INVESTIGATION OF THYROID HORMONE STATUS AMONGOBESE WOMEN ATTENDING OF THE ENDOCRINE OUTPATIENT DEPARTMENT IN A TERTIARY LEVEL HOSPITAL

Submitted by

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A Thesis Report Submitted to the Department of Pharmacy, East West University, In Partial Fulfillment of the Requirements for the Degree of Masters of Molecular & Clinical Pharmacy

Declaration by the Candidate

I, **Tanzina Bente Satter**, hereby declare that, **"Investigation of thyroid hormone status among obese women attending of the endocrine outpatient department in a tertiary level hospital"** submitted by me to the Department of Pharmacy, East West University, in partial fulfillment of the requirements for the Degree of Masters of Pharmacy (M.Pharm) is a confide record of original research work carried out by me under the supervision and guidance of **Md. Anisur Rahman**, Senior Lecturer, Department of Pharmacy, East West University, Bangladesh. I also declare that no part of this report has been or is being submitted elsewhere for the award of any Degree.

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Certificate by the Supervisor

This is to certify that the dissertation entitle **"Investigation of thyroid hormone status among obese women attending of the endocrine outpatient department in a tertiary level hospital"**, submitted to the Department of Pharmacy, East West University, in partial fulfillment of the requirements for the Degree of Masters of Pharmacy , was carried out by Tanzina Bente Satter , ID No. 2014-03-79-031 under my supervision and no part of this dissertation has been or is being submitted elsewhere for the award of any Degree.

_____

Md. Anisur Rahman

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Endorsement by the Chairperson

This is to certify that the entitled **"Investigation of thyroid hormone status among obese women attending of the endocrine outpatient department in a tertiary level hospital"**, is a genuine research work carried out by Tanzina Bente Satter, ID No# 2014-03-79-031under the supervision of Md. Anisur Rahman (Senior Lecturer, East West University, Dhaka). I further certify that no part of the thesis has been submitted for any other degree and all the resources of the information in this connection are duly acknowledged.

_____

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Tanzina Bente Satter

DEDICATION

This research paper dedicated

To

My beloved parents

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ABSTRACT

This work was proposed to determine the status of thyroid hormone among obese women attending in the endocrine outpatient department in a tertiary level hospital. The study was performedon 800 obese women patients aged between 20-78years. Weight, height, Body mass index(BMI) and thyroid status reports that showed patient's TSH and FT4 levels were collected from Sir Solimullah Medical College & Hospital, Mitford, Dhaka from 2015-2016.In this study, the highest proportion of obese women patients was found 35% and weight ranges from 70-84kg. The lowest proportion of obese women patients was found 2%between58-67kg weights. According to BMI-wise allocation of obese women patients, the highest percentages was 62% where BMI ranges from 41- 50kg/m². In this BMI ranges, hyperthyroidism patients were found larger than hypothyroidism patients. Some patient's BMI were high from normal level of BMI but they had no thyroid disorder. Some Patients were found in this study who was suffering from subclinical hypothyroidism. Among 800 obese women patients, the number of hypothyroid women patients was300 that arelarger than 200 patients who were suffering from hyperthyroid problem. In this work, number of population was not large. This study exposes that most of the obese women suffered from thyroid problem whether it is hypothyroidism or hyperthyroidism. However further study with larger population is required to consolidate this result.

Key words: TSH, FT4, Height, Weight, BMI, Hypothyroidism, Hyperthyroidism, Subclinical Hypothyroidism, Obese.

Chapter: 1

Introduction

1.1 Introduction

The rapid emergence of overweight and obesity in developing countries has been recognized as a major public health problem in most regions of the world (World Health Organization, 2013). WHO estimates that at least 500 million adults (greater than 10%) are obese, with higher rates among women than men (Alwan, 2011). The prevalence of overweight-obesity in women of Bangladesh increased substantially from 2.7% in 1996 to 8.9% in 2006 (Balarajan and Villamor, 2009). There are some objectives to determine the status of thyroid hormone among obese women attending in the endocrine outpatient department in a tertiary level hospital.The specific objectives that are needed to do this work are:

- To assess the obese women attending in the endocrine outpatient department.
- To measure T3, T4 and TSH level of the obese women attending in the endocrine outpatient department.
- To determine the status of thyroid hormone among obese women attending of the endocrine outpatient department.

1.2 Pathophysiology of obesity:

The pathophysiology of obesity is complex and still poorly understood, but is includes genetic, environmental, behavioral and psychological factors (Haslam and James). Family studies suggest that heredity may explain up to 67% of the population variance in BMI (Maes et al., 1997). Obesity is associated with an increased risk of diabetes, dyslipidemia, kidney disease, cardiovascular disease, all-cause mortality and cancer (Golden et al., 2009). As a consequence, in developed countries, increasing rates of obesity may lead to a decline in the overall life expectancy (Olshansky et al., 2005).

Obesity is linked to many endocrine abnormalities including thyroid dysfunction (Kokkoris and Pi-Sunyer, 2003, Reinehr, 2010). Several clinical studies evaluated the issue of hormonal changes associated with obesity (Kokkoris and Pi-Sunyer, 2003). Thyroid dysfunction has been extensively investigated in obese subjects(Asvold et al., 2009, Reinehr, 2010). Evidence suggests that slight variations in thyroid function contribute to the development of regional obesity and the tendency to gain weight (Knudsen et al., 2005). The normal level of TSH is0.3-5.0pmol/L

and normal level of FT4 is 9.5-25.55pmol/L. Furthermore BMI has been negatively associated with serum free T4 (FT4) and higher TSH levels among slightly overweight euthyroid individuals thereby resulting in a positive correlation between TSH and the progressive increase in weight with time (Knudsen et al., 2005, Fox et al., 2008). Thyroid dysfunction is associated with changes in body weight and composition, body temperature and total and resting energy expenditure independently of physical activity. Moreover, weight gain often develops after treatment of thyroid dysfunction (Hoogwerf and Nuttall, 1984). Both subclinical and overt hypothyroidism are frequently associated with weight gain, decreased thermogenesis and metabolic rate (Hoogwerf and Nuttall, 1984, Asvold et al., 2009).

1.3 Thyroid gland:(Brady, 2015)

The thyroid gland is a butterfly-shaped organ located in the base of our neck. It releases hormones that control metabolism—the way our body uses energy. The thyroid is part of the endocrine system, which is made up of glands that produce, store, and release hormones into the bloodstream so the hormones can reach the body's cells.

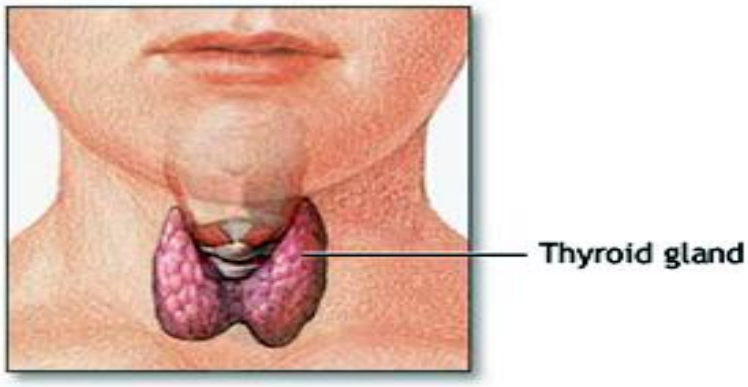

Figure 1.3: Thyroid gland (Wechter, 2014)

The thyroid gland uses iodine from the foods we eat to make two main hormones:

1. Triiodothyronine (T3)
2. Thyroxine (T4)

It is important that T3 and T4 levels are neither too high nor too low. Two glands in the brain the hypothalamus and the pituitary communicate to maintain T3 and T4 balance.

The hypothalamus produces TSH Releasing Hormone (TRH) that signals the pituitary to tell the thyroid gland to produce more or less of T3 and T4 by either increasing or decreasing the release of a hormone called thyroid stimulating hormone (TSH).

1.4 Pathophysiology of thyroid:

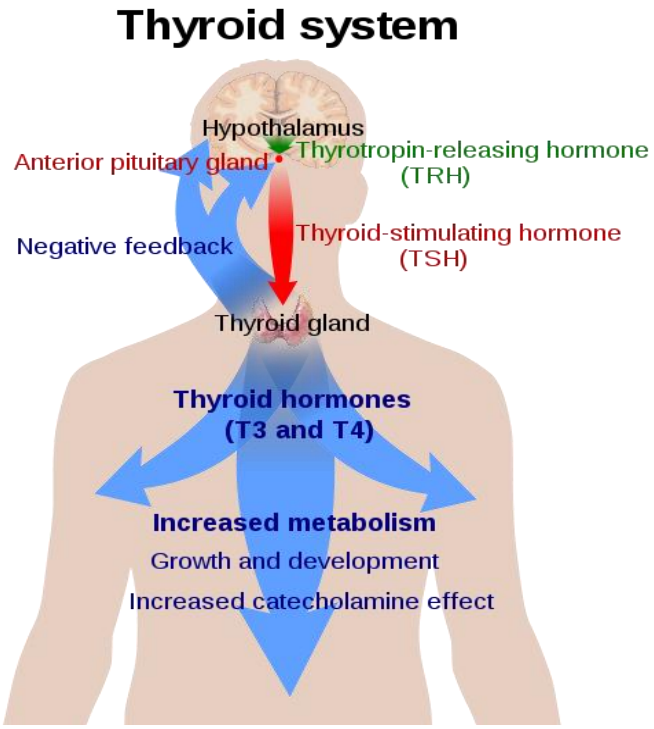

Figure 1.4: Diagram of the hypothalamic–pituitary–thyroid axis (Haggstrom, 2009)

The hypothalamus secretes TRH (green), which stimulates the production of TSH (red) by the pituitary gland. This in turn stimulates the production of thyroxine by the thyroid (blue). Thyroxine levels decrease TRH and TSH production by a negative feedback process.

1.5 Thyroid disease:(emedicinehealth, 2010)

There are some thyroid diseases include:

1. Hypothyroidism
2. Hyperthyroidism
3. Subclinical hypothyroidism

1.6 Hypothyroidism:

Hypothyroidism occurs when the thyroid gland does not produce enough energy generating thyroid hormones. Weight gain is a classic symptom of this dysfunction. In such cases levels of thyroid stimulating hormone (TSH) may rise in an attempt to spur more production andsecretion of thyroid hormones from thyroid gland (Kotkiewskiet al,. 1997).

1.7 Causes of hypothyroidism:(emedicinehealth, 2014)

The most common cause of hypothyroidism is-

- Hashimoto's thyroiditis. This causes the body's natural defenses-the immune system-to produce antibodies that over time destroy thyroid tissue.
- Iodine deficiency is the number one cause of hypothyroidism.
- Thyroid surgery- Removing all or a large portion of your thyroid gland can diminish or halt hormone production. In that case, we'll need to take thyroid hormone for life.
- Radioactive iodine therapy- It can destroy the thyroid gland, leading to hypothyroidism.
- External beam radiation-Radiation used to treat cancers of the head and neck can affect your thyroid gland and may lead to hypothyroidism.

Less common causes include:

- Infections- Viral and bacterial infections can temporarily damage the thyroid gland.
- Medicines-Some medicines can interfere with normal production of thyroid hormone. Lithium is one of the most common medicines that cause hypothyroidism. Others include amiodarone (such as Cordarone or Pacerone) and interferonalfa (such as Intron A or Roferon A).

- Excessive iodine which, in food or medicines, can reduce the function of the thyroid gland.
- Congenital hypothyroidism-Some babies are born with a defective thyroid gland or no thyroid gland. In most cases, the thyroid gland didn't develop normally for unknown reasons, but some children have an inherited form of the disorder. Often, infants with congenital hypothyroidism appear normal at birth. That's one reason why most states now require newborn thyroid screening.
- In rare cases, disorders of the pituitary gland or the hypothalamus (secondary and tertiary forms of hypothyroidism). The pituitary gland and hypothalamus produce hormones that control the thyroid and, as a result, affect its ability to produce thyroid hormone.
- Some women develop hypothyroidism during or after pregnancy (postpartum hypothyroidism), often because they produce antibodies to their own thyroid gland.

1.8 Sign and symptoms of hypothyroidism:(Pruthi, 2015)

The sign and symptoms of hypothyroidism are nonspecific and may be confused with those of other clinical conditions, especially in postpartum women and the elderly.Patients with severe hypothyroidism generally present with a group of sign and symptoms that may include-

- lethargy,
- weight gain,
- cold intolerance,
- decreased sweating,
- slowed heart rate,
- impaired memory,
- Muscle weakness,
- infertility,
- hair loss,
- dry skin,
- forgetfulness,
- Constipation and depression.

Not all of these sign and symptoms occur in every patient, and many may be blunted in patients with mild hypothyroidism (Hueston. 2001). Hypothyroidism is ten times more common in women than men and its prevalence increase s with age. The prevalence of thyroid dysfunction, by definition, is testing patients in various geographic regions, primary care clinics and in population that have not been screened previously (Ahmed et al., 2013). Thyroid function test panel is commonly used for screening and evaluating thyroid dysfunctions. The American Thyroid Association recommends that adults must be screened for thyroid dysfunction by measurement of the serum T3, T4, TSH concentration at the age 35 years and every 5 years thereafter (Ladensonet al., 2000).

1.9 Who can develop hypothyroidism?(Pruthi, 2015)

Anyone can develop hypothyroidism, anyone at an increased risk if he/she:

- Is a woman older than age 60
- Has an autoimmune disease
- Has a family history of thyroid disease
- Has other autoimmune diseases, such as rheumatoid arthritis or lupus, a chronic inflammatory condition
- Has been treated with radioactive iodine or anti-thyroid medications
- Received radiation to your neck or upper chest
- Has had thyroid surgery (partial thyroidectomy)
- Has been pregnant or delivered a baby within the past six months

1.10 Complications:(Pruthi, 2015)

Some Complications that untreated hypothyroidism can lead to a number of health problems:

- **Goiter.** Constant stimulation of thyroid to release more hormones may cause the gland to become larger — a condition known as a goiter. Hashimoto's thyroiditis is one of the most common causes of a goiter. Although generally not uncomfortable, a large goiter can affect your appearance and may interfere with swallowing or breathing.

- **Heart problems.** Hypothyroidism may also be associated with an increased risk of heart disease, primarily because high levels of low-density lipoprotein (LDL) cholesterol — the "bad" cholesterol — can occur in people with an underactive thyroid. Even subclinical hypothyroidism, a mild or early form of hypothyroidism in which symptoms have not yet developed, can cause an increase in total cholesterol levels and impair the pumping ability of your heart. Hypothyroidism can also lead to an enlarged heart and heart failure.
- **Mental health issues.** Depression may occur early in hypothyroidism and may become more severe over time. Hypothyroidism can also cause slowed mental functioning.
- **Peripheral neuropathy.** Long-term uncontrolled hypothyroidism can cause damage to peripheral nerves — the nerves that carry information from your brain and spinal cord to the rest of body, for example-arms and legs. Signs and symptoms of peripheral neuropathy may include pain, numbness and tingling in the area affected by the nerve damage. It may also cause muscle weakness or loss of muscle control.
- **Myxedema.** This rare, life-threatening condition is the result of long-term, undiagnosed hypothyroidism. Its signs and symptoms include intense cold intolerance and drowsiness followed by profound lethargy and unconsciousness. A myxedema coma may be triggered by sedatives, infection or other stress on body. If anyonehas signs or symptoms of myxedema, they need immediate emergency medical treatment.
- **Infertility.** Low levels of thyroid hormone can interfere with ovulation, which impairs fertility. In addition, some of the causes of hypothyroidism such as autoimmune disorder that can also impair fertility.
- **Birth defects.** Babies born to women with untreated thyroid disease may have a higher risk of birth defects than may babies born to healthy mothers. These children are also more prone to serious intellectual and developmental problems. Infants with untreated hypothyroidism present at birth are at risk of serious problems with both physical and mental development. But if this condition is diagnosed within the first few months of life, the chances of normal development are excellent.

1.11 Diagnosis of hypothyroidism:(Vellanki,2015)

The diagnosis of hypothyroidism, Health care providers usually diagnoses hypothyroidism by a thorough physical examination, medical history and through blood tests.

- Physical exam is that the doctor will check thyroid gland and look for changes such as dry skin, swelling, slower reflexes, and a slower heart rate.
- By Blood tests, there are two blood tests that are used in the diagnosis of hypothyroidism. The most common blood test used is the TSH test. It detects the amounts of thyroid stimulating hormone (TSH) in the blood. If the TSH reading is above normal then the patient is usually considered to have hypothyroidism; if TSH levels are below normal then the patient is considered to have hyperthyroidism.
- Additional blood tests used to confirm the diagnosis or determine the cause of hypothyroidism are the T4 test and the thyroid autoantibody test. It is often helpful for a doctor to run a complete thyroid panel, testing levels of T3 and T4, TSH and thyroid autoantibodies in order to fully establish the health and activity of the thyroid gland. This can help reduce the likelihood that a single normal reading for, say, thyroxine, masks an underlying issue with TSH or another key element of thyroid function.

1.12Treatment with medicine:(Mclntosh, 2015)

The majority of people with hypothyroidism are treated with one of the synthetic forms of the T4 thyroid hormone Levothyroxine (L-thyroxine). Thyroid hormone influences growth and maturation of tissues. It is involved in normal growth, metabolism, and development.

- Levothyroxine (LT4) is generally considered to be the treatment of choice for patients with hypothyroidism.
- Liothyronine (LT3) is a synthetic form of the natural thyroid hormone (T3) converted from T4. It is not intended for use as sole maintenance therapy, but in rare cases it can be used together with LT4 in small doses (5-15 µg/day).
- Iodine is an essential mineral for thyroid function, but people with autoimmune thyroid disease can be particularly sensitive to the effects of iodine, meaning that it can trigger or worsen hypothyroidism.

- Other thyroid hormone replacements are available but are not often recommended for replacement therapy. These include: desiccated thyroid hormone, T3 (triiodothyronine), and combinations of thyroid hormones T3 and T4.

1.13 Who take thyroid hormone medicine?(Kim, 2014)

People with hypothyroidism who take thyroid hormone medicine usually notice:

- Improved energy level.
- Gradual weight loss (in people with severe hypothyroidism at the time of diagnosis).
- Improved mood and mental function (thinking, memory).
- Improved pumping action of the heart and improved digestive tract function.
- Reduction in the size of an enlarged thyroid gland (goiter), if you have one.
- Improved growth, school performance, and behavior in children. Children whose growth has been delayed because of hypothyroidism start growing normally again when they are getting adequate doses of thyroid hormone.
- Lower cholesterol and triglyceride levels.

1.14 Effectiveness of thyroid replacement hormones:

The effectiveness of thyroid replacement hormones may be decreased when given with drugs such as calcium carbonate, ferrous sulphate, cholestyramine (Questran) and colestipol (Colestid) that binds thyroid replacement hormones and prevent their absorption. This interaction may be reduced by separating the administration of these drugs from thyroid replacement hormones by four hours. (Ogbru,2015)

1.15 Treatment of Hypothyroidism:

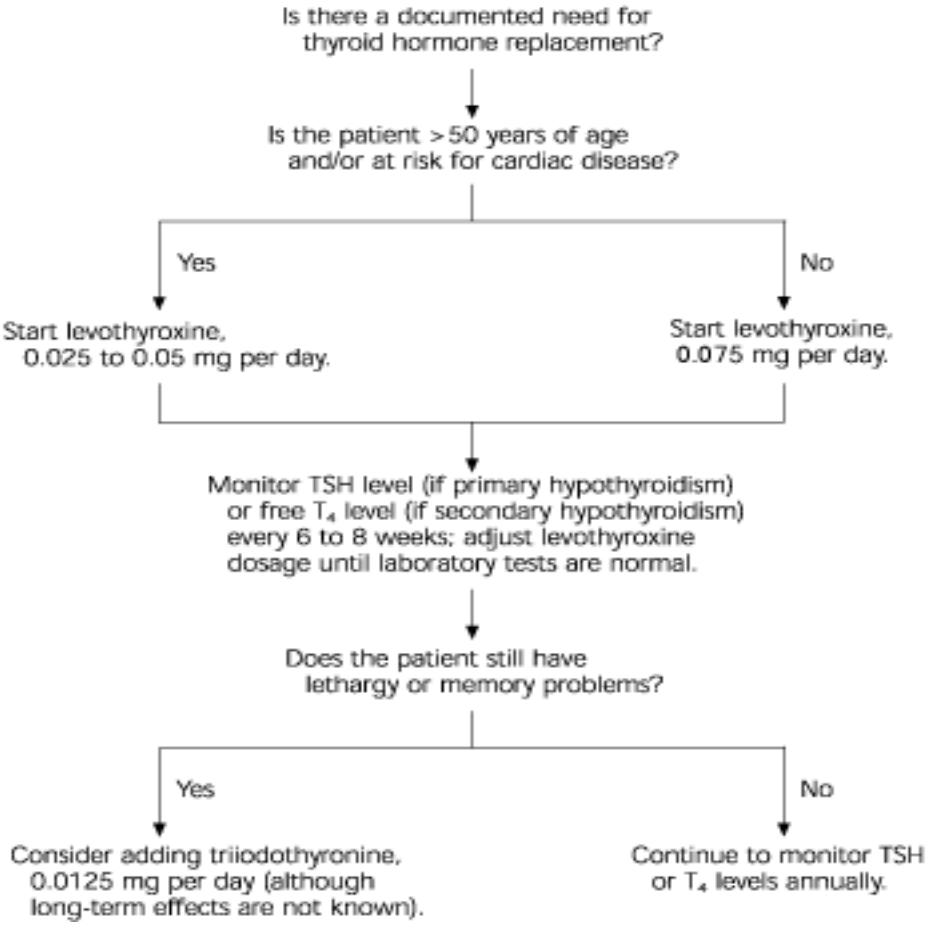

Figure1.12:Initiation and monitoring of treatment for hypothyroidism. (TSH = thyroid-stimulating hormone; T4 = thyroxine) (Hueston, 2001)

1.16 Hyperthyroidism:

Hyperthyroidism is a condition in which the thyroid gland is overactive and makes excessive amounts of thyroid hormone than our body needs. (Aleppo, 2015) Hyperthyroidism occurs when the thyroid makes too much tetraiodothyronine (T4) and thyroid stimulating hormone (TSH) is decreased from normal level. (Verneda et al., 2015)

1.17 Causes of hyperthyroidism:(Robonson, 2015&Verneda et al., 2015).

There are several causes of hyperthyroidism. These are –

- Graves' disease: It is an auto-immune disorder. It causes antibodies to stimulate the thyroid to secrete too much hormone.
- Excess iodine, a key ingredient in T4 and T3
- Inflammation of the thyroid (thyroiditis) that causes T4 and T3 to leak out of the gland
- Tumors of the ovaries or testes
- Benign tumors of the thyroid or pituitary gland
- Large amounts of tetraiodothyronine taken through dietary supplements or medication
- Thyroid nodule: One or more lumps, or nodules, can grow in the thyroid gland, gradually increasing the gland's activity and the amount of thyroid hormone in blood.

1.18Symptoms of hyperthyroidism:(Robonson, 2015 &Verneda et al., 2015)

Symptoms of hyperthyroidism are given below:

- Nervousness
- irritability
- increased perspiration
- heart racing
- hand tremors
- anxiety
- difficulty sleeping
- thinning of the skin
- hair loss
- muscular weakness
- weight loss
- difficulty concentrating

1.19 Diagnosis of hyperthyroidism:

Hyperthyroidism is diagnosed based on symptoms, physical exam, and blood tests to measure levels of thyroid stimulating hormone (TSH) and thyroid hormones T_3 and T_4. Doctor may also decide to order either an ultrasound or a nuclear medicine scan of thyroid to see if it has nodules, or whether it is inflamed or overactive. (Aleppo. 2015)

1.20 Treatment of hyperthyroidism:(Robonson, 2015 &Wisse, 2015)

Treatment depends on the cause and severity of symptoms. Hyperthyroidism is usually treated with one or more of the following:

- Antithyroid medicines (propylthiouracil or methimazole)
- Radioactive iodine to destroy the thyroid gland and stop the excess production of hormones
- Surgery to remove the thyroid
- Beta-blockers to slow down heart rate. These medicines do not lower thyroid hormone levels but help relieve symptoms related to a rapid heart rate.

1.21Complications of Hyperthyroidism:(Wisse, 2015)

Complications linked to hyperthyroidism include:

- Irregular heart rhythm (atrial fibrillation)
- Congestive heart failure
- Miscarriage
- Osteoporosis and bone fractures (hyperthyroidism causes your bones to lose calcium faster than usual)

Surgery-related complications, including:

- Scarring of the neck
- Hoarseness due to nerve damage to the voice box
- Low calcium level due to damage to the parathyroid glands (located near the thyroid gland)

- Hypothyroidism (underactive thyroid)

1.22 Subclinical hypothyroidism:(Fatourechi, 2009)

Subclinical hypothyroidism (SCH) is defined as a serum thyroid-stimulating hormone (TSH) level above the upper limit of normal despite normal levels of serum free thyroxine. Serum TSH measurement is the necessary test for diagnosis of mild thyroid failure when the peripheral thyroid hormone levels are within normal laboratory range. Subclinical hypothyroidism or mild thyroid failure is a common problem, with a prevalence of 3% to 8% in the population without known thyroid disease. The prevalence increases with age and is higher in women.

1.23 Causes of Subclinical hypothyroidism:

The commonest causes for subclinical hypothyroidism are autoimmune thyroiditis (Hashimoto's disease) and previous treatment for hyperthyroidism. Treatment of hyperthyroidism with radioiodine results in hypothyroidism in at least 50% of patients with Graves' disease (depending upon the dose administered), although a lower proportion in those with toxic nodular hyperthyroidism development of subclinical hypothyroidism typically preceding overt thyroid failure(Manji, N. et al. 2009).Partial thyroidectomy for hyperthyroidism or nodular goitre is associated with a similar risk of development of hypothyroidism, which is again first identified by a rise in serum TSH(Franklyn, 2013).

1.24 Symptoms and Signs of Subclinical hypothyroidism:(Vaz, 2016)

With advancing age, subclinical hypothyroidism may be even more common as TSH does tend to rise with age and typically presents with milder symptoms in older people. One may present with mild non-specific symptoms of hypothyroidism, such as fatigue, constipation and depression. A mild thyroid gland enlargement or goiter may be seen. In some studies treatment with thyroid hormone was associated with a significant decrease in goiter in cases of subclinical hypothyroidism.

1.25 Treatment of Subclinical hypothyroidism:(Vaz, 2016)

Treatment with thyroxine should be given to women and men with subclinical hypothyroidism in whom serum TSH concentration is raised and who have detectable levels of microsomal thyroid peroxidase antibodies. The aim of thyroxine therapy should be to restore serum TSH concentration to within the reference range: levels below this range are possibly associated with an increased risk of developing atrial fibrillation.

Subclinical hypothyroidism is always treated during pregnancy and preferably also when a patient is trying to conceive. Hypothyroidism in pregnancy is treated differently than in non-pregnant individuals.

1.26 Rationale of the research:

Obesity and thyroid dysfunction are common diseases. Hypothyroidism has often thought to be the cause of obesity. In recent years, there has been an increasing attention to thyroid function in obese patients. But the prevalence of hypothyroidism among obese women is not known in our country. The finding of the study might give the clinicians an idea regarding the investigation of thyroid hormone status in obese women and consequently they will be particularly alert for the screening their thyroid dysfunction.

Chapter: 2
Literature Review

In twentieth century, some researchers (Bertoli et al., 2002) took an attempt tostudy on the effect of subclinical hypothyroidism and obesity on whole-body and regional bone mineral content. This study showed that Subclinical thyroidhypofunction and obesity seem to affect BMD differently in the body segments. A condition of subclinical hypothyroidism should be considered when evaluating subjects for osteoporosis.

After 3 years,Ribaudowith researchers team(Ribaudo et al., 2005) worked on Relationship of thyroid function with body mass index, leptin, insulin sensitivity and adiponectin in euthyroid obese women. This study showed that TSH and BMI were positively related. TSH has been found to be correlated also with leptin adjusted for BMI. TSH could represent a marker of altered energy balance in severe, but uncomplicated obesewomen.

In 2009,another scientist(Julia, 2009) worked on Effect of treatment with levothyroxine in the lipid profile of the patients with subclinical hypothyroidism. This study was no significant differences were detected in TC or in LDL-c after treatment with levothyroxine. Nonsignificant reductions were found in TC (-4 mg/dl; p=0.77) and LDL-c (-10 mg/dl; p=0.31) when euthyroidism was achieved, as well as in TC (-10mg/dl; p=0.58) after 5+/-3 years of treatment.

In the same year, Veronelliand his researchers team (Veronelli et al., 2009) worked on Sexual dysfunction is frequent in premenopausal women with diabetes, obesity, and hypothyroidism, and correlates with markers of increased cardiovascular risk. These study indicated an increased prevalence of sexual dysfunction in diabetic, in obese, and in hypothyroid women, associated with markers of cardiovascular risk.

After few months,other scientists (Hassan et al., 2009) worked on Association between hypothyroidism and hepatocellular carcinoma.This study noted significant elevated risk association between hypothyroidism and HCC in women that was independent of established HCC risk factors. Experimental investigations are necessary for thorough assessment of the relationship between thyroid disorders and HCC.

After two months, some researchers(Ittermann et al., 2009) studied on Subclinical hyperthyroidism and blood pressure in a population. The result was Subclinical hyperthyroidism is not associated with changes in blood pressure, pulse pressure or incident hypertension.

After few months, other researchers(Chung et al., 2011) worked on Hyperthyroidism and female urinary incontinence. They showed that patients with hyperthyroidism were more likely to have UI (Urinary incontinence) during the 3-year follow-up period than the comparison patients.

In the same year, Lopezand his co-workers(Lopezet al., 2011) worked on Subclinical hypothyroidism and cardiovascular risk factors. Theyobserved a common pattern in the management of subclinical hypothyroidism, requiring the implementation and promotion of practice guidelines in primary care.

In 2011, Farasatandhis researchers team(Farasat et al., 2011) studied on Serum Thyroid and its regulatory hormone levels in obese women with sedentary lifestyle. The aim of this study was to investigate the thyroid hormones (T3, T4) and its regulatory hormone (TSH) levels in obese women with sedentary life style. It was observed that thyroid functions were normal in range in all subjects but when comparison was done between the groups using one way ANOVA, theserum T3 concentration was significantly low in obese and overweight subjects in comparison with normal weight subjects ($p \leq 0.005$). Serum T4 concentration was significantly lowers in overweight and obese subjects in comparison to normal weight ($p \leq 0.005$). Serum TSH concentration was significantly higher in obese in comparison with normal weight ($p \leq 0.005$) while it was not significantly higher in overweight subjects ($p \geq 0.05$).

In the next year, other scientists(Ayyagari et al., 2012)worked on Obesity, polycystic ovarian syndrome and thyroiddysfunction in women with epilepsy. The result was WWE (Women with epilepsy) on VAL (Sodium Valproate) and CBZ (Carbamazepine) had significant weight gain compared to DPH (Phenytoin) users. Despite weight gain, there was no difference in the incidence of PCOS between the users of VAL, CBZ and DPH.

After few months, Westerinkwith other researchers (Westerink et al., 2012) worked on Relation between thyroid-stimulating hormone and the occurrence of cardiovascular events and mortality in patients with manifest vascular diseases. Their result was Higher TSH levels within the normal range are associated with an increased risk of myocardial infarction, in patients with clinical manifest vascular disease. This relation is most prominent in patients without visceral obesity.

After 4 months, two researchers (Diez& Iglesias, 2012) took an attempt to study on the analysis of the relative risk for hypothyroidism in patients with Type 2 diabetes. The results favour screening for hypothyroidism in patients with Type 2 diabetes older than 65 years, especially in the presence of diabetic macroangiopathy or treatment with metformin.

Then Hammed I.K. (Hammed, 2012)worked on Subclinical Hypothyrodism and Central Adiposity. His result was 13.5 %(n=18) of the studied population had subclinical hypothyroidism.

In the same year, Ismozherova NV and Andeev AN(Ismoz herova & Andeev, 2012) worked on the frequency and structure of cardiac rhythm disturbances in the women presenting with abdominal obesity during the postmenopausal period. They observed that women presenting with abdominal obesity during the postmenopausal period are characterized by the high frequency of cardiac rhythm disturbances and ischemia. The elevated risk of ventricular extrasystole in the postmenopausal period is associated with AO, coronary heart disease, and chronic heart failure.

After 1year, Karasoy and fellow researchers(Karasoy et al., 2013) studied on Obesity is a risk factor for atrial fibrillation among fertile young women. The result was Obesity is a risk factor for AF (atrial fibrillation) among young and essentially healthy fertile women despite the low incidence of AF. These results may have implications for prevention of AF (atrial fibrillation).

Few months later, Anjaneya Prasad and fellow researchers (Prasad et al., 2013) worked on Subclinical Hypothyroidism in Obese Patients in Rural General Hospital.TSH levels were significantly higher in morbidly obesepatients and in females than in male patients.

After 5 months, two scientists (Das &Shaini,2013) worked on prevalence of Thyroid Hormone Dysfunction among Female Patients.The prevalence of hypothyroidism and hyperthyroidism in females are 19.1% and 13.7% respectively and also shows that prevalence of hypothyroidism is more common in females of hilly areas (23.8%) compared to valley or plain areas (16.2%).

In same month, Tigenwith his researchersteam (Tigen et al., 2013)tried to study on Cardiac changes with subclinical hypothyroidism in obesewomen. The result Cardiac structural and functional deteriorations may be related with subclinical hypothyroidism in obese subjects.

In the same year,Nekrasova(Nekrasova et al., 2013) worked on Hematological disturbances in subclinical hypothyroidism and their dynamics during substitution therapy. The aim was to estimate dynamics of hematological disturbances in autoimmune thyroiditis and subclinical hypothyroidism (SH) during substitution therapy and without it and to elucidate factors promoting successful correction.

In the same year, one scientist (Adriana, 2013)worked on prevelance of obesity in adul patients with diabetes mellitus type 2 and autoimmune chronicthyroiditis. 67.94% had different types of obesity. The obesity was more frequent in men than in women. Regarding the type of android obesity, 39.62% had typeI, 37.73 % typeII and 22.64 % typeIII. Also, 64.15 %had hypertension and dyslipidemia79.24 %. Android type was represented an increased risk of cardiovascular morbidity-mortality, particularly for atherosclerotic cardiovascular disease. The association of thyroid disease, which over time can evolve with hypothyroidism, is an additional risk factor for atherosclerotic cardiovascular disease.

Next year, Gowachirapant (Gowachirapant, 2014) worked on Overweight increases risk of first trimester hypothyroxinaemia in iodine-deficient pregnant women. Their result was Iodine-deficient pregnant women who are overweight have higher risk of hypothyroxinaemia in the first trimester compared to normal weight women. The overweight a potential risk factor for thyroid dysfunction in pregnant women in iodine-deficient areas.

After 2 months, Nakamuraand his researchers team (Nakamura et al., 2014) studied on association between a serum thyroid-stimulating hormone concentration within the normal range and indices of obesity in Japanese men and women. Their result was a significant interaction between the TSH level and the smoking status on body weight and a significant association between the TSH level and body weight in nonsmokers, but not in current smokers. No significant associations were observed between the TSH level and the anthropometric indices in women.

After 3 months, Mamtaniand his teammate(Mamtani et al., 2014) worked onincreased waist circumference is independently associated with hypothyroidism in Mexican Americans: replicative evidence from two large, population-based studies. Their result was central obesity (defined as WC $\geq$ 102 cm in men and $\geq$88 cm in women) was associated with clinical and subclinical hypothyroidism independent of age, sex, BMI and type 2 diabetes in both datasets. Estimated prevalence of hypothyroidism was consistently high in those with central obesity, especially below 45yrs of age.

After 2 months,some scientists(Jaiswal et al., 2014) studied on High prevalence of maternal hypothyroidism despite adequate iodine status in Indian pregnant women in the first trimester. Their result was Women consuming vegetarian diets did not have significantly lower iodine intakes or higher risk of hypothyroidism than those consuming mixed diets, but overweight/obesity and anemia predicted thyroid insufficiency.

In the same year,other researchers(Ismailov&Abdurazzakova,2014) tried to study on Prevalenceofsubclinicalhypothyroidismamongfemaleresidentsof Andijan region in Uzbekistan. Prevalence of subclinical hypothyroidism with TSH concentrations > 4.05

mIU/l and normal FT4 among female, aged from 18 to 65 was found 12.4%. It confidently increased to 28.3% when TSH upper limit was reduced (> 2.5 mIU/l). Regardless of TSH upper limit subclinical hypothyroidism frequency is higher among women over 40 years of age than among those under 30.

After 1 year, another groups(Farishta et al., 2015) worked on Insulin resistance and thyroid hypofunction in obese women. They found that 46% of these SH subjects are having insulin resistance while 24% of patients with normal thyroid function are having insulin resistance as estimated by HOMA IR.

After that study, some scientists(Gupta et al., 2015) worked on a correlation between thyroid stimulating hormone and body mass index in women with subclinical hypothyroidism.Thyroid profile (TSH and T3) was significantly (<0.05) different between subclinical hypothyroidism women and normal women. Women with subclinical hypothyroidism were having higher TSH (13.01±4.41 vs. 2.61±0.79) compared with normal healthy control group along with different T3 (0.94±0.17±1.09±0.26) between the groups. The serum concentration of FT4 was not significant between the groups. The body mass index, higher (28.81±3.47 vs. 22.62±1.57) in subclinical hypothyroidism women, was highly significant (<0.001). BMI was positively correlated with TSH in SCH (0.36) group as well as normal control (0.50) group. The correlation was significant (<0.05) in both the groups.This result suggests that estimation of thyroid profile, also within the normal range, could be one of several factors acting in concert to determine body weight. However, this parallel increase in BMI due to weight gain along with increase in TSH may further leads to overt hypothyroidism if left untreated.

In the same year, IngerAakre and his teammate(Aakre et al., 2015) worked on excessive iodine intake and thyroid dysfunction among lactating Saharawi women. The main objective was to describe iodine status and the prevalence of thyroid dysfunction among lactating women in areas with high iodine (HI) and very high iodine (VHI) concentrations in drinking water. They discovered that being from VHI area was associated with higher urinary iodine concentration (UIC) and breast milk iodine concentration (BMIC). Thyroid dysfunction and/or positive thyroid antibodies were

found in 33.3% of the women, of which 18.9% had hypothyroidism and 8.1% had hyperthyroidism and 6.3% had positive antibodies with normal thyroid function. The high prevalence of thyroid dysfunction may be caused by excessive iodine intake over several years.

After the above study, ZhianDezayeeand his teammate(Dezayee et al., 2015)tried to study on thyroid hormones protect Type 2 diabetes in obese patients against cardio metabolic risk factors. The serum levels of T3 and T4 attended higher level in women compared with men while the TSH levels are less in women than in men. The significant positive correlations between the TSH and the cardio metabolic risk factors (except fasting serum glucose and hsCRP) were observed. It concludes that the thyroid gland function is disturbed in obese T2D patients and thyroid hormones were significantly and inversely correlated with cardio metabolic risk factors which were prominently observed in men.

Chapter: 3

Materials & Methods

3.1 Main outcome variable:

The main outcome variable of the study is to determine the investigation of thyroid hormonestatus among obese women attending in the endocrine outpatient department in a tertiary level hospital.

3.2 Study preparation:

Women attending in the endocrine outpatient department whose BMI ≥ 25 kg/m²were the study population.

3.3 Sample size:

To determine the sample size, a total of 800 patients with relevant symptoms were initially included in the study.

3.4 Sampling method:

The subjects meeting the predefined eligibility criteria were selected purpositively from the study population.

3.5 Inclusion:

- BMI ≥ 25 kg/m²
- Age >18 years
- Sex: Female
- Clinical features of hypothyroidism, hyperthyroidism and subclinical may hypothyroidismor may not present.

3.6 Exclusion:

- Pregnant women
- Patient with secondary hypothyroidism
- Thyroid carcinoma
- Sex: Male
- Previously diagnosed hypothyroid
- Patient on thyroxin
- BMI < 25 kg/m

3.7Operational definitions:

Subclinical hypothyroidism:

Raised serum hypothyroidism THS with normal total T3 and T4

Overt hypothyroidism:

Elevated serum THS and low total T3 and T4 (Verma et al., 2008).

Over weight: 25-29.9 kg/m²

Obese class 1: 30-39.9 kg/m²

Obese class 2: 35-39.9 kg/m²

Obese class 3: 40 kg/m² (World Health Organization, 2004)

3.8 Research Question:

What is the investigation of thyroid hormone status among obese women attending in the endocrine outpatient department in a tertiary level hospital?

3.9 Procedure of preparing & organizing materials:

Data were collected using a structured questionnaire (Research Instrument) containing all the variables of interest. Collected data were checked daily and edited (if needed) in Sir Salimullah Medical College and Hospital, Mitford, Dhaka. Data collection periods were 4th October, 2015 to 7th February, 2016.Height was taken using standard apparatus with the subjects wearing light clothing and without shoes. Weight was measured in the upright position with a weighting scale to the nearest 0.01kilogram (kg). Height was measured to the nearest 0.1cm by using a non-stretching tape. Obesity index or body mass index (BMI) was calculated as weight (kg) divided by height squared (m²) to estimate overall body fat distribution (Greenspan and Gardner, 2004).

3.10 Procedure of data collection:

Data were collected by interviewing the patients, anthropometric measurements and laboratory investigations. Data were collected ensuring the privacy and confidentiality as far as possible. Before data collection, the detail of the study was explained to each eligible respondent and written informed consent was taken.

3.11 Data analysis:

After completion of data collection, data analysis was made with the help of analytical software Windows 2007(Microsoft Excel).

Chapter: 4

Result

Number of obesewomen patients age-wise

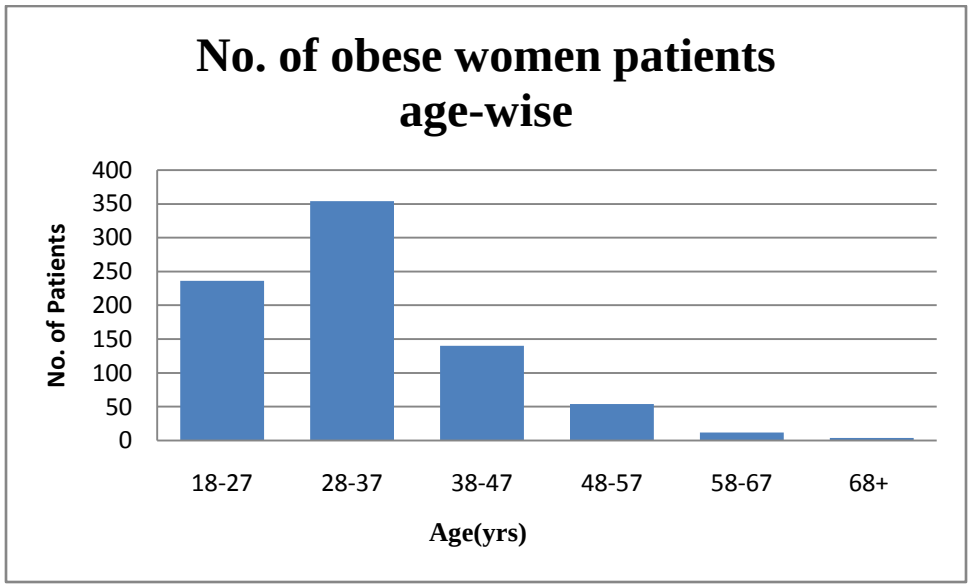

Figure4.1: Number of obese women patients age-wise

Age-wise distribution of obese women patients

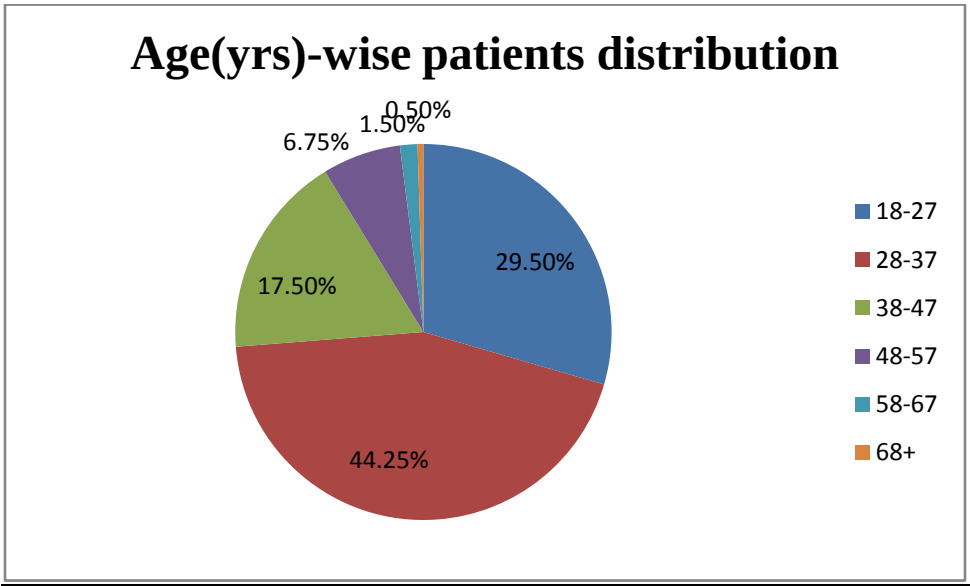

Figure 4.2: Age-wise distribution of obese women patients

Number of obese women patients weight-wise

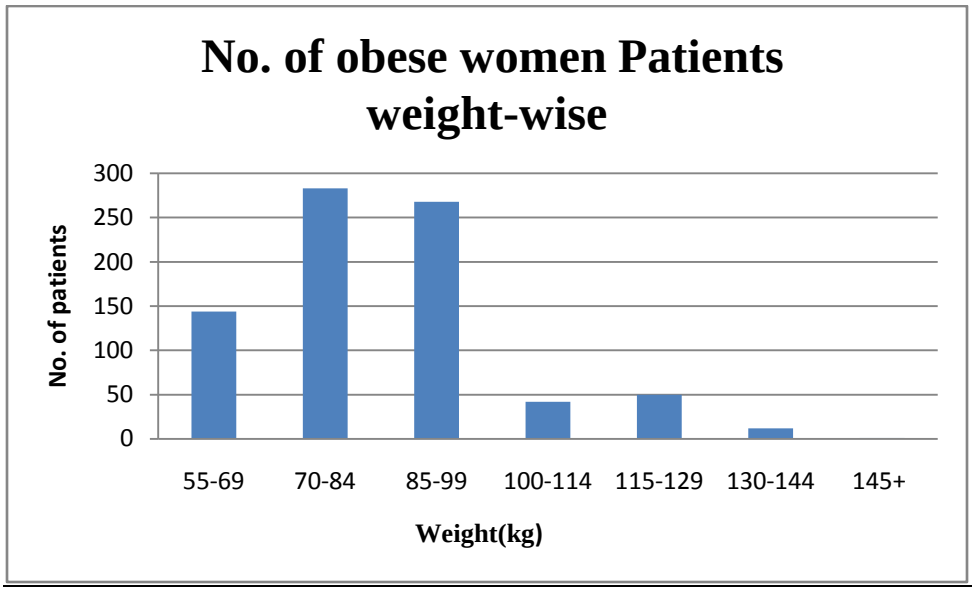

Figure4.3:Number of obese women patients weight-wise

Weight-wise allocation of obese women patients

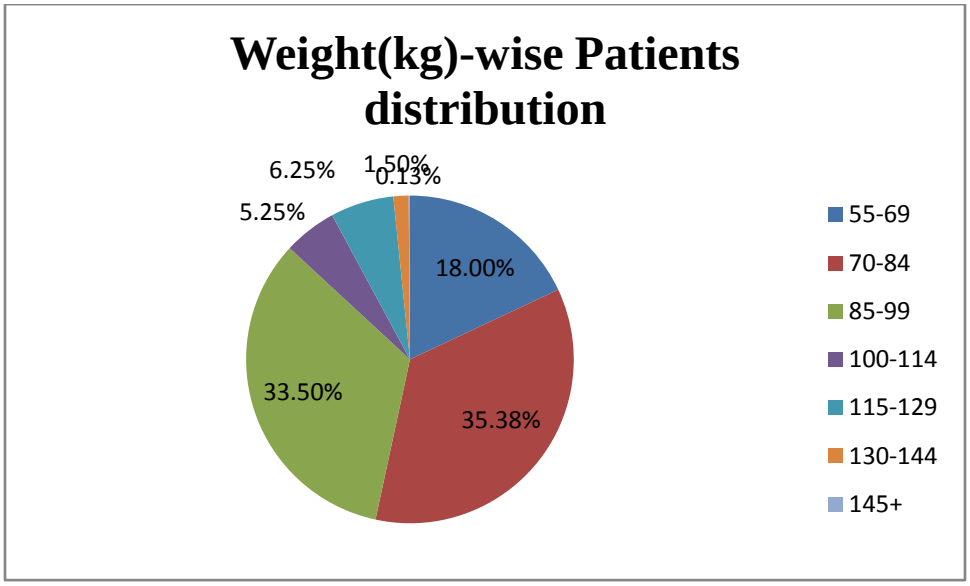

Figure4.4:Weight-wise allocation of obese women patient

Number of obese women patients height-wise

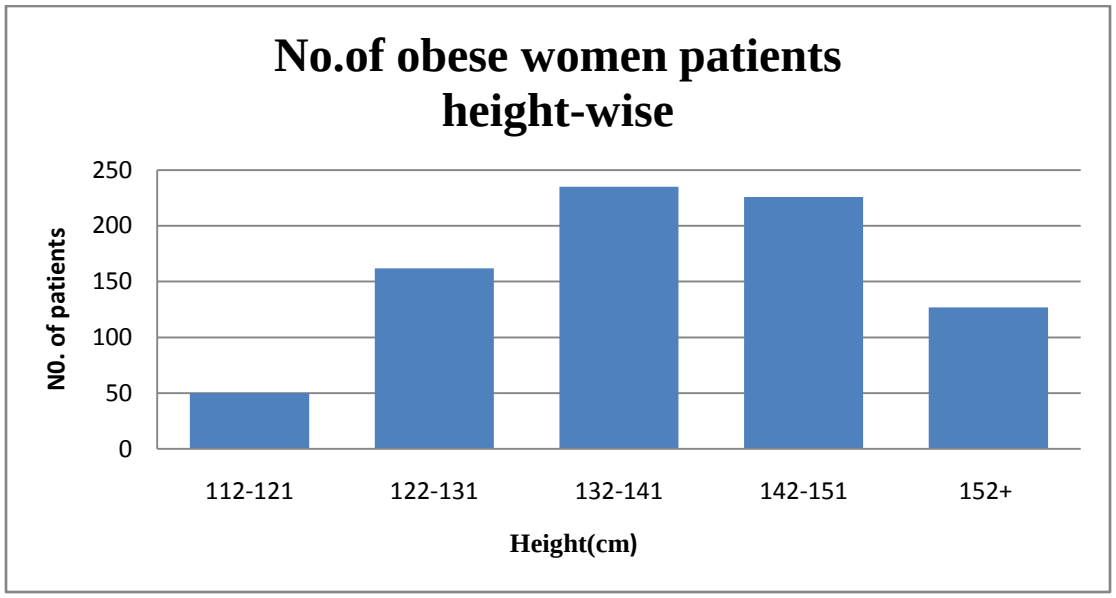

Figure4.5:Number of obese women patients height-wise

Height-wise distribution of obese women patients

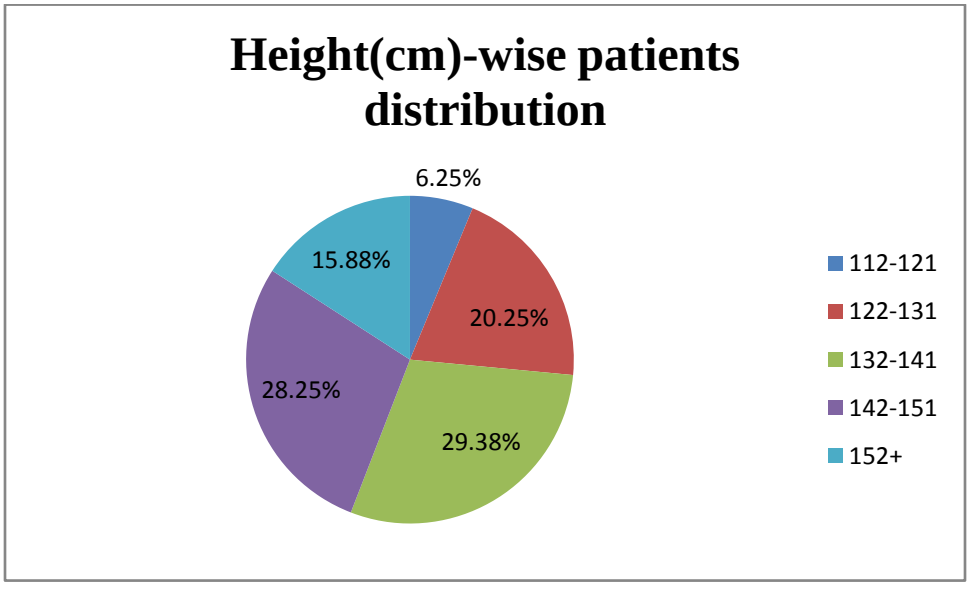

Figure4.6:Height-wise distribution of obese women patient

Number of obese women patients BMI-wise

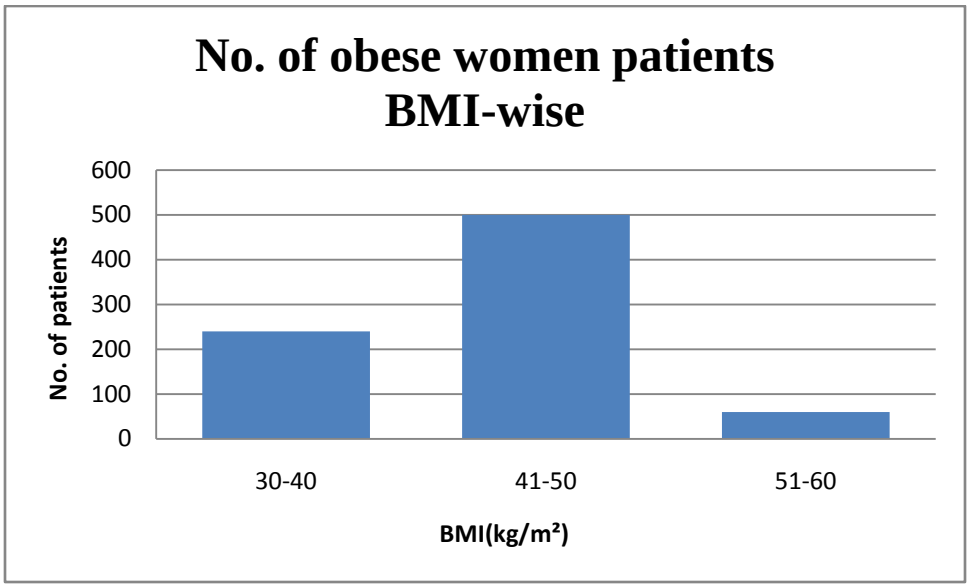

Figure4.7: Number of obese women patients BMI-wise

BMI-wise allocation of obese women patients

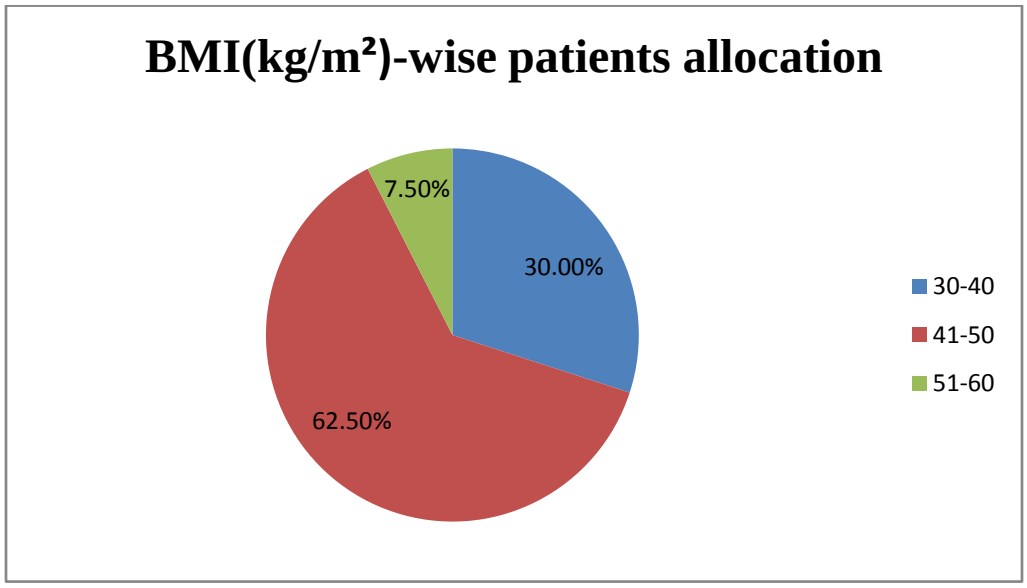

Figure4.8: BMI-wise allocation of obese women patients

Number of obese women patients Thyroid Status-wise

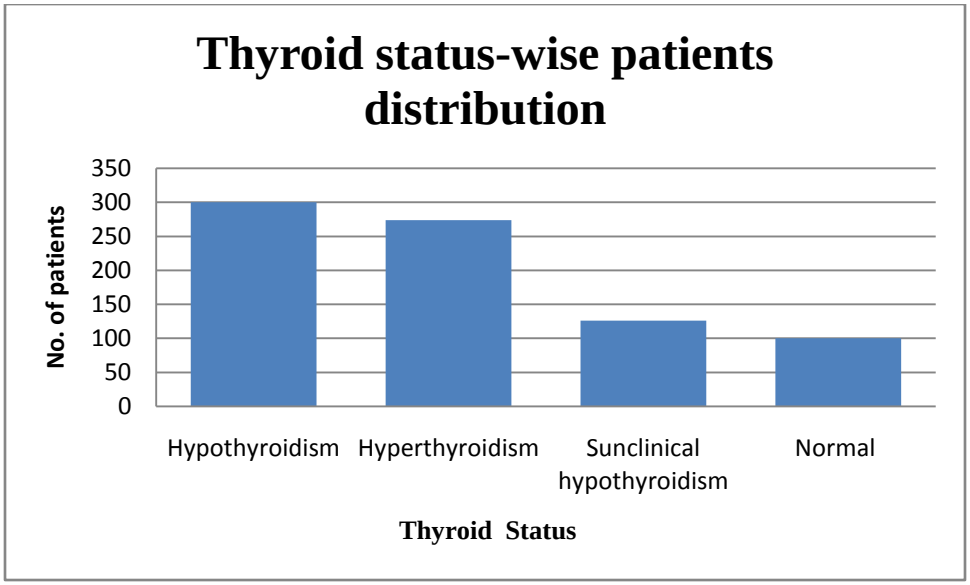

Figure4.9: number of obese women patients thyroid status-wise

Thyroid status-wise distribution of obese women patients

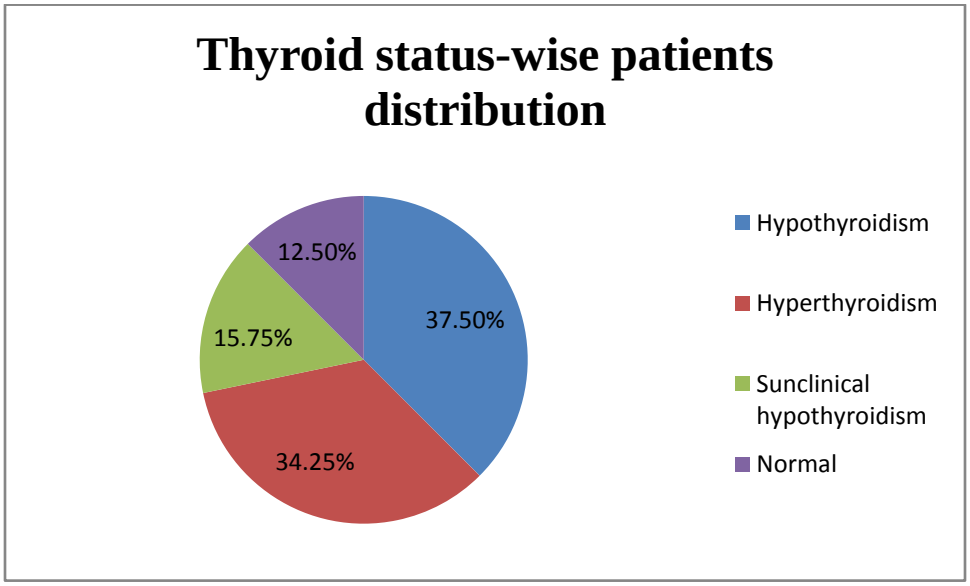

Figure4.10: Thyroid status-wise distribution of obese women patients

Chapter: 5
Discussion

About 200 million people in the world have hypothyroidism. Hypothyroidism is treatable; however, untreated hypothyroidism can produce serious results in other parts of the body. Improved public awareness and understanding of hypothyroidism will enable patients and their families to cope more effectively with the sometimes disturbing thyroid illness. In this way individuals will also be better equipped to play a role in alerting their physicians to a suspected thyroid condition that may otherwise be difficult to diagnose in the sometimes slowly developing initial phases.

The sample was collected from Sir Solimullah Medical College & Hospital, Mitford, Dhaka from 4th Oct, 2015 to 7thFeb; 2016.the study was done in which 800 obese women patients aged between 20-78yrs, weight, height, BMI and thyroid status report were taken.

In this study, the highest % of obese women patients were found 44% and age ranges from 28-37yrs (fig 4.2). In this age range, number of hyperthyroidism patients was found more than patients suffering from hypothyroidism. When TSH levels are high from normal level and FT4 levels are reduced from normal levels, then hypothyroidism is occurred. When TSH levels are low from normal level and FT4 levels are increased from normal levels, then hyperthyroidism is occurred. Subclinical hypothyroidism is occurred when TSH levels are increased from normal levels and FT4 is normal (Davidsons, 2014). Where among 350 obese women patients hypothyroidism was 131, hyperthyroidism was 141, subclinical hypothyroidism was 42 and though women were obese but they had no thyroid problem. The number of obese women patients was reduced by increasing age. That was age range 58-78yrs, the % of obese women patients was 1-2%. There hypothyroidism patients were found more than hyperthyroidism patients.

Weight of obese women patients was collected from the patient's information paper. According to weight-wise allocation of obese women patients, the highest percentages were 35% ranges from 70-84kg (fig. 4.4). In this weight range, hypothyroidism patients were found more than hyperthyroidism patients. Among 284 obese women patients hypothyroidism was 112, hyperthyroidism was 79, subclinical hypothyroidism was 60 and no thyroid disorder patients were 33. Above 130kg, the number of obese women patients was less that was 0-2%. There were no subclinical hypothyroidism patients. There were hypothyroidism patients, hyperthyroidism patients and normal patients and the number of patients was almost similar. Probable reason for weight gain due to lack of physical activity.

The highest % of obese women patients was found 30% and height ranges from 132-141cm (fig. 4.6). According to this height range, the number of hypothyroidism patients was found 93, where hyperthyroidism patients were found 69. Subclinical hypothyroidism patients were found 49 and 49 patients had no thyroid problem. The lowest number of obese patients was found 6% and height ranges from 112-121cm. Then the height ranges from 142-151cm showed 28% and above 152cm, the number of obese patients was 16%.

According to BMI-wise allocation of obese women patients, the highest percentages is 62% where BMI ranges from 41- 50kg/m² (fig 4.8). Here hyperthyroidism patients were found larger than hypothyroidism patients. Among 500 obese women patients, hypothyroidism patients were found 150, hyperthyroidism was 225 and subclinical hypothyroidism patients were 80.Some patient's BMI were high from normal level of BMI but they had no thyroid disorder. The number of this type of women was 44.Then the BMI ranges from 30 to 40 kg/m² showed 30% and the rest percentages showed ranges from 51- 60 kg/m².

Chapter: 6
Conclusion

The work was done on 800 obese women patients of various age groups, among them hypothyroid patients were found more than the women suffering from hyperthyroid problem. Here also found less number of patients who had no thyroid problem. So, it is probable cause that obese women patients are mostly hypothyroid and as a complications of hypothyroid obesity, heart disease, hypertension, infertility, ischemic heart disease results. As most females are affected, so they give a birth hypothyroid baby called cretinism (Steve, 2015) and which is the burden for a country. So, the determination of thyroid problem and proper management may help to improve overall health status of a country. The population of this study was not big. So, further study is needed to be done with larger population to verify the outcome of this study.

Chapter: 7
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Appendix