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# Subclinical hypothyroidism in elderly women attending an outpatient clinic

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## Summary

**Background:** The object was to determine the frequency of subclinical hypothyroidism (SH) in elderly women and study its relation to serum lipids, hypertension, diabetes, and ischemic heart disease.

**Material/Methods:** A sample of 257 patients was randomly selected among women above the age of 50 visiting the King Abdulaziz University outpatient clinic. All were examined for thyroid function. Positive cases of SH were further tested for thyroid antibodies, hypothyroid symptoms, and goiter. Data were collected from the cases and a control group regarding age, presence of hypertension, diabetes, and ischemic heart disease, and lipoprotein levels and body mass index (BMI) values. Comparative analysis was performed between the cases and controls regarding dyslipidemia, BMI, hypertension, diabetes, and ischemic heart disease after age adjustment with logistic regression.

**Results:** Ninety patients out of 257 (35%) had SH. Positive thyroid antibodies were present in 55 (61%), goiter in 8 (9%), and hypothyroid symptoms in 22 (24%). In multiple regression analysis, SH cases were found to have lower risk for hypertension, ischemic heart disease, and diabetes than the controls after adjustment for age: OR 1.5 (95% CI: 0.8–2.83), 2.17 (0.75–6.28), 2.67 (1.50–4.76), respectively; the p-values were found to be significant for diabetes (0.19, 0.14, <0.001). However, there were no significant differences between cases and controls regarding measurements of LDL and cholesterol: 3.3±1.1 mmol/l and 5.5±1.2 mmol/l vs. 3.4±0.9 mmol/l and 5.4±1.1 mmol/l, respectively.

**Conclusions:** There is a high prevalence of SH among our sample, with no increased risk of hypertension, hyperlipidemia, ischemic heart disease, or diabetes.

**key words:** subclinical hypothyroidism • elderly women • ischemic heart disease

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## BACKGROUND

Subclinical hypothyroidism (SH) is defined as an asymptomatic state characterized by normal serum concentration of free thyroxine and an elevated serum concentration of thyroid stimulating hormone (TSH) [1]. This biochemical state has been given a variety of other names, including mild thyroid failure, as well as compensated, early, late, mild, minimally symptomatic, and pre-clinical hypothyroidism [2,3]. Although the term SH is widely used, mild hypothyroidism may be more appropriate, and is defined as an isolated elevated serum thyrotrophin level in the setting of normal serum thyroid hormone levels, in the presence or absence of symptoms [4]. SH is a common disorder with prevalence ranging from 1–10% of the, mostly adult, population [5–9], with the highest rate approaching 26% in elderly women [6,10–12]. The effect of SH on serum lipid levels and cardiovascular disease is controversial [10,12–14].

To the best of our knowledge, no studies on SH had been conducted in Saudi Arabia. The aim of our work was to estimate the prevalence of SH among women above the age of 50 attending outpatient clinics at the King Abdulaziz University Hospital (K.AU.H) over the period of one year to study its relation to serum lipids, hypertension, diabetes, and ischemic heart disease, and to compare our findings with those reported in the literature. We chose elderly women, as the condition is highly prevalent in them.

## MATERIAL AND METHODS

Women above the age of 50 years attending the outpatient medical clinic at K.AU.H, a teaching hospital in Jeddah in the western province of Kingdom of Saudi Arabia, from January 2000 to January 2001 were studied. Those with known thyroid disease, a history of neck irradiation, chronic renal failure, known hyperlipidemic, severe illness (such as infection, recent myocardial infarction, severe heart failure, or recent intensive care admission), or taking pharmaceuticals such as beta-blockers, amiodarone, interferon-alfa were excluded. A sample of 300 women was randomly selected. All the participating women were examined for thyroid function. Women with SH (defined as TSH >4.2 mU/l with normal free T4 and free T3) were considered as cases, and women without subclinical hypothyroidism were considered as controls. Laboratory measurements and clinical assessments were carried out on all the participants.

### Measurements

Thyroid function (free T4, free T3, and TSH) and lipoprotein levels, i.e. low density lipoprotein (LDL), high-density lipoprotein (HDL), total cholesterol (TC), and triglyceride (TG), were measured. Those with abnormal results repeated the test after 4 weeks. For patients with SH, thyroid antibodies (microsomal and thyroid peroxidase) were measured. Thyroid function test in our hospital is done using the electrochemolumences method. The normal range for TSH is 0.27–4.2 mU/l, for free T4 12–22 pmol/l, and for free T3 0.27–7.1 pmol/l, while thyroid antibodies were determined using the indirect hemagglutination technique.

### Clinical assessments

Participants with SH were examined for the presence of goiter and symptoms of hypothyroidism.

### Analytical methods

The following data were collected from all the study group: age, body mass index (BMI), presence of hypertension (defined as blood pressure >140/90 mmHg on more than one occasion, or the patient is known to be hypertensive), diabetes mellitus (defined as fasting blood glucose >7 mmol/l on two consecutive readings one month apart, or the patient is known to be diabetic), ischemic heart disease (IHD) (defined as angina or myocardial infarction by self report or by analysis of a standard 12-lead electrocardiogram), and history of stroke. Comparison between cases with SH and normal control subjects of similar age and ethnic group was done with regard to the presence of IHD, stroke, hypertension, and diabetes mellitus, as well as BMI, and serum lipid values.

### Statistical analysis

Statistical analysis was done using the Statistical Package for Social Sciences (SPSS 9.2). Different statistical methods were used as appropriate. Mean ±SD was determined for quantitative data and frequency for categorical variables. The independent t-test was performed on all continuous variables. The normal distribution of the data was checked before any t-test. The chi-square test was used to analyze group difference for categorical variables. In logistic regression models, age was adjusted for the estimation of each or all the independent effects of hypertension, ischemic heart disease, and diabetes. Goodness-of-fit of the logistic regression model was assessed using the test described by Hosmer and Lemeshow, and an adequate fit was obtained for all models used in this study. A p-value $<0.05$ was considered significant.

## RESULTS

Three hundred women were studied from a total number of 8449 women above the age of 50 who visited the medical clinic during the study period. Forty-three were lost before follow-up, and the remaining 257 participated in this study. Ninety women were found to have the criteria set for the definition of SH, which meant a rate of 35%. Patients with SH were regarded as cases and the remaining were the control group. There were differences in the mean age distribution among the cases and controls; these differences were adjusted in our analysis of the results. The mean age for patients with SH was 55.8±7.2 years. Mean TSH was 10.64 mU/l (range: 4.8–28.8), free T4 was 15.36 pmol/l (range: 12.1–22), and free T3 was 4.2 pmol/l (range: 2.87–6.43). Most of the patients with SH had a TSH level below 10 mU/l (Table 1). Positive thyroid antibodies (both microsomal and thyroid peroxidase) were found in 55/90 (61%), while goiter was present in 8/90 (9%).

**Table 1.** TSH levels in patients with subclinical hypothyroidism.

| TSH level in mU/l | Number of patients (%) Total No.=90 |
|---|---|
| <5 | 6 (7) |
| 5–10 | 45 (50) |
| >10 | 39 (43) |

**Table 2.** Logistic regression showing each independent risk factor in cases with subclinical hypothyroidism and controls, adjusted for age.

| | Odd ratio | 95% CI | P value |
|---|---|---|---|
| Diabetes mellitus | 2.99 | 1.70–5.25 | <0.001 |
| Hypertension | 2.07 | 1.15–3.71 | 0.01 |
| Ischemic heart disease | 2.85 | 1.03–7.85 | 0.04 |

Hypothyroid symptoms were reported in 22/90 (24%). Fatigability was the most common complaint, followed by constipation, infertility, cold intolerance and weight gain, these rates being 19 (20%), 14 (16%), 11 (12%), 6 (7%), and 4 (4%), respectively. In logistic regression analysis (Table 2), cases with SH were less likely to develop hypertension, diabetes, and ischemic heart disease than controls after adjustment for age.

The p values all indicated significant correlation. However, after taking all the above factors into consideration in multiple regression (Table 3), diabetes alone was found to be still significantly less likely to develop among the cases of SH than the controls. In addition, the results of the measurement of BMI and lipoprotein levels were not significantly different between cases with SH and the control group (Table 4).

## Discussion

SH is highly prevalent in elderly women. A prevalence of 11–26% had been reported [6,11,12,15], while our study showed that 35% of the elderly women attending the outpatient clinic had SH. This higher prevalence in our population could be due to environmental or genetic factors, which should be verified in further studies. Surveys that stratified TSH levels indicate a predominance of TSH <10 mU/l, which accounts for 55–85% of cases [5,7,16,17]. Almost 60% of our patients had TSH <10 mU/l. Studies that have reported thyroid antibody test on subjects with elevated TSH demonstrated seropositivity rates from 20–78% [6,9,10,18], which is not far from our results. Goiter is twice as prevalent among patients with SH [10]. It is found in 9% of our patients.

Several studies have suggested that mild symptoms of hypothyroidism are more prevalent in patients with SH than in age-matched controls [11,14,19]; fatigability and weight gain were the most frequent [20], but not all studies have found this to be true [21]. Twenty-four percent of our patients had symptoms, fatigability being the most common.

**Table 3.** Logistic regression showing combined independent risk factors in cases with subclinical hypothyroidism and controls, adjusted for age.

| | Odd ratio | 95% CI | P value |
|---|---|---|---|
| Diabetes mellitus | 2.67 | 1.50–4.76 | <0.001 |
| Hypertension | 1.51 | 0.8–2.83 | 0.19 |
| Ischemic heart disease | 2.17 | 0.75–6.28 | 0.14 |

**Table 4.** Comparison of different measurements between cases of subclinical hypothyroidism and controls.

| Variable | Patients with SH N=90 | Controls N=167 | P value |
|---|---|---|---|
| BMI (mean±SD) | 29.5±5.3 | 30.6±5.6 | 0.2 |
| TC (mean±SD) mmol/l | 5.5±1.2 | 5.4±1.1 | 0.3 |
| TG (mean±SD) mmol/l | 1.9±1.3 | 1.5±.9 | 0.4 |
| LDL (mean±SD) mmol/l | 3.2±1.1 | 3.3±0.8 | 0.9 |
| HDL (mean±SD) mmol/l | 1.2±0.4 | 1.1±0.2 | 0.1 |

SH – subclinical hypothyroidism; BMI – body mass index; TC – total cholesterol; TG – triglyceride; LDL – low-density lipoprotein; HDL – high-density lipoprotein

There have been three published randomized prospective placebo-controlled trials on the therapy of symptoms in patients with SH [22–24]. Two reported significant improvement in the symptoms of hypothyroidism, whereas the third found no benefit of therapy [22–24]. The benefit of therapy was related to TSH level, being more in those whose mean serum TSH was 12.7 mU/l at base line [23]. In women with SH and ovulatory dysfunction, thyroxin therapy may restore fertility [25]. Case-control and cross-sectional studies on the association between SH and cardiovascular diseases have been done, but results were controversial [10,12–14,26–29]. A 20-year follow-up study of the original Whickham survey [30] showed no association between elevated TSH and increased risk of IHD, while a report of 1149 women from Rotterdam showed increased atherosclerotic vascular disease and myocardial infarction in patients with SH [12]. Our results did not show a significant increase in IHD in patients with SH compared with controls. Several studies on the association between SH and dyslipidemia have been done. The initial Whickhan study observed that lipid levels were not associated with TSH elevation after age adjustment [10]. The Colorado study and others noted significantly elevated LDL cholesterol in subjects with SH [11,31]. A report from Rotterdam noted that SH subjects actually had lower total cholesterol [12]. Our results are in agreement with those previous reports that showed no association. Women with SH did not differ from controls with regard to BMI, hypertension, and diabetes in the previous studies [12,21]. Our study showed this to be true with regard to hypertension and BMI, while, interestingly, women with SH had a significantly lower rate of diabetes than the controls.

A recent analysis concluded that screening for and treating mild thyroid failure in all adults over 35 years of age

is as cost-effective as many other screening procedures [32]. There is documented evidence that many (but not all) effects are improved or corrected when L-thyroxin replacement is instituted. L-thyroxin treatment was recommended for the majority of patients with mild thyroid failure, particularly those with symptoms, goiter, positive thyroid antibodies, and those who are pregnant. However, despite these positive indications that treatment carries some benefits, the benefit-to-risk ratio of treatment remains to be determined, given the lack of outcome data and the considerable risk of TSH suppression in patients on L-thyroxin replacement. Keeping in mind that these patients (with SH) are usually elderly individuals, the prescription of thyroid hormone (for life) for poorly established indications compounds the increasing problem of polypharmacy and drug interaction in them.

## CONCLUSIONS

Further multi-center randomized studies are needed in our community to study the relation between SH and cardiovascular disease and risk factors. Large-scale, controlled intervention and outcome trials are needed to assess the potential benefit of L-thyroxin treatment in subjects with SH, so further recommendation regarding screening for thyroid disease in the community will be influenced by the results of these studies.

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