

Thyroid Dysfunction in Elderly Patients

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Abstract

Introduction: The aim of this study was to determine the prevalence of thyroid dysfunction in an elderly in-patient population in a restructured hospital. **Methods:** This was a prospective observational study performed on consecutive patients admitted into a geriatric ward in a restructured hospital in Singapore over a period of 3 months. Thyroid function tests (free thyroxine and thyroid stimulating hormone) were performed on all patients during routine blood screening. For those with abnormal thyroid function tests, further investigations including thyroid autoantibodies and anterior pituitary hormone measurements were performed where indicated. Demographic data, the presence of sepsis, hypoalbuminaemia and patients' functional status as well as other thyroid-related data were captured. **Results:** A total of 184 patients were screened and 62 (33.7%) patients were found to have abnormal thyroid function tests. The mean age was 83.8 years (SD 6.2). Twenty (32.3%) were males and 42 (67.7%) were females. Thirty-three (53.2%) patients had sepsis on admission, 29 (46.8%) were functionally dependent and 22 (35.5%) had hypoalbuminaemia. The prevalence of thyroid disorders were as follows: 1 (0.5%), 4 (2.2%), 9 (4.9%), 15 (8.2%) and 33 (17.9%) patients had hyperthyroidism, subclinical hypothyroidism, primary hypothyroidism, secondary hypothyroidism and sick euthyroid syndrome, respectively. Cross-tabulating sick euthyroid syndrome against functional dependence, hypoalbuminaemia and sepsis did not reveal any significant association (Fisher's exact test, $P = 0.44$, $P = 0.42$ and $P = 0.61$, respectively). **Conclusion:** There was a high prevalence of thyroid dysfunction in the elderly in-patient population. We would advocate a lower threshold for screening elderly in-patients for thyroid dysfunction.

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Key words: Secondary hypothyroidism, Sepsis, Sick euthyroid, Thyroid antibodies

Introduction

Symptoms and signs of thyroid dysfunction in the elderly tend to be atypical and may be mistakenly attributed to the ageing process. Currently, thyroid function tests are performed on patients who manifest signs and symptoms of overt thyroid disease or as part of the investigations for dementia in the older patient. This will, therefore, miss patients with more subtle signs of the disease who may benefit from treatment or further follow-up.

With increasing age, there are anatomical and physiological changes occurring within the thyroid gland.¹ The production of thyroxine (T4) is reduced but serum T4 levels remain unchanged as there is a concomitant reduction in T4 clearance. Triiodothyronine (T3) production is also reduced and levels may be slightly lower than that of younger adults but remain within the normal range.² Basal thyroid stimulating hormone (TSH) levels are normal in the elderly. Overall, the thyroid gland is able to produce a normal amount of thyroid hormone throughout life.

There have been studies advocating screening of thyroid

disease in the elderly in view of the increased incidence in this age group³⁻⁷ as well as the morbidity and complications associated with overt and subclinical thyroid disease.⁸⁻¹⁴ There are however, very little data on the prevalence of thyroid dysfunction in the elderly in Singapore though there have been studies carried out in other populations.¹⁵⁻¹⁹

The aim of this study was to determine the prevalence of thyroid dysfunction in elderly patients admitted to a geriatric ward in a restructured hospital.

Materials and Methods

Subjects

All admissions to a 38-bedded geriatric ward in a restructured hospital were prospectively screened for thyroid dysfunction from September 2001 to December 2001. The admissions were largely unselected elderly patients above the age of 75, admitted from the Accident and Emergency Department, with a few patients admitted from the specialist outpatient clinic. Each patient was screened once during the study period. Blood was drawn for free thyroxine (fT4)

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and thyroid stimulating hormone (TSH) on admission or on the next working day.

Demographic data, the presence of sepsis, functional dependence (determined by patients being in a chairbound or bedbound state), and hypoalbuminaemia (defined as serum albumin <30 g/L) were documented.

Data extracted from history taking included any history of thyroid disease, thyroidectomy or radioactive iodine treatment as well as any ingestion of medications that may affect thyroid function. Presence of a goitre and/or atrial fibrillation was also documented.

The algorithm for investigations is shown in Fig. 1.

Patients with normal fT4 and TSH were deemed to be euthyroid and no more investigations were done for them.

Patients with TSH of more than 10 mU/L were deemed to have primary hypothyroidism while those with values between 5 and 10 mU/L were deemed to have subclinical hypothyroidism. Patients currently on treatment for primary hypothyroidism were deemed to have primary hypothyroidism (those who were euthyroid were not included).

Patients with low TSH had their total triiodothyronine (T3) done if the fT4 was normal. Those with high fT4 and/or high T3 were deemed to have hyperthyroidism. Patients currently on treatment for hyperthyroidism were deemed to have hyperthyroidism (those who were euthyroid were not included).

Patients with normal TSH and low fT4, and those with low TSH and low or normal fT4 or T3 had their anterior pituitary hormones evaluated (Fig. 1). Females with inappropriately low LH or FSH were deemed to have hypogonadotropic hypogonadism, and combined with inappropriately low TSH were deemed to have secondary hypothyroidism. Males found to have low or normal levels of LH or FSH in the presence of low serum testosterone levels were also deemed to have hypogonadotropic hypogonadism, and combined with inappropriately low TSH were diagnosed with secondary hypothyroidism.¹² Patients with secondary hypothyroidism had a magnetic resonance imaging (MRI) of the pituitary done.

For the above patients, if their LH and FSH levels were appropriate, they were deemed to have subclinical hyperthyroidism if the fT4 and total T3 were normal. On the other hand, patients with low fT4 and / or total T3 were labelled as sick euthyroid.

Assays

Thyroid function tests were determined using the second generation AxSYM Immunoanalyser, thyroid stimulating hormone (TSH) and free thyroxine (fT4) being measured by MEIA and total triiodothyronine (T3) by FPIA. Free

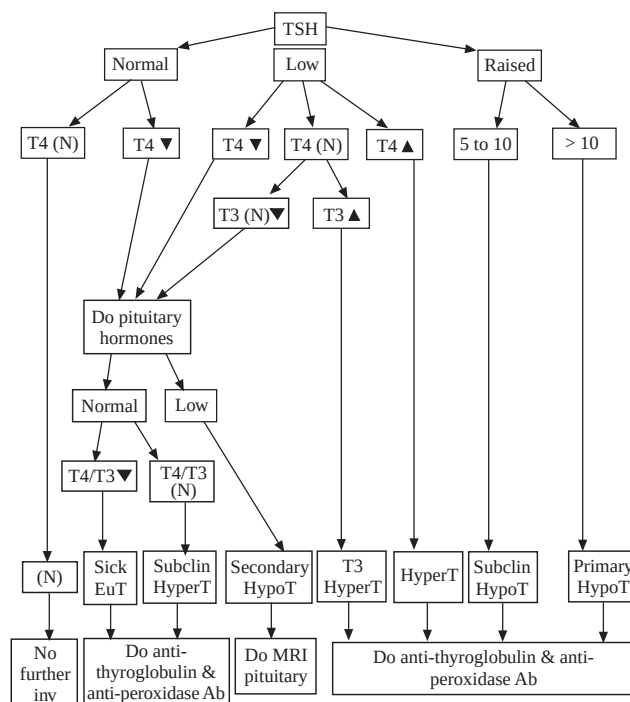


Fig. 1. Algorithm to ascertain thyroid status in elderly in-patients.

triiodothyronine (fT3) was not available in our laboratory. The normal reference ranges were as follows: TSH 0.5–5.0 mU/L, fT4 10.3–31.0 pmol/L and T3 1.2–3.4 nmol/L.

Anti-thyroglobulin antibodies (anti-Tg Ab) and anti-peroxidase antibodies (anti-TPO Ab) were measured by radio-immuno assay (RIA). The normal laboratory ranges were: anti-Tg Ab 0.0–60.0 U/mL and anti-TPO Ab 0.0–60.0 U/mL.

Luteinising hormone (LH), follicle-stimulating hormone (FSH), prolactin and testosterone were determined by EC methodology on Elecsys 1010 (first generation). Insulin-like growth factor (IGF-1) and adrenocorticotrophic hormone (ACTH) were measured using radio-immuno assay (RIA) and immuno-radiometric assay (IRMA) respectively. Reference ranges for the above tests were: LH 0.8–6.1 IU/L (males), 13.2–45.7 IU/L (post-menopausal females); FSH 1.6–11.0 IU/L (males), 48.6–143.9 IU/L (post-menopausal females); prolactin 60–630 mIU/L (males), 80–630 mIU/L (females); testosterone 9.1–55.2 nmol/L; IGF-1 114–492 microg/L and ACTH 9–52 ng/L.

Statistics

Statistical analysis was carried out using SPSS 10.0.

Results

Over the study period of 3 months, a total of 184 patients were screened and 62 (33.7%) patients were found to have abnormal thyroid function tests. The mean age was 83.8

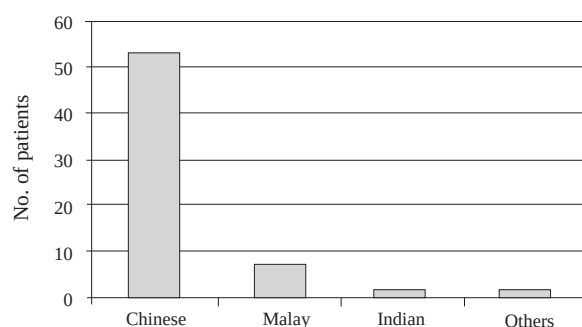


Fig. 2. Racial distribution of patients with abnormal thyroid function tests.

years (SD 6.2). Of these 62 patients, 20 (32.3%) were males and 42 (67.7%) were females. There were 53 (85.5%) Chinese, 7 (11.3%) Malays, 1 (1.6%) Indian and 1 (1.6%) patient of another race (Fig. 2).

Thirty-three (53.2%) patients had sepsis on admission, 29 (46.8%) were functionally dependent and 22 (35.5%) had hypoalbuminaemia. Only 1 (1.6%) patient had a previous thyroidectomy, none had received radioactive iodine in the past, 6 (9.7%) were on thyroxine, 1 (1.6%) was taking carbimazole, 2 (3.2%) were on amiodarone and 1 (1.6%) patient was taking systemic steroids. Three (4.8%) patients had a goitre and 6 (9.7%) had atrial fibrillation.

It was found that among the 62 patients with abnormal thyroid function tests, 1 (1.6%) patient had hyperthyroidism, 4 (6.5%) patients had subclinical hypothyroidism, 9 (14.5%) patients had primary hypothyroidism, 15 (24.2%) patients had secondary hypothyroidism and 33 (53.2%) patients had sick euthyroid syndrome (Fig. 3).

In patients diagnosed with subclinical and primary hypothyroidism (a total of 13 patients), 6 (46.2%) patients were found to have anti-TG Ab positive and 7 (53.8%) patients had anti-TPO Ab positive. Five (38.5%) patients had both antibodies positive whilst 8 (61.5%) patients had at least one positive antibody.

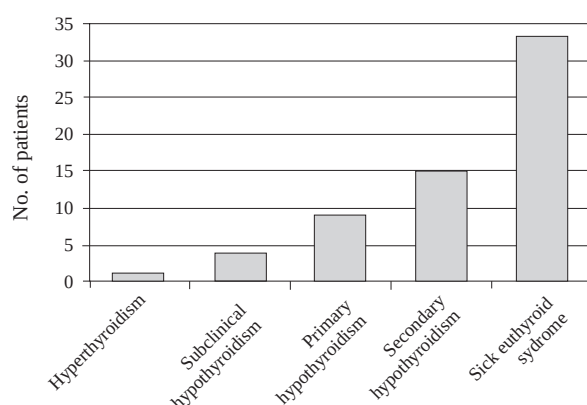


Fig. 3. Types of thyroid dysfunction in patients with abnormal thyroid function tests.

In the 15 patients diagnosed with secondary hypothyroidism, all 15 (100%) patients had low concentrations of LH and IGF-1, 12 (80%) patients had low FSH levels, 2 (13.3%) had low ACTH levels and all had normal prolactin levels. Of these 15 patients, 6 (40%) had MRI of the pituitary and 1 (6.7%) patient was found to have a pituitary microadenoma. The rest either refused MRI or died.

Cross-tabulating sick euthyroid syndrome against patients' functional status, hypoalbuminaemia and sepsis did not reveal any association (Fisher's exact test, $P = 0.44$, $P = 0.42$ and $P = 0.61$, respectively).

Discussion

In this study, the prevalence of thyroid dysfunction in the elderly in-patient population was 33.7%. Other studies have shown prevalence rates of 6.9% to 17.2%,^{4,13-15,17} though the definition of thyroid dysfunction varies between studies and the majority of these studies did not include the diagnoses of sick euthyroid syndrome or secondary hypothyroidism.

The prevalence rate for hyperthyroidism was low (0.5%, 1 out of 184), comparable with those of other studies.^{4,7,19} This was the same for subclinical hypothyroidism (2.2%, 4 out of 184)^{18,20-23} and primary hypothyroidism (4.9%, 9 out of 184),^{6,18,19} though in a Taiwan study, their rate was higher at 34.8%.¹⁵

One of the interesting findings in our study was the high prevalence (8.2%, 15 out of 184) of secondary hypothyroidism, that is, hypothyroidism secondary to pituitary dysfunction. It has been reported that if two trophic hormones are deficient, panhypopituitarism is likely.¹² Therefore, we attempted to establish at least two trophic hormone deficiencies to diagnose pituitary dysfunction. After inappropriate TSH levels were noted, we used LH and FSH levels to establish hypogonadotropic hypogonadism in the patients. Females with inappropriately low LH or FSH and males with low or normal levels of LH or FSH in the presence of low serum testosterone levels were deemed to have hypogonadotropic hypogonadism.¹² In the 15 patients with secondary hypothyroidism, all had concomitantly low IGF-1 levels and 2 (13.3%) had low ACTH levels. We did not rely on the IGF-1 levels for diagnosis of hypopituitarism because IGF-1 levels may be decreased in the elderly, malnourished and chronically sick.²⁴

The reason why such a high prevalence of secondary hypothyroidism occurred in our study population is unclear. Pituitary-cell destruction has been reported to account for more than 95% of cases of hypopituitarism. Larger adenomas (more than 10 mm), and not microadenomas, commonly cause insufficient secretion of one or more

trophic hormones.¹² Five patients in our study had normal MRI of the pituitary with only 1 having a pituitary microadenoma. In our study, pituitary-cell destruction probably was not the main cause of hypopituitarism. As the majority of our patients were frail, sickly and elderly, they probably had pituitary impairment from degenerative changes. Hypopituitarism in them would have remained undiagnosed unless the diagnosis was suspected and measurement of pituitary hormones was done, as has been shown in some case reports.²⁵

All 6 patients who were treated with thyroxine had TSH levels >5 mU/L. This may indicate the need for an increment in their thyroxine dosage. However, cautious replacement is required in elderly patients and in patients with ischaemic heart disease, and this may therefore account for the subtherapeutic TSH values.

Thyroid antibodies were performed to ascertain the aetiology of primary and subclinical hypothyroidism. As most of the patients were antibody positive, probably the majority of patients in the study with primary and subclinical hypothyroidism had an autoimmune aetiology.

Studies have shown the presence of sick euthyroid syndrome in patients with acute illnesses^{26,27} though the mechanism of these hormonal responses remained little understood. In sick euthyroid syndrome, the consistent finding is a decrease in serum T3 concentrations. This is largely due to reduced conversion from T4.²⁸ FT4 and TSH levels may be low or normal. It has been debated whether this hormonal response represents part of an adaptive response which lowers tissue energy requirement in the face of systemic illness or a maladaptive response which induces damaging tissue hypothyroidism. It has also been shown that the degree of thyroid function disturbance correlates with disease severity.²⁶

Some studies^{13,29} have shown resolution of the thyroid dysfunction after the acute illness and others³⁰ advocate re-assessment of the thyroid status when the acute illness is resolved.

Hypoalbuminaemia is associated with increased morbidity in hospitalised patients³¹ and can therefore reflect the severity of the patients' illness. It may also be used as a marker of poor nutritional status although in the presence of an acute illness, this correlation lacks sensitivity. Nevertheless, in one study,³² serum albumin testing has been found to be a good prognostic tool in chronically ill patients.

In our study, we could not find any association between sick euthyroid syndrome with either hypoalbuminaemia, functional dependency or sepsis. The lack of association could be also due to our small sample size. Whether treatment would be beneficial for these patients remains

controversial. In order to ascertain this, larger future trials would be required.

Conclusion

There was a high prevalence (33.7%) of thyroid dysfunction in the elderly in-patient population. We would advocate a lower threshold for screening elderly in-patients for thyroid dysfunction as newly diagnosed thyroid disease would either require treatment or follow-up and those already known to have thyroid disease may require optimisation of therapy. For those diagnosed with sick euthyroid syndrome, it may be useful re-assessing their thyroid status after resolution of the acute illness.

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