

Original article:

Hypothyroidism in patients with type 2 diabetes and its relation to depression, excessive daytime sleepiness, and glycated hemoglobin in Tabuk, Saudi Arabia, A case-control study

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Abstract:

Introduction: Diabetes mellitus and hypothyroidism are common health problems, both hypothyroidism and diabetes can lead to depression and excessive daytime sleepiness necessitating special consideration in management

Objectives: we aimed to study hypothyroidism in diabetes mellitus, and its relation to depression, daytime sleepiness, and HbA1c.

Material & Methods: This case-control study conducted at King Khalid Hospital, Saudi Arabia among 178 diabetic patients and 100 controls during the period From March to June 2015. Patients were invited to sign a written informed consent, then interviewed using a standard questionnaire based on the Beck Depression Inventory, the Epworth Sleepiness Scale, and demographic data. A blood sample was taken for thyroid function tests and glycated hemoglobin. The ethical committee of King Khalid Hospital approved the research, and the chi-square test used to compare categorical data, A P-value of <0.05 was considered significant

Observations & Results: Hypothyroidism was evident in 16.2% of diabetic vs.0% in controls patients, daytime sleepiness in 6.7% vs. 0% controls, while depression was concluded in 61.8% of diabetic patients vs. 30% of control subjects. No statistically significant difference was found between diabetic patients with hypothyroidism and those with normal thyroid function regarding depression, excessive daytime sleepiness, and Glycated hemoglobin P-value<0.05.

Conclusions: Hypothyroidism was more prevalent among diabetic patients compared to control subjects, no relationship was observed between hypothyroidism, depression, excessive daytime sleepiness, and HbA1c.

Keywords: Hypothyroidism, diabetes, depression, sleepiness.

Introduction:

Diabetes mellitus is a global epidemic with 415 million people living with the disease. In the Middle East and North Africa, the number is 35.4 million, and this figure is expected to reach 72.1 million by the year 2040, according to World Health Organization, three million people die from diabetes mellitus or its complications every year, and the number is expected to double by the year 2030. The prevalence of diabetes mellitus in Saudi Arabia is 17.6% as one of the highest rate worldwide [1-3].

Hypothyroidism is a common health issue worldwide with 4-5% prevalence and 4-15% of subclinical hypothyroidism [4]. In Saudi Arabia, 7% of the populations had hypothyroidism [5]. Diabetes mellitus and thyroid dysfunction are the most common two endocrine disorders worldwide. Furthermore, the relationship is bidirectional with prediabetes predisposing to thyroid dysfunction in the form of low free T3, increased reverse T3, and normal free T4 and TSH, on the other hand, thyroid dysfunction is

associated with both types of diabetes mellitus [6]. The biguanide metformin a principal first line drug in type 2 diabetes is linked to thyroid hormone reduction in untreated hypothyroidism (7). Hypothyroidism had been associated with insulin resistance while the relationship between subclinical hypothyroidism and diabetes is controversial, moreover, hypothyroidism when to co-exist with diabetes mellitus substantially increase both macrovascular and microvascular complications (8). Insomnia manifested by failure to initiate or maintain sleep is common in patients with depression, on the other hand, people with obstructive sleep apnea and excessive daytime sleepiness are more prone to depression, however most of the scales used for the diagnosis of depression inquire about fatigability and insomnia and not daytime sleepiness, so the latter may be underestimated (9) Data about hypothyroidism, depression, and daytime sleepiness among patients with diabetes in Saudi Arabia are scarce and mostly on type 1 diabetes. Thus, we conducted this research to study the relation of hypothyroidism, depression, and daytime sleepiness among patients with type 2 diabetes mellitus in the diabetes Center-Tabuk, Saudi Arabia.

Subjects and Methods:

This case-control study conducted at the Diabetes Center at King Khalid Hospital in Tabuk during the period March to June 2015. One hundred and seventy-eight patients with type 2 diabetes were asked to sign a written informed consent form then interviewed using a structured questionnaire. Information collected include demographic data, duration of diabetes, height, weight, and body mass index [BMI] as calculated by the formula: $\text{body mass index} = \text{weight} / (\text{height in meters})^2$. Hypothyroid status was confirmed by the history of hypothyroidism, if on thyroxine replacement for thyroid failure or thyroid function tests. Depression was assessed by the Beck Depression Inventory-11 (BDI-11) a well-validated questionnaire for the diagnosis of depression (10), the Epworth Sleepiness Scale (ESS) was used for the daytime sleepiness assessment, the (ESS) had been previously validated (11). A blood sample was taken for Glycated hemoglobin estimation for the degree of control using a glycol hemoglobin reagent set from HB1C Siemens Healthcare Diagnostics Newark, DE 19714, USA. Comparisons then were undertaken between diabetic patients and healthy controls, and patients with and without hypothyroidism. The ethical committees of both the University of Tabuk, and King Khalid Hospital approved the research and the Statistical Package for Social Sciences (SPSS version 20) was used, the chi-square test was used to compare categorical data with a P-value of < 0.05 considered significant.

Observations & results

They were 178 diabetic patients and 100 healthy control subjects their age ranged from 28-75 years with a mean of 47.6 ± 12.32 , their body mass index was 28.93 ± 5.75 , the duration of diabetes mellitus was 6.72 ± 5.86 , HbA1c was 8.6 ± 4.1 , the Epworth Sleepiness Score was, 4.43 ± 2.52 , and the total sleeping hours/night was 7.44 ± 1.19 hours Table No (1).

Table No (2) illustrated the comparison between diabetic and control subjects in which hypothyroidism was commoner among diabetic patients as compared to control subjects (16.2% vs. 0%) with high significant statistical difference P-value < 0.001, depression was found in 61.8% in diabetic patients and 30% of control P-value < 0.001, the daytime sleepiness was evident in 6.7% of diabetic patients and not found in control subjects P-value < 0.001, sleeping less than 6 hours/night was reported in 19.6% of

patient and 19% of healthy controls with no significant statistical difference P-value 0.893, a significant statistical difference was reported between patients and control as regarding failure to initiate sleep (92.7%vs.85%) P-value 0.041, while no significant difference was found regarding the inability to maintain sleep (7.3%vs. 14%) P-value 0.070. In the current study poor diabetes control was evident in 34.4% of hypothyroid patients and 32.8% of patients without hypothyroidism P-value 0.597 with no significant statistical difference, the daytime sleepiness was concluded in 4.3% of hypothyroidism as compared to patients with normal thyroid function 7.3% and P-value 0.439. Table No (3) depicted the comparison between diabetic patients hypothyroidism and those with normal thyroid function.

Table No. (1): Characteristics of the study group

Character	Mean± SD
Age	47.6±12.32
Sleeping hours/night	7.44±1.19
ESS	4.43±2.52
BMI	28.93±5.75
Duration of diabetes	6.72±5.86
HbA1c	8.6±4.1

Table No (2): Comparison between diabetic patients and control subjects regarding hypothyroidism, depression, anxiety and sleep character

Character	Diabetic No=178	Controls No=100	P-value
Hypothyroidism	29 (16.2%)	0 (0%)	0.000
Depression	110(61.8%)	30(30%)	0.000
Daytime sleepiness	12 (6.7%)	0 (0%)	0.008
Sleeping< 6hours	35 (19.6%)	19 (19%)	0.893
Failure to initiate sleep	165 (92.7%)	85 (85%)	0.041
Failure to maintain sleep	13 (7.3%)	14 (14%)	0.070

Table No (3): Comparison between diabetic patients with and without hypothyroidism regarding depression, anxiety and sleep character

Character	Hypothyroid No=29	Normal No=149	P-value
Depression	15 (51.7%)	95(63.7%)	0.322
Daytime sleepiness	1 (3.4%)	11 (7.3%)	0.439
Sleeping< 6hours	5 (17.2%)	30 (20.1%)	0.720
Failure to initiate sleep	28 (96.5%)	137 (91.9%)	0.383
Failure to maintain sleep	1 (3.4%)	12 (8%)	0.383
HbA1c> 8	10 (34.4%)	49 (32.8%)	0.597

Discussion:

In hypothyroidism glucose absorption from the gastrointestinal tract and glucose utilization by peripheral tissues are slowed, also insulin secretion decrease and its half-life increase leading to reduced requirements, which may result in higher glucose level after the introduction of thyroxine and In the present study hypothyroidism was found in 16.2% in (normalization of thyroid function 12). diabetic patients and not detected in control subjects with a high significant statistical difference, similarly Akbar et al. (13) in his study in Saudi diabetic patients concluded a prevalence of 16%. Research conducted in Spain (14) found similar finding of hypothyroidism among patients with diabetes mellitus. In accordance with the present results, Algefri et al. reported clinical hypothyroidism in 15.3% of patients with diabetes mellitus (15). The current finding was higher than studies conducted in Jordan (16), this can be explained by the high prevalence (26%) of latent autoimmune diabetes of adult (LADA) in Saudi Type 2 diabetics (13). In the present study hypothyroidism was commoner among

Females 23 (79.3%) a previous survey conducted in Saudi Arabia concluded similar results (14). In the current research, depression was concluded in 61.8% of diabetic patients with a high significant statistical difference between patients and control similar to Palizqir in Iran who reported depression in % of diabetic patients (17). The current data concluded excessive daytime sleepiness in 6.7% of diabetic patients in accordance with Cho et al., who observed daytime sleepiness in 8.5% of diabetic patients (18). The association of thyroid function and depression is controversial; the current data observed no significant statistical difference regarding depression among hypothyroid diabetic patients and diabetic patients with normal thyroid function; similar previous researchers reported no association between thyroid function and depression (19,20).

In contradiction to the present study Itermann et al. (21) concluded the association between untreated hypothyroidism and depression, one plausible explanation can be all of the patients in the current study were on thyroxine therapy Recent research (22) concluded that no significant difference in HOMA-IR and BMI values among high normal and high TSH levels. Similarly, the current study showed no significant difference between hypothyroid patients and normal thyroid function regarding the glycated hemoglobin. In the present study patients with hypothyroidism had similar ESS score to non-hypothyroid, in accordance to Shinno et al. (23) who observed an improvement in ESS in hypothyroid patients after receiving thyroxine therapy.

Conclusion:

Hypothyroidism was commoner among patients with diabetes mellitus, but not associated with depression, excessive daytime sleepiness, and glycated hemoglobin. Limitation of the present study are: the small size of the survey group, single-center study, and we cannot control for other variables that affect HbA1c like anemia, the reliance on a self-reported questionnaire to assess depression, and daytime sleepiness is more prone to subjectivity.

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