RELATION BETWEEN TIROID STATUS WITH GLYCEMIC CONTROL OF TYPE 2 DM PATIENTS AT RSPAD GATOT SOEBROTO

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ABSTRACT

Background: Diabetes Mellitus (DM) is a group of symptoms that arise due to increased blood sugar levels. Diabetes Mellitus type 2 has a higher risk of developing thyroid dysfunction. Thyroid dysfunction can affect various body metabolism and result in insulin resistance, significantly affecting glycemic control in DM patients. This study aimed to determine the relation between thyroid status as assessed by the level of thyroid-stimulating hormone (TSH), free thyroxine (FT4), and glycemic control (HbA1c).
Subjects and Method: A cross-sectional study. A sample of 38 DM patients was selected by purposive sampling. The dependent variable was glycemic control. The independent variables were TSH and FT4. Patients were classified into 4 quartiles (Q) based on their TSH and FT4 levels. Statistic test used was non parametric for category group of variables, which was Chi square test.
Results: Mean of fasting blood glucose was 200,56 mg/dL (modus 137 mg/dL), mean of 2 hours post prandial blood glucose was 247 mg/dL (modus 305 mg/dL). Subjetcs with poor glycemic control dominated as much as 76%. Most subjects had TSH level at Q4 (36%), while most of the subjects had FT4 level at Q1 (34%). The results showed that 38 samples with poor glycemic control were 72% in the 4th quartile (Q4) (> 3.1750 mU / L) TSH, and 64.7% were in Q1 (≤ 11.8400) FT4. The analysis showed that there was a significant relation between TSH (p = 0.047) and FT4 (p = 0.041) with glycemic control in type 2 DM patients.
Conclusion: FT4 and TSH levels relate to glycemic control in type 2 DM patients

Keywords: TSH, FT4, HbA1c, Diabetes Mellitus

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BACKGROUND

Diabetes mellitus (DM) is a collection of symptoms that arise in a person caused by an increase in blood glucose levels due to abnormalities in insulin secretion, insulin action or both (PERKENI, 2015). In 2015 there were 415 million cases of DM in the world and an estimated number every year (IDF, 2015). Indonesia is in the 7th position of the top 10 countries with the most DM sufferers in the world in 2015 (IDF, 2015). The incidence of DM in Indonesia at ≥ 15 years of age is 6.9%. Around 12 million sufferers and DKI Jakarta is in second place for areas with the most DM incidence in Indonesia (RISKESDAS, 2013).

According to the *World Health Organization* (WHO) In 2016 uncontrolled DM will cause complications that can be life-threatening, therefore controlling blood sugar levels plays an important role in preventing DM complications. Chronic hyperglycemia that occurs in DM can cause toxic effects on cells (Campos, 2012) which

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can lead to the formation of *Reactive Oxygen Species* (ROS). Increased levels of ROS in DM sufferers can cause oxidative stress which can trigger an inflammatory reaction. This can cause a deiodinase enzyme disorder that affects changes in thyroid hormones.

Insulin and thyroid hormone play an important role in the body's metabolic processes. if there is a disturbance in the thyroid hormone it can cause unfavorable effects for people with diabetes (Hage *et al*, 2011). These effects can affect metabolic control (blood sugar levels) in DM patients and can increase the risk of further complications (microvascular and macrovascular in the body's organs). Whereas in Indonesia there are not many thyroid function checks in DM patients routinely (Pramono, 2015).

According to research conducted by Ramesh *et al.* (2015) stated that the prevalence of thyroid disorders is higher in patients with type 2 diabetes than non-DM patients, with hypothyroid disorders being the most common. In addition, Billic-Komarica et al. (2012) stated that there was a strong relationship between TSH and HbA1c. Based on the description above, the researcher wanted to find out more about the relationship between thyroid status and glycemic control in type 2 DM patients at RSPAD Gatot Soebroto.

SUBJECTS AND METHOD

1. Study Design

A cross-sectional study with purposive sampling.

2. Population and Sample

The population was DM patients in RSPAD Hospital and samples that met the criteria were 50 people.

3. Study Variables

The inclusion criteria were type 2 DM patients. The exclusion criteria were no red blood cell abnormalities such as anemia.

4. Definition of Operational Study

Glycemic control is blood sugar control of type 2 DM patients in the last 3 months categorized as HbA1c <7% (controlled) and HbA1c> 7% (uncontrolled).

Thyroid status is the thyroid hormone status measured by looking at the level ofhormone *free thyroxine* 4(FT4) divided into 4 quartiles; Q1 (11,8400 ng / dL), Q2 (11,8401-15.5500 ng / dL), Q3 (15,5501-17.6525 ng / dL) and Q4 (> 17.6525 ng / dL). Thyroid status was also measured by looking at *thyroid stimulating hormonelevels* (TSH) which were divided into 4 quartiles; Q1 (≤0.6875 mU / L), Q2 (0.6876-1.5200 mU / L), Q3 (1.52001-3.1750 mU / L), Q4 (> 3.1750 mU / L).

5. Data Analysis

Bivariate analysis looked at the relationship between glycemic control and thyroid status in type 2 DM patients.

6. Study Ethics

This study has received ethical approval from the Health Research Ethics Commission of the Faculty of Medicine, National Development University "Veteran" Jakarta with number: B / 1164 / VII / 2017 / KEPK.

RESULTS

Number of respondents 50 patients consisting of 62 % female and 38% male. Age range was 26- over 65 years, 44% were 46-55 years old. The highest percentage of BMI is obesity 1 (36%).

The frequency distribution of TSH levels for Type 2 DM patients at RSPAD Gatot Soebroto is divided into Q1, Q2, Q3, and Q4 with the highest frequency at RSPAD Gatot Soebroto in 2017, namely in Q4 as

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many as 18 people (36%) and the smallest frequency, namely Q1 as many as 10 people (20%).

The frequency distribution of FT4 levels of Type 2 DM patients at RSPAD Gatot Soebroto is divided into Q1, Q2, Q3, and Q4 with the highest frequency of respondents at RSPAD Gatot Soebroto in 2017, namely in Q1 as many as 17 people (34%) and the smallest frequency in the Q4 group, namely 9 people (18%).

The frequency distribution of HbA1c levels in Type 2 DM patients at the Gatot Soebroto Army Hospital is divided into controlled and uncontrolled with the largest percentage in the Gatot Soebroto Army Hospital in 2017, namely in the uncontrolled group of 76% (38 people).

Percentage of uncontrolled HbA1c also increases at higher TSH levels. The results of the analysis of the relationship between TSH levels and glycemic control in type 2 DM patients showed that the percentage of uncontrolled glycemic control seen from HbA1c in each quartile (Q1,2 and Q3,4) was higher than that of controlled glycemic controls.

Based on the statistical test, the value of p = 0.047 The TSH Q3-4 hormone had a significant risk of worsening glycemic control 3.8 times compared to TSH Q1-2 (OR = 3.8; p value = 0.047).

The percentage of uncontrolled HbA1c also increased at higher levels of FT4. The results of the analysis of the relationship between FT4 and glycemic control in type 2 DM patients found that the percentage of uncontrolled glycemic control seen from HbA1c in each quartile (Q1,2 and Q3,4) was higher than that of controlled glycemic control. Based on the statistical test, the value of p = 0.041 FT4 Q1-2 hormone has 0.2 times the risk of worsening glycemic control compared to FT4 Q3-4 (OR = 0.2; p value = 0.041).

DISCUSSION

This study shows the results of the analysis that has been carried out with thetest *Chi-Square*, it was found that the p value = 0.047 for the relationship between TSH and glycemic control. This result is supported by research conducted by Acharya *et al.* (2016) which stated that there was a positive correlation between TSH and HbA1c (p = 0.397). In addition, Ram *et al.* (2017) reported that there was a positive correlation between serum TSH and HbA1c levels (r = 0.35, p = <0.0001).

This is also reinforced by research conducted by Petrosyan (2015) which states that when TSH is in the *low normal range*, the number of patients with poor glycemic control (HbA1c> 7%) decreased from 27.5% to 12.5% (p = 0.02). This could be because TSH can affect other networks (Felske, 2015). According to Csaba & Phíllinger (2009) some tissues such as adipose tissue and bone express TSH. In addition, Felske (2015) also stated that TSH affects insulin through several mechanisms. One of them is TSH activates lipolysis in adipocytes (Gagnon *et al.*, 2010).

In this study, it shows the results of the analysis that has been carried out with thetest *Chi-square*, it was found that the p value = 0.041 for the relationship between FT4 levels and glycemic control. This result is supported by research conducted by Sohal *et al.* (2016) who reported that 26 out of 30 hypothyroid patients found an increase in HbA1c levels (p = <0.005).

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1. Sample Characteristics

Table 1. Sample Characteristics

Characteristics	Category	Frequency	Percentage
Gender	Male	19	38%
	Female	31	62%
Age	Early Adult (26-35)	1	2%
	Late Adult (36-45)		
	Early Elderly (46-55)	3	6%
	Late Elderly (56-65)		
	Elderly> 65	22	44%
		14	28%
	Skininess	10	20%
	Normal		
BMI	Pre Obesity	1	2%
	Obesity I	11	22%
	Obesity II	14	28%
		18	36%
	Q1	6	12%
	Q2		
FT4	Q3	17	34%
	Q4	12	24%
		12	24%
	Q1	9	18%
	Q2		
TSH	Q3	10	20%
	Q4	11	22%
		11 11	22%
	<7%	18	36%
	> 7%		
HbA1c		12	24%
		38	76%

Table 2. Analysis of the Relationship between TSH and FT4 Levels on HbA1c in Type 2 DM Patients

Thyroid Status	HbA1c				OR	p value
	> 7%		<7%			
	N	%	N	%		
TSH						
Q1-2	13	61.9	8	38.1	3.8	0.047
Q3-4	25	86.2	4	13.8		
FT4						
Q1-2	19	65.5	10	34.5	0.2	0.041
Q3-4	19	90.5	2	9.5		

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This is reinforced by the theory stated by Ray S (2016) which states that thyroid hormone has an effect on glucose and lipid metabolism and directly affects insulin regulation and *glucose disposal* in peripheral tissues. In addition, according to Brenta (2010), the effect of thyroid hormone on blood glucose control is through several mechanisms, namely modification of insulin levels and influencing *uptake* glucosein peripheral tissues.

The thyroid hormone represented by FT4 can affect blood glucose control which is important for DM sufferers. Archarya *et al*. (2016) also reported that thyroid hormone disorders in patients with diabetes were characterized by an increase in TSH and a decrease in FT3 and FT4. This thyroid hormone-influenced effect has an adverse effect on the disease course of DM patients.

In conclusion, there is a significant relationship between TSH and FT4 with glycemic control in type 2 DM patients.

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