Irish Journal of Medical Science (1971 -) (2020) 189:171–175
https://doi.org/10.1007/s11845-019-02082-9

ORIGINAL ARTICLE

The prevalence and incidence of thyroid dysfunction in patients with diabetes - a longitudinal follow-up study

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Received: 28 November 2018 / Accepted: 6 August 2019 / Published online: 20 August 2019

Abstract

Background Thyroid dysfunction (TD) occurs in 13.4% of diabetic patients, which has prompted recommendations for annual thyroid screening in patients with diabetes. However, recommendations for annual screening should be based on disease incidence rather than prevalence.

Methods In 1997–1998, seven hundred and thirty patients (618 type 2 diabetes, 55% male; 112 type 1 diabetes, 47% male) were sequentially screened for TD. The 639 patients with normal thyroid function were followed from 1999 to 2006, with annual thyroid function tests.

Results A total of 21/112 (19%) with type 1 diabetes (T1DM) and 70/618 (11%) with type 2 diabetes (T2DM) had TD. TD was more frequent in females ($p < 0.05$) and T1DM ($p = 0.04$). The mean annual rate of conversion to abnormal tests was 2.1%. At 8 years, there were 100 new cases of TD representing 15.6% of the cohort (17 T1DM and 83 T2DM). TD was more frequent in females ($p < 0.05$), but there was no difference in the incidence of new TD between T1DM and T2DM ($p = 0.39$).

Conclusions Our data confirms the high prevalence of TD in diabetic patients, in concordance with the results from other series. We found only 25 treatable cases of new thyroid disease from 639 patients in the 8-year follow-up, less than 0.5% per year. The low incidence of treatable thyroid disease challenges the need for annual screening for thyroid abnormalities in patients with type 2 diabetes.

Keywords Diabetes mellitus · Incidence · Prevalence · Thyroid disease · Thyroid dysfunction

Background

Thyroid disorders are common in the general population [1]. It has been reported that 7.5% of women and 2.8% of men in all ages in Whickham, UK, had abnormal serum thyroid stimulating hormone (TSH) concentration [2]. The Colorado Thyroid Disease Prevalence Study reported that 11.7% of subjects attending a statewide health fair had abnormal serum TSH concentration [3]. The prevalence of thyroid dysfunction increases with advancing age [4–8]. In 20 years of follow-up, the Whickham study reported a mean annual incidence of spontaneous hypothyroidism of 4% per annum, but a higher incidence of 27% per annum in women with positive thyroid antibodies [2]. The incidence may vary with ethnicity, as higher rates of 15–30% have been reported in Indian patients [9, 10] and in 40% of Greek patients [11]. A 2015 meta-analysis of 61 studies showed that subclinical hypothyroidism was more common in patients with diabetes and predisposed them to higher complication rates [12].

Thyroid disorders are the most prevalent autoimmune diseases in patients with diabetes, occurring in 12–24% of patients with type 1 diabetes (T1DM) and in 3–6% of people with type 2 diabetes (T2DM) [13–16]. As the published data suggests an increased prevalence of thyroid dysfunction in subjects with T1DM and T2DM, regular screening for thyroid dysfunction is recommended [13, 14, 17]. However, the recommendations for thyroid screening have been made on the basis of prevalence data; in a prospective study, the incidence of abnormal thyroid function was only 1% of patients per annum [18].

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Aims

The aim of this study was to determine the incidence of new thyroid dysfunction in a diabetic population attending our outpatient clinics from 1997 to 2006.

Methods

We identified a sample of 730 consecutive patients attending our Diabetes Outpatient Clinic from 1997 to 2006. This large adult diabetic clinic serves a predominantly urban, Irish population. As part of their annual review assessment, all patients had thyroid function tests (TFT) with measurement of TSH and free thyroxine (FT4). The diagnosis of TD had been established either in the Diabetes Outpatient Clinic or during interim patient reviews with their general practitioners. All the respective patients were included in our analysis. Data were collected from annual review spreadsheets and a computerized laboratory database.

Patients with newly diagnosed or previously treated thyroid disease in 1997–1998 provided prevalence data, and the patient cohort with normal thyroid function tests, who had thyroid function measured annually thereafter, provided incidence data.

Measurements of thyroid function

Serum TSH and FT4 concentrations were measured by Auto Delfia and Beckman DXI 800 assays. The normal ranges for FT4 and TSH were 7–16 pmol/l and 0.5–4.2 mU/l, respectively. According to the results of thyroid function tests, patients were divided into five groups: (1) normal, when TSH and T4 were in normal range; (2) overt hypothyroidism, when total TSH was > 4.2 mU/l and F4 was < 7 pmol/l; (3) subclinical hypothyroidism, when FT4 was within normal limits but TSH > 4.2 mU/l; (4) overt hyperthyroidism, when the serum TSH value was suppressed to < 0.03 mU/l and F4 was > 16 pmol/l; (5) subclinical hyperthyroidism, when FT4 was within normal limits but TSH < 0.1 mU/l.

Treatment was initiated for the patients diagnosed with subclinical hypothyroidism on the basis of a serum TSH concentration greater than 10 mU/l, strongly positive thyroid antibodies, or development of symptoms.

The patients with newly diagnosed subclinical hyperthyroidism were treated if they met one the following criteria: (1) age 65 years or older; (2) associated co-morbidities, such as heart disease or osteoporosis; (3) symptoms of hyperthyroidism; (4) postmenopausal not taking estrogen or bisphosphonates.

Statistical analysis

Statistical analysis was performed using SPSS, version 11.5. Categorical variables were compared by chi-square test. Statistical significance was defined as $p < 0.05$. Values are presented as percentage or median (range).

Results

Prevalence of thyroid disease

The median age of our cohort of 730 patients who attended the diabetic clinic in 1997/1998 was 60 years (range 20–91).

The group is composed of 112 (15%) patients with T1DM, 53 (47%) females and 59 (53%) males, and 618 (85%) patients with T2DM, 275 (45%) females and 343 (55%) males. Patients with T2DM were older (median 64 years, range 32–78) compared with the patients diagnosed with T1DM (median 24 years, range 16–66) ($p < 0.001.9$).

We found that of the 730 patients, 91 had previous or newly diagnosed thyroid dysfunction. Hypothyroidism was identified in 15, hyperthyroidism in 9, subclinical hypothyroidism in 48, and subclinical hyperthyroidism in 17, and 2 patients had thyroid surgery and hypothyroidism as a result.

The prevalence of thyroid dysfunction was highest (26%) in female T1DM patients and lowest (8%) in male T2DM patients (Table 1). The frequency of thyroid dysfunction was statistically higher in patients with T1DM (19%) than T2DM (11%) ($p = 0.04$, chi-square) and also in females than males ($p < 0.05$, chi-square) in both types of diabetes.

Annual incidence of new thyroid disease

At baseline, 693 patients had normal thyroid function and proceeded to have annual TFT from 1999 to 2006. New thyroid dysfunction was found in 100 patients during this 8-year period. This gave a mean annual incidence of thyroid dysfunction of 2.6% in patients with T1DM and 2.0% in patients with T2DM ($p = 0.39$, chi-square) (Table 2).

Table 1 Prevalence of thyroid dysfunction in the initial cohort in 1997/1998. Prevalence data from work of Perros et al. is given for comparison [14]

	Gender	*n* (%)	Perros et al. 1995 (%)
Type 1 diabetes	Male	7 (12%)	12%
N = 21 (19%)*	Female	14 (26%)	31%
Type 2 diabetes	Male	28 (8%)	7%
N = 70 (11%)*	Female	42 (15%)	11%

*$p = 0.037$ type 1 vs type 2 diabetes

Table 2 Annual incidence of newly diagnosed thyroid dysfunction from 1999 to 2006

	Type 1 diabetes *n* (%)	Type 2 diabetes *n* (%)
1999	2 (2.2%)	19 (3.5%)
2000	4 (4.5%)	9 (1.7%)
2001	3 (3.5%)	10 (1.9%)
2002	2 (2.5%)	13 (2.5%)
2003	2 (2.5%)	12 (2.4%)
2004	1 (1.3%)	6 (1.2%)
2005	1 (1.3%)	4 (0.8%)
2006	2 (2.6%)	10 (2.1%)
Mean %	2.6%	2.0%

Overt hypothyroidism was diagnosed in 7 patients, overt hyperthyroidism in 2 patients, subclinical hypothyroidism in 48 patients, and subclinical hyperthyroidism in 43 patients.

Females in both type 1 and type 2 diabetes mellitus categories had higher frequency of new thyroid dysfunction than males ($p < 0.05$, chi-square) (Table 3). Patients with T2DM and an initial presentation TSH of 1.0–3.0 mU/l had a decreased probability for development of thyroid dysfunction (odds ratio, 0.57; 95% CI, 0.36–0.92; $p = 0.02$; risk ratio, 0.63; 95% CI, 0.42–0.93; $p = 0.02$) compared with the patients with TSH level above or below these levels during 8 years of follow-up.

Newly diagnosed patients with hypo- and hyperthyroidism were treated accordingly, but only 14 patients with subclinical hypothyroidism and 2 with subclinical hyperthyroidism met the treatment criteria mentioned in the "Methods" section above.

Conclusions

This prospective study reconfirms the association between thyroid dysfunction and diabetes. Previously reported prevalence of thyroid dysfunction in patients with diabetes varies widely between studies. Cross-sectional studies have reported a prevalence of thyroid dysfunction in 12–24% of female patients with T1DM and 6% of male patients with T1DM, as well as in 3–6% of patients with T2DM [14–16, 19]. These studies have provided a rationale for routine screening for thyroid dysfunction to be incorporated into the annual review of diabetic patients. Screening for thyroid dysfunction may prevent the development of symptomatic thyroid disease and may allow early treatment of hyperlipidemia [5, 20] and prevention of metabolic bone disorders [22]. Subclinical hypothyroidism is a strong indicator for atherosclerotic disease and acute coronary events, particularly in the elderly population [21]. Untreated hypothyroidism has been associated with worse metabolic control, including dyslipidemia [11], higher rates of microvascular complications [12], and increased rates of coronary artery disease in type 2 diabetes [23]. In one study, thyroid hormone replacement has been associated with lower rates of acute coronary insufficiency and cerebrovascular disease [24], so appropriate screening and treatment may reduce the burden of disease in diabetes.

Table 3 Total number of new cases of thyroid dysfunction in 8 years of follow-up

	Gender	*n* (%)	*p***
Type 1 diabetes	Male	4 (8.3%)	0.01
N = 17 (18.7%)	Female	13 (28.9%)	
Type 2 diabetes	Male	33 (10.5%)	0.0004
N = 83 (15.1%)	Female	50 (21.5%)	

***p* values represent the difference in thyroid abnormalities according to gender

However, our study reveals a relatively low incidence of new thyroid dysfunction at annual screening. Of the 639 patients screened annually from 1999 to 2006 in this study, only seven patients developed overt hypothyroidism which needed treatment with thyroxine. Overt hyperthyroidism was diagnosed in 2 patients, who were treated with oral medications.

Fourteen of the 48 patients with subclinical hypothyroidism were treated with thyroxine, and only 2 patients out of 43 diagnosed with subclinical hyperthyroidism needed treatment with oral thyroid medications.

The high incidence of thyroid disease in our large, unselected cohort of patients with diabetes was similar to that reported in a Scottish population by Perros and colleagues [14]. In addition, the low annual incidence of thyroid disease requiring treatment, less than 0.5%, was similar to that reported in the Scottish study. Although the prevalence of thyroid dysfunction was higher in patients with type 1 diabetes, the annual incidence of thyroid dysfunction was similar in type 1 and type 2 diabetes.

Our prevalence data and data from other studies show strong associations between type1 diabetes and autoimmune thyroid disease, which probably justifies annual screening for thyroid disease in patients with type 1 diabetes. However, the low incidence of thyroid dysfunction requiring treatment which we report challenges the need for annual screening for thyroid abnormalities in male patients with type 2 diabetes who have normal thyroid function at diagnosis. The Edinburgh group has also challenged the need for screening for thyroid disease in type 2 diabetes, except for those in the upper quartile of the reference range for TSH [18]. In this particular cohort of patients, the prevalence rates of new hypothyroidism are significantly higher. Longitudinal studies have demonstrated that female gender, TSH, and TPO antibody titer are the strongest risk factors predicting the presence of overt hypothyroidism at follow-up.

The risk of progression to overt hypothyroidism increases as the initial serum TSH level increases. In the Whickham survey, a baseline serum TSH concentration above 2 mU/l was associated with an increased risk of hypothyroidism at the 20-year follow-up [2].

A more recent longitudinal study conducted in West Australia confirmed the findings of the Whickham study and suggested that the use of TSH cutoffs of 2.5–4.0 mU/l, combined with thyroid antibodies (antibodies to thyroid peroxidase or thyroglobulin antibodies), provides a clinically useful estimate of the long-term risk of hypothyroidism [25].

However, an argument against screening patients with a TSH in the upper limit of the normal reference range or mild TSH elevations has been the increased incidence of spontaneous reversion of elevated TSH to normal, reported to be as high as 40–50% [26–29].

There is an obvious need for more definitive data with regard to the risk stratification and the management of these patients.

Based on the current evidence, we believe it is reasonable to measure TPO thyroid antibodies in patients with diabetes and a TSH in the upper quartile and continue screening for TD on a yearly basis.

We consider that our data strengthens the recommendation that annual screening for thyroid disease is not required in patients with type 2 diabetes and normal plasma TSH concentration, other than those with borderline high plasma TSH.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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