BODY COMPOSITION IN PATIENTS WITH THYROID DISEASE USING BIOELECTRICAL IMPEDANCE ANALYSIS

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TABLE OF CONTENTS

Contents

ABBREVIATIONS

BCM	Body cell mass
BIA	Bioelectrical impedance analysis
BMI	Body mass index
CT	Computed X-ray Tomography
DXA	Dual X-ray absorptometry
ECW	Extracellular water
HUSM	Hospital Universiti Sains Malaysia
ICW	Intracellular water
HSD	Honestly Significant Difference
MNG	Multinodular goitre
MRI	Magnetic resonance imaging
TSH	Thyroid stimulation hormone
TBW	Total body water
T4	Thyroxine
T3	Triiodothyronine

ABSTRAK

Latar belakang:

Hormon tiroid adalah hormon yang penting dalam metabolisma tubuh. Penyakit berkaitan tiroid boleh meliputi tahap hormon tiroid yang tinggi atau tahap hormon tiroid yang rendah. Ke dua-dua keadaan tiroid hormon yang tinggi atau rendah akan menggangu metabolisma tubuh dan mengubah kandungan komposisi tubuh. Kajian ini akan mengkaji kandungan komposisi tubuh di dalam kumpulan hormon tiroid yang tinggi, rendah dan normal.

Kaedah:

Ini adalah kajian keratan rentas yang melibatkan 47 orang pesakit yang disahkan menghidap penyakit berkaitan kalenjar tiroid iaitu penyakit Grave Disease, Multinodular Goitre (MNG) dan lain-lain seperti thyroiditis dan congenital hypothyroid, berumur di antara 21 hingga 45 tahun. Pesakit akan dikategorikan ke dalam 3 kumpulan iaitu hyperthyroid, hypothyroid dan euthyroid berdasarkan keputusan darah hormon tiroid. Komposisi tubuh iaitu komposisi lemak, air dan berat badan tanpa lemak akan diukur menggunakan mesin 'Bioelectrical Impedance Analysis (BIA) Bodystat® Quadscan. Data akan di nilai untuk membuat perbandingan komposisi tubuh di antara 3 kumpulan tersebut.

Keputusan:

Sejumlah 47 orang pesakit yang menghidap penyakit berkaitan tiroid telah di analisa. Majoriti pesakit adalah perempuan (85.1%) dengan purata umur 32.85 (±7.43) tahun. 18 orang pesakit (38.3%) adalah hyperthyroid, 11 orang pesakit (23.4%) adalah hypothyroid dan 18 orang pesakit (38.3%) adalah euthyroid. Komposisi tubuh di ukur

dan di analisis di antara 3 kumpulan tersebut. Komposisi lemak badan adalah lebih tinggi di dalam pesakit hypothyroid berbanding pesakit hyperthyroid dengan nilai *P*=0.047. Kandungan air keseluruhan, juga lebih tinggi di dalam pesakit hypothyroid, berbanding pesakit hyperthyroid dengan nilai *P*=0.05,. Berat badan tanpa lemak juga lebih tinggi di dalam pesakit hypothyroid berbanding pesakit hyperthyroid dengan nilai *P*=0.03.

Kesimpulan:

Tahap hormon tiroid yang abnormal mempengaruhi komposisi tubuh, di mana tahap hormon tiroid yang rendah menyebabkan lemak badan, kandungan air dan berat badan tanpa lemak yang lebih tinggi berbanding pesakit dengan status hormon tiroid yang tinggi.

ABSTRACT

Background:

Thyroid hormone is an important hormone for body metabolism. Diseases affecting thyroid gland can cause either hyperthyroid or hypothyroid state. Both of these condition can alter body metabolism and causing changes in body composition. This study will compare body composition in 3 different thyroid state which were hyperthyroid, hypothyroid and euthyroid.

Methods:

This was a cross sectional study involving 47 patients who have been diagnosed with thyroid disease such as Grave's Disease, Multinodular Goitre (MNG), thyroiditis and congenital hypothyroid, age between 21 to 45 years old. Patients were divided into 3 groups which were hyperthyroid, hypothyroid and euthyroid group based on thyroid function test result. Body composition (body fat, body water and lean weight) were measured for each patients using Bioelectrical Impedance Analysis machine (Bodystat®Quadscan). Data was analyzed to compare body composition in all 3 groups.

Results:

A total number of 47 patients who had thyroid disease were analysed. Majority of the patients were female (85.1%) with mean age of 32.85 (±7.43) year old. 18 (38.3%) patients were in hyperthyroid group, 11 (23.4%) patients were in hypothyroid groups and 18 (38.3%) patients were in euthyroid groups. Body composition were measured and analysed between 3 groups. Total body fat was higher in hypothyroid group as compare to hyperthyroid group [F (2,44)=3.279, *P*=0.047]. Total body water (TBW) was also higher in hypothyroid group compare to hyperthyroid group with statistically

significant differrence; *P*=0.05. Lean weight was also higher in hypothyroid group compare to hyperthroid group with statistically significant differrence; *P*=0.03.

Conclusion:

Thyroid hormone dysfunction cause significant changes in body composition in which hypothyroid state as compare to hyperthyroid patient cause higher total body fat, body water and lean weight.

CHAPTER 1: INTRODUCTION

Thyroid disorder were among one of the most common endocrine diseases in Malaysia. There were few study done on the prevalence of thyroid disease in Malaysia. From previous study, Thyroid Disorder in Malaysia: A Nationwide Multicentre Study (MyENDO:Thyroid) , it showed that prevalence of thyroid dysfunction among Malaysian adult population were 2.1% for hypothyroidism and 3.4% for hyperthyroidism (Shahar *et al.*, 2017).

Thyroid hormone is an important hormone in our body. It is produced by thyroid gland. Its synthesis and secretion are maintained within limits by a regulatory mechanism that is very sensitive to small changes in circulating hormone concentrations. There are two biologically active thyroid hormones: thyroxine (T4) and 3,5,3'-triiodothyronine (T3). T4 is solely a product of the thyroid gland, whereas T3 is a product of the thyroid gland and other tissues, in which it is produced by deiodination of T4. Thyroid hormones play a crucial role in human body. It regulates metabolic process essential for normal growth and development, and regulating metabolism in adult (Mullur *et al.*, 2014). They also affect the function of almost every organ system.

Thyroid hormone dysfunction can cause either hyperthyroidism or hypothyroidism. Hyperthyroidism, a state of excess thyroid hormone, promotes a hypermetabolic state characterized by increased resting energy expenditure, weight loss, reduced cholesterol level, increased lipolysis and gluconeogenesis. While hypothyroidism, a state of reduced thyroid hormone level is associated with hypometabolism characterized by reduced resting energy expenditure, weight gain, increased cholesterol level, reduced lipolysis and gluconeogenesis. It is known that thyroid hormones status correlates with body weight and energy expenditure (Fox CS *et*

a.l., 2008). There was positive association between change of serum TSH concentration and weight change (Bjergverd *et al.*, 2014). Because of the changes in weight, alteration of thyroid hormone level can cause changes in body mass index (BMI). There has been found a positive correlation between BMI and various thyroid hormone level in which higher thyroid hormone level associated with lower BMI (Anastasios *et al.*, 2013).

Body composition were used to describe the percentage of fat, muscle, bone and water in human body. Assessment of body composition have an important role in physical and clinical assessment of nutrition status, as well as in the management of non-communicable chronic disease. There were various methods for body composition assessment including anthropometry, computed X-ray tomography (CT), magnetic resonance imaging (MRI), bone densitometry (DXA) and bioelectrical impedance analysis (BIA). Choice of method to use depend on which compartment to assess, cost, validity, applicability of the technique, availability of the equipment and risk associated with exposure radiation (Kyle U *et al.*, 2004).

In this study, biolectrical impedance analysis (BIA) were used for body composition assessment. This method were widely used mainly because of its rapid processing of information, non-invasiveness, relatively inexpensive and used a portable instrument of easy handling. BIA method consist of the passage of a painless electrical current of low amplitude through the organism, applied by means of cables connected to electrodes and conductive surfaces. Body composition were determined by measuring the resistance of the body as a conductor to a small electrical current (Duren *et al.*, 2008).

As mentioned earlier, thyroid hormone plays an important role in regulating body metabolism and energy comsumption. Studies showed that thyroid hormone

dysfunction cause changes in body weight and BMI. Hyperthyroid assocated with weight loss, while hypothyroidism may cause modest increase in weight (Hoogwerf *et al*., 1984). In view of this, we hypothesize that, thyroid dysfunction also can cause alteration in body composition. However, there were few studies on effects of thyroid hormone dysfunction on body composition. From previous study, body composition in hyperthyroid Grave's patients characterized by lowered body cell mass (BCM) and eleveted extracellular water (ECW) (Hu *et al.,* 1995). Another study showed that hyperthyroid patients had significantly lower body weight and fat mass than hypothyroid patients (Adam *et al.*, 2016).

In this study, assessment of body composition using BIA were done in patients with thyroid disease, in 3 different thyroid status which were hyperthyroid, hypothyroid and euthyroid, age between 21-45 years old. Perhaps, the result of this study will help in the nutritional assessment and management of patients with thyroid disease. In addition, there was no similar study done in Malaysia.

CHAPTER 2: OBJECTIVES OF STUDY

2.1 General objective

2.1.1 To study body composition (body fat, body water and lean weight) in patients with thyroid disease in 3 different thyroid status (hyperthyroid, hypothyroid and euthyroid) using bioelectrical impedance analysis (BIA).

2.2 Specific objectives

2.2.1 To compare body fat composition in patients with hyperthyroid, hypothyroid and euthyroid using bioelectrical impedance analysis (BIA).

2.2.2 To compare body water composition (total body water, intracellular water and extracellular water) in patients with hyperthyroid, hypothyroid and euthyroid using bioelectrical impedance analysis (BIA).

2.2.3 To compare lean weight in patients with hyperthyroid, hypothyroid and euthyroid using bioelectrical impedance analysis (BIA).

CHAPTER 3: MANUSCRIPT

3.1 TITLE: BODY COMPOSITION IN PATIENTS WITH THYROID DISEASE USING BIOELECTRICAL IMPEDANCE ANALYSIS

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3.2 ABSTRACT

Background:

Thyroid hormone is an important hormone for body metabolism. Diseases affecting thyroid gland can cause either hyperthyroid or hypothyroid state. Both of these condition can alter body metabolism and causing changes in body composition. This study will compare body composition in 3 different thyroid state which were hyperthyroid, hypothyroid and euthyroid.

Methods:

This was a cross sectional study involving 47 patients who have been diagnosed with thyroid disease such as Grave's Disease, Multinodular Goitre (MNG), thyroiditis and congenital hypothyroid, age between 21 to 45 years old. Patients were divided into 3 groups; hyperthyroid, hypothyroid and euthyroid group based on thyroid function test result. Body composition (body fat, body water and lean weight) were measured for each patients using Bioelectrical Impedance Analysis machine (Bodystat®Quadscan).

Results:

A total number of 47 patients who had thyroid disease were analysed. Majority of the patient were female (85.1%) with mean age of 32.85 (±7.43) year old. 18 (38.3%) patients were in hyperthyroid group, 11 (23.4%) patients were in hypothyroid group and 18 (38.3%) patients were in euthyroid group. Body composition were measured and analysed between 3 groups. Total body fat were higher in hypothyroid group as compare to hyperthyroid group [F (2,44)=3.279, P=0.047]. Total body water (TBW) were also higher in hypothyroid group with statistically significant differrence; P=0.05.

Lean weight were also higher in hypothyroid group compare to hyperthroid group with statistically significant differrence; *P*=0.03.

Conclusion:

Thyroid hormone dysfunction cause significant changes in body composition in which hypothyroid patients as compare to hyperthyroid patients had higher total body fat, total body water and lean weight.

KEYWORDS: *Thyroid disease, Hyperthyroid, Hypothyroid, Euthyroid, Body composition, Total body fat, Total body water(TBW), Lean weight, Intracellular water (ICW), Extracellular water (ECW).*

3.3 INTRODUCTION

Thyroid hormone is an important hormone in our body. It is produced by thyroid gland. Its synthesis and secretion are maintained within limits by a regulatory mechanism that is very sensitive to small changes in circulating hormone concentrations. Thyroid hormones play a crucial role in human body. It regulates metabolic process essential for normal growth and development, and regulating metabolism in adult.(1) They also affect the function of almost every organ system.

Thyroid hormone dysfunction can cause either hyperthyroidism or hypothyroidism. Hyperthyroidism, a state of excess thyroid hormone, promotes a hypermetabolic state characterized by increased resting energy expenditure, weight loss, reduced cholesterol level, increased lipolysis and gluconeogenesis. While hypothyroidism, a state of reduced thyroid hormone level is associated with hypometabolism characterized by reduced resting energy expenditure, weight gain, increased cholesterol level, reduced lipolysis and gluconeogenesis. It is known that thyroid hormones status correlates with body weight and energy expenditure. (2) There was positive association between change of serum TSH concentration and weight change.(3) Because of the changes in weight, alteration of thyroid hormone level can cause changes in body mass index (BMI). There has been found a positive correlation between BMI and various thyroid hormone level in which higher thyroid hormone level associated with lower BMI.(4)

Body composition were used to describe the percentage of fat, muscle, bone and water in human body. There were various methods for body composition assessment including anthropometry, computed X-ray tomography (CT), magnetic resonance imaging (MRI), bone densitometry (DXA) and bioelectrical impedance analysis (BIA).

In this study, biolectrical impedance analysis (BIA) were used for body composition assessment. This method were widely used mainly because of its rapid processing of information, non-invasiveness, relatively inexpensive and used a portable instrument of easy handling. BIA method consisting of the passage of a painless electrical current of low amplitude through the organism, applied by means of cables connected to electrodes and conductive surfaces. Body composition were determined by measuring the resistance of the body as a conductor to a small electrical current. (5)

As mentioned earlier, thyroid hormone plays an important role in regulating body metabolism and energy comsumption. Studies showed that thyroid hormone dysfunction cause changes in body weight and BMI. Hyperthyroid assocated with weight loss, while hypothyroidism may cause modest increase in weight.(6) In view of this, we hypothesize that, thyroid dysfunction also can cause alteration in body composition. However, there were few studies on effects of thyroid hormone dysfunction on body composition. In this present study, we applied BIA to the investigation of body composition in patients with three different thyroid status; hyperthyroid, hypothyroid and euthyroid.

3.4 SUBJECTS AND METHOD

3.4.1 SUBJECTS

The present study was a cross sectional study, conducted from May 2019 until August 2019 involving patients with thyroid disease attended follow up at Endocrine Clinic, Hospital USM, age between 21-45 years old. A total of 47 patients fulfilled the inclusion and exclusion criteria and included in this study. The inclusions criteria were any patients with thyroid diseases, age between 21 to 45 years old with biochemical hyperthyroid, hypothyroid or euthyroid for more than 3 months. The following patients were excluded from the study : pregnant lady, post menopausal lady, breast feeding, patients who had chronic kidney disease, chronic liver disease, chronic gastrointestinal disease or any malignancy, patients who is on medication such as steroid, hormone replacement therapy, antiepileptic or immunosuppressive drugs that can affect body composition. Out of 47 patients, 18 patients were in hyperthyroid , 11 patients were in hypothyroid and 18 patients were in euthyroid state. All patients provided their written informed consent for paticipations before entering the study. For all patients, sociodemographic data, height, weight and BMI were obtained during clinic visit. Their blood investigations result were reviewed from Laboratory Information System (LIS) for thyroid function test. All available thyroid function test within last 12 months were recorded for each subjects.

3.4.2 BODY COMPOSITION ANALYSIS

Body composition analysis were performed by means of Bioelectrical Impedance Analysis Bodystat® Quadscan 4000 (Bodystat Ltd., Douglas, Isle Of Man). Body composition were calculated by the machine by measuring the flow of current through the body at four different frequencies 5, 50, 100 and 200 kHz. This multifrequencies allow the current to penetrate cell membrane as well as pass through extracellular and intracellular component. All body composition measurement were done at the bed side during same setting. To minimize the confounder for body composition such as food intake, physical activity and hydration status, subjects advised not to take any meals or drink 4 to 5 hours prior to the test, not exercise 12 hours prior to the test and not taking any alcohol or caffeine for 24 hours prior to the test . Subjects were given another date or time for body composition measurement if they did not fullfil any of the above recommendations.

3.4.3 STATISTICAL ANALYSIS

All the data collected were entered into SPSS database. The statistical analysis was performed with IBM Statistic Program for Social Sciences (SPSS version 24) software. Sociodemographic and clinical characteristic were tabulated for descriptive statistics. The numerical data were described in mean and standard deviation (SD) while categorical data were described in frequency and percentages. The numerical data comparing within groups were analysed using One Way ANOVA. A p-value of less than 0.05 ($p<0.05$) was considered to be statistically significant.

An ethical clearance was sought and obtained from Jawatankuasa Etika Penyelidikan Manusia Universiti Sains Malaysia (JEPeM) (USM/JEPeM/19040243).

The study complied with acceptable international standards including the Declaration of Helsinki.

3.5 RESULTS

Baseline sociodemographic and clinical characteristic of patients

A total of 47 patients with thyroid diseases were included in this study. From 47 patients, 40 (85.1%) patients were female while 7 (14.9%) were male. Majority of the patients in this study were Malay (95.7%) while only 2 (4.3%) were Chinese. 27 (57.4%) patients were diagnosed with Grave Disease, 10 (21.3%) with Multinodular Goitre and the other 10 (21.3%) patients diagnosed with other diagnosis which were Hashimoto Thyroditis, thyroiditis and congenital hypothyroid. (Table 1)

Among these patients, 18 (38.3%) patients were in hyperthyroid group, 11 (23.4%) patients in hypothyroid group and 18 (38.3%) patients in euthyroid group. The mean disease duration was 60 (±57.14) month while mean duration of current thyroid status (hyperthyroid, hypothyroid or euthyroid) was 7.13 (±4.07) month. Mean weight and BMI was higher in hypothyroid group with a mean (SD) of 73.13 (±17.93) and 27.83 (±4.78) respectively, with statistically significant difference between group (P <0.05). (Table 2) The mean age of patients was 32.85 (±7.43) years, range from 21 to 45 years old. There were no statistically significant association between age and thyroid status (Table 3).

Comparison of body fat composition in hyperthyroid, hypothyroid and euthyroid patients.

There was a statistically significant difference in mean total body fat (P = 0.047) between 3 groups. There was significant difference between hypothyroid and hyperthyroid patients (P=0.05) with patients in hypothyroid state have an average 6.69kg more fat compare with patients in hyperthyroid state. There were no significant difference in body fat composition between other group (P>0.05).(Table 4 and 5)

Comparison of body water composition in hyperthyroid, hypothyroid and euthyroid patients.

Body water composition were divided into 3 categories which were total body water (TBW), intracellular water (ICW) and extracellular water (ECW). For TBW composition, there was a statistically significant difference in mean TBW (P=0.05). There was a statistically significant difference of TBW composition between hypothyroid and hyperthyroid group (P=0.04) (Table 3) in which patients with hypothyroid have an average 6.34 liter more TBW compare to hyperthyroid patients (Table 5).

For ECW composition, there was no statistically significance difference noted in between 3 groups (P=0.139). For ICW composition, there was also no significant difference noted between 3 groups (P=0.072). From the finding above, we found that there were a statistically signicant differrence in total body water composition between hypothyroid and hyperthyroid patients, but no statistically sigificant difference for ICW and ECW .(Table 4 and 5)

Comparison of lean weight in hyperthyroid, hypothyroid and euthyroid patients.

For lean weight composition, there was a statistically significant difference noted in between 3 groups (P=0.039). Statistically significant difference noted between hypothyroid and hyperthyroid patients (P=0.036), in which hypothyroid patient have an average 3.5kg more dry lean weight compare to hyperthyroid patients. There were no statistically significant difference noted between other groups (P>0.05). (Table 4 and 5)

3.6 DISCUSSION

Thyroid disease is one of the commonest endocrine disorder. Several studies were done to study the effect of thyroid disease on body composition. This study was done to assess body composition in patients with known thyroid disease at 3 different thyroid hormone status.

Our study involved 47 patients with thyroid disease who were under treatment at Endocrie Clinic HUSM. Majority of the patients were female with mean age of 32.85 (±7.43), and 57.1% of the patients was diagnosed with Grave's disease. Data from previous study showed almost similar sociodemographic pattern. A study by Shahar *et al*, showed that majority of patients with thyroid disease in Malaysian adult population were female, with ratio female to male ratio was 2:1. (7) Grave disease were the commonest cause of hyperthyroidism and were more prevalence in women compare to men. (8)

In this study, patient with hypothyroid state had more weight and BMI as compare to hyperthyroid and euthyroid patients. Compared with other study, there were a relationship between obesity and thyroid hormone. Verma *et al*, showed that obesity

were more common in overt hypothyrodism (46% vs 34%) as compare to subclinical hypothyroid. (9) In a case-control study of patients with newly diagnosed overt autoimmune hypothyroidism identified in a population study versus matched euthyroid controls from the same background population, the patients weighed on average 7 kg more than the controls. (10)

For body composition assesment, our study demonstrate that body composition are associated with variation in thyroid hormone level. We found that patient with hypothyroid have more body fat, more total body water and more dry lean weight compare to hyperthyroid patients in this cohort. Previous study on body composition and thyroid status have a variable results. Findings in this study were similar with study done by Adam Stangierski *et al* as they found that hyperthyroid patient have lower body weight and fat mass as compare to hypothyroid patients. (11) Study by Hu *et al*, in which assessemnt of body composition done using BIA in 11 patients with hyperthyroid Grave disease, showed that hyperthyroid patient have increased ECW and lower body cell mass (BCM). (12) Another study of body composition in hyperthyroid patients using DXA scan showed that hyperthyroid patients have higher body fat and lower dry lean weight. (13)

In our study, body fat and lean weight were lower in hyperthyroid patients compare to hypothyroid patients. Hyperthyroidism increases protein turnover leading to the loss of muscle mass , accelerates thermogenesis and induces gluconeogenesis and lipolysis by metabolising amino acids from muscles and free fatty acids from adipose tissue (11). Hyperthyroid state also promotes calorigenesis by enhancing transmembrane Na/K-ATPase activity due to increase number of pumps. The increased transmenbrane exchange may result in loss of ICW and expansion of ECW (13). However, in our study we found no significant changes in ICW and ECW between 3 groups.

This difference in findings of the above result was attributed by few factors, such as relatively low number of patients in our study, different method of body composition used and also effect of confounding factor such as diet intake, physical activities and water intake that may affect the result. Further study with much larger patients with controlled confounding factor is needed in the future for better outcome and results.

3.7 CONCLUSION

The variations of thyroid hormone level can cause changes in body composition especially those with hypothyroid and hyperthyroid state. It may guide health care provider in nutrition management and advice for the patients with thyroid disease.

There are several limitations in our study. This study was a cross sectional study done at one centre only which was Hospital Universiti Sains Malaysia (HUSM), Kubang Kerian, Kelantan and due to the time constraint, only a small number of patients involved in this study. This might not represent Kelantan population as a whole. A much larger sample is needed to represent overall population. The cohort also limited to young adult age between 21 to 45 years old, which might not represent all age group of adults.

In addition, there are several limitations in using BIA to accurately determine body composition. Factors that may influence BIA measurement includes wrong lead or sensor placement, hydration status, excessive physical activities prior to the test, food consumptions, room temperature and medical condition such as peripheral edema and cutaneous disease that may affect electrode-skin electrical transmission. Besides that, different BIA machine may produced different value due to variations in manufactures