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ORIGINAL ARTICLE

Increased Admissions Due to Cardiac Complications of Thyrotoxicosis in Māori

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Background As thyrotoxicosis is a risk factor for atrial fibrillation, current guidelines recommend measuring a thyroid-stimulating hormone level in patients with this disorder. Hyperthyroidism may also be associated with other heart diseases including cardiac ischaemia and cardiac failure. Currently, the prevalence of thyrotoxicosis in cardiac admissions in the absence of a rhythm disorder is unknown.

Aims The aims of this study were: 1) to calculate the prevalence of admissions for thyrotoxicosis-associated cardiac disease, 2) determine the type of cardiac disease i.e. dysrhythmic, ischaemic or cardiac failure, and 3) to assess whether Māori are over-represented amongst patients admitted to hospital with cardiac complications of thyrotoxicosis.

Methods A retrospective review of admissions with both thyrotoxicosis and cardiac disease from 1 January 2005 to 31 December 2012 inclusive.

Results Seventy-two patients were identified as being admitted for a cardiac complication of thyrotoxicosis, giving a mean of nine admissions per year. Dysrhythmia was the cause for admission in 32 patients, ischaemia in 12, cardiac failure in 11 and mixed cardiac disease in 17. Graves' disease and amiodarone-induced were the most common causes of the thyrotoxicosis (25 and 19 cases, respectively). Of the cohort 26 (36.1%) were Māori (compared to 16.8% of all cardiac admissions over the same period). Māori were more likely to present with cardiac failure than non-Māori (57.7% vs. 26.1%, p = 0.008 respectively).

Conclusions Māori are over-represented amongst patients admitted with cardiac complications of thyrotoxicosis and more often present with cardiac failure than non-Māori. Measurement of thyroid function should be considered in patients presenting not only with atrial fibrillation but also in patients presenting with cardiac failure, particularly if they are Māori.

Keywords Hyperthyroidism • Graves' disease • Congestive heart failure • Atrial fibrillation • Toxic multinodular goitre

Introduction

Thyrotoxicosis is a common endocrine disorder, which, when untreated, results in significant morbidity and premature mortality [1]. Cardiovascular disease is a common cause of admission to hospital and is associated with a significant health burden in the community. Hyperthyroidism is a known risk factor for cardiac failure and cardiac dysrhythmias, particularly atrial fibrillation [2–4].

A retrospective study assessing rates of thyroid dysfunction in 250 patients presenting to a New Zealand district hospital with atrial fibrillation reported that 5.2% of these patients had either overt or subclinical hyperthyroidism [5]. The ethnic distribution of patients presenting with atrial

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fibrillation was reported to be consistent with that expected for the population, although no ethnicity data was provided for those identified to have thyroid dysfunction.

An Australian group reported that Māori presenting with cardiac complications of thyrotoxicosis comprised one-third of the cases presenting to their unit despite only representing 0.007% of their regional population [6]. It was suggested by these authors that Māori women might be at increased risk of cardiac complications of thyrotoxicosis. Māori have previously been reported to have an increased rate of admission and mortality from cardiac failure when compared with the non-Māori population [7]. However, there is no data available on rates of thyrotoxicosis in Māori presenting with cardiac failure.

Current guidelines recommend that patients presenting with atrial fibrillation should have thyroid function measured [8]. Whether thyroid testing should also be routinely performed in patients presenting with ischaemic heart disease and heart failure is less clear.

The aims of this study were: 1) to calculate the prevalence of admission for documented thyrotoxicosis-associated cardiac disease, 2) determine the type of cardiac disease i.e. dysrhythmia, ischaemia or cardiac failure, and 3) to assess whether Māori are over-burdened with cardiac complications of thyrotoxicosis.

Methods

In this retrospective, population-based cohort study, hospital coding using ICD10 codes was used to identify all hospital admissions to Waikato Hospital, a 600-bed tertiary New Zealand Hospital, in which both cardiac disease and thyrotoxicosis were treated during the same admission over the period 1 January 2005 to 31 December 2012, inclusive. Data was obtained from hospital notes, electronic health records, laboratory, and radiology records.

Two searches were carried out. The first included all patients admitted and coded with thyrotoxicosis as the primary diagnosis during that period, identifying 561 admissions. For this search the following codes were used:

E011 – Iodine-deficiency-related multinodular (endemic) goiter
E050 – Thyrotoxicosis with diffuse goitre
E051 – Thyrotoxicosis with toxic single thyroid nodule
E052 – Thyrotoxicosis with toxic multinodular goitre
E054 – Thyrotoxicosis factitia
E055 – Thyroid crisis or storm
E058 – Other thyrotoxicosis
E059 – Thyrotoxicosis, unspecified
E079 – Disorder of thyroid, unspecified

Of the 561 admissions, 215 patients were identified as having been admitted to cardiology, general medicine or endocrinology services with most of the remainder being admitted for thyroidectomy and so excluded. Following electronic review of the patient's clinical records, 71 patients were confirmed as having acute cardiac involvement contributing to their admission. A second search was undertaken of all the cardiac admissions during the same time period, where thyrotoxicosis (using the same codes as above) was coded as a secondary diagnosis or complication. Following review of the electronic notes to determine patients who were thyrotoxic at the time of admission, 36 patients were identified. Patients who developed thyrotoxicosis secondary to treatment of their cardiac condition during that admission were excluded. This second search yielded only one additional patient who had not been identified by the first search and resulted in a total of 72 patients for analysis.

The electronic notes of all 72 patients were reviewed in detail and data extracted including: age, gender, ethnicity, cause of thyrotoxicosis (based on clinical, laboratory and imaging results and classified as Graves' disease, toxic multinodular goitre, amiodarone-induced, thyroiditis, and levothyroxine overuse), highest free thyroid hormone values, acute cardiac diagnosis resulting in the current hospitalisation (classified as cardiac failure, ischaemia/infarction, dysrhythmia or mixed). Prevalence of thyrotoxicosis within cardiac admissions was calculated using cardiac discharge data for the same period as the denominator and those patients in the cohort who were discharged by a cardiology team as the numerator. In all cases, ethnicity was taken from hospital records, with a prioritisation approach used to classify a single ethnicity to individuals. Ethnicity was then classified into Māori and non-Māori groupings.

This study was registered with the institutional review committee and was conducted in accordance with the New Zealand National Health Advisory Committee's Ethical Guidelines for Observational Studies, and with permission of the Endocrine Department.

Statistical analysis was performed using Stata v 13.1 (StataCorp. 2013. Stata Statistical Software: Release 13. College Station, TX.) Mann-Whitney tests were used for continuous variables (as all were non-parametric) and chi-square or Fisher's exact test for categorical variables (depending on cell frequencies). A $p < 0.05$ was used to reject the null hypothesis, unless otherwise specified.

Results

Overall there were 35,337 cardiac admissions during the period studied. Māori accounted for 16.8% of the total cardiac admissions during this time period, which parallels the Māori population in the region (2013 census 17.3% of the Waikato DHB adult population were Māori) [9]. The breakdown of discharge (by coded ICD10 principal diagnosis) included: ischaemic heart disease—12,352 (35.0%), tachyarrhythmias—4455 (12.6%), and heart failure and cardiomyopathies—3586 (10.1%). These 20,393 were used to investigate the prevalence of thyrotoxicosis within cardiac admissions. When looking by cardiac diagnosis Māori comprised 13.7% of patients presenting with ischaemic heart disease, 27.8% with cardiac failure and 16.8% of those with tachyarrhythmia.

A total of 72 patients were identified as having thyrotoxicosis-associated cardiac disease giving an average of nine admissions per annum. Details are shown in Table 1. Graves' disease was the cause of the thyrotoxicosis in 25 patients (34.8%), amiodarone-induced thyrotoxicosis in 19 patients (26.4%), toxic multinodular goitre in 18 (25%), excess levothyroxine replacement in five (6.9%) and other causes comprised the remaining five cases. The majority (51, 70.8%) were admitted to a cardiology service, with the remaining 29.2% being treated by a medical team.

Using the 51 patients admitted to the cardiology service, the prevalence of thyrotoxicosis within all cardiac hospitalisations was 14.4 per 10,000 admissions (95% CI 10.8, 19.0). When limited to hospitalisations for cardiac ischaemic, heart failure and tachyarrhythmia the prevalence of thyrotoxicosis was 25.0 per 10,000 admissions (95% CI 18.6, 32.9). There were no cases of thyrotoxicosis coded in the group of ''other'' cardiac diagnoses, which comprised 14, 944 discharges.

Patients with concurrent thyrotoxicosis were more likely to present with a tachyarrhythmia—47 cases (65.3%), compared to heart failure (27 cases [37.5%]) or cardiac ischaemia (16 cases [22.2%]). Mixed disease was present in 17 of 72 patients (>2 diagnoses). All patients with levothyroxine over-replacement presented with a tachyarrhythmia (atrial fibrillation in four and ventricular tachycardia in one patient) and varied in severity of thyrotoxicosis with an FT_4 level up to 49 pmol/L.

Māori comprised 36.1% of those with thyrotoxicosis-associated cardiac admissions. The prevalence of thyrotoxicosis

Table 1 Characteristics of patients with thyrotoxicosis-associated cardiac admissions.

Median age (range)		59.5 (23–88)
Gender	Female	48 (66.7%)
Ethnicity	Māori	26 (36.1%)
	Non-Māori	46 (63.9%)
Median length of stay (range)		5 days (0–30)
		– Māori 5 (1–23)
		p = 0.6334
		– Non-Māori 5 (0–30)
Thyrotoxicosis cause	Graves' disease	25 (34.8%)
	AIT	19 (26.4%)
	TMNG	18 (25%)
	Thyroxine	5 (6.9%)
	Other	5 (6.9%)
Cardiac diagnosis[a]	Tachyarrhythmia	47/72 (65.3%)
		– Māori 14/26 (53.8%)
		p = 0.126[b]
		– Non-Māori 33/46 (71.7%)
	Heart failure	27/72 (37.5%)
		– Maori 15/26 (57.7%)
		p = 0.008[b]
		– Non-Maori 12/46 (26.1%)
	Cardiac ischaemia	16/72 (22.2%)
		– Maori 5/26 (19.2%)
		p = 0.646[b]
		– Non-Maori 11/46 (23.9%)
Severity of thyrotoxicosis	Mild	28/72 (38.9%)
FT_4 (RR 12–22 pmol/L)	– FT_4 <30 pmol/L	– Māori 8/26
		– Non-Māori 20/46
	Moderate	17/72 (23.6%)
	– FT4 31–50 pmol/L	– Māori 7/26
		p = 0.543
		– Non-Māori 10/46
	Severe	27/72 (37.5%)
	– FT4 >51 pmol/L	– Māori 11/26
		– Non-Māori 16/46

Abbreviations: AIT, amiodarone-induced thyrotoxicosis; TMNG, toxic multinodular goitre; FT_4, free thyroxine level; RR, reference range.

[a]Patients may have more than one diagnosis so total adds up to more than the total number of patients.

[b]Bonferroni adjustment used to recognise multiple diagnoses, $p < 0.017$ used to reject the null hypothesis.

within Māori admitted with cardiac ischaemic, heart failure and tachyarrhythmia was higher than that seen in non-Māori with the same diagnoses, particularly in those under the age of 65 (overall 46.7 per 10,000 admissions vs. 20.6 per 10,000 admissions; aged 65 and under prevalence rate ratio 1.1 [95% CI 0.1, 4.5; p = 0.8573]; aged over 65 prevalence rate ratio 2.3 [95%CI 1.0, 4.9; p = 0.0271]). Māori admitted with thyrotoxicosis-associated cardiac disease were younger than non-Māori (median age 56.5 vs. 65.5 years, p = 0.003) and presented with less dysrhythmia and more cardiac failure (53.9% vs. 71.7%, p = 0.126 and 57.7% vs. 26.1%, p = 0.008 respectively, Figure 1). There was no difference in severity of thyrotoxicosis between Māori and non-Māori (p = 0.568) unless patients with amiodarone-induced thyrotoxicosis (AIT) were excluded. AIT accounted for 11 of 16 cases of severe thyrotoxicosis in non-Māori whereas Māori were no more likely to have AIT than expected for the population demographics (3/19 Māori).

Discussion

Admissions for cardiac complications of thyrotoxicosis were relatively infrequent, averaging just less than one admission per month compared to 368 monthly cardiac admissions over the same time period. Amongst admissions for cardiac conditions that were potentially thyrotoxicosis-related (cardiac ischaemia, tachyarrhythmias and heart failure) the prevalence of thyrotoxicosis was 25.0 per 10,000 admissions. Tachyarrhythmias were the most common thyrotoxicosis-associated cardiac admissions but over one-third of hyperthyroid patients admitted had heart failure and almost one-quarter experienced an acute ischaemic cardiac event. In 23.6% of patients more than one of these cardiac complications were present. Approximately one-third of the cases of thyrotoxicosis were iatrogenic with over one-quarter of the cohort having amiodarone-induced thyrotoxicosis. This is a much higher proportion of amiodarone-induced thyrotoxicosis than would normally be expected in a general thyrotoxic cohort and is likely to reflect the underlying cardiac disease in this cohort. Interestingly, while often considered relatively benign, levothyroxine over-replacement comprised almost 7% of the thyrotoxic cohort, particularly affecting older non-Māori and all had tachyarrhythmias (atrial fibrillation or ventricular tachycardia).

From this retrospective study, Māori appear to have a greater burden of disease than non- Māori when admitted with thyrotoxicosis-associated cardiac disease. Māori patients were younger when compared with non-Māori, reflective of the Māori population demographic, although there was no difference in severity of thyrotoxicosis between the two groups. In addition, the type of cardiac involvement differed between the two groups with Māori patients more commonly experiencing cardiac failure than non-Māori. This parallels the known increased rate of admissions for heart failure in Māori as compared to non-Māori [7], which was also seen within this study period.

A significant limitation of this study is that being retrospective, the reasons for the ethnic disparity could not be identified. Possible contributors to these ethnic differences include the concepts that both the cardiac and/or thyroid

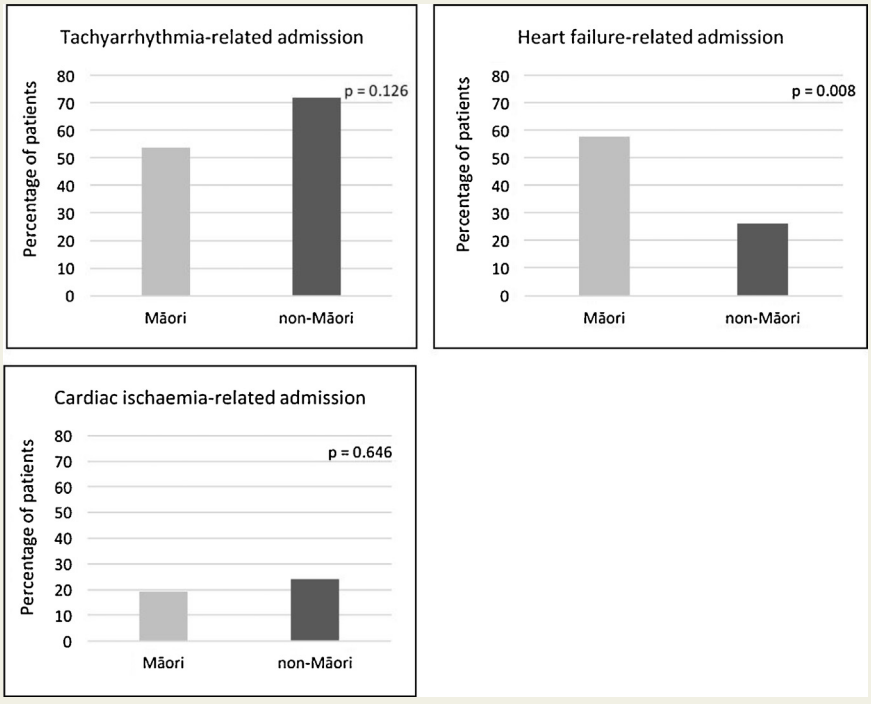

Figure 1 Percentage of patients presenting with tachyarrhythmia, heart failure or cardiac ischaemia, by ethnicity.

disease in Māori is more severe, or that Māori have higher rates of underlying cardiac disease, such as the known higher rate of rheumatic heart disease when they develop thyrotoxicosis, or that both conditions are more prevalent. It was not clear from the notes as to the duration of thyrotoxicosis prior to presentation, treatment duration, and whether the treatment of their thyrotoxicosis was optimal. The duration of untreated disease during initial work up of thyrotoxicosis is longer in Māori than non-Māori (unpublished observations) and barriers to care in other areas have been shown to contribute to more severe presentations and outcomes for Māori [10]. In addition, there are likely social factors contributing to the discrepancy. Māori are overrepresented in lower socioeconomic deciles [11], which reduces access to medical care. It is possible that a delay in receiving treatment, or under-treatment of thyrotoxicosis may result in a higher rate of cardiac dysfunction.

This health disparity seen for Māori can also be adversely affected by other important comorbidities such as obesity, hypertension, rheumatic heart disease, metabolic syndrome and diabetes mellitus, also known to disproportionately affect Māori [12,13]. Prospective work in this area, accurately quantifying the disparity and reviewing the individual, social and health care factors that influence it, is needed to identify areas to make improvements.

Current recommendations are to screen for hyperthyroidism in patients with atrial fibrillation. Given the potential role of thyrotoxicosis in heart failure, and the prevalence of thyrotoxicosis, particularly in Māori, noted in this study it might be suggested that these patients should also be assessed for hyperthyroidism. As this study is retrospective and notes based, it only illustrates the hyperthyroidism that was identified and coded, not what existed, as there may have been additional patients with undiagnosed thyrotoxicosis. There is the potential to under-count thyrotoxicosis in this population, particularly in Māori if there was a bias in testing. This could be avoided with a well-designed prospective cohort study. Interestingly, there were no cases of thyrotoxicosis in any of the other cardiac diagnoses despite this group being almost 15,000 patients and a background prevalence of thyrotoxicosis in our community of 0.2% [14]. This suggests that a significant number of cases of thyrotoxicosis were missed in these cardiac patients. This is important as not only is thyrotoxicosis very treatable, but thyrotoxicosis is also associated with an increased risk of cardiovascular mortality [15]. In addition, development of a euthyroid state should be expected to improve the cardiac status.

Conclusions

Māori are over-represented amongst patients admitted with cardiac complications of thyrotoxicosis and more often present with cardiac failure than non-Māori. Measurement of thyroid function should be considered in patients presenting not only with atrial fibrillation but patients presenting with cardiac failure, particularly if they are Māori. Further work is needed to understand this disparity, determine whether it also occurs in other indigenous populations and identify effective interventions.

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