# Comparative Study of Hospitalization Characteristics and Predictors between Hypothyroidism and Hyperthyroidism of patients in the United States

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**Comparative Study for Hospitalization Characteristics and Predictors between Hypothyroidism and Hyperthyroidism of Inpatients in the United States**

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## ABSTRACT

**BACKGROUND**:

Hypo- and hyperthyroidism are the most common types of autoimmune diseases of the thyroid gland. Although the prevalence of overt hypo- and hyperthyroidism is 0.3% and 0.5%, respectively, the majority of patients with these disorders suffer from cardiovascular complications, which are considered to be a significant risk of mortality. The thyroid disorders and their complications affect patient quality of life and life spans, and elevate the government's economic burdens regarding health care. The objective of the present study is to highlight the similarities and differences of hypo- and hyperthyroidism in terms of risk factors related to hospitalization outcomes such as mortality, length of stay, and total medical charges when there is a presence of cardiovascular and other complications.

**METHOD**:

The study implemented a cross-sectional design to achieve the primary objectives. Data were downloaded and extracted, with permission, from Nationwide Inpatient Sample (NIS). A total of 721,958 patients with hypo- and hyperthyroidism were admitted to hospitals in the United States in 2012. The collected data included patient demographic characteristics, such as age, gender, race, insurance type, and income. Patient medical information included the number of medical procedures, chronic diseases, co-morbidities, and the type of thyroid disorder. Statistical Package for the Social Sciences (SPSS) version 22 was used to analyze the data of the present study, and all outcomes with a p-value less than 0.05 were found to be significant.

Multinomial logistic regression and multiple linear regressions (the dummy method) were the appropriate statistical tests to determine the predictors of the study outcomes.

**RESULTS**:

A descriptive analysis of the present study revealed the highest incidences of thyroid disorders to be in those who were older than 80 years of age (29.3%), white (76.7%), female (74.9%), on Medicare (68.2%), and who had a household income in the 25th percentile (27.1%). Patient medical information showed the highest comorbidities to be hypertension (63.8%), fluid-electrolyte disorders (29.1%) and uncomplicated diabetes (24.4%). The incidence of mortality for patients with thyroid diseases was 2.4%. The mean (± SD) length of hospital stay and total medical charges were 5.06 (±6.113) days and $41829.47 (±60920.47), respectively. There was a higher prevalence of hypothyroidism than hyperthyroidism (97% vs. 3%). Overall mortality showed a higher incidence of hypothyroidism than of hyperthyroidism (2.4% vs. 1.75%). The incidence of mortality increased with cardiovascular complications, to 5.42% vs. 4.87% for congestive heart failure (CHF) and 2.47% vs. 1.99% for hypertension (HT), for patients with hypo- and hyperthyroidism, respectively. Risk factors for patients with hyperthyroidism related to length of stay were paralysis, weight loss, pulmonary circulation, fluid and electrolyte disorders, age, neurological disorders, coagulopathy, psychosis, and the number of procedures. Risk factors of length of stay for patients with hypothyroidism patients were weight loss, paralysis, fluid and electrolyte disorders, age, the number of procedures, and insurance type.

Risk factors of total charges for hyperthyroidism patients were Hispanic or Asian-Pacific Islander descent, younger than 30 years of age, paralysis, the number of procedures, weight loss, fluid and electrolyte disorders, coagulopathy, and neurological disorders. In patients with hypothyroidism of Hispanic or Asian-Pacific

Islander descent who were younger than 30 years of age, risk factors related to total medical charges of patients with were the number of procedures, weight loss, coagulopathy, paralysis, and fluid and electrolyte disorders. Risk factors for patients with hyperthyroidism related to mortality were the number of procedures, age, metastasis, fluid and electrolyte disorders, insurance type, and renal failure. Risk factors for patients with hypothyroidism related to mortality were the number of procedures, age, fluid and electrolyte disorders, metastasis, weight loss, and coagulation.

**CONCLUSION**:

Several factors were observed to increase the risk of mortality, the total medical charges, and the length of stay for patients included in the present study. Comorbidities can increase cost and mortality, which are considered to be serious risks for patient outcomes. Similarities found in risk factors between hypo- and hyperthyroidism were attributed to the physiological changes of thyroid function, which worsened the patients' health statuses; however, differences were found depending on the strength of each risk factor in relation to each type of thyroid disorder. These risks also increased the cost and mortality for patients with cardiovascular diseases. The government and researchers are required to manage preventable risk factors to minimize incidences of mortality and to control the costs of therapy and health services administered to patients with thyroid diseases.

# CHAPTER I

# INTRODUCTION

## 1.1 Background of thyroid diseases

Thyroid hormones play a role in human body activities, such as cell growth, neural performance, metabolic processes, and regulation of energy[1]. Therefore, the abnormal secretion of thyroid hormones induces disturbances in normal activities of the body which can result in autoimmune diseases such as hyperthyroidism and hypothyroidism[2]. A high concentration of thyroid hormones in tissues is due to the incremental release and synthesis of hormones or endogenous or exogenous thyroid-related sources. The common causes of excessive production of thyroid hormones are Graves's disease, toxic multinodular goiter, and toxic adenoma, while the common cause of excessive release of thyroid hormones is thyroiditis[3]. Hypothyroidism associated with a deficiency can be induced by several etiological factors, such as environmental (geographic location), pharmacological (medications such as amiodaron and lithium), medical (neoplastic, hormonal secretion disorders and inflammations), and other conditions[78].

## 1.2 Historical background of thyroid diseases

Goiters were first identified by Hindus around 1500 BC. Herbs and seaweed were also reportedly used in ancient China to treat similar symptoms. In his writing, Hippocrates also mentioned an awareness of these types of illnesses. However, it was not until 1786 that thyroid disease, especially adults' goiters, was first diagnosed by

Caleb Hillier Parry. He followed up patients, reporting symptoms such as enlarged eyeballs, agitation, distress, and palpitations. However, in 1802, Giuseppe Flajani was the first to publish information about this disease. In 1833, Robert James Graves, the Irish medical scientist, found the relationship between hyperthyroidism and cardiac dysfunction. The description of hyperthyroidism begun by Graves and then was completed by the German doctor Adolph von Basedow. Graves characterized the main signs of Graves's disease as goiter, exophthalmos, and irregular heartbeats. The first thyroidectomy was performed by Ludwig Rehn on a patient with Graves's disease. In 1909, William Osler observed toxicity due to thyroid hormone hyper secretions on body organs. The term hyperthyroidism was coined by Charles Mayo in 1907 to describe over-production of hormones by the thyroid gland. In 1930, the pituitary gland was discovered to be the main source of toxic materials. In 1952, Adams and co-workers first used long-acting thyroid stimulators for management of hyperthyroidism[4,5].

Myxedema, a form of hypothyroidism, was first diagnosed by Thomas Blizzard Curling in the mid-19th century after observing the swollen fat tissue around the necks of two of his patients. However, the full description of myxedema was first reported by William Gull in 1873, while William Ord in 1878 investigated the condition by autopsy. Later, many researchers started experimental treatments and determined the main causes of myxedema. Reverdin and Kocher detected the symptoms of this disease. Kocher also reported the main features of myxedema after performing thyroidectomies on 30 patients. Also, Victor Horsley found the occurrence of myxedema in dogs after thyroidectomy procedures. Felix Semon ended the controversy surrounding myxedema by identifying its association with thyroid gland function disorders. George Murray experimented with several treatment options

for myxedema using glycerin extract injections, while Hector Mackenzie administered thyroid oral extract to his patients, which was considered the early use of thyroxin. For other causes of hypothyroidism, Riedel in 1896 diagnosed chronic thyroiditis, and Hashimoto's disease was reported first in 1912. These diseases supported clinicians and researchers in their differentiation among types, causes, and features of hypothyroidism disorders[4,79].

### 1.3 Pathophysiology and etiology of thyroid diseases

#### 1.3.1 Hyperthyroidism

The etiology of hyperthyroidism as an autoimmune disease remains unknown. It is believed that the main cause for abnormality in physiological activities is either due to genetic susceptibility and/or environmental conditions, which are attributed to immune tolerance to thyroid antigens and may induce more immune reactions against the thyroid gland[6,7]. Hyperthyroidism is a thyrotoxicosis with hyper-production and secretion of thyroid hormones. Main etiologies of hyperthyroidism and Graves's disease, subacute thyroiditis, thyroid autonomy, and thyrotoxicosis factitia[8].

Pathogenicity of Graves's disease was attributed to autoimmunity and the presence of thyroid-stimulating hormone (TSH) receptor antibodies. It is considered an autoimmune disease due to the binding and stimulation of antibodies to TSH receptors called thyrotropin receptor antibodies (TRAb) or thyroid-stimulating immunoglobulin (TSI). IgG antibodies are antagonists of TSH receptors and are detected in more than 80% of untreated hyperthyroidism patients[9]. Recent studies showed that the extracellular A-subunit of the TSH receptor is the immunogen of Graves's disease, which is responsible for the autoimmunity of this type of hyperthyroidism disease[10]. The main mechanisms of autoimmune reaction of Graves's disease are (1) T-cell

function failure, (2) molecular mimicry, (3) activation of thyroid T-cells, and (4) expression of major histo-compatibility complex (MHC) by thyroid cells[8].

Subacute thyroiditis is known as giant cell thyroiditis and is related to viral thyroid inflammation; it has a higher incidence among females than males. The virus binds to the human leucocyte antigen (HLA) of macrophages[11].

Factitial thyrotoxicosis is a hidden activity of thyroid hormones. It is more prevalent among subjects in the medical field for those who are more reaching and using medications containing thyroid hormones. Thyroid autonomy, the fourth etiology of hyperthyroidism, is associated with abnormalities of the thyroid nodules[8].

### 1.3.2 Hypothyroidism

The main etiology of hypothyroidism is attributed to the abnormal synthesis and secretion of thyroid hormones thyroxine (T4) and triiodothyronine (T3) which are associated with the functions of body organs. These hormones are influenced by other hormones secreted by the pituitary gland and hypothalamus. Thyrotropin-releasing hormone (TRH) is produced by the hypothalamus, while TSH is released by thyrotropic cells of the anterior pituitary gland. Secretion of TRH and TSH is dependent on the negative feedback system of thyroid hormones; that is, elevation of T3 and T4 hormones stimulates the inhibition mechanism of synthesis and the secretion of TRH and TSH, and vice versa[80]. Comorbidities may affect the normal structure and function of the thyroid gland, which is associated with the stability of secretion and conversion of T4 to T3. Related conditions include cancer, infection, and other inflammatory diseases. Medications and radiation also contribute to the occurrence of hypothyroidism. Recent researchers attributed the severity and incidence of hypothyroidism to genetic susceptibility[82], while others found

environmental variations for ingestion of iodine-containing compounds with a higher percentage of hypothyroidism[81].

## 1.4 Epidemiology of thyroid diseases

### 1.4.1 Hyperthyroidism

Recent reviews showed that the prevalence of hyperthyroidism ranges globally from 0.2% to 1.3%. In 1977, in the United Kingdom, the estimated incidence of patients with hyperthyroidism was from 100 to 200 cases per 100,000 per year, with a higher incidence among females than males. This incidence was reported to be lower in the United States by 30 cases per 100,000 per year from 1935 to 1967. This incidence changed after a study by the National Health and Nutrition Examination Survey (NHANES III) found the overall prevalence of patients with hyperthyroidism to be 1.3% in the United States. The incidence of global hyperthyroidism varies based on sensitivity, type of iodine products used, and nutritional status. For example, the incidence of overt hyperthyroidism is higher in Europe than in the United States (0.7% vs. 0.5%, respectively), while lower incidences are reported in Australia (0.3%) and the highest incidence are found in China (1.2%)[12].

### 1.4.2 Hypothyroidism

Previous studies reported the prevalence of hypothyroidism in the United States, Europe, and Japan to be 0.6 to 12 per 1,000 women and 1.3 to 4.0 per 1,000 men[83]. The NHANES reported the prevalence of overt hypothyroidism of Americans to be 0.3%, and subclinical hypothyroidism to be 4.3%[84]. Hypothyroidism is a common thyroid disease in India with a reported incidence of one in per 10 persons[85]. Globally, variations of the prevalence of hypothyroidism were found to be based on iodine

deficiency. Findings show that the US is the most densely populated country with insufficient iodine in the diet of its population[1].

### 1.5 Goals and objectives

The main objectives of this study are to determine the following:

1) Whether there is a significant association between mortality and the type of thyroid disease.

2) Whether there is a significant association between mortality and the type of thyroid disease in patients with Chronic Heart Failure (CHF).

3) Whether there is a significant association between mortality and the type of thyroid disease of patients with Hypertension HT.

4) Whether there are predictors for length of stay of hyper- and hypothyroidism in patients with CHF.

5) Whether there are predictors for length of stay of hyper- and hypothyroidism in patients with HT.

6) Whether there are predictors for total charges in patients with hyper- and hypothyroidism.

7) Whether there are predictors for total charges of hyper- and hypothyroidism in patients with CHF.

8) Whether there are predictors for total charges of hyper- and hypothyroidism in patients with HT.

9) Whether there are predictors for mortality in patients with hyper- and hypothyroidism.

10) Whether there are predictors for mortality of hyper- and hypothyroidism in patients with CHF.

11) Whether there are predictors for mortality of hyper- and hypothyroidism in patients with HT.

### 1.6 Research hypotheses

**Hypothesis 1:** There is a significant association between the type of thyroid disease and risk of mortality.

Null Hypothesis: H0 = H1

Alternative Hypothesis: H0 ≠ H1

**Hypothesis 2:** There is significant association between type of thyroid disease and risk of mortality in patient with CHF

Null Hypothesis: H0 = H1

Alternative Hypothesis: H0 ≠ H1

**Hypothesis 3**: There is an association between type of thyroid disease and risk of mortality in patients with HT

Null Hypothesis: H0 = H1

Alternative Hypothesis: H0 ≠ H1

**Hypothesis 4:** There are significant predictors for length of stay for patients with hyper- and hypothyroidism

Null Hypothesis: H0 = H1

Alternative Hypothesis: H0 ≠ H1

**Hypothesis 5:** There are significant predictors for length of stay of hyper- and hypothyroidism in patients with CHF

Null Hypothesis: H0 = H1

Alternative Hypothesis: H0 ≠ H1

**Hypothesis 6:** There are significant predictors for length of stay of hyper- and hypothyroidism in patients with HT

Null Hypothesis: H0 = H1

Alternative Hypothesis: H0 ≠ H1

**Hypothesis 7:** There are significant predictors for total charges in patients with hyper- and hypothyroidism

Null Hypothesis: H0 = H1

Alternative Hypothesis: H0 ≠ H1

**Hypothesis 8:** There are significant predictors for total charges of hyper- and hypothyroidism in patients with CHF

Null Hypothesis: H0 = H1

Alternative Hypothesis: H0 ≠ H1

**Hypothesis 9:** There are significant predictors for total charges of hyper- and hypothyroidism in patients with HT

Null Hypothesis: H0 = H1

Alternative Hypothesis: H0 ≠ H1

**Hypothesis 10:** There are significant predictors for mortality in patients with hyper- and hypothyroidism

Null Hypothesis: H0 = H1

Alternative Hypothesis: H0 ≠ H1

**Hypothesis 11:** There are significant predictors for mortality of hyper- and hypothyroidism in patients with CHF

Null Hypothesis: H0 = H1

Alternative Hypothesis: H0 ≠ H1

**Hypothesis 12:** There is significant predictors for mortality of hyper- and hypothyroidism in patients with HT

Null Hypothesis: H0 = H1

Alternative Hypothesis: H0 ≠ H1

## 1.7 Statement of the problem

There are divided opinions regarding the association between thyroid disorders and cardiovascular diseases and their impact on mortality in the United States[13]. Among the reviewed patient data, there was found to be an increase in the incidence of mortality with the occurrence of comorbidities, especially in patients with cardiovascular diseases, which elevated the percentage of comorbidity-related deaths. A high incidence of mortality was related to cardiovascular diseases in patients with thyroid disease[14,86]. Other studies showed higher incidences of mortality according to the type and number of risk factors[15,16].

A high prevalence of thyroid disease and complications in patients living in the United States was observed, with approximately 3.45 million patients[17]. The cost associated with thyroid disease and comorbidities is a burden to American patients and the US health system, which has a major negative influence on patients' quality of life and increases psychological hardships. Several studies estimated the cost for thyroid cancer to rise to as high as $150 billion by 2020[18], while other researchers hypothesized that the cost of thyroid therapy would reach $9 million annually from 2004 to 2012[19]. However, very few studies highlighted the total cost and mortality rate for patients with thyroid disease who have comorbid cardiovascular diseases in the United States.

### 1.8 Definition of terms

The definition of medical terms used in this study is illustrated in Table 1.

**Table 1 Definitions of terms**

| Term | Definition |
|---|---|
| Symptoms | Any medical, physical and/or mental disorders related to a specific disease |
| Diagnosis | Examination and identification of an illness, according to the symptoms and clinical evaluation |
| Healthy | Free from any illness or disease |
| Disorder | Abnormality of the body's physical or mental status |
| Medication | Drugs used to treat a special disorder or disease |
| Hyperthyroidism | Abnormal production and over-secretion of thyroid gland hormones |
| Hypothyroidism | Inadequate production and abnormal functions of thyroid gland hormones |
| Graves's disease | The common and frequent cause of hyperthyroidism, where antibodies attack the thyroid gland |
| Hashimoto's thyroiditis (HT) | Is the most common cause of hypothyroidism, where lymphocytic infiltration after destruction of thyroid parenchymal tissue |
| Thyroidectomy | The total or partial surgical removal of the thyroid gland |

## 1.9 Importance of the study

Hypo- and hyperthyroidism are autoimmune diseases observed to be more prevalent among females than males. Few studies have shown the impact of cardiovascular diseases, such as congestive heart failure and hypertension, on the incidence of mortality, total charges in health-care activities or length of hospital stay of patients with thyroid disease in the United States. Moreover, very few studies determined the link between major risk factors contributing to the high incidence of mortality, longer length of stay, and overestimation of total charges between hypo- and hyperthyroidism disorders. The present study will reveal the similarities and differences of risk factors and predictors of mortality, total charges and length of hospital stay between hypo- and hyperthyroidism with congestive heart failure and hypertension as the main comorbidities of hyperthyroidism patients. This comparison is not mentioned in previous studies, especially for a large sample size of patients in the United States.

# CHAPTER II

# LITERATURE REVIEW

## 2.1 Introduction

Hypothyroidism and hyperthyroidism are major diseases of the thyroid gland caused by abnormal production and secretion of thyroid hormones. These diseases are exacerbated by the presence of other comorbidities and the incidence of circulatory mortality[20]. There are several risk factors, as reported by studies, associated with thyroid gland diseases, which determine the severity and complications of these disorders[21]. This chapter reviews the causes, diagnoses, types, symptoms, risk factors, complications, comorbidities, mortality, and cardiac complications of hypo- and hyperthyroidism.

## 2.2 Causes of Thyroid gland diseases

### 2.2.1 Hyperthyroidism

There are many causes of hyperthyroidism which differ in incidence, pathophysiological characteristics, and severity of the disease. However, the main categories for causes of hyperthyroidism are[22]

1. Circulating thyroid stimulators

a) Graves' disease: the most common type with disorder of thyroid stimulating immunoglobulins[23]. Pathogenic mechanism is autoimmunity and TSH receptor antibodies.

b) Neonatal Graves' disease: a very rare type with disorder of thyroid stimulating immunoglobulins[24].

c) Thyrotropin secreting tumor: a rare type of hyperthyroidism accompanied with pituitary adenoma[25].

d) Hyperemesis gravidarum: an uncommon type and related to human chorionic gonadotropin secretion[26].

e) Choriocarcinoma: a rare type and related to human chorionic gonadotropin secretion[27].

f) Abnormal thyrotropin receptor: a very rare type and related to human chorionic gonadotropin secretion[28].

2. Thyroidal autonomy

a) Toxic multinodular goiter: a common type and related to activation of mutations in thyrotropin receptor or G protein gene[29].

b) Toxic solitary adenoma: a common type and related to the activation of mutations in thyrotropin receptor or G protein gene[30].

c) Congenital hyperthyroidism: a very rare type and related to the activation of mutations in thyrotropin receptor[28].

d) Hyperthyroidism of Iodine reasons: uncommon in the United States, and is attributed to the excessive amount of iodine due to disorders of thyroid hormone secretion[31].

3. Thyroiditis

a) Subacute thyroiditis: an uncommon type and related due to viral infections[32]

b) Postpartum thyroiditis: common and attributed to the autoimmune disorders[40].

c) Thyroiditis of drugs: uncommon and is attributed to the adverse drug reactions of amiodaron, lithium and interferon[41].

d) Acute thyroiditis: uncommon and related to infection of the thyroid gland[33].

4. Exogenous thyroid hormone

a) Iatrogenic[34]: common due to the ingestion of thyroid hormone products

b) Factitious[35]: a rare type due to ingestion of thyroid hormone products

5. Ectopic thyroid tissues

a) Struma ovarii[37]: rare and due to ovarian teratoma thyroid tissue

b) Metastatic thyroid cancer[38]: a rare type attributed to large tumor secreting hormone

c) Pituitary resistance to thyroid hormone[39]: a rare type due to mutation of thyroid hormone tissues with higher rate of secretion and lower rate of responses.

### 2.2.2 Hypothyroidism

Hypothyroidism, based on the type of disorder, is classified into primary and secondary types. The primary type is associated with the defects of production and secretion of thyroid hormones inside the gland, while the secondary type refers to the abnormality of secretion of the pituitary gland's thyroid-stimulating hormones (TRH or TSH)[1,87].

**Primary hypothyroidism**

1- Autoimmune disorders

a) Hashimoto disease or chronic thyroiditis[88]

b) Subacute thyroiditis90: seasonal and more prevalent in females and in those ages 40-50 years

c) Silent thyroiditis: It is more prevalent in females than males, and in those 30-40 years of age.

d) Postpartumthyroiditis89: occurs within the first six months after delivery about 3%-8% of total pregnancies

2- Iatrogenic

a) Thyroidectomy[91]: Thyroid surgery is accompanied with lipid peroxide oxidation

b) Radioactive therapy[92]: occurs during the first year of use of radioactive iodine due to destructive effects of radiation to thyroid tissues.

c) Anti thyroid hormone medications: Excessive use of anti thyroid will increase the possibility of hypothyroidism.

3- Miscellaneous

a) Iodine deficiency[93]: inadequate production of thyroid hormones due to loss of iodine. About 2 billion individuals have the deficiency of Iodide intake.

b) Excess Iodine[94]: more levels of iodine induce hypothyroidism, especially in newborns babies.

4- Medications [95,96] (amiodarone, Lithium, monoclonal antibodies, sodium valproate, tyrosine kinase, and immune checkpoint inhibitors)

5- Systemic illness[97]: like systemic lupus erythematosus (SLE), In this case you see several chronic inflammations of organs including thyroid gland.

6- Thyroid agenesis[98]: also known as congenital hypothyroidism, due to defects of growth of newborn babies.

7- Abnormality of thyroid hormone production

8- Thyroid hormones resistance[99]: Occursdue to mutations of THRB gene receptors

9- Genetic variations[82]: Occurs due to the genetic defects that induce hypothyroidism. This may also be associated with congenital hypothyroidism.

10- Infections (viral)[100]: Hepatitis C is considered one of the most common causes of hypothyroidism

11- Malignancy[101]: Anticancer agents inhibit the growth factor signaling impair in the blood flow.

**Secondary hypothyroidism**

1- Tumors[102]: Chemotherapeutic agents increase the TSH hormone level which induces hypothyroidism

2- Surgery[103]: Surgical interventions (like Cardiopulmonary Bypass) cause secondary hypothyroidism

3- Infections[104,111]: Infection is a major cause of myxoedema coma of hypothyroidism

4- Medications[101, 105, 111] (dopamine, somatostatin, and others)

5- Hypothalamus and pituitary dysfunctions[106]: Dysfunctions of pituitary and hypothalamus hormones induce secondary hypothyroidism. These dysfunctions are either

a) Lymphoma [109]
b) Hemochromatosis [107]
c) Histiocytosis [108]
d) Sarcoidosis[110]

6- Resistance to TSH or TRH[111]: resistance of hormones induces hypothyroidism.

7- Genetic variations[111]: Mutation of genes of RH receptor, TSHß, pituitary transcription factors (Pit-1, PROP1, LHX3, LHX4, HESX1), or LEPr, IGSF1 induces secondary hypothyroidism.

## 2.3 Diagnosis of thyroid diseases

Thyroid disease is diagnosed by laboratory and clinical tests, as well as by signs and symptoms.

### 2.3.1 Hyperthyroidism

**a) Laboratory diagnosis**

1) Depends on the concentrations of hormones, such as low TSH and elevated T3 and T4 serum concentration.

2) High levels of radioactive iodine uptake (RAIU) by the thyroid gland, which is more specific at the current time, because the level determines the type of thyroid disorder[42,47].

When RAIU increases, the diagnosis can be

1. TSH-induced hyperthyroidism
2. TSH-secreting tumors
3. Pituitary resistance to T4
4. Thyroid stimulators other than TSH
5. Graves' disease
6. Trophoblastic disease
7. Thyroid autonomy
8. Adenoma
9. Goiter

When the RAIU decreases, the diagnosis can be

1. Inflammatory thyroid disease
2. Subacute thyroiditis

3. Ectopic thyroid tissue
4. Struma ovarii
5. Metastatic follicular carcinoma
6. Ingestion of thyroid hormone or external sources of iodine
7. Medication stimulating thyroid diseases

**b) Symptoms and clinical features**

There are several signs and symptoms of hyperthyroid disease. The primary symptoms are the following: (1) fatigue and weakness, (2) heat intolerance, (3) excessive sweating, (4) shakes and tremors, (5) palpitation, (6) weight loss, (7) increased appetite, (8) weight loss, (9) anxiety, (10) mood changes, (11) hyperactivity, (12) hyper-defecation, (13) sleeping difficulty, (14) thinning hair and brittle nails, (15) menstrual irregularities, and (16) erectile dysfunction.

The signs of hyperthyroidism are these: (1) tachycardia, (2) arrhythmia, (3) hypertension, (4) hyperactivity, (5) hyperreflexia, (6) muscle weakness, (7) warm and moist skin, (8) tremors, and (9) a staring gaze and eyelid retraction[45,46].

However, other symptomatic findings are associated with specific etiologies, such as the following:

1. Painful and tender goiter with fever in cases of subacute thyroiditis,
2. Nodules of thyroid autonomy,
3. Non-enlarged thyroid gland of thyrotoxicosis factitia,

4. Tender goiter vascularized, acropachy, dermopathy, and ophthalmological disturbances of Graves' disease43.

### 2.3.2 Hypothyroidism

**a) Laboratory diagnosis**

1. TSH: Elevated TSH found with primary hypothyroidism with low levels of TSH and secondary hypothyroidism87.
2. Free thyroxine: Low free thyroxin observed with primary hypothyroidism Not elevation of thyroxine with secondary hypothyroidism[114].
3. Globulin
4. Albumin
5. Transthyretin
6. Hashimoto thyroiditis.
7. Ultrasound imaging[115]
8. Goiter biopsy
9. Lipid metabolism: the increase of low-density lipoproteins (LDL) and apolipoprotein B due to decreased hepatic clearance and hepatic receptors. Also, increase of high-density lipoprotein (HDL)[112,113].

**b) Symptoms and clinical features**

There are several symptoms associated with the different stages and type of hypothyroidism. Therefore, these symptoms are categorized into into 3 segments: early, late and children/teens[116].

1. Early: 1) Cold sensitivity, 2) Depression, 3) Constipation, 4) Fatigue, 5) Joint and/or muscle pain, 6) Dry skin, 7) Thin/brittle hair and nails, 8) Weakness, 9) Unintentional weight gain

2. Late: 1) Abnormal sense of smell and taste, 2) Hoarse voice, 3) Facial and Extremity edema, slow speech, 5) Thick skin, 6) Bradycardia, 7) Slow mentation

3. Children/teens: 1) Jaundice, 2) Choking, 3) Big tongue, 4) Puffy face, 5) Thrive difficulty, 6) Constipation, 7) Excessive sleeping, 8) Poor muscle tone, 9) Delay of mental and physical development

### 2.4 Risk factors of thyroid diseases

#### 2.4.1 Hyperthyroidism

Several risk factors contribute to high incidence of hyperthyroidism. These risk factors differ based on the type and cause of hyperthyroidism[43].

1. Genetic: hyperthyroidism such as Graves's disease is more commonly found in families, especially with the presence of common concurrent diseases, such as diabetes mellitus type 1 and Addison's disease. This is associated with the similarity of thyroid genes among families such as HLA, CTLA-4, PTPN22, CD40, and FCRL348-50.

2. Infections: these contribute to autoimmunity of the thyroid gland, especially the mechanism of the activation of T-cells[57].

3. Stress: psychological status also showed a high impact on the incidence and severity of hyperthyroidism, which affects the levels of ACTH and cortisol due to suppression of the immune system[59].

4. Gender: autoimmune diseases including hyperthyroidism are more related to chromosome X. Therefore, women are more susceptible to the incidence of hyperthyroidism than men, because women carry two X chromosomes (2 X) while men carry one[51].

5. Pregnancy: Graves's disease is the most common cause of hyperthyroidism during pregnancy. However, the onset of Graves is uncommon during pregnancy[56].

6. Iodine and medications: some medications containing iodine, or medications similar to amiodarone, may contribute to the high incidence of hyperthyroidism[55].

7. Irradiation: radiation is one of the most obvious reasons for hyperthyroidism because of alteration and changes of T-cell activation[1].

8. Smoking: this is a trigger for high incidences of hyperthyroidism and complications due to its effect on the immune system[44].

9. Alcohol consumption: alcohol consumption will affect the functions of the thyroid gland[52].

10. Age: elderly patients are at higher risk of developing hyperthyroidism than young patients[53,54].

### 2.4.2 Hypothyroidism

Several risk factors contribute to high incidence of hypothyroidism. Those risk factors were as follows:

1. Gender: incidence of hypothyroidism is more commonly observed in females than in males[117].

2. Iodine deficiency: low levels of iodine are considered a significant risk factor for the occurrence of hypothyroidism[118].

3. Iodine excess: excess iodine is considered a trigger of hypothyroidism, especially in newborn babies[94].

4. The transition from iodine deficiency to sufficiency: an increased level of iodine will induce elevation of thioperoxide antibodies, which will increase the incidence of hypothyroidism[119].

5. Autoimmune diseases: existence of other autoimmune conditions contributes to the higher incidence of hypothyroidism, especially in those with Hashimoto's thyroiditis and rheumatoid arthritis[120].

6. Genetic variations: more than 10% of the cases of patients with hypothyroidism were attributed to genetic differences[82].

7. Selenium deficiency: this is a significant risk factor in newly-diagnosed hypothyroidism, where low levels of selenium were observed compared to healthy individuals.

8. Drugs: several drugs considered as a cause and/or reversible therapy to hypothyroid patients[87].

9. Reducing the TSH secretion (like glucocorticoids, opiates, dopamine, bromocriptine, phentolamine, octreotide, and growth hormone).

10. Thyroid hormone synthesis/release (amiodarone, iodine, thionamides, thiocyanate, aminoglutethimide, perchlorate, lithium, and cytokines).

11. Thyroid hormone metabolism (rifampicin, phenytoin, carbamazepine, barbiturates, tyrosine kinase inhibitors, growth hormone, glucocorticoids, propylthiouracil, β-blockers, iodinated contrast agents, and clomipramine).

12. Thyroxin binding globulin (estrogen, selective estrogen receptor modulators, opiates, mitotane, clofibrate, perphenazine, and 5-fluorouracil).

13. Thyroid hormone absorption (calcium compounds, sucralfate, aluminum hydroxide, ferrous compounds, cholestyramine, colesevelam, proton pump inhibitors, H2 blockers).

14. Syndromic conditions: About 25% of patients with Down's syndrome have primary hypothyroidism[121]. In addition, about 13% of patients with Turner syndrome have hypothyroidism[122].

15. Age: elderly individuals are at higher risk of developing hypothyroidism than younger patients[123].

## 2.5 Treatment of thyroid diseases

### 2.5.1 Hyperthyroidism

The treatment of hyperthyroidism disease involves pharmacotherapy, radiation, and surgery. There are several advantages and disadvantages to each type of treatment[60-62].

1. Methimazole and propylthiouracil: these are the most commonly used for pharmacotherapy for the treatment of hyperthyroidism. The main advantages are the low cost and risks, and the non-invasive administration. The main disadvantages are the low cure rate (30–80%), adverse reactions, and drug compliance. Methimazole is the first line therapy to treat children, adolescents, and those with congenital hyperthyroidism.

2. Radioactive iodine: Advantages are characterized by low cost and better adjustment of quality of life. The disadvantages are permanent hypothyroidism, worsening vision, effects on pregnancy and breastfeeding, and risk of exacerbation of hyperthyroidism. This is considered the best treatment option for toxic multinodular goiters.

3. Surgery: The main advantage of surgery for hyperthyroidism patients is the rapid, effective, and appropriate treatment for large-sized goiters. The disadvantages are cost, permanent hypothyroidism, pain, and post-surgical scarring. In some cases, surgery may be the best choice for congenital hyperthyroidism due to the adverse effects of medications. Complications include nerve damage and hypothyroidism. It is

the best type of treatment for suspected nodules and alternative therapy for patients who refuse the radioactive iodine therapy method.

Two-thirds of American endocrinologists preferred the use of radioiodine as their primary therapy, while 20% of UK and Europeans endocrinologists favored this method as a first-line therapy. In South Korea, 10% of physicians preferred thyroidectomy as the main therapy plan for their hyperthyroid patients, while in Africa, they preferred medications and surgery[58,63].

### 2.5.2 Hypothyroidism

Treatment of hypothyroidism disease involves pharmacotherapy and hormone replacement

1. Levothyroxine: also called L-thyroxin, this is used for the treatment of overt hypothyroidism. Levothyroxine is safer than liothyronine and offers a better quality of life and lower incidences of adverse effects, such as pain, fatigue, anxiety, Cognitive problems, and depression[124]. Overdosing on levothyroxine may lead to hyperthyroidism. Minimizing the bone mass of women and arterial fibrillation are the main related side effects of suppression of the TSH. Supplemental requirements were lower in hypothyroidism patients than other patients because of the dysfunction of the thyroid gland; moreover, hypothyroidism patients with gastrointestinal problems or bowel bypass surgery need special cares and certain medications and/or diets, like calcium, dietary soy, sucralfate, and fibers because of the lower ability of absorption[125,128].

2. Liothyronine: this is active form of the thyroid hormone in body tissues. This type of medication showed significant reduction in body weight and improvement of lipid profile. Levothyroxine is preferred to liothyronine since no improvement was noticed in the cardiovascular health nor the quality of life by using the latter. This medication improved the level of T3 for a subgroup of patients[126].

3. Pig thyroid extract: New US laboratories (Forest Laboratories, Inc., New York, NY) found that the use of extracts from pigs' thyroid glands are effective as a means of treatment because they contain T4 and T3 with ratio equals to 4:1. However, no previous studies showed a significant difference between pig thyroid extract and levothyroxine[124].

4. Monitoring of thyroid function: Annual monitoring of thyroid function is required after the stability of thyroid hormone functions after 6 to 8 weeks of initiation of therapy or in case of changing the dose of levothyroxine[127].

## 2.6 Cardiac complications of thyroid diseases

### 2.6.1 Hyperthyroidism

Thyroid hormones contribute to cardiovascular diseases by influencing the cardiac myocyte by regulating the cardiac expression genes, which affects the contractility and relaxation of the cardiac muscle. On the other hand, the T3 hormone induces some changes in the membrane ion channels of cardiac cells and the intracellular signaling pathways[64,65], which increases the heart rate, contractility of the left ventricle, and blood volume. Thyroid hormones also contribute to the reduction of resistance in peripheral arterioles and the arterial blood pressure by increasing the absorption of sodium through the activation of the renin-angiotensin-aldosterone system. The estimated increments of cardiac output with hyperthyroidism are 50–300% [66].

There are several signs and symptoms of thyroid hormonal abnormalities that affect the cardiovascular system, such as tachycardia, palpitation, dyspnea, exercise intolerance, and increased pulse rate. Thyroid hormone disorders were found to be significantly related to the future existence of serious comorbidities, including angina, atrial fibrillation, cardiac hypertrophy, peripheral edema, systolic hypertension, and congestive heart failure[67].

Chest pain and EKG changes are the most commonly reported symptoms with elderly hyperthyroid patients, which leads to cardiac ischemia and increases the oxygen demands needed for the increased rates of contractility and workload induced by

overproduction of thyroid hormones. Also, few differences were observed between elderly and young hyperthyroid patients in the incidence of cardiac complications[68,69].

**a) Atrial fibrillation**

Atrial fibrillation is the most commonly reported disorder related to thyrotoxicosis. Sinus tachycardia is a significant disturbance observed in most hyperthyroidism patients. The prevalence of hyperthyroidism patients with atrial fibrillation ranges from 2% to 20%. About 15% of elderly hyperthyroid patients older than 70 years develop atrial fibrillation. Ischemic disease and congestive heart failure are the most common prognoses of atrial fibrillation induced by hyperthyroidism[70,71].

Treatment of atrial fibrillation is done by controlling the abnormal contractility and heart rates by blockage of beta receptors. Selective and non-selective beta-blockers are appropriate in the management of cardiac disorders. Digitalis is appropriate for stabilizing heart rate, but it requires high doses, which increases the probability of toxicity and incidences of adverse drug reactions. However, medication like calcium channel blockers is not encouraged to be used for hyperthyroidism due to cardiac collapse and acute hypotension after blocking the calcium channels of smooth muscle cells[72,73].

**b) Heart failure**

Increases in the incidence and severity of atrial fibrillation may elevate the occurrence of heart failure, if not controlled, in most patients with hyperthyroidism. High rates of tachycardia and ischemia that are directly induced by abnormal elevation of thyroid

hormones contribute to congestive heart failure. Heart failure is more predominant in patients with hyperthyroidism older than 60 years[71].

Pulmonary hypertension, peripheral edema, and neck vein distension are the main signs of congestive heart failure[74]. Beta-blockers are the most appropriate antihypertensive agents for the treatment of congestive heart failure induced by hyperthyroidism. Diuretics and digitalis are also appropriate treatment options for pulmonary hypertension[75]. Radioiodine hyperthyroidism therapy is safe to be given with beta-blockers; therefore, beta-blockers are the drugs of choice for congestive heart failure in patients with hyperthyroidism[16].

### 2.6.2 Hypothyroidism

Mechanisms of thyroid hormones on the cellular mechanisms of the cardiovascular system revealed the association between thyroid hormone disorders and cardiovascular diseases by influencing the cardiac contractility, diastolic hypertension, vascular resistance, and rhythm disturbances[129]. Hypothyroidism reduces the thermogenesis of tissues by 5% to 8% and increases the resistance of arterioles due to the effect of T3 on the cells of smooth muscles, which in turn will induce an abnormal increment of blood pressure and abnormal cardiac outputs. The thyroid hormone mechanism's effect on the heart muscle is important for expression of the cardiac gene and the regulation of $Ca^2$-ATPase activity[130].

Several pathophysiological symptoms of hypothyroidism that impact the cardiovascular system include decrease of cardiac contractility, reduction of cardiac outputs, elevation of peripheral vascular resistance, reduction of blood volume, abnormality of capillary permeability, dyspnea, intolerance, and increase in the incidence of angina. The signs of cardiovascular problems are a reduction of pulse

rate, higher diastolic BP, cardiomegaly, edema, abnormal Electrocardiogram (EKG) with ST-T changes, and prolonged systolic intervals[111].

**a) Atherosclerosis**

There is an increase in the occurrence of atherosclerosis in hypothyroidism patients because of atheromatous changes[131]. Most patients with myxedema have atherosclerosis, especially patients 60 years old or older. Atherosclerosis is not accelerated for hypothyroidism patients on therapy of congestive heart failure or angina pectoris. However, atherosclerosis has a higher incidence with patients complaining of myxedema hypothyroidism and hypertension[111].

Several studies reported the association between the abnormal elevation in levels of lipoproteins and the prevalence of subclinical hypothyroidism. Therefore, as a prognosis of this type of complication, atherosclerosis, and hypothyroidism, there is a significant relationship between the hypothyroidism and the occurrence of cardiovascular consequences[123,133].

**b) Angina pectoris**

Anginal pectoris, like atherosclerosis, is encountered in myxedema hypothyroidism patients. Inadequate oxygen for myocardium cells and high demands for cardiac output and oxygen supplies, due to the abnormal physiological thyroid functions, induces the angina attack and chest pain of hypothyroidism patients. Treatment of angina must be re-evaluated after performing the angiography for coronary artery disease because angina occurs at any time, especially after starting hypothyroidism therapy[111].

### c) Heart failure

Progression of heart failure is influenced by the endocrine activation because the thyroid hormones are essential parameters for the homeostasis of heart functions, including the heart rate, pulse, cardiac outputs, and muscle contraction[134]. In addition to the direct effects of thyroid dysfunction on disorders of the cardiovascular system, other risk factors have also contributed to the severity and incidence of heart failure, such as atherosclerosis, hypertension, and others[135].

Several studies have found an association between the hypothyroidism and congestive heart failure. However, some of these studies investigated the mortality related to congestive heart failure and abnormal TSH levels of hypothyroidism[137]. Others found a reduction of T3 and T4 thyroid hormone levels of congestive heart failure patients[136]. Moreover, these studies observed the relationship between the increase in the incidence of hypothyroidism and the number of hospital admissions for heart failure[138].

## 2.7 Mortality of thyroid diseases

### 2.7.1 Hyperthyroidism

There is an increased incidence of mortality with hyperthyroidism disease. Reduction of TSH levels worsens the health status, which elevates the possibility of death for treated and untreated hyperthyroidism patients[76]. Types of hyperthyroidism have been associated with mortality, such as subclinical and overt hyperthyroidism, depending on the time duration of therapy and levels of TSH[15,77].

### 2.7.2 Hypothyroidism

An increase in the incidence of hypothyroidism and comorbidities, including those involving the cardiovascular, neurological, metabolism, psychiatric, respiratory, musculoskeletal, gastrointestinal, reproductive, hematopoietic and endocrine systems, contributes to the high incidence of mortality[111]. Cardiovascular risk showed a higher incidence of mortality compared to other complications. There is a 5% and 9% lifetime risk of overt and subclinical hypothyroidism, respectively. However, a limited number of studies determined a difference between subclinical and overt hypothyroidism in the incidence of mortality[139]. Other studies confirmed the relationship between levels of TSH and heart failure-related mortality[140].

## 2.8 Research gap

There have been many global studies conducted to determine the prevalence of hyperthyroidism patients, involving risk factors, mortality, and comorbidities. However, several gaps were seen in these studies, which affected the validity and generalization of their main findings. Short duration and small sample size of observations were considered as the main limitations of these studies[138,139]. Also, genetic studies of hyperthyroidism patients and gene relationships with mortality require far more attention from researchers. Patients outcomes, such as duration of hospital stay and total cost, were not much discussed in previous studies, especially those related to cardiovascular events. Therefore, there is a need for studies involving predictors and risk factors of mortality, length of stay, and total cost that link thyroid disorders with cardiovascular diseases to support the health-care systems with the new findings and to control their complications and minimizing the incidence of mortality in the United States. Finally, there are studies involving the predictors of mortality, length of stay and total cost for thyroid disease patients, but no study has yet

discussed the differences of these predictors between the hypo- and hyperthyroidism diseases.

## 2.9 Summary

There are several types of thyroid diseases with different causes, diagnoses, and therapies. There is an obvious relationship between thyroid disorders and cardiovascular risks, which elevates the rate of mortality and increases the total cost and length of stay. All these outcomes are considered as financial and mental burdens to the government and patients' quality of life. Identifying and controlling the preventable risk factors may contribute to enhancing of health and minimizing problematic health events.

# CHAPTER III

# MATERIAL AND METHODS

## 3.1 Nationwide inpatient sample data

Data from Nationwide Inpatient Sample (NIS) was used to achieve the objectives of the present study. Permission for downloading and approval of the use of these data were obtained. The NIS data were commonly used by most clinicians and researchers in their studies, especially related to the influence of patients' information effects on the patients' length of stay, total charges, and mortality. The main patients' information in the NIS database were demographics, hospital characteristics, insurance types, types and years of admissions, and comorbidities.

## 3.2 Data and methods

The NIS dataset used in the present study is related to the patients with hyper-andhypothyroid diseases. A total of 721,958 visits were made by patients with hyper- and hypothyroidism to 1,050 hospitals in 44 states in 2012. The main variables of NIS dataset involved patients' information like health and financial statuses, hospital information, other non-clinical information. Data included information on patients' comorbidities, number of procedures and chronic conditions, discharge status, socio-demographic characteristics, length of hospital stay, total charges of health care services, and incidence of mortality. NIS stated the codes and groups of each variable, to give an example, information related to inpatients payments were reported like the type of insurance (Medicare, Medicaid, and others).

This study segmented NIS data into three types of stages, based on the objectives and hypotheses: the first segment included all hyper- and hypothyroidism patients; second hyper- and hypothyroidism patients with congestive heart failure (CHF); and third hyper- and hypothyroidism patients with hypertension (HT).

The variables of NIS datasets are classified in the present study to either dependent or independent variables. Dependent variables of the present study are the length of hospital stay, total charges, and incidence of mortality. Patients' demographic characteristics (age, gender, race, etc.), type of insurance, household income, comorbidities, and other clinical variables were considered as independent variables. SPSS version 22 is used to analyze the data of the present study through the most appropriate statistical tests based on approving the assumptions. All results with p values less than 0.05 were considered as significant. Statistical tests used in the present study were chi-square, Pearson correlation, multinomial logistic regression and multiple linear regression (dummy method). The Chi-square test is used to find the association between variables (like race categories) and mortality. The Pearson correlation test is used to determine the type and strength of correlation between two or more numerical variables like the relationship between the number of procedures and length of hospital stay/total charges. A multinomial logistic regression test is used to determine the predictors of mortality. The multiple linear regressions (dummy method) are used to determine the predictors of length of hospital stay/total charges.

### 3.3 Data variables, research questions, statistical analysis procedures

The NIS dataset used in the present study covered the patients for the year-2012. All variables involved to achieve the objectives of this study are illustrated in Table 2.

**Table 2 Data variables used for the analysis**

| Study variables | Original variables in NIS | Variables description |
|---|---|---|
| AGE | AGE | Age in years; Numerical Variable |
| MORTALITY | DIED | The patient did not die during hospitalization (DIED=0); The patient died during hospitalization (DIED=1), Categorical Variable |
| GENDER | FEMALE | Gender of patient FEMALE = 1 is Female; FEMALE= 0 is Male; Categorical Variable |
| TOTAL CHARGE | TOTCHG | Total charges, Numerical Variable |
| RACE | RACE | 1 = White, 2 = Black, 3 = Hispanic, 4 = Asian/Pacific, 5 = Native Am., 6 = Other; Categorical Variable |
| INSURANCE TYPE | PAY1 | 1=Medicare, 2=Medicaid, 3=Private insurance,4=Self-pay,5=No charge,6=Other; Categorical Variable |
| NUMBER OF PROCEDURES | NPR | The number of procedures performed while the patient was hospitalized; Numerical Variable |
| SOCIO_ ECONOMIC STATUS | ZIPINC_QRTL | Median household income for patient's ZIP Code, 1= 76th to 100th percentile, 2= 26th to 50th percentile, 3= 51st to 75th percentile, 4= 0-25th percentile; Categorical Variable |
| COMORBIDITIES | CM_AIDS, CM_ALCOHOL, CM_ANEMDEF, | Acquired immune deficiency syndrome, alcohol abuse, deficiency anemias, rheumatoid arthritis/collagen vascular |

| | | |
|---|---|---|
| | CM_ARTH, CM_BLDLOSS, CM_CHF, CM_CHRNLUNG, CM_COAG, CM_DEPRESS, CM_DM, CM_DMCX, CM_DRUG, CM_HTN_C, CM_HYPOTHY, CM_LIVER, CM_LYMPH, CM_LYTES, CM_METS, CM_NEURO, CM_OBESE, CM_PARA, CM_PERIVASC, CM_PSYCH, CM_PULMCIRC, CM_RENLFAIL, CM_TUMOR, CM_ULCER, CM_VALVE, CM_WGHTLOSS | diseases, chronic blood loss anemia, congestive heart failure, chronic pulmonary disease, coagulopathy, depression, diabetes uncomplicated, diabetes with chronic complications, drug abuse, hypertension , hypothyroidism, liver disease, lymphoma, fluid and electrolyte disorders, metastatic cancer, other neurological disorders, obesity, paralysis, peripheral vascular disorders, psychoses, pulmonary circulation disorders, renal failure, solid tumor without metastasis, peptic ulcer disease excluding bleeding, valvular disease, weight loss;<br><br>Categorical variable |
| LENGTH OF STAY | LOS | The number of days the patient was<br><br>hospitalized; Numerical Variable |
| Number of chronic conditions | CHRONIC | Number of chronic conditions; Numerical variable |

### 3.4 Study hypotheses and statistical tests

In order to answer the research questions, 22 hypotheses were tested by using different statistical tests. All research questions, hypotheses, outcomes, independent variables, and statistical tests are illustrated in Table 3.

**Table 3 Study hypotheses, research questions, and appropriate statistical tests**

| Research question | Hypotheses | Independent variables | Outcomes variables | Inferential statistical analysis |
|---|---|---|---|---|
| Is there an association between mortality and type of thyroid disease? | Hypothesis 1 | Type of thyroid disease | Mortality | Chi-square |
| Is there an association between mortality and type of thyroid disease of patients with CHF? | Hypothesis 2 | Type of thyroid disease | Mortality | Chi-square |
| Is there an association between mortality and type of thyroid disease of patients with HT? | Hypothesis 3 | Type of thyroid disease | Mortality | Chi-square |
| Are there predictors for the length of stay of patients with hyper- and hypothyroidism? | Hypothesis 4 | Patients' information & comorbidities | Length of stay | Multiple linear regression |
| Are there predictors for the length of stay of patients with hyper- and hypothyroidism CHF? | Hypothesis 5 | Patients' information & comorbidities | Length of stay | Multiple linear regression |
| Are there predictors for the length of stay of patients with hyper- and hypothyroidism HT? | Hypothesis 6 | Patients' information & comorbidities | Length of stay | Multiple linear regression |
| Are there predictors for total charges of patients with hyper- and hypothyroidism? | Hypothesis 7 | Patients' information & comorbidities | Total charges | Multiple linear regression |
| Are there predictors for total charges of patients with hyper- and hypothyroidism CHF? | Hypothesis 8 | Patients' information & comorbidities | Total charges | Multiple linear regression |

| | | | | |
|---|---|---|---|---|
| Are there predictors for total charges of patients with hyper- and hypothyroidism HT? | Hypothesis 9 | Patients' information & comorbidities | Total charges | Multiple linear regression |
| Are there predictors for mortality of patients with hyper- and hypothyroidism? | Hypothesis 10 | Patients' information & comorbidities | Mortality | Multinomial logistic regression |
| Are there predictors for mortality of patients with hyper- and hypothyroidism CHF? | Hypothesis 11 | Patients' information & comorbidities | Mortality | Multinomial logistic regression |
| Are there predictors for mortality of patients with hyper- and hypothyroidism HT? | Hypothesis 12 | Patients' information & comorbidities | Mortality | Multinomial logistic regression |

Patients' information related to hyper- and hypothyroidism was extracted from the NIS database after checking the codes and entries of 721,958 patients who visited hospitals in 2012. The analysis and results of the present study are fully outlined in the next chapter

# CHAPTER IV

# RESULTS AND ANALYSIS

## 4.1 Introduction

This chapter contained the results including descriptive and statistical analysis. Statistical Package for the Social Sciences (SPSS) version 22 used for the analysis of NIS dataset for the year 2012, involved patients with 721,958 patients suffered of hypo- and hyperthyroidism, and those complained of concurrent congestive heart failure and hypertension are 93,141 & 460,331 patients respectively. ICD-9-CM codes for hyperthyroidism are 24200, 24210, 24220, 24230, 24240, 24280, 24290, and 7753, while for hypothyroidism are 243, 2449, 2440, 2448, 3540, 37633, 7011, and 7018. The results with p values less than 0.05 were considered as significant.

## 4.2 Demographic characteristics and health information

### 4.2.1 Age

The patients were categorized into age groups, where highest incidence was observed with those aged elder than 80 years old by 29.3% followed by those aged 70-80 years (22.3%), 61-70 years (19.3%), while lowest percentages showed with patients aged equal and younger than 30 (3.5%) respectively, as shown in Table 4.

**Table 4 Patients age groups**

| Age groups | | Frequency | Percent |
|---|---|---|---|
| | ≤30 | 25188 | 3.5 |
| | 31-40 | 34188 | 4.7 |
| | 41-50 | 52699 | 7.3 |
| | 51-60 | 98216 | 13.6 |
| | 61-70 | 139380 | 19.3 |
| | 71-80 | 160907 | 22.3 |
| | >80 | 211314 | 29.3 |
| | Total | 721892 | 100.0 |
| Missing | System | 66 | .009 |
| Total | | 721958 | 100.0 |

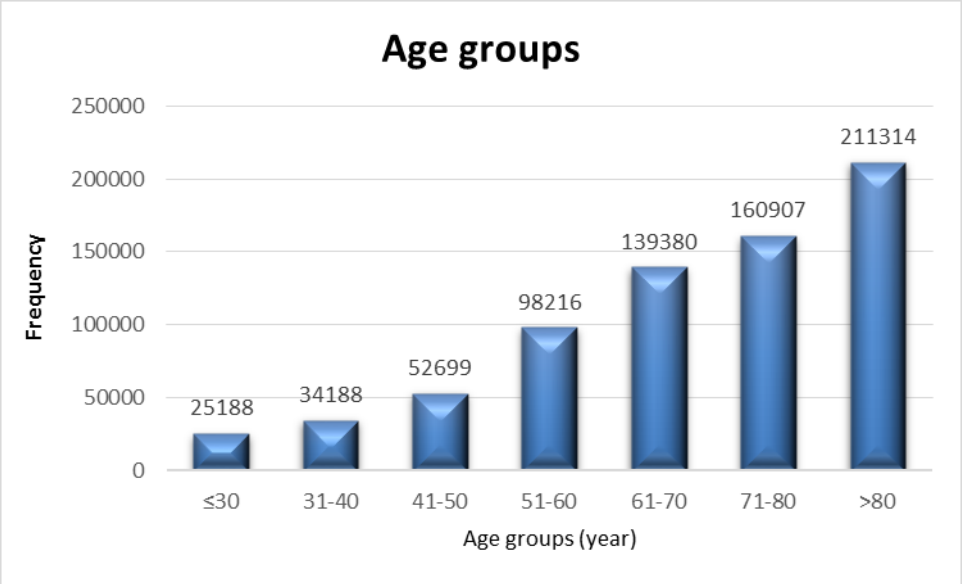



**Figure 1Age groups of thyroid disease patients**

### 4.2.2 Race

White patients occupied the highest incidences of hyperthyroidism by 76.7%, followed by Black race patients (7%), and others, as shown in Table 5

**Table 5 Patients and race groups**

| Race | | Frequency | Percent |
|---|---|---|---|
| | White | 554033 | 76.7 |
| | Black | 50506 | 7.0 |
| | Hispanic | 46717 | 6.5 |
| | Asian or Pacific Islander | 10402 | 1.4 |
| | Native American | 4135 | .6 |
| | Others | 18265 | 2.5 |
| | Total | 684058 | 94.8 |
| Missing | System | 37900 | 5.2 |
| Total | | 721958 | 100.0 |

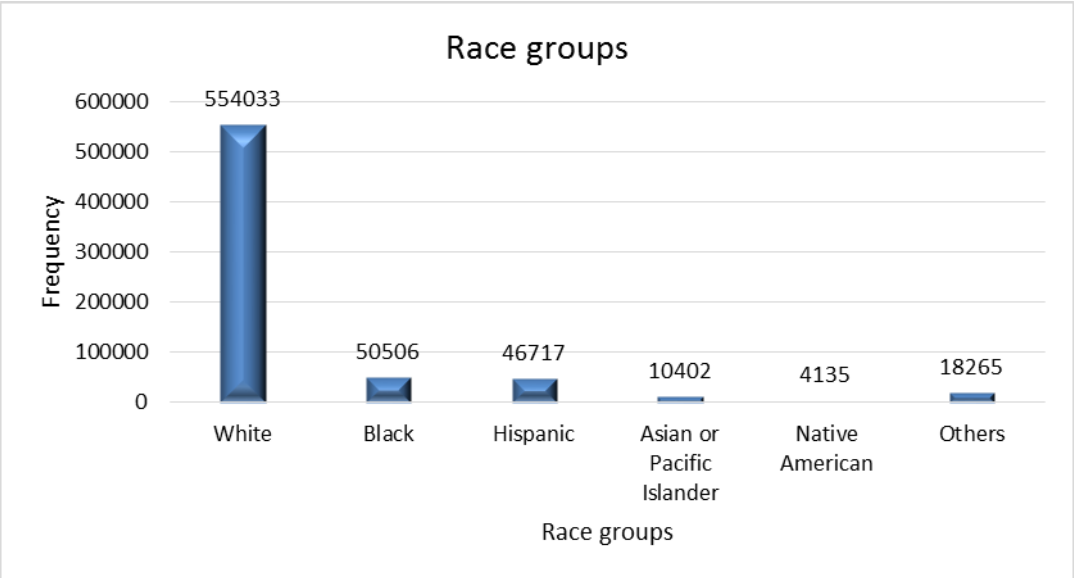



**Figure 2Incidence of hyperthyroidism among races**

### 4.2.3 Gender

Females showed higher incidence of thyroid diseases than males (74.9% vs. 25.1%), as shown in Table 6.

**Table 6 Incidence of thyroid diseases between genders**

| Genders | | Frequency | Percent |
|---|---|---|---|
| | Male | 181210 | 25.1 |
| | Female | 540710 | 74.9 |
| | Total | 721920 | 100.0 |
| Missing | System | 38 | .0 |
| Total | | 721958 | 100.0 |

### 4.2.4 Health insurance

Medicare was the main form of health insurance with highest incidence by 68.2%, followed by 20.2% of Private (HMO), 7.1% of Medicaid, and others as shown in Table 7.

**Table 7 Thyroid diseases and health insurance**

| Health insurance | | Frequency | Percent |
|---|---|---|---|
| | Medicare | 492730 | 68.2 |
| | Medicaid | 51059 | 7.1 |
| | Private including HMO | 145920 | 20.2 |
| | Self-pay | 14825 | 2.1 |
| | No charge | 1326 | .2 |
| | Others | 14873 | 2.1 |
| | Total | 720733 | 99.8 |
| Missing | System | 1225 | .2 |
| Total | | 721958 | 100.0 |

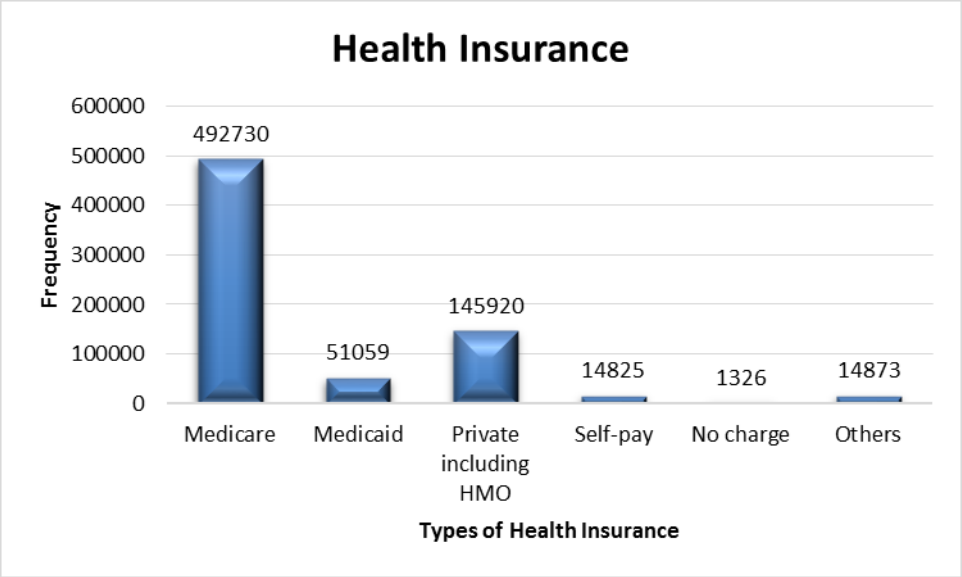



**Figure 3Insurance types of thyroid disease patients**

### 4.2.5 Patients' Comorbidities

Highest incidence of comorbidities of thyroid disease patients observed with hypertension by 63.8%, followed by fluid and electrolyte disorders (29.1%), and diabetes uncomplicated (24.4%), while comorbidities with lowest incidence were peptic ulcer disease excluding bleeding (0.04%) and acquired immune deficiency syndrome (0.1%), as shown in Table 8.

**Table 8 Thyroid diseases and patients' comorbidities**

| Comorbidities | Frequency | Percent |
|---|---|---|
| 1. Hypertension (combine uncomplicated and complicated) | 460331 | 63.8 |
| 2. Fluid and electrolyte disorders | 209824 | 29.1 |
| 3. Diabetes, uncomplicated | 175859 | 24.4 |
| 4. Chronic pulmonary disease | 168383 | 23.3 |
| 5. Deficiency anemias | 164884 | 22.8 |
| 6. Renal failure | 125649 | 17.4 |

| | | |
|---|---|---|
| 7. Depression | 118287 | 16.4 |
| 8. Obesity | 103309 | 14.3 |
| 9. Congestive heart failure | 93141 | 12.9 |
| 10. Other neurological disorders | 79481 | 11.0 |
| 11. Peripheral vascular disorders | 53434 | 7.4 |
| 12. Psychoses | 43254 | 6.0 |
| 13. Valvular disease | 42097 | 5.8 |
| 14. Diabetes with chronic complications | 42102 | 5.8 |
| 15. Weight loss | 39573 | 5.5 |
| 16. Coagulopathy | 38634 | 5.4 |
| 17. Rheumatoid arthritis/collagen vascular diseases | 33444 | 4.6 |
| 18. Pulmonary circulation disorders | 23092 | 3.2 |
| 19. Liver disease | 21109 | 2.9 |
| 20. Paralysis | 18266 | 2.5 |
| 21. Alcohol abuse | 17569 | 2.4 |
| 22. Drug abuse | 15340 | 2.1 |
| 23. Solid tumor without metastasis | 15094 | 2.1 |
| 24. Metastatic cancer | 15088 | 2.1 |
| 25. Chronic blood loss anemia | 11748 | 1.6 |
| 26. Lymphoma | 7201 | 1.0 |
| 27. Acquired immune deficiency syndrome | 628 | .1 |
| 28. Peptic ulcer disease excluding bleeding | 264 | .04 |

### 4.2.6 Mortality

The incidence of mortality of thyroid disease patients was about 2.4%, as shown in Table 9

**Table 9 Mortality of thyroid diseases**

| Mortality | | Frequency | Percent |
|---|---|---|---|
| | did not die during hospitalization | 704626 | 97.6 |
| | died during hospitalization | 17186 | 2.4 |
| | Total | 721812 | 100.0 |
| Missing | System | 146 | .02 |
| Total | | 721958 | 100.0 |

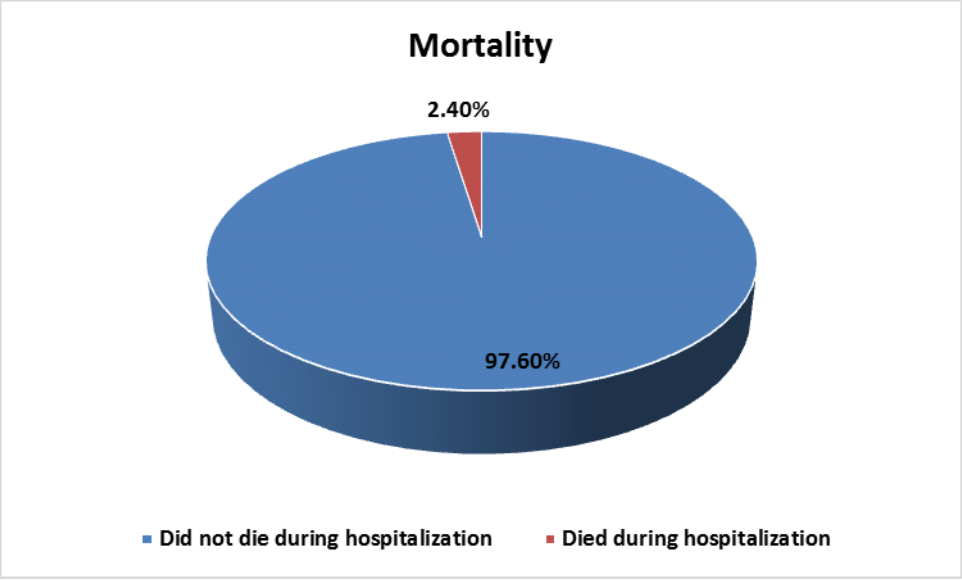



**Figure 4Mortality of the thyroid disease patients**

### 4.2.7 Length of stay and total charge

The mean (±SD) length of stay for patients with thyroid diseases was 5.06 (±6.113) days. The mean (±SD) total cost was $41829.47 (±$60920.47), as shown in Table 10.

**Table 10 Length of hospital stay and total charge of thyroid disease patients**

| Parameters | Mean | Median | ± SD | Skewness | Kurtosis |
|---|---|---|---|---|---|
| Length of hospital stay (days) | 5.06 | 3.00 | 6.113 | 10.896 | 311.73 |
| Total cost ($) | 41829.47 | 25741.0 | 60920.47 | 11.790 | 376.47 |

### 4.2.8 Median household income

Four levels of median household income were observed in this study are 0-25th percentile, 26th to 50th percentile, 51st to 75th percentile, and 76th to 100th percentile. The percentages of median income of hyperthyroidism patients are; 22.2%, 24.8%, 27.1% and 27.1% for the 76th to 100th percentile, 26th to 50th percentile, 51st to 75th percentile, and 0-25th percentile respectively, as shown in Table 11,

**Table 11 Median household income of thyroid disease patients**

| Levels of household income | | Frequency | Percent |
|---|---|---|---|
| | 76th to 100th percentile | 160163 | 22.2 |
| | 26th to 50th percentile | 179141 | 24.8 |
| | 51st to 75th percentile | 173772 | 24.1 |
| | 0-25th percentile | 195514 | 27.1 |
| | Total | 708590 | 98.1 |
| Missing | System | 13368 | 1.9 |
| Total | | 721958 | 100.0 |

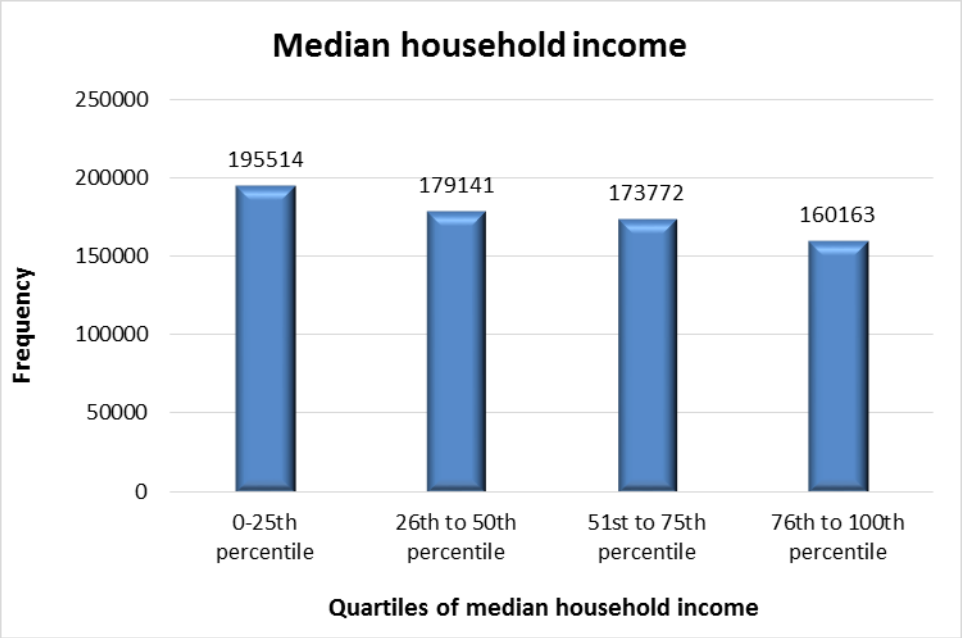



**Figure 5 Median household incomes of thyroid disease patients**

### 4.2.9 Types of thyroid diseases

The incidence for types of thyroid diseases are 3% and 97% for hyperthyroidism and hypothyroidism respectively, as shown in Table 12.

**Table 12 Incidence for types of thyroid diseases**

| Thyroid diseases | Frequency | Percent |
|---|---|---|
| Hypothyroidism | 699991 | 97.0 |
| Hyperthyroidism | 21967 | 3.0 |
| Total | 721958 | 100.0 |

### 4.2.10 Number of procedures and number of chronic diseases

The mean (±SD) number of procedures for patients with thyroid diseases is 1.55 (±2.143). The mean (±SD) number of chronic diseases is 7.18 (±3.208), as shown in Table 13

**Table 13 Number of procedures and number of chronic diseases of thyroid disease patients**

| Parameters | Mean | Median | ± SD | Skewness | Kurtosis |
|---|---|---|---|---|---|
| Number of procedures | 1.55 | 1.00 | 2.143 | 2.453 | 9.742 |
| Number of chronic diseases | 7.18 | 7.00 | 3.208 | .422 | .047 |

### 4.3 Thyroid diseases and demographic characteristics

#### 4.3.1 Congestive Heart Failure

**a) Gender**

Females occupied higher incidence of hyperthyroidism compared to males (72.316% vs. 70.675%), while the incidence of hypothyroidism showed higher with males by 29.325% than of females (27.684%), as shown in Figure 6.

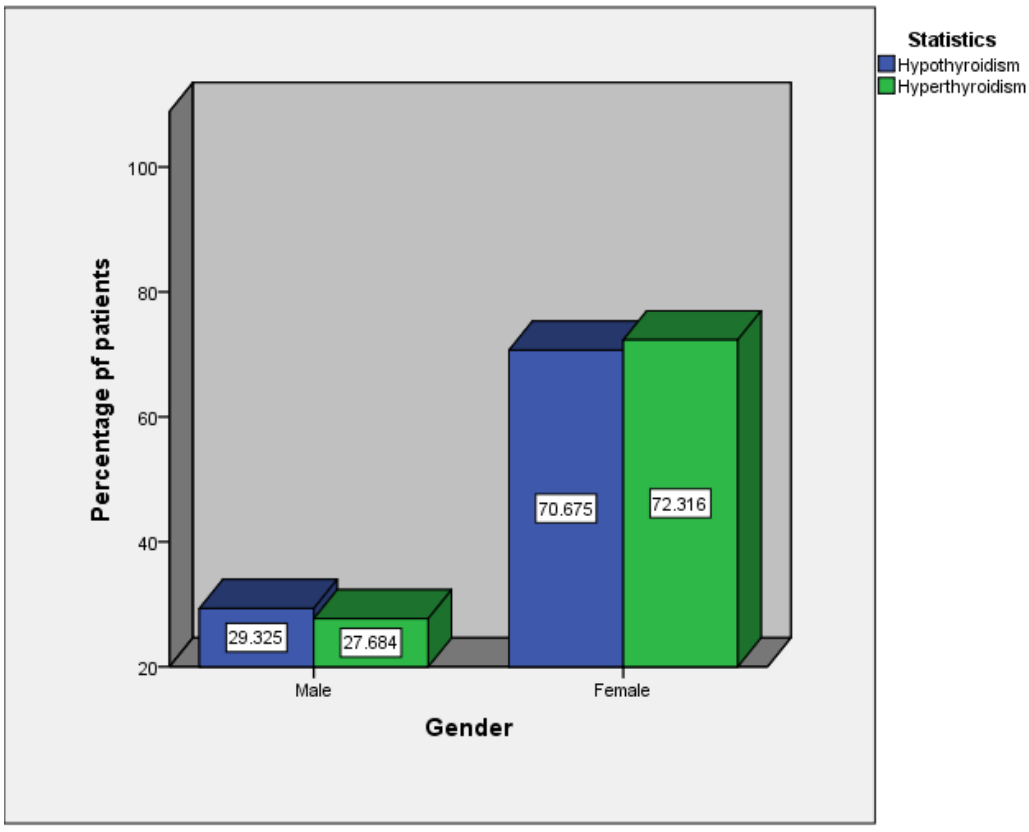



**Figure 6 Thyroid diseases and gender of CHF patients**

**b) Insurance company**

Medicare showed highest incidence of patients with thyroid diseases. However higher percentage was seen with hypothyroidism (86.18%) than of hypothyroidism (73.88%). Hyperthyroidism patients showed higher incidence of Medicaid (10.23%) than of hypothyroidism patients (4.42%), while patients with private including HMO showed higher incidence with hyperthyroidism (10.8%) than of hypothyroidism patients (7.41%), as shown in Figure 7.

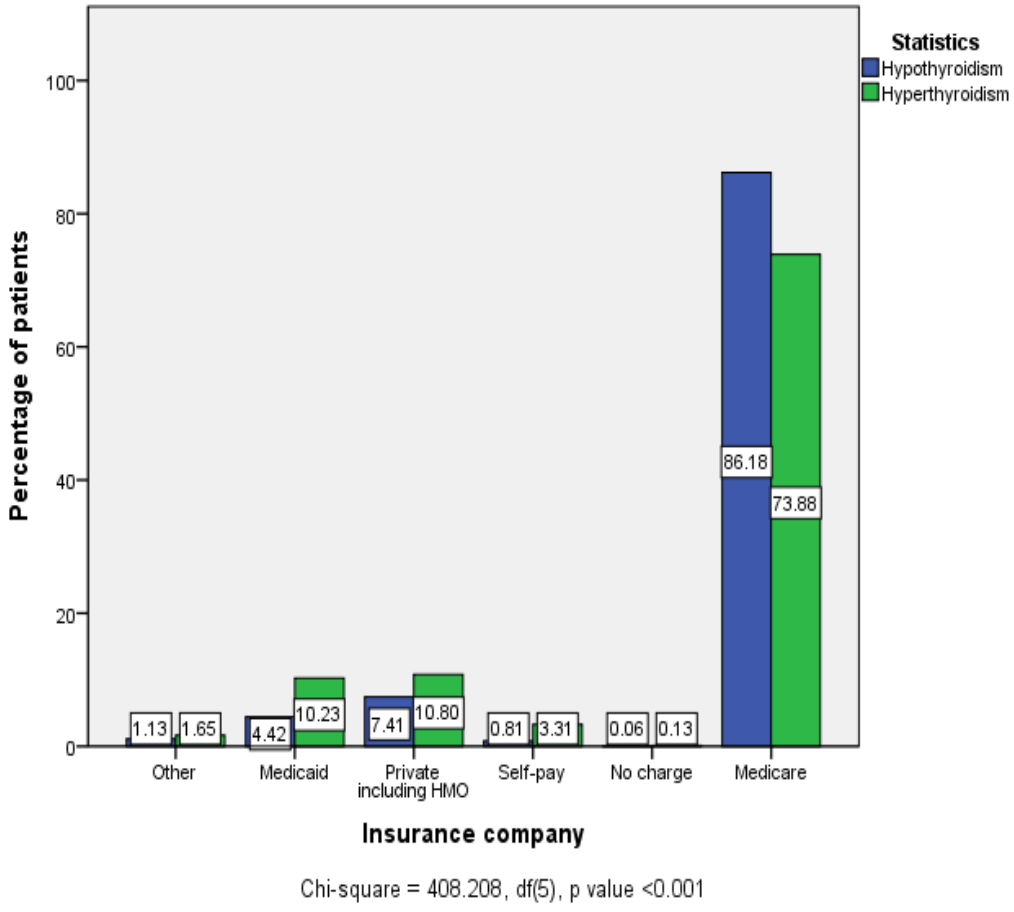



**Figure 7 Thyroid diseases and insurance type of CHF patients**

**c) Race**

White race patients occupied highest incidence of thyroid diseases compared to other races, however higher percentage was obtained for those with hypothyroidism than with hyperthyroidism (81.75% vs. 63.03%). Black race patients got higher incidence of hyperthyroidism (24.05%) than of hypothyroidism (8.28%), as shown in Figure 8.

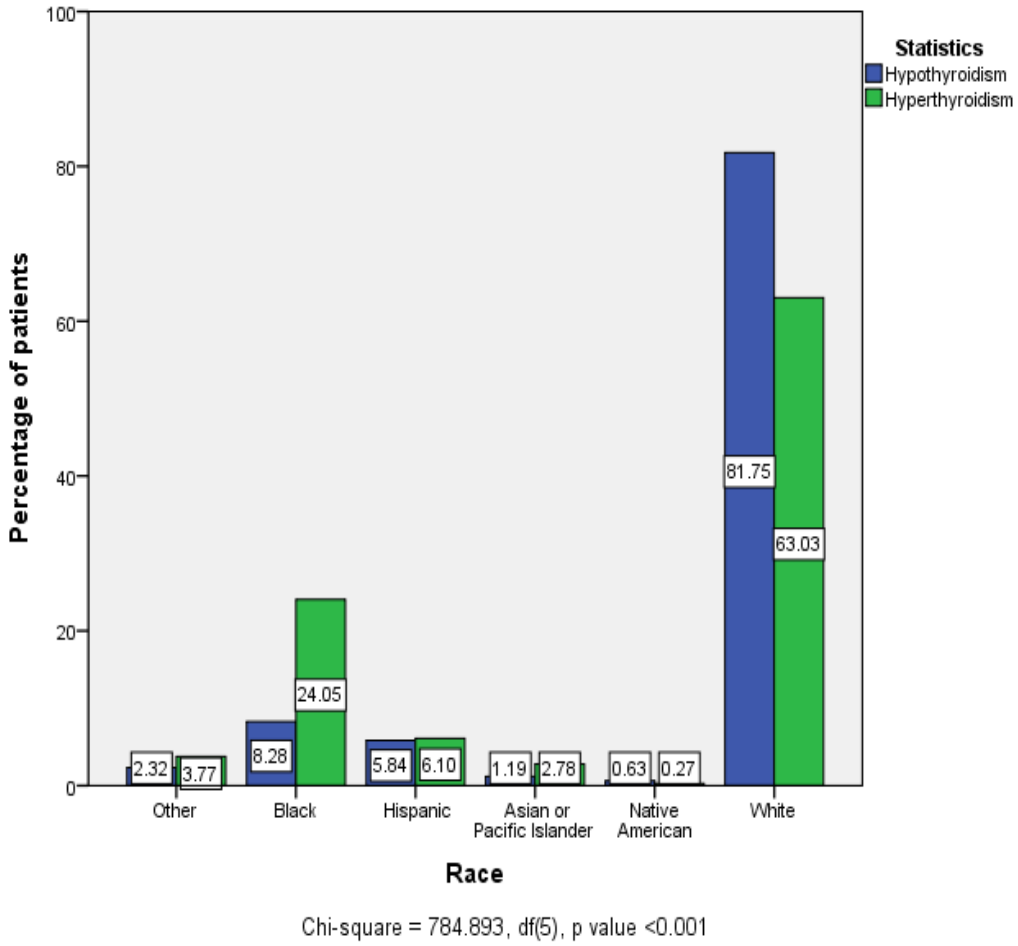



**Figure 8 Thyroid diseases and race of CHF patients**

**d) Median household income**

Higher percentages of patients are those with 0-25th percentile of median household income than other incomes, however higher percentage was seen with hyperthyroidism (33.14%) than of hypothyroidism (30.28%). Patients with 26-50th percentile income showed higher incidence of hypothyroidism (25.77%) and of hyperthyroidism (23.69%), as shown in Figure 9.

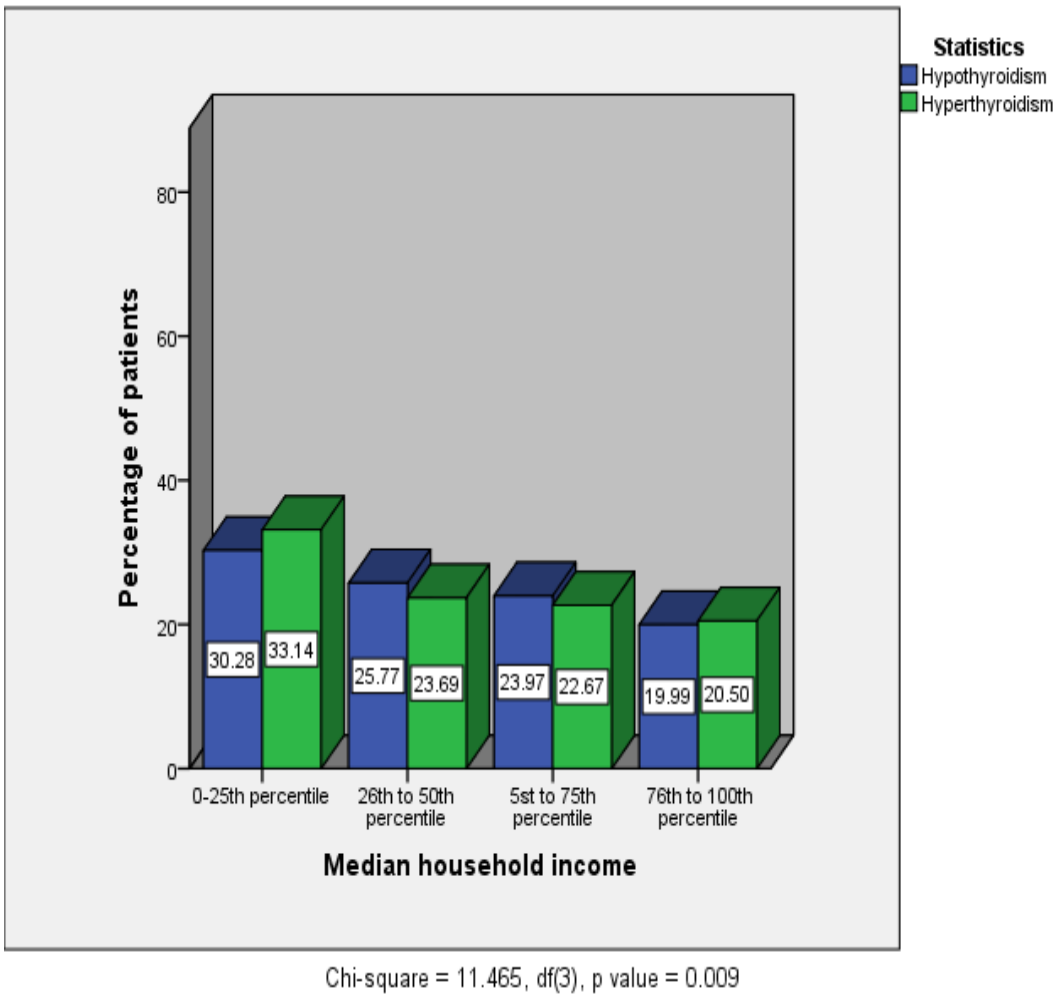



Figure 9 Thyroid diseases and median household incomes of CHF patients

**e) Age**

Patients aged elder than 80 years old were obtained highest incidence of thyroid diseases than other age categories, however higher incidence was obtained with hypothyroidism (46.72%) than of hyperthyroidism (34.07%). Patients aged 71-80 years got higher incidence of hypothyroidism (26%) than of hyperthyroidism (22.6%), as shown in Figure 10.

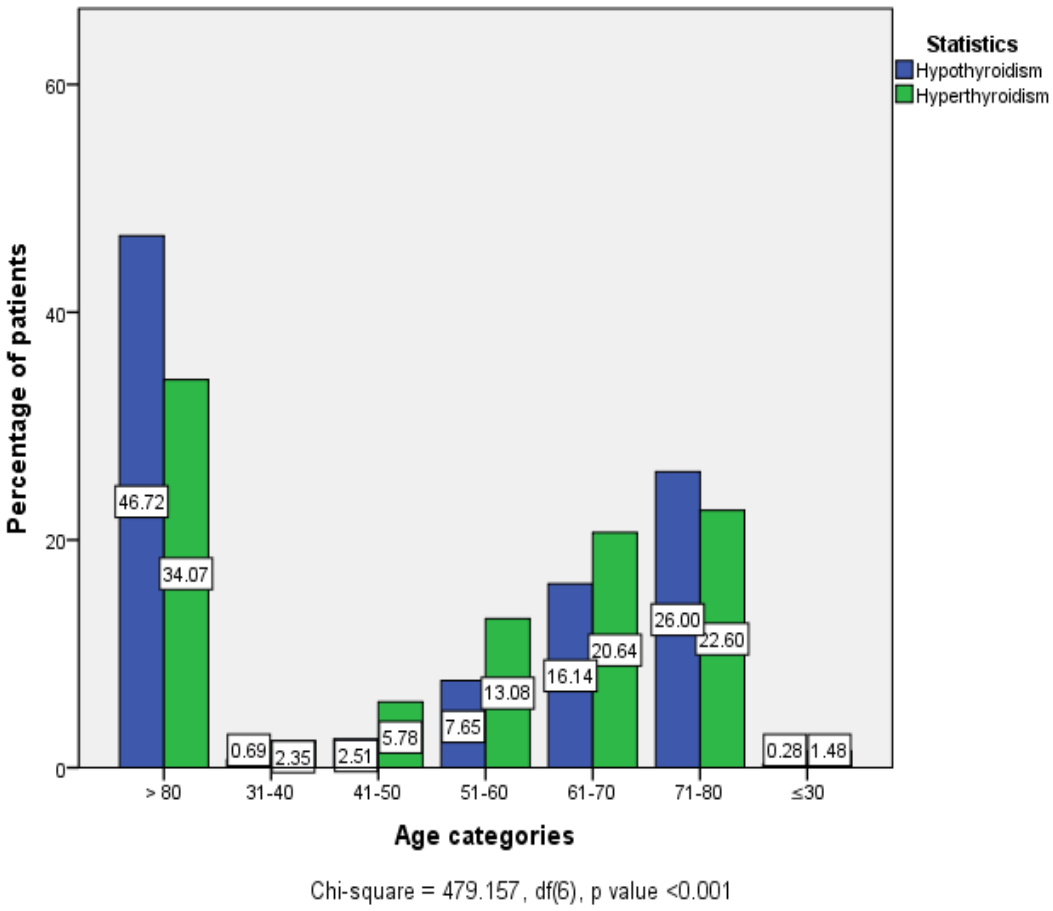
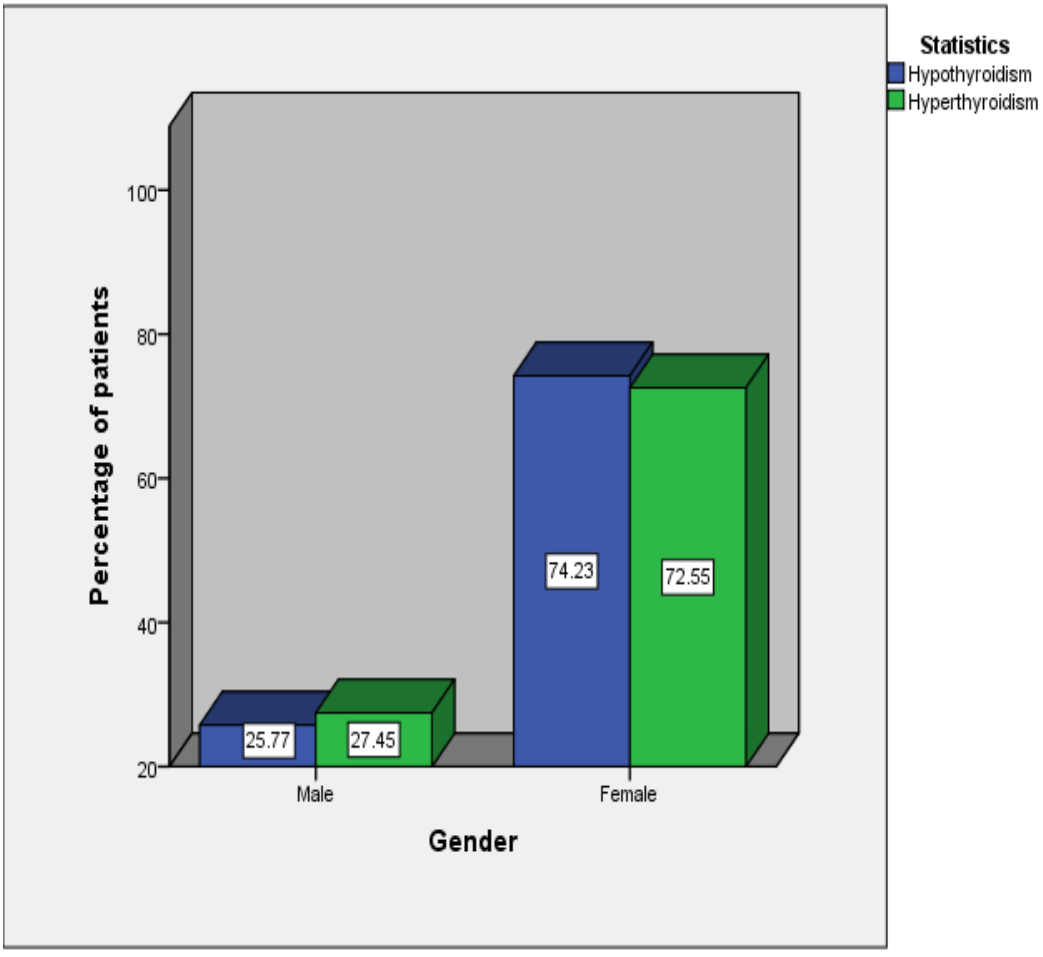



**Figure 10 Thyroid diseases and age categories of CHF patients**

### 4.3.2 Hypertension

**a) Gender**

Females occupied higher incidences of thyroid diseases, however higher incidence of hypothyroidism disease (74.23%) than of hypothyroidism (72.55%). Hyperthyroidism got higher incidence of hyperthyroidism (27.45%) than of hypothyroidism (25.77%), as shown in Figure 11.




Chi-square= 17.176, df(1), p value < 0.001

**Figure 11 Thyroid diseases and gender of hypertension patients**

**b) Insurance company**

Medicare insurance occupied the highest incidence of thyroid diseases, however higher incidence showed with hypothyroidism (76.63%) than of hypothyroidism (62.38%). Private including HMO insurance showed higher incidence of hyperthyroidism patients than of hypothyroidism patients (18.45% vs. 14.97%), as shown in Figure 12.

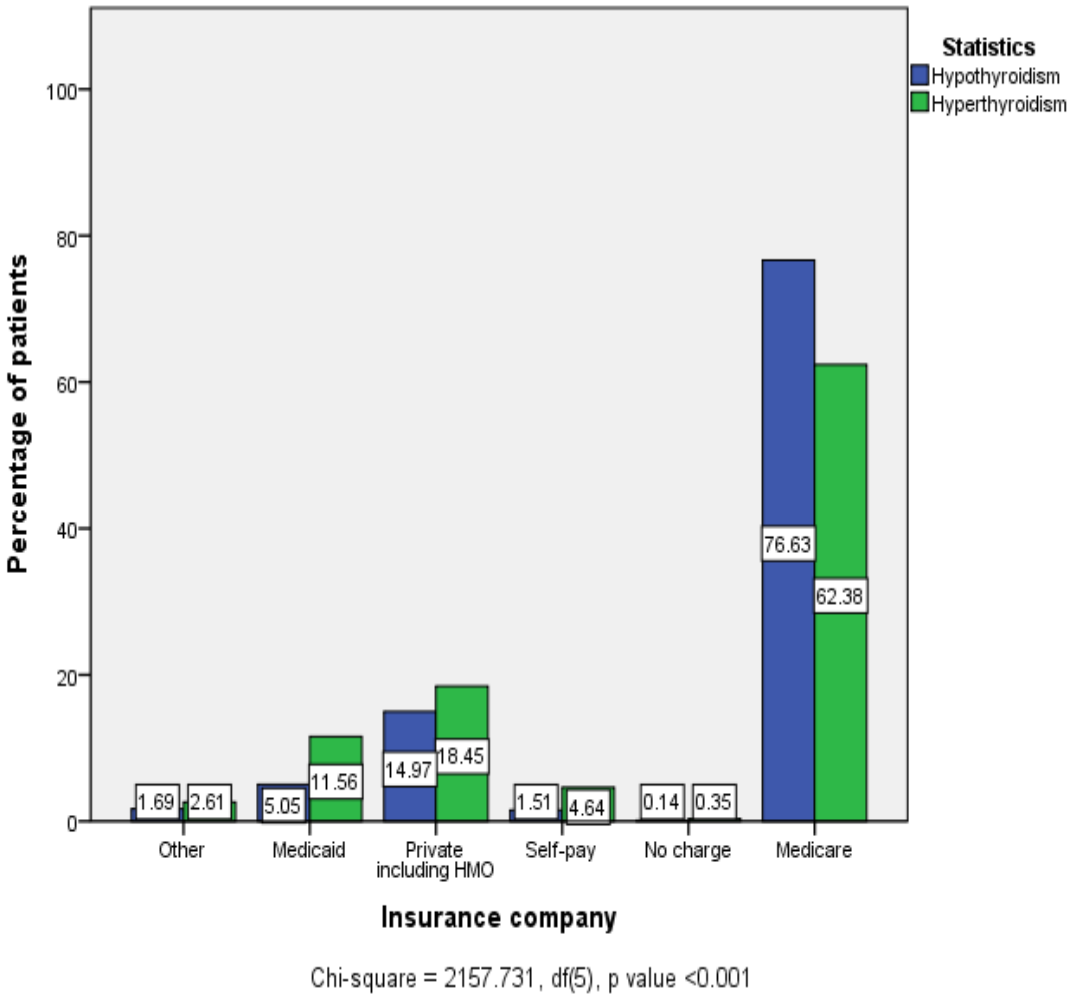



**Figure 12 Thyroid diseases and insurance type of hypertension patients**

**c) Race**

White race patients got highest incidence of thyroid diseases than other races, however, higher incidence observed with hypothyroidism than hyperthyroidism (81.38% vs. 61.37%). Black race patients showed higher incidence of hyperthyroidism than or hypothyroidism (24.02% vs. 7.71%), as shown in Figure 13.

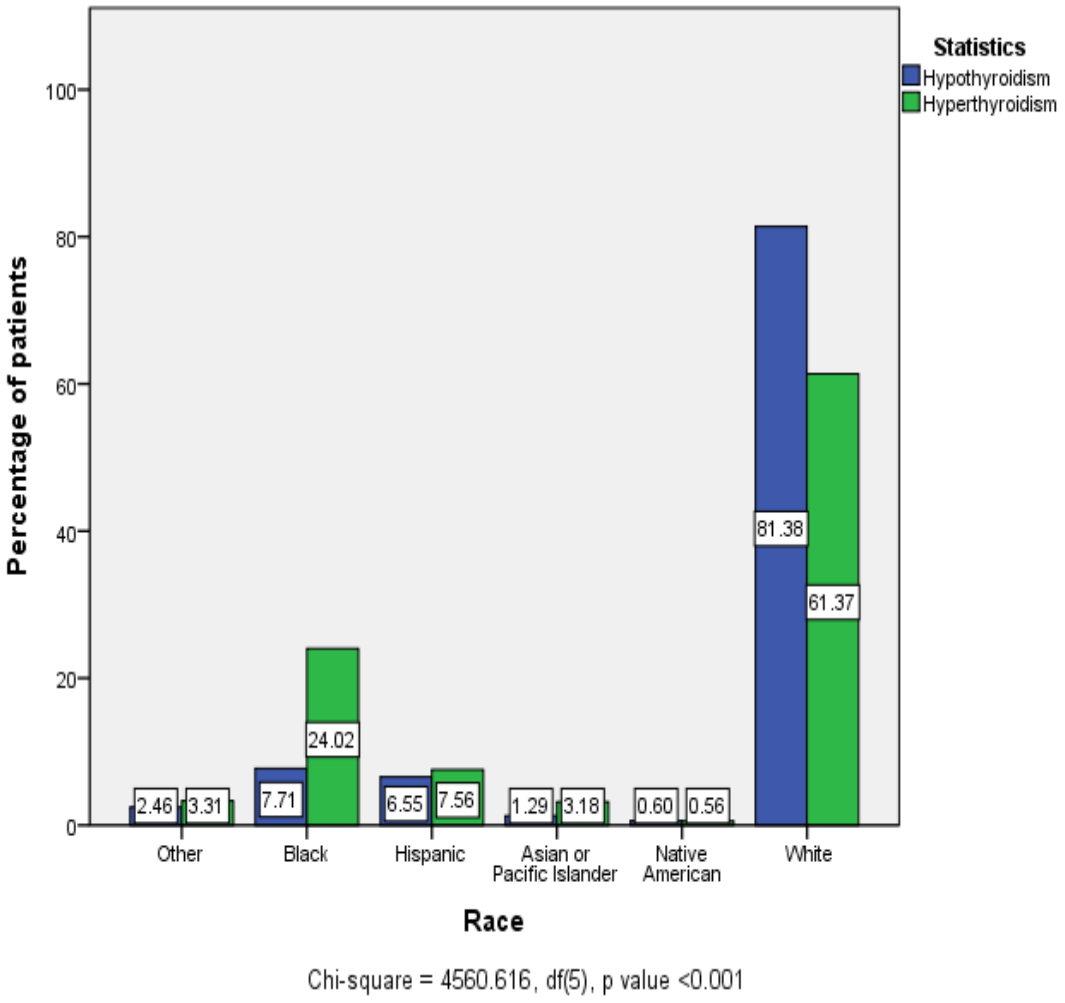



**Figure 13 Thyroid diseases and race of hypertension patients**

**d) Median household income**

Patients with 0-25th percentile median income got highest incidence of thyroid diseases, however higher incidence of hyperthyroidism disease then of hypothyroidism (32.8% vs. 28.55%). Hypothyroidism disease patients got higher incidence of 26th-50th percentile than of hyperthyroidism disease patients (25.56% vs. 23.87%), as shown in Figure 14.

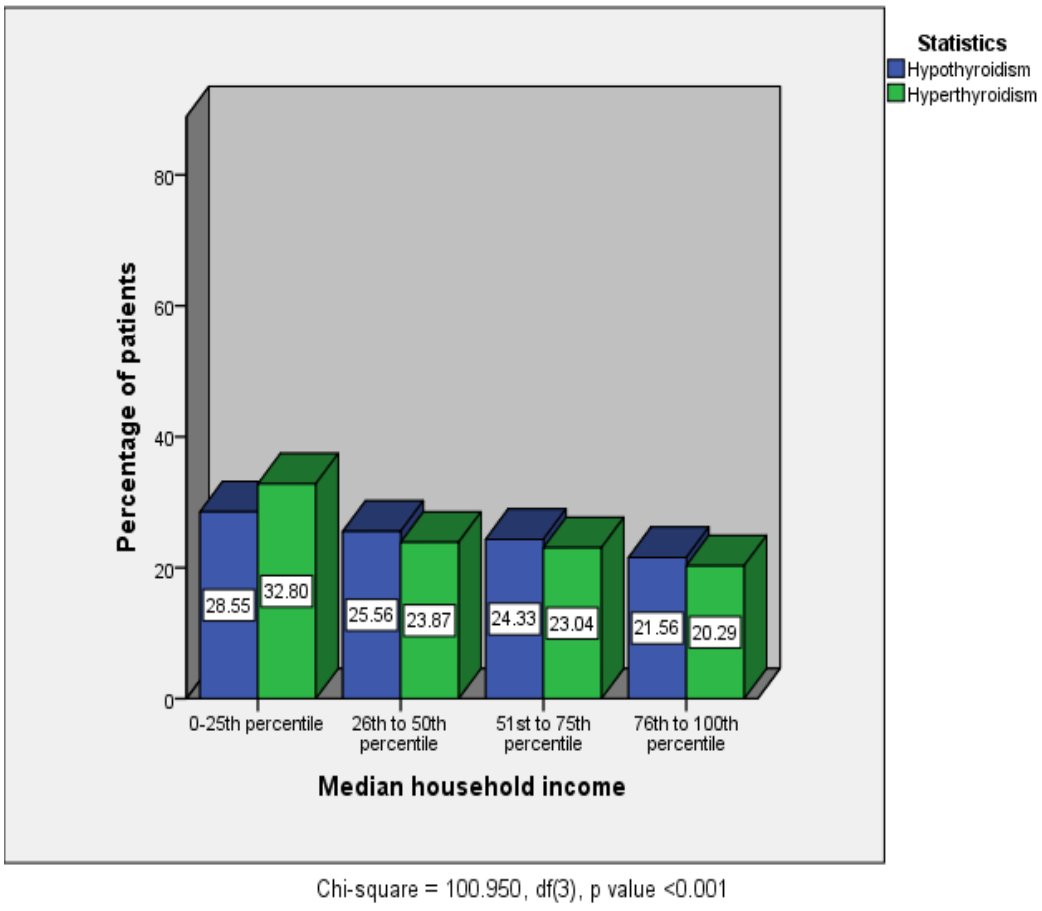



**Figure 14 Thyroid diseases and median household incomes of hypertension patients**

**e) Age**

Patients aged elder than 80 years got highest incidences of thyroid diseases, however higher percentage was seen with hypothyroidism than of hyperthyroidism (34.39% vs. 22.6%). Patients aged 70-80 years got higher incidence of hypothyroidism (25.66%) than of hyperthyroidism (21.92%), as shown in Figure 15.

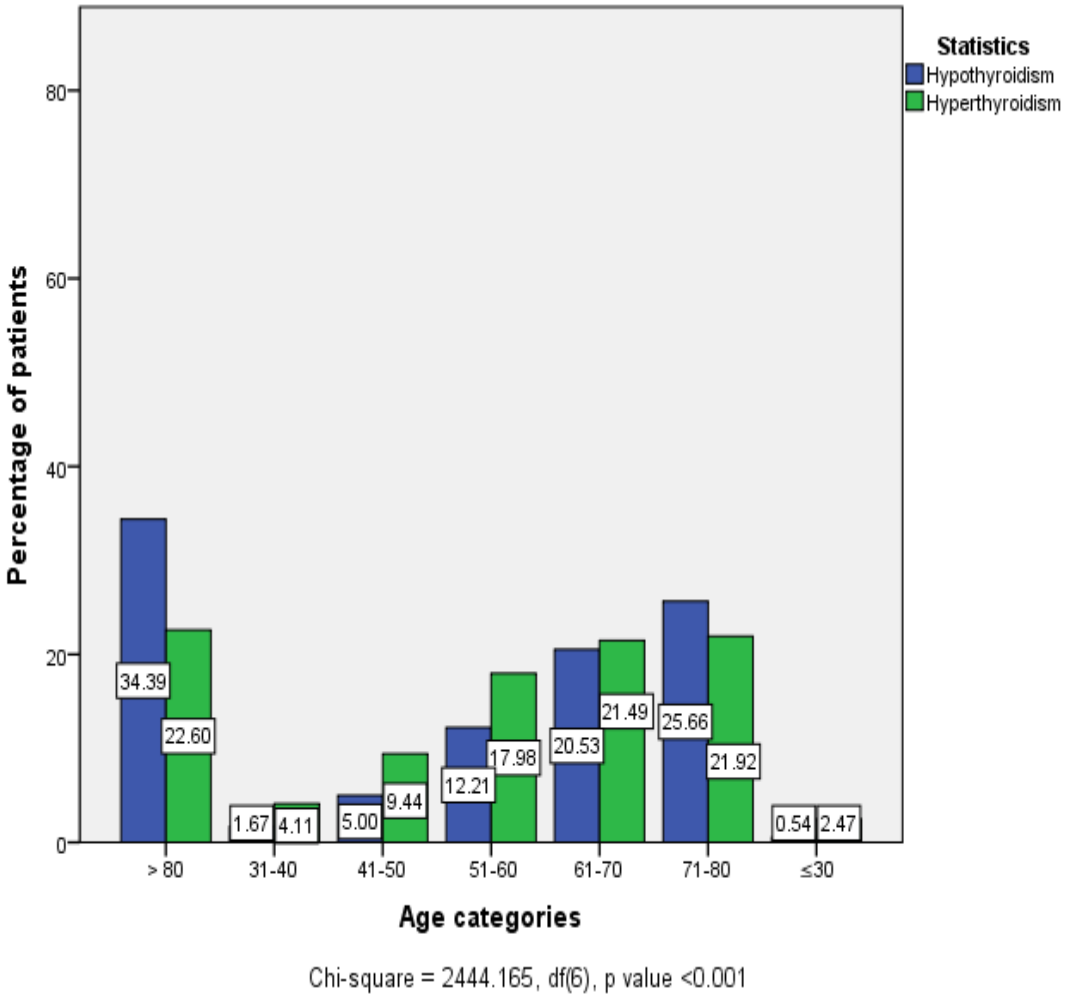



**Figure 15 Thyroid diseases and age categories of hypertension patients**

### 4.4 Mortality incidence and thyroid diseases

#### 4.4.1 Overall mortality and thyroid diseases (Hypothesis 1)

Mortality showed higher incidence of those with hypothyroidism disease than of hyperthyroidism (2.4% vs. 1.75%), as shown in Figure 16.

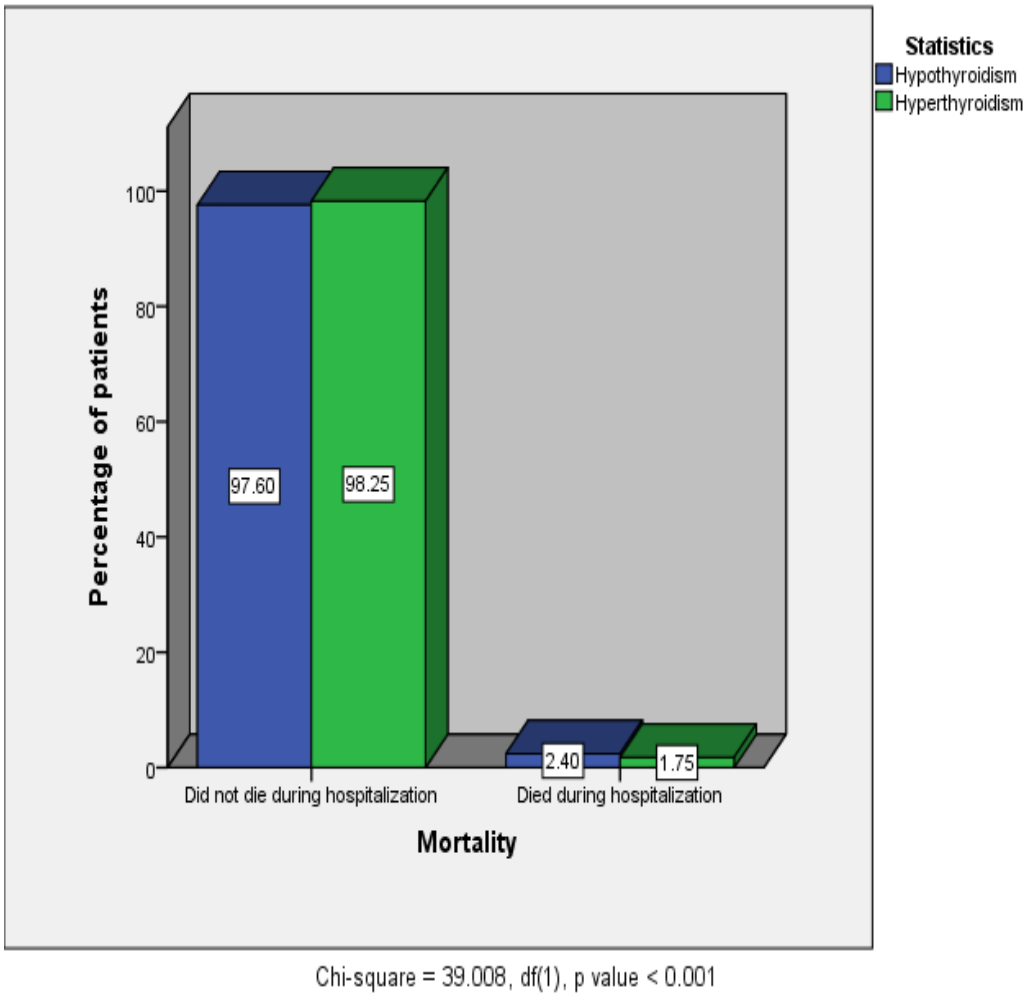



**Figure 16 Mortality and thyroid diseases**

### 4.4.2 Mortality and CHF of thyroid disease patients (Hypothesis 2)

Mortality showed higher incidence of those with hypothyroidism disease than of hyperthyroidism (4.42% vs. 4.87%), as shown in Figure 17.

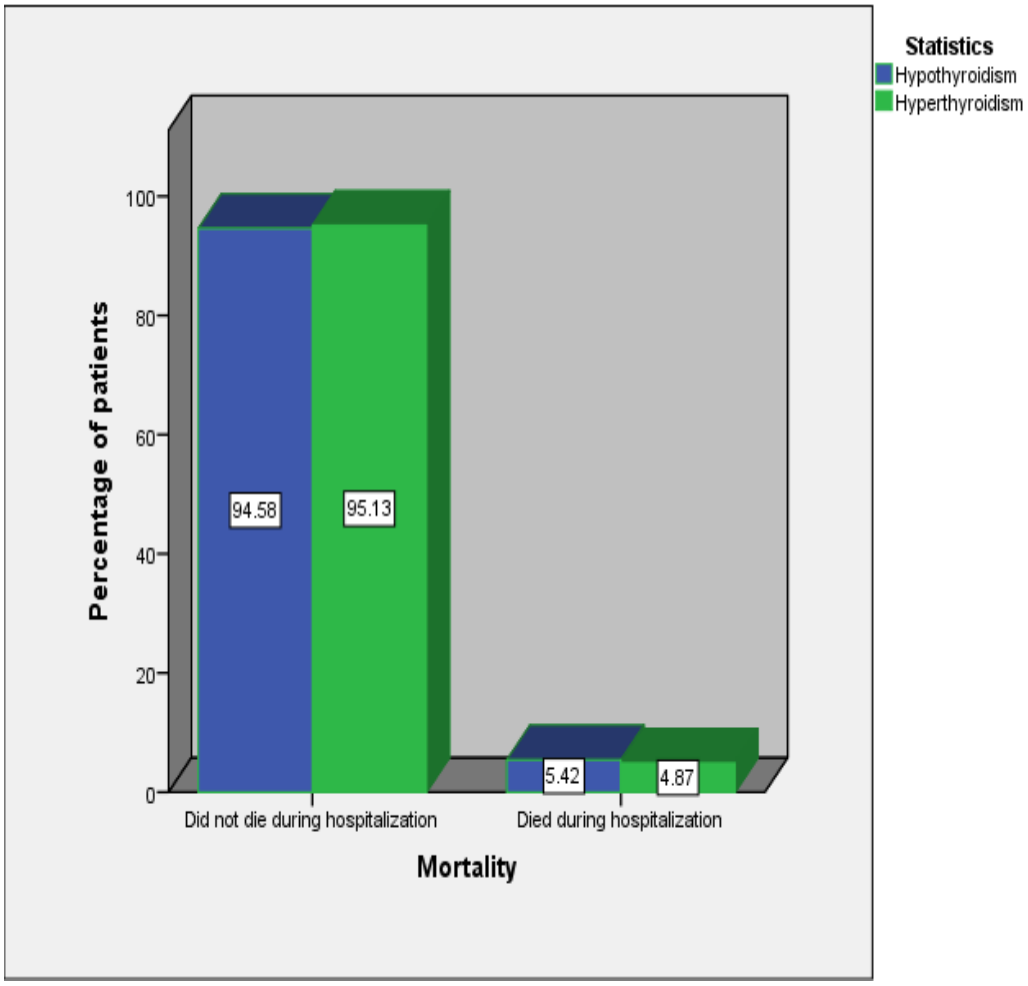



**Figure 17 Mortality and thyroid diseases of CHF patients**

### 4.4.3 Mortality and hypertension of thyroid disease patients (Hypothesis 3)

Mortality showed higher incidence of those with hypothyroidism disease than of hyperthyroidism (2.47% vs. 1.99%), as shown in Figure 18.

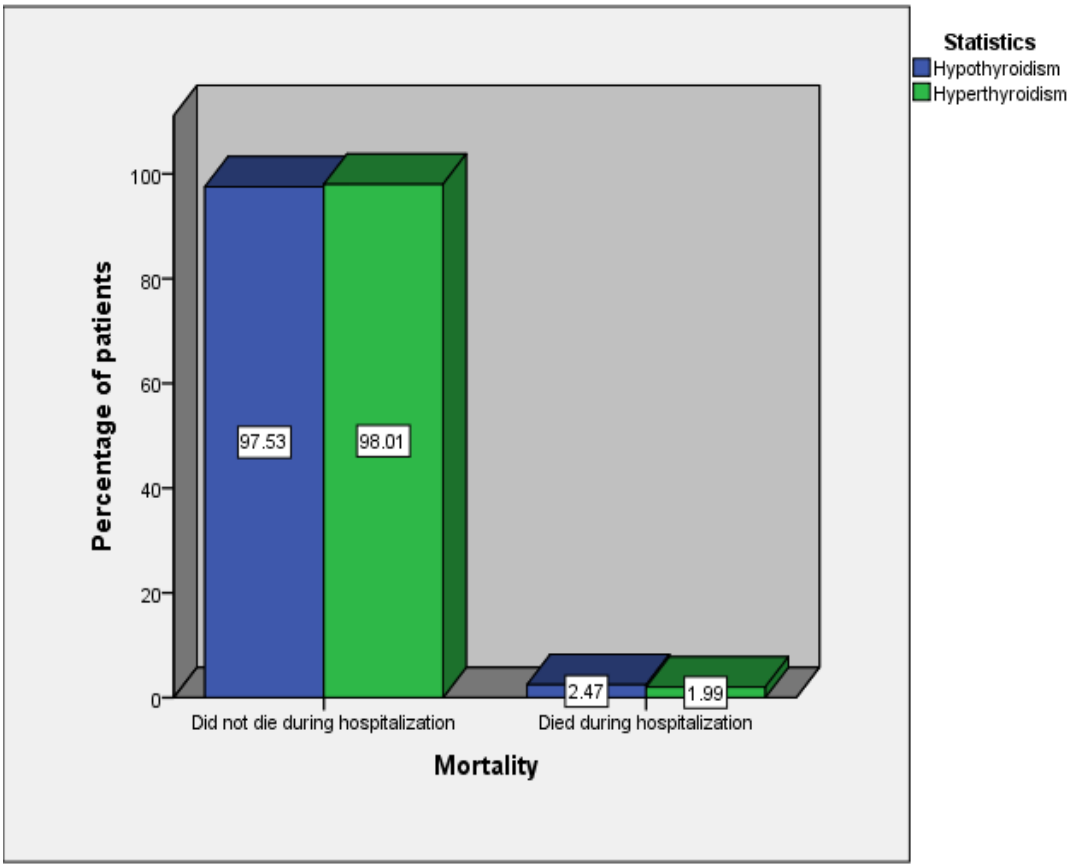



**Figure 18 Mortality and thyroid diseases of hypertension patients**

### 4.4.4 Mortality and gender

Males got higher incidences of mortality compared to males, however higher incidence of females' mortality was observed with hypothyroidism (67.49% vs. 64.58%). Inversely, males got higher incidences of mortality with hyperthyroidism than hypothyroidism (35.42% vs. 32.51%), as shown in Figure 19.

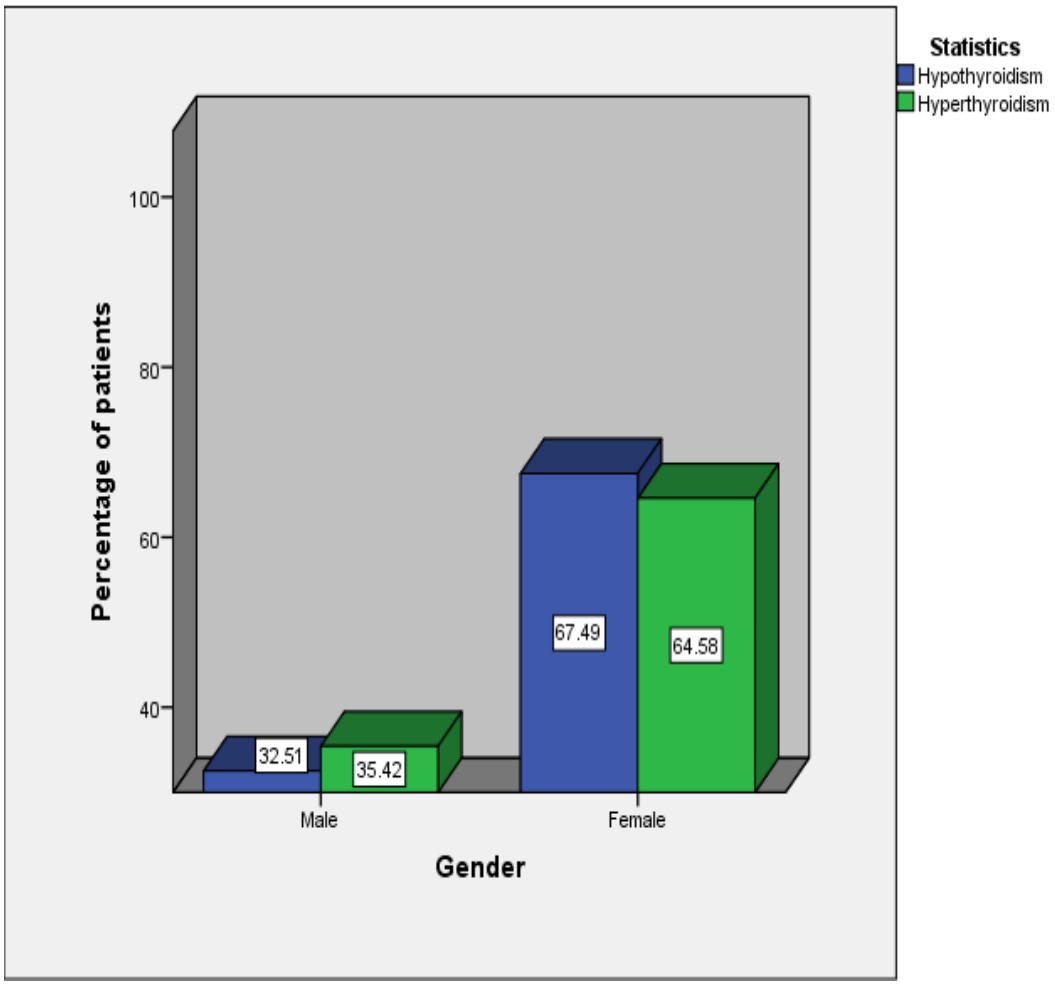



**Figure 19 Mortality and gender**

### 4.4.5 Mortality and insurance type

Highest incidences of mortality was observed with Medicare than other types of insurance, however higher mortality observed with hypothyroidism (81.27%) than of hyperthyroidism (75%). Private including HMO insurance type showed higher incidence of mortality with hyperthyroidism than of hypothyroidism (13.8% vs. 10.93%), as shown in Figure 20.

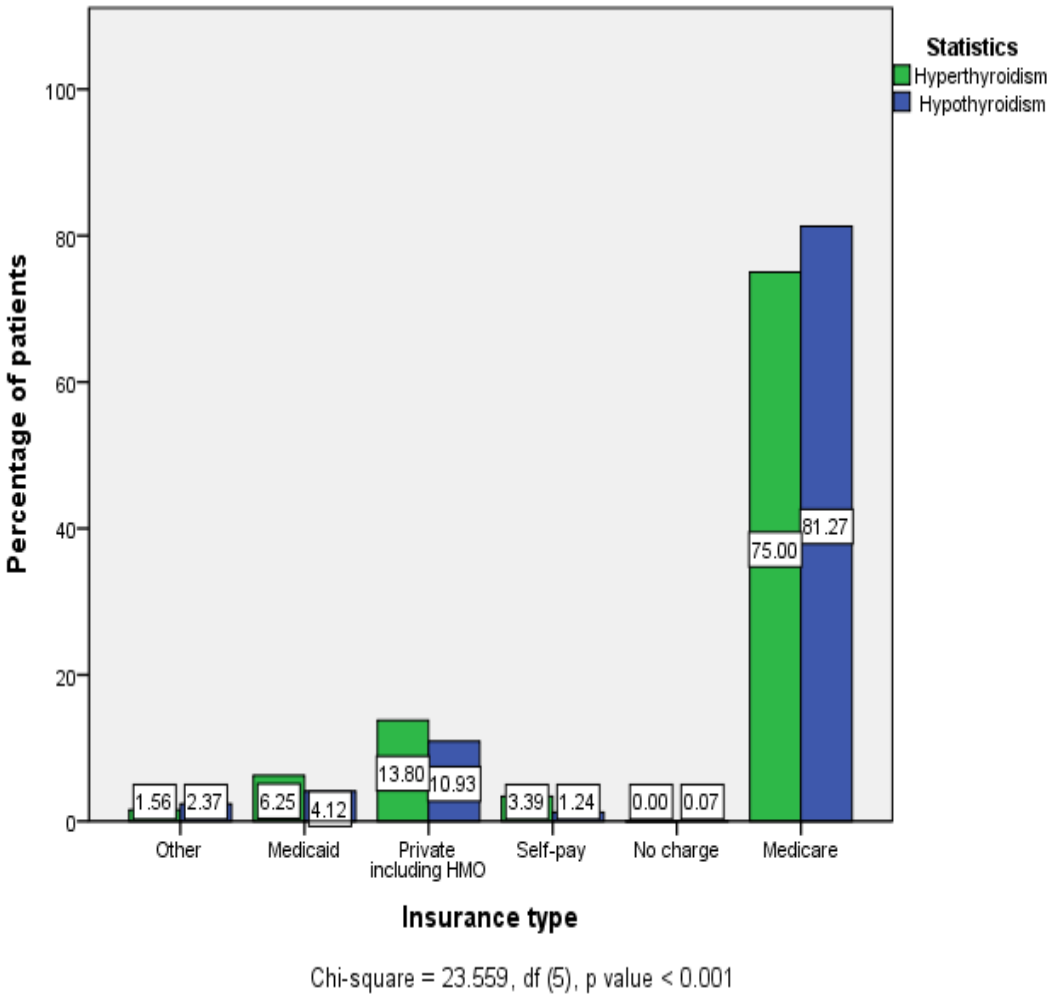



**Figure 20 Mortality and insurance type**

### 4.4.6 Mortality and race

White race patients showed highest incidences of mortality compared to other races, however the incidence of those with hypothyroidism got higher incidence than of hyperthyroidism (82.17% vs. 72.33%). Black race patients got higher mortality with hyperthyroidism than of hypothyroidism (16.99% vs. 6.8%), as shown in Figure 21.

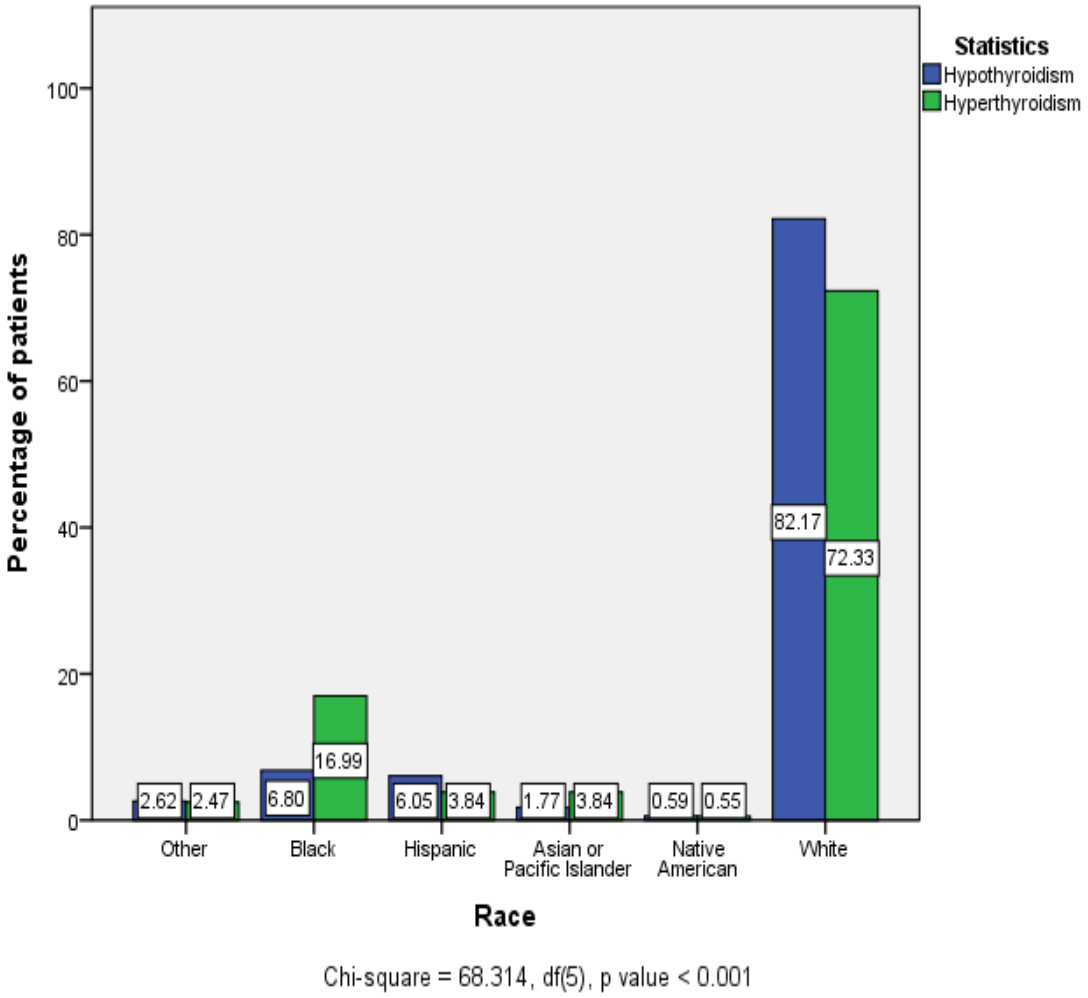



**Figure 21 Mortality and race**

### 4.4.7 Mortality and median household income

Highest incidences of mortality observed with those have income 0-25th percentile than other incomes, however higher incidence was seen in those have hypothyroidism than of hyperthyroidism (28.01% vs. 26.6%). Hyperthyroidism patients with 26th-50th percentile income got higher incidence of mortality than of hypothyroidism (25% vs. 24.73%), as shown in Figure 22.

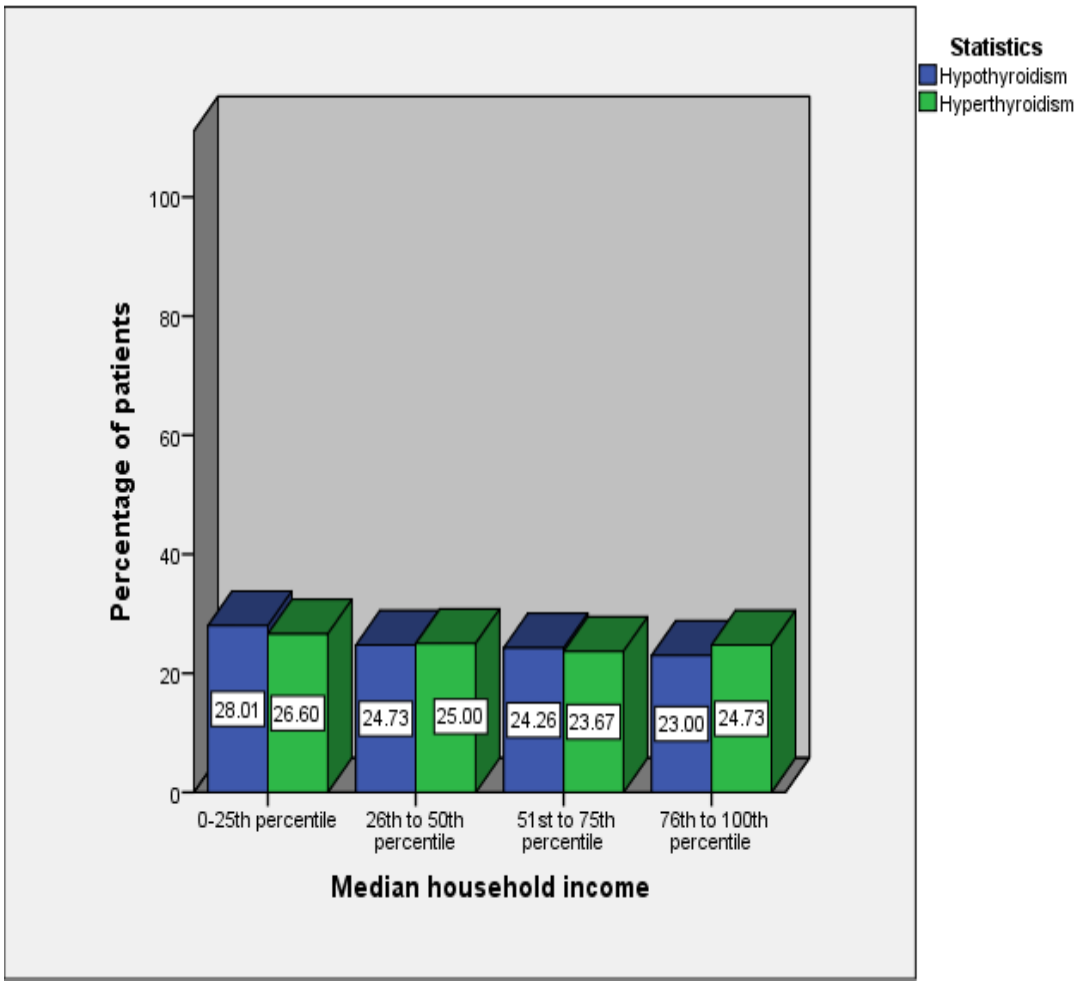



**Figure 22 Mortality and median household income**

### 4.4.8 Mortality and age

Patients aged elder than 80 years old got higher incidences of mortality than other ages, however higher incidences observed with those got hypothyroidism than of hyperthyroidism (50.71% vs. 39.58%). Patients aged 71-80 years got higher incidence of mortality with hyperthyroidism than of hypothyroidism (24.74% vs. 23.39%), as shown in Figure 23.

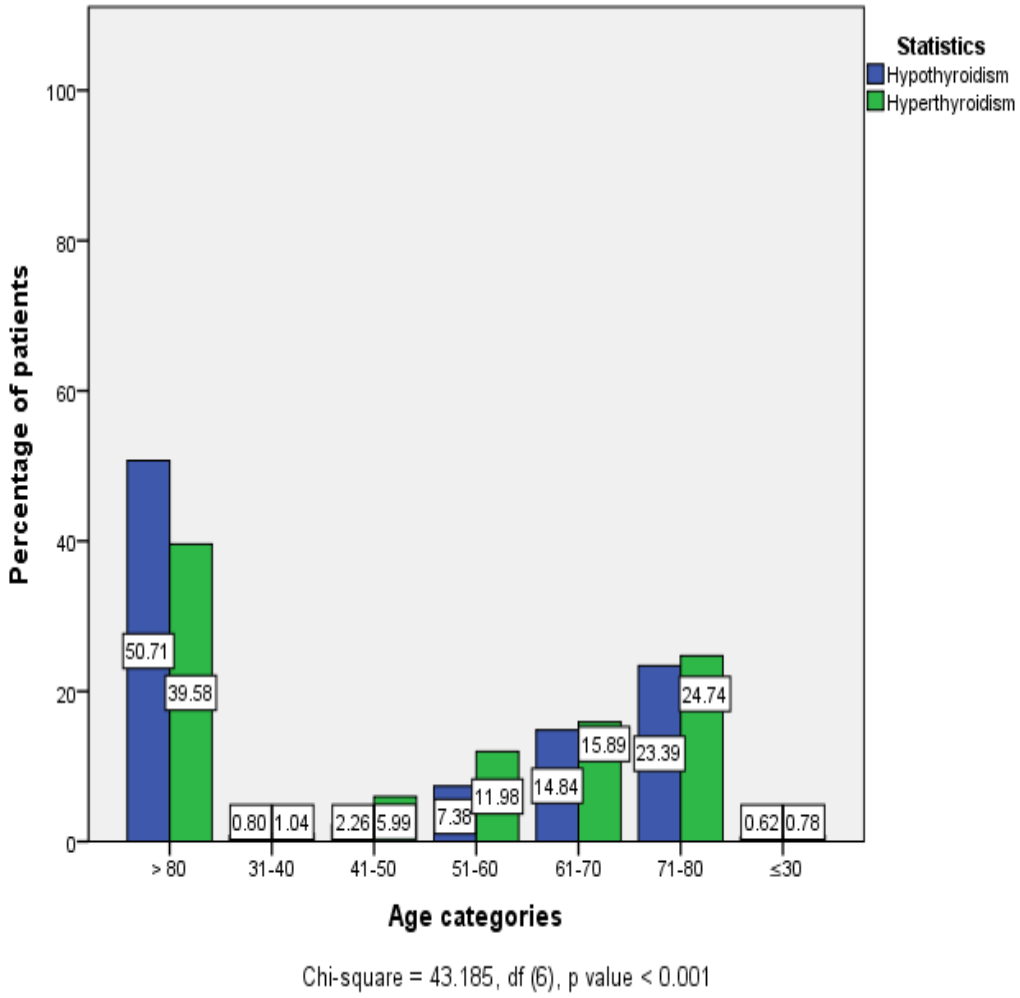



**Figure 23 Mortality and age**

## 4.5 Predictors of length of hospital stay

### 4.5.1 Predictors and Differences in length of hospital stay between hyper- and hypothyroidism patients (Hypothesis 4)

Multiple linear regression (dummy method) is used to find out the predictors of length of hospital stay for thyroid disease patients. Assumptions must be proceeded to approve the final results of regression model. These assumptions are

**Assumption 1,** dependent variables should be continuous: Length of hospital stay is continuous. This assumption is accepted.

**Assumption 2,** two or more independent variables (numerical, ordinal, or categorical): Comorbidities, age categories, gender, race, type of insurance, and household income are categorical, while number of procedures and number of chronic diseases are numerical. All groups were re-categorized to be appropriate for dummy method of analysis. This assumption is accepted.

**Assumption 3, independence of observations** or **independence of residuals**: The value of Durbin-Watson for length of stay should be ranged between 1 and 3, or near to 2 as ideal result. The value of Durbin-Watson of length of stay is 1.949 and 1.918 for hyper and hypothyroidism respectively. This assumption is accepted.

**Assumption 4, linear relationship between the dependent and independent variable(s):** Significant relationships between dependent and independent variables. This assumption is accepted.

**Assumption 5, data must show homoscedasticity: Results showed that the dots along of scatter plot are homogenous and with same distance around the linear fit line, as shown in Figures below. This assumption is accepted.**

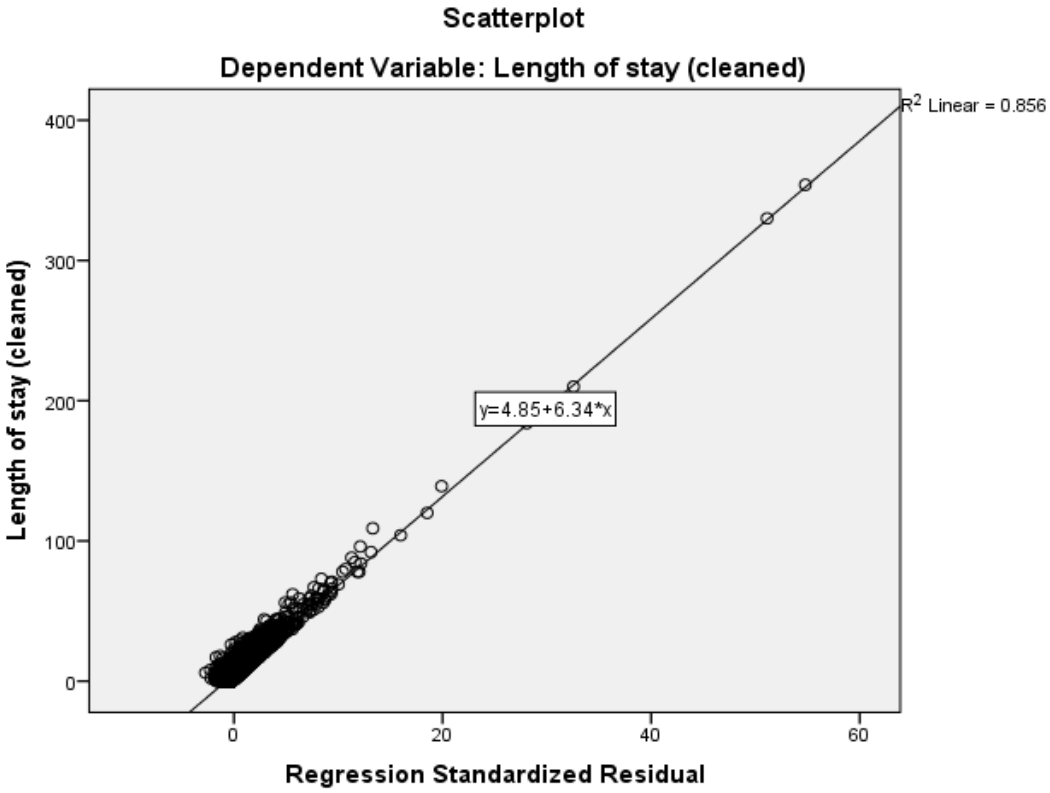



**Figure 24 Homoscedasticity of Length of hospital stay for hyperthyroidism patients**

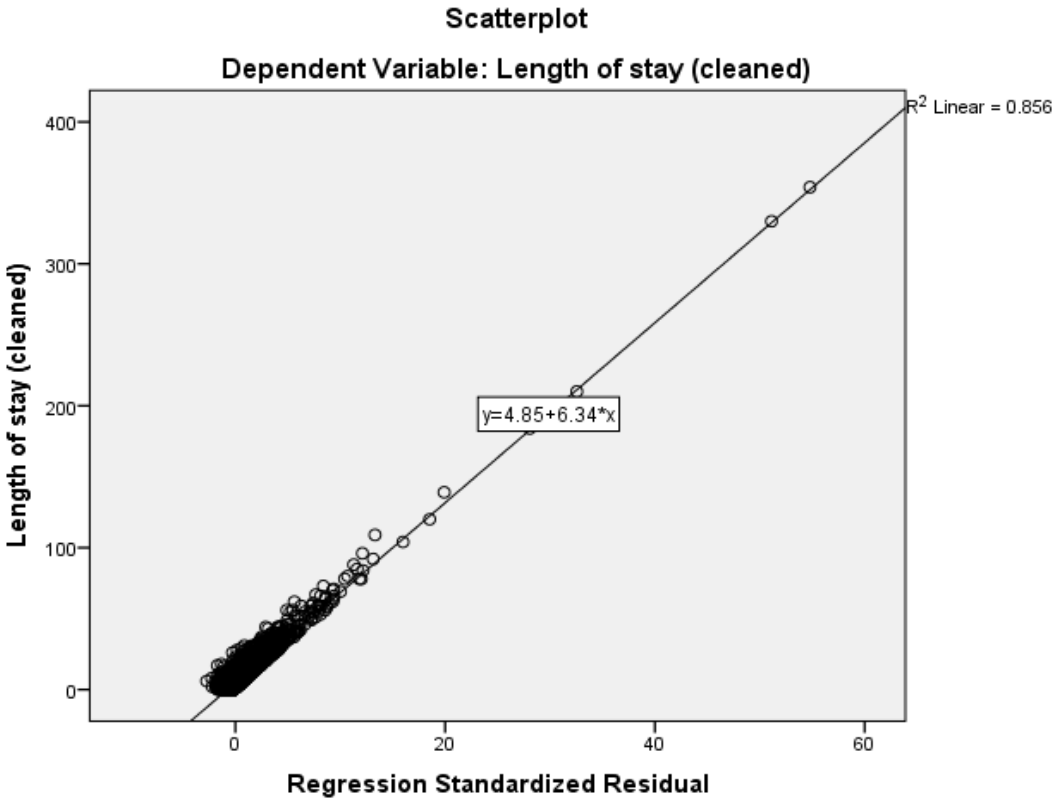



**Figure 25 Homoscedasticity of Length of hospital stay for hyperthyroidism patients**

**Assumption 6,** data must not show multicollinearity: Collinearity diagnostics is used to determine the multicollinearity. The VIF results must be less than 2 or near to 1 as ideal results. All results of variables are less than 2. This assumption is accepted.

**Assumption 7, no significant outliers:** The cut point for the outliers while using Cook's distance is (4/n), which equals to 0.00001. There were 557 and 21,580 cases of hyper- and hypothyroidism, which were considered as outliers. These cases were excluded in regression model.

**Assumption 8,** the residuals must be normally distributed: The residuals are normal distributed, as shown in Figures above.

After accepting all assumptions for the length of stay, the final models for the predictors of hyper- and hypothyroidism patients are shown in Table 14

Paralysis is the predictor with highest effects on length of hospital stay for hyperthyroidism patients with 1.984 days, followed by weight loss (1.651 days), pulmonary circulation disorders (1.407 days), fluid and electrolyte disorders (1.226 days). The factors more related to reduction of length of hospital stay were private including HMO insurance type (-0.929 days), followed by no charge (-0.850 days) and self-pay (-0.746 days).

The length of hospital stay of hyperthyroidism = 3.090-.241 (female) + .594 (number of procedures) -.297( Asian and Pacific Islander) -.656 (Native American) -.715 (Other insurances) -.558 (Medicaid) -.929 (Private including HMO) -.746 (self-pay) -.850 (No charge) -.181 (income 26th-50th percentile) -.121 (income 51th-75th percentile) -.195 (income 76th-100th percentile) +.293 (alcohol abuse) + .798 (Deficiency anemias) + .305 (Chronic pulmonary disease) + 1.067 (Coagulopathy) + .159 (depression) + .259 (DM, uncomplicated) + .474(DM with chronic complications) + .363(drug abuse) + 1.226 (Fluid and electrolyte disorders) + .596 (Metastatic cancer) + .561 (other neurological disorders) + .163 (Obesity) + 1.984 (Paralysis) + .527 (Psychoses) + 1.407 (Pulmonary circulation disorders) + .160 (renal failure) + .461 (valvulardisease) + 1.651 (Weight loss).

Weight loss is the predictor with highest effects on length of hospital stay for hypothyroidism patients with 1.997 days, followed by paralysis (1.484 days), and fluid and electrolyte disorders (1.065 days). The factors more related to reduction of length of hospital stay were age 31-40 years (-.807 days), followed by age equal and younger than 30 years (-.681 days) and age 41-50 years (-.627 days).

The length of hospital stay of hypothyroidism = 3.240 - .054 (female) + .528 (number of procedures) -.681 (Age ≤ 30) -.807 (Age 31-40) -.627(Age 41-50) -.474(Age 51-60) -.466(Age 61-70) -.319(Age 71-80) -.083(other races) +.175(other races) -.136 (Hispanic) - .273 (Asian and Pacific Islander) -.484 (Native American) -.462 (Other insurances) + .070 (Medicaid) -.444 (Private including HMO) -.379 (self-pay) -.416 (No charge) -.115 (income 26th-50th percentile) -.145 (income 51th-75th percentile) -.177 (income 76th-100th percentile) + .614 (Acquired immune deficiency) +.347 (alcohol abuse) + .686 (Deficiency anemias) + .362 (Chronic pulmonary disease) + .754 (Coagulopathy) + .049 (depression) + .117 (DM, uncomplicated) + .432 (DM with chronic complications) + .646 (drug abuse) + .150 (lymphoma) + 1.065 (Fluid and electrolyte disorders) + .531 (Metastatic cancer) + .471 (other neurological disorders) + .332 (Obesity) + 1.484 (Paralysis) + .421 (Psychoses) + .861 (Pulmonary circulation disorders) + .181 (renal failure) + .191 (solid tumor without metastasis) + .763 (peptic ulcer) + .244 (valvular disease) + 1.997 (Weight loss).

As main comparison between predictors of length of stay for hyper- and hypothyroidism diseases, similarity observed in predictors affected on longer hospital stay, but higher for paralysis and weight loss for hyper- and hypothyroidism respectively. In other word, contribution of paralysis to the hospital stay was higher with hyperthyroidism than to hypothyroidism, while weight loss effect was higher for hypothyroidism than to hyperthyroidism.

**Table 14 Predictors of hospital of length stay of hyper- and hypothyroidism patients**

| Predictors | Hyperthyroidism | | | | Hypothyroidism | | | |
|---|---|---|---|---|---|---|---|---|
| | B | SE | 95% CI | | B | SE | 95% CI | |
| | | | Lower Bound | Upper Bound | | | Lower Bound | Upper Bound |
| (Constant) | 3.090 | .076 | 2.942 | 3.239 | 3.240 | .013 | 3.214 | |
| Female | -.241 | .050 | -.340 | -.142 | -.054 | .009 | -.072 | -.037 |
| Number of procedures | .594 | .011 | .572 | .616 | .528 | .002 | .525 | .532 |
| Age ≤ 30 | | | | | -.681 | .025 | -.729 | -.632 |
| Age 31-40 | | | | | -.807 | .021 | -.849 | -.766 |
| Age 41-50 | | | | | -.627 | .018 | -.662 | -.592 |
| Age 51-60 | | | | | -.474 | .015 | -.503 | -.445 |
| Age 61-70 | .013 | .060 | -.104 | .130 | -.466 | .012 | -.489 | -.443 |
| Age 71-80 | -.015 | .065 | -.142 | .113 | -.319 | .011 | -.340 | -.298 |
| Other races | -.036 | .119 | -.269 | .197 | -.083 | .024 | -.131 | -.035 |
| Black | .014 | .057 | -.098 | .126 | .175 | .016 | .145 | .206 |
| Hispanic | -.147 | .079 | -.301 | .007 | -.136 | .016 | -.167 | -.106 |
| Asian Pacific Islander | -.297 | .119 | -.529 | -.064 | -.273 | .033 | -.338 | -.208 |
| Native American | -.656 | .282 | -1.209 | -.103 | -.484 | .052 | -.587 | -.381 |
| Other insurance | -.715 | .127 | -.963 | -.467 | -.462 | .028 | -.516 | -.407 |
| Medicaid | -.558 | .069 | -.694 | -.423 | .070 | .018 | .036 | .105 |
| Private including HMO | -.929 | .058 | -1.042 | -.816 | -.444 | .012 | -.467 | -.421 |
| Self-pay | -.746 | .098 | -.938 | -.555 | -.379 | .029 | -.436 | -.323 |
| No charge | -.850 | .355 | -1.546 | -.154 | -.416 | .103 | -.619 | -.214 |
| Income 26th-50th percentile | -.181 | .058 | -.295 | -.067 | -.115 | .010 | -.135 | -.094 |
| Income 51st-75th percentile | -.121 | .059 | -.237 | -.005 | -.145 | .010 | -.166 | -.125 |
| Income 75th-100th percentile | -.195 | .062 | -.317 | -.073 | -.177 | .011 | -.198 | -.156 |
| Acquired immune deficiency | .966 | .561 | -.133 | 2.065 | .614 | .203 | .217 | 1.011 |
| Alcohol abuse | .293 | .128 | .043 | .544 | .347 | .026 | .296 | .398 |
| Deficiency anemias | .798 | .055 | .690 | .906 | .686 | .009 | .668 | .705 |
| Rheumatoid arthritis | .217 | .118 | -.015 | .448 | .018 | .018 | -.017 | .053 |
| Chronic pulmonary disease | .305 | .053 | .201 | .409 | .362 | .009 | .345 | .380 |
| Coagulopathy | 1.067 | .104 | .862 | 1.272 | .754 | .017 | .720 | .788 |
| Depression | .159 | .067 | .028 | .291 | .049 | .010 | .029 | .069 |
| DM, uncomplicated | .259 | .056 | .149 | .369 | .117 | .009 | .099 | .135 |
| DM with chronic complications | .474 | .110 | .258 | .690 | .432 | .017 | .399 | .465 |
| Drug abuse | .363 | .110 | .147 | .580 | .646 | .028 | .591 | .702 |
| Liver disease | .030 | .145 | -.255 | .315 | | | | |
| Lymphoma | .154 | .290 | -.415 | .722 | .150 | .039 | .073 | .227 |
| Fluid and electrolyte disorders | 1.226 | .050 | 1.127 | 1.324 | 1.065 | .009 | 1.049 | 1.082 |
| Metastatic cancer | .596 | .162 | .278 | .914 | .531 | .027 | .478 | .583 |
| Other neurological disorders | .561 | .082 | .400 | .723 | .471 | .012 | .447 | .495 |
| Obesity | .163 | .070 | .027 | .300 | .332 | .011 | .310 | .354 |
| Paralysis | 1.984 | .155 | 1.681 | 2.287 | 1.484 | .025 | 1.434 | 1.533 |
| Peripheral vascular disease | -.086 | .096 | -.276 | .103 | -.001 | .015 | -.030 | .028 |
| Psychoses | .527 | .098 | .335 | .719 | .421 | .016 | .389 | .453 |
| Pulmonary circulation disorders | 1.407 | .126 | 1.161 | 1.654 | .861 | .022 | .817 | .904 |
| Renal failure | .160 | .073 | .017 | .303 | .181 | .011 | .160 | .202 |
| Solid tumor without metastasis | .086 | .164 | -.236 | .407 | .191 | .027 | .139 | .244 |
| Peptic ulcer disease | -.060 | 1.554 | -3.106 | 2.986 | .763 | .385 | .008 | 1.518 |
| Valvular disease | .461 | .101 | .263 | .659 | .244 | .016 | .212 | .277 |
| Weight loss | 1.651 | .091 | 1.473 | 1.830 | 1.997 | .017 | 1.963 | 2.032 |

* Multiple linear regression: R = 0.493 (adjust $R^2$ = .241), df (42), p <0.001. Reference: White, male, age ≥80 years, Medicare, 0-25th percentile income, and no comorbidities.

† Multiple linear regression: R = 0.452 (adjust $R^2$ = .204), df (45), p <0.001. Reference: White, male, age ≥80 years, Medicare, 0-25th percentile income, and no comorbidities

### 4.5.2 Predictors and Differences in length of hospital stay between hyper- and hypothyroidism among hypertension and CHF patients

**a) CHF (Hypothesis 5)**

Multiple linear regression (dummy method) is used to find out the predictors of length of hospital stay for thyroid disease patients suffered of CHF.

The value of Durbin-Watson for length of stay should be ranged between 1 and 3, or near to 2 as ideal result. The value of Durbin-Watson of length of stay is 1.930 and1.912 for hyper and hypothyroidism respectively. **Collinearity diagnostics is used to determine the multicollinearity. The VIF results must be less than 2 or near to 1 as ideal results. All results of variables are less than 2.**

Weight loss is the predictor with highest effects on length of hospital stay for hyperthyroidism CHF patients with 3.550 days, followed by those aged equal and younger than 30 years (2.823 days), paralysis (2.551 days), other neurological disorder (1.549 days), coagulopathy (1.50 days), and number of procedures (1.297 days). The factor more related to reduction of length of hospital stay was female (-0.322 days).

People aged equal and younger than 30 years is the predictor with highest effects on length of hospital stay for hypothyroidism patients with 2.639 days, followed by weight loss (2.325 days), paralysis (1.884 days), number of procedures (1.276 days), and Medicaid (1.235 days). The factors more related to reduction of length of hospital stay were age 31-40 years (-.998 days), followed by age 41-50 years (-.583 days) and age 51-60 years (-.536 days), as shown in Table 15.

As comparison between hyper-and hypothyroidism of CHF patients weight loss found highest risk factor length of stay for hyperthyroidism disease, while those aged equal and younger than 30 years old showed highest with hypothyroidism disease.

**Table 15 Predictors of hospital of length stay of hyper- and hypothyroidism for CHF patients**

| Predictors | Hyperthyroidism | | | | Hypothyroidism | | | |
|---|---|---|---|---|---|---|---|---|
| | B | SE | 95% CI | | B | SE | 95% CI | |
| | | | Lower Bound | Upper Bound | | | Lower Bound | Upper Bound |
| (Constant) | 3.527 | .437 | 2.670 | 4.385 | 3.533 | .062 | 3.410 | 3.655 |
| Female | -.322 | .290 | -.890 | .246 | .061 | .044 | -.026 | .147 |
| Number of procedures | 1.297 | .058 | 1.183 | 1.411 | 1.276 | .009 | 1.258 | 1.294 |
| Age ≤ 30 | 2.823 | 1.116 | .633 | 5.012 | 2.639 | .375 | 1.904 | 3.374 |
| Age 31-40 | .736 | .922 | -1.071 | 2.544 | -.998 | .244 | -1.476 | -.520 |
| Age 41-50 | .242 | .643 | -1.019 | 1.504 | -.583 | .137 | -.851 | -.316 |
| Age 51-60 | -.029 | .491 | -.993 | .934 | -.536 | .087 | -.707 | -.365 |
| Age 61-70 | -.157 | .380 | -.902 | .589 | -.289 | .062 | -.410 | -.167 |
| Age 71-80 | -.299 | .348 | -.982 | .383 | -.125 | .050 | -.222 | -.027 |
| Other races | .136 | .679 | -1.197 | 1.468 | .283 | .135 | .019 | .547 |
| Black | -.164 | .329 | -.809 | .481 | .096 | .076 | -.052 | .244 |
| Hispanic | .127 | .552 | -.955 | 1.209 | .086 | .087 | -.086 | .257 |
| Asian Pacific Islander | -.894 | .787 | -2.438 | .650 | -.352 | .187 | -.719 | .016 |
| Native American | -3.056 | 2.443 | -7.847 | 1.735 | -.249 | .256 | -.751 | .253 |
| Other insurance | -.777 | 1.005 | -2.748 | 1.194 | .140 | .188 | -.228 | .509 |
| Medicaid | -.860 | .502 | -1.844 | .123 | 1.235 | .106 | 1.027 | 1.443 |
| Private including HMO | .090 | .443 | -.778 | .958 | -.005 | .079 | -.160 | .149 |
| Self-pay | -.553 | .774 | -2.071 | .965 | .233 | .224 | -.205 | .671 |
| No charge | -.725 | 3.494 | -7.576 | 6.126 | -.795 | .801 | -2.365 | .776 |
| Income 26th-50th percentile | .122 | .342 | -.549 | .794 | -.135 | .053 | -.239 | -.031 |
| Income 51st-75th percentile | -.170 | .353 | -.862 | .523 | -.120 | .054 | -.226 | -.014 |
| Income 75th-100th percentile | -.044 | .367 | -.765 | .676 | -.084 | .058 | -.197 | .030 |
| Acquired immune deficiency | -.615 | 2.709 | -5.927 | 4.697 | -.633 | .781 | -2.164 | .898 |
| Alcohol abuse | -.948 | .809 | -2.536 | .639 | .090 | .159 | -.221 | .401 |
| Deficiency anemias | .652 | .277 | .109 | 1.195 | .411 | .042 | .328 | .494 |
| Rheumatoid arthritis | -.766 | .652 | -2.045 | .513 | -.143 | .090 | -.319 | .033 |
| Chronic pulmonary disease | -.262 | .271 | -.793 | .268 | .209 | .042 | .128 | .291 |
| Coagulopathy | 1.500 | .464 | .590 | 2.410 | .614 | .075 | .467 | .762 |
| Depression | .258 | .378 | -.484 | 1.000 | .207 | .053 | .102 | .312 |
| DM, uncomplicated | .124 | .290 | -.445 | .692 | -.042 | .045 | -.130 | .046 |
| DM with chronic complications | .380 | .481 | -.563 | 1.324 | .220 | .069 | .086 | .355 |
| Drug abuse | .095 | .840 | -1.553 | 1.743 | .195 | .181 | -.160 | .550 |
| Lymphoma | -2.006 | 1.359 | -4.671 | .659 | .372 | .180 | .020 | .725 |
| Fluid and electrolyte disorders | .969 | .262 | .456 | 1.483 | .899 | .041 | .819 | .980 |
| Metastatic cancer | .489 | .989 | -1.449 | 2.428 | .083 | .160 | -.231 | .398 |
| Other neurological disorders | 1.549 | .417 | .731 | 2.367 | .357 | .058 | .243 | .471 |
| Obesity | .777 | .385 | .023 | 1.532 | .332 | .055 | .224 | .441 |
| Paralysis | 2.551 | .681 | 1.216 | 3.886 | 1.884 | .114 | 1.660 | 2.107 |
| Peripheral vascular disease | .092 | .426 | -.743 | .928 | | | | |
| Psychoses | .774 | .582 | -.367 | 1.915 | .897 | .089 | .723 | 1.071 |
| Pulmonary circulation disorders | .705 | .361 | -.003 | 1.413 | .437 | .061 | .317 | .556 |
| Renal failure | .017 | .306 | -.583 | .618 | | | | |
| Solid tumor without metastasis | -.669 | .853 | -2.341 | 1.003 | .580 | .137 | .312 | .848 |
| Peptic ulcer disease | -.625 | 4.269 | -8.997 | 7.747 | .907 | 1.07 | -1.181 | 2.996 |
| Valvular disease | .721 | .330 | .075 | 1.367 | | | | |
| Weight loss | 3.550 | .426 | 2.714 | 4.386 | 2.325 | .072 | 2.183 | 2.467 |

* Multiple linear regression: R = 0.521 (adjust $R^2$ = .271), df (45), p <0.001.

Reference: White, male, age ≥80 years, Medicare, 0-25th percentile income, and no comorbidities.

† Multiple linear regression: R = 0.473 (adjust $R^2$ = .224), df (42), p <0.001. Reference: White, male, age ≥80 years, Medicare, 0-25th percentile income, and no comorbidities

**b) HT (Hypothesis 6)**

Multiple linear regression (dummy method) is used to find out the predictors of length of hospital stay for thyroid disease patients suffered HT.

The value of Durbin-Watson for length of stay should be ranged between 1 and 3, or near to 2 as ideal result. The value of Durbin-Watson of length of stay is 1.931 and1.899 for hyper and hypothyroidism respectively. **Collinearity diagnostics is used to determine the multi-collinearity. The VIF results must be less than 2 or near to 1 as ideal results. All results of variables are less than 2.**

Paralysis is the predictor with highest effects on length of hospital stay for hyperthyroidism HT patients with 3.920 days, followed by weight loss (2.348 days), pulmonary circulation disorders (1.707 days), fluid and electrolyte disorders (1.361 days), coagulopathy (1.325 days), and psychoses (1.165 days). The factors more related to reduction of length of hospital stay were age 31-40 years (-0.89 days), followed by other types of insurance (-.751 days), age 41-50 years (-.588 days), private including HMO (-.573 days), and age 71-80 years (-.45 days).

Paralysis is the predictor with highest effects on length of hospital stay for hypothyroidism patients with 2.840 days, followed by weight loss (2.744 days), fluid and electrolyte disorders (1.178 days), and pulmonary circulation disorders (1.134 days). The factors more related to reduction of length of hospital stay were age 41-50 years (-.511 days), followed by age 31-40 years (-.419 days), age 51-60 years (-.415 days) and age 61-70 years (-.403 days), as shown in Table 16.

As comparison between hyper-and hypothyroidism of HT patients, paralysis is the risk factor with highest contribution for long length of stay.

**Table 16 Predictors of hospital of length stay of hyper- and hypothyroidism for HT patients**

| Predictors | Hyperthyroidism | | | | Hypothyroidism | | | |
|---|---|---|---|---|---|---|---|---|
| | B | SE | 95% CI | | B | SE | 95% CI | |
| | | | Lower Bound | Upper Bound | | | Lower Bound | Upper Bound |
| (Constant) | 3.236 | .194 | 2.855 | 3.617 | 3.053 | .027 | 3.000 | 3.106 |
| Female | -.210 | .122 | -.449 | .028 | -.056 | .019 | -.092 | -.019 |
| Number of procedures | .892 | .024 | .844 | .939 | .740 | .004 | .733 | .747 |
| Age ≤ 30 | -.483 | .381 | -1.230 | .263 | .839 | .111 | .622 | 1.057 |
| Age 31-40 | -.890 | .312 | -1.502 | -.278 | -.419 | .066 | -.548 | -.289 |
| Age 41-50 | -.588 | .239 | -1.056 | -.119 | -.511 | .042 | -.595 | -.428 |
| Age 51-60 | -.248 | .199 | -.638 | .142 | -.415 | .032 | -.477 | -.353 |
| Age 61-70 | -.391 | .170 | -.724 | -.059 | -.403 | .024 | -.450 | -.356 |
| Age 71-80 | -.450 | .160 | -.764 | -.137 | -.311 | .021 | -.352 | -.270 |
| Other races | .736 | .304 | .140 | 1.333 | .235 | .053 | .131 | .338 |
| Black | .143 | .138 | -.127 | .413 | .359 | .031 | .298 | .421 |
| Hispanic | -.096 | .212 | -.511 | .319 | -.063 | .033 | -.128 | .003 |
| Asian Pacific Islander | .272 | .312 | -.339 | .883 | .120 | .073 | -.023 | .262 |
| Native American | -.375 | .724 | -1.794 | 1.044 | -.337 | .105 | -.543 | -.131 |
| Other insurance | -.751 | .346 | -1.429 | -.073 | -.346 | .063 | -.469 | -.223 |
| Medicaid | .042 | .201 | -.352 | .435 | .813 | .040 | .733 | .892 |
| Private including HMO | -.573 | .164 | -.895 | -.251 | -.394 | .026 | -.445 | -.343 |
| Self-pay | -.320 | .279 | -.866 | .227 | -.088 | .067 | -.220 | .044 |
| No charge | -1.158 | .898 | -2.918 | .603 | -.148 | .212 | -.563 | .266 |
| Income 26th-50th percentile | -.322 | .143 | -.603 | -.042 | -.141 | .022 | -.183 | -.098 |
| Income 51st-75th percentile | -.214 | .146 | -.500 | .071 | -.144 | .022 | -.187 | -.101 |
| Income 75th-100th percentile | -.257 | .155 | -.560 | .046 | -.139 | .023 | -.185 | -.094 |
| Acquired immune deficiency | .489 | 1.160 | -1.784 | 2.762 | .670 | .319 | .045 | 1.294 |
| Alcohol abuse | .754 | .325 | .118 | 1.391 | .576 | .057 | .464 | .687 |
| Deficiency anemias | .881 | .130 | .627 | 1.136 | .757 | .019 | .718 | .795 |
| Rheumatoid arthritis | -.155 | .272 | -.689 | .378 | .005 | .037 | -.068 | .078 |
| Chronic pulmonary disease | .023 | .125 | -.221 | .267 | .342 | .019 | .305 | .378 |
| Coagulopathy | 1.325 | .249 | .836 | 1.813 | .967 | .036 | .896 | 1.038 |
| Depression | .125 | .159 | -.187 | .437 | .093 | .021 | .051 | .135 |
| DM, uncomplicated | .277 | .123 | .036 | .519 | .102 | .018 | .067 | .138 |
| DM with chronic complications | .202 | .232 | -.254 | .657 | .521 | .033 | .456 | .587 |
| Drug abuse | .608 | .310 | .001 | 1.216 | .902 | .065 | .774 | 1.030 |
| Liver disease | -.020 | .343 | -.693 | .652 | .057 | .050 | -.041 | .154 |
| Lymphoma | .255 | .639 | -.998 | 1.508 | .591 | .082 | .431 | .751 |
| Fluid and electrolyte disorders | 1.361 | .119 | 1.129 | 1.594 | 1.178 | .018 | 1.143 | 1.213 |
| Metastatic cancer | .312 | .382 | -.437 | 1.061 | .738 | .058 | .625 | .851 |
| Other neurological disorders | .593 | .193 | .215 | .971 | .677 | .026 | .627 | .727 |
| Obesity | .160 | .159 | -.152 | .472 | .314 | .023 | .269 | .359 |
| Paralysis | 3.920 | .330 | 3.273 | 4.567 | 2.840 | .050 | 2.742 | 2.938 |
| Peripheral vascular disease | -.245 | .204 | -.644 | .154 | -.085 | .028 | -.141 | -.030 |
| Psychoses | 1.165 | .236 | .704 | 1.627 | .804 | .035 | .735 | .873 |
| Pulmonary circulation disorders | 1.707 | .285 | 1.148 | 2.266 | 1.134 | .045 | 1.046 | 1.222 |
| Renal failure | .213 | .149 | -.079 | .506 | .211 | .021 | .170 | .251 |
| Solid tumor without metastasis | .181 | .388 | -.579 | .941 | .536 | .056 | .427 | .645 |
| Peptic ulcer disease | -.651 | 2.183 | -4.929 | 3.628 | -.015 | .406 | -.811 | .781 |
| Valvular disease | .283 | .226 | -.161 | .727 | .336 | .033 | .272 | .401 |
| Weight loss | 2.348 | .218 | 1.921 | 2.775 | 2.744 | .036 | 2.673 | 2.815 |

* Multiple linear regression: R = 0.418 (adjust $R^2$ = .172), df (46), p <0.001. Reference: White, male, age ≥80 years, Medicare, 0-25th percentile income, and no comorbidities.

† Multiple linear regression: R = 0.385 (adjust $R^2$ = .148), df (46), p <0.001. Reference: White, male, age ≥80 years, Medicare, 0-25th percentile income, and no comorbidities

## 4.6 Predictors of total charges

### 4.6.1 Predictors and Differences in total charges between hyper- and hypothyroidism patients (Hypothesis 7)

Multiple linear regression (dummy method) is used to find out the predictors of total charges for thyroid disease patients. Assumptions must be proceeded to approve the final results of regression model. These assumptions are

**Assumption 1,dependent variables should be continuous:** Total charges is continuous. This assumption is accepted.

**Assumption 2, two or more independent variables (numerical, ordinal, or categorical):** Comorbidities, age categories, gender, race, type of insurance, and household income are categorical, while number of procedures and number of chronic diseases are numerical. All groups were recategorized to be appropriate for dummy method of analysis. This assumption is accepted.

**Assumption 3, independence of observations or independence of residuals**: The value of Durbin-Watson for total charges should be ranged between 1 and 3, or near to 2 as ideal result. The value of Durbin-Watson of total charges is 1.563 and 1.502 for hyper and hypothyroidism respectively. This assumption is accepted.

**Assumption 4, linear relationship between the dependent and independent variable(s):** Significant relationships between dependent and independent variables. This assumption is accepted.

**Assumption 5, data must show homoscedasticity:** Results showed that the dots along of scatter plot are homogenous and with same distance around the linear fit line, as shown in Figures below. This assumption is accepted.

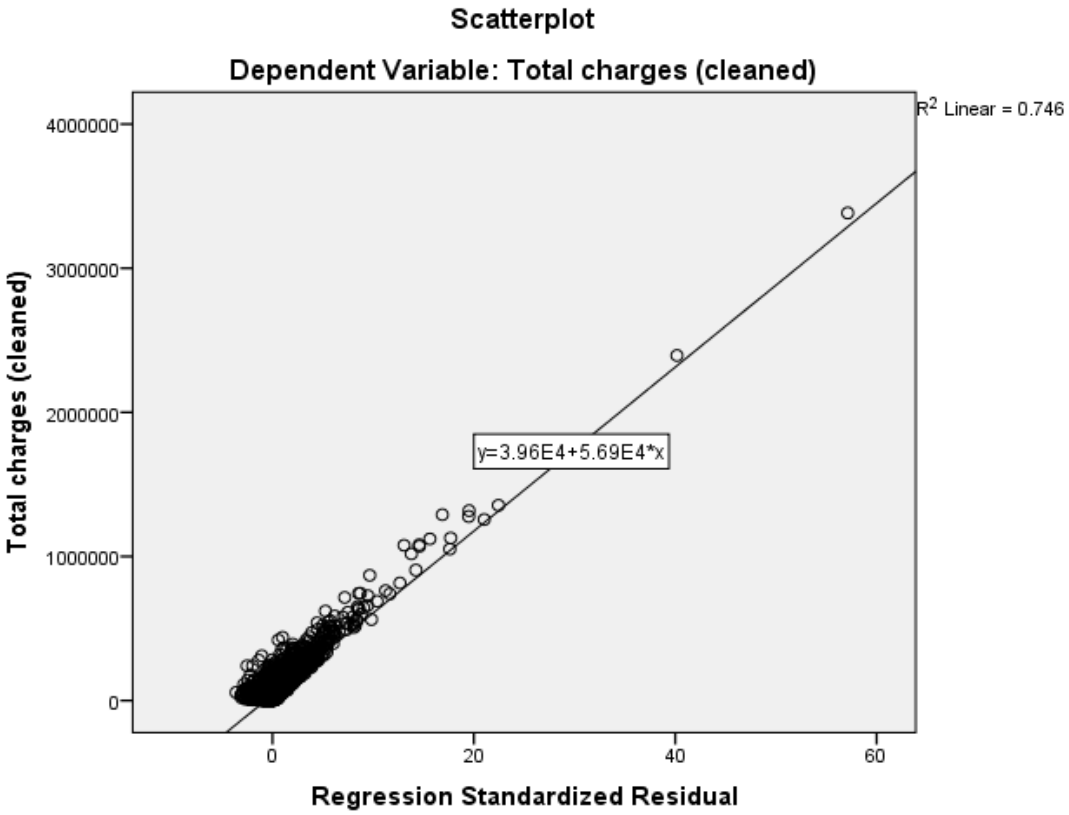



**Figure 26 Homoscedasticity of Total charges for hyperthyroidism patients**

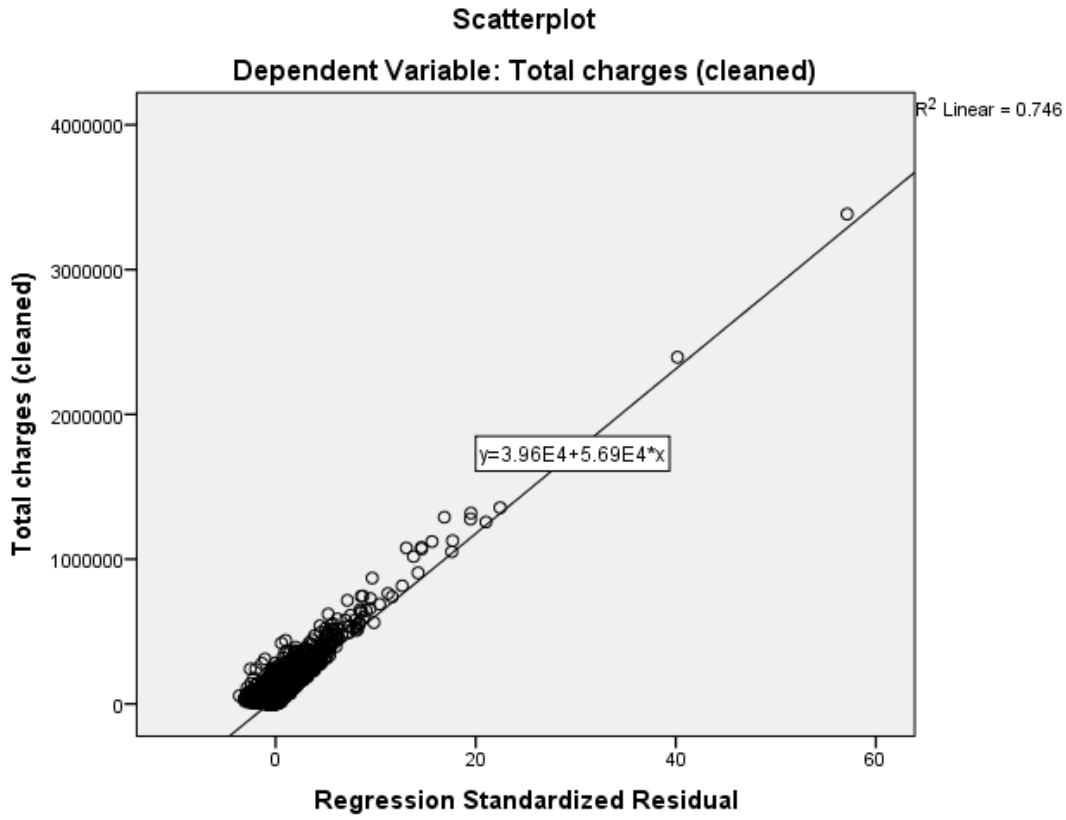



**Figure 27 Homoscedasticity of Total charges for hyperthyroidism patients**

**Assumption 6, data must not show multicollinearity:** Collinearity diagnostics is used to determine the multicollinearity. The VIF results must be less than 2 or near to 1 as ideal results. All results of variables are less than 2. This assumption is accepted.

**Assumption 7, no significant outliers:** The cut point for the outliers while using Cook's distance is (4/n), which equals to 0.00001. There were 565 and 21,089 cases of hyper- and hypothyroidism, which were considered as outliers. These cases were excluded in regression model.

**Assumption 8, the residuals must be normally distributed:** The residuals are normal distributed, as shown in Figures above.

After accepting all assumptions for the total charges, the final models for the predictors of hyper- and hypothyroidism patients are shown in Table 17

Paralysis is the predictor with highest effects on total charges for hyperthyroidism patients with $12696.31, followed by number of procedures ($9789.22), weight loss ($8072.45), fluid and electrolyte disorders ($6802.94), Hispanic ($6421.82), and coagulopathy ($6337.61). The factors more related to reduction of total charges were chronic blood loss anemia ($-12502.07), followed by Medicaid ($-3812.24), and female ($-3043.27).

The total charges of hyperthyroidism = 14213.54-3043.27 (female) + 9789.22 (number of procedures)+ 3390.14 (age 61-70) + 1023.21 (age 71-80) + 6421.82 (Hispanic) + 3544.81 (Asian Pacific Islander) -2690.67 (Other insurances) -3812.24 (Medicaid) -2865.00 (Private including HMO)+ 3612.22 (income 51th-75th percentile) + 4989.09 (income 76th-100th percentile) + 3765.88 (Deficiency anemias) +2740.86 (Rheumatoid arthritis) -12502.07 (Chronic blood loss anemia) + 2701.24 (CHF) + 2844.68 (Chronic pulmonary disease) + 6337.61 (Coagulopathy) + 1651.69 (DM, uncomplicated) + 3026.12 (DM with chronic complications) + 2380.56 (Hypertension) + 2638.74 (liver disease) + 6802.94 (Fluid and electrolyte disorders) + 1255.47 (Obesity) + 12696.31 (Paralysis) + 3301.13 (Psychoses) + 5130.38 (Pulmonary circulation disorders) + 1715.44 (valvular disease) + 8072.45 (Weight loss).

Number of procedures is the predictor with highest effects on total charges for hypothyroidism patients with $ 10488.75, followed by weight loss ($ 8719.31), Hispanic ($8142.07), coagulopathy ($7032.12), paralysis ($6859.13), and fluid and electrolyte disorders ($5162.30). The factors more related to reduction of total charges

were age equal and under 30 years ($-10409.71), followed by 31-40 years ($-10087.37), and chronic blood loss anemia ($-6282.42).

The total charges of hypothyroidism = 15036.29-1429.50 (female) + 10488.78 (number of procedures) -10409.71(age ≤ 30 ) -10087.37 (Age 31-40) -2423.11 (Age 41-50) +452.32 (Age 51-60) + 1495.99 (Age 61-70) +1049.69 (Age 71-80) + 651.85 (other races) + 1146.39 (Black) + 8142.07 (Hispanic) + 2984.51 (Asian Pacific Islander) -2837.60 (Native American) -1466.11 (Other insurances) -684.47 (Medicaid) -1411.70 (Private including HMO) -1134.30 (Self-pay) -2357.03 (No charge) + 525.12 (26th-50th percentile) + 3096.64 (income 51th-75th percentile) + 5530.29 (income 76th-100th percentile)+ 3093.42 (Acquired immune deficiency) + 2913.64 (Deficiency anemias) -6282.42 (Chronic blood loss anemia)+ 1955.09 (CHF) + 2128.17 (Chronic pulmonary disease) +7032.12 (Coagulopathy) + 605.07 (DM with chronic complications) + 2239.58 (Drug abuse)+ 1254.25 (Hypertension) -773.63 (liver disease) + 5162.30 (Fluid and electrolyte disorders)+ 594.19 (Metastatic cancer)+ 996.74 (Other neurological disorders) + 3301.95 (Obesity) + 6859.13 (Paralysis)+ 439.34 (Peripheral vascular disease) + 1966.08 (Psychoses) + 3585.73 (Pulmonary circulation disorders) -903.53 (Renal failure) -969.98 (Solid tumor without metastasis) + 543.38 (valvular disease) + 8719.31 (Weight loss).

As main comparison between predictors of total charges for hyper- and hypothyroidism diseases, similarity observed in predictors affected on total charges, but higher for paralysis and number of procedures for hyper- and hypothyroidism respectively. In other word, contribution of paralysis to the total charges was higher with hyperthyroidism than to hypothyroidism, while number of procedures effect was higher for hypothyroidism than to hyperthyroidism.

**Table 17 Predictors of total charges of hyper- and hypothyroidism patients**

| Predictors | Hyperthyroidism | | | | Hypothyroidism | | | |
|---|---|---|---|---|---|---|---|---|
| | B | SE | 95% CI | | B | SE | 95% CI | |
| | | | Lower Bound | Upper Bound | | | Lower Bound | Upper Bound |
| (Constant) | 14213.54 | 691.23 | 12858.68 | 15568.39 | 15036.29 | 124.02 | 14793.21 | 15279.36 |
| Female | -3043.27 | 436.59 | -3899.03 | -2187.51 | -1429.50 | 76.10 | -1578.65 | -1280.36 |
| No. of procedures | 9789.22 | 101.99 | 9589.31 | 9989.13 | 10488.78 | 17.25 | 10454.97 | 10522.58 |
| Age ≤ 30 | | | | | -10409.71 | 214.81 | -10830.73 | -9988.69 |
| Age 31-40 | | | | | -10087.37 | 185.09 | -10450.13 | -9724.60 |
| Age 41-50 | | | | | -2423.11 | 155.21 | -2727.32 | -2118.90 |
| Age 51-60 | | | | | 452.32 | 126.71 | 203.98 | 700.67 |
| Age 61-70 | 3390.14 | 518.81 | 2373.24 | 4407.04 | 1495.99 | 101.62 | 1296.82 | 1695.16 |
| Age 71-80 | 1023.21 | 567.38 | -88.90 | 2135.32 | 1049.69 | 91.23 | 870.88 | 1228.51 |
| Other races | .46 | 1019.39 | -1997.62 | 1998.54 | 651.85 | 209.93 | 240.41 | 1063.30 |
| Black | 736.50 | 495.26 | -234.25 | 1707.26 | 1146.39 | 134.41 | 882.95 | 1409.83 |
| Hispanic | 6421.82 | 688.85 | 5071.61 | 7772.02 | 8142.07 | 135.79 | 7875.92 | 8408.21 |
| Asian Pacific Islander | 3544.81 | 1073.20 | 1441.25 | 5648.37 | 2984.51 | 295.39 | 2405.56 | 3563.46 |
| Native American | -3376.59 | 2416.23 | -8112.59 | 1359.41 | -2837.60 | 442.18 | -3704.25 | -1970.95 |
| Other insurance | -2690.67 | 1080.90 | -4809.32 | -572.02 | -1466.11 | 236.53 | -1929.69 | -1002.53 |
| Medicaid | -3812.24 | 602.31 | -4992.80 | -2631.67 | -684.47 | 149.98 | -978.41 | -390.52 |
| Private including HMO | -2865.00 | 510.30 | -3865.23 | -1864.76 | -1411.70 | 101.55 | -1610.73 | -1212.66 |
| Self-pay | -1243.05 | 842.69 | -2894.79 | 408.68 | -1134.30 | 244.99 | -1614.47 | -654.14 |
| No charge | -4799.03 | 3029.53 | -10737.15 | 1139.09 | -2357.03 | 836.14 | -3995.84 | -718.21 |
| Income26th-50th percentile | -365.28 | 499.86 | -1345.03 | 614.48 | 525.12 | 87.97 | 352.70 | 697.53 |
| Income 51st-75th percentile | 3612.22 | 511.10 | 2610.42 | 4614.02 | 3096.64 | 89.43 | 2921.37 | 3271.91 |
| Income75th-100th percentile | 4989.09 | 540.73 | 3929.22 | 6048.97 | 5530.29 | 92.98 | 5348.05 | 5712.53 |
| Acquired immune deficiency | 3738.21 | 4631.47 | -5339.83 | 12816.26 | 3093.42 | 1535.19 | 84.49 | 6102.35 |
| Alcohol abuse | 1300.45 | 1101.84 | -859.24 | 3460.14 | -404.50 | 222.39 | -840.38 | 31.39 |
| Deficiency anemias | 3765.88 | 482.36 | 2820.42 | 4711.34 | 2913.64 | 80.86 | 2755.14 | 3072.13 |
| Rheumatoid arthritis | 2740.86 | 1022.59 | 736.51 | 4745.22 | 57.45 | 153.44 | -243.29 | 358.18 |
| Chronic blood loss anemia | -12502.07 | 1322.83 | -15094.92 | -9909.23 | -6282.42 | 265.12 | -6802.05 | -5762.79 |
| Congestive heart failure | 2701.24 | 648.77 | 1429.60 | 3972.88 | 1955.09 | 102.88 | 1753.46 | 2156.72 |
| Chronic pulmonary disease | 2844.68 | 463.10 | 1936.96 | 3752.40 | 2128.17 | 77.61 | 1976.07 | 2280.28 |
| Coagulopathy | 6337.61 | 915.44 | 4543.28 | 8131.95 | 7032.12 | 150.98 | 6736.20 | 7328.04 |
| Depression | 131.90 | 580.15 | -1005.24 | 1269.04 | 68.29 | 87.44 | -103.08 | 239.67 |
| DM, uncomplicated | 1651.69 | 490.82 | 689.65 | 2613.72 | 26.08 | 78.34 | -127.47 | 179.62 |
| DM with chronic complications | 3026.12 | 991.23 | 1083.23 | 4969.02 | 605.07 | 147.86 | 315.27 | 894.88 |
| Drug abuse | 1365.81 | 947.97 | -492.27 | 3223.90 | 2239.58 | 238.87 | 1771.40 | 2707.76 |
| Hypertension | 2380.56 | 404.80 | 1587.12 | 3174.00 | 1254.25 | 72.31 | 1112.52 | 1395.99 |
| Liver disease | 2638.74 | 1262.47 | 164.20 | 5113.27 | -773.63 | 199.79 | -1165.21 | -382.05 |
| Lymphoma | -825.27 | 2539.13 | -5802.15 | 4151.62 | -336.26 | 335.64 | -994.10 | 321.57 |
| Fluid and electrolyte disorders | 6802.94 | 436.23 | 5947.89 | 7657.99 | 5162.30 | 73.56 | 5018.12 | 5306.47 |
| Metastatic cancer | 1613.30 | 1412.50 | -1155.30 | 4381.91 | 594.19 | 231.27 | 140.91 | 1047.48 |
| Other neurological disorders | 1382.76 | 707.05 | -3.12 | 2768.64 | 996.74 | 103.80 | 793.30 | 1200.18 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Obesity | 1255.47 | 612.29 | 55.34 | 2455.61 | 3301.95 | 96.40 | 3113.02 | 3490.89 |
| Paralysis | 12696.31 | 1324.69 | 10099.81 | 15292.81 | 6859.13 | 212.38 | 6442.86 | 7275.39 |
| Peripheral vascular disease | -1276.86 | 864.28 | -2970.92 | 417.19 | 439.34 | 128.05 | 188.37 | 690.30 |
| Psychoses | 3301.13 | 845.62 | 1643.65 | 4958.61 | 1966.08 | 139.69 | 1692.30 | 2239.86 |
| Pulmonary circulation disorders | 5130.38 | 1111.48 | 2951.80 | 7308.97 | 3585.73 | 193.71 | 3206.06 | 3965.40 |
| Renal failure | -397.75 | 641.42 | -1654.98 | 859.49 | -903.53 | 92.16 | -1084.15 | -722.90 |
| Solid tumor without metastasis | -1025.73 | 1438.73 | -3845.75 | 1794.30 | -969.98 | 228.11 | -1417.05 | -522.90 |
| Peptic ulcer disease | -5020.05 | 9374.75 | -23395.29 | 13355.19 | -2463.61 | 2711.78 | -7778.60 | 2851.39 |
| Valvular disease | 1715.44 | 889.53 | -28.11 | 3459.00 | 543.38 | 143.10 | 262.90 | 823.86 |
| Weight loss | 8072.45 | 800.89 | 6502.63 | 9642.26 | 8719.31 | 151.05 | 8423.25 | 9015.36 |

* Multiple linear regression: R = 0.602 (adjust $R^2$ = .361), df (45), p <0.001.

Reference: White, male, age ≥80 years, Medicare, 0-25th percentile income, and no comorbidities.

† Multiple linear regression: R = 0.632 (adjust $R^2$ = .400), df (49), p <0.001.

Reference: White, male, age ≥80 years, Medicare, 0-25th percentile income, and no comorbidities

### 4.6.2 Predictors and Differences in total charges between hyper- and hypothyroidism among hypertension and CHF patients

**a) CHF (Hypothesis 8)**

Multiple linear regressions (dummy method) is used to find out the predictors of total charges for thyroid disease patients suffered of CHF

The value of Durbin-Watson for total charges should be ranged between 1 and 3, or near to 2 as ideal result. The value of Durbin-Watson of total charges is 1.929 and 1.641 for hyper and hypothyroidism respectively. Collinearity diagnostics is used to determine the multicollinearity. The VIF results must be less than 2 or near to 1 as ideal results. All results of variables are less than 2.

People aged equal and younger than 30 years is the predictor with highest effects on total charges with $184,185.01, followed by Hispanic ($33786.66), coagulopathy ($32729.10), weight loss ($28405.24), other neurological disorders ($26715.82), and number of procedures ($15475.84). However, there are no factors related to reduction of total charges of hyperthyroidism CHF patients.

People aged equal and younger than 30 years is the predictor with highest effects on total charges for hypothyroidism patients with $ 44446.49, followed by Hispanic ($ 18937.76), number of procedures ($17503.83), Asian Pacific Islander ($ 16900.84), weight loss ($15874.59), paralysis ($10880.09), and coagulopathy ($9547.39). Native American is the only factor related with reduction of total charges of hypothyroidism CHF patients ($-5679.82), as shown in Table 18.

As comparison between hyper-and hypothyroidism of CHF patients, patients aged equal and younger than 30 years showed highest risk factor of total charges for hyper- and hypothyroidism patients.

**Table 18 Predictors of total charges of hyper- and hypothyroidism for CHF patients**

| Predictors | Hyperthyroidism | | | | Hypothyroidism | | | |
|---|---|---|---|---|---|---|---|---|
| | B | SE | 95% CI | | B | SE | 95% CI | |
| | | | Lower Bound | Upper Bound | | | Lower Bound | Upper Bound |
| (Constant) | 10268.91 | 7167.23 | -3786.36 | 24324.18 | 7695.38 | 595.23 | 6528.74 | 8862.02 |
| Female | -1658.67 | 4748.11 | -10969.95 | 7652.61 | 199.19 | 426.48 | -636.72 | 1035.09 |
| No. of procedures | 15475.84 | 968.29 | 13576.97 | 17374.70 | 17503.83 | 90.80 | 17325.86 | 17681.80 |
| Age ≤ 30 | 184185.01 | 18358.65 | 148182.82 | 220187.20 | 44446.49 | 3634.27 | 37323.37 | 51569.61 |
| Age 31-40 | 7029.86 | 15011.20 | -22407.83 | 36467.55 | 90.56 | 2346.70 | -4508.96 | 4690.07 |
| Age 41-50 | 15945.86 | 10663.42 | -4965.61 | 36857.32 | 4606.68 | 1316.28 | 2026.79 | 7186.57 |
| Age 51-60 | 998.73 | 8090.06 | -14866.26 | 16863.73 | 1146.41 | 838.80 | -497.62 | 2790.44 |
| Age 61-70 | -2774.52 | 6239.17 | -15009.84 | 9460.80 | 2076.56 | 592.74 | 914.80 | 3238.31 |
| Age 71-80 | -5506.16 | 5714.86 | -16713.28 | 5700.96 | 268.20 | 477.04 | -666.79 | 1203.19 |
| Other races | -3480.42 | 11168.68 | -25382.73 | 18421.89 | 4508.06 | 1297.77 | 1964.44 | 7051.67 |
| Black | -2533.50 | 5398.83 | -13120.86 | 8053.87 | 867.83 | 733.77 | -570.36 | 2306.01 |
| Hispanic | 33786.66 | 9075.15 | 15989.86 | 51583.46 | 18937.76 | 845.75 | 17280.10 | 20595.43 |
| Asian Pacific Islander | 3696.73 | 13408.91 | -22598.77 | 29992.24 | 16900.84 | 1854.56 | 13265.92 | 20535.75 |
| Native American | -20431.59 | 39555.95 | -98002.69 | 57139.51 | -5679.82 | 2496.74 | -10573.41 | -786.23 |
| Other insurance | -3770.61 | 16288.54 | -35713.21 | 28171.99 | 750.54 | 1800.18 | -2777.80 | 4278.87 |
| Medicaid | -6354.90 | 8246.74 | -22527.14 | 9817.34 | 3041.49 | 1023.57 | 1035.31 | 5047.68 |
| Private including HMO | 4788.85 | 7286.23 | -9499.79 | 19077.49 | 814.76 | 761.92 | -678.58 | 2308.11 |
| Self-pay | -15809.49 | 12683.90 | -40683.22 | 9064.24 | -3329.79 | 2149.04 | -7541.89 | 882.32 |
| No charge | -78077.41 | 56580.23 | -189033.94 | 32879.13 | -7675.62 | 7661.28 | -22691.66 | 7340.41 |
| Income26th-50th percentile | -3179.62 | 5596.49 | -14154.61 | 7795.37 | 42.45 | 510.60 | -958.33 | 1043.22 |
| Income 51st-75th percentile | 1942.26 | 5785.88 | -9404.13 | 13288.65 | 5069.76 | 524.65 | 4041.46 | 6098.07 |
| Income75th-100th percentile | 5211.64 | 6051.58 | -6655.79 | 17079.07 | 9833.46 | 561.67 | 8732.60 | 10934.33 |
| Acquired immune deficiency | -3973.66 | 43897.60 | -90058.95 | 82111.64 | -12576.14 | 7467.82 | -27213.00 | 2060.72 |
| Alcohol abuse | -8972.12 | 13176.98 | -34812.81 | 16868.58 | -955.74 | 1533.94 | -3962.25 | 2050.78 |
| Deficiency anemias | 1442.19 | 4580.44 | -7540.27 | 10424.66 | 1848.95 | 407.24 | 1050.76 | 2647.14 |
| Rheumatoid arthritis | -7991.13 | 11059.21 | -29678.76 | 13696.51 | -1352.64 | 870.32 | -3058.47 | 353.18 |
| Chronic blood loss anemia | -14462.88 | 16973.79 | -47749.28 | 18823.52 | | | | |
| Chronic pulmonary disease | 9025.77 | 4446.10 | 306.75 | 17744.79 | 2920.64 | 404.23 | 2128.35 | 3712.93 |
| Coagulopathy | 32729.10 | 7668.26 | 17691.28 | 47766.91 | 9547.39 | 729.77 | 8117.06 | 10977.73 |
| Depression | 2777.34 | 6188.31 | -9358.24 | 14912.92 | -166.95 | 515.86 | -1178.03 | 844.14 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| DM, uncomplicated | 1331.40 | 4748.30 | -7980.25 | 10643.05 | | | | |
| DM with chronic complic. | 175.50 | 8040.58 | -15592.47 | 15943.47 | | | | |
| Drug abuse | -22236.35 | 13843.01 | -49383.15 | 4910.46 | 3643.64 | 1762.93 | 188.31 | 7098.96 |
| Liver disease | 3077.34 | 12755.94 | -21937.66 | 28092.34 | | | | |
| Lymphoma | -17611.68 | 22613.39 | -61957.63 | 26734.26 | -856.37 | 1742.79 | -4272.21 | 2559.48 |
| Fluid and electrolyte disorders | 4271.01 | 4300.39 | -4162.26 | 12704.28 | 7364.45 | 395.75 | 6588.78 | 8140.12 |
| Metastatic cancer | 5317.14 | 16236.80 | -26524.01 | 37158.29 | 1539.73 | 1562.02 | -1521.80 | 4601.27 |
| Other neurological disorders | 26715.82 | 6815.87 | 13349.57 | 40082.07 | 1782.94 | 563.00 | 679.46 | 2886.42 |
| Obesity | 10282.72 | 6311.70 | -2094.82 | 22660.26 | 4490.72 | 531.86 | 3448.28 | 5533.16 |
| Paralysis | 6563.97 | 11221.95 | -15442.81 | 28570.75 | 10880.09 | 1112.81 | 8699.01 | 13061.18 |
| Peripheral vascular disease | -5967.34 | 7080.58 | -19852.70 | 7918.03 | | | | |
| Psychoses | 8808.03 | 9793.96 | -10398.40 | 28014.45 | 6506.84 | 868.97 | 4803.66 | 8210.01 |
| Pulmonary circulation dis. | -1038.96 | 5955.55 | -12718.08 | 10640.16 | 1821.10 | 603.60 | 638.05 | 3004.15 |
| Renal failure | -2349.73 | 5047.19 | -12247.51 | 7548.06 | | | | |
| Solid tumor without metas. | -2832.66 | 13941.41 | -30172.44 | 24507.11 | 2228.28 | 1321.70 | -362.25 | 4818.80 |
| Peptic ulcer disease | 3867.07 | 97392.55 | -187124.37 | 194858.51 | -3093.96 | 10718.67 | -24102.45 | 17914.53 |
| Valvular disease | 6312.43 | 5416.63 | -4309.84 | 16934.69 | 504.62 | 508.70 | -492.44 | 1501.67 |
| Weight loss | 28405.24 | 7099.61 | 14482.57 | 42327.91 | 15874.59 | 708.28 | 14486.37 | 17262.82 |

* Multiple linear regression: R = 0.442 (adjust $R^2$ = .179), df (47), p <0.001.

Reference: White, male, age ≥80 years, Medicare, 0-25th percentile income, and no comorbidities.

† Multiple linear regression: R = 0.591 (adjust $R^2$ = .349), df (41), p <0.001.

Reference: White, male, age ≥80 years, Medicare, 0-25th percentile income, and no comorbidities

**b) HT (Hypothesis 9)**

Multiple linear regression (dummy method) is used to find out the predictors of total charges for thyroid disease patients suffered of HT.

The value of Durbin-Watson for total charges should be ranged between 1 and 3, or near to 2 as ideal result. The value of Durbin-Watson of total charges is 1.671 and 1.607 for hyper and hypothyroidism respectively. Collinearity diagnostics is used to determine the multicollinearity. The VIF results must be less than 2 or near to 1 as ideal results. All results of variables are less than 2.

Weight loss is the predictor with highest effects on total charges of hyperthyroidism HT patients with $17965.52, followed by paralysis ($14261.19), number of procedures ($14162.73), Asian Pacific Islander ($ 12993.40), coagulopathy ($11821.54), and Hispanic ($10510.52). However, there are no factors related to reduction of total charges of hyperthyroidism HT patients.

Weight loss is the predictor with highest effects on total charges for hypothyroidism patients with $ 15414.48, followed by number of procedures ($14066.62), coagulopathy ($13920.17), paralysis ($12800.66), Hispanic ($ 12589.97), and Asian Pacific Islander ($ 12265.67). Native American is the factor related with highest reduction of total charges of hypothyroidism HT patients ($-4595.35), followed by patients aged 31-40 years ($-3673.04), Self-pay ($-2043.25), patients aged 41-50 years ($-1623.70), and female ($-1460.00), as shown in Table 19.

As comparison between hyper-and hypothyroidism of HT patients, weight loss showed highest risk factor of total charges for hyper- and hypothyroidism patients.

**Table 19 Predictors of total charges of hyper- and hypothyroidism for HT patients**

| Predictors | Hyperthyroidism | | | | Hypothyroidism | | | |
|---|---|---|---|---|---|---|---|---|
| | B | SE | 95% CI | | B | SE | 95% CI | |
| | | | Lower Bound | Upper Bound | | | Lower Bound | Upper Bound |
| (Constant) | 10490.97 | 1625.28 | 7305.16 | 13676.78 | 11127.17 | 245.22 | 10646.55 | 11607.80 |
| Female | -1415.41 | 1025.90 | -3426.34 | 595.53 | -1460.00 | 168.61 | -1790.46 | -1129.53 |
| No. of procedures | 14162.73 | 203.76 | 13763.32 | 14562.14 | 14066.62 | 33.72 | 14000.52 | 14132.71 |
| Age ≤ 30 | -2556.08 | 3192.69 | -8814.29 | 3702.12 | 4583.50 | 1002.37 | 2618.89 | 6548.11 |
| Age 31-40 | -3482.86 | 2623.03 | -8624.45 | 1658.73 | -3673.04 | 596.57 | -4842.29 | -2503.79 |
| Age 41-50 | 323.17 | 2013.02 | -3622.69 | 4269.02 | -1623.70 | 383.92 | -2376.18 | -871.22 |
| Age 51-60 | 3924.96 | 1671.38 | 648.78 | 7201.15 | 396.71 | 285.31 | -162.49 | 955.91 |
| Age 61-70 | 1693.51 | 1430.40 | -1110.31 | 4497.33 | 1291.13 | 217.90 | 864.06 | 1718.20 |
| Age 71-80 | -1708.90 | 1350.36 | -4355.83 | 938.03 | 1039.67 | 191.45 | 664.44 | 1414.91 |
| Other races | 3136.59 | 2539.11 | -1840.50 | 8113.67 | 3089.16 | 475.46 | 2157.27 | 4021.05 |
| Black | 905.22 | 1160.89 | -1370.32 | 3180.75 | 1897.59 | 285.12 | 1338.77 | 2456.41 |
| Hispanic | 10510.52 | 1800.02 | 6982.17 | 14038.87 | 12589.97 | 303.94 | 11994.25 | 13185.68 |
| Asian Pacific Islander | 12993.40 | 2733.33 | 7635.62 | 18351.18 | 12265.67 | 670.84 | 10950.84 | 13580.49 |
| Native American | -1066.84 | 6110.72 | -13044.89 | 10911.20 | -4595.35 | 957.86 | -6472.73 | -2717.97 |
| Other insurance | -1615.80 | 2877.94 | -7257.04 | 4025.44 | -894.76 | 564.90 | -2001.95 | 212.43 |
| Medicaid | 69.16 | 1683.92 | -3231.61 | 3369.93 | 1809.97 | 364.79 | 1094.99 | 2524.95 |
| Private including HMO | -2742.28 | 1384.27 | -5455.69 | -28.87 | -343.00 | 234.77 | -803.13 | 117.14 |
| Self-pay | 372.89 | 2333.05 | -4200.28 | 4946.05 | -2043.25 | 606.21 | -3231.39 | -855.10 |
| No charge | -8303.86 | 7464.45 | -22935.44 | 6327.72 | -3641.32 | 1898.11 | -7361.55 | 78.91 |
| Income26th-50th percentile | -475.02 | 1199.24 | -2825.73 | 1875.68 | 382.43 | 195.41 | -.56 | 765.42 |
| Income 51st-75th percentile | 4669.57 | 1226.62 | 2265.19 | 7073.94 | 3814.42 | 199.31 | 3423.78 | 4205.07 |
| Income75th-100th percentile | 5239.83 | 1305.38 | 2681.07 | 7798.59 | 7413.29 | 208.75 | 7004.14 | 7822.44 |
| Acquired immune deficiency | 417.70 | 10047.33 | -19276.77 | 20112.16 | 6801.46 | 2898.51 | 1120.47 | 12482.46 |
| Alcohol abuse | 6235.20 | 2747.88 | 848.90 | 11621.50 | -569.97 | 516.72 | -1582.71 | 442.78 |
| Deficiency anemias | 2086.12 | 1095.71 | -61.65 | 4233.89 | 3457.44 | 176.56 | 3111.39 | 3803.49 |
| Rheumatoid arthritis | 1244.24 | 2300.50 | -3265.13 | 5753.61 | 163.18 | 338.45 | -500.17 | 826.53 |
| Chronic pulmonary disease | 1984.47 | 1049.24 | -72.21 | 4041.16 | 2960.78 | 169.33 | 2628.90 | 3292.65 |
| Coagulopathy | 11821.54 | 2107.49 | 7690.51 | 15952.57 | 13920.17 | 329.25 | 13274.85 | 14565.48 |
| Depression | 297.25 | 1336.42 | -2322.35 | 2916.86 | -334.50 | 194.16 | -715.06 | 46.05 |
| DM, uncomplicated | 1516.03 | 1034.73 | -512.21 | 3544.27 | -145.21 | 165.20 | -468.99 | 178.57 |
| DM with chronic complic. | 1418.74 | 1998.66 | -2498.97 | 5336.46 | 823.31 | 306.38 | 222.81 | 1423.81 |
| Drug abuse | -2895.71 | 2607.04 | -8005.94 | 2214.52 | 3216.43 | 594.26 | 2051.71 | 4381.16 |
| Liver disease | 4498.21 | 2906.31 | -1198.64 | 10195.07 | -613.22 | 452.22 | -1499.56 | 273.12 |
| Lymphoma | 3361.98 | 5412.22 | -7246.89 | 13970.84 | 1787.28 | 739.57 | 337.74 | 3236.82 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Fluid and electrolyte disorders | 8920.99 | 998.81 | 6963.16 | 10878.82 | 7564.05 | 160.44 | 7249.60 | 7878.49 |
| Metastatic cancer | -4363.11 | 3224.00 | -10682.69 | 1956.48 | 1014.23 | 523.12 | -11.07 | 2039.53 |
| Other neurological disorders | 1101.35 | 1622.02 | -2078.07 | 4280.78 | 1646.24 | 232.18 | 1191.18 | 2101.29 |
| Obesity | 2153.22 | 1351.10 | -495.17 | 4801.60 | 3752.18 | 208.29 | 3343.94 | 4160.42 |
| Paralysis | 14261.19 | 2787.26 | 8797.70 | 19724.68 | 12800.66 | 455.70 | 11907.50 | 13693.83 |
| Peripheral vascular disorders | | | | | -93.30 | 260.57 | -604.01 | 417.41 |
| Psychoses | 3843.44 | 2005.27 | -87.24 | 7774.12 | 3816.98 | 323.58 | 3182.78 | 4451.18 |
| Pulmonary circulation dis. | 8497.26 | 2414.11 | 3765.20 | 13229.32 | 5970.12 | 408.29 | 5169.88 | 6770.37 |
| Renal failure | 3370.70 | 1260.98 | 898.97 | 5842.43 | -283.87 | 186.23 | -648.88 | 81.13 |
| Solid tumor without metas. | -927.87 | 3273.42 | -7344.32 | 5488.58 | 441.93 | 503.94 | -545.78 | 1429.64 |
| Peptic ulcer disease | -7467.63 | 21438.25 | -49490.21 | 34554.96 | -3474.81 | 3706.76 | -10739.95 | 3790.33 |
| Valvular disease | 2201.77 | 1907.94 | -1538.12 | 5941.66 | 1300.65 | 300.11 | 712.43 | 1888.86 |
| Weight loss | 17965.52 | 1857.51 | 14324.48 | 21606.56 | 15414.48 | 333.31 | 14761.20 | 16067.76 |

* Multiple linear regression: R = 0.585 (adjust $R^2$ = .340), df (45), p <0.001.

Reference: White, male, age ≥80 years, Medicare, 0-25th percentile income, and no comorbidities.

† Multiple linear regression: R = 0.572 (adjust $R^2$ = .327), df (46), p <0.001.

Reference: White, male, age ≥80 years, Medicare, 0-25th percentile income, and no comorbidities

### 4.7 Predictors of mortality

#### 4.7.1 Predictors of mortality for hyper- and hypothyroidism patients (Hypothesis10)

Multinomial logistic regression is the appropriate statistical test used to determine the predictors of mortality for hyper- and hypothyroidism patients. Six assumptions were tested to approve the results of logistic regression model.

**Assumption 1**: The dependent variable must be nominal. The mortality is nominal. This assumption is accepted.

**Assumption 2**: The independent variables are continuous, ordinal, or nominal; Comorbidities, age categories, gender, race, type of insurance, and household income are categorical, while number of procedures and number of chronic diseases are numerical. This assumption is accepted.

**Assumption 3**: Independence of observation. All subjects of dependent variables were different. This assumption is accepted.

**Assumption 4**: Eight patients were considered as outliers of hyper- and hypothyroidism diseases (4 each), and those were excluded in the model. This assumption is accepted.

Number of procedure showed highest incidence of mortality of hyperthyroidism patients ($\chi2$ = 154.422, df (1), p value < 0.001), followed by age categories ($\chi2$= 76.194, df (6), p value < 0.001), metastasis ($\chi2$= 34.692, df (1), p value < 0.001), fluid and electrolyte disorders ($\chi2$= 27.986, df (1), p value <0.001), and others.

Age considered as significant predictor for mortality of hyperthyroidism patients, where those aged elder than 80 years showed highest increment in the incidence of mortality by 1,645% (OR = 11.645), followed by patients aged 71-80 years (583.1%, OR = 6.831), patients aged 61-70 years (289.5%, OR = 3.895), and patients aged 51-

60 years (276.4%, OR= 3.764) than those aged equal and younger than 30 years. Self-pay higher than Medicare by 88.6% (OR = 1.886). Males got higher incidence of mortality than females by 270% (OR= 1.270). Number of procedures and chronic diseases showed significant associations with mortality by 23% (OR= 1.23) and 7.3% (OR = 1.073) respectively. Patients with metastatic cancer, chronic pulmonary disorder, coagulopathy, fluid and electrolyte disorder, pulmonary circulation disorders, and other neurological disorders got higher incidence of mortality by 279.3% (OR=3.973), 28.8% (OR= 1.288), 95.3% (OR = 1.953), 83% (OR= 1.83), 120.7% (OR= 2.207), and 51.8% (OR= 1.518) than those without, respectively.

Number of procedure showed highest incidence of mortality of hypothyroidism patients ($\chi^2$ = 4002.360, df (1), p vale < 0.001), followed by age categories ($\chi$2= 3370.489, df (6), p value < 0.001), Fluid and electrolyte disorders ($\chi$2= 2373.123, df (1), p value <0.001), metastasis ($\chi$2= 541.925, df (1), p value < 0.001), and others.

Age considered as significant predictor for mortality of hypothyroidism patients, where those aged elder than 80 years showed highest increment in the incidence of mortality by 680.2% (OR = 7.802), followed by patients aged 71-80 years (312%, OR = 4.120), and patients aged 61-70 years (183.6%, OR = 2.836) than those aged equal and younger than 30 years. Other insurance patients got higher mortality than Medicare by 118.9% (OR = 2.189), followed by Self-pay (61.6%, OR = 1.616), Medicaid (36.7%, OR=1.367), and no charge (11.3%, OR= 1.113). Males got higher incidence of mortality than females by 21.7% (OR= 1.217). Asian Pacific Islander got higher incidence of mortality by 16.2% (OR = 1.162) than White race patients. Number of procedures and chronic diseases showed significant associations with mortality by 18.9% (OR= 1.189) and 2.4% (OR = 1.024) respectively. Patients with chronic pulmonary disorder, coagulopathy, uncomplicated DM, liver disease,

lymphoma, fluid and electrolyte disorder, metastatic cancer, other neurological disorders, paralysis, Peripheral vascular disease, pulmonary circulation disorders, renal failure, Solid tumor without metastasis, Valvular disease, and weight loss got higher incidence of mortality by 22.8% (OR= 1.228), 79.2% (OR = 1.792), 4.9% (OR= 1.049), 56.7% (OR= 1.567),47.8% (OR= 1.478), 129.3% (OR= 2.293), 160.9% (OR= 2.609), 33.7% (OR= 1.337), 42.4% (OR= 1.424), 9.1% (OR= 1.091), 64.1% (OR= 1.641), 31.2% (OR= 1.312), 48.6% (OR= 1.486), 6.1% (OR= 1.061) and 73.6% (OR= 1.736) than those without, respectively, as shown in Table 20.

## Table 20 Predictors of mortality for hyper- and hypothyroidism patients

| | | Hyperthyroidism | | | Hypothyroidism | | |
|---|---|---|---|---|---|---|---|
| | | Exp(B) | 95% CI for Exp(B) | | Exp(B) | 95% CI for Exp(B) | |
| | | | Lower | Upper | | Lower | Upper |
| Intercept | | | | | | | |
| No. of chronic dis. | | 1.073 | 1.028 | 1.120 | 1.024 | 1.017 | 1.031 |
| No. of procedures | | 1.230 | 1.193 | 1.267 | 1.189 | 1.183 | 1.195 |
| Gender | Male | 1.270 | 1.005 | 1.604 | 1.217 | 1.174 | 1.260 |
| | Female (ref.) | . | . | . | . | . | . |
| Race | Others | .559 | .277 | 1.128 | .973 | .879 | 1.078 |
| | Black | .854 | .634 | 1.150 | 1.008 | .945 | 1.076 |
| | Hispanic | .440 | .245 | .790 | .934 | .872 | 1.001 |
| | Asian/Pacific Islander | 1.005 | .568 | 1.779 | 1.162 | 1.025 | 1.316 |
| | Native American | 1.335 | .318 | 5.604 | 1.116 | .905 | 1.378 |
| | White (ref.) | . | . | . | . | . | . |
| Age (years) | >80 | 11.645 | 3.511 | 38.620 | 7.802 | 6.357 | 9.575 |
| | 31-40 | .961 | .212 | 4.360 | .902 | .691 | 1.177 |
| | 41-50 | 3.056 | .895 | 10.427 | 1.306 | 1.044 | 1.633 |
| | 51-60 | 3.764 | 1.147 | 12.352 | 1.989 | 1.617 | 2.446 |
| | 61-70 | 3.895 | 1.176 | 12.903 | 2.836 | 2.310 | 3.481 |
| | 71-80 | 6.831 | 2.050 | 22.762 | 4.120 | 3.353 | 5.061 |
| | ≤30(ref.) | . | . | . | . | . | . |
| Type of insurance | Others | .996 | .417 | 2.378 | 2.189 | 1.961 | 2.444 |
| | Medicaid | .790 | .474 | 1.317 | 1.367 | 1.248 | 1.496 |
| | Private (HMO) | .956 | .663 | 1.378 | 1.113 | 1.050 | 1.180 |
| | Self-pay | 1.886 | 1.004 | 3.542 | 1.616 | 1.392 | 1.875 |
| | No charge | | | | .960 | .519 | 1.773 |
| | Medicare (ref.) | . | . | . | . | . | . |
| Deficiency anemias | Yes | 1.034 | .812 | 1.316 | | | |
| | No (ref.) | . | . | . | | | |
| Chronic pulmonary dis. | Yes | 1.288 | 1.009 | 1.643 | 1.228 | 1.183 | 1.275 |
| | No (ref.) | . | . | . | . | . | . |
| Coagulopathy | Yes | 1.953 | 1.417 | 2.690 | 1.792 | 1.706 | 1.882 |
| | No (ref.) | . | . | . | . | . | . |
| Diabetes, uncomplicated | Yes | 1.130 | .878 | 1.455 | 1.049 | 1.010 | 1.089 |
| | No (ref.) | . | . | . | . | . | . |
| Drug abuse | Yes | .479 | .737 | .317 | | | |
| | No (ref.) | . | . | . | | | |
| Liver disease | Yes | .114 | 1.555 | .900 | .000 | 1.567 | 1.448 |
| | No (ref.) | . | . | . | . | . | . |
| Lymphoma | Yes | .244 | 1.737 | .686 | .000 | 1.478 | 1.308 |
| | No (ref.) | . | . | . | . | . | . |
| Fluid and electrolyte dis. | Yes | .000 | 1.830 | 1.465 | .000 | 2.293 | 2.217 |
| | No (ref.) | . | . | . | . | . | . |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Metastatic cancer | Yes | .000 | 3.973 | 2.648 | .000 | 2.609 | 2.426 |
| | No (ref.) | . | . | . | . | . | . |
| Other neurological dis. | Yes | .011 | 1.518 | 1.102 | .000 | 1.337 | 1.278 |
| | No (ref.) | . | . | . | . | . | . |
| Paralysis | Yes | | | | .000 | 1.424 | 1.312 |
| | No (ref.) | | | | . | . | . |
| Peripheral vascular dis. | Yes | .351 | 1.176 | .836 | .001 | 1.091 | 1.036 |
| | No (ref.) | . | . | . | . | . | . |
| Pulmonary circulation dis. | Yes | .000 | 2.207 | 1.535 | .000 | 1.641 | 1.537 |
| | No (ref.) | . | . | . | . | . | . |
| Renal failure | Yes | .107 | 1.254 | .952 | .000 | 1.312 | 1.262 |
| | No (ref.) | . | . | . | . | . | . |
| Solid tumor without metas. | Yes | .203 | 1.462 | .815 | .000 | 1.486 | 1.361 |
| | No (ref.) | . | . | . | . | . | . |
| Valvular disease | Yes | .305 | .811 | .544 | .045 | 1.061 | 1.001 |
| | No (ref.) | . | . | . | . | . | . |
| Weight loss | Yes | .078 | 1.317 | .970 | .000 | 1.736 | 1.657 |
| | No (ref.) | . | . | . | . | . | . |

* Multinomial logistic regression. Model of fitting: $\chi^2$ = 665.409, df(35) p <0.001.

The reference category is: did not die during hospitalization

† Multinomial logistic regression. Model of fitting: $\chi^2$ = 18551.042, df(34) p <0.001.

The reference category is: did not die during hospitalization

### 4.7.2 Predictors of mortality for hyper- and hypothyroidism CHF and HT patients

**a) CHF (Hypothesis 11)**

Multinomial logistic regression is the appropriate statistical test used to determine the predictors of mortality for hyper- and hypothyroidism CHF patients. Six assumptions were tested to approve the results of logistic regression model. All these assumptions were tested and approved.

Number of procedure showed highest incidence of mortality of hyperthyroidism CHF patients ($\chi2$ = 44.592, df (1), p value < 0.001), followed by age categories ($\chi2$= 31.587, df (6), p value < 0.001), and metastasis ($\chi2$= 10.672, df (1), p value = 0.001).

Number of procedures considered as significant predictor for mortality of hyperthyroidism patients by 25.3% (OR= 1.253) with increase number of procedures. Patients with metastasis showed higher incidence of mortality by 378.2% (OR = 4.782) than those without.

Number of procedure showed highest incidence of mortality of hypothyroidism patients ($\chi2$ = 1264.273, df (1), p vale < 0.001), followed by age categories ($\chi2$= 421.919, df (6), p value < 0.001), Fluid and electrolyte disorders ($\chi2$= 291.869, df (1), p value <0.001), weight loss ($\chi2$= 107.146, df (1), p value <0.001), coagulation ( $\chi2$= 75.997, df (1), p value < 0.001), metastasis ($\chi2$= 69.869, df (1), p value < 0.001), and others.

Age considered as significant predictor for mortality of hypothyroidism CHF patients, where those aged elder than 80 years showed highest increment in the incidence of mortality by 44.4% (OR = 1.444). Other insurance patients got higher mortality than Medicare by 120% (OR = 2.200), followed by Self-pay (68.4%, OR = 1.684), and

private (HMO) (25.8%, OR=1.258) than Medicare. Males got higher incidence of mortality than females by 21.3% (OR= 1.213). Number of procedures showed significant associations with mortality by 21% (OR= 1.210). Patients with coagulopathy, liver disease, fluid and electrolyte disorder, metastatic cancer, other neurological disorders, peripheral vascular disease, pulmonary circulation disorders, renal failure, solid tumor without metastasis, and weight loss got higher incidence of mortality by 54% (OR= 1.540), 30.6% (OR = 1.306), 72.1% (OR= 1.721), 128.6% (OR= 2.286), 21.2% (OR= 1.212), 16.1% (OR= 1.161), 31% (OR= 1.310), 18.6% (OR= 1.186), 34.2% (OR= 1.342), and 60.8% (OR= 1.608) than those without respectively as shown in Table 21.

## Table 21 Predictors of mortality for hyper- and hypothyroidism CHF patients

| | | Hyperthyroidism | | | Hypothyroidism | | |
|---|---|---|---|---|---|---|---|
| | | Exp(B) | 95% CI for Exp(B) | | Exp(B) | 95% CI for Exp(B) | |
| | | | Lower | Upper | | Lower | Upper |
| Intercept | | | | | | | |
| No. of chronic dis. | | 1.033 | .964 | 1.106 | .954 | .942 | .966 |
| No. of procedures | | 1.253 | 1.178 | 1.333 | 1.210 | 1.198 | 1.222 |
| Gender | Male | | | | 1.213 | 1.136 | 1.295 |
| | Female (ref.) | | | | . | . | . |
| Race | Others | | | | .942 | .775 | 1.145 |
| | Black | | | | .902 | .799 | 1.018 |
| | Hispanic | | | | .977 | .857 | 1.114 |
| | Asian/Pacific Isl. | | | | 1.141 | .893 | 1.459 |
| | Native American | | | | .991 | .654 | 1.504 |
| | White (ref.) | | | | . | . | . |
| Income | 0-25th percent. | | | | 1.040 | .953 | 1.136 |
| | 26th-50th percent. | | | | .993 | .907 | 1.086 |
| | 51st-75th percent. | | | | 1.018 | .931 | 1.114 |
| | 75th-100th percent | | | | . | . | . |
| Age (years) | >80 | 2.797 | .349 | 22.441 | 2.688 | 1.444 | 5.003 |
| | 31-40 | | | | .939 | .432 | 2.041 |
| | 41-50 | 1.021 | .108 | 9.682 | .696 | .355 | 1.366 |
| | 51-60 | .528 | .057 | 4.870 | .876 | .466 | 1.645 |
| | 61-70 | 1.008 | .120 | 8.441 | 1.321 | .709 | 2.462 |
| | 71-80 | 1.598 | .194 | 13.175 | 1.712 | .918 | 3.191 |
| | ≤30(ref.) | . | . | . | . | . | . |
| Type of insurance | Others | | | | 2.200 | 1.737 | 2.787 |
| | Medicaid | | | | 1.164 | .964 | 1.407 |
| | Private (HMO) | | | | 1.258 | 1.113 | 1.422 |
| | Self-pay | | | | 1.684 | 1.205 | 2.354 |
| | No charge | | | | .882 | .176 | 4.426 |
| | Medicare (ref.) | | | | . | . | . |
| Coagulopathy | Yes | 1.772 | .989 | 3.177 | 1.540 | 1.402 | 1.692 |
| | No (ref.) | . | . | . | . | . | . |
| Diabetes, uncomplicated | Yes | | | | 1.069 | .999 | 1.144 |
| | No (ref.) | | | | . | . | . |
| Drug abuse | Yes | | | | 1.025 | .733 | 1.434 |
| | No (ref.) | | | | . | . | . |
| Liver disease | Yes | | | | 1.306 | 1.113 | 1.534 |
| | No (ref.) | | | | . | . | . |
| Lymphoma | Yes | | | | 1.222 | .957 | 1.561 |
| | No (ref.) | | | | . | . | . |
| Fluid and electrolyte | Yes | 1.489 | .998 | 2.219 | 1.721 | 1.617 | 1.832 |
| dis. | No (ref.) | . | . | . | . | . | . |
| Metastatic cancer | Yes | 4.782 | 2.053 | 11.140 | 2.286 | 1.913 | 2.733 |
| | No (ref.) | . | . | . | . | . | . |
| Other neurological dis. | Yes | | | | 1.212 | 1.112 | 1.322 |
| | No (ref.) | | | | . | . | . |
| Paralysis | Yes | | | | 1.084 | .915 | 1.284 |
| | No (ref.) | | | | . | . | . |
| Peripheral vascular dis. | Yes | | | | 1.161 | 1.060 | 1.272 |
| | No (ref.) | | | | . | . | . |
| Psychosis | Yes | | | | .939 | .803 | 1.098 |
| | No (ref.) | | | | . | . | . |
| Pulmonary circulation | Yes | | | | 1.310 | 1.199 | 1.432 |
| dis. | No (ref.) | | | | . | . | . |
| Renal failure | Yes | | | | 1.186 | 1.109 | 1.267 |
| | No (ref.) | | | | . | . | . |
| Solid tumor without | Yes | | | | 1.342 | 1.119 | 1.609 |
| metas. | No (ref.) | | | | . | . | . |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Valvular disease | Yes | | | | .993 | .917 | 1.076 |
| | No (ref.) | | | | . | . | . |
| Weight loss | Yes | 1.063 | .600 | 1.883 | 1.608 | 1.474 | 1.753 |
| | No (ref.) | . | . | . | . | . | . |

* Multinomial logistic regression. Model of fitting: $\chi^2$ = 100.556, df(12) p <0.001.

The reference category is: did not die during hospitalization

† Multinomial logistic regression. Model of fitting: $\chi^2$ = 2903.218, df(38) p <0.001.

The reference category is: did not die during hospitalization

**b) HT (Hypothesis 12)**

Multinomial logistic regression is the appropriate statistical test used to determine the predictors of mortality for hyper- and hypothyroidism HT patients. Six assumptions were tested to approve the results of logistic regression model. All these assumptions were tested and approved.

Number of procedure showed highest incidence of mortality of hyperthyroidism HT patients ($\chi2 = 73.538$, df (1), p value < 0.001), followed by metastasis ($\chi2 = 17.305$, df (1), p value < 0.001), insurance type ($\chi2 =12.338$, df (1), p value = 0.03), renal failure ($\chi2 =11.275$ df (1), p value = 0.001), and others.

Number of procedures and chronic diseases showed significant associations with mortality by 19.4% (OR= 1.194) and 8.2% (OR = 1.082) respectively. White race showed higher incidences of mortality than Black and Hispanic race patients by 45% and 112.8% respectively. Medicare patients got higher incidence of mortality than Medicaid by 140.3%. Patients with coagulopathy, fluid and electrolyte disorder, metastatic cancer, other neurological disorders, pulmonary circulation disorders, renal failure, and weight loss got higher incidence of mortality by 86.4% (OR=1.864), 49.7% (OR= 1.497), 261.1% (OR = 3.611), 110.4% (OR= 2.104), 73.7% (OR= 1.737), 74.6% (OR= 1.746), and 52.9% (OR = 1.529) than those without, respectively.

Number of procedure showed highest incidence of mortality of hypothyroidism patients ($\chi2 = 78.043$, df (1), p vale < 0.001), followed by fluid and electrolyte disorders ($\chi2= 24.778$, df (1), p value <0.001), age categories ($\chi2= 24.062$, df (6), p value = 0.001), metastasis ($\chi2= 15.022$, df (1), p value < 0.001), number of chronic diseases ($\chi2= 11.309$, df (1), p value <0.001), and others.

Number of procedures and chronic diseases showed significant associations with mortality by 28.9% (OR= 1.289) and 12.8% (OR = 1.128) respectively. Patients aged elder than 80 years got higher mortality by 548.2% (OR= 6.482), followed by those aged 71-80 years (270.9%, OR= 3.709) than those aged equal or younger than 30 years. Private HMO patients got lower incidence of mortality by 101.2% than those with Medicare. Medicare patients got higher incidence of mortality than Medicaid by 140.3%. Patients with coagulopathy, Diabetes, uncomplicated, liver disease, fluid and electrolyte disorder, metastatic cancer, and pulmonary circulation disorders got higher incidence of mortality by 82.4% (OR=1.824), 57.7% (OR= 1.577), 126.4% (OR = 2.264), 153.9% (OR= 2.539), 307.4% (OR= 4.074), and 91.3% (OR= 1.913) than those without respectively, as shown in Table 22.

## Table 22 Predictors of mortality for hyper- and hypothyroidism HT patients

| | | Hyperthyroidism | | | Hypothyroidism | | |
|---|---|---|---|---|---|---|---|
| | | Exp(B) | 95% CI for Exp(B) | | Exp(B) | 95% CI for Exp(B) | |
| | | | Lower | Upper | | Lower | Upper |
| Intercept | | | | | | | |
| No. of chronic dis. | | 1.082 | 1.028 | 1.140 | 1.128 | 1.053 | 1.209 |
| No. of procedures | | 1.194 | 1.151 | 1.239 | 1.289 | 1.223 | 1.358 |
| Gender | Male | 1.055 | .782 | 1.424 | 1.316 | .906 | 1.911 |
| | Female (ref.) | . | . | . | . | . | . |
| Race | Others | .503 | .198 | 1.280 | .651 | .226 | 1.877 |
| | Black | .686 | .477 | .988 | .956 | .574 | 1.594 |
| | Hispanic | .470 | .229 | .968 | .379 | .141 | 1.017 |
| | Asian/Pacific Isl. | .668 | .286 | 1.561 | 1.914 | .847 | 4.321 |
| | Native American | 1.012 | .137 | 7.483 | 1.475 | .184 | 11.795 |
| | White (ref.) | . | . | . | . | . | . |
| Age (years) | >80 | | | | 6.482 | 1.793 | 23.440 |
| | 31-40 | | | | .628 | .120 | 3.291 |
| | 41-50 | | | | 2.706 | .752 | 9.746 |
| | 51-60 | | | | 3.339 | .967 | 11.537 |
| | 61-70 | | | | 2.946 | .823 | 10.543 |
| | 71-80 | | | | 3.709 | 1.007 | 13.656 |
| | ≤30(ref.) | | | | . | . | . |
| Type of insurance | Others | .367 | .087 | 1.542 | 1.091 | .365 | 3.259 |
| | Medicaid | .416 | .214 | .810 | .557 | .265 | 1.172 |
| | Private (HMO) | .725 | .483 | 1.090 | .497 | .274 | .900 |
| | Self-pay | .870 | .348 | 2.172 | 1.184 | .495 | 2.831 |
| | Medicare (ref.) | . | . | . | . | . | . |
| Deficiency anemia | Yes | .989 | .728 | 1.344 | 1.040 | .697 | 1.552 |
| | No (ref.) | . | . | . | . | . | . |
| Blood loss anemia | Yes | .239 | .032 | 1.781 | .331 | .059 | 1.871 |
| | No (ref.) | . | . | . | . | . | . |
| Coagulopathy | Yes | 1.864 | 1.220 | 2.847 | 1.824 | 1.110 | 2.995 |
| | No (ref.) | . | . | . | . | . | . |
| Diabetes, uncomplicated | Yes | | | | 1.577 | 1.032 | 2.412 |
| | No (ref.) | | | | . | . | . |
| Drug abuse | Yes | .387 | .094 | 1.598 | | | |
| | No (ref.) | . | . | . | | | |
| Liver disease | Yes | | | | 2.264 | 1.088 | 4.710 |
| | No (ref.) | | | | . | . | . |
| Lymphoma | Yes | | | | | | |
| | No (ref.) | | | | | | |
| Fluid and electrolyte | Yes | 1.497 | 1.127 | 1.988 | 2.539 | 1.756 | 3.671 |
| dis. | No (ref.) | . | . | . | . | . | . |
| Metastatic cancer | Yes | 3.611 | 2.120 | 6.150 | 4.074 | 2.155 | 7.704 |
| | No (ref.) | . | . | . | . | . | . |
| Other neurological dis. | Yes | 1.737 | 1.167 | 2.586 | 1.146 | .659 | 1.991 |
| | No (ref.) | . | . | . | . | . | . |
| Paralysis | Yes | | | | 1.325 | .567 | 3.097 |
| | No (ref.) | | | | . | . | . |
| Peripheral vascular dis. | Yes | 1.162 | .766 | 1.763 | 1.330 | .730 | 2.421 |
| | No (ref.) | . | . | . | . | . | . |
| Psychosis | Yes | | | | | | |
| | No (ref.) | | | | | | |
| Pulmonary circulation | Yes | 2.104 | 1.316 | 3.366 | 1.913 | 1.077 | 3.398 |
| dis. | No (ref.) | . | . | . | . | . | . |
| Renal failure | Yes | 1.746 | 1.269 | 2.402 | .713 | .383 | 1.328 |
| | No (ref.) | . | . | . | . | . | . |
| Solid tumor without | Yes | 1.584 | .754 | 3.328 | | | |
| metas. | No (ref.) | . | . | . | | | |
| Valvular disease | Yes | 1.196 | .757 | 1.888 | | | |
| | No (ref.) | . | . | . | | | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Weight loss | Yes | 1.529 | 1.030 | 2.268 | .940 | .572 | 1.545 |
| | No (ref.) | . | . | . | . | . | . |

* Multinomial logistic regression. Model of fitting: $\chi^2$ = 281.701, df(26) p <0.001.

The reference category is: did not die during hospitalization

† Multinomial logistic regression. Model of fitting: $\chi^2$ = 375.988, df(32) p <0.001.

The reference category is: did not die during hospitalization

# CHAPTER V

# DISCUSSION AND IMITATIONS

## 5.1 Discussion

### 5.1.1 Introduction

This study highlights the main outcomes related to patients with thyroid diseases admitted to United States hospitals in 2012. This study aimed to investigate the impact of the patients' sociodemographic characteristics, diseases, and other medical conditions on their total cost, length of hospital stay, and mortality induced by thyroid diseases. This study showed the comparisons in predictors of length of stay, total cost and mortality between hypo- and hyperthyroidism on one hand, and the relationship among thyroid diseases and cardiovascular complications on the other. This study revealed several needs for revisions of therapy plans to reduce the cost of health-care services, length of stay, and mortality which, in turn, will enhance patients' quality of life.

### 5.1.2 Patients' sociodemographic and medical information

These data were obtained from the NIS database and involved 721,958 patients for the year 2012. The highest incidence of patients admitted to hospitals were for patients 80 years of age and older (29.3%), white (76.7%), female (74.9%), insured under Medicare (68.2%), and with a household income ranging from the 0 to 25th percentile (27.1%). Hypertension was the comorbidity with highest incidence compared to others by 63.8%, followed by fluid and electrolyte disorders (29.1%), uncomplicated Diabetes Mellites (DM) (24.4%), chronic pulmonary disease (23.3%), and deficiency anemia (22.8%), while the lowest incidences were observed with peptic ulcer (0.04%), followed by acquired immune deficiency syndrome (0.1%), lymphoma

(1%), and chronic blood loss anemia (1.6%). A significant association was found between the dependent outcomes (mortality, length of stay, and total cost) and independent variables (comorbidities and patient sociodemographic profiles), as mentioned in the literature review.

Incidence of mortality for thyroid diseases, hypo- and hyperthyroidism disorders, is 2.4% of total patients, as shown in Figure 4. This incidence is within the range (2% to 3.6%) reported by Mahal et al. about the mortality of patients involving hypothyroidism only[141], but higher than 0.06–1.49% reported by Abraham et al., which is attributed to including only the thyroid disease patients after thyroidectomy[142].

The median length of stay for patients in the present study was three days (Table 10), which is lower than results of Mahal et al. by one day because their study conducted for hypothyroidism patients who complained of congestive heart failure only[141]. The mean for length of hospital stay of the present study is 5.06 days, which is higher than that reported by Sullivan et al. (4.3 days) because this study followed only hyperthyroidism patients[143]. The present study found the median cost to patients with thyroid disease to be $25,741, which is higher than the median cost reported by Mahal et al. [141] ($20,312) because they involved only hypothyroidism patients which required fewer charges and a lower number of surgical procedures.

Incidence of hypothyroidism was found to be higher than that of hyperthyroidism in US patients in 2012, as shown in Table 12. Hypothyroidism is more common than hyperthyroidism; therefore, the majority of patients in the present study who complained of hypothyroidism and due to some hyperthyroidism patients got the surgery or radiotherapy, who later suffer of future hypothyroidism. This result

concurs with the findings of previous studies that found a higher prevalence of hypothyroidism than hyperthyroidism[15,144,145].

### 5.1.3 Demographics related to heart failure and thyroid disease conditions

Although males are more affected by cardiovascular diseases, thyroid disease in females showed higher incidence of congestive heart failure than in males in both hypo- and hyperthyroidism disorders. Females had a higher incidence of hyperthyroidism with CHF compared to males, as shown in Figure 6. The interaction effect for gender on the association between CHF and the type of thyroid disease was also supported by a previous study[141]. Mahal et al. showed that the rate of female patients with congestive heart failure was 69.4%, which was higher than 30.6% for males and very similar to the results of the present study. However, the main limitations related to the results of the present study is that it involved hypothyroidism patients only.

A significant association was found between the type of insurance and the types of thyroid diseases for those with congestive heart failure-related thyroid disorders, as shown in Figure 7. However, higher incidences were observed for hypothyroidism with Medicare than other types of insurances. Another significant association was found between the median household income and the thyroid-heart failure conditions, as shown in Figure 9. Higher incidence of heart failure-thyroid diseases (hyperthyroidism 33.14% and hypothyroidism 30.28%) occurred in the 0 to 25th percentile income range than in other incomes. Unfortunately, no literature stated the association between the type of insurance and household income with thyroid-heart failure conditions. White patients showed the highest incidence of congestive heart failure induced by thyroid diseases with 81.75% and 63.03% for hypo- and hyperthyroidism, respectively (Figure 8), which is in line with findings of a previous

study[141]. Rodondi et al. discussed the contribution of race to coronary heart disease (CHD), CHD mortality, and total mortality induced by thyroid diseases. They stated that there was a higher incidence of CHD events with white race patients than those of other races[146]. Rodondi et al. also reported no effects for age as a risk factor for the CHF induced by thyroid diseases. This can possibly be attributed to their focus on subclinical hypothyroidism only and their small sample size. The present study showed a significant impact on those 80 years and older by heart failure induced by thyroid diseases (hypothyroidism 46.72% and hyperthyroidism 34.07%). However, the present study is supported by the findings of Mahal et al., who found a significant association between age and CHF-thyroid disorder conditions, but they also were limited to studying only hypothyroidism patients.

### 5.1.4 Demographic and hypertension-thyroid disease conditions

Shinkov et al. explored the difference between genders based on the interaction of the arterial blood pressure and thyroid diseases. They found thyroid disease in males had a higher percentage of hypertension than in females[147]. Six-Merker et al. found females had higher incidences of cardiovascular hazards than males with thyroid diseases[148], while Liu et al. showed the hypertension-hypothyroidism in females was a more significant risk factor than in males[150]. However, their study involved only the hypothyroidism patients, which is its main limitations. The present study revealed that the higher incidence of heart failure-thyroid diseases was in females than in males. With females, higher incidences of hypertension were observed in hypothyroidism than in hyperthyroidism (74.23% vs. 72.55%), while males had higher incidences with hyperthyroidism than hypothyroidism (27.45% vs. 25.77%), as shown in Figure 11. Marzouka et al. determined that there was an impact for racial differences on the hypertension induced by thyroid diseases [149], but their study involved hypothyroidism

diseases only. This result supported the findings of the present study, where there were higher incidences of hypertension-hypothyroidism than of hyperthyroidism in white patients, while hypertension-hyperthyroidism was higher than hypothyroidism in black patients, as shown in Figure 13.

No information exists in the literature about the impact of the type of insurance and median household income on the hypertension induced by thyroid diseases. Patients with Medicare insurance showed the highest incidence of thyroid diseases than those with other types of insurance. Also, there were higher incidences of patients with hypertension-hypothyroidism than those with hypertension-hyperthyroidism (76.63% vs. 62.38%) as shown in Figure 12. Patients with a median income in the 0 to 25th percentile showed the highest incidence of hypothyroidism compared to others. Patients with hypertension-hyperthyroidism who ranged within 0-25 percentile got higher than those with hypertension-hypothyroidism (32.8% vs. 28.55%) as shown in Figure 14. This can be attributed to the need for more insurance coverage due to the high cost of surgical procedures and radiation therapy. Age also played a role in the complications of cardiovascular events induced by thyroid diseases. Liu et al. stated the there was a significant contribution of age to the hypertension-hypothyroidism condition[150]. This finding supported the results of the present study, where there were higher incidences of hypertension induced by hypothyroidism than by hyperthyroidism (34.39% vs. 22.6%), as shown in Figure 15.

### 5.1.5 Mortality, thyroid diseases, and patients' demographic characteristics

The present study revealed the significant association between mortality and type of thyroid disease, where there was a higher incidence of mortality found with hypothyroidism (2.4%) than hyperthyroidism (1.75%), as shown in Figure 16. Laulund et al. found the incidence of mortality to be higher with hypothyroidism than

with hyperthyroidism[15]. The incidence of mortality because of CHF-hypothyroidism was higher than that of hyperthyroidism (5.42% vs. 4.87%), as shown in Figure 17. Previous studies showed a higher incidence of mortality in CHF-hypothyroidism patients than in CH-hyperthyroidism patients[140,145]. This finding supports the findings of the present study. The incidence of mortality for HT-hypothyroidism was significantly higher than that of HT-hyperthyroidism (2.47% vs. 1.99%), as shown in Figure 18. This result is in line with outcomes reported by Martin et al. and Grossman et al., where a higher incidence of mortality was induced by hypertension with subtypes of hypothyroidism than with subtypes of hyperthyroidism[151,152].

Females showed higher incidences of mortality with hypothyroidism than with hyperthyroidism (67.49% vs. 64.58%), and vice versa for males, as shown in Figure 19. This result was similar to findings obtained by previous studies[15,141]. White patients had a higher incidence of mortality induced by hypothyroidism (82.17%) than with hyperthyroidism (72.33%), while black patients had higher mortality with hyperthyroidism than with hypothyroidism, as shown in Figure 21. Previous studies also stated the role of race in mortality induced by thyroid diseases, which supported the results of the present study[141,151]. No previous studies highlighted the effects of insurance type and income on mortality according to type of thyroid disease. Higher incidences were observed in hypothyroidism patients with 0 to 25th percentile income range and with Medicare insurance, as shown in Figures 20 and 22. Patients 80 years and older had higher incidences of mortality induced by hypothyroidism (50.71%) than with hyperthyroidism (39.58%), as shown in Figure 23. Several studies proved that age is considered a significant moderator for mortality induced by thyroid diseases; however, they are limited to a specific thyroid disorder[141,145,153], which supported the results of the present study.

### 5.1.6 Risk factors (predictors) of total charges, length of stay, and comorbidity

#### a) Total charges

Very few studies involved the total charges for hospitalization of thyroid disease patients. Studies in the literature have highlighted the impact of comorbidities and the complications of thyroid diseases, which are higher than for factors such as demographic and other medical information[161]. The main limitations of these studies was that they were not involved with the comorbidities that showed the greatest influence on the total charges of health-care services, which is considered another novel factor described in the present study.

Hypokalemic periodic paralysis is rare life-threatening complication of hyperthyroidism which is characterized by hypokalemia and paralysis attacks[154]. Most of the previous studies discussed this complication as case report studies[155–158]; however, these cohort studies involved small sample sizes[159]. Misdiagnosis of the hypokalemic periodic paralysis of hyperthyroidism ends up costing the patients and insurance companies a lot of money due to treatment screening and other health-care services[160]. Although screening for hyperthyroidism is not expensive, the cost will be high for females aged 50 years and older[162]. However, the cost was high for those in the present study because the majority of individuals were females who had had several thyroidectomy procedures, radiation, and therapy[163,177]. The number of procedures was another high risk factor for high total charges. Weight loss is the sign and complication common observed with hyperthyroidism patients; therefore, it is definitely related to the cost of health-care services, where higher prophylactic steps are taken to improve this disorder. Asban et al. presented evidence for the hazard ratio of weight loss as the highest related comorbidity compared to other factors, which supported the results of the present study[164]. Sosa et al. highlighted the economic

outcomes of US patients from 2004 to 2009, and they observed that Hispanic and black patients had the highest total charges than other races[165]. Their study supported the outcomes of the present study because Hispanic patients had higher charges than patients of other races. A significant association was found between coagulopathy and thyroid dysfunction. Squizzato et al. discussed that the coagulation-fibrinolytic system is influenced by thyroid disorders (hyper- and hypothyroidism) that require the attention of clinicians to control this comorbidity and the high cost of health-care services [166,171]. Therefore, the present study revealed that coagulopathy is one of highest risk factors of hyperthyroidism expenditures.

For risk factors influencing the total charges for patients with hypothyroidism, the predictors with the highest incidences are number of procedures, weight loss, Hispanic race, coagulopathy, paralysis, and fluid and electrolyte disorders. Previous studies showed the effect of the number of procedures on the total expenditures of hypothyroidism patients[167,168], which supported the outcomes of the present study. The number of procedures, in the present study, contributed the highest high total charges for hypothyroidism patients. Weight loss is not a comorbidity for hypothyroidism patients, but thyroid medications induced weight loss as a type of adverse event, which also related to high levels of expenditures; that is, high expenditures were related to the fees for medications which significantly related to this adverse effect. This factor was also reported by several studies on successful therapy plans for hypothyroidism patients[169,170]. The Hispanic race was found to be a significant predictor for high cost of hypothyroidism when compared to other races. This result was also highlighted by a previous study[161]. Coagulation was another significant comorbidity for abnormally high total charges related to treatment for hypothyroidism[166,171]. Also, paralysis is not only found with hyperthyroidism, but

some thyroid disorders such as thyroiditis may induce paralysis and hypothyroidism[172]. The most common reason for paralysis, as mentioned in the literature, is attributed to complications of thyroidectomy where unilateral and bilateral vocal cord paralysis may result after performed thyroid surgeries[173], which contribute to high costs of health-care services[177]. Fluid and electrolyte disorders are considered significant comorbidities of hypothyroidism disease[174], which supported the results of the present study.

All comorbidities increased the rate of hospital expenditures because of the involvement of additional procedures and health-care services. Therefore, there was little similarity in predictors between hypo- and hyperthyroidism due to both being autoimmune diseases[167]. The present study involved total charges of CHF and HT for hypo- and hyperthyroidism patients, which added significant risk factors related to paralysis, number of procedures, race, coagulopathy, and weight loss. Patients younger than 30 years old showed high incidences of HT and CHF for thyroid disorders, which in turn increased the rate of expenditures. The reason for high total charges was that the newly-diagnosed individuals with cardiovascular diseases required many plans for therapy to stabilize their health status. Moreover, the present study involved patients aged 80 years and older as the main reference for the other ages. The HF and CHF of thyroid disorder conditions were also discussed by Jung et al.[175] and Park et al.[176], which supported the results of the present study.

**b) Length of hospital stay**

A limited number of studies highlighted the predictors of length of hospital stay for thyroid disease patients. Paralysis, weight loss, pulmonary circulation disorders, and

fluid and electrolyte disorders were found to be the most common risk factors for length of hospital stay for hyperthyroidism patients.

Gardner et al. highlighted the influence of vocal fold paralysis, unilateral and bilateral, as the main complication of hyperthyroidism disorder after performed thyroidectomy procedure and long length of stay[177]. This finding concurs with the results of the present study, where paralysis was the highest risk factor for longer lengths of stay for hyperthyroidism patients. Weight loss has been found to be the main complication accompanied with thyrotoxicosis and thyroid storm, which increased the length of hospital stay[178,179]. This is in line with the findings of the present study, where weight loss was a risk factor for the length of stay of hyperthyroidism patients. Previous studies investigated the association between length of hospital stay and pulmonary circulation problems of thyroid disease patients[180,181]. Therefore, the present study showed long lengths of stay due to the pulmonary circulation as a comorbidity of hyperthyroid disease. Fluid and electrolyte disorders are complications of thyroid disorders (hypo- and hyperthyroidism)[174]; therefore, the present study showed long lengths of stay because additional health-care services are used to control this risk.

Unfortunately, no study has yet highlighted the direct association between weight loss of hypothyroidism and length of hospital stay. Researchers stated the association between weight loss and hyperthyroidism therapy[170]. The present study found a significant impact for weight loss, as a comorbidity of hyperthyroidism, on the length of hospital stay. Paralysis (unilateral and bilateral) is induced due to the thyroidectomy procedures which contribute to the high cost of health-care services[173,177]. Fluid and electrolyte disorders also contributed to longer lengths of stay due to the common abnormality of thyroid hormones, as more time was required

to control this complication[174]. Patients younger than 30 years old showed high incidences of HT and CHF for thyroid disorders which, especially for those newly diagnosed for CHF and HT with hypothyroidism disorders[175,176], increased the length of hospital stay found in the present study. However, this was attributed for considering patients aged 80 years and older as the reference for other ages. The number of procedures significantly associated with length of stay of thyroid disease patients[182] was in line with the findings of the present study. No published studies have yet found the direct effects for the pulmonary circulation disorders, psychosis, and coagulation on the length of stay. However, most of these complications provide serious signs for CHF and HT diseases which require more health-care services and observation of the patients' health status.

**c) Mortality**

Several risk factors for the mortality of hyperthyroidism patients were obtained in the present study, including number of procedures, age, metastasis, and fluid and electrolyte disorders. The present study revealed the number of procedures showed the highest association to mortality of hyperthyroidism patients. Although thyroidectomy is considered as having a low risk of mortality compared with other surgical procedures[183], an increase in the number of other procedures may be considered as a cause of mortality[184]. Palace et al. reported that thyroid dysfunction may complicate surgical procedures and postoperative recovery[185]; therefore, this is also considered as another risk for mortality. Age is considered as a significant predictor for mortality, especially for elderly patients[186,187]. Thus, patients 80 years and older had the highest incidences of mortality compared to other age groups. Previous studies stated that metastasis is a strong predictor of mortality, which supports the results of the present study[188,189]. Abnormalities of mineral levels for

sodium, magnesium, potassium, and phosphate, during thyroid dysfunction, are also associated with mortality for thyroid disease patients[174,190]. This finding supports the results of the present study, where electrolyte disorders were found to be significant risk factors for hyperthyroidism disorder.

Predictors of hypothyroidism disorder were similar to predictors of hyperthyroidism disease, where higher mortalities were associated with number of procedures, age, fluid and electrolyte disorders, and metastasis. Surgical procedures were considered as a risk factor for mortality[185], which supports the results of the present study. Elderly patients had higher incidences of mortality[191], where those 80 years and older had the highest incidences compared to others. The similarity between hypo- and hyperthyroidism for electrolyte disorders was attributed to the physiological changes and abnormal thyroid functions which increased the risks of mortality because of abnormal functions of body organs, such as the liver, kidneys, and heart[174]. Metastasis and thyroid cancers are dependent on age as the main predictor for mortality of patients with thyroid dysfunctions[192,193]. Gaddey et al. proved the association between weight loss and mortality because of malignancy, gastrointestinal diseases, and psychiatric conditions, which influence thyroid hormones functions[194]. Ordookhani et al. showed the elevation in incidence of mortality because of the difficulty of the body to maintain homeostasis, and because several factors of coagulation (VIII, IX, XI, VII, and plasminogen activator-1) were detected with hypothyroidism[195]. This finding supports the results of the present study, where there was a significant positive association between mortality and coagulation.

For patients with HT and CHF thyroid disorders, other predictors increased the risks of mortality, such as type of insurance and renal failure. Unfortunately, no study stated the relationship for type of insurance and mortality, while a significant

relationship was found between renal and cardiovascular disease, which were considered as serious comorbidities.

The novel approach of the present study involved comparisons between hypo- and hyperthyroidism, which investigated the similarities in risk factors but found differences in the significance of the association with patients' parameters, such as mortality, length of hospital stay, and total charges. Several justifications were not proven, yet were involved in the present study, including thyroid storm, paralysis, and others, which contributed to the reevaluation of the risk factors, especially with patients who complained of cardiovascular diseases.

### 5.2 Study limitations

Several limitations were involved in the present study which related to the type of data used. First, this study depended on secondary data obtained from NIS, where not all information was included such as laboratory data and type of thyroid disorder (overt and subclinical). Moreover, several patients' data were not complete and were missing information, such as medical history, number of admissions, signs/symptoms of thyroid disorders, pharmacotherapy, type of surgery, and radiation treatment. Moreover, some of that information was essential to this study regarding the diagnosis and treatment of thyroid disorders, stages of diseases, and duration of therapy, type of medications and doses, and dates of surgical procedures.

# CHAPTER VI

# CONCLUSION AND FUTURE RESEARCH

## 6.1 Study summary

This study highlighted important thyroid disease patient outcomes related to predictors of hospitalization parameters in U.S. hospitals. The common factors that affected both the patients' and society's quality of life and quality of health-care services were the length of hospital stay, total medical charges, and mortality, which are considered dependent variables of the study. The independent variables of the present study involved patient sociodemographic characteristics and medical information. Sociodemographic data included age, gender, race, type of insurance, and income level. Patient medical information included the number of procedures and chronic diseases, comorbidities, and the type of thyroid disorder. The total number of patients was 721,958 for the year 2012. Multiple linear regression (the dummy method) and multinomial logistic regression were used to determine the risk factors and to achieve the objectives of the present study.

Descriptive analysis was implemented to measure incidences in the study sample. The highest incidences of thyroid disorders were observed in those who were over 80 years of age, white, female, on Medicare, and had a household income in the 25th percentile. The highest incidences of comorbidities were seen with hypertension, fluid and electrolyte disorders, and uncomplicated diabetes. There was a higher incidence of hypothyroidism than of hyperthyroidism. The distribution of congestive heart failure (CHF)in patients with hypothyroidism, according to patient demographic characteristics, was observed in those who were male, on Medicare, white, had an

income in the 25th percentile, and over 80 years of age. The distribution of hypertension (HT) in patients with thyroid diseases was observed in those who were female, on Medicare, white, had an income in the 25th percentile, and were over 80 years of age. The distribution of mortality according to the type of thyroid disorder was higher in patients with hypothyroidism and CHF or HT than those with hyperthyroidism.

Risk factors for patients with hyperthyroidism related to the length of stay were paralysis, weight loss, pulmonary circulation, fluid and electrolyte disorders, age, neurological disorders, coagulopathy, psychosis, and the number of procedures. Risk factors for patients with hypothyroidism related to the length of stay were weight loss, paralysis, fluid and electrolyte disorders, age, the number of procedures, and the type of insurance. Risk factors for patients with hyperthyroidism related to total medical charges were paralysis, the number of procedures, weight loss, fluid and electrolyte disorders, race, coagulopathy, age, and neurological disorders. Risk factors for patients with hypothyroidism related to total medical charges were the number of procedures, weight loss, race, coagulopathy, paralysis, fluid and electrolyte disorders, and age. Risk factors for patients with hyperthyroidism related to mortality were the number of procedures, age, metastasis, fluid and electrolyte disorders, insurance type, and renal failure. Risk factors for patients with hypothyroidism related to mortality were the number of procedures, age, fluid and electrolyte disorders, metastasis, weight loss, and coagulation.

Although there were similarities among the predictors between hypo- and hypothyroidism, differences were found in etiology and the association of these disorders to comorbidities. Moreover, they involved different strengths of associations based on the direct or indirect influence of the type of disorder and type of

comorbidity. Several comorbidities were also related to cardiovascular diseases, such as coagulopathy and renal failure, and the relationship between metastasis and mortality.

Researchers are urgently required to update the guidelines and plans of therapy for patients with thyroid disorders to obtain comprehensive diagnoses for all diseases and comorbidities. Reviewing the quality of services to control preventable predictors could affect the total medical charges and length of stay and minimize incidences of mortality due to the effect on patients' life spans and the government's economic burden regarding health-care services.

**6.2 Future research**

Clinical trials are needed to help determine the risk factors of thyroid disorders based on thyroid hormone levels, using laboratory and screening techniques, and their association to mortality, length of stay, and total medical charges. The implementation of intervention studies is important to update the knowledge and practice of health-care professionals regarding thyroid disorders and their future complications. Consequences of thyroid disorders such as cardiovascular disease, thyroid storm, and paralysis need to be investigated in other scientific terms, such as in genetic association trials and causality studies, to determine the proper therapy and optimal health services to be administered to thyroid patients.

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