

Original article

**Proportion of Subclinical Hypothyroidism in Patients
with Diabetes Mellitus**

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Abstract:

Background: According to some recent studies, a connection exists between type 2 diabetes mellitus (T2DM) and the occurrence of subclinical hypothyroid (SCH). This purpose of this research was therefore, to determine the proportion of SCH in those diagnosed with T2DM. **Materials and Methods:** Data was obtained for this cross-sectional study by analyzing 278 patients suffering from T2DM for at least 1 year. The collected data include glycemic control (HbA1c) and thyroid hormone. Those with triiodothyronine (fT3), thyroxine (fT4), and TSH (≥ 4 μ IU/ml) were suffered from SCH and examined with ultrasonographic (USG) for clinical screening of thyroid diseases. **Results:** Approximately 7.2% patients with T2DM were above 60 years with significant differences in number of men and women diagnosed with diabetes mellitus. There is also a significant correlation between HbA1c and SCH in T2DM. Among 20 subjects with SCH, USG thyroid suggested thyroiditis in 15 subjects. **Conclusions:** The prevalence of SCH among T2DM patients is high, therefore, all those with T2DM need to be examined for thyroid dysfunction.

Keywords: type 2 diabetes mellitus, subclinical hypothyroidism,

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Introduction

Some of the commonest endocrine diseases in adults are diabetes mellitus and thyroid dysfunction.¹ SCH is the most common thyroid dysfunction with an overall prevalence of 12-16%.^{2,3,4} It is high in diabetic patients, which confirms that the disease is a secondary result of an autoimmune reaction.^{5,6} Furthermore, it is characterized as thyroid stimulating hormones (TSH) irrespective of the presence of free triiodothyronine (fT3) and thyroxine (fT4), without the inclusion of clinical signs, and in the absence of other causes of elevated serum TSH.^{7,8}

The T2DM patients with SCH stand a higher chance of experiencing cardiovascular complications.⁹ Therefore, it is important to screen patients with

diabetes because most are asymptomatic. This research aims to determine the occurrence of SCH in Indonesian T2DM patients using clinical routine.

Materials and Methods

The data used to carry out this cross-sectional study was obtained from a sample of two hundred and seventy-eight adult outpatients from the metabolic-endocrine division of Cipto Mangunkusumo Hospital in Jakarta, diagnosed with T2DM for at least one year. Subjects with type 1 diabetes mellitus and pre-existing thyroid diseases were excluded from this study. Data were retrieved from medical records and laboratory tests between March to April 2016. The level of HbA1c, serum cholesterol, triglyceride, LDL and HDL were also observed. The patients with

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triiodothyronine (fT3), thyroxine (fT4), and TSH (≥ 4 μ IU/ml) were diagnosed with SCH and analyzed with USG explorations of the thyroid gland used to screen for thyroid diseases.

Statistical Analysis

Windows version 15.0 was used to carry out the statistical analysis. In addition, the Chi-square test was utilized to categorize variables in the two groups. The test was considered statistically significant, using a two-tailed p -value of <0.05 .

Results

Two hundred and seventy-eight adults diagnosed with diabetes were studied. The age range was 37–86 years (median: 60 years), comprising 116 males (42%) and 162 females (58%), with the populations bio-data shown in table 1. The study shows that the proportion of SCH in T2DM is 20 subjects (7.2%), with only 2 diagnosed with overt hypothyroidism. Table 2 shows that all subjects with SCH have a serum TSH between 4-10 mIU/L with the majority above 60 years. In addition, table 3 showed no differences in the proportion between women and men. This study, therefore, aims to examine the relationship between SCH and glycemic control in patients with T2DM. The analysis showed patients suffering from T2DM with poor glycemic control (HbA1C >7) stand a greater risk of 3.664 times in developing SCH compared to those with good glycemic control as shown in Table 4. The study showed that among the 20 patients diagnosed with SCH, and USG thyroid analysis, 15 had thyroiditis while the rest showed nodular or multi-nodular goiter.

Discussion

One of the most prevalent diseases of the endocrine system is hypothyroidism. According to studies, diabetic patients have a greater occurrence of thyroid disorders with autoimmunity termed a major cause of thyroid-dysfunction.¹⁰ Therefore, patients with autoimmune disease stand a risk of being diagnosed with other types of diseases. A number of reports have shown that SCH is one of the most common thyroid disorder.^{2,3,4} **The best screening test for** thyroid disease, with increased values is by measuring the serum TSH which is used to determine the early stage of hypothyroidism. The condition overtly develops in patients with low free T4 and raised TSH. However, there is an uncertain rise in TSH among diabetic patients due to a complex interdependent interaction.¹¹

SCH is difficult to diagnose because symptoms do not occur, which is often overlooked. This study showed that the 7.2% of those with T2DM suffered from SCH. The result also provides a vivid picture of the presence of SCH in T2DM patients, although the frequency is lower than those described by authors from other studies.^{2,3,4} The present study shows that the risk of SCH increases with age.^{12,13} However, there were no significant difference between men and women suffering from SCH due to a low number of subjects. According to various studies, women have a greater percentage of having SCH compared to men.¹ There is great variability in diabetic patients, due to the varying diagnostic criteria of SCH, degree of iodine intake, varying TSH assays, and large population.¹⁴

Thyroid USG is one of the most sensitive techniques used to examine abnormalities in the thyroid gland. It is also used to examine its structure. Meanwhile, auto-immune thyroiditis is the common cause of SCH which is a milder form of hypothyroidism, thereby making it difficult to detect thyroiditis antibody. Thyroid USG is also crucial in the differential diagnosis of hypothyroidism and provides early evidence for thyroid autoimmunity.^{15,16} The typical appearance of autoimmune thyroiditis includes inhomogenous and hypoechogenic patterns. In this study, among the 20 patients with SCH, thyroid USG analysis, 15 showed inhomogenous and hypoechogenic patterns while the rest had nodular or multi-nodular goiters. This echographic pattern indicated that thyroiditis is associated with the development of SCH and Hashimoto's disease.

HbA1c is a blood test performed to monitor the controlled blood glucose level in patients with diabetes. The higher the number, the more difficult it is to control the diseases. This study showed that patients with poor glycemic control (HbA1C >7) have approximately 3.664 times greater risk of being diagnosed with SCH compared to those with T2DM. The correlation between HbA1c and SCH in T2DM patient is significant, due to insulin resistance, thereby leading to poor glycemic control.^{17,18}

No establishment has been developed to test patients with thyroid by determining their serum TSH levels. According to previous researches, those diagnosed with SCH have an increase rate of contacting cardiovascular diseases.¹⁹ Meanwhile, this study showed a high frequency of SCH in

T2DM patients. The essential ramification of SCH is its high rate to clinical hypothyroidism, which leads to an increase in cardiovascular risk. Therefore, screening for thyroid disease among old patients with poor glycemic control helps in detecting complications early. Before using the screening technique on diabetic population, Large-scale randomized trials need to be carried out on diabetic patients, before routine screening on the entire population.

Limitation of the study: There are some limitations of this research. This is due to the use of a cross-sectional design, which made it difficult to fully establish the causality between T2DM and SCH. The second limitation is the use of a convenience sample to determine treated diabetic patients. Thirdly, the number of subjects was limited.

Conclusion and Recommendations

This study showed that the incidence of SCH caused by autoimmune thyroiditis is higher among diabetic patients. In addition, patients diagnosed with SCH stand a higher rate of contacting hypothyroidism. Therefore, screening for thyroid disease needs to be considered in elderly diabetic patients, due to the high prevalence of SCH as comorbidity as well as the classical risk factors, arising from an undiagnosed SCH. This tends to allow early detection and possible correction of complications, thereby improving general patient care.²⁰

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Disclosure statement: The authors declare no conflicts of interest.

Ethical approval issue: This research received approval from the Ethics Committee Faculty of medicine, University of Indonesia.

Individual authors contribution: Idea owner of this study: HH, LAP, DSH, IS., Data gathering: HH, LAP, DSH, IS., Writing and submitting manuscript: HH, LAP, DSH, FNA, IS, SS., Editing and approval of final draft: HH, LAP, DSH, FNA, IS, SS.

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TABLE

Table 1. Clinical characteristics of the study participants

Characteristics	Category	Total (n %)
Sex	Male	128 (42,8)
	Female	171 (57,2)
Age	median	60 (37-86)
	≥ 60 y.o	140 (50,4)
	< 60 y.o	138 (49,6)
Glycemic control	HbA1c ≥ 7%	153 (51,2)
	HbA1c < 7%	146 (48,8)
Thyroid status	Euthyroid	256 (93,8)
	Subclinical hypothyroid	20 (7,20)
	Overt hypothyroid	2 (0,72)

Table 2. The proportion of hypothyroid in patients with type 2 diabetes associated with age

Variable	Total n (%)	SCH n (%)	Overt hypothyroid n (%)	Euthyroid n (%)
Sex				
Male	116 (41,7)	10 (3,6)	0 (0,00)	106 (38,10)
Female	162 (58,3)	10 (3,6)	2 (0,72)	129 (55,70)
Total	278 (100)	20 (7,2)	2 (0,72)	256 (93,80)

Table 3. The proportion of hypothyroid in patients with type 2 diabetes associated with sex

Variable	Total subject n (%)	SCH n (%)	Overt hypothyroid n (%)	Euthyroid n (%)
Age				
≥ 60 y.o	140 (50,4)	12 (4,32)	1 (0,36)	127 (45,68)
< 60 y.o	138 (49,6)	8 (2,88)	1 (0,36)	129 (46,40)
Total	278 (100)	20 (7,2)	2 (0,72)	256 (93,80)

Table 4: Relation of glucose control (HbA1c) with SCH in patients with type 2 diabetes

Variabel	SCH		OR (95% CI)	P
	Yes	No		
HbA1c				
≥ 7	16 (12,6)	127 (88,8)	3,664 (1,257-10,680)	0,010
< 7	4 (3,1)	131 (96,9)		

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