyroxine alone does not provide relief of symptoms (Torio, 2012).

1.4.7.3 Thyroid extract

Thyroid extract or natural thyroid hormone is pig thyroid gland that has been dried and crushed in powder form. This is not a recommended thyroid hormone replacement because the amount of T_4 and T_3 can be variable and there can be an excess T_3 in this preparation (Torio, 2012).

1.4.8 Side Effects and Complicationons

The only dangers of thyroxine are caused by taking too little or too much. If too little, is taken then hypothyroidism will continue. If too much, is taken symptoms of hyperthyroidism—an overactive thyroid gland will be developed. The most common symptoms of too much thyroid hormone are fatigue but inability to sleep, greater appetite, nervousness, shakiness, feeling hot when other people are cold, and trouble exercising because of weak muscles, shortness of breath , and a racing, skipping heart. Patients who have hyperthyroid symptoms at any time during thyroxine replacement therapy should have their TSH tested. If it is low, indicating too much thyroid hormone, their dose needs to be lower (Torio, 2012).

1.4.9 Follow-up

Follow up is needed to check TSH about every 6 to 10 weeks after a thyroxine dose change. Patient may need tests more often she is pregnant or if taking a medicine that interferes with body's ability to use thyroxine. The goal of treatment is to get and keep the TSH in the normal range. Babies with hypothyroidism must get all their daily treatments and have their TSH levels checked as they grow, to prevent mental retardation and stunted growth. Once the patient is settled into a thyroxine dose, he can return for TSH tests about once a year (American thyroid association, 2014).

Patient needs to return TSH test soon if any of the following is seen

- If symptoms return or get worse
- If to change thyroxine dose or brand, or change taking pills with or without food
- In case of gaining or losing a lot of weight
- To start or stop taking a drug that can interfere with absorbing thyroxine (such as certain antacids, calcium supplements and iron tablets), or to change the dose of such a drug
- To try stopping thyroxine treatment
- If patient thinks of doing well enough not to need thyroxine treatment any longer then patient should try it only under doctor's close supervision, rather than stopping the pills completely (American thyroid association, 2014).

1.5 Worldwide conditions of thyroid disease

About 200 million people in the world have some form of thyroid disease and about 20 million approximately 1 in 13 or 7.35% people in USA suffering from thyroid disease. Among them, undiagnosed prevalence of Thyroid disorders about 13 million, so the undiagnosed prevalence rate is 1 in 20 or 4.78% (Health grade inc, 2015).

Females are 5 times more likely to develop a hypothyroid disease condition over males. 1 in 8 women during their life time has the risk of thyroid disease in the US. 27 per 1000 people having goiter and 1 in 4000 babies suffer from thyroid disease. 20% of people with Diabetes will experience an onset of thyroid disorder (Health grade inc, 2015).

1.5.1 Worldwide condition of hypothyroidism

In iodine-replete communities, the prevalence of spontaneous hypothyroidism is between 1 and 2%, and it is more common in older women and 10 times more common in women than in men. Studies in Northern Europe, Japan and the USA have found the prevalence to range between 0.6 and 12 per 1000 women and between 1.3 and 4.0 per 1000 in men investigated (Vanderpump, 2011).

Other factors associated with a higher risk of developing clinical hypothyroidism include being an older woman (up to 20% of women over age 60 have subclinical hypothyroidism), having a goiter (enlarged thyroid gland) or thyroid antibodies, or harboring immune factors that suggest an autoimmune condition (University of Maryland Medical Center, 2015).

1.5.1.1 Conditions of Subclinical hypothyroidism

In the original Whickham survey in Northeast England, 8% of women (10% of women over 55 years of age) and 3% of men had subclinical hypothyroidism (Vanderpump, 2011).

In the Colorado study, 9.4% of the subjects had a high-serum TSH concentration, of which 9.0% had subclinical hypothyroidism. Among those with a high-serum TSH concentration, 74% had a value between 5.1 and 10 mIU/l and 26% had a value >10 mIU/l. The percentage of subjects with a high-serum TSH concentration was higher for

women than for men in each decade of age, and ranged from 4 to 21% in women and 3 to 16% in men (Vanderpump, 2011).

In the National Health and Nutrition Examination Survey (NHANES III) serum TSH concentrations increased with age in both men and women and were higher in whites than in blacks, independent of serum anti-thyroid antibody concentrations. Approximately 2% of adolescents aged 12–19 years had a serum TSH >4.5 mIU/l (Vanderpump, 2011).

Studies of elderly persons have confirmed the high prevalence of a raised serum TSH in this age group, with ~10% of subjects >60 years in a single general practice in Birmingham, UK having serum TSH values above the reference range. More recent data from Birmingham suggest that there is now an increased awareness of thyroid disease and testing of thyroid function and perhaps earlier use of levothyroxine in mild thyroid failure. A community-based sample of 5960 participants aged ≥65 years demonstrated a lower prevalence of subclinical hypothyroidism of 2.9% (95% confidence interval (CI): 2.6–3.1%) (Vanderpump, 2011).

A further analysis of the NHANES III data suggests that the reference range for serum TSH rises with age as the 97.5 centile for those subjects aged >80 was 7.49 mIU/l and 70% had a serum TSH greater than the population defined upper limit of the reference range of 4.5 mIU/l of whom only 40% were anti-thyroid antibody positive. Data from a US cohort aged 70–79 years found that black subjects had a significantly lower prevalence of subclinical hypothyroidism (2% in men and 3% in women), as compared with white subjects (4% in men and 6% in women). Subclinical hypothyroidism is found at higher frequency (18% in Iceland and 24% in Hungary) in areas where iodine intake is high, but most cases are not of autoimmune origin. In surveys of hospital in-patients, the point prevalence rates were similar being between 3 and 6% with most subjects reverting to normal thyroid function 3 months following the acute illness. (Vanderpump, 2011)

Spontaneous recovery has also been described in subjects with subclinical hypothyroidism, although the frequency of this phenomenon is unclear. In one study, 37% of patients normalized their serum TSH levels over a mean follow-up time of 32 months. Normalization of serum TSH concentrations is more likely to occur in patients with negative antithyroid antibodies and serum TSH levels <10 mIU/l, and within the first 2 years after diagnosis (Vanderpump, 2011).

1.5.1.2 Overt hypothyroidism

Each year, about 2 - 5% of people with subclinical thyroid go on to develop overt hypothyroidism (Vanderpump, 2011).

Overt hypothyroidism was found in 7% of 558 subjects aged between 85 and 89 years in Leiden, Netherlands. A lower prevalence is seen in areas of iodine deficiency (Vanderpump, 2011).

1.5.1.3 Congenital hypothyroidism

Congenital hypothyroidism affects about one newborn in 3500–4000 births and is the most treatable cause of mental retardation. In iodine-replete areas, 85% of the cases are due to sporadic developmental defects of the thyroid gland (thyroid dysgenesis), such as the arrested migration of the embryonic thyroid (ectopic thyroid) or a complete absence of thyroid tissue (athyreosis) (Vanderpump, 2011).

The remaining 15% have thyroid dyshormonogenesis defects transmitted by an autosomal recessive mode of inheritance (Vanderpump, 2011).

Clinical diagnosis occurs in <5% of newborns with hypothyroidism because symptoms and signs are often minimal. As a result, it is not possible to predict which infants are likely to be affected. Without prompt diagnosis and treatment most affected children gradually develop growth failure, irreversible mental retardation and a variety of neuropsychological deficits (Vanderpump, 2011).

1.5.2 Studies done on thyroid disease in some other countries

1.5.2.1 Thyroid disorders in India: An epidemiological perspective

Thyroid diseases are common worldwide. In India too, there is a significant burden of thyroid diseases. According to a projection from various studies on thyroid disease, it has been estimated that about 42 million people in India suffer from thyroid diseases. Five common thyroid diseases in India: (1) hypothyroidism, (2) hyperthyroidism, (3) goitre and iodine deficiency disorders, (4) Hashimoto's thyroiditis, and (5) thyroid cancer. 50% of people in the community have microscopic nodules, 3.5% have occult papillary

carcinoma, 15% have palpable goitres, 10% demonstrate an abnormal thyroid-stimulating hormone level, and 5% of women have overt hypothyroidism or hyperthyroidism (Unnikrishnan and menon, 2011).

1.5.2.2 Epidemiology of thyroid disorder in Australia

According to the National Health Survey, that is conducted by the Australian Bureau of Statistics. This study, which has received a lot of publicity on the internet, reported average prevalence rates of 9.5% for hypothyroidism and 2.2% for hyperthyroidism. The combined prevalence of 11.7% is much higher than earlier studies (Stevens, 2000).

The results for the prevalence of overt hypothyroidism and hyperthyroidism are given in the table

Table1.4: Australian prevalence of Hyper & Hypo Thyroidism (Stevens, 2000).

Age	Female		Male		Female to Male
	Number	%	Number	%	
20 & under	16,065	0.60%	4,055	0.14%	3.96
21 to 30	26,891	1.91%	7,856	0.55%	3.42
31 to 40	50,631	3.46%	15,361	1.06%	3.30
41 to 50	83,833	6.28%	23,349	1.74%	3.59
51 to 60	107,289	11.25%	25,563	2.59%	4.20
61 to 70	136,747	19.30%	25,274	3.68%	5.41
71 to 80	166,344	29.22%	21,869	4.85%	7.61
Over 80	123,815	41.85%	9,504	6.26%	13.03
Totals	711,614	7.56%	132,831	1.43%	5.36

1.5.2.3 Epidemiology of thyroid disorder in Bangladeshi population

Although there is no established data on the whole number of patients‘ suffering from Hypothyroidism in Bangladesh, but it is can be assumed from some studies, which are done on patients to assume the percentage of people suffering from Under reactive thyroid disorder. A study shows that, Prevalence of hypothyroidism was 15%, and

prevalence of hyperprolactinemia was 43% and 21% in primary and secondary infertility respectively (Akhter and Hassan, 2008). Again a study shows- The overall occurrence of thyroid disease was estimated to be 20.43 %. The spectrum of thyroid disorders showed highest incidence of diffuse goitre (7.35 %), followed by subclinical hypothyroidism (6.59%), hypothyroidism (4.97%), hyperthyroidism (0.86%) and sub-clinical hyperthyroidism (0.65 %) (Paul *et.al*., 2006).

1.5.3 Statistics by Country for Thyroid disorders

The following table attempts to extrapolate the above prevalence rate for Thyroid disorders to the populations of various countries and regions

Table1.5: Prevalence of Thyroid disease of different countries in the world (right diagnosis.com, 2012).

Country/Region	Prevalence	Population Estimated Used
Thyroid disorders in North America		
USA	21,592,308	293,655,405
Canada	2,390,284	32,507,874
Thyroid disease in south America		
Brazil	13,536,845	184,101,109
Columbia	3,111,086	42,310,775
Thyroid disease in Europe		
Britain (United Kingdom)	4,431,669	60,270,708
Denmark	398,043	5,413,392
Thyroid disease in Asia		
China	95,503,499	1,298,847,624
Japan	9,362,720	127,333,002

Bangladesh	10,392,681	1,065,070,607
India	78,314,013	159,196,336
Pakistan	11,705,612	19,905,165

CHAPTER 2

LITERETURE REVIEW

Literature Review

2.1 Thyroid Disorders in Khulna District: A Community Based Study

This study reports the prevalence of thyroid diseases and their relationship to autoimmunity in a population of Khulna district where goitre is not endemic. Of the total 925 individual studied, 527 was female and 398 was male with age ranges from 2-62 years (mean 19.86::!:13.62years). The overall occurrence of thyroid disease was estimated to be 20.43%. The spectrum ofthyroid disorders showed highest incidence of diffuse goitre (7.35 %), followed by sub-clinical hypothyroidism (6.59%), hypothyroidism (4.97%), hyperthyroidism (0.86%) and sub-clinical hyperthyroidism (0.65 %). The incidence of thyroid disorders was observed to be highest in the 11-45 years age group (79.89%). Female outnumbered male, the ratio being 2.5: 1 with preponderance offemale subjects in all disease groups. The prevalence of all goitre was 10.49%. TMAb estimation was performed in 318 samples, of them 48 cases (l5.09%) was found to be autoimmune thyroid disease. Of the total sub-clinical and overt hypothyroidism, the incidence of autoimmune thyroid disease was 29.29% and non-goitrous thyroid dysfunction was more common than goitrous one. Three of 38(7.89%) euthyroid goitrous subjects showed positive antibody. Interestingly, 16 of 181(8.84%) individual had a positive antibody, which was considered normal by neck examination. Goitre prevalence of 10.49% in this study indicates the region to be a mild iodine deficient area. Chronic autoimmune disease is likely to be one of the etiological factors for thyroid disorders in this southern zone (Paul *et al.*, 2006).

2.2 Congenital Hypothyroidism in the Southern Bangladesh

Congenital hypothyroidism is the commonest preventable cause of mental retardation. It is more prevalent in endemic goiter regions like Bangladesh. 1353 samples were eventually assayed for TSH. Among the study population 88.2% hailed from Khulna district and the rest of the cases came from neighboring districts. Male to female baby ratio was 1.2:1. Regarding the birth weight 33.4% babies were low birth weight. TSH above 10 was found in 35 babies among whom one baby was hypothyroid and the other member of the twin was also hypothyroid although the TSH level was below 10. None of newborn had TSH level above 20. Thus frequency of congenital hypothyroidism was 1.5 per thousand living newborn (Rasul *et al*, 2006).

2.3 Cross sectional evaluation of thyroid hormone levels in non-diabetic and diabetic patients in Bangladeshi population

Diabetes mellitus (DM) and thyroid dysfunction are the common disorders in human being and diabetes mellitus in many cases is found to be associated with disordered thyroid function. In this study 140 healthy non-diabetic subjects and 140 diabetic subjects were investigated for fasting blood sugar (FBS), total triidothyronine (T3), total thyroxin (T4), free triidothyronine (FT3), free thyroxine (FT4) and thyroid stimulating hormone (TSH). Out of 140 diabetic subjects studied, 70% had euthyroidism (normal), 18.6% had hypothyroidism, and 11.4% had hyperthyroidism. Serum T3, T4 and FT3 levels were low, TSH and FT4 levels were high in diabetic subjects whereas, in non-diabetic subjects all these levels were normal. All the diabetic subjects had high fasting blood sugar levels (10.82 Â± 2.72). Statically no significant differences were observed in serum T4 ($p = 0.791$) and BMI ($p = 0.477$) levels between non-diabetic and diabetic subjects. Fasting blood sugar was found to be significantly correlated with TSH, FT3 levels and others parameter were not that much significant. In this study, 30% diabetic patients were found to abnormal thyroid hormone levels. The prevalence of thyroid disorder was higher in women (17.1%) than in men (12.9%), while hyperthyroidism were higher in males (13.3%) than in females (10%) and hypothyroidism was higher in females (20%) than in males (16.7%) (Alam *et al*, 2013).

2.4 Assessment of Sub-Clinical Hypothyroidism and Hyperthyroidism status in adult patients.

It is reported that most patients who were found to have sub-clinical hyperthyroidism depicts TSH values between 0.1 to 0.45 µIU/L and those with sub clinical hypothyroidism between 4.5 to 10 µIU/L. In this respect, studies were carried out during January 2006-Dec 2007 in 230 adult patients (98 males, 132 females) for evaluation of sub-clinical thyroid disease. TSH and thyroid hormones (T3 T4, FT3 and FT4) levels of all patients were determined by standard methods to assess the extent of the sub-clinical status. In female group which comprised of 132 patients, a total of n = 28 (21.20%) exhibited sub-clinical thyroid disorders [n = 18; 13.63% Sub-clinical hypothyroidism, n = 10; 7.57% sub-clinical hyperthyroidism], whereas 59 (44.69%) exhibited true-thyroid disorder. Subsequent assessment in males shows that out of 98 patients; n = 15 patients (15.30%) showed sub-clinical thyroid disorders [n = 9; 9.18% sub-clinical hypothyroidism; n = 6; 6.12% sub-clinical hyperthyroidism], whereas 20 (20.40%)

exhibited true thyroid disorder. In both gender groups, 45 and 63 individuals were without any sub-clinical or true thyroid disease, respectively and thus presented as normal. It is concluded that sub-clinical thyroid dysfunction prevails in females with 12.17% occurrence whereas 6.52% in males. Furthermore, the evaluation and subsequent presence of sub-clinical conditions predicts future progression to overt disease (Alam *et al*, 2010).

2.5 Thyroid function and psychiatric morbidity in patients with manic disorder receiving lithium therapy

Euthyroid hyperthyroxinemia as a result of a transient increase in thyroid-stimulating hormone (TSH) levels may contribute to the development of manic disorder. Lithium has a potent short-term antithyroidal effect that may account for its antimanic action. At baseline, the free thyroxine level (FT4, 16.23 +/- 3.11 pmol/L) was at the high end of the normal range, whereas the free triiodothyronine (FT3, 4.24 +/- 0.65 pmol/L) and TSH (1.47 +/- 0.73 mIU/L) levels were within the normal range. All patients were clinically euthyroid, but five of them (11%) had elevated FT4 levels. Baseline FT3 and FT4 levels were positively correlated with past psychiatric morbidity. The FT4 level at baseline and after 1 month of treatment was positively correlated with scores on the Brief Psychiatric Rating Scale ($p < 0.02$) and negatively correlated with scores on the Global Assessment Scale ($p < 0.005$). During the first month of treatment, the reduction of FT3 and FT4 levels was significantly correlated with a decrease in psychiatric symptoms. By 6 months, the FT3 level was no longer significantly different from that at the baseline, but FT4 levels remained significantly lower. The TSH level increased progressively from baseline to 6 months. Multilevel models showed that FT4 and serum lithium levels were positively and negatively associated with psychiatric symptoms, respectively. The findings of the study lend support to the notion that euthyroid hyperthyroxinemia contributes to acute mania and suggest that lithium's short-term antimanic action may be mediated by its antithyroid effect (Lee *et al*, 2000).

2.6 Pattern of hypothyroid cases in Bangladeshi People: A pilot study

Diabetic patients have a higher prevalence of thyroid disorders than the general population, this may influence diabetic management. Fifty-two diabetic patients were consecutively selected from diabetic patients attending the out-patient department of BIRDEM. Fifty control subjects were selected from non-diabetic patients who attended the out-patient department of BIRDEM for routine check-ups as advised by their attending physicians. The subjects in both groups were above 30 years of age. The concentration of thyroid stimulating hormone (TSH), free triiodothyronine (FT3) and thyroxine (FT4) were evaluated using a Microparticle Enzyme Immunoassay (MEIA) procedure. Patients with type 2 diabetes had significantly lower serum FT3 levels ($p=0.000$) compared to the control groups. There were no significant differences observed in serum FT4 ($p=0.339$) and TSH ($p=0.216$) levels between the control and study subjects. All the diabetic patients had high fasting blood glucose levels (12.15±2.12). We conclude that FT3 levels were altered in these study patients with uncontrolled diabetes (Islam *et al.,* 2008).

2.7 Thyroid Disorder in Far Western Part of Nepal: A Hospital Based Study

This study was conducted to know the status of thyroid disorder in people of far western region of Nepal. The percentage of thyroid disorders was 33.66% in people of far western region of Nepal. The people were highly affected by overt hyperthyroidism (14.9%) followed by subclinical hyperthyroidism (9.9%). The subclinical hypothyroidism was 7.9% while 1% overt hypothyroidism only. Serum fT3, fT4 and TSH level were significantly different in male and females. Similarly, fT3, fT4 and TSH levels show statistically significant differences in different thyroid disorders. The fT3 and fT4 level in overt hyperthyroidism and subclinical hypothyroidism showed statistically significant differences when compared with euthyroidism group. Likewise, TSH level also shows statistically significant in all the thyroid disorders when compared with euthyroidism group. The fT3 and fT4 levels were statistically insignificant in all the age groups whereas TSH level showed statistically significant different in all the age groups. The fT3 and fT4 level in 21-40 years showed statistically significant when compared with serum level of fT3 and fT4 of 0-20 years. Similarly, serum level of TSH in 21-40 and 41-60 years also showed statistically significant when compared with serum level of TSH of 0-

20 years. The people residing in far western region have risk for thyroid disorders. They were suffering with thyroid disorder, especially overt hyperthyroidism (14.9%) and subclinical hyperthyroidism (9.9%). Further studies are required to characterize the reasons for this high prevalence of overt hyperthyroidism and subclinical hyperthyroidism (Yadav *et al.*, 2012).

2.8 Hypothyroidism in adults: A review and recent advances in management

Hypothyroidism is a common endocrine disorder resulting from deficiency of thyroid hormone or, more rarely, from their impaired activity at tissue level. In its clinically overt form, hypothyroidism is a relatively common condition, with an approximate prevalence of 2% in adult women and 0.2% in adult men. Deficiency of the hormone has a wide range of effects, because all metabolically active cells require thyroid hormone. The clinical features of hypothyroidism are dependent on the patient's age, the presence of other disease, and the rate at which hypothyroidism develops. Early detection and proper management is very important. Under treatment leads to disease progression with gradual worsening of symptoms and further metabolic derangements. Fortunately, in most patients older than 3 years, the signs and symptoms of hypothyroidism are reversed with thyroid hormone treatment. A constant reminder on progress in management of the disease is needed. Thus, the aim of this review is to bring to notice the recent advances in the diagnosis and management of hypothyroidism and to highlight the risks involved in the global movement from consuming organic animals (as the world moves towards inorganic foods, which inhibits thyroid hormones (Bello and Bakari, 2012).

2.9 Screening and treatment of Thyroid Dysfunction: An evidence review for the US preventive services task forces

Hyperthyroidism and hypothyroidism are common conditions that have lifelong effects on health. About 5% of U.S. adults report having thyroid disease or taking thyroid medication.1,2 In a cross-sectional study of 2,799 well-functioning adults aged 70-79, 9.7% of black women, 6% of white women, 3.2% of black men, and 2.2% of white men reported a history of hyperthyroidism.3 In the same study, 6.2% of black women, 16.5% of white women, 1.7% of black men, and 5.6% of white men reported a history of hypothyroidism. Hyperthyroidism has several causes. Graves' disease, the most common

intrinsic cause, is an autoimmune disorder associated with the development of long-acting thyroid stimulating antibodies (LATS). Single or multiple thyroid nodules that produce thyroid hormones can also cause hyperthyroidism. The use of excessive doses of the thyroid hormone supplement levothyroxine is also a common cause. The most common cause of hypothyroidism is thyroiditis due to antithyroid antibodies, a condition called "Hashimoto's thyroiditis." Another common cause of hypothyroidism is prior treatment for Graves' disease with surgery or radioiodine. Consequences of untreated hyperthyroidism include atrial fibrillation, congestive heart failure, osteoporosis, and neuropsychiatric disorders. Both hyperthyroidism and hypothyroidism cause symptoms that reduce functional status and quality of life (Helfand, 2004).

2.10 Prevalence of hypothyroidism in adults: An epidemiological study in eight cities of India

Hypothyroidism is believed to be a common health issue in India, as it is worldwide. However, there is a paucity of data on the prevalence of hypothyroidism in adult population of India.. Thyroid abnormalities were diagnosed on the basis of laboratory results (serum FT3, FT4 and Thyroid Stimulating Hormone [TSH]). Patients with history of hypothyroidism and receiving levothyroxine therapy or those with serum free T4 <0.89 ng/dl and TSH >5.50 μU/ml, were categorized as hypothyroid. The prevalence of self reported and undetected hypothyroidism, and anti-thyroid peroxidase (anti-TPO) antibody positivity was assessed. Inland cities showed a higher prevalence of hypothyroidism as compared to coastal cities. A significantly higher ($P < 0.05$) proportion of females vs. males (15.86% vs 5.02%) and older vs. younger (13.11% vs 7.53%), adults were diagnosed with hypothyroidism. Additionally, 8.02% (n = 430) patients were diagnosed to have subclinical hypothyroidism (normal serum free T4 and TSH >5.50 μIU/ml). Anti – TPO antibodies suggesting autoimmunity were detected in 21.85% (n = 1171) patients. The prevalence of hypothyroidism was high, affecting approximately one in 10 adults in the study population. Female gender and older age were found to have significant association with hypothyroidism. Subclinical hypothyroidism and anti-TPO antibody positivity were the other common observations (Unnikrishnan *et al.,* 2013).

2.11 Hypothyroidism—A Question towards Quality and Patient Centricity

The metabolic and endocrine disorders are either increasing across the globe or may have been observed with more focus in recent years. It is not uncommon now to find out neither patients of endocrine and metabolic disorders nor a physician of the associated diseases. Out of 102 patients of the study, 80 patients fell into the inclusion criteria, while 22 were excluded. A total of 80 patients were registered in the incorporate duration. Among the total samples 36 (42.9%) were males and 44 (52.4%) were females. Mean age males and females included in the study were 34.89 ± 17.73 and 33.36 ± 13.73 years respectively. The systolic and diastolic blood pressure (120/80 mg Hg) was observed in 18 (40.9%) females' and 13 (36.1%) males' patients (Rehman *et al.*, 2015).

2.12 Sub-clinical hypothyroidism and hyperprolactinemia in infertile women: Bangladesh perspective after universal salt iodination

Hypothyroidism is an accepted cause of infertility and habitual abortion. Prevalence of subclinical hyperthyroidism and hypothyroidism was 6.5% and 15%, and prevalence of hyperprolactinemia was 43% and 21% in primary and secondary infertility respectively. Mean TSH level was higher in secondary infertility (3.6 +/- 3.7mIU/L) than primary infertility (2.3 +/- 2.7mIU/L), though the difference was not statistically significant ($P < 0.11$). Mean prolactin level in primary infertility (495 +/-340nmol/L) was higher than secondary infertility (340 +/- 310nmol/L), showing a significant statistical difference ($p<.05$). Prevalence of hyperprolactinemia was higher in primary infertility and prevalence of sub-clinical hypothyroidism was higher in secondary infertility, showing no correlation between TSH and prolactin levels in these two groups (Akhter and Hassan, 2008).

2.13 Epidemiology of thyroid diseases in Africa

The reported prevalence rates of endemic goiter range from 1% to 90% depending on the area of study with myxedematous cretinism still a prominent feature of IDD in only a few regions of the continent. The extent of autoimmune thyroid disorders remains unknown because of underdiagnosis and underreporting but the few available studies note a prevalence rate of 1.2% to 9.9% of which Graves diseases is the commonest of these

groups of disorders. Rarer causes of thyroid dysfunction such as thyroid tuberculosis and amiodarone related causes are also documented in this review. The onset of new thyroid diseases following amiodarone usage was documented in 27.6% of persons treated for arrhythmia. Reports on thyroid malignancies (CA) in Africa abound and differentiated thyroid malignancies are noted to occur more commonly than the other forms of thyroid CA. The documented prevalence rates of thyroid CA in the African continent are as follows (papillary: 6.7–72.1%, follicular: 4.9–68%, anaplastic: 5–21.4%, and medullary: 2.6%–13.8%). For the differentiated thyroid CA, there is a changing trend toward the more frequent occurrence of papillary CA compared to follicular CA and this may be attributable to widespread iodization programs. Our review shows that diagnosis and evaluation of thyroid disorders are reliant in most regions of the continent on clinical acumen and suboptimal diagnostic facilities and expertise are what obtain in many practices. The frequently employed management options of thyroid disorders in the continent are pharmacological and surgical treatment modalities (Ogbera and kuku, 2011).

2.14 Prevalence of thyroid disease, thyroid dysfunction and thyroid peroxidase antibodies in a large, unselected population. The Health Study of Nord-Trùndelag (HUNT)

It is done to examine the prevalence of thyroid disease and dysfunction including thyroid autoimmunity in Norway. The prevalence of former diagnosed hyperthyroidism was 2.5% in females and 0.6% in males, hypothyroidism 4.8% and 0.9%, and goitre 2.9% and 0.4% respectively. In both sexes the prevalence increased with age. In individuals without a history of thyroid disease the median, 2.5 and 97.5 percentiles for TSH (mU/l) were 1.80 and 0.49±5.70 for females and 1.50 and 0.56±4.60 for males. The TSH values increased with age. When excluding individuals with positive thyroid peroxidase antibodies (TPOAb) (> 200 U/ml), the 97.5 percentiles dropped to 3.60 mU/l and 3.40 mU/l respectively. The prevalence of pathological TSH values in females and males were TSH$10 mU/l 0.90% and 0.37%; TSH 4.1±9.9 mU/l 5.1% and 3.7%; and TSH#0.05 mU/l 0.45% and 0.20% respectively The prevalence of positive TPOAb (> 200U/ml) was 13.9% in females and 2.8% in males. In females the lowest percentage (7.9%) of positive TPOAb was seen with TSH 0.2± 1.9 mU/l and increased both with lower and higher levels of TSH. The percentage of males with positive TPOAb was lower than in females

in all TSH groups except for those with TSH> 10 mU/l (85% TPOAb positive). In spite of a high prevalence of recognised thyroid disease in the population a considerable number of inhabitants have undiagnosed thyroid dysfunction and also positive TPOAb (Bjuro *et al*., 2000).

Significance of the study

Hypothyroidism is the most common Thyroid disorder in both in the developed and less developed world. About 2-3 percent of Americans have hypothyroidism and as many as 10-15% have mild hypothyroidism. More than half of those with hypothyroidism do not know they have it (American Thyroid Association, 2014). Females are 5 times more likely to develop a hypothyroid disease condition over males. 20% of people with Diabetes will experience an onset of a thyroid disorder. Each year, about 2 - 5% of people with subclinical thyroid go on to develop overt hypothyroidism (University of Maryland Medical Center, 2014). Hypothyroidism is now the most common disease among men and women in Bangladesh. It is assumed that, Prevalence of hypothyroidism was 15% (Akhter and Hassan, 2008). Among them more than half of the population is being unaware about this disease because the clinical features of Hypothyroidism are not specific and many of these symptoms are often confused with other health conditions. Moreover, the unawareness these patients may lead them to suffer from serious illness like goitre, thyrotoxicosis, thyroid cancer and thyroid papillary carcinoma.

Symptoms of hypothyroidism usually appear slowly over several months or years but this disease is a slow killer which may further develop many other physical and mental problems.

If not detected earlier sometimes hypothyroidism may lead to thyroid carcinomas and may cause death. Thyroid disorder is very crucial in female fertility and the risk of hypothyroidism increases during pregnancy, after delivery and around menopause. Lack of awareness and early detection program in developing country is a main reason for thyroid disease.

The study done in Bangladesh on thyroid disordered patients' prevalence level checking is very few. There is no study focusing particularly on hypothyroidism. Again is difficult to calculate the prevalence on the general people, so we have targeted the diagnosing thyroid disordered patients to conduct our study and our target was to estimate the prevalence of hypothyroidism and to judge the level of knowledge about thyroid dysfunction, early warning signs, and therapeutic and screening approaches of hypothyroidism.

Our main focus is to get the idea about knowledge level about hypothyroidism, risk factors and their treatment pattern and how much they are complying with their medication and treatment pattern. Again, as it is a hormonal disorder, the patient's must be conscious and consistence about their treatment and medication. From this study, we can calculate their conditions whether their hormone levels are in control by taking medications or relapse occurred when they stopped their treatment.

From this study we will also get idea about their family history of thyroid disorder or any other endocrine disorder and the relationship with the patient. However, we can estimate the approximate number of patients who have been diagnosed and how much the aware about this disease, how they are treated, and their willingness and also awareness to control their hormone level.

Study Goal and Objective:

- To find out Prevalence of hypothyroidism among endocrine disorder in Bangladesh
- To identify the signs and symptoms, diagnosis, treatment pattern and medication of Hypothyroidism
- To assess the knowledge of patients regarding their disease.

CHAPTER 3

METHODOLOGY

Study Method

3.1 Study area

Permissions were taken from the authorized members of the following hospitals before interview.

- The Institute of Nuclear Medicine & Ultrasound (INMU) Bangabandhu Sheikh Mujib Medical University (BSMMU), Shahbagh , Dhaka-1000
- Central Hospital Ltd, 18,Green Road, Dhaka-1205
- Popular Diagnostic Centre, House # 16, Road # 2, Dhanmondi R/A, Dhaka – 1205
- Thyroid Clinic, 20, Green Road, Dhaka-1205
- Sir Salimullah Medical College Mitford Hospital, Mitford road, Dhaka-1205
- Mymensingh Medical College Hospital

3.2 Total Number of participants

Data was collected from 273 endocrine disordered patients.

3.3 Inclusion criteria

- All patients having endocrine disorder and who are previously diagnosed.
- Participants always included a general population of both sexes without age restriction.

3.4 Exclusion Criteria

- Unwilling to participate or unable to comply with protocol requirements.

3.5 Procedure

- For collecting data, a questionnaire was prepared according to required information.
- The collected data were analyzed with the help of Microsoft Office Excel and filtered out accordingly for analysis. Some graphical representations were made from those analysis statuses.

CHAPTER 4

RESULTS

Result

4.1 Participants having endocrine disorder

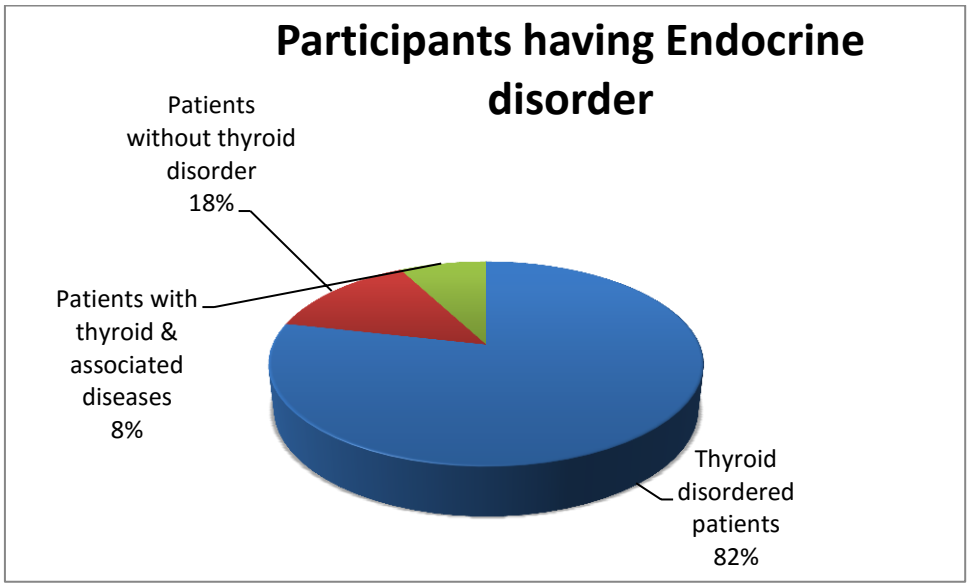

Figure 4.1: Participants having endocrine disorder

Looking at the above histogram, showing the distribution of percentage of endocrine disorder of the participants it is seen that 82% of the total number of patients had thyroid disorder. 18% of the patients did not have thyroid diseases but having others Endocrine diseases like glucose homeostasis disorder (diabetes) and tumor of endocrine gland. Moreover among 223 thyroid patients, 8% patients had thyroid disease as well as other associated disease like diabetes, hypertension and cardiovascular diseases.

4.2 Percent of participating population suffering from various endocrine diseases

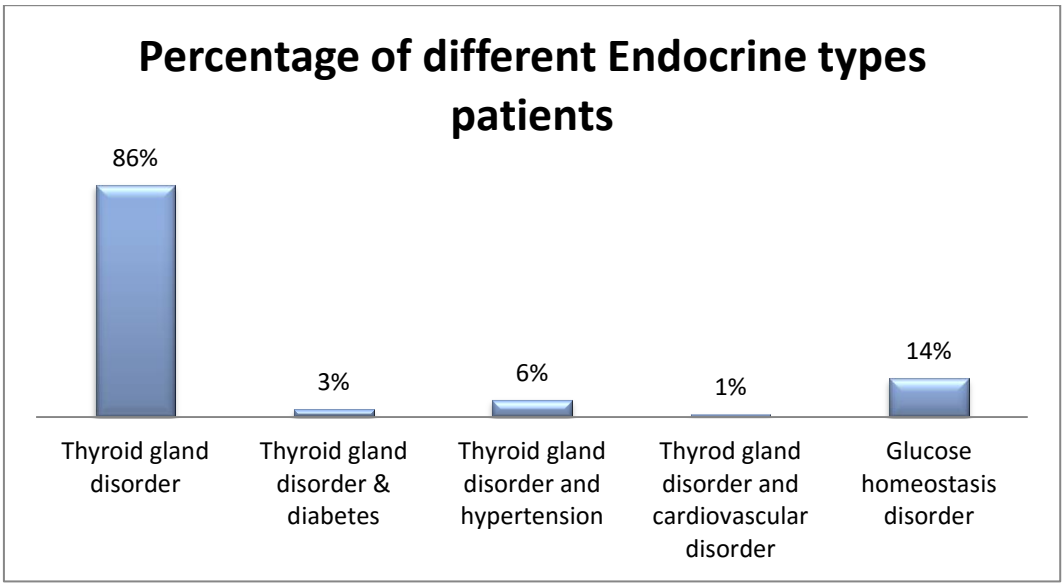

Figure 4.2: Patients suffering from various endocrine diseases

Among 273 participants 86% had Thyroid gland disorder and 14% had glucose homeostasis disorder. Again from total 223 thyroid patients, 3% had both thyroid disease and diabetes, 6% had both thyroid disease and hypertension and 1% had both thyroid and cardiovascular disease.

4.3 Age distribution of the respondents

The patients were divided into four different age groups and these age groups are shown in the figure below.

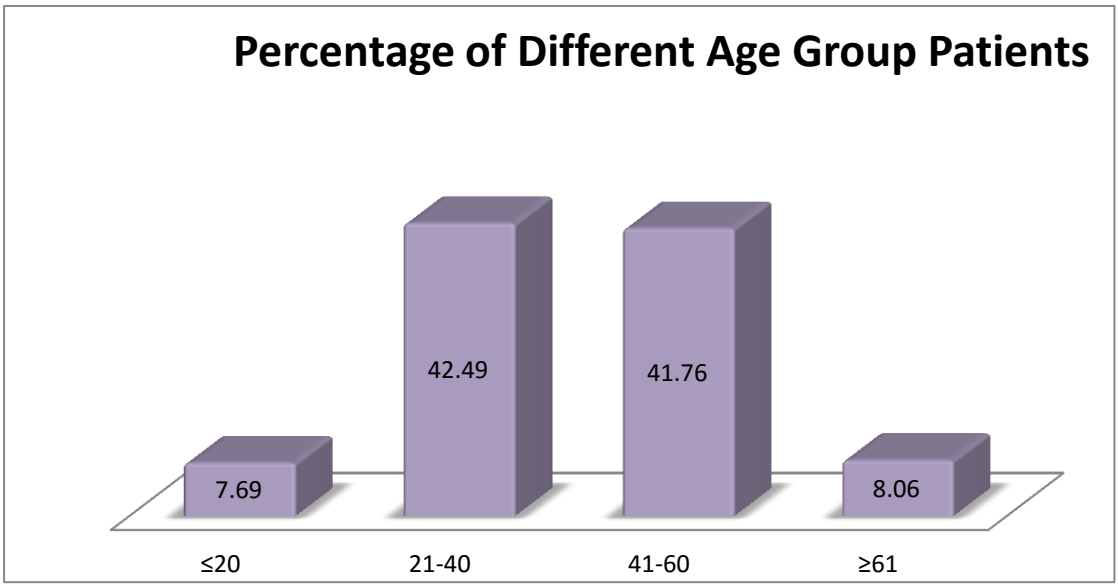

Figure 4.3: Respondents Age distribution (year)

The histogram says that among the respondent patients, majority of them are in the age limit 21-40 (42.49%), then age 41-60 are of 41.76% then below 20 years are of 7.69% and rest of patients are over 60 years having 8.06%.

4.4 Sex of thyroid disordered patients

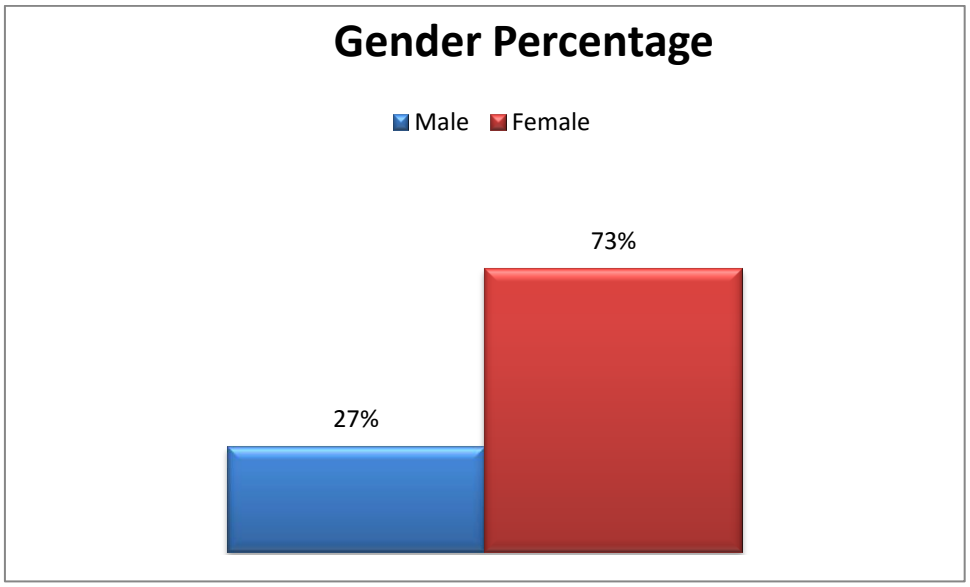

Figure 4.4: Percentage of Male and female patient having hyperthyroidism

It is observed from the histogram that 27% are male and 73% are female. So, the analysis shows maximum patients are female and it is about 3 times than the male patient.

4.5 Marital status of patients

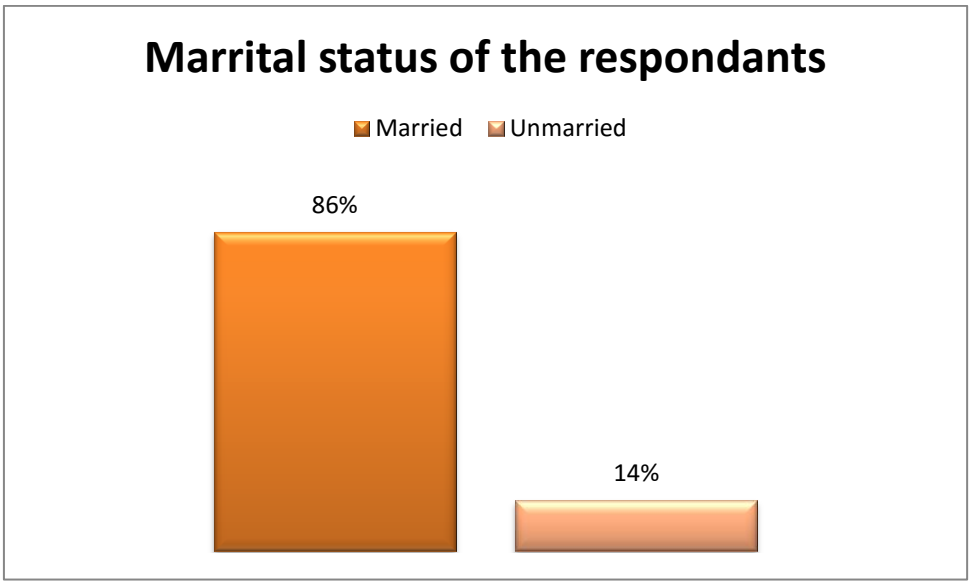

Figure 4.5: Marital status of the respondents

The analysis shows most of the patients are married and it is 86%. The rest 14% of patients are unmarried.

4.6 Educational Status of the respondents

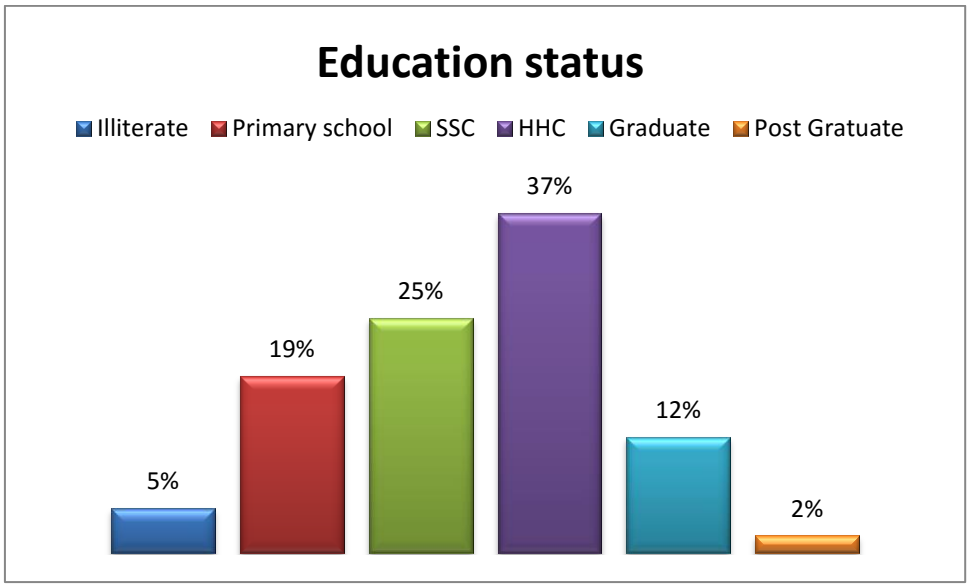

Figure 4.6: Percentage of the Educational status of sample population

The recorded data shows that, 5% are illiterate, 19% have primary education, 25% passed SSC and 37% have their HSC and 14% patients are Graduates and post graduates within the respondent patients.

4.7 Occupational status of patients

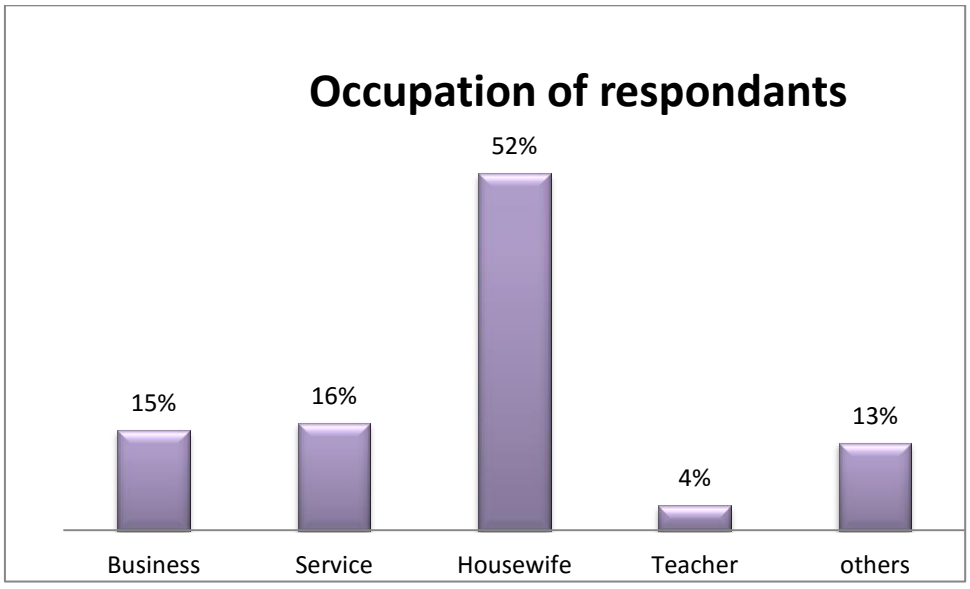

Figure 4.7: Occupational status of patients

Here it is observed majority of the patients are house wife. Businessman, Service holder also holds a large portion.

Among 273 Endocrine patients, majority 52% are housewife, 16% are service holder, 15% doing business, 4% are teacher and 13% are from other various profession

4.8 BMI status of Hyperthyroid containing patients

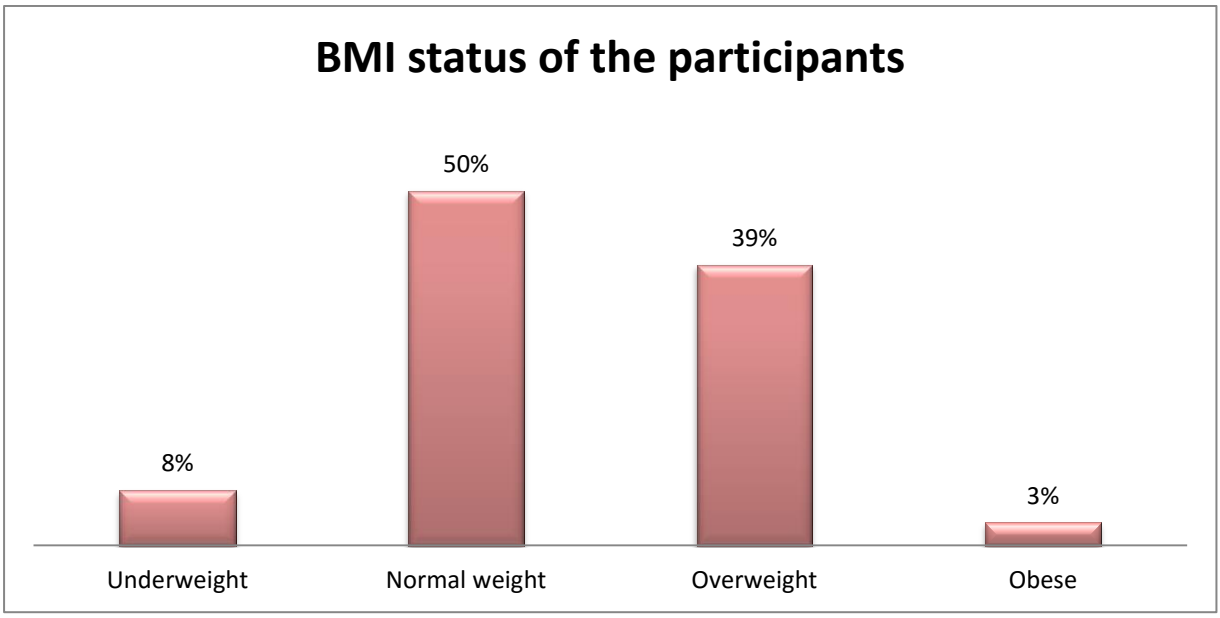

Figure 4.8: BMI status of the respondents

From the recorded data, half of the patients were found with normal body mass index. According to BMI standard < 18.5 are underweight, 18-24.5 are normal weight, 25-29.9 are overweight, and obese are >30.

Here, the histogram shows that, 8% patients are underweight, 50% are normal, 39% are overweight and 3 % are obese of all participant patients.

4.9 Types of thyroid disorder

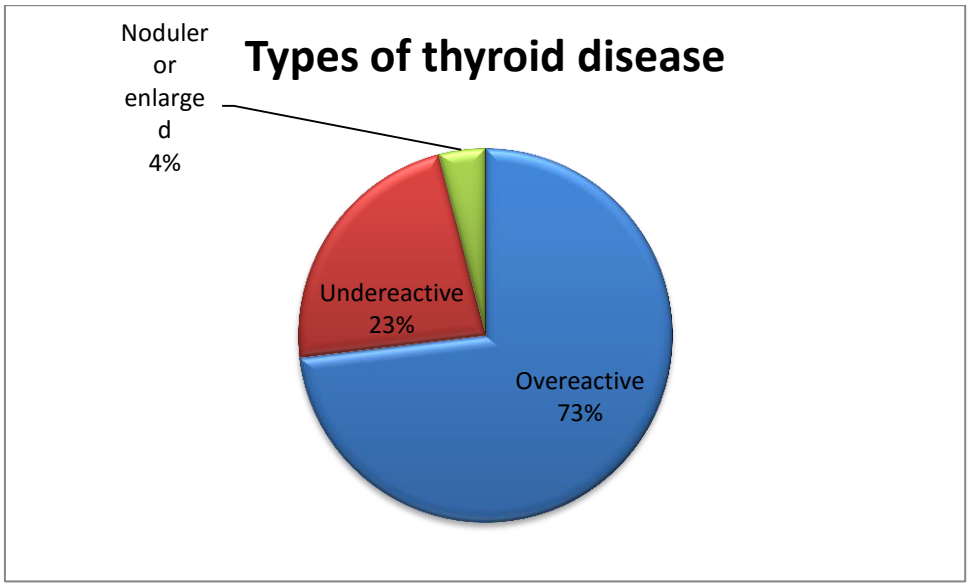

Figure 4.9: Types of thyroid disorder

Among 223 patients having thyroid disorder, 23% are having unreactive thyroid (Hypothyroidism), 73% having overactive thyroid (Hyperthyroidism) and 4% have nodular or enlarged thyroid gland

4.10 History of Thyroid disorder

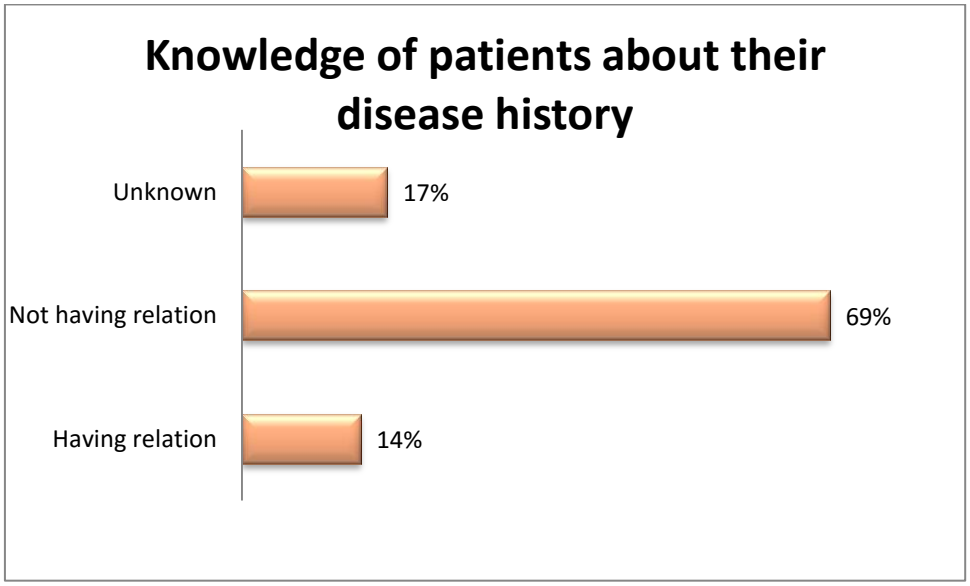

Fig 4.10: History of Thyroid disorder in patients.

Among all the patients 14% have their family history, 17% do not know the reason and past family history, 69% patients said they do not have any family history of this disease, although they were not very confident.

4.11 Relation with them

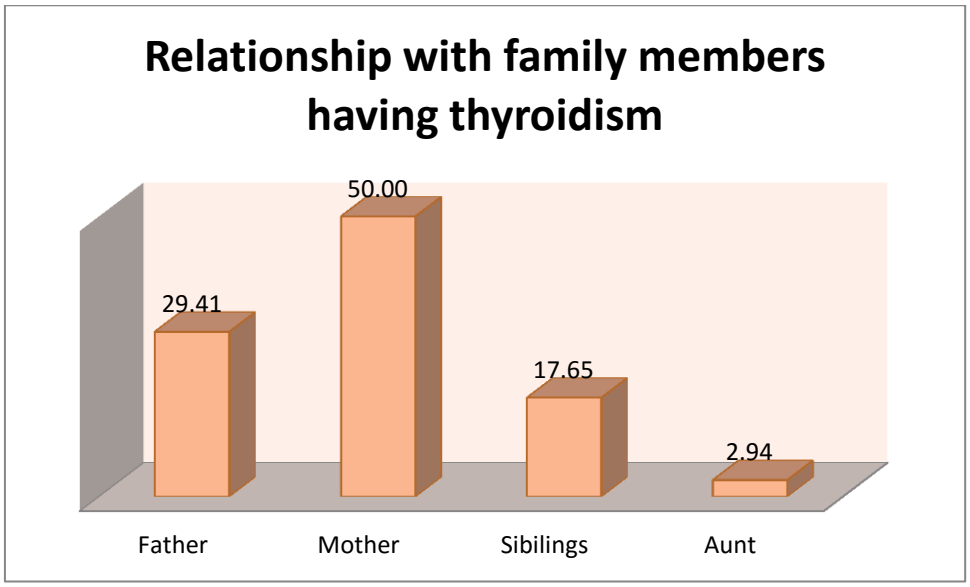

Figure 4.11: Family history having thyroid disease (in percent)

The histogram shows that among the patients having family history 29% had previous history of father, 50% had previous history of mother, 17% siblings and 3% from aunts.

4.12 Types of Thyroid disease

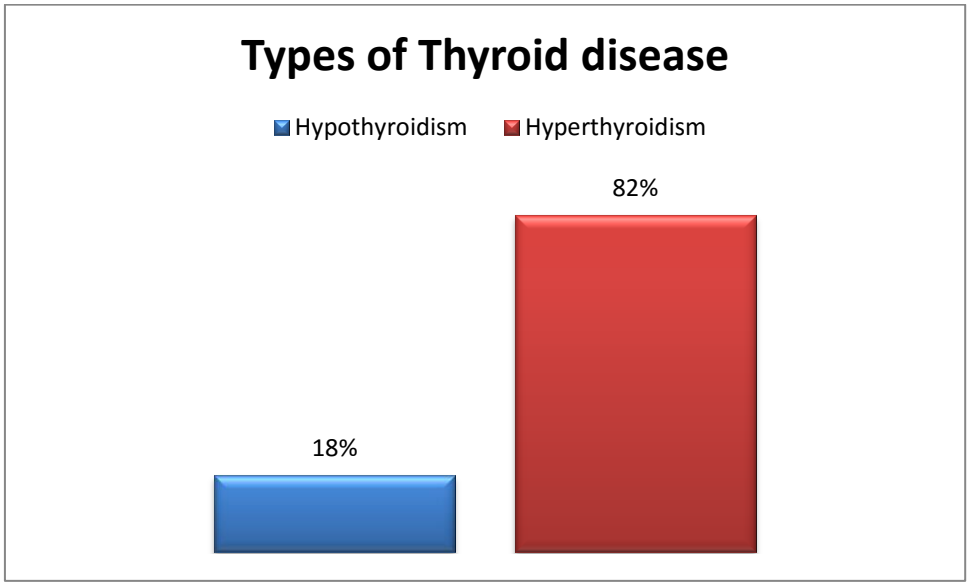

Figure 4.12: Types of Hyper and Hypothyroidism

Majority of the patients (82%) found from the study suffering from hyperthyroidism and the rest 18% are hypothyroid patients.

4.13 Percentage of Hypothyroid patient types

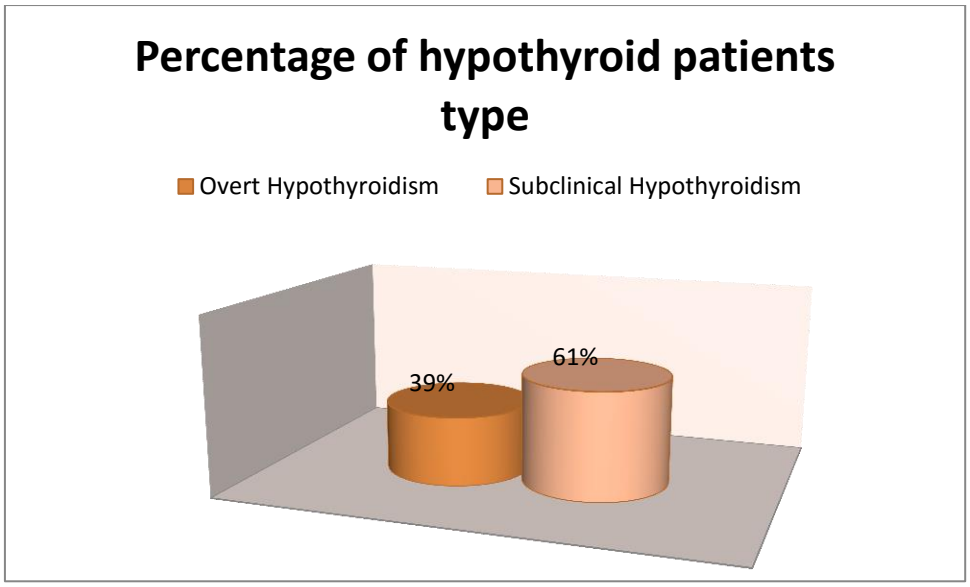

Figure 4.13: Hypothyroidism types percentage

From the histogram it is easily understandable that the ratio of two types of hypothyroidism is pretty near to each other, where subclinical hypothyroidism is higher (61%) than overt hypothyroidism (39%).

4.14 Duration of the patients suffering from hypothyroidism

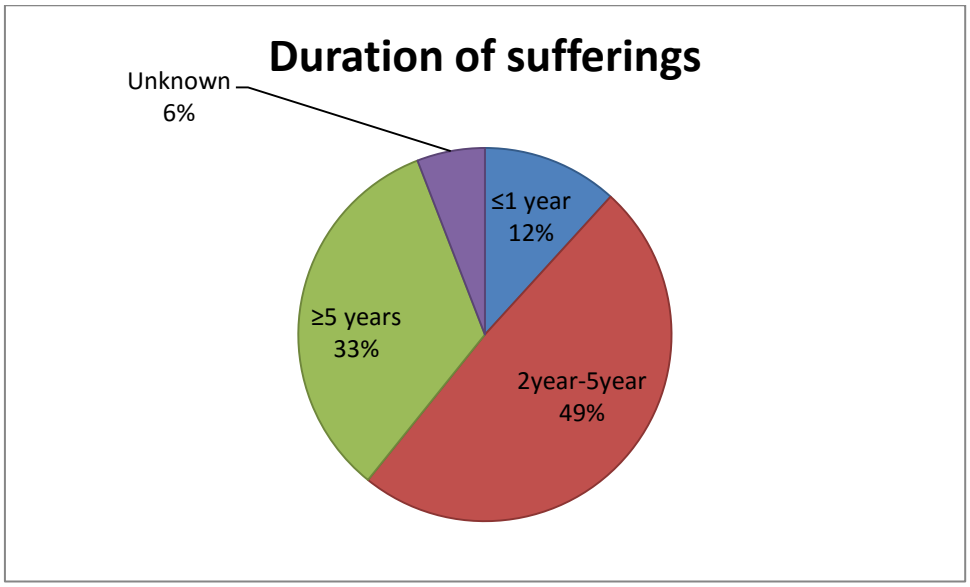

Figure 4.14: Duration of sufferings (in years)

The pie chart shows, among patients, 49% patients are suffering from this disorder 2-5 years, 33% are suffering for more than 5 years and 12% of them are suffering for 1years or less than 1 year and 6% don't know how long they are suffering.

4.15 Symptoms of hypothyroidism

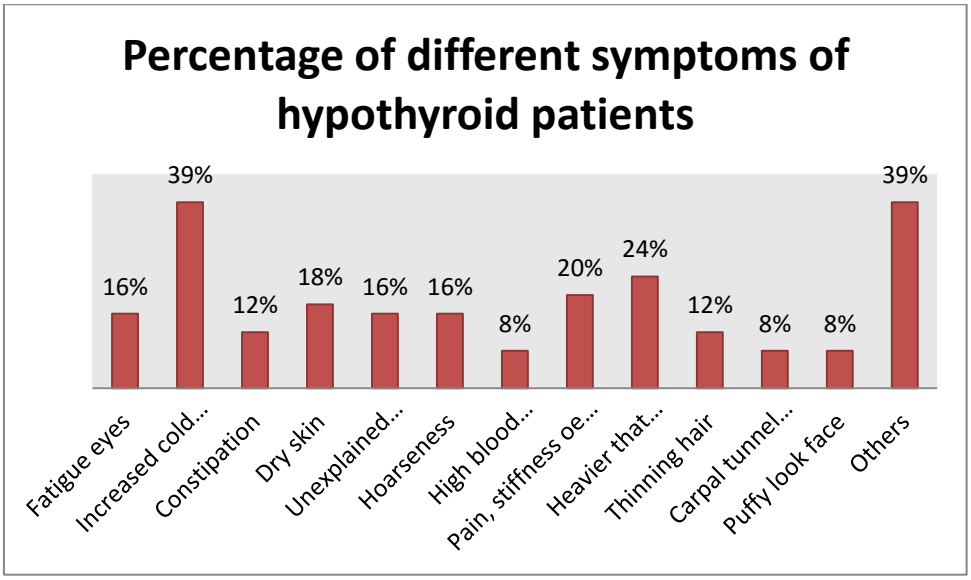

Figure 4.15: symptoms of hypothyroidism

In most of the cases patients cannot understand any prominent symptoms of hypothyroidism, for this most of the patients (39%) having different other symptoms rather than hypothyroidism. Moreover, the most common symptom is increased sensitivity to cold and it is also approximately 39%. Besides, 16% of patients having fatigue eyes, 12% have constipation, dry skin is seen in 18%, unexplained weight gain is found in 16%, hoarseness percentage is also same 16%. 8% of total patients, have high blood pressure, 20% have pain, stiffness in joint, 24% women have iregulation in menstruation, thinning hair in 12%, carpal tunnel syndrome and puffy face both are seen in 8%.

4.16 Type of tests for determining hypothyroidism

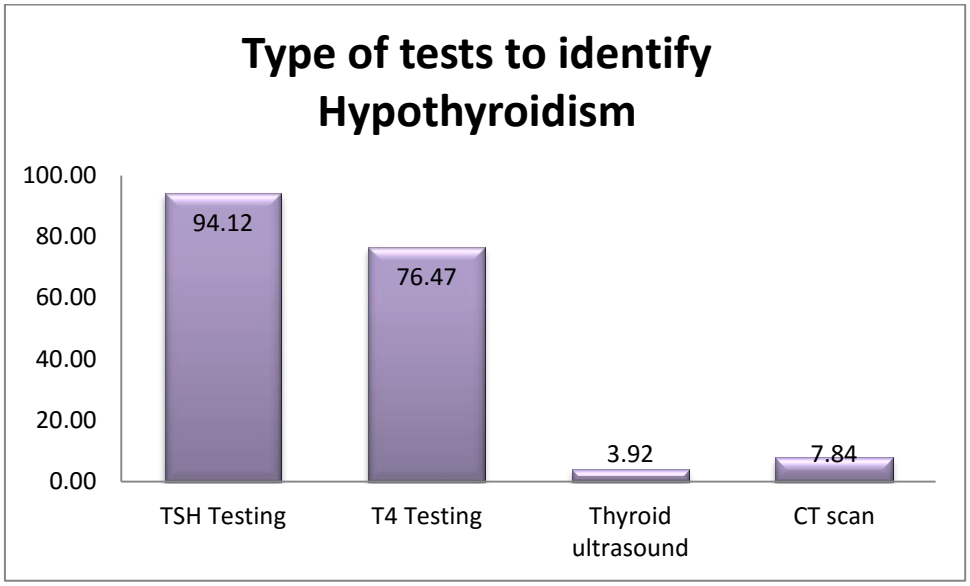

Figure 4.16: tests for determining hypothyroidism

For determining hypothyroidism, among 52 hypothyroid patients most of them (94%) did TSH test and 76% did T4 test, thyroid ultrasound test 4%, and 9% were for CT scan.

4.17 Types of treatments

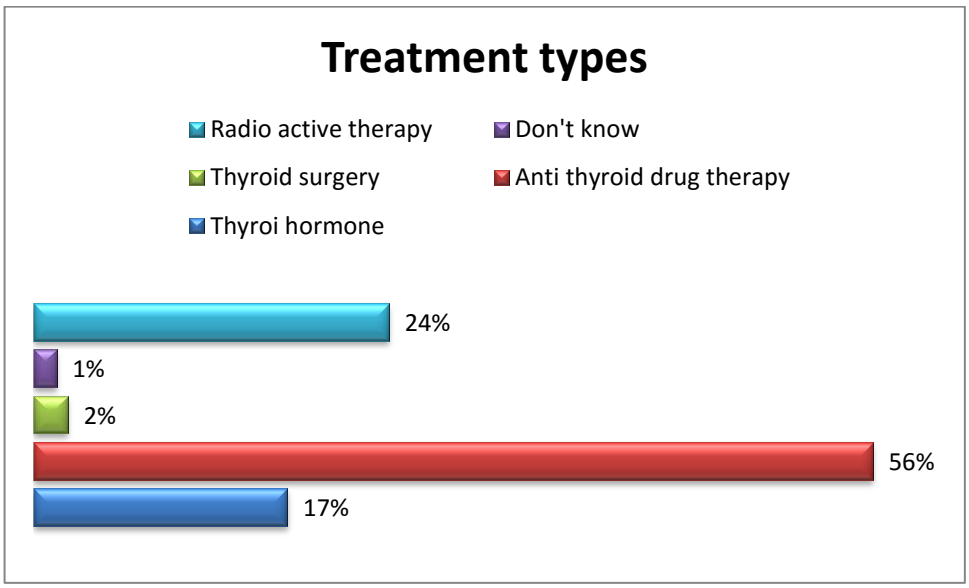

Figure 4.17: Type of treatments of thyroid patients

In this study, among 223 thyroid majority of the patients were found taking anti-thyroid drug therapy, 17% of them are treated with thyroid hormone therapy, 56% are treated with anti-thyroid drug therapy, 24% are taking radio iodine therapy, 2% have thyroid surgery, and 1% do not know what actually they take.

4.18 Medications prescribed for thyroid disordered patients

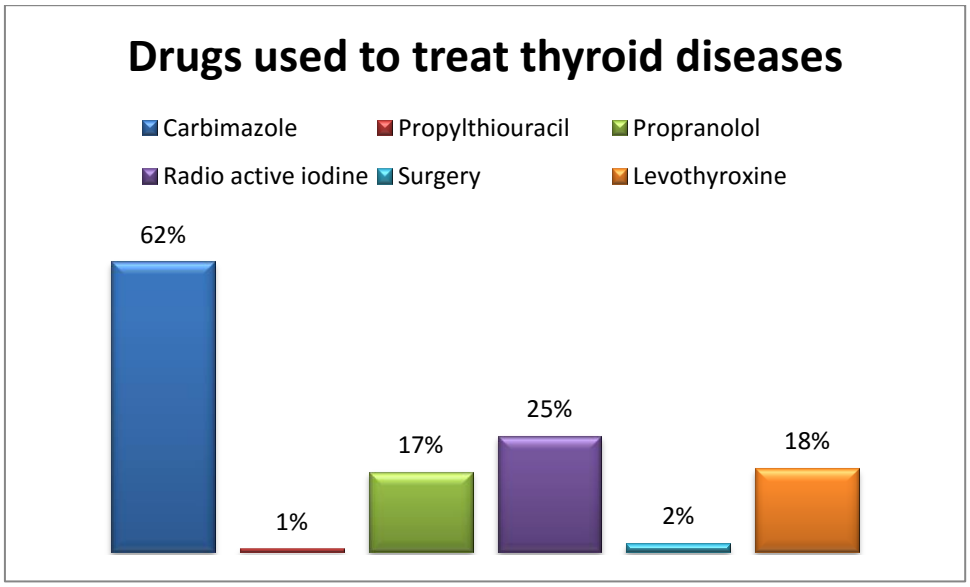

Figure 4.18: Medication taken by thyroid disordered patients

Looking at the above histogram it is observed that, majority of the patients were prescribed antithyroid drug mainly carbimazole 62%. This is because most of our studied respondents were hyperthyroid patients. Only 1% of hyperthyroid patients take propulthiouracil. Along with antithyroid drugs, 17% take beta blocker, mainly propranolol. 25% patients treated with radioactive iodine 131. 2% went for surgery. All hypothyroid patients (18%) are treated with synthetic hormone therapy mainly levothyroxine as their severity is less than Hyperthyroidism patients.

4.19 Medication taking time

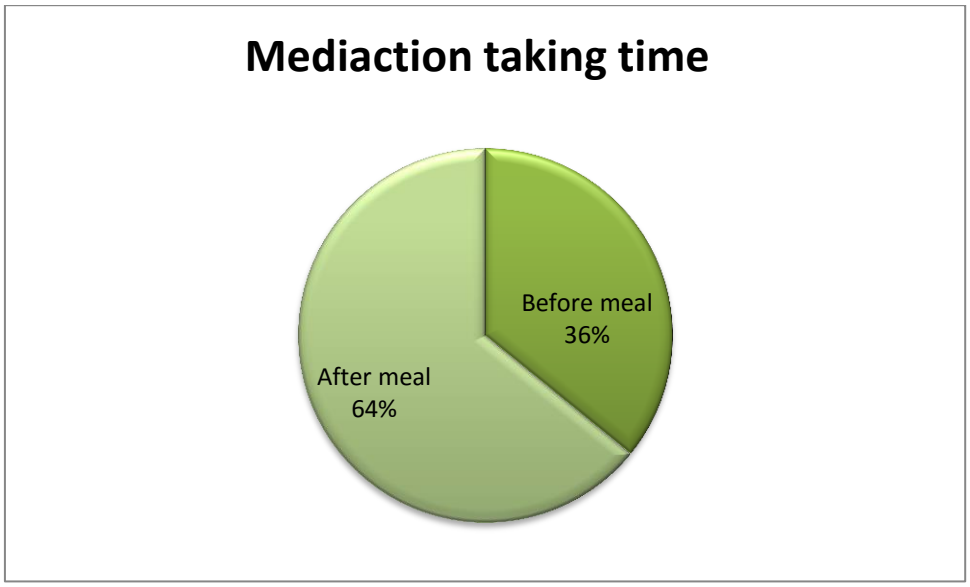

Figure 4.19: Medication taking time

Pie chart shows that, among 223 thyroid patients, 64% takes their medicine after meal and 36% takes before meal.

4.20 Frequency of dosing

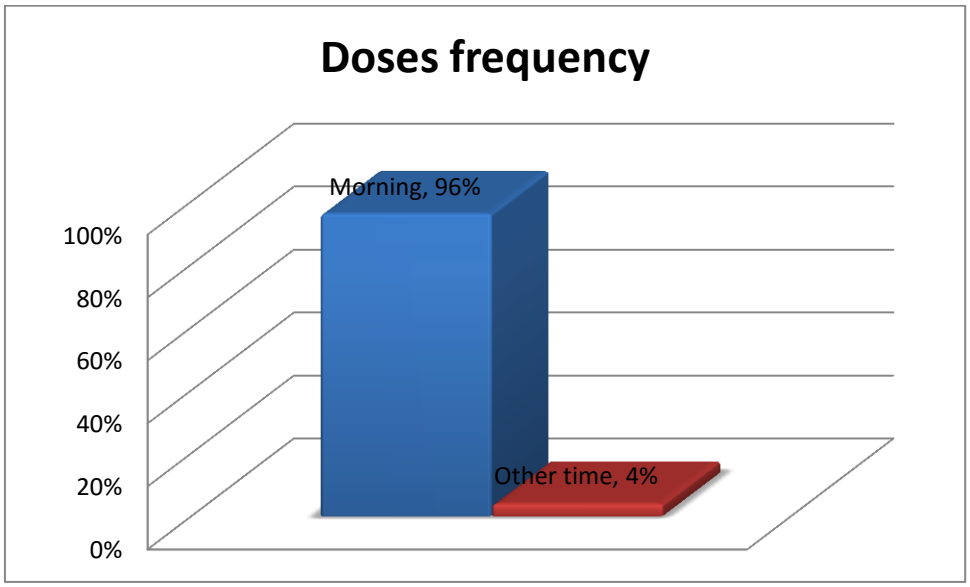

Figure 4.20: frequency of dosing

Basically levothyroxine is prescribed to take at morning, for this reason among 51 hypothyroid patients, majority (96%) take medicine at morning. Only a few patients 4% is prescribed to take medicine at other time

4.21 Complications after having hypothyroid medication

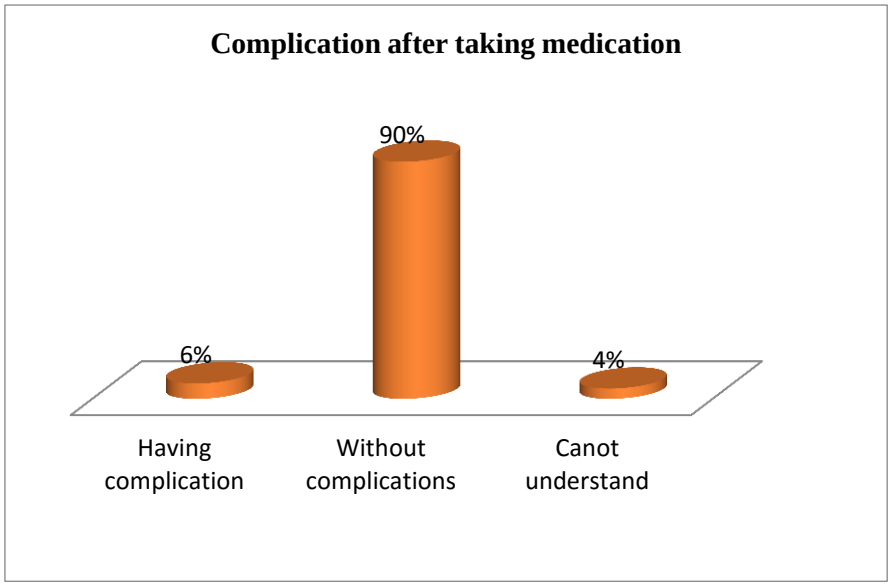

Figure 4.21: Complications after taking medicines

Most of the patients do not find any complication after medication and the percentage is 90. Again 6% had some complications and 4% cannot understand whether they are facing any complications or not.

4.22 Medication on time

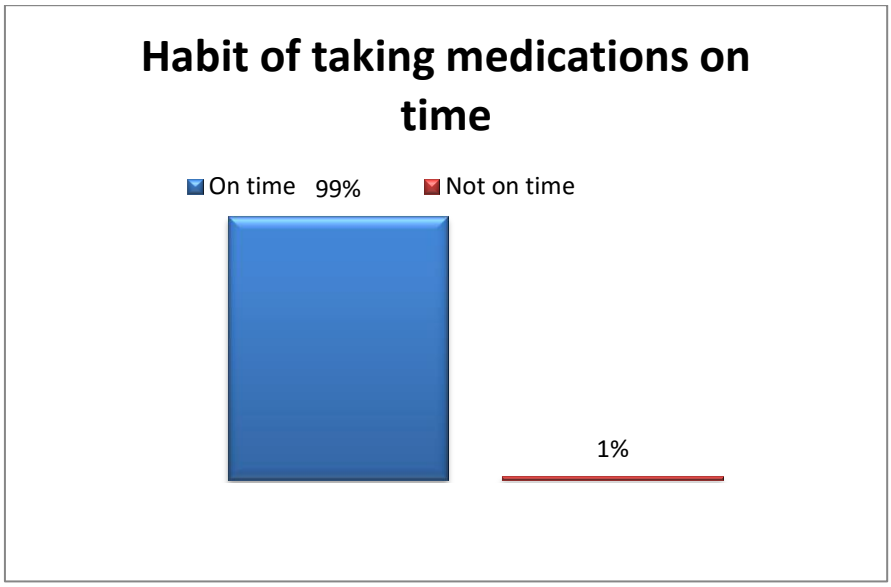

Figure 4.22: Habit of taking medications on time

99% patients take their medication on time and 1% does not regular in taking their medicine.

4.23 Perception about disease recovery

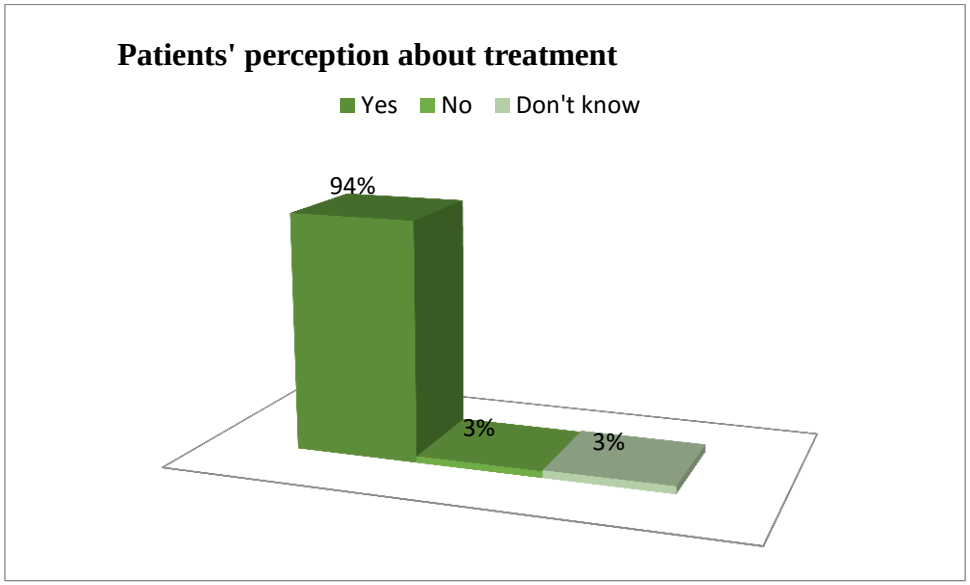

Figure 4.23: Perception about disease recovery

Majority of the respondents 94% aspect they will recover but only 3% don't think that they might be fully recovered and 3% people don't know their fate.

4.24 Satisfactory level of Physician's consultancy and assistance

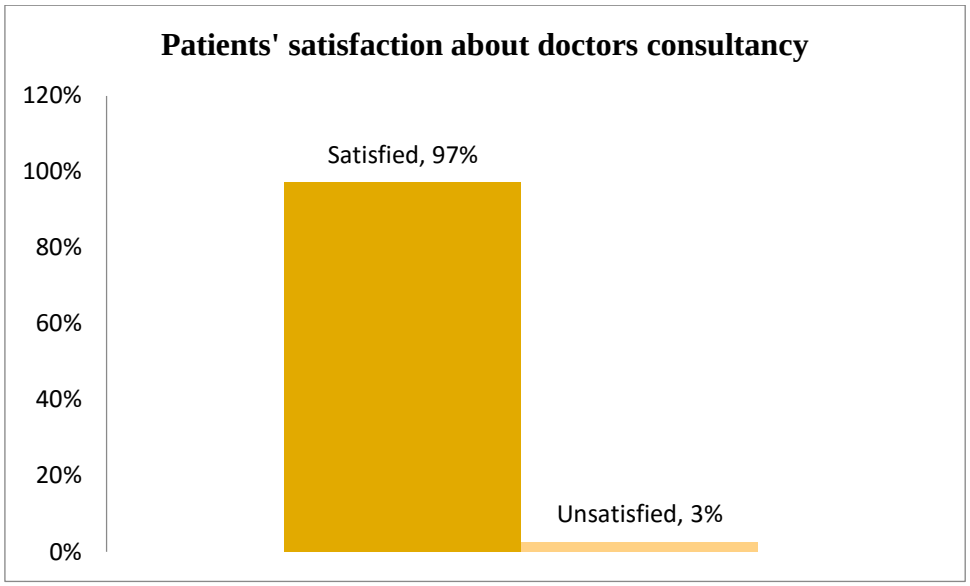

Figure 4.24: Physician's consultancy in satisfied range

It is observed from the recorded data that almost all patients 97% are satisfied about doctor's consultancy and only 3% shows dissatisfaction.

4.25 Regular in check up among the patients

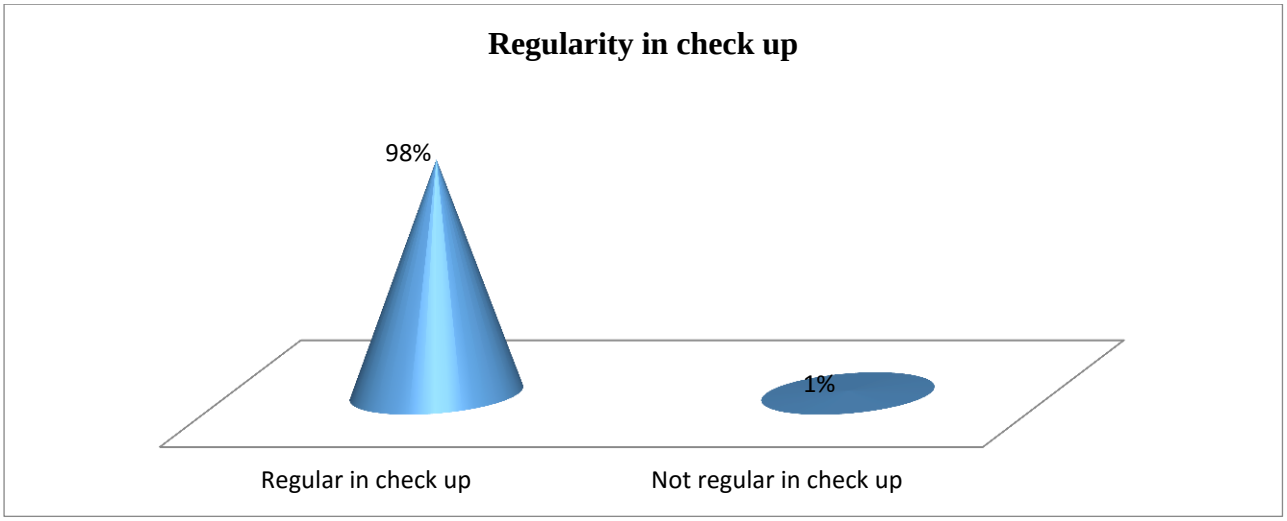

Figure 4.25: Regular in check up

Survey result was very pleasing in this case that almost all the patients were regular having check up. The figure clearly shows up that 98% percent among the patients were in regular checkup and only 2% of them were not regularly checking them up.

4.26 Complexity of dosage administration /treatment form

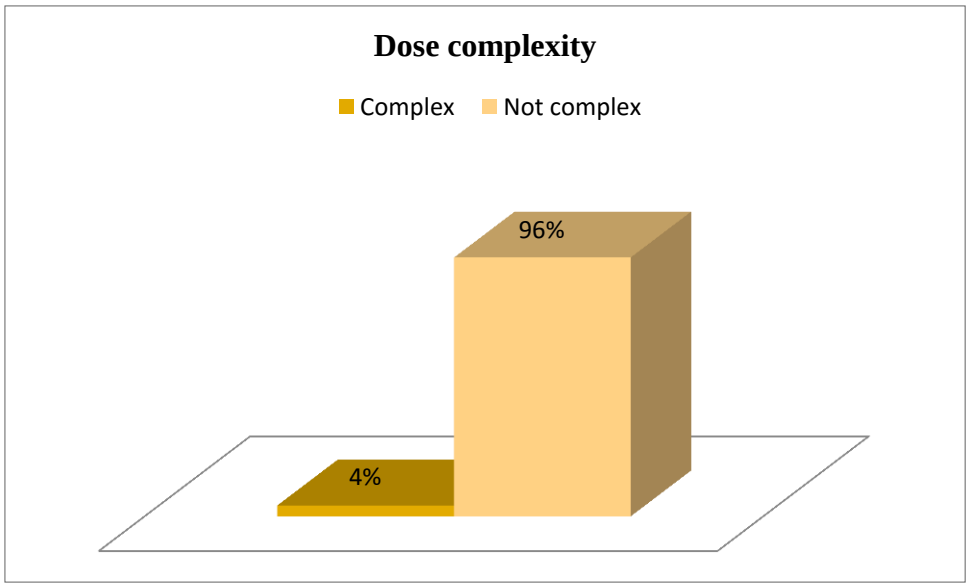

Figure 4.26: Complexity of dosage administration to the patient

Most of the patient were satisfied with their dosage administration or pattern and they didn't find any complexity in their dosage pattern but a little complains about their dosage administration or pattern. The figure makes the sense more clear about the response of the survey during the questioning. As 96% responded negative on the question about the complexity of the dosage pattern. On the other hand only 4% found that it was complex to them.

4.27 Missed dose recovery pattern

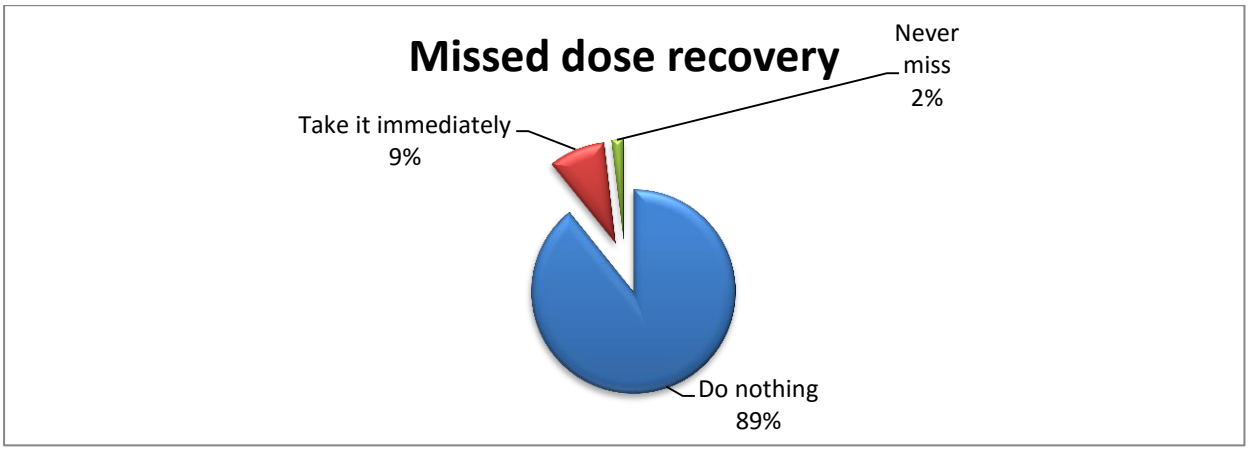

Fig 4.27 Missed dose recovery pattern when they missed dose

Survey result shows that most of the patients were very reluctant about the medicine what they took. From the pie chart of data above the most significant items are 89% patients do nothing if they miss up any regular medicine, 9% took the medicine immediately and 2% responded that they never miss medicine

4.28 Maintaining Weight among the Patients

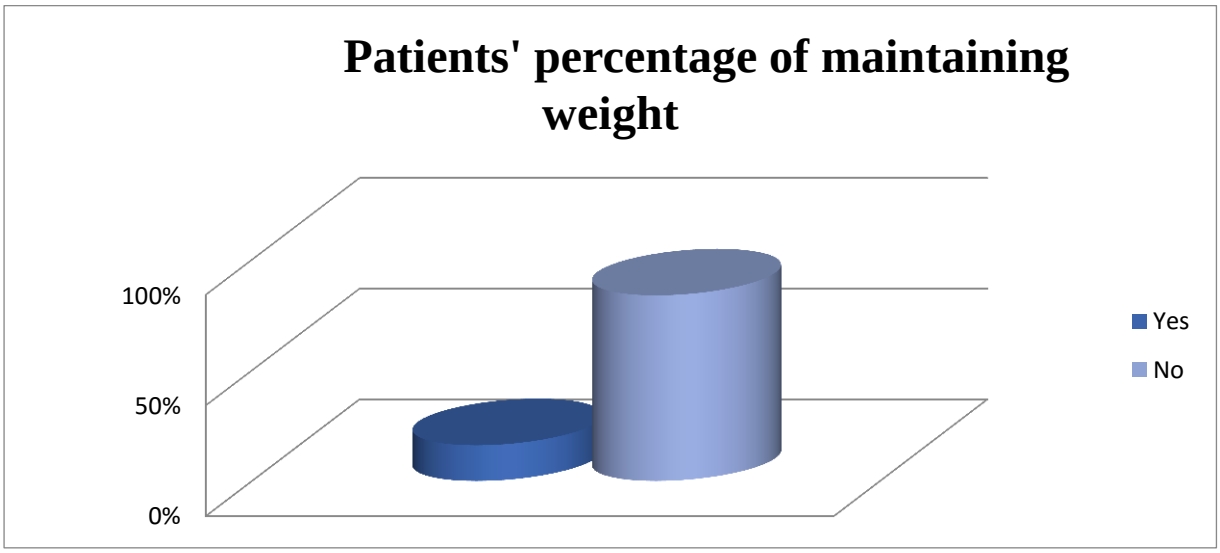

Figure 4.28: Percentage of patients maintaining their weight

This part of survey result shows that maximum patients were not conscious about maintaining their excessive weight. The figure shows the result of the survey conducted

by the researcher. It shows among the sample patients only 16% maintain their weight and rest 84% were not at all aware of maintaining their weight. Again the survey brings out that how the aware people maintains there weight.

4.29 Methods of weight controlling

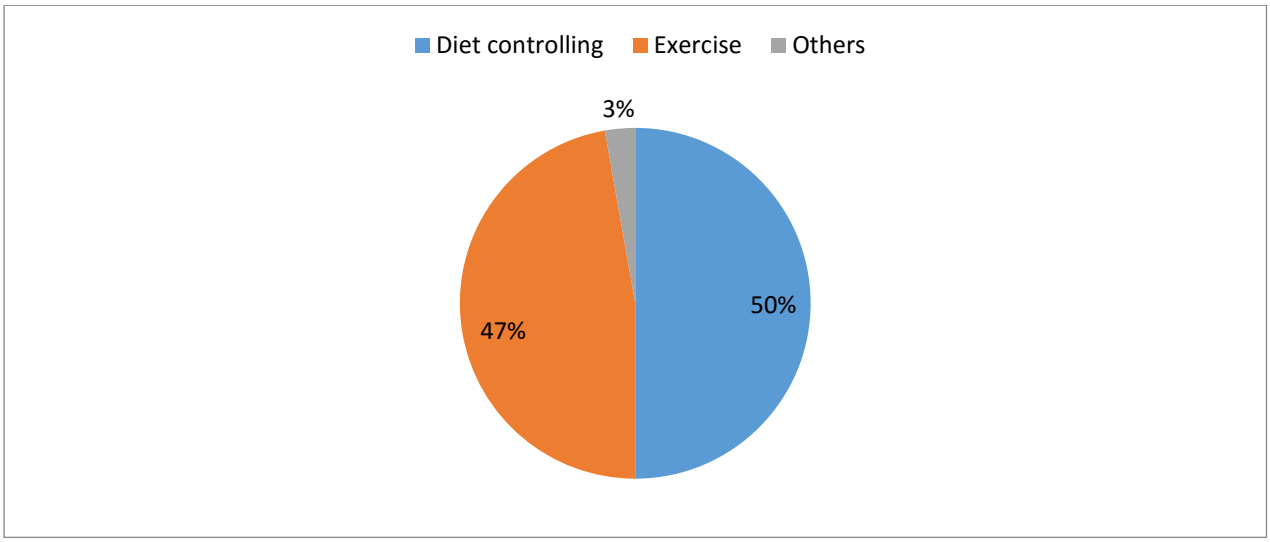

Figure 4.29: Methods used for controlling patients' weight

The pie chat shows that among the aware patients half of them that means, 50% were having diet control and another 47% were taking exercise. Again 3% were having other measures to control their weight.

4.30 Other health problems

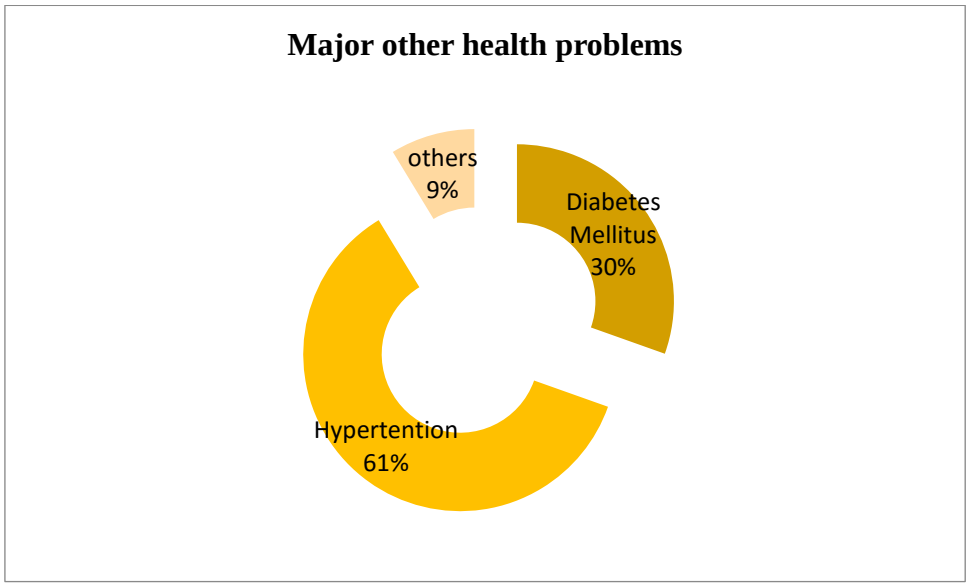

Figure 4.30: Percentage of other major health problems

Total 23 patients found who have some other major problems along with thyroid disease. Among them 61% has hypertension, 30 % has diabetes mellitus and 9% has other problems.

CHAPTER 5

DISCUSSION

Discussion

About 200 million people in the world have some form of thyroid disease. Thyroid diseases for the most part are treatable; however, untreated thyroid disease can produce serious results sometimes in many other parts of the body (Sahni, 2015). The diagnosis of thyroid disease can be particularly challenging. In particular, people may not associate the signs and symptoms with the disease process and thus may not bring them to the attention of themselves against thyroid disorder. For this reasons, if early detection of these disorders would be possible then, it would not become any life threatening problem. Although in Bangladesh the number of thyroid patients are increasing day by day, till now, there is no direct study has been conducted on endocrine patients having thyroid disorder. For this reasons, we have conducted a survey on 273 endocrine disordered patients. Here, our study mainly focused on, Patients' diagnosis, treatment pattern, and patient's knowledge about the disease as well as their awareness that we included in our questionnaire and this study was done in 6 renowned institutions of Dhaka, Bangladesh.

From our study, among our total 273 endocrine patients we have found 223 (82%) with thyroid disorder and rest 50 (19%) have other endocrine disorder mainly glucose homeostasis disorder and tumor of endocrine gland. Basically diabetes is considered as one of the risk factor of thyroid disease and we got 39 (14%) diabetes patients. Moreover, we found 22 (8%) thyroid patients with some other health complications like diabetes (3%) hypertension (6%) and cardiovascular disease (1%).

According to American Thyroid Association prevalence of thyroid disorders is estimated about 2.0% in female and 0.2% in male. In our study, out of 223 thyroid disordered patients 23% are having hypothyroidism,73% having hyperthyroidism and only 4% having nodular thyroid gland.

The prevalence and incidence of thyroid disorders is influenced primarily by sex and age. Thyroid disorders are more common in women than men (DeRuiter, 2002). Among the functional disorder of the thyroid, hypothyroidism is the most common with prevalence ranged from 1.0%- 11.7% in female and 0.9%- 5.14% in male (Sapini, Rokiah & Zuraida, 2009).

Females are 5 times more likely to develop a hypothyroid disease condition over males (Health grade inc, 2015). This study also supports that, Thyroid disease was observed highest in female. We found the female (73%) male (23%) ratio was 2.7:1.

It was found that, majority of the patients are in the age limit 21-40 (42.49%), then age 41-60 are of 41.76%, so middle age usually vulnerable for thyroid disease. However, according to American thyroid association, hyperthyroidism mostly occurs in more than 60 years old people American thyroid association, 2016). As claimed by a study of Malaysia which is quite similar to ours that, Thyroid disease usually develops between the second and the fourth decades of life (sapini, Rokiah & Zuraida, 2009). In accordance to, National Health and Nutrition Examination Survey serum TSH concentrations increased with age in both men and women (Vanderpump, 2011). As stated by Australian bureau of statistics, 71-80 years mostly suffer from thyroid disease and the prevalence is 41.84% (Stevens, 2000). In contrast, in our country this disorder develops in a younger age.

Thyroid dysfunction is associated with changes in body weight as overweight is a symptom of hypothyroidism and sometimes weight is reduced in hyperthyroidism. For this reason BMI is important to estimate body fat. In our study we found that, most of the patients are normal weighted (50%) although the percentage of over weight is not that much low (39%). This is because some hypothyroid patients gained weight due to this disease. However, some conscious patients maintain their health by controlling their diet and taking some kind of physical exercise although they are only 16% of total thyroid dysfunctional patients.

In women and men aged older than 74 years screened at a Colorado health fair, the prevalence of hypothyroidism (defined as a serum thyrotropin greater than 10 mU/L) was 21% and 16%, respectively (Roberts & Ladenson, 2004). We have seen that from 51 hypothyroid disordered patients 57% male and 43% female having hypothyroidism.

However among these 51 hypothyroid patients, the prevalence of subclinical hypothyroidism is estimated to be 61% and overt hypothyroidism is 39%. Again in accordance to a Bangladeshi study, sub-clinical hypothyroidism (6.59%), an overt hypothyroidism (4.97%) but this study is not done only the diseased person like ours, here random subjects were chosen (Paul *et al.,* 2006).

We have also found that most of the patients have been suffering from hypothyroidism around the range of 2 to 5 years. Majority of our patients do not perceive any distinguished symptoms of hypothyroidism however, we found the predominant symptoms are- increased sensitivity to cold, joint paint or swelling, fatigue eyes, weight gain and hoarseness, dry skin, constipation. As claimed by a report, among the important clinical features of hypothyroidism are apathy, fatigue, cold intolerance, slow speech, weight gain, coarse feature and facial puffiness (Sapini, Rokiah & Zuraida, 2009). It is observed that in case of diagnosis almost all the patients (around 95%) did THS test to determine hypothyroidism as well as the percentage of FT_4 testing patients also high (76.47%). After identifying hypothyroidism, all of the patients were prescribed synthetic thyroid hormone, levothyroxine. Hereafter in our study we have seen the most common brand of levothyroxine is thyrox manufactured by Reneta limited. Nearly all of the hypothyroid patients (96%) take their medicine at morning, before meal and 99% patients take their medicine regularly. Henceforth 96% patients were satisfied with their dosage administration or pattern and they did not find any complexity in their dosage pattern.

It is interesting that, 94% believe that they will fully recover as they are facing positive outcome after treatment and they are satisfied with physician consultancy and assistance. For this reason we also found that 98% percent among the patients were in regular checkup and only 2% of them were not regularly checking them up. As, around 76% patients were educated that means at least passed SSC, nearly 83% could provide their family history of the disease and among them 14% have family history of thyroid disease. Majority (50%) got their disorder from their mother.

CHAPTER 6

CONCLUSION

Conclusion

This study indicated that the current condition of hypothyroid disorder in Bangladesh which covers the prevalence of hypothyroid patients among thyroid disordered patients, family history of the disease, consciousness and acquaintance of patients about hypothyroidism furthermore, the study also exhibited the treatment pattern and compliance of hypothyroid patients. From this study it can be concluded that awareness of patients is affected by their educational level and family history of the disease. Conducting survey we found they were conscious about their treatment but still they do not have any clear perception about their disease. From this study the need for strategic plan to increase the awareness of patients about hypothyroidism is recommended. Although this study does not represent the whole country so need to further study in larger sphere. We think, for having better understanding on hypothyroidism in our country this study should be done on a handsome number of patients not only in Dhaka city but also in other districts and rural regions in Bangladesh. In those study we can include the not only the hypothyroid patients but also general people both in urban and rural areas that will help people to become conscious about this disease.

CHAPTER 7

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