



Analysis of Ft4 and Tsh Levels in Controlled and Uncontrolled Type 2 Diabetes Patients

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Abstract: Diabetes melitus (DM) is a group of metabolic disease with the characteristic of hyperglycemia which occurs due to disturbance in insulin secretion, insulin work, or both. Diabetes melitus and thyroid disorder are endocrine disorders that are closely associated each other. This study aimed to determine the correlation between thyroid function in controlled and uncontrolled type 2 DM patients.

This is a retrospective study using secondary data from medical record. Data were collected from patients diagnosed with type 2 DM by the clinicians and were categorized into controlled and uncontrolled type 2 DM with FT4 and TSH assessment data. Data were analyzed with *Independent T-Test* and *Mann-Whitney test* using SPSS.

This study investigated 53 participants, divided into controlled DM (18.9%) and uncontrolled DM (81.1%). The population was dominated by females (75.5%) with the average age of 57.45 years old. The prevalence of thyroid function in this study were normal (84.95%), subclinical hyperthyroid (9.4%), and hyperthyroid (5.7%). There was no significant difference found in FT4 and TSH levels between controlled and uncontrolled type 2 DM patients with FT4 level (1.46 ng/dl \pm 0.59 vs 1.36 ng/dl \pm 0.66, $p = 0.490$) and TSH (1.66 μ IU/ml \pm 1.13 vs 1.07 μ IU/ml \pm 0.05, $p = 0.515$).

Conclusion: There was no significant difference of FT4 and TSH levels between controlled and uncontrolled type 2 DM

Keywords: FT4, TSH, Type 2 Diabetes Melitus

I. INTRODUCTION

Diabetes mellitus (DM) is one of metabolic disease characterized by hyperglycemia that occurs due to impaired insulin secretion, insulin mechanism of action or both. The prevalence of DM in 2017 worldwide is 451 million and estimated to reach 693 million in 2045. Increasing incidence of DM will be followed by an increase of its complications. Good glycemic control is a preventive measure to prevent complications. The American Diabetes Association (ADA) recommends measurement of HbA1c as long-term glycemic control marker in type 2 DM patients.

Diabetes mellitus and thyroid disorders are endocrine disorders that are related to one another. Thyroid hormones affect carbohydrate metabolism including insulin in hyperthyroid and hypothyroid states, thus

affecting glucose metabolism in type 2 diabetes. The correlation between DM and thyroid dysfunction has a very complex mechanism and involves many roles, including the synthesis of thyrotropin releasing hormone (TRH), thyroid stimulating hormone (TSH), and insulin resistance. Untreated thyroid dysfunction can interfere with metabolic control of DM patients hence the management of the disease becomes more complex.

The first study that showed the relationship between DM and thyroid function was published in 1979. Other studies have been carried out and have shown different estimates of the prevalence of thyroid dysfunction. The prevalence of thyroid dysfunction is greater in DM patients compared to non-DM patients. The prevalence of thyroid dysfunction in the general population is around 6.6-13.4% while in the diabetic population is around 20-24%.

Research conducted by Pasupathi et al. found that out of 100 DM patients, the prevalence of hypothyroidism and hyperthyroidism reached up to 28 and 17%. Research conducted by Imam et al. (2017) regarding thyroid dysfunction in type 2 DM patients at Cipto Mangunkusumo Hospital Jakarta showed that around 7.59% patients with type 2 DM patients have hypothyroidism while 2.31% type 2 DM patients had hyperthyroidism with a total of 9.9% type 2 DM patients had thyroid dysfunction. Research conducted by Sajeda A et al. (2017) in the Department of Endocrinology, Rangpur Medical College and Diabetic Association Rangpur in India mentioned that out of 50 newly diagnosed diabetic patients experienced a change in thyroid function, becoming towards hypothyroidism.

The American Thyroid Association (ATA), The British Thyroid Association and the American Diabetes Association (ADA) recommend routine TSH screening in patients with risk factors including type 2 diabetes. Currently, many are not aware of the complications caused by DM and thyroid disorders. Although thyroid disorders are common in patients with DM, they are often neglected and undiagnosed in the early stages.

In Indonesia, there is no policy regarding screening of thyroid function in DM patients due to the lack of evidence in the form of research that states the prevalence and relationship between thyroid function and DM patients, especially in Makassar. Therefore, the aim of this research is to search for differences of FT4 and TSH levels in controlled and uncontrolled type 2 DM patients.

II. RESEARCH OBJECTIVES

This study aims to observe the differences of FT4 and TSH in controlled and uncontrolled type 2 diabetes mellitus patients.

III. INDENTATIONS AND EQUATIONS

This study was conducted retrospectively by taking data from patients diagnosed with type 2 Diabetes Mellitus at Dr. Wahidin Sudirohusodo Hospital, Makassar from January 2017 to May 2019. Data was taken at the medical record installation at Dr. Wahidin Sudirohusodo Hospital.

Inclusion criteria were all patients aged ≥ 18 years diagnosed with type 2 diabetes who had thyroid examination results (FT4 and TSH) and HbA1c at Dr. Wahidin Sudirohusodo General Hospital from January 2017 to May 2019. Exclusion criteria were patients who received thyroid therapy and those with missing examination data (HbA1c, FT4 and TSH). Patient data with type 2 diabetes were grouped into controlled type 2 diabetes if the HbA1c level was ≤ 7 and uncontrolled if the HbA1c level > 7 and laboratory data search was carried out for FT4 and TSH levels. The results of HbA1c examination were obtained using the immunoturbidimetric method, while the FT4 and TSH levels were obtained by the Enzyme-linked immunosorbent assay (ELISA).

Data analysis was performed using SPSS and normality test was carried out using Kolmogorov-Smirnov and statistical tests using the Independent T-Test on normally distributed data and the Mann-Whitney Test on data

that were not normally distributed on the FT4 and TSH values in controlled and uncontrolled DM type 2 patients. The test results are significant if the p value <0.05.

Ethical clearance was obtained from the Health Research Ethics Commission, Hasanuddin University Faculty of Medicine - Dr. Wahidin Sudirohusodo Hospital Makassar No. 350 / UN4.6.4.5.31 / PP36 / 2019.

IV. FIGURES AND TABLES

Table 1. Shows the total subjects were 53 patients with a mean age of 57.45 years with the most susceptible age range of 29-79 years. Subjects were mostly women (75.5%), had uncontrolled diabetes (81.1%) and had normal levels of FT4 (77.4%) and TSH (81.1%). The prevalence of subjects with normal thyroid function, subclinical hyperthyroidism, hyperthyroidism were 84.95%, 9.4% and 5.7%, respectively.

Table 1. Characteristics of Subjects

Characteristics	N (%)	Mean ± SD	Min - Max
Gender			
- Female	40 (75.5)		
- Male	13 (24.5)		
Age		57.45 ± 10.37	29 - 79
Type of DM (HbA1C (%))			
- Controlled DM	10 (18.9)		
- Uncontrolled DM	43 (81.1)		
Type of Examination:			
FT4 (ng / dl)		1.38 ± 0.64	0.55 - 4.90
- Normal	42 (77.4)		
- No Normal	11 (20.8)		
TSH (µIU / ml)		1.46 ± 1.07	0.05 - 4.41
- Normal	44 (81.1)		
- Abnormal	9 (17.0)		
Subjects:			
- Normal thyroid function	45 (84.9 %)		
- Subclinical hyperthyroidism	5 (9.4%)		
- Hyperthyroid	3 (5.7%)		

Source: Secondary data

Table 2 shows the characteristics of subjects classified into controlled and uncontrolled DM type 2 groups. The results of the HbA1c on controlled and uncontrolled diabetes mellitus groups were significantly different (p <0.001), however there was no significant difference between FT4 and TSH (p = 0.490, p = 0.515) in controlled and uncontrolled group therefore it can be concluded that there was no significant differences of thyroid function in patients with controlled and uncontrolled type 2 diabetes.

Table 2. Differences in Controlled and Uncontrolled Thyroid Hormones

	Controlled DM			Uncontrolled DM			P
	SD	Mean	Min-Max	SD	Mean	Min-Max	
FT4 (ng/dl)	0, .59	1,46	1,02-2,52	0, 66	1.36	0.55-4.90	0.490 **

TSH (μ IU/ml)	1.13	1.66	0.05-3.46	0.05	1.07	0.05-4.41	0.515 *
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* Independent T-Test ** Mann-Whitneytest

This research was conducted from May to June 2019 using medical record data from January 2017 to May 2019 at Dr. Wahidin Sudirohusodo Hospital. This study used retrospective research design involving 53 subjects who met the inclusion and exclusion criteria.

The results showed women are more likely to have diabetes with an average age of 57.45 years. Research conducted by Nur (2015) in Banda Aceh stated that DM patients with HbA1c \geq 6.5% were most commonly found in women. Riskesdas 2007 also stated that the prevalence of DM was higher in women by 6.4% compared to men at 4.9%. Women have a greater chance of developing DM due to a greater increase in body mass index (BMI).

Increased incidence of DM is closely related to ageing. DM patients tend to be found in the older age group. This can be seen from research which showed that the majority of DM patients are elderly (46-65 years). Insulin resistance in the elderly can be caused by several factors, namely changes in body composition, decrease the amount of muscle mass (from 19% to 12%), an increase of adipose tissue (from 14% to 30%) resulting in reduced number and sensitivity of insulin receptors.

This study was not able to show a significant difference between FT4 and TSH in patients with controlled and uncontrolled DM. Similar result was also found in a study conducted by Al-Geffari et al. (2013) which showed poor glycemic control is not associated with thyroid dysfunction, and it is not a risk factor for thyroid dysfunction in type 2 diabetes. The prevalence of thyroid dysfunction reported by Al-Geffari et al. (2013) are hypothyroidism (25.3%), clinical hypothyroidism (15.3%), subclinical hypothyroidism (9.5%) and hyperthyroidism (3.2%). Similar results was also obtained by Ernita (2013) in Sleman which stated that there is no relationship between thyroid status, glucose levels and anemia in women of childbearing age. The same result was also found by Anik (2016) in Magelang which stated that thyroid status was not related to glucose levels and nutritional status in women of childbearing age.

Research regarding the prevalence of type 2 diabetes mellitus patients and its relation to thyroid dysfunction conducted by Mardianto et al (2010) in Adam Malik Hospital, Medan also stated that from 40 subjects, only 10% had thyroid function disorders. Research conducted by Imam et al (2017) in Cipto Mangunkusumo Hospital, Jakarta stated that 273 out of 303 subjects (90.1%) were euthyroid and only 9.9% of DM patients had thyroid dysfunction.

Studies in various countries regarding glucose control with thyroid dysfunction in type 2 diabetes show mixed results. Based on the guidelines for controlling thyroid disorders from the Ministry of Health in 2017, the risk factors for thyroid disorders consist of: age, sex, genetics, stress, family history of autoimmune-related diseases, contrast substances containing iodine, drugs and diet. None of the above risk factors states that type 2 diabetes mellitus can cause thyroid dysfunction.

Research conducted by Al-Geffari et al. (2013) stated that other causes of thyroid dysfunction in type 2 diabetes mellitus are family history of thyroid dysfunction. Patients with family history of thyroid dysfunction had a higher chance of developing thyroid dysfunction. However, family history of type 2 diabetes does not increase the risk of thyroid dysfunction. In this study, it was also stated that duration of illness, more than 10 years, was also a contributing factor of thyroid dysfunction. The limitation of this study is the usage of secondary data, hence data regarding duration of illness and family history of thyroid dysfunction can not be obtained.

The results of this study are not in line with research conducted by Cho et al. (2016) which stated that the risk of subclinical hypothyroidism was higher in the group with poor glycemic control at HbA1c levels \geq 9% compared to HbA1c levels $<$ 7%. Research conducted by Pandji (2016) in RSUD Dr. Moewardi, Surakarta stated that

glycemic control is related to thyroid dysfunction in type 2 DM patients with the most common dysfunction of subclinical hypothyroidism (61.54%).

Thyroid gland is the largest endocrine gland in the human body, located at the front of the neck. The thyroid gland produces thyroid hormones namely tyrosine (T4) and triiodothyronine (T3). The formation of thyroid hormone is influenced by a feedback mechanism involving the thyroid stimulating hormone (TSH). When production of thyroid hormone increases, the production of TSH decreases, and vice versa. Therefore, if the production of thyroid hormone decreases, the TSH will increase.

Thyroid hormone plays a physiological role in various metabolic processes (protein, carbohydrates, fat) and physiological activities in almost all organ systems. Lack or excess of thyroid hormone will interfere with various metabolic processes and activities, physiology, as well as growth and development of various tissues.

V. CONCLUSION

There is no significant difference between FT4 and TSH in controlled and uncontrolled type 2 DM patients.

VI. SUGGESTIONS

It is necessary to carry out further research using primary data by including other variables such as duration of diabetes and family history of thyroid disease

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