Prevalence and Awareness of Hyperthyroidism among Endocrine Disordered Patients of Bangladesh.

A research report submitted to the Department of Pharmacy, East West University, in Partial fulfillment of the requirement for the degree of Bachelor of Pharmacy

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Declaration by the Research Candidate

I, Noor-E-Raihan Nisa , hereby declare that the dissertation entitled "Awareness and Prevalence of Hyperthyroidism in Endocrine Disordered Patients of Bangladesh." submitted to the Department of Pharmacy, East West University in the partial fulfillment of the requirement for the award of the degree Bachelor of Pharmacy is a bonafied record of original research work carried out by me , under the supervision and guidance of **Ms. Nigar Sultana Tithi, Senior Lecturer**, Department of Pharmacy, East West University. The research has not formed the basis for the award of any other degree/diploma/fellowship or other similar title to any candidate of any university.

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Abstract

Thyroid disorder is the second most common endocrine disorder in women both in the developed and less developed world and it is rising significantly. So, a study was conducted on 273 endocrine disordered patients in 6 renowned institutions to know the prevalence of Hyperthyroidism, common symptoms, their diagnostic pattern, treatment pattern, knowledge level and also their awareness regarding these diseases in Bangladesh. This survey was conducted by face to face interview of patients and on the basis of their prescriptions and medical test reports and Obtained data are analyzed by Microsoft excel. Among 173 endocrine disordered patients the prevalence of hyperthyroidism patients in our country is 81.68%. Women are the main victim of hyperthyroidism (73%). The highest suffering age was 21-40 years. 14% provided positive family history and 50% of them got from their mother. The most common diagnosis test is blood test (100%) because it is effective and cheap. Hyperthyroidism having patients are treated mainly with antithyroid drugs (Carbimazol) because most of the patients in our country are subclinical patients. Majority, patients 85% were educated they are at least to primary level, so they were conscious about their diagnosis and were found to take medication timely. But unfortunately their knowledge level about their disease history and perception about recovery was not so satisfactory. Majority had difficulty in sleep (63.8%) and memory loss, weight loss, fatigue, agitation as their symptoms. Prevalence of hyperthyroidism among endocrine patients in this study is very high also. From our so study we find that, knowledge level of patients of our country is relatively poor and needs to be improved. So, some steps should be taken by the authority with the help of professionals to make them aware of this disease.

Key words: Thyroid gland, Endocrine system, Hyperthyroidism, TSH test, Prevalence, Medication, Knowledge level.

Chapter 1

Introduction

1 Introduction

1.1 Overview

Hyperthyroidism is a condition in which the thyroid gland produces too much thyroid hormone such as T4, T3, or both. This can cause rapid heart rate, elevated blood pressure, and hand tremors, as well as a host of other symptoms. Diagnosis of the overactive thyroid and treatment of the underlying cause can relieve symptoms and prevent complications. The thyroid gland produces hormones which regulates the body's metabolism, and affects critical body functions such as energy levels and heart rate. These hormones influence every cell, tissue and organ in the body. About 200 million people worldwide including about 20 million Americans have some form of thyroid disease, and more than 12 percent of the U.S. population will develop a thyroid condition during their lifetime. Perhaps the most stunning statistic is that up to 60 percent of those with thyroid disease are unaware of their condition and that women are five to eight times more likely than men to have thyroid problems. The earliest references said to thyroid gland were in 1600 BC when the Chinese used burnt sponge and seaweed for the treatment of goiters- which is an enlargement of the thyroid gland. In 15 AD, Celsus first described it as a tumour of the neck (bronchoceole). In 150 AD, Galen, a pioneer in modern medicine suggested the use of burnt sponge for the treatment of goiter and also claimed (incorrectly) that the role of thyroid was to lubricate the larynx. In children, an underactive thyroid can be fatal, which is why they are tested for a deficiency at birth. The thyroid gland is a hormone factory. Under normal conditions, the factory foreman -- the molecule calling the shots -- is the aptly named thyroid-stimulating hormone. Called TSH for short, this hormone attaches to a receptor on the thyroid cell surface, triggering a series of signals that provoke the gland to pump out thyroid hormones (News medical, 2016).

Hyperthyroidism is generally treatable with no long-term adverse effects and only rarely is life threatening. In most cases, the problem causing hyperthyroidism can be cured, or the symptoms can be eliminated or greatly reduced. Side effects of medications used to treat hyperthyroidism may be more in older people. Surgical removal of a portion of the thyroid (subtotal thyroidectomy) is generally effective but can result in inadequate production of thyroid hormone in the body. Older people are also at high risk for complications such as cardiac failure. If left untreated, however, hyperthyroidism places under stress on the heart and many other organs.

Hyperthyroidism caused by grave disease (autoimmune disease where the thyroid is overactive, producing an excessive amount of thyroid hormones) usually gets worse over time. It has many complications, some of which are severe and affect quality of life. If they were treated with anti-thyroid drugs, prolonged remissions of the illness may occur. Radioactive iodine also is an effective treatment for grave's disease. It is almost always used in patients with overproducing thyroid nodules. However, this treatment may come with hypothyroidism as its complication. Fortunately, this condition can be easily treated with daily thyroid replacement medication (Allthyroid.org, 2015).

1.2 The Thyroid gland

The thyroid is a butterfly-shaped gland that sits low on the front of the neck. It lies below of Adam's apple, along the front of the windpipe. The thyroid has two side lobes, connected by a bridge (isthmus) in the middle. When the thyroid is its normal size, it can't feel. Brownish-red in color, the thyroid is rich with blood vessels. Nerves important for voice quality also pass through the thyroid. The thyroid secretes several hormones, collectively called thyroid hormones. The main hormone is thyroxine, also called T4. Thyroid hormones have a major impact on the following functions: growth, use of energy and oxygen, heat production, fertility, the use of vitamins, proteins, carbohydrates, fats, electrolytes & water, immune regulation in the intestine. These hormones can also alter the actions of other hormones and drugs. During infancy and childhood, adequate thyroid hormone is crucial for brain development (Nytimes, 2013).

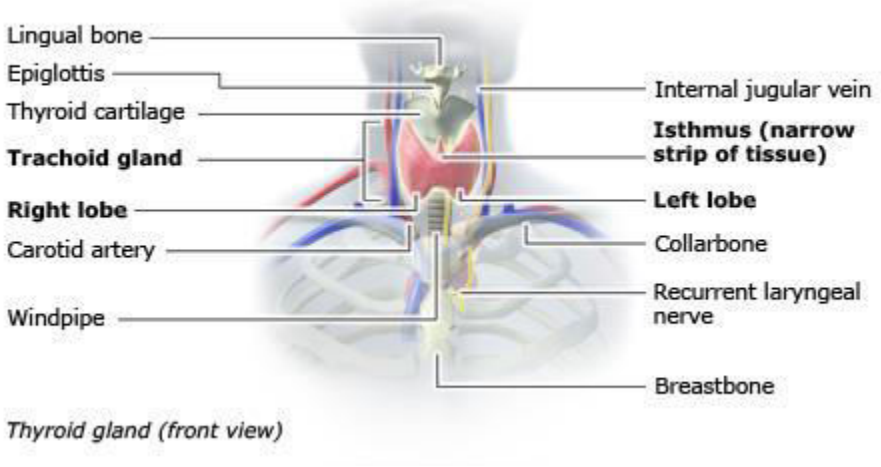


Fig 1.1: Thyroid gland

1.3 Pathophysiology

In healthy patients, the hypothalamus produces thyrotropin-releasing hormone (TRH), which stimulates the anterior pituitary gland to secrete thyroid-stimulating hormone (TSH); this in turn triggers the thyroid gland to synthesize thyroid hormone.

Thyroid hormone concentration is regulated by negative feedback by circulating free hormone primarily on the anterior pituitary gland and to a lesser extent on the hypothalamus. The secretion of TRH is also partially regulated by higher cortical centers.

The thyroid gland produces the prohormone thyroxine (T4), which is deiodinated primarily by the liver and kidneys to its active form, triiodothyronine (T3). The thyroid gland also produces a small amount of T3 directly. T4 and T3 exist in 2 forms: a free, unbound portion that is biologically active and a portion that is protein bound to thyroid-binding globulin (TBG). Despite consisting of less than 0.5% of total circulating hormone, free or unbound T4 and T3 levels best correlate with the patient's clinical status (Medscape,2014).

1.4 Function of the thyroid gland

The thyroid gland is part of the endocrine system of the body. This is the organ of the endocrine system that secretes hormones. The primary function of thyroid gland is to secrete

thyroid hormones. The thyroid hormones are involved in regulating many of its bodily functions, such as breathing, heart rate, temperature, how quickly burn calories, and digestion, among other functions. Babies and children need adequate amounts of thyroid hormones for brain development and growth (Fitsweb.uchc.edu, 2016).

1.5 Hormones of the thyroid gland

The 2 main thyroid hormones are T3 (triiodothyronine) and T4 (thyroxine). T3 and T4 regulate body's temperature, metabolism and heart rate.

The amount of thyroid hormones secreted is controlled by another hormone, called thyroid stimulating hormone (TSH), which is released from the pituitary gland in the brain. TSH stimulates the thyroid to make T3 and T4. Blood tests are done for TSH levels when doctors investigate for thyroid disease. T3 and T4 may also be tested for.

Note that different laboratories may have different reference ranges for normal, so always follow the advice of the doctor.

T3 or triiodothyronine

T3 tests can help diagnose an overactive thyroid (hyperthyroidism). The usual accepted normal range for free T3 (which measures T3 in the bloodstream, but not T3 bound to protein in your body) is between 3.1 pmol/L and 6.8 pmol/L.

T4 (thyroxine)

The normal range usually quoted for free thyroxine (T4) is 12-22 pmol/L. In people with hyperthyroidism (overactive thyroid), free T4 is usually above 22 pmol/L. And for those with hypothyroidism (underactive thyroid), free T4 is usuallly below 12 pmol/L.

Calcitonin

Another hormone that’s produced in your thyroid gland is called calcitonin. This hormone, secreted by a small population of cells known as C cells, is involved in regulating the level of calcium and phosphate in your blood.

The levels of calcitonin are driven by the amount of calcium in your blood. When your blood calcium levels decrease, less calcitonin is secreted and vice versa - when your blood calcium levels increase, levels of calcitonin increase. Calcium and phosphate are both involved in the formation of bones (Fitsweb.uchc.edu, 2016).

1.6 Thyroid hormone synthesis

The main function of the thyroid gland is to make hormones, T4 and T3, which are essential for the regulation of metabolic processes throughout the body. The thyroid contains two hormones, L-thyroxine (tetraiodothyronine, T_4) and L-triiodothyronine (T_3).Iodine is an indispensable component of the thyroid hormones, comprising 65% of T_4's weight, and 58% of T_3's. The thyroid hormones are the only iodine-containing compounds with established physiologic significance in vertebrates.

The first step in the synthesis of thyroid hormones is the organification of iodine. Iodide is taken up, converted to iodine, and then condensed onto tyrosine residues which reside along the polypeptide backbone of a protein molecule called thyroglobulin. This reaction results in either a mono-iodinated tyrosine (MIT) or di-iodinated tyrosine (DIT) being incorporated into thyroglobulin. This newly formed iodothyroglobulin forms one of the most important constituents of the colloid material, present in the follicle of the thyroid unit (Fitsweb.uchc,edu, 2016).

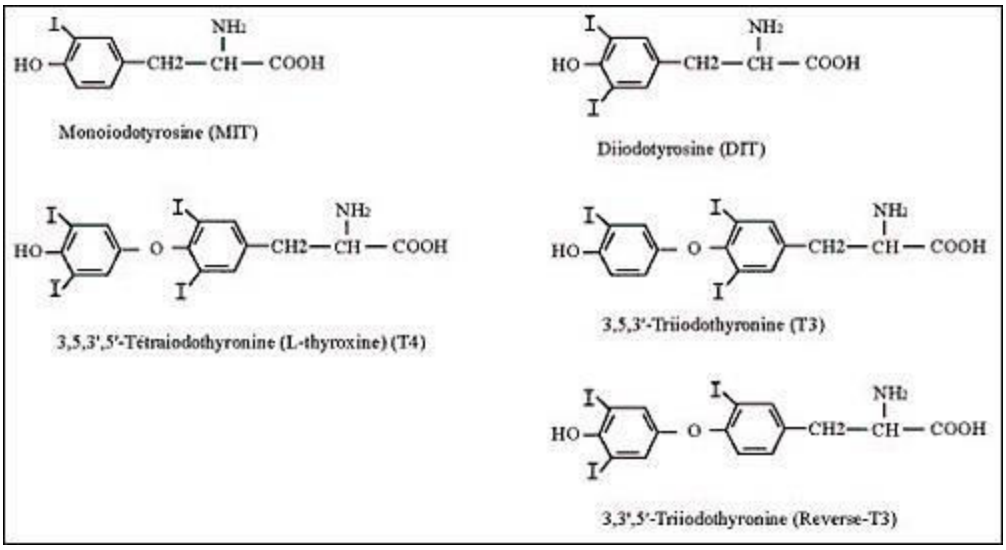


Fig 1.2: Structures of thyroid hormones.

The other synthetic reaction that is closely linked to organification is a coupling reaction, where iodotyrosine molecules are coupled together. If two di-iodotyrosine molecules couple together, the result is the formation of thyroxin (T4). If a di-iodotyrosine and a mono-iodotyrosine are coupled together, the result is the formation of tri-iodothyronine (T3).

From the perspective of the formation of thyroid hormone, the major coupling reaction is the di-iodotyrosine coupling to produce T4. Although T3 is more biologically active than T4, the major production of T3 actually occurs outside of the thyroid gland. The majority of T3 is produced by peripheral conversion from T4 in a deiodination reaction involving a specific enzyme which removes one iodine from the outer ring of T4.

The T3 and T4 released from the thyroid by proteolysis reach the bloodstream where they are bound to thyroid hormone binding proteins. The major thyroid hormone binding protein is thyroxin binding globulin (TBG) which accounts for about 75% of the bound hormone.

In order to attain normal levels of thyroid hormone synthesis, an adequate supply of iodine is essential. The recommended minimum intake of iodine is 150 micrograms a day. Intake of less than 50 micrograms a day is associated with goiter. High iodine levels inhibit iodide oxidation and organification. Additionally, iodine excess inhibits thyroglobulin proteolysis

(this is the principal mechanism for the antithyroid effect of inorganic iodine in patients with thyrotoxicosis) (Fitsweb.uchc.edu, 2016).

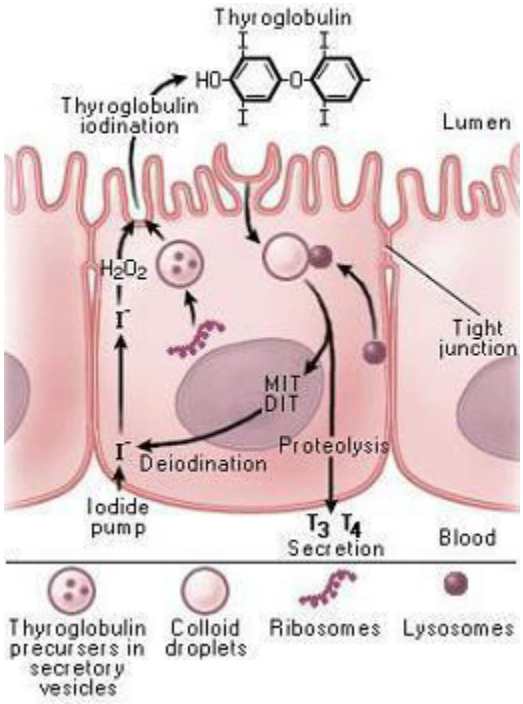


Fig 1.3: Thyroid hormone synthesis

1.7 Thyroid hormone regulation

The production of T4 and T3 in the thyroid gland is regulated by the hypothalamus and pituitary gland. To ensure stable levels of thyroid hormones, the hypothalamus monitors circulating thyroid hormone levels and responds to low levels by releasing thyrotropin-releasing hormone (TRH).This is produced in a region in the brain called the hypothalamus, which monitors thyrotropin level..This TRH then stimulates the pituitary to release thyroid stimulating hormone (TSH). Thyrotropin (also called thyroid-stimulating hormone or TSH) is another very important hormone in the process. It is secreted by the pituitary gland; this hormone directly influences the process of iodine trapping and thyroid hormone production. When thyroxine levels drop even slightly, the pituitary gland goes into action to pump up secretion of thyrotropin so that it can stimulate thyroxine production. So, when T4 levels fall, TSH levels increase. When thyroid hormone levels increase, production of TSH decreases, which in turn slows the release of new hormone from the thyroid gland. Cold temperatures, can also

increase TRH levels. This is thought to be an intrinsic mechanism that helps keep us warm in cold weather. Elevated levels of cortisol, as seen during stress and in conditions such as Cushing's syndrome, lowers TRH, TSH and thyroid hormone levels as well. The thyroid gland needs iodine and the amino acid L-tyrosine to make T4 and T3. A diet deficient in iodine can limit how much T4 the thyroid gland can produce and lead to hypothyroidism.T3 is the biologically active form of thyroid hormone. The majority of T3 is produced in the peripheral tissues by conversion of T4 to T3 by a selenium-dependent enzyme. Various factors including nutrient deficiencies, drugs, and chemical toxicity may interfere with conversion of T4 to T3.Another related enzyme converts T4 to an inactive form of T3 called reverse T3 (rT3). Reverse T3 does not have thyroid hormone activity; instead it blocks the thyroid hormone receptors in the cell hindering action of regular T3.Ninety-nine percent of circulating thyroid hormones are bound to carrier proteins, rendering them metabolically inactive. The remaining "free" thyroid hormone, the majority of which is T3, binds to and activates thyroid hormone receptors; exerting biological activity. Very small changes in the amount of carrier proteins will affect the percentage of unbound hormones. Oral contraceptives, pregnancy, and conventional female hormone replacement therapy may increase thyroid carrier protein levels and, thereby, lower the amount of free thyroid hormone available. Thyroid needs iodine (a chemical element that's an essential part of our diet) in order to manufacture these thyroid hormones. Iodine plays an important role in the function of the thyroid gland. It is the chief component of thyroid hormones, and is essential for their production. Iodine is obtained from the water we drink and the food we eat. Iodides ingested orally are absorbed from the gastrointestinal tract. Iodine is removed from the circulating blood by the cells of the thyroid gland and used for synthesis of the thyroid hormones. The basal membrane of the thyroid cell has the specific ability to pump the iodide actively to the interior of the cell, using a pump called the sodium-iodide symporter (NIS). This is called iodide trapping. In a normal gland, the iodide pump concentrates the iodide to about 30 times its concentration in the blood (Lifeextension, 2016).

1.8 Common types of thyroid problems

- Goiter: A general term for thyroid swelling. Goiters can be harmless, or can represent iodine deficiency or a condition associated with thyroid inflammation called Hashimoto's thyroiditis. Signs & symptoms of the goiter are: a visible swelling at the base of the neck that may be particularly obvious when shave or put on makeup, a tight feeling in throat, difficulty swallowing & breathing.
- Thyroiditis: Inflammation of the thyroid, usually from a viral infection or autoimmune condition. Thyroiditis can be painful. The signs & symptoms of this type of thyroid disease are: painful goiter, pain in front of neck radiating to the jaw and ears, painful swallowing, fever, malaise, nausea, vomiting, increased heart rate, palpitations, hyperactivity.
- Hyperthyroidism: Excessive thyroid hormone production. Hyperthyroidism is most often caused by Graves's disease or an overactive thyroid nodule. Symptoms of hyperthyroidism is: Nervousness, fatigue, weakness, palpitations, heat intolerance, excessive sweating, dyspnea, diarrhea, insomnia, oligomenorrhea. Signs of this disease are: weight loss, hair loss, tachycardia, proximal myopathy, warm, moist skin, hyperkinesis, stare, lid leg, emotional liability, hyperactive reflexes, and thyroid enlargement.
- Hypothyroidism: Low production of thyroid hormone. Thyroid damage caused by autoimmune disease is the most common cause of hypothyroidism. Sign & symptoms of this disease are: fatigue, increased sensitivity to cold, dry skin, weight gain, puffy face, muscle weakness, elevated blood cholesterol level, pain, stiffness or swelling in joints, muscle aches, tenderness and stiffness, depression and impaired memory.
- Grave's disease: An autoimmune condition in which the thyroid is over stimulated, causing hyperthyroidism. Its signs & symptoms are: increased sweating, weight loss, nervousness, hand tremors, anxiety, an irregular or rapid heartbeat & enlargement of the thyroid gland.
- Thyroid cancer: An uncommon form of cancer, thyroid cancer is usually curable. Surgery, radiation and hormone treatments may be used to treat thyroid cancer. Its signs & symptoms are: a lump in the neck, swelling in the neck, pain in front of the neck, sometimes going up to the ears, trouble swallowing, hoarseness or other voice changes that do not go away, trouble breathing & a constant cough that is not due to a cold.

- Thyroid nodule: A small abnormal mass or lump in the thyroid gland. Thyroid nodules are extremely common. Few are cancerous. They may secrete excess hormones, causing hyperthyroidism, or cause no problems. Signs & symptoms of this disease are: unexplained weight loss, intolerance to heat, tremor, nervousness & rapid or irregular heartbeat.
- Thyroid storm: A rare form of hyperthyroidism in which extremely high thyroid hormone levels cause severe illness. Signs & symptoms of this disease are: high fever, persistent sweating, shaking, agitation, restlessness, confusion, diarrhea, tachycardia, unconsciousness (Healthline, 2015).

1.9 Hyperthyroidism

Hyperthyroidism means an overactive thyroid gland. When the thyroid gland is overactive it makes too much thyroxine. The extra thyroxine causes many of the body's functions to speed up. In contrast, if have hypothyroidism, body make too little thyroxine; this causes many of the body's functions to slow down**.**Thyrotoxicosis is a term that may be used by doctors instead of hyperthyroidism. The two terms mean much the same (Patient. my heath, 2015).

1.10 Classification of hyperthyroidism

Hyperthyroidism can be classified into 2 different types.

1.10.1 Overt hyperthyroidism

Overt hyperthyroidism is defined as the syndrome of hyperthyroidism associated with suppressed TSH and elevated serum levels of T4 or T3. Most patients with overt hyperthyroidism have a dramatic constellation of symptoms. These symptoms characteristically include anxiety, emotional liability, weakness, tremor, palpitations, heat intolerance, increased perspiration, and weight loss despite a normal or increased appetite.

While the combination of weight loss and increased appetite is a characteristic finding, some patients gain weight, in particular younger patients, due to excessive appetite stimulation. Other symptoms that may be present include hyper defecation (not diarrhea), urinary

frequency, oligomenorrhea or amenorrhea in women, and gynecomastia and erectile dysfunction in men (Uptodate, 2015).

1.10.2 Subclinical hyperthyroidism

Subclinical hyperthyroidism is a condition that develops when the amount of thyroid stimulating hormone (TSH) in the blood is low. TSH is made in the brain and controls how much thyroid hormone is made. Thyroid hormones help control body temperature, heart rate, growth, and weight. Subclinical hyperthyroidism can lead to hyperthyroidism. The most common cause of true subclinical hyperthyroidism is toxic nodular goiter, especially in the elderly. Subclinical hyperthyroidism is associated with increased risks of coronary heart disease (CHD) mortality and incident atrial fibrillation, with highest risks of CHD mortality and atrial fibrillation when thyrotropin level is lower than 0.10 mIU/L. (Uptodate ,2015).

1.11 Hyperthyroidism in neonates

This condition occurs rarely and is principally seen in newborn babies of mothers who have Graves' disease. It occurs in around one out of 70 pregnancies with Graves' disease. Occasionally it is seen in neonates of euthyroid mothers. Maternal TSH-receptor antibody levels may be high. Clinical features vary but may include tachycardia, pulmonary hypertension and cardiopulmonary failure. Neonates commonly develop tachycardia and are treated with carbimazole and beta-blockers once the diagnosis is confirmed (Patient.myhealth, 2015).

1.12 Hyperthyroidism in children

- Girls have a higher incidence than boys.
- Thyrotoxicosis is less common in children than in adults, with an incidence in the UK and Ireland of 0.9 per 100,000 per year, of which 96% of cases are autoimmune.
- The onset of symptoms may be insidious and subsequently associated with a delay in diagnosis.

- Weight loss, tiredness, change in behavior and heat intolerance are the most common symptoms.
- Pediatric patients are treated in a similar fashion to adults: anti-thyroid medication, radio-iodine (for adolescents) and surgery (Patient. my heath, 2015).

1.13 Signs & symptoms of hyperthyroidism

Symptoms and signs are different for each person. Here are the most common ones:

- Nervousness
- Irritability
- Sweating more than normal
- Thinning of the skin
- Fine, brittle hair
- Weak muscles, especially in the upper arms and thighs
- Shaky hands
- Fast heartbeat (palpitations)
- High blood pressure
- More bowel movements than normal
- Weight loss
- Problems sleeping
- Prominent eyes
- Sensitivity to bright light
- Confusion
- Irregular menstrual cycle in women
- Tiredness (fatigue)
- Thyroid gland is larger than normal (goiter)

1.14 Causes of hyperthyroidism

Follicular thyroid cancer

Though cases such as this are rare, some individual who have thyroid cancer may go onto develop hyperthyroidism as a result of the cancer cells in the thyroid gland beginning to produce thyroxine or triiodothyronine.

Grave's disease

Grave's disease is considered to be the most common cause of hyperthyroidism. The autoimmune condition, which weakens the immune system by mistaking healthy substances I the body for dangerous and toxic substances before attacking them, can be genetic and occurs at any age. According to NHS information, the condition is more common among women, notably those who are aged between 20 and 40 and is also more likely to develop in individuals who smoke. In a healthy and normal immune system, the body manufactures antibodies which protect it from bacteria and infection. In an autoimmune disorder such as Graves ' disease, the antibodies begin attacking healthy tissue instead. The reason for this is unknown but in the case of Graves ' disease it could result in what is known as graves' opthalmopathy, which causes the eyes to bulge out of their sockets often causing double vision and also commonly leading onto the development of hyperthyroidism (Nutririonist, 2016).

Iodine supplements

The food we eat will usually contain enough iodine to keep the thyroid gland producing thyroid hormones. However, individuals who decide to take extra iodine using supplements can find that this results in overproduction of the thyroid hormones. This form of hyperthyroidism is known as iodine-induces hyperthyroidism and in most cases will usually only occurs if non-toxic nodules are present in the thyroid gland (Nutririonist, 2016).

Amiodarone

Amiodarone is a form of medication which is used to treat heart irregularities. The drug works by correcting the rhythm of the heart and slowing a heart that is beating too fast. Individuals who have non-toxic nodules in their thyroid gland may find that taking amiodarone can induce hyperthyroidism as it contains iodine (Nutritionist, 2016).

Thyroid nodules

Approximately 2% of men & 8% women develop thyroid lumps or nodules at some point during their lives. In 95% of cases these lumps are benign, but for a small number of individuals they are malignant. Even though for most individuals with thyroid lumps the risk of developing cancer will be minor, the nodules can still contain what is known as 'abnormal thyroid tissue', which hinders the regular production of thyroid hormones, subsequently resulting in an over active thyroid. If only a single thyroid nodule or lump develops in your thyroid gland, this is known as a toxic thyroid nodule, and if two thyroid lumps or nodules develop, this is known as a toxic multinodular goiter, which after Graves ' disease is said to be the second most common cause of hyperthyroidism, accounting for approximately 5% of cases. Thyroid nodules are more common among those with a history of thyroid cancer so it is worth making yourself aware of your family medical history. The nodules themselves may cause slight discomfort though in most cases individuals either spot them in the minor or are alerted to them by friends or family before they become aware of persistent pain (Nutritionist, 2016).

1.15 Risk factors

Gender: the incidence of thyroid disorders is reported to be higher in women than in men.

Age: the risk of developing thyroid disease is elevated in individuals 50 years of age, and above.

Stress: it has been observed that major stress may contribute to disturbances in thyroid function. However, the majority of studies examining this effect have been conducted in psychiatric patients, and the results may therefore be influenced by the study population.

Family history: patients with a family history of thyroid disease are at an increased risk of developing an autoimmune thyroid condition. Similarly, a family history of autoimmune disease also increases the risk of thyroid disorders, albeit to a lesser extent.

Thyroid surgery / medical treatment: Treatment of hepatitis C with interferon 2α has been associated with increased risk of thyroid dysfunction, which usually resolved upon discontinuation of treatment. Recent exposure to a surgical antiseptic that includes iodine (such as Povidone) can increase the risk of temporary thyroiditis, hypothyroidism or hyperthyroidism.

Radiation Exposure: exposure of the neck area to radiation, such as in the treatment of head or neck cancer, or accidental environmental exposure, increases the risk of autoimmune thyroid disease and thyroid cancer. Medical tests that use iodine-based contrast enhancing dyes can slightly increase the risk of developing a temporary thyroiditis, hypothyroidism or hyperthyroidism.

Pregnancy: the risk of developing thyroid disorders increases during pregnancy. Increased levels of human chorionic gonadotropin (hCG) and estrogen are thought to be responsible for alterations in the levels of thyroid hormones.

Smoking: thiocyanate in cigarettes adversely affects the thyroid. Smokers, therefore, have an increased risk of developing autoimmune thyroid diseases, and smoking can exacerbate existing symptoms of thyroid disease.

Diet: insufficient dietary iodine increases the risk of hypothyroidism (most common in developing countries). In contrast, dietary supplementation with iodine-containing herbal remedies among individuals with sufficient dietary iodine intake can increase the risk of autoimmune thyroid disease. In susceptible people (usually those with underlying thyroid autoantibodies), foods containing goitrogens (chemicals that can promote goitre) can induce hypothyroidism when eaten raw and in large quantities. Some foods that are high in goitrogens include cabbage, brussel sprouts, broccoli, turnips, rutabagas, kohlrabi, radishes, cauliflower, African cassava, millet, soy and kale (Myhivclinic.org, 2016).

1.16 Complications

Hyperthyroidism can lead to a number of complications:

Heart problems Some of the most serious complications of hyperthyroidism involve the heart. These include a rapid heart rate, a heart rhythm disorder called atrial fibrillation and congestive heart failure — a condition in which the heart can't circulate enough blood to meet of the body's needs. These complications generally are reversible with appropriate treatment.

Brittle bones Untreated hyperthyroidism can also lead to weak, brittle bones (osteoporosis). The strength of the bones depends, in part, on the amount of calcium and other minerals they contain. Too much thyroid hormone interferes with body's ability to incorporate calcium into bones.

Eye problems People with Graves' ophthalmopathy develop eye problems, including bulging, red or swollen eyes, sensitivity to light, and blurring or double vision. Untreated, severe eye problems can lead to vision loss.

Red, swollen skin In rare cases, people with Graves' disease develop Graves' dermopathy, which affects the skin, causing redness and swelling, often on the shins and feet.

Thyrotoxic crisis Hyperthyroidism also places at risk of thyrotoxic crisis —a sudden intensification of the symptoms, leading to a fever, a rapid pulse and even delirium. If this occurs, seek immediate medical care.

Osteoporosis

If it does not treat hyperthyroidism, it also runs the risk of developing osteoporosis. It can gradually lose bone mineral density because uncontrolled hyperthyroidism can cause the body to pull calcium and phosphate out of the bones and to excrete too much calcium and phosphorous (through the urine and stool). It needs calcium and phosphorous to maintain healthy bones, so if bones aren't absorbing enough those minerals or losing them at an increased rate, they can become less dense. This can also make the body temporarily hungrier

for calcium after thyroid surgery. Eventually, it may develop osteoporosis—meaning that bones aren't as strong as they should be and making prone to fractures (Endocrineweb, 2014).

Pregnancy problems

Miscarriage, preterm birth, preeclampsia (high blood pressure during pregnancy), fetal thyroid dysfunction, and poor fetal growth are all possible complications of untreated hyperthyroidism (Everyday, 2016).

1.17 Test & diagnosis of hyperthyroidism

The proper treatment of hyperthyroidism depends on recognition of the signs & symptoms of the disease and determination of the etiology. Diagnosing thyroid disease is a process that can incorporate numerous factors, including clinical evaluation, blood tests, imaging tests, biopsies and other tests. Various types of thyroid tests are given below:

1.17.1 Clinical Evaluation

A clinical part of detecting and diagnosing thyroid disease is the clinical evaluation conducted by a trained practitioner. As part of a through clinical evaluation, practitioner typically should do the following:

- Feel(also known as "palpating") the neck
- Listen to thyroid using a stethoscope
- Test the reflexes
- Check the heart rate, rhythm and blood pressure
- Measure the weight
- Measure body temperature
- Examine the face
- Examine the eyes
- Observe the general quality and quantity of hair
- Examine the skin
- Examine nails and hands

- Review other clinical signs (About, 2016).

1.17.2 Thyroid blood tests

A diagnosis can be confirmed with blood tests that measure the levels of thyroxine and TSH in the blood. The blood tests that may be done as part of a thyroid diagnosis include the following:

1.17.2.1 TSH tests

The TSH (or Thyroid Stimulating Hormone) assay has been recognized as an exquisitely sensitive indicator of thyroid status. TSH assays have therefore been widely adopted as the first-line thyroid function test. Reference range of the TSH is 0.5-4.70 µIU/mL. In ambulatory patients with intact hypothalamic and pituitary function, a normal TSH result excludes hypo- or hyperthyroidism; whereas elevated and suppressed TSH results are diagnostic of hypo- and hyperthyroidism, respectively. Abnormal TSH results are generally confirmed with a complementary determination of thyroid hormone levels (Msd, 2015).

1.17.2.2 Total T4/ Total Thyroxine

The T4 (or Thyroxin) assay complements the TSH assay, and is used to confirm a thyroid disorder when suggested by an abnormal TSH. Furthermore, the T4 assay may become the first-line assay in conditions that are known to possibly compromise the reliability of TSH results. For example, several months may be required for the dynamics of the regulatory mechanism (along the hypothalamic-pituitary-thyroid axis) to fully equilibrate after a treatment regimen is initiated or significantly altered; during this time TSH results may be misleading. Secondary and tertiary hypothyroidism are other conditions in which TSH results may be misleading, and the differential diagnosis is likely to rely on T4 (Free T4) results complemented by the characteristic profile of TSH results obtained during a TRH-stimulation testing procedure. Reference range of the free T4 is the 4.5-12.5 µg/dL.

The free form of the hormone (Free T4) is generally considered to provide the more reliable indicator of true thyroid status, because only the free form of the hormone is physiologically active. The total hormone concentration (Total T4) is dependent on the concentration of

thyroid transport proteins, specifically thyroid binding globulin (TBG), which is influenced by many common factors (Msd, 2015).

1.17.2.3 Total T3/Total Triiodothyronine

The T3 (or Triiodothyronine) assay is another assay which is used in the diagnosis of thyroid disorders. In developing hyperthyroidism, the Free T3 concentration is a more sensitive indicator of developing disease than is T4 (free T4), and the former is therefore preferred for confirming hyperthyroidism that has already been suggested by a suppressed TSH result. However, the reverse is true for hypothyroidism. In developing hypothyroidism, T4 (free T4) is the more sensitive indicator of developing disease than is T3 (Free T3), and is therefore preferred for confirming hypothyroidism that has already been suggested by an elevated TSH result. Its reference range is 2.3-4.2 pg/mL.

The T3 assay is also useful for diagnosing a variant of hyperthyroidism known as T3 thyrotoxicosis, wherein T4 levels remain within the thyroid range.

1.17.2.4 T3 resin uptake

The T3 Resin Uptake assay is used in calculating the Free Thyroxin Index (FTI). It is interpreted in conjunction with a Total T4 or Total T3 and corrects for abnormal Thyroid Binding Globulin (TBG) to give an estimate of the amount of unbound (free) T4 available. With the ability to calculate Free T4 (nowadays), the Free T4 assay is now preferred over the Free Thyroxin Index or T3 Resin Uptake.

- Free T3/ Free Triiodothyronine
- Thyroglobulin/Thyroid binding globulin/TBG
- Reverse T3
- Thyroid peroxidase antibodies/Antithyroid Peroxidase antibodies
- Antithyroid microsomal antibodies/Antimicrosomal antibodies
- Thyroglobulin antibodies/ Antithyroglobulin antibodies
- Thyroid receptor antibodies

- Thyroid stimulating immunoglobulins (Msd,2015).

1.17.2.5 Thyroid biopsy/Fine needle aspiration

Fine Needle Aspiration (FNA) has become the single-most important step in the evaluation of a thyroid nodule. A number of recent studies have confirmed the high accuracy of FNA, with sensitivities and specificities in the range of greater than 80% and 90%, respectively. The accuracy in diagnosing thyroid abnormalities is dependant both on the expertise of the cytopathologist interpreting the biopsy specimen, as well as the physician performing the biopsy.

Provided adequate sample is removed on biopsy, FNA of thyroid nodules can be used to categorize tissue into the following categories: malignant, benign, thyroiditis, follicular neoplasm, suspicious, or non-diagnostic. The technique has decreased unnecessary operative procedures in patients with benign nodules and increased the probability that surgery will be performed on those with malignant disease. The one drawback lies with hypocellular samples and aspirates with high follicular cellularity. Hypocellular aspirates may be encountered in cystic nodules. Aspirates with a high follicular cellularity suggest follicular neoplasm, however, FNA cannot reliably distinguish a benign follicular neoplasm from a malignant one, and thus surgical resection remains the necessary recourse to obtain a definitive diagnosis. Below is an example of a fine needle aspiration from a nodule containing papillary carcinoma. Notice that the cells form papillary structures, the cells have internuclear inclusions (INI), and that the nuclei show grooves.(Msd, 2015).

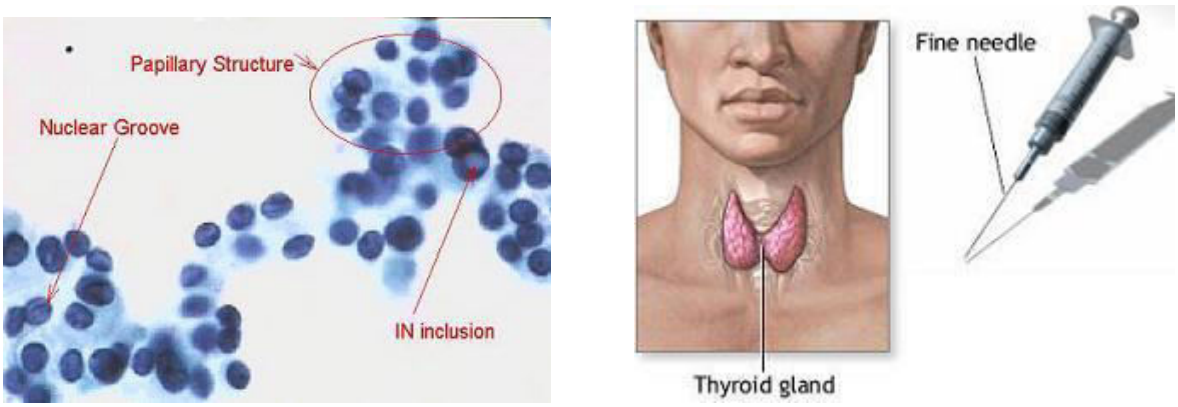
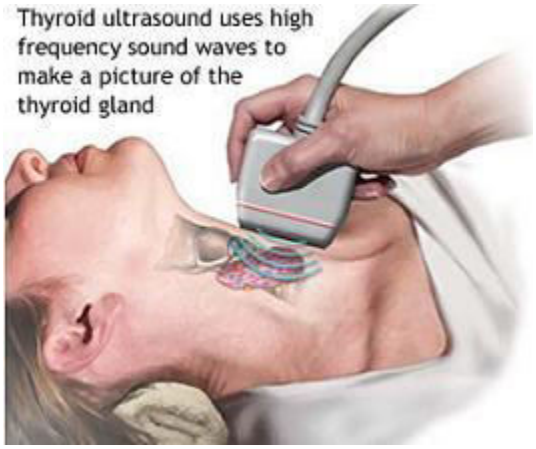


Fig1.4: Fine needle aspiration.

1.18. Thyroid imaging tests

A number of imaging tests are performed for diagnosis of various thyroid conditions. These tests include:

1.18.1 Ultrasound



Similar in its use for evaluating a breast mass, ultrasound can be used to assess a thyroid nodule. Its advantage over physical exam alone lies in its ability to distinguish solid from cystic nodules, whether more than one nodule exists, and the exact size and extent of a nodule. In fact, ultrasound can be used to assess the size and shape of the thyroid gland itself. Because of the recent advances in this form of imaging technology, ultrasound has become quite sensitive a modality, particularly when assessing size and numbers of nodules.

Ultrasound characteristics which suggest a benign nodule include:

Nodule filled with fluid (likely a cyst)

Multiple nodules throughout the gland (likely a multinodular goiter)

No blood flowing through nodule (again, likely a cyst)
Sharp edges seen around nodule

Ultrasound characteristics which suggest malignancy include:

Solid or complex appearing nodules
Blood flowing through nodule
Unclean (rough) edges around nodule

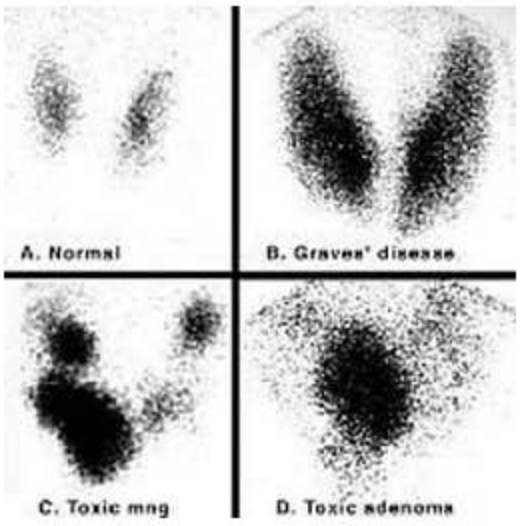
Ultrasound can also be used in conjunction with fine needle aspiration (FNA) in guiding a biopsy. Its only drawbacks are in its inability to distinguish benign from malignant disease or determine the functional status of the thyroid gland.

Ultrasound can also be used to assess (in the same manner) the four parathyroid glands that lie within, or next to, the thyroid gland. Normal parathyroid glands are often difficult to see on ultrasound and cannot be felt during physical examination; however, abnormal parathyroid glands may be enlarged and detectable by ultrasound.

As ultrasound does not involve the use of radiation, it is a safe imaging technique for use during pregnancy and poses no harm to the developing fetus.

1.18.2 Thyroid Scan

The thyroid glands' ability to concentrate iodine and certain radioactive isotopes has been exploited in a nuclear imaging technique known as the thyroid scan.



Radioactive isotopes are special forms of elements that undergo a process called decay in which they change from higher energy states to lower energy states. As they undergo this change, they release small bursts of energy in the form of radiation that can be detected by special cameras.

The tissue that makes up the thyroid gland is unique in that it is able to take up and trap iodine and certain other molecules of similar size. When radioactive isotopes of these substances (tracers) are swallowed or injected into the bloodstream, they are taken up by the thyroid gland. As they decay, a special camera can detect the energy that is released, creating a picture of the thyroid gland. The radioactive isotopes that are most commonly used as tracers to perform thyroid scans are called 123-Iodine, 99m-Technetium pertechnetate and 131-Iodine.

Nuclear imaging and the thyroid scan can be used to distinguish a nodule as hot, warm, or cold, based on the relative amount of uptake of radioactive isotope. Hot nodules take up excessive amounts of isotope and indicate autonomously functioning nodules. They appear very dark on thyroid scan (see picture to right) in relation to normal thyroid tissue. Warm nodules appear gray and suggest normal thyroid function. Cold nodules take up minimal amounts of radioactive isotope and therefore indicate hypo functional or nonfunctional thyroid tissue.

Hot nodules are rarely malignant; however, warm or cold nodules are malignant in 5-8% of cases and require further workup (biopsy, removal, etc.). Unfortunately, solitary thyroid nodules are hot in only about 10% of cases and 90% of cold nodules are not malignant. Thus, nuclear imaging (regardless of whether it is used in conjunction with ultrasound or not) is associated with a low yield of cancer diagnoses (Connecticut, 2016).

1.18.3 Other diagnostic tests and procedures

Practitioner sometimes uses other diagnostic tests and procedures to identify thyroid dysfunction. The use of these tests is considered controversial to mainstream practitioners, but many of these tests are well-accepted and in use among alternative, integrative and holistic physicians. These tests include:

- Iodine patch tests
- Saliva testing
- Urinary testing
- Basal body temperature testing

1.19 Treatment

There are three treatments for hyperthyroidism. Antithyroid medicine and radioactive iodine are the ones doctors use most often. In rare cases, surgery may be done. Hyperthyroidism can lead to more serious problems. So even if symptoms are not bothering, it still needs treatment.

The kind of treatment that have depends on anyone's age, what is causing his hyperthyroidism, how much thyroid hormone of body is making, and other medical conditions he may have. Each kind of treatment has benefits and risks. Discuss the benefits and risks of each kind of treatment with doctor. For some people, more than one kind of treatment may be needed.

1.19.1 Initial treatment

Initial treatment for hyperthyroidism usually is anti thyroid medicine or radioactive iodine therapy. If patients have a lot of symptoms, doctor may recommend that patient take antithyroid medicine first to help him to feel better. Then he can decide whether to have radioactive iodine therapy.

- Antithyroid medicines work best if he have mild hyperthyroidism, if this is the first time he is being treated for Graves' disease, if he is younger than 50, or if his thyroid gland is only swollen a little bit (small goiter).
- Radioactive iodine is often recommended if patient have Graves' disease and are older than 50, or if he have thyroid nodules (toxic multinodular goiter) that are releasing too much thyroid hormone. Radioactive iodine is not used if:
    - Patient is pregnant or she wants to become pregnant within 6 months of treatment.
    - She is breast-feeding.
    - She has thyroiditis or another kind of hyperthyroidism that is often temporary.

If has symptoms such as a fast heartbeat, tremors, sweating, nervousness, or dry, patients may take some additional medicines to treat those symptoms.

Surgery is not usually part of initial treatment. It may need surgery if thyroid gland is so big that patient has a hard time swallowing or breathing. Or it may need surgery if a single large thyroid nodule is releasing too much thyroid hormone (Msd, 2015).

1.19.2 Ongoing treatment

During and after treatment for hyperthyroidism, patient will have regular blood tests to check his levels of thyroid-stimulating hormone (TSH). He will also have regular thyroid hormone tests to check his levels of hormones called T4 and T3. These tests are a good way to know how well his treatment is working. If his symptoms do not go away after his initial treatment, he may need to repeat the treatment or try a different treatment.

- If patients have Graves' disease and have been taking antithyroid medicine but his hyperthyroidism has not improved, he can continue to take antithyroid medicine or he can try radioactive iodine therapy.
- If patient have lots of side effects from antithyroid medicines and radioactive iodine is not an option for him, he may need surgery to remove all or part of his thyroid gland (thyroidectomy).

Sometimes treatment cures his hyperthyroidism but may cause hypothyroidism (Msd, 2015).

1.19.3 Treatment if the condition gets worse

If radioactive iodine or antithyroid medicines are not working well, you may need:

- Another treatment of radioactive iodine.
- Surgery to remove all or part of the thyroid gland (thyroidectomy).

After treatment with radioactive iodine, it may develop hypothyroidism (too little thyroid hormone). Call doctor if patient have any of the symptoms of hypothyroidism such as gaining weight, feeling tired, or feeling cold more often than usual. If patient have

hypothyroidism, it may need to take thyroid hormone medicine for the rest of life (Webmd, 2014).

1.20 Drugs uses in hyperthyroidism

Drug	Side effects	Comments
Thionamides		
Carbimazole Mehimazole Propylthiouracil	Allergic reactions (usually rashes) Nausea Loss of taste Infection due to a low white blood cell count Liver dysfunction Joint aching	Decrease the production of thyroid hormones
Nonmetallic element		
Iodine	Rash	Decrease the production and release of thyroid hormones
Radioactive isotope		
Radioactive iodine	Hypothyroidism	Destroys the thyroid gland
Beta blockers		
Atenolol Metoprolol Propranolol	In people with lung disease, may cause wheezing Can worsen symptoms of peripheral vascular disease Can cause depression May reduce blood pressure (hypotension)	Block many of the stimulating effects of excess thyroid hormones on other organs

Table1.1: Drugs uses in hyperthyroidism (Msd, 2015)

1.21 Clinical efficacy of anti thyroid drugs

In many tissues, hyperthyroidism is associated with an increased number of beta-adrenergic receptors. The ensuing increase in beta-adrenergic activity is responsible for many of the symptoms associated with this disorder. It also explains the ability of beta blockers to ameliorate rapidly many of the symptoms, including palpitations, tachycardia, tremulousness, anxiety and heat intolerance. In a small randomized trial, patients receiving beta blockers with methimazole, compared with patients receiving methimazole alone, had a lower heart rate and improvement in fatigability, shortness of breath, and physical functioning after four weeks of therapy.

Propranolol in high doses (above 160 mg/day) also slowly decreases serum triiodothyronine (T3) concentrations by as much as 30 percent, via inhibition of the 5'-monodeiodinase that converts thyroxine (T4) to T3. Propranolol is highly lipid soluble, allowing it to become sufficiently concentrated in tissues to inhibit monodeiodinase activity. This effect of propranolol is slow, occurring over 7 to 10 days, and contributes little to the therapeutic effects of the drug. Atenolol, alprenolol, and metoprolol similarly cause minimal reductions in serum T3 concentrations, whereas sotalol and nadolol do not.

Despite this theoretical advantage of propranolol and related drugs, the small effect and slow onset severely limit their usefulness for reducing serum T3 concentrations. If deiodinase inhibition is considered important in a patient with severe hyperthyroidism (eg, thyroid storm or impending thyroid storm), it is best achieved by the addition of an iodinated radiocontrast agent to the medical regimen (these agents are currently not available in the United States), or the use of propylthiouracil (PTU) (Uptodate, 2015).

1.22 Contraindications of anti thyroid drugs

Adverse reactions associated with levothyroxine therapy are primarily those of hyperthyroidism due to therapeutic over dosage. They include the following:

- **General**-Fatigue, increased appetite, weight loss, heat intolerance, fever, excessive sweating;

- **Central Nervous System**-Headache, hyperactivity, nervousness, anxiety, irritability, emotional liability, insomnia.

- **Musculoskeletal**-Tremors, muscle & weakness.

- **Cardiovascular**-Palpitations, tachycardia, arrhythmias, increased pulse and blood pressure, heart failure, angina, myocardial infarction, cardiac arrest;

- **Respiratory**-Dyspnea.

- **Gastrointestinal**-Diarrhea, vomiting, abdominal cramps and elevations in liver function tests;
- **Dermatologic**-Hair loss, flushing;
- **Endocrine**-Decreased bone mineral density;

- **Reproductive**-Menstrual irregularities, impaired fertility.

Pseudotumor cerebri and slipped capital femoral epiphysis have been reported in children receiving levothyroxine therapy. Overtreatment may result in craniosynostosis in infants and premature closure of the epiphyses in children with resultant compromised adult height.
Seizures have been reported rarely with the institution of levothyroxine therapy.Inadequate levothyroxine dosage will produce or fail to ameliorate the signs and symptoms of hypothyroidism.Hypersensitivity reactions to inactive ingredients have occurred in patients treated with thyroid hormone products. These include urticaria, pruritus, skin rash, flushing, angioedema, various GI symptoms (abdominal pain, nausea, vomiting and diarrhea), fever, arthralgia, serum sickness and wheezing. Hypersensitivity to levothyroxine itself is not known to occur (Rxlist, 2015).

Potassium iodide:

Iodide can cross the placenta & cause fetal goiter.

Radioavtive I-131:

Pregnancy or nursing mothers.

Methimazole:

Pregnancy & nursing mothers- methimazole is found in breast milk & is contraindicated in nursing mothers. It can cause fetal harm when administered to a pregnant woman (Tmedweb, 2013).

Chapter 2

Literature review

2.1 Primary hyperthyroidism – diagnosis and treatment. Indications and contraindications for radioiodine therapy

Isotope therapy is one of the methods used in primary hyperthyroidism. The therapy is based on short-range beta radiation emitted from radioactive iodine. Radioiodine administration must always be preceded by pharmacological normalization of thyroid function. Otherwise, post-radiation thyrocyte destruction and thyroid hormones release may lead to hyperthyroidism exacerbation. Indications for radioiodine therapy in Graves-Basedow disease include recurrent hyperthyroidism after thyrostatic treatment or thyroidectomy and side-effects observed during thyrostatic treatment. In toxic nodule, isotope therapy is the first choice therapy. Radioiodine is absorbed only in autonomous nodule. Therefore, it destroys only this area and does not damage the remaining thyroid tissue. In toxic goitre, radioiodine is used mostly in recurrent nodules. Absolute contraindications for radioiodine treatment are pregnancy and lactation. Relative contraindications are thyroid nodules suspected of malignancy and age under 15 years. In patients with thyroid nodules suspected of malignancy, radioiodine treatment may be applied as a preparation for surgery, if thyrostatic drugs are ineffective or contraindicated. In children, radioiodine therapy should be considered in recurrent toxic goitre and when thyrostatic drugs are ineffective. In patients with Graves-Basedow disease and thyroid-associated orbitopathy, radioiodine treatment may increase the inflammatory process and exacerbate the ophthalmological symptoms. However, thyroid-associated orbitopathy cannot be considered as a contraindication for isotope therapy. The potential carcinogenic properties of radioiodine, especially associated with tissues with high iodine uptake (thyroid, salivary glands, stomach, intestine, urinary tract, breast), have not been confirmed (Gurqul *et.al*, 2011).

2.2 Chinese herbal medicines for hyperthyroidism

Hyperthyroidism is a disease in which excessive amounts of thyroid hormones circulate in the blood. Patients, among other things suffer from tachycardia, warm moist skin and raised body temperature. The treatment of hyperthyroidism includes symptom relief and therapy with antithyroid medications, radioiodine and thyroidectomy. Medicinal herbs are used alone or in combination with antithyroid agents to treat hyperthyroidism in China and some other countries.

Objective: To assess the effects of Chinese herbal medicines for treating hyperthyroidism.

Search methods Studies were obtained from computerized searches of medline, embase, The Cochrane Library, the Chinese Biomedical Database.

Selection criteria: Randomised controlled trials comparing the effects of Chinese herbal medicines alone with Chinese herbal medicines combined with antithyroid drugs, radioiodine or both.

Data collection and analysis: Three authors interviewed authors of all potentially relevant studies by telephone to verify randomization procedures. One author entered data into a data extraction form and another author verified the results of this procedure.

Main results: Thirteen relevant trials with 1770 participants were included. All of them were of low quality. Fifty-two studies still need to be assessed because the original authors could not be interviewed. None of these trials analyzed mortality, health related quality of life, economic outcomes or compliance. Compared to anti thyroid drugs alone the results showed that Chinese herbal medicines combined with anti thyroid drugs may offer benefits in lowering relapse rates, reducing the incidence of adverse effects, relieving symptoms, improving thyroid antibody status and thyroid function. Two trials investigated Chinese herbal medicine versus radioiodine and reported improvements in anxiety, tachycardia and heat intolerance. However, thyroid function - with the exception of restored thyroid stimulating hormone (TSH) - was not significantly altered.

Authors' conclusions: The results suggest that traditional Chinese herbal medicines added to other routine treatment have a therapeutic potential for people with hyperthyroidism. However, due to methodological limitations, we could not identify a well-designed trial to provide strong evidence for Chinese traditional herbal medicine in the treatment of hyperthyroidism. Thus, we currently cannot recommend any single preparation or formulation for clinical use (Cochrane library, 2006).

2.3 The mechanisms of atrial fibrillation in hyperthyroidism

Atrial fibrillation (AF) is a complex condition with several possible contributing factors. The rapid and irregular heartbeat produced by AF increases the risk of blood clot formation inside the heart. These clots may eventually become dislodged, causing embolism, stroke and other disorders. AF occurs in up to 15% of patients with hyperthyroidism compared to 4% of people in the general population and is more common in men and in patients with triiodothyronine (T_3) toxicosis. The incidence of AF increases with advancing age. Also, subclinical hyperthyroidism is a risk factor associated with a 3-fold increase in development of AF. Thyrotoxicosis exerts marked influences on electrical impulse generation (chronotropic effect) and conduction (dromotropic effect). Several potential mechanisms could be invoked for the effect of thyroid hormones on AF risk, including elevation of left atrial pressure secondary to increased left ventricular mass and impaired ventricular relaxation, ischemia resulting from increased resting heart rate, and increased atrial eopic activity. Reentry has been postulated as one of the main mechanisms leading to AF. AF is more likely if effective refractory periods are short and conduction is slow. Hyperthyroidism is associated with shortening of action potential duration which may also contribute to AF. (Dabrowa *et.al*, 2009)

2.4 Management of the Solitary Thyroid Nodule

Thyroid nodules are common, with up to 8% of the adult population having palpable nodules. With the use of ultrasound, up to 10 times more nodules are likely to be detected. Increasing numbers of nodules are being detected serendipitously because of the rising use of imaging to investigate unrelated conditions. The primary aim in investigating a thyroid nodule is to exclude the possibility of malignancy, which occurs in about 5% of nodules. This begins with a thorough history, including previous exposure to radiation and any family history of thyroid cancer or other endocrine diseases. Clinical examination of the neck should focus on the thyroid nodule and the gland itself, but also the presence of any cervical lymphadenopathy. Biochemical assessment of the thyroid needs to be followed by thyroid ultrasound, which may demonstrate features that are associated with a higher chance of the nodule being

malignant. Fine-needle aspiration biopsy is crucial in the investigation of a thyroid nodule. It provides highly accurate cytologic information about the nodule from which a definitive management plan can be formulated. The challenge remains in the management of nodules that fall under the "indeterminate" category. These may be subject to more surgical intervention than is required because histological examination is the only way in which a malignancy can be excluded. Surgery followed by radioactive iodine ablation is the mainstay of treatment for differentiated thyroid cancers, and the majority of patients can expect high cure rates (Yeung *et.al,* 2007).

2.5 Atrial fibrillation and arterial embolism in hyperthyroidism

Atrial fibrillation or flutter was present in 70 of 381 patients with uncontrolled hyperthyroidism; return to stable sinus rhythm occurred in 39 with antithyroid and anti-arrhythmic treatment. One third of the patients who reverted did so in the first week of treatment while still hyperthyroid. As expected, reversion was more likely in younger patients, and in those with arrhythmia of recent onset, without evidence of other heart disease. Eight patients with arrhythmia had proven (five) or probable (three) major arterial embolic episodes. Four of these eight patients died. Embolism tended to occur at an early stage, during uncontrolled hyperthyroidism, in patients with both atrial fibrillation and cardiac failure. These findings suggest that prophylactic anticoagulation may be appropriate in this high risk group, although more extensive studies are necessary before effective prevention of embolism can be claimed (Hurley *et.al*, 2008).

2.6 The treatment of hyperthyroidism with radioactive iodine

Roentgen treatment has been used for hyperthyroidism for many years. In 1923 Means and Holmes[1] pointed out that in this form of treatment about one third of the patients are cured, another third improved and another third not affected. Since 1923 ordinary iodine by mouth has been used as a preoperative method of quieting the hyperactive thyroid in preparation for surgery. Under iodine alone occasionally the patient and the doctor have been agreeably surprised to find that the symptoms and signs of hyperthyroidism disappeared, and a

permanent remission apparently was effected. That x-ray treatment and iodine treatment sometimes cure hyperthyroidism led to the hope that someday a more effective, nonsurgical agent would be found. Then the MacKenzies[2] and Astwood[3] discovered that several chemical compounds inhibit the function of the thyroid in hyperthyroidism as well as under other circumstances (Chapman *et.al,* 1946).

2.7 Treatment Guidelines for Patients with Hyperthyroidism and Hypothyroidism

Its objective is to develop a set of minimum clinical guidelines for use by primary care physicians in the evaluation and management of patients with hyperthyroidism and hypothyroidism.Guidelines were developed by a nine-member ad hoc Standards of Care Committee of the American Thyroid Association (the authors of this article). The participants were selected by the committee chair and the president of the American Thyroid Association on the basis of their clinical experience. The committee members represented different geographic areas within the United States, in order to take into account different practice styles.Guidelines were developed on the basis of expert opinion of the participants, as well as on available published information.Input was obtained from all of the participants, each of whom wrote an initial section of the document. A complete draft document was then written by three participants (P.A.S., D.S.C., and E.G.L.) and resubmitted to the entire committee for revision. The revised document was then submitted to the entire membership of the American Thyroid Association for written comments, which were then reviewed (mainly by P.A.S., D.S.C., and E.G.L.). Many of the suggestions of the American Thyroid Association members were incorporated into the final draft, which was then approved by the Executive Council of the American Thyroid Association. The entire process, from initial drafts to final approval, took approximately 18 months. A set of minimum clinical guidelines for the diagnosis and treatment of hyperthyroidism and hypothyroidism were developed by consensus of a group of experienced thyroidologists. The guidelines are intended to be used by physicians in their care of patients with thyroid disorders, with the expectation that more effective care can be provided, and at a cost savings (Singer *et.al,* 1995).

2.8 Mortality after the Treatment of Hyperthyroidism with Radioactive Iodine

Hyperthyroidism affects many organ systems, but the effects are usually considered reversible. The long-term effects of hyperthyroidism on mortality are not known. We conducted a population-based study of mortality in a cohort of 7209 subjects with hyperthyroidism that was treated with radioactive iodine in Birmingham, United Kingdom, between 1950 and 1989. The vital status of the subjects was determined on March 1, 1996, and causes of death were ascertained for those who had died. The data on the causes of death were compared with data on age-specific mortality in England and Wales. The standardized mortality ratio was used as a measure of relative risk, and the effect of covariates on mortality was assessed by regression analysis. During 105,028 person-years of follow-up, 3611 subjects died; the expected number of deaths was 3186 (standardized mortality ratio, 1.1; 95 percent confidence interval, 1.1 to 1.2; P<0.001). The risk was increased for deaths due to thyroid disease (106 excess deaths; standardized mortality ratio, 24.8; 95 percent confidence interval, 20.4 to 29.9), cardiovascular disease (240 excess deaths; standardized mortality ratio, 1.2; 95 percent confidence interval, 1.2 to 1.3), and cerebrovascular disease (159 excess deaths; standardized mortality ratio, 1.4; 95 percent confidence interval, 1.2 to 1.5), as well as fracture of the femur (26 excess deaths; standardized mortality ratio, 2.9; 95 percent confidence interval, 2.0 to 3.9). The excess mortality was most evident in the first year after radioiodine therapy and declined thereafter. Among patients with hyperthyroidism treated with radioiodine, mortality from all causes and mortality due to cardiovascular and cerebrovascular disease and fracture are increased (Franklyn *et.al*, 1998).

2.9 Germline mutations in the thyrotropin receptor gene cause non−autoimmune autosomal dominant hyperthyroidism

The thyrotropin receptor (TSHR), a member of the large family of G protein−coupled receptors, controls both the function and growth of thyroid cells via stimulation of adenylyl cyclase. We report two different mutations in the *TSHR*gene of affected members of two large pedigrees with non−autoimmune autosomal dominant hyperthyroidism (toxic thyroid hyperplasia), that involve residues in the third (Val509Ala) and seventh (Cys672Tyr)

transmembrane segments. When expressed by transfection in COS−7 cells, the mutated receptors display a higher constitutive activation of adenylyl cyclase than wild type. This new disease entity is the germline counterpart of hyperfunctioning thyroid adenomas, in which different somatic mutations with similar functional characteristics have been demonstrated (Duprez *et al*, 1994).

2.10 Late radiation effects in roentgen therapy for hyperthyroidism

Radioactive iodine, especially the isotope of 8 day half-life, I^{131}, has been employed in the treatment of hyperthyroidism in several clinics during recent years, a total of several hundred patients probably having received the material. The question of the possibility of late radiation changes leading to malignant degeneration has been raised and cannot be disregarded. Serious sequelae to radiation therapy usually appear several years after the treatment; hence such damage from radioiodine would not be expected for some time. If it is to be feared that this will be a serious hazard, the use of the material ought to be very sharply restricted until sufficient time has elapsed to ascertain the late results in persons already treated (Quimby *et.al,* 1949).

2.11 Bone metabolism during anti-thyroid drug treatment of endogenous subclinical hyperthyroidism

There is recent evidence that both exogenous and endogenous subclinical thyrotoxicoses are associated with decreased bone mineral density. Scanty information is available on bone metabolism in these conditions when euthyroidism is restored. We evaluated the effect of anti-thyroid drug treatment on bone metabolism in endogenous subclinical hyperthyroidism. Prospective follow-up study over 2 years during treatment with methimazole, with an untreated control group. Sixteen post-menopausal women with endogenous subclinical hyperthyroidism associated with multinodular goitre, eight of whom were treated with methimazole.Serum concentrations of free T4, total T3, and TSH, osteocalcin, urinary excretion of hydroxyproline and forearm bone mineral density were

measured at regular intervals.Significant changes in serum osteocalcin concentration or urinary hydroxyproline excretion were not observed in either group. Distal, but not proximal, forearm bone mineral density, expressed as a percentage of the base-line value, was significantly ($P < 0.05$) higher in the treated than in the untreated subjects in the second year of treatment.Treatment with methimazole in post-menopausal women with endogenous subclinical hyperthyroidism associated with multinodular goitre can prevent excessive loss of bone, at least in the distal forearm (Mudde *et.al*, 1994).

Significance of the Study

Thyroid disorder is the second most common endocrine disorder in women both in the developed and less developed world (Hechtman, 2011). It is estimated that 200 million worldwide have a Thyroid Disorder of these 27 million people about half are undiagnosed. 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. 50% of children with parents having a thyroid disorder may develop a thyroid disorder themselves by age 40. (Thyroidu.com). Again, Hyperthyroidism affects 2-5% of all women mainly between 20 and 40 years old. One study estimated the incidence to be 1-2 cases/1000 per year with women affected 10 times more often than men. (myVMC, 2014). Each year, about 2 - 5% of people with subclinical thyroid go on to develop overt hypothyroidism.(University of Maryland Medical Center, 2014). Thyroid disorder is now the most common disease among men and women in Bangladesh. It is guessed that, more than 10,392,681 people having any kind of thyroid disorder. Among them more than half of the population is being unaware about this disease. . Because of their unawareness these patients may suffer from goiter, thyrotoxicosis, thyroid cancer and thyroid papillary carcinoma, gravies disease, etc. As this disease does not have such significant signs and symptoms generally no one can understand that. But this disease is a slow killer which may further develop many other physical and mental problems. Sometimes hyperthyroidism may lead to thyroid carcinomas and may cause death. Hyperthyroidism is very crucial in female fertility. Most of the persons having thyroid disorder are female and the patient's aged between 25-40 may be infertile due to some thyroid disorders. Although there is not any specific statistical calculation of government in our country, but some studies which are done on some diagnosed patients like that - 113 infertile women during their first visit for infertility evaluation. Prevalence of sub-clinical hyperthyroidism was 6.5% and prevalence of hyperprolactinemia was 43% and 21% in primary and secondary infertility respectively (Akhter N. and Hassan S., 2008). From a study done between March and August 2014, indicates that, Females were found with higher rate of thyroid dysfunction (78.3%) with male (21.7%) (Moslem F. et.al, 2015). So, we can see that, a high percentage of female are suffering from this disorder. Lack of awareness and early detection program in developing country is a main reason for escalating the morbidity.

The study done in Bangladesh on thyroid disordered patients' prevalence level checking is very few. There was a study done in an urban hospital that was efficacy of radioiodine therapy for hyperthyroidism. The purpose of this study is to evaluate the efficacy of the radio-iodine for eradicating hyperthyroidism and the problems of follow-up. Every patient was discussed about the radiation safety aspects of I- 131 therapy. They were warned beforehand that they would probably become hypothyroid in future and may need life-long thyroxin replacement therapy and they agreed to this (Faruk S.et.al, 2001). Another study was in Khulna medical college to assess the degree of effectiveness of radioiodine therapy in case of hyperthyroidism (Alam J.et.al, 2003). There is no direct study focusing on hyperthyroidism. But is difficult to calculate the prevalence on the general people, so we have the diagnosed patients to conduct our study and our target was to judge the level of knowledge about thyroid dysfunction, early warning signs, and therapeutic and screening approaches.

Because, if we do the study on them, we will get idea what is there knowledge level about hyperthyroidism, risk factors and their treatment pattern and how much they are complying with their medication and treatment pattern.

We are serving this study as; these diseases can lead to severe infertility problem to both male and female. These may also causes CNS problem, cardiovascular problem, integumentary and various ENT problems. So, we can say these are vital reason for many diseases but as most of the people do not notice this as a reason for their sufferings, they do not take treatment and this hormonal disease may hamper their physical conditions a lot. 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. But 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 examine the prevalence of hyperthyroidism in Bangladeshi patients.
- The common symptoms, diagnosis, treatment pattern and medication of hyperthyroidism.
- Awareness among the patients regarding their disease.

Chapter 3

Study Method

3 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
- Thyroid Clinic, 20, Green Road, Dhaka-1205
- Mymensingh medical hospital, Mymensingh
- Sir salimullah medical College Mitford Hospital, Mitford road, Dhaka-1205

3.2 Total Number of Participants

Data was collected from 273 thyroid 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

4 Results

4.1 Participants having endocrine disorder

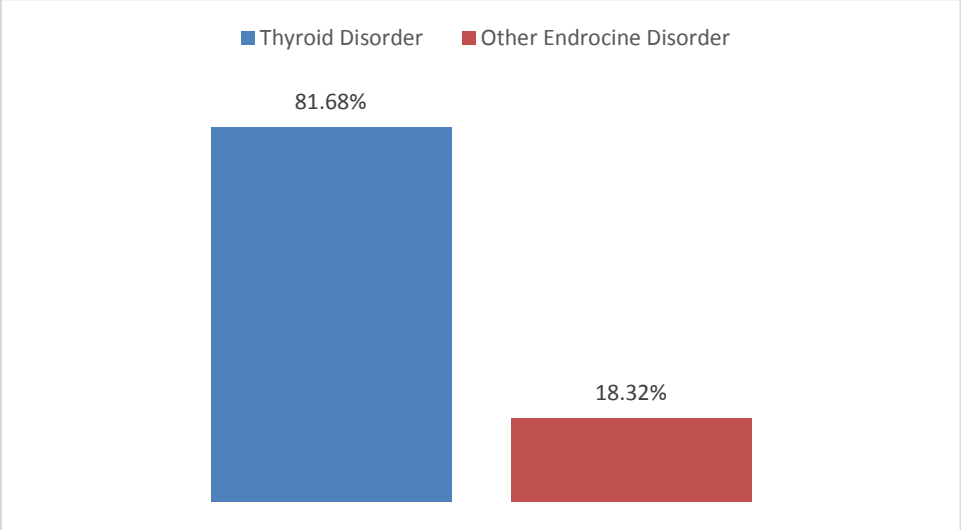


Fig 4.1: participants having endocrine disorder

Among 273 endocrine disordered patients 81.68% patients having thyroid disorder and 18.32% patients having other endocrine disorders, like glucose homeostasis disorder, diabetes, sex hormone disorder or tumor of endocrine gland.

4.2 Age of Patients having thyroid disorder

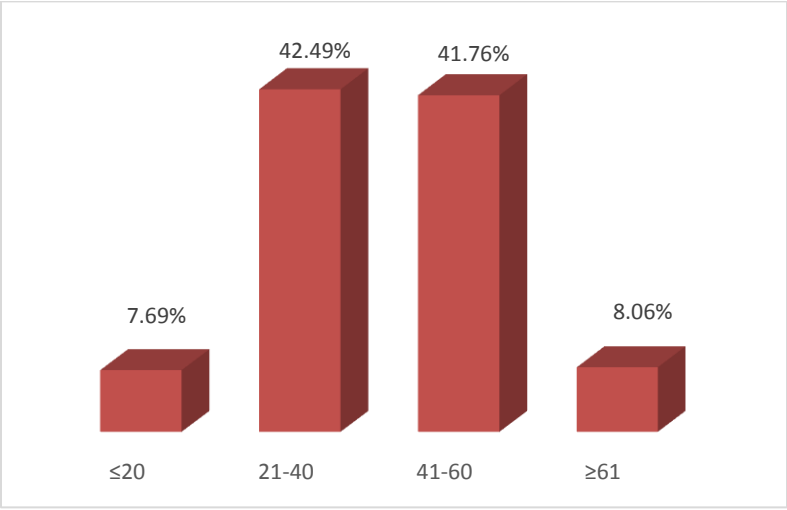


Fig 4.2: Age distribution among thyroid disordered patients

Among 273 patients , majority of them are in the age limit below 20 (7.69%), then age 21-40 are of 42.49% then age 41-60 years are of 41.76% and rest of patients are of age above 61 years having 8.06%.

4.3 Sex of thyroid disordered patients

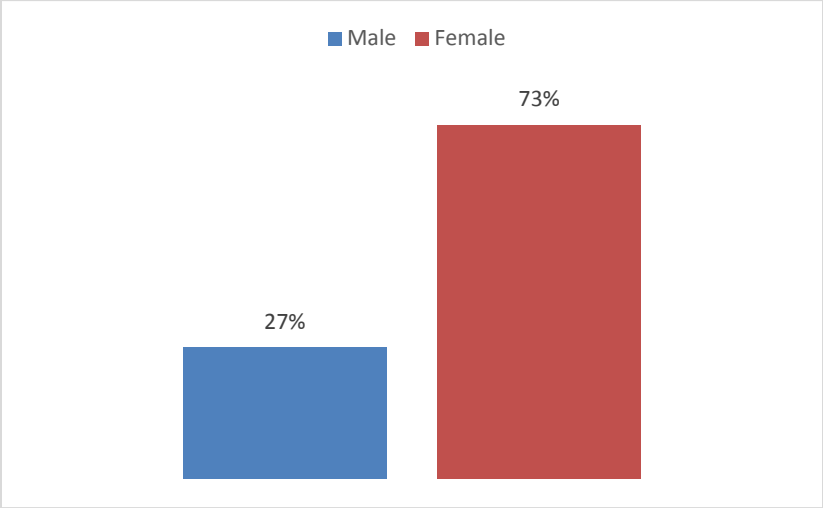


Fig 4.3: Gender of patients

Among 273 patients suffering from thyroid disorder, majority 73% are female and only 27% are male.

4.4 Marital status of patients

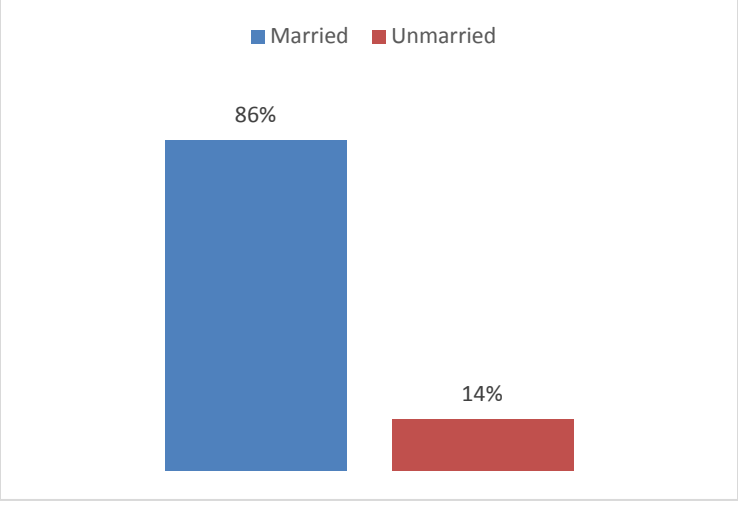


Fig 4.4: Marital status of thyroid disordered patients

Among 273 patients having thyroid disorder, 86% are married and 14% are unmarried.

4.5 Education level of patients

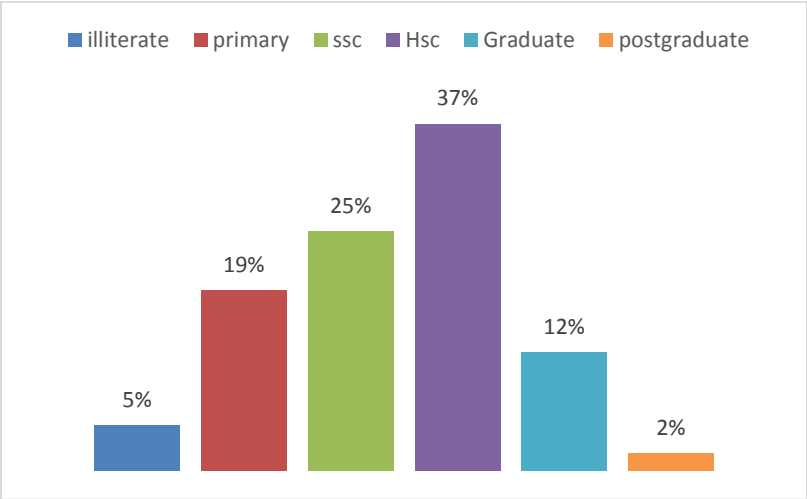


Fig 4.5: Education level of patients

Among 273 patients are given their data and according to that, 5% are illiterate, 19% have primary education, 25% passed SSC and 37% have their HSC. 12% patients are Graduates and 2% are post graduates.

4.6 Occupational statuses of patients

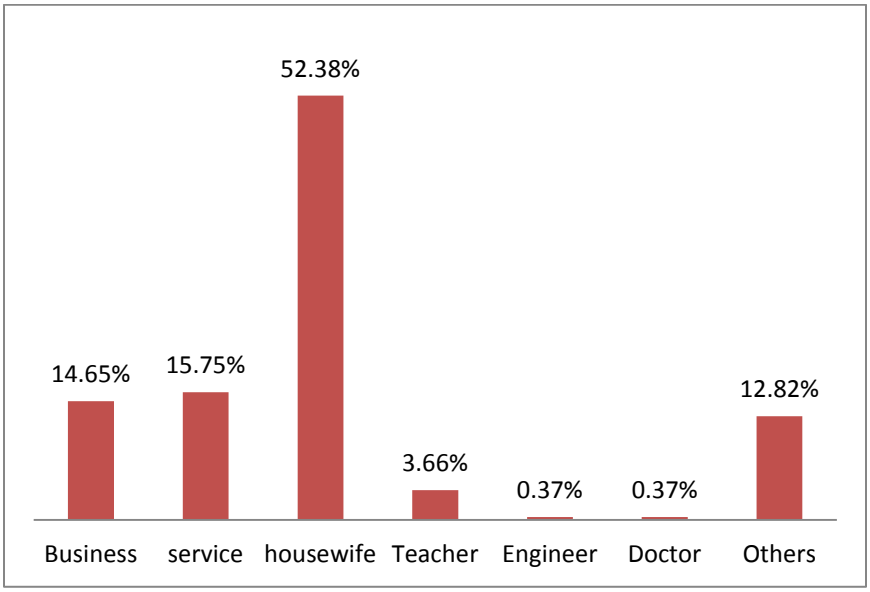


Fig 4.6: Occupational status of the patients

Among them, majority 52.38% are housewife, then 15.75% are service holder, 14.65% are doing business, 12.82% are from others occupations, 3.66% are teacher, 0.37% are engineer and 0.37% are doctor.

4.7 BMI status of the patients

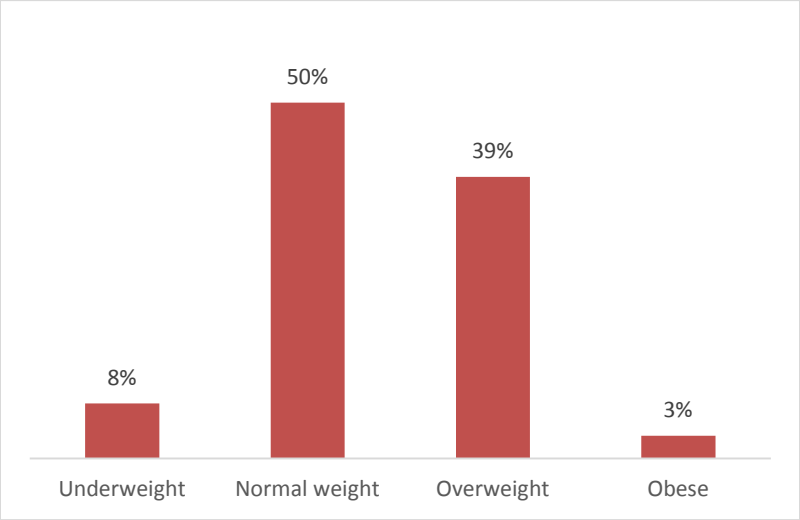


Fig 4.7: BMI status of the patients

According to BMI standard < 18.5 are underweight, 18-24.5 are normal weight, 25-29.9 are overweight, and obese are >30. Here, 8% patients are underweight, 50 %are normal, 39% are overweight and 3% are obese of all 221 participant patients.

4.8 Types of thyroid disorder

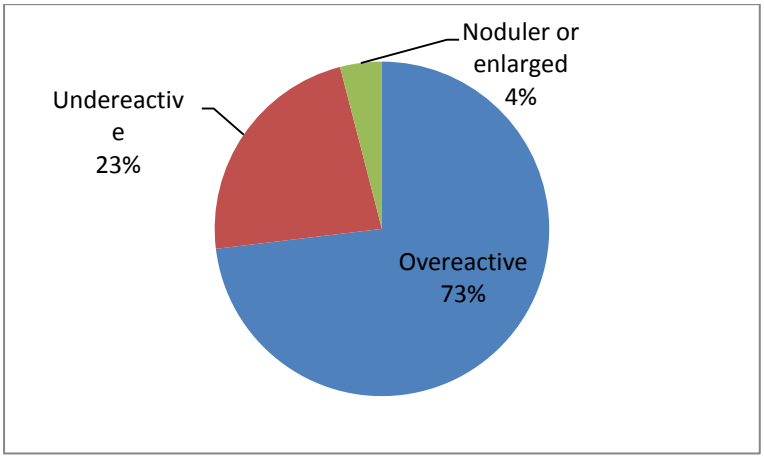


Fig 4.8: Types of thyroid disorder

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

4.9 History of thyroid disorder

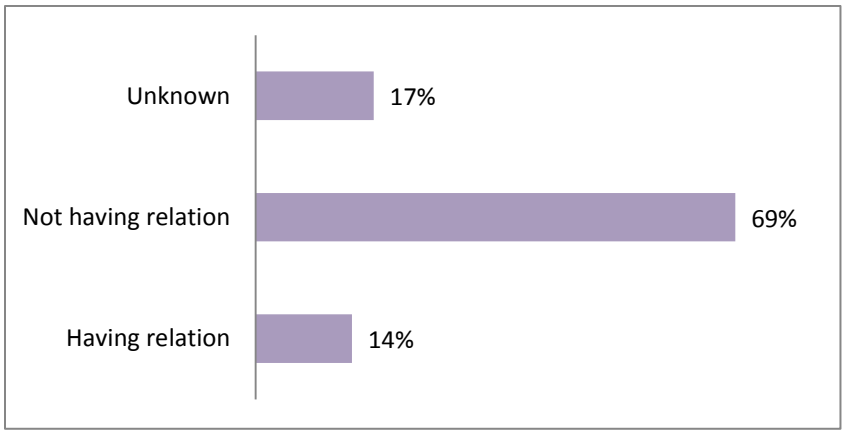


Fig 4.9: History of Thyroid disorder in patients

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

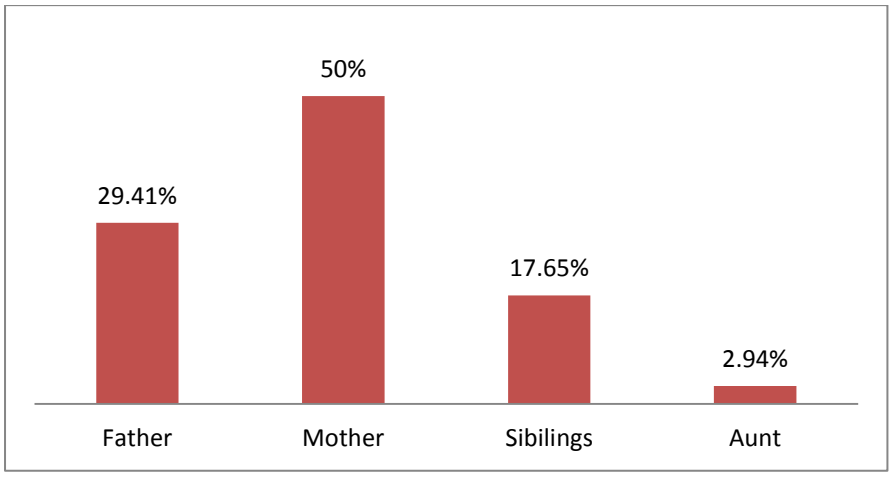


Fig 4.9.1: relation of patients with their family members having thyroid disorder

Among the 14% patients who have family histories, 50% got their disease from their mother, 29.41% got their disease from their father,17.65% got their disease from their siblings and 2.94% having this disorder as their aunt are also suffering from it.

4.10 Types of endocrine disorder among patients

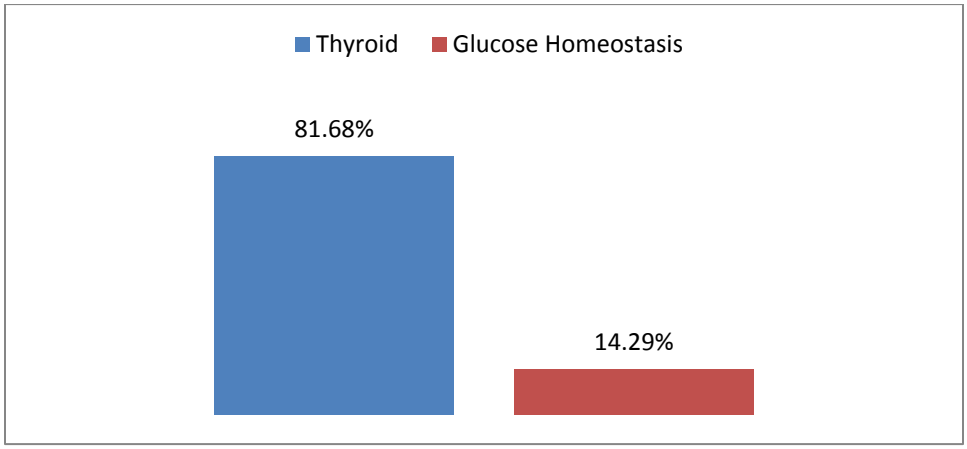


Fig 4.10: Types of endocrine disorder

Of 273 patients 81.68% are suffering from thyroid, and 14.29% are suffering from glucose homeostasis. 4.03% are suffering from tumor.

4.11 Types of hyperthyroidism

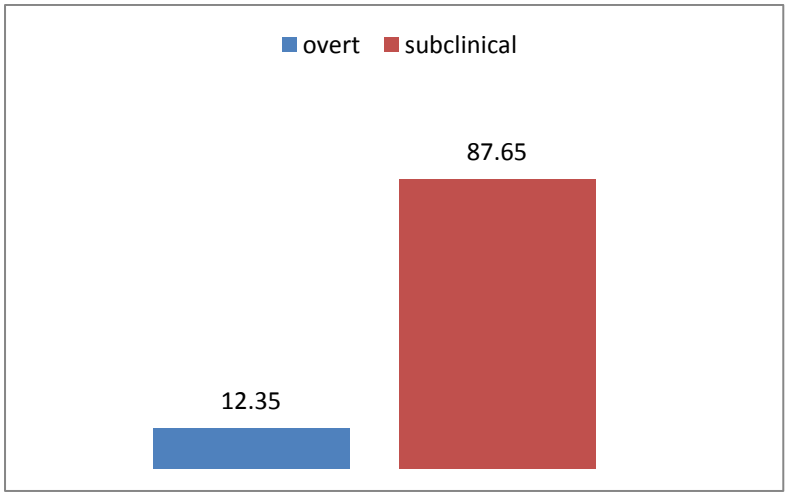


Fig 4.11: Types of Hyperthyroidism

Among 162 hyperthyroidism patients, 12.35% are suffering from overt and 87.65% are suffering from subclinical hyperthyroidism.

4.12 Duration of sufferings

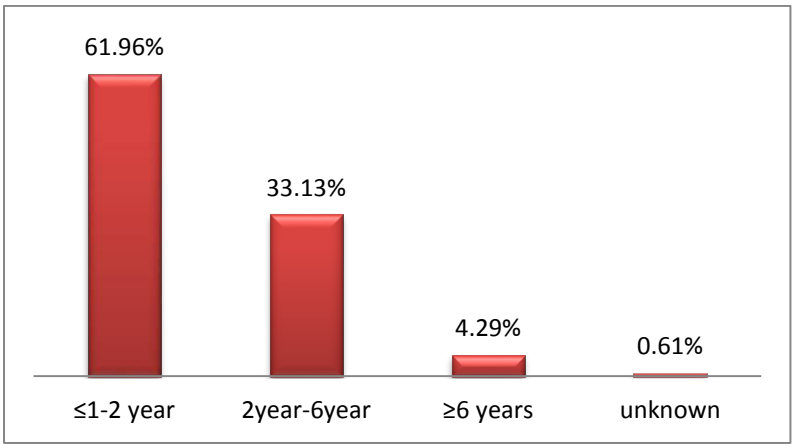


Fig 4.12: Duration of sufferings (in years)

Among 163 patients, 61.96% hyperthyoridism containing patients are suffering from this disorder below 1 year to 2 years, 33.13% are suffering for 2 years to 6 years and 4.29% of them are suffering for more than 6years.Again, 0.61% patients are do not know about their duration.

4.13 Causes of Hyperthyroidism

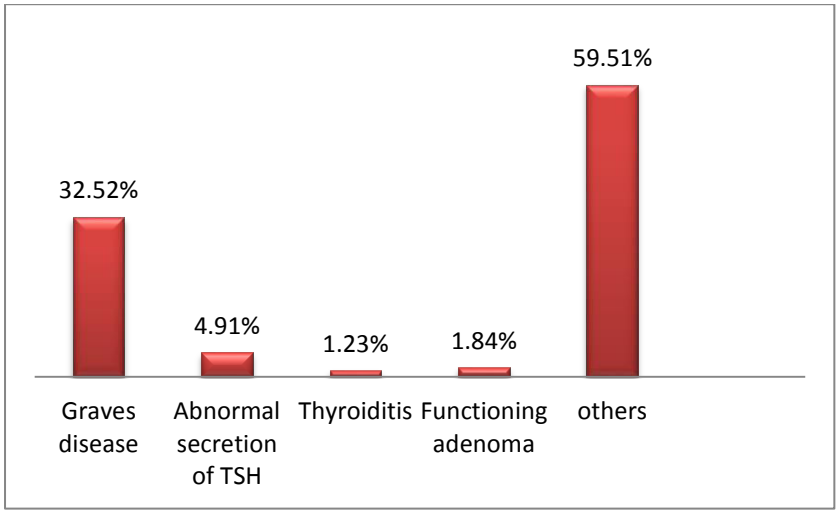


Fig 4.13: Causes of hyperthyroidism

Of all thyroid disorder containing patients 32.52% have Graves' disease, 4.91% have abnormal secretion of TSH, and 1.84% has functioning adenoma or toxic multinodular goiter, and 1.23% having thyroiditis and 59.51% patients do not know their cause – why they are having their disorder.

4.14 Symptoms of hyperthyroidism

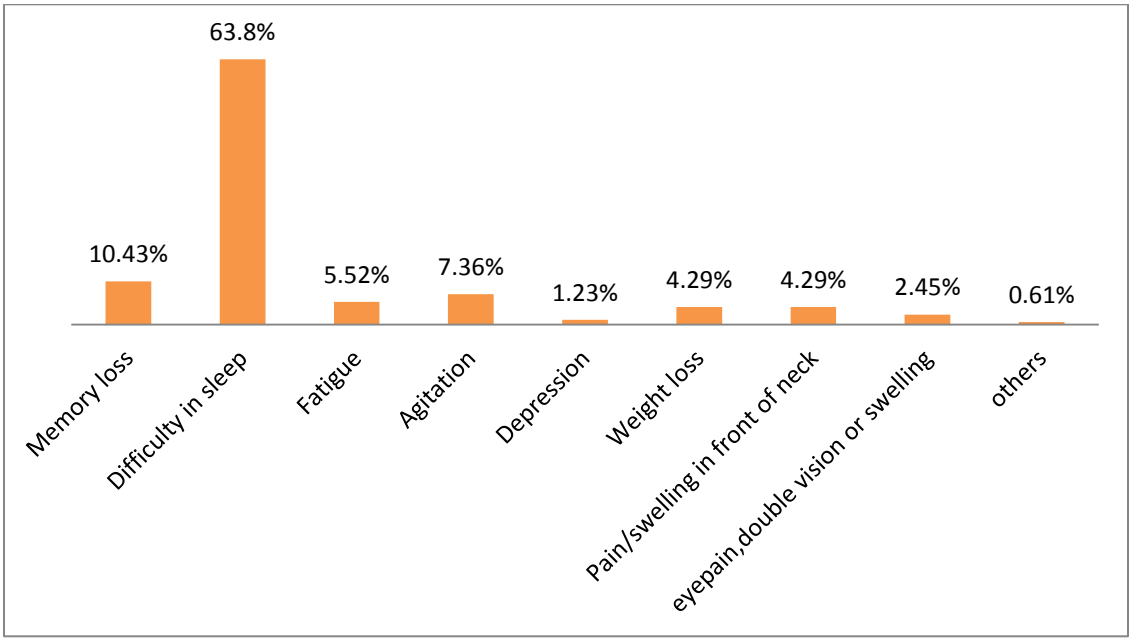


Fig 4.14: Symptoms of hyperthyroidism

Of all Hyperthyroid disordered patients approximately- 5.52% have fatigue eyes, 10.43% have memory loss, 63.8% have difficulty in sleep, 7.36% have agitation, 4.29% having unexpected weight loss,1.23 having depression,4.29% having pain or swelling in front of the neck,2.45% having eye pain or double vision & 54% cannot understand their symptoms clearly.

4.15 Types of test for determining hyperthyroidism

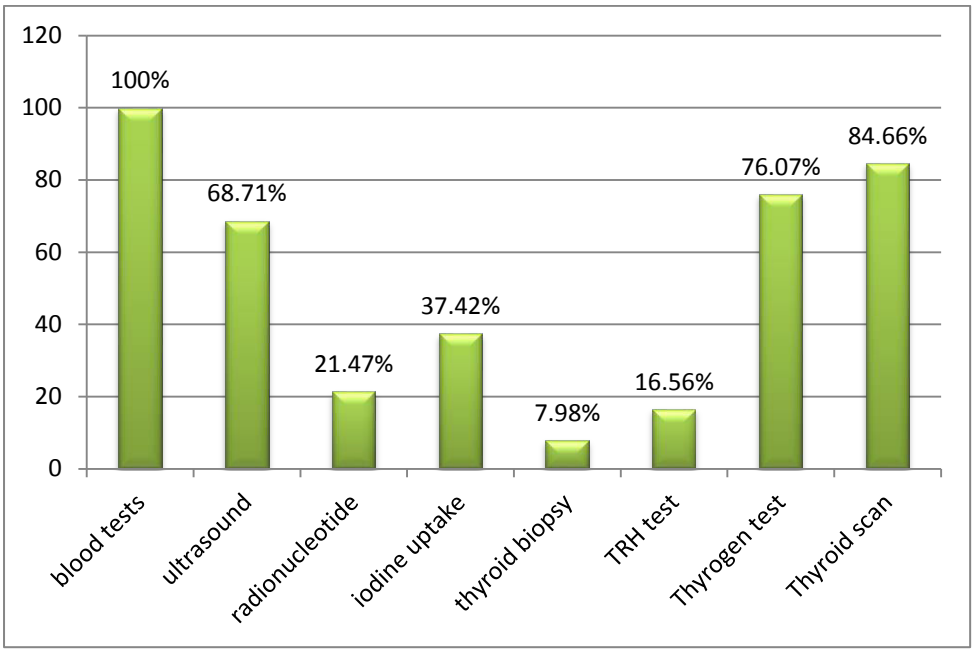


Fig 4.15: Type of tests for hyperthyroidism diagnosis

For determining hyperthyroidism, physicians suggest to do blood test 100%, TRH Test 16.56%, ultrasound examination 68.71%, iodine uptake test 37.42%, thyroid scan 84.66%, radionucleotide test 21.47%, thyrogen test 76.07% & in some cases thyroid biopsy 7.98 % if there is any surgery.

4.16 Blood tests

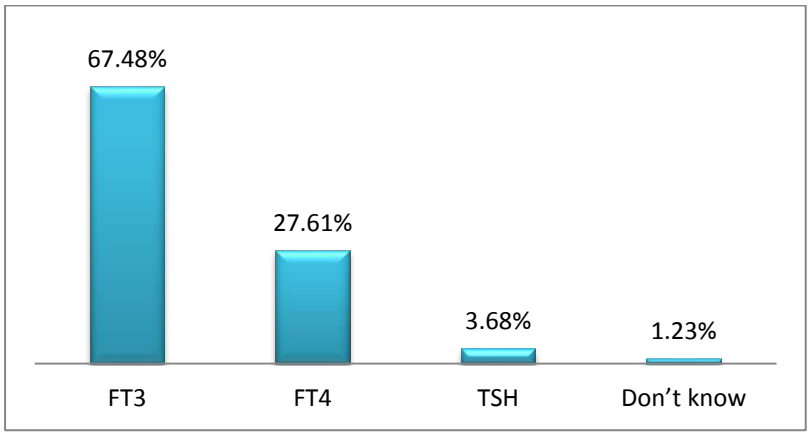


Fig 4.16: Blood tests used for knowing patient's condition after treatment

Physicians check TSH level the most 3.68% then FT4 level 27.61%, FT3 level 67.48% & 1.23% have know any idea about their blood tests. For knowing patients' response towards the treatment pattern, or whether they have to change the treatment.

4.17 Treatment

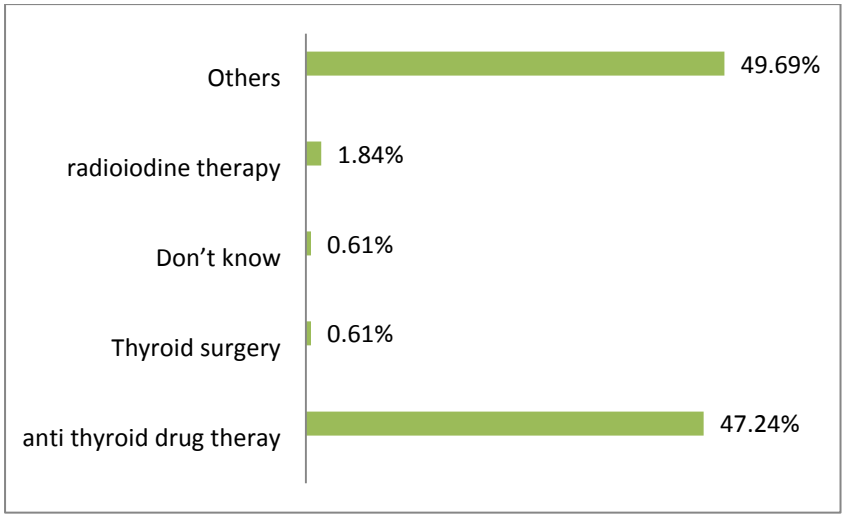


Fig 4.17: Percent of Treatment types for hyperthyroid patients

Majority 49.69% of them are treated which they have no idea about their treatment, 47.24% are treated with anti-thyroid drug therapy, 1.84% are taking radio iodine therapy, 0.61% have thyroid surgery, & 0.61% do not take any therapy.

4.18 Medications prescribed to hyperthyroid patients

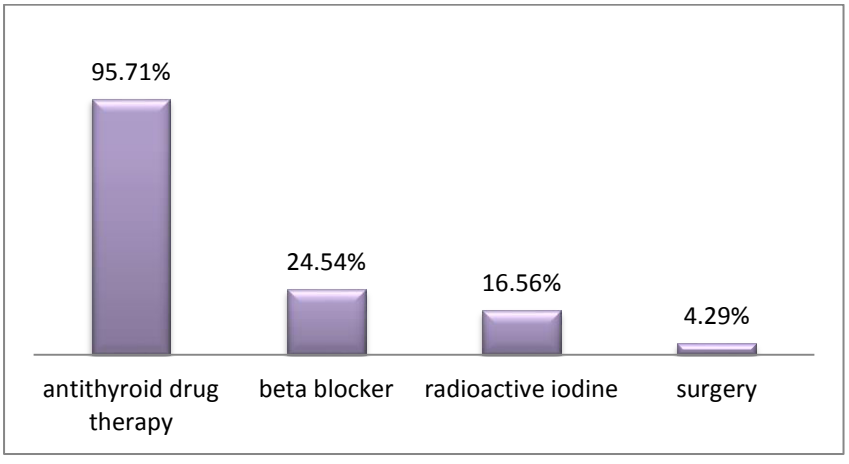


Fig 4.18: Medications suggest for hyperthyroid patients

Among 163 patients 95.71% are treated with anti-thyroid drug, 24.54% are taken beta blockers, 16.56% takes radioactive iodine & 4.29% are treated with surgery.

4.19 Medications suggest for thyroid disordered patients

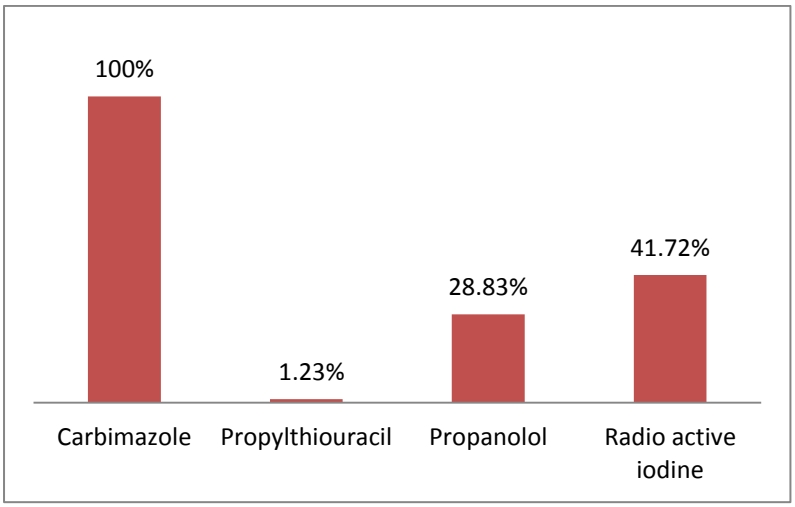


Fig 4.19: Percent of medications taken by patients

Majority of hyperthyroidism patients are treated with anti thyroid drugs, and mainly carbimazole 100%, in addition with this 28.83% patients are treated with Beta blockers specially propranolol, some are given PTU 1.23% only, if any adverse response to carbimazol, some patients after taking anti- hyperthyroid treatment may develop hypothyroidism, in that case they are given Levothyroxine, and some are treated with radioactive iodine 41.72%.

4.20 Medication taking time

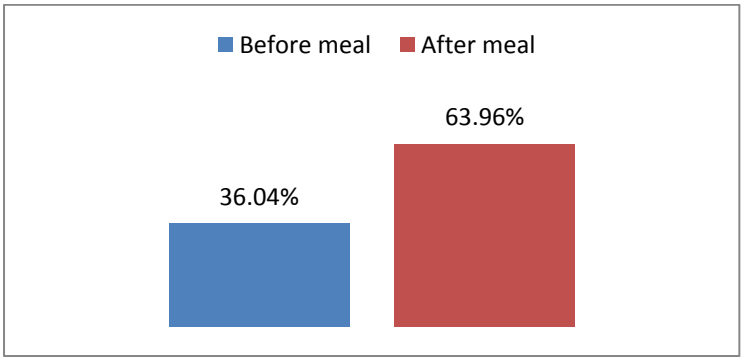


Fig 4.20: Medication taking time

Among 222 participating patients 36.05% takes their medication before meal, 63.96% takes their medication after meal. Among these 36.05 % patients, who takes medication before meal-

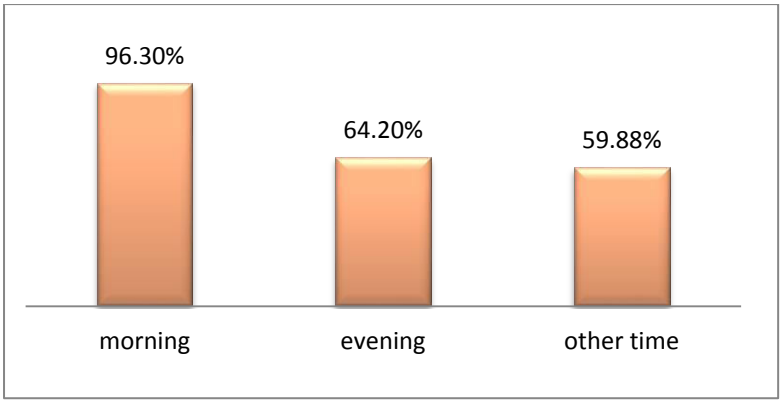


Fig 4.20.1: Medication taking time before meal

Among 36.05% patients, 96.30% takes their medication in morning, 64.20% takes in evening and 59.88% takes in other time.

4.21 Complexity of dosage administration /treatment form

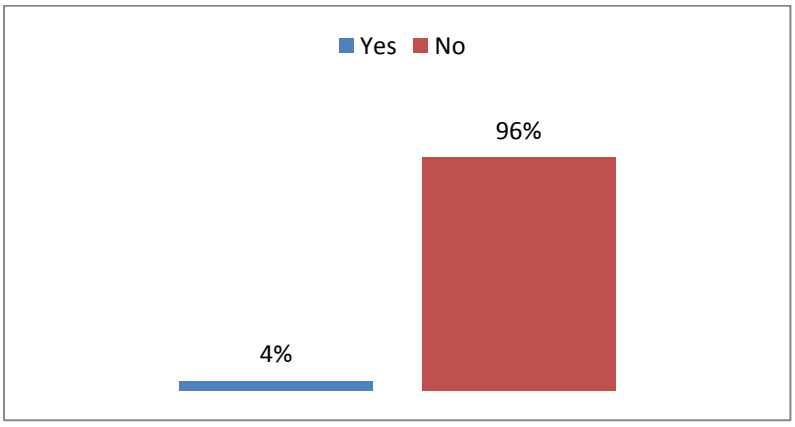


Fig 4.21: complexity of dosage administration /treatment form

Among 223 patients, 96% patient's do not facing any problem but only 4% of that claimed that they have some mild problems.

4.22 Medication on time

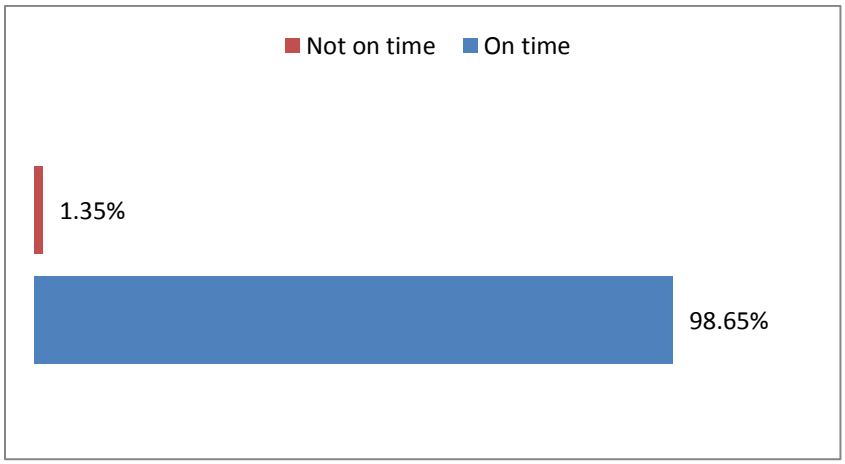


Fig 4.22: Habit of taking medication on time

98.65% patients take their medication on time and 1.35% does not regular in taking their medicine.

4.23 Perception about disease recovery

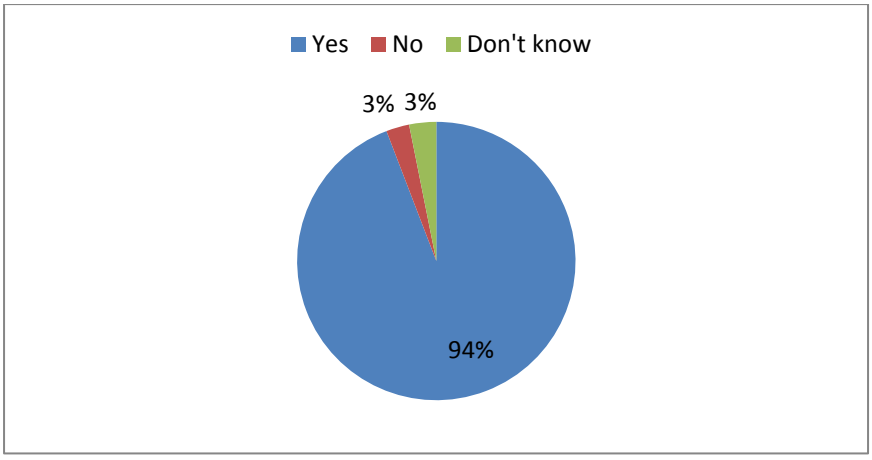


Fig 4.23: Perception about disease recovery

94% of patients think that they will recover but 3% don't think that they might be fully recovered & 3% people don't know their fate.

4.24 Satisfactory level of Physician's consultancy and assistance

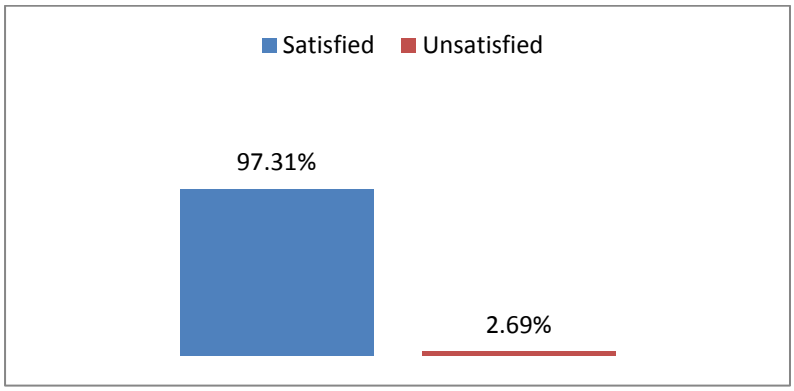


Fig 4.24: Physician's consultancy in satisfied range

Almost all patients 97.31% are satisfied about doctor's consultancy and only 2.69% shows dissatisfaction.

4.25 Regular in check up

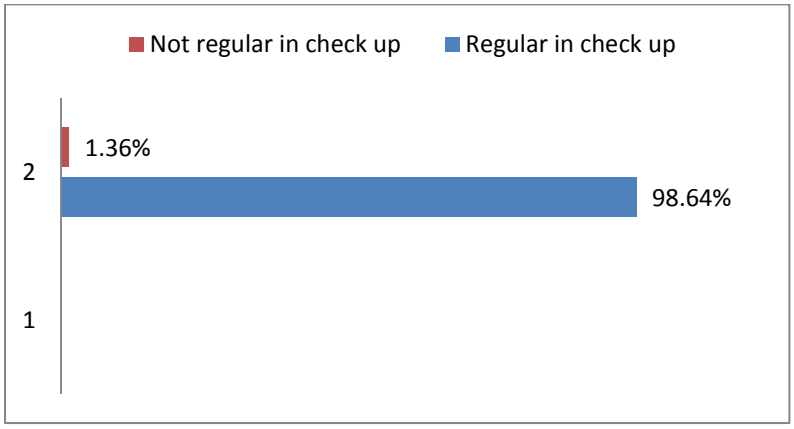


Fig 4.25: Regular in check up as routine work

98.64 % of all patients were regular in checkup. And 1.36% was not regular in checkup.

4.26 Missed dose recovery patterns

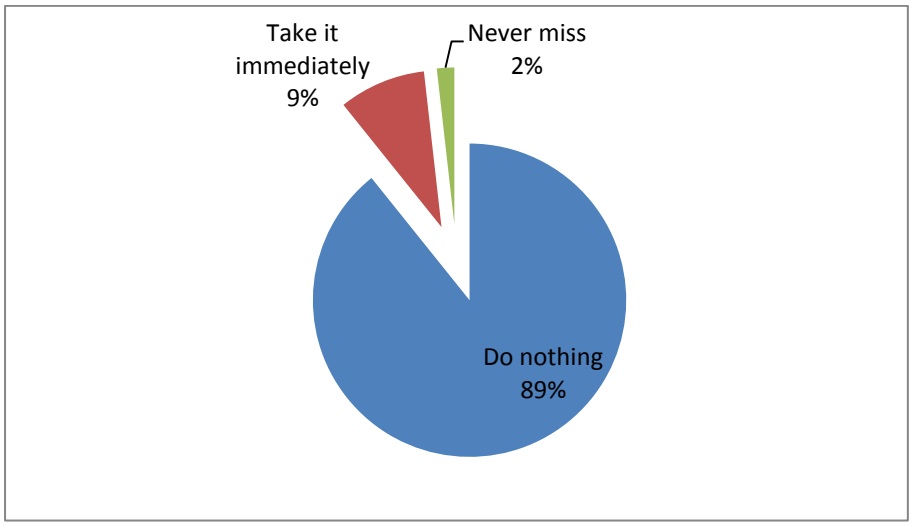


Fig 4.26: Missed dose recovery pattern when they missed dose

89% irregular patients' just do nothing if they missed any dose, and some patients about 9% take their missed dose immediately & 2% never miss their dose.

4.27 Maintaining their weight

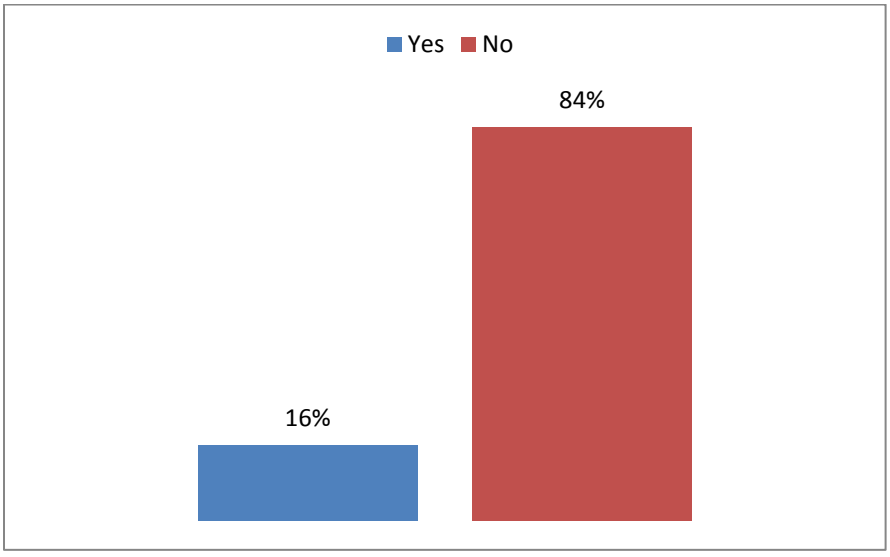


Fig 4.27: Percentage of patients maintaining their weight

16% patients of total patients try to maintain their weight. And 84% are not conscious about their body weight.

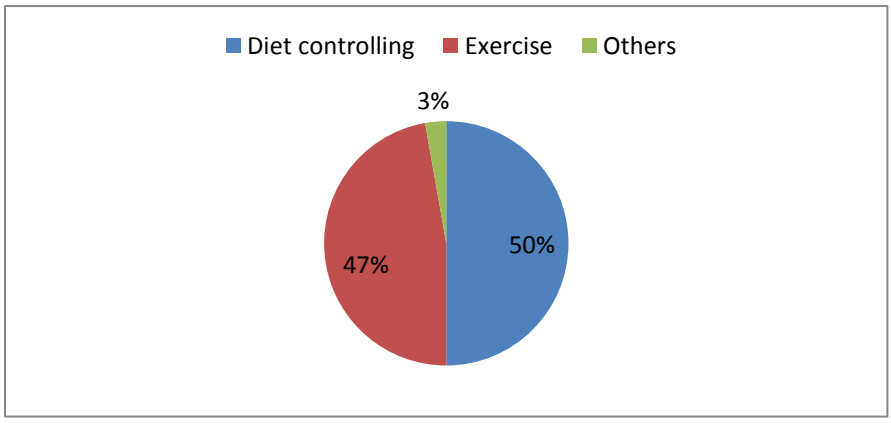


Fig 4.27.1: Methods used for controlling patients' weight

47% doing some exercise, 50 % controls their diet and 3% doing nothing for maintaining health.

Chapter 5

Discussion

5 Discussion

Thyroid disorder is the second most common endocrine disorder in women both in the developed and less developed world (Hechtman, 2011).Thyroid disorders are conditions that affect the thyroid gland, a butterfly-shaped gland in the front of the neck. The thyroid has important roles to regulate numerous metabolic processes throughout the body. Different types of thyroid disorders affect either its structure or function. Women are more likely than men to have thyroid disease. One in eight women will develop thyroid problems during her lifetime. Thyroid disorders for the most part are treatable; however, untreated thyroid disease can produce serious results in other parts of the body. Improved public awareness and understanding of thyroid disorders will enable patients and their families to cope more effectively with the sometimes disturbing course of thyroid illness. There is few study held on hyperthyroidism in Bangladesh but we have conducted a survey on 273 patients study on hyperthyroidism. Here, we mainly focused on patient's diagnosis, treatment pattern and patient's knowledge pattern and also their awareness and this study was done in 6 renowned institutions of Dhaka and Mymensingh, Bangladesh.

In our study, we got 81.68% of endocrine disordered patients having thyroid disorder and majority patients have 59.7% of hyperthyroidism. Others have glucose homeostasis disorder 14.29% who are also have chance to have thyroid disorder & rest have only 4.03% tumor. Here, among 163 hyperthyroidism patients, 87.65% subclinical hyperthyroidism and 12.35% overt hyperthyroidism.

Females are more vulnerable than males to thyroid disorders. We have found the same result in our study where 73% female and 27% male had thyroid disorders. Similarly, in another study in America, the prevalence of hyperthyroidism in community-based studies has been estimated at 2% for women and 0.2 % for men (Reid and wheeler, 2005).

In our study we got, majority of patients are in the age limit 21-40 years were of (42.49%), age and 41-60 years were of (41.76%). But according to American Thyroid Association hyperthyroidism mostly occurs in more than 60 years old people. Again, according to Australian bureau of statistics, 51- over 80 years old Australian people having more thyroid

disorder in terms of hypo- and hyperthyroidism (Thyroid flyer, 2000). On the other hand, in our country this disorder develops in a younger age.

In our study we found that, majority of the BMI status of patients with endocrine disorders were normal weighted (50%) and a high prevalence of overweight 39%were found. So, some conscious patients maintain their health by controlling their diet and taking some kind of physical exercise although they are only 16% of total patients.

In 163 hyperthyroid containing patients, 12.35% are suffering from overt hyperthyroidism, and 87.65% were suffering from subclinical hyperthyroidism. Where in an Indian study, subclinical hyperthyroidism was detected in 5.1% cases of Juvenile autoimmune thyroiditis, and none had overt hyperthyroidism (John, 2008). Among them most of the people were sufferings for more than 1 year. Although most of the patients do not know the cause of hyperthyroidism (59.51%), but Graves' diseases was in high percentage (32.52%),which is similar to a study of Kentucky, Graves' disease is the most common cause of hyperthyroidism, accounting for 60 to 80 percent of all cases (Weetman, 2000). Majority has difficulty in sleep (63.8%), memory loss (10.43%) these patients are mostly treated with anti-thyroid drugs (95.71%), and beta blocker (24.54%).which is also supported by American Thyroid Association. In our study majority of people did blood tests (100%), thyroid scan (84.66%), thyrogen test (76.07%) and ultrasound (68.71%). In blood tests majority of patients did FT3 test (67.48%).In our study we see that patients are treated with carbimazole where in America patients were mostly treated with methimazole and propylthyouracil(thyroid.org, 2012).

Again, in our study we found, 94% of patients think that they will recover. 98.64% of all patients were regular in checkup.98.65% patients take their medication on time and 96% don't found their treatment pattern complex, but 4% claimed that they have some mild problems. Although, 85% patients were educated and at least passed SSC, but unfortunately, only 14% can provide their family history and among them, majority (50%) got their disorder from their mother. So, we can say from our study, the majority of patients are concerned about their disease and taking their medications regularly. Because most of the people were educated so they were more conscious with their diagnosis, treatment and medication, but at the same time they were having lack of consciousness about the risk factors and family history.

Chapter 6

Conclusion

6 Conclusion

In conclusion, the results of the present study revealed the prevalence of thyroid disordered patients and the rate of hyperthyroidism among them, their consciousness and perception about their disorder and moreover their treatment pattern and compliance. It had been found that the knowledge about patients having family history of thyroid disorder is very low in both educated and the illiterate patients. Most of the patients were women. But most patients are not as severe as they were suffering from have sub clinical hyper thyroidism. Majority were quite healthy as their BMI was in normal range, and as most patients are educated, they were conscious about their treatment. But still they do not have any clear perception about their disease. They do not know the severity of their disease and treatment outcome. On the other hand awareness would lead to early detection and reduce the stage at diagnosis, potentially improve patient's knowledge and more cost effective treatment should be easily provided. So, efforts should be made by Government and Non- Governmental agencies to improve the knowledge about thyroid disorder. Here in this study we only focused on Hyperthyroidism but further studies can be done on other thyroid related disorder to widen this study in large sphere.

Chapter 7

References

7 References

Akhter, N., Hassan, S. (2008) Sub-clinical hypothyroidism and hyperprolactinemia in infertile women: Bangladesh perspective after universal salt iodination, The Internet Journal of Endocrinology, 5(1), p.357-563.

Bielecka-Dabrowa, A., Mikhailidis, D., Rysz, J. and Banach, M. (2009). The mechanisms of atrial fibrillation in hyperthyroidism. *Thyroid Research*, [online] 2(1), p.4. Available at: https://thyroidresearchjournal.biomedcentral.com/articles/10.1186/1756-6614-2-4[Accessed 20 Jun. 2016].

Cancer.org. (2015). *Signs and symptoms of thyroid cancer*. [online] Available at: http://www.cancer.org/cancer/thyroidcancer/detailedguide/thyroid-cancer-signs-symptoms [Accessed 5 Apr. 2016].

Chapman, E. and Evans, R. (1946). The treatment of hyperthyroidism with radioactive iodine.journal of the American medical association.[online] 131(2),p.86. Available at: http://jama.jamanetwork.com/article.aspx?articleid=285751 [Accessed 20 Jun. 2016].

Duprez, L., Parma, J., Van Sande, J., Allgeier, A., Leclère, J., Schvartz, C., Delisle, M., Decoulx, M., Orgiazzi, J., Dumont, J. and Vassart, G. (1994). Germline mutations in the thyrotropin receptor gene cause non–autoimmune autosomal dominant hyperthyroidism. *Nature Genetics*, [online] 7(3), pp.396-401. Available at: http://www.nature.com/ng/journal/v7/n3/abs/ng0794-396.html [Accessed 20 Jun. 2016].

Fitsweb.uchc.edu.(2016).*DiagnosticTests*.[online] Available at: http://fitsweb.uchc.edu/student/selectives/Luzietti/Thyroid_diagnostics.htm [Accessed 5 Apr. 2016].

Franklyn, j. and Boelaert, k. (2005). thyroid hormone in heath and disease. *society for endocrinology*.Journal of endocrinology,p.1-15 Available at: http://joe.endocrinology-journals.org/content/187/1/1.full.pdf+html [Accessed at 20 june,2016]

Franklyn, J. and Boelaert, K. (2012). Thyrotoxicosis. *The Lancet*, 379(9821), pp.1155-1166.

Franklyn, J. and Sheppard, M. (1998). *Mortality after the Treatment of Hyperthyroidism with Radioactive Iodine* —New England Journal of Medicine [online]. Available at: http://www.nejm.org/doi/full/10.1056/NEJM199803123381103 [Accessed 20 Jun. 2016].

Hechtman, L. (2011) Clinical Naturopathic Medicine. 3rd edition, Elsevier Australia.

Hoque, R. and Hossain, S. (2001). *Untitled Document*. [online] Orion-group.net. Available at: http://www.orion-group.net/journals/Journals/Vol13_Sep2002/7.html [Accessed 20 Jun. 2016].

Hurley, D., Hunter, A., Hewett, M. and Stockigt, J. (1981). Atrial Fibrillation and Arterial Embolism in Hyperthyroidism. *Australian and New Zealand Journal of Medicine*, [online]11(3), pp.391-393 Available at: http://onlinelibrary.wiley.com/doi/10.1111/j.1445-5994.1981.tb03519.x/abstract [Accessed 20 Jun. 2016].

John, M. (2008) Burden of Thyroid Diseases in India. Need for Aggressive Diagnosis, Medicine Update, 18, p. 334-341

Lam, P. (2015). *Graves' Disease: Causes, Symptoms and Treatments*. [online] Medical News Today. Available at: http://www.medicalnewstoday.com/articles/170005.php [Accessed 5 Apr. 2016].

Marks, l. (n.d.). *What Is Hyperthyroidism?*. [online] EverydayHealth.com. Available at: http://www.everydayhealth.com/hyperthyroidism/guide/ [Accessed 5 Apr. 2016].

Mathur, R. (2015). *hyperthyroidism*. [online] medicinenet.com. Available at: http://www.medicinenet.com/hyperthyroidism/page2.htm [Accessed 5 Apr. 2016].

Mayoclinic.org. (2014). *Goiter Symptoms - Mayo Clinic*. [online] Available at: http://www.mayoclinic.org/diseases-conditions/goiter/basics/symptoms/CON-20021266 [Accessed 5 Apr. 2016].

Mayoclinic.org. (2015). *Symptoms and causes - Hypothyroidism - Mayo Clinic*. [online] Available at: http://www.mayoclinic.org/diseases-conditions/hypothyroidism/symptoms-causes/dxc-20155382 [Accessed 5 Apr. 2016].

Mayoclinic.org. (2015). *Thyroid nodules Symptoms - Mayo Clinic*. [online] Available at: http://www.mayoclinic.org/diseases-conditions/thyroid-nodules/basics/symptoms/CON-20021546 [Accessed 5 Apr. 2016].

MD, K. (n.d.). *Hyperthyroidism Complications*. [online] EndocrineWeb. Available at: http://www.endocrineweb.com/conditions/hyperthyroidism/hyperthyroidism-complications [Accessed 5 Apr. 2016].

Moslem, F., Bithi, S.T., Biswas, A. (2015) Prevalence of Thyroid Dysfunction Among Type-2 Diabetes Patients in an Urban Diabetes Hospital, Bangladesh. Open Science Journal of Clinical Medicine. 3(3), pp. 98-102

Moore, K. (2016). *Thyroid Storm*. [online] Healthline. Available at: http://www.healthline.com/health/thyroid-storm#Symptoms3 [Accessed 5 Apr. 2016].

Myhivclinic.org. (n.d.). *Thyroid Disease â€“ Risk Factors*. [online] Available at: http://myhivclinic.org/thyroid-disease/disease-information-overview/risk-factors [Accessed 5 Apr. 2016].

Mythyroide.blogspot.com. (2010). *Hyperthyroidism: Prognosis*. [online] Available at: http://mythyroide.blogspot.com/2010/12/prognosis_6867.html [Accessed 5 Apr. 2016].

Mudde, A., Houben, A. and Kruseman, A. (1994). Bone metabolism during anti-thyroid drug treatment of endogenous subclinical hyperthyroidism. *ClinEndocrinol*, [online] 41(4), pp.421-424. Available at: http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2265.1994.tb02571.x/full [Accessed 20 Jun. 2016].

myVMC, (2003) Hyperthyroidism | myVMC. [online] Available at: http://www.myvmc.com/diseases/hyperthyroidism/ [Accessed 19 Sep. 2015].

Newson, D. (2016). *Hyperthyroidism (overactive thyroid). Medical information | Patient*. [online] Patient. Available at: http://patient.info/doctor/hyperthyroidism [Accessed 5 Apr. 2016].

Newson, D. (2016). *Hyperthyroidism (overactive thyroid). Medical information | Patient*. [online] Patient. Available at: http://patient.info/doctor/hyperthyroidism [Accessed 5 Apr.

2016].

Nutritionist-resource.org.uk. (2016). *Hyperthyroidism (Overactive Thyroid) - Nutritionist Resource*. [online] Available at: http://www.nutritionist-resource.org.uk/articles/hyperthyroidism.html [Accessed 5 Apr. 2016].

Nytimes.com. (2016). *HypothyroidismÂ Background - Hypothyroidism Health Information - NY Times Health*. [online] Available at: http://www.nytimes.com/health/guides/disease/hypothyroidism/background.html [Accessed 5 Apr. 2016].

Provet.co.uk. (2013). Provet healthcare information- *Classification of Hypothyroidism*. [online] Available at: http://www.provet.co.uk/health/diseases/hypothyroidismclass.htm [Accessed 5 Apr. 2016].

Quimby, E. and Werner, S. (1949). Late radiation effects in roentgen therapy for hyperthyroidism. Journal of the American medical association, [online] 140(12), p.1046. Available at: http://jama.jamanetwork.com/article.aspx?articleid=305111 [Accessed 20 Jun. 2016].

Reid, J. R., Wheeler, S.F. (2005) Hyperthyroidism: Diagnosis and Treatment, American Family Physician, 72 (4), p. 624-629 Available at: http://www.aafp.org/afp/2005/0815/p623.pdf [Accessed on 26 Nov.2015]

Rightdiagnosis.com. (2015). *Symptoms of Subacute Thyroiditis - RightDiagnosis.com*. [online] Available at: http://www.rightdiagnosis.com/s/subacute_thyroiditis/symptoms.htm [Accessed 5 Apr. 2016].

Ross, d. (n.d.). *Beta blockers in the treatment of hyperthyroidism*. [online] Uptodate.com. Available at: http://www.uptodate.com/contents/beta-blockers-in-the-treatment-of-hyperthyroidism [Accessed 5 Apr. 2016].

RxList. (2015). *Synthroid (Levothyroxine Sodium) Drug Information: Side Effects and Drug Interactions - Prescribing Information at RxList*. [online] Available at: http://www.rxlist.com/synthroid-drug/side-effects-interactions.htm [Accessed 5 Apr. 2016].

Schraga, E. (n.d.). *Hyperthyroidism, Thyroid Storm, and Graves Disease: Background, Pathophysiology, Epidemiology*. [online] Emedicine.medscape.com. Available at: http://emedicine.medscape.com/article/767130-overview#a5 [Accessed 5 Apr. 2016].

Shaha, A., Alam, M., Rashid, M., Hoque, M., Khasru, M. and Ahasan, H. (2008). Radio-iodine Therapy in Hyperthyroidism- A Study of 50 Cases. *J. Medicine*, [online] 9(1). Available at: http://www.banglajol.info/index.php/JOM/article/view/1422 [Accessed 20 Jun. 2016].

Shomon, M. and Shomon, M. (2016). *Thyroid Diagnosis: How to Get Tested*. [online] About.com Health. Available at: http://thyroid.about.com/od/gettestedanddiagnosed/a/testdiagnose.htm [Accessed 5 Apr. 2016].

Shomon, M. and Shomon, M. (n.d.). *Thyroid Diagnosis: How to Get Tested*. [online] About.com Health. Available at: http://thyroid.about.com/od/gettestedanddiagnosed/a/testdiagnose.htm [Accessed 5 Apr. 2016].

Singer, P. and Cooper, D. (1995). Treatment Guidelines for Patients with Hyperthyroidism and Hypothyroidism. *JAMA*, [online] 273(10), p.808. Available at: http://jama.jamanetwork.com/article.aspx?articleid=387402 [Accessed 20 Jun. 2016].

Steven, D. E. (2014) University of Maryland Medical Center hypothyroidism. Available at: http://umm.edu/health/medical/altmed/condition/hypothyroidism

Thyroid.org (2012) American Thyroid Association hypothyroidism. Available at: http://www.thyroid.org/hypothyroidism/ [Accessed on 26 Nov.2015]

Tmedweb.tulane.edu. (n.d.). *antithyroid_drugs [TUSOM | Pharmwiki]*. [online] Available at: http://tmedweb.tulane.edu/pharmwiki/doku.php/antithyroid_drugs [Accessed 5 Apr. 2016].

WebMD. (2016). *Hyperthyroidism-Treatment Overview*. [online] Available at: http://www.webmd.com/women/tc/hyperthyroidism-treatment-overview [Accessed 5 Apr.

2016].

Yeung, M. and Serpell, J. (2008). Management of the Solitary Thyroid Nodule. *The Oncologist*, [online] 13(2), pp.105-112. Available at: http://theoncologist.alphamedpress.org/content/13/2/105.short [Accessed 20 Jun. 2016].

Zeng, X. and yuan, Y, Wu, T, Yan L, Su H. (2009). Chinese herbal medicines for hyperthyroidism. The Cochrane library. [Online](2). Available at: http://www.ncbi.nlm.nih.gov/pubmedhealth/PMH0013474/ [Accessed 20 Jun. 2016].