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ORIGINAL ARTICLE

Subclinical Thyroid Disorders In Postmenopausal Women Of Iran

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ABSTRACT

Objectives: The present Cross-sectional study was aimed to investigate the prevalence of subclinical thyroid disorders in postmenopausal women in a community on the northwest of Iran.

Methods: By using the records of the local household registry, a sample of 1000 subjects aged between 60 and 89 years (mean 64.5±5.4) were included in our survey. Tests of thyroid function including TSH concentration in all subjects and free T4 concentration, free T3 concentration and anti-microsomal antibodies in those with abnormal TSH were conducted.

Results: Eight hundred and seventy three (87.3) subjects were euthyroid, as indicated by their serum TSH concentrations. The overall prevalence of thyroid dysfunction in the samples was 12.7%. The prevalence of subclinical hypothyroidism and subclinical hyperthyroidism was 5.8% and 4.1%, respectively. High titers of anti-microsomal antibodies were found in 60.6% of the patients with high TSH levels.

Conclusion: The prevalence of abnormal biochemical thyroid function reported here is substantial and confirms previous reports from other populations. We found that the prevalence of thyroid dysfunction is high in the elderly female population of East Azerbaijan. The results from this study provide the baseline information to settle public health plans and to track the changes.

Key Words: Anti-microsomal antibody, subclinical hypothyroidism, subclinical hyperthyroidism, postmenopausal women

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Introduction

The advent of automated sensitive assays for thyroid hormones and thyroid-stimulating hormone (TSH) and the increasingly widespread use of such tests have led to a substantial increase in the identification of mild thyroid dysfunction, especially in elderly patients. Previous studies on the prevalence of thyroid disease in Iran and other countries have included patients of all ages [1],[2],[3],[4],[5],[6],[7],[8] and have reached differing conclusions. Most of these studies have examined only a small number of elderly patients; furthermore, recent developments in tests of thyroid function mean that previously undetected biochemical abnormalities may become evident.

The potential consequences of subclinical hypothyroidism are much less well established and although elevated TSH levels in the elderly have been recently suggested to confer a mortality advantage [9], most of the literature refers to adverse consequences such as the possibility of cardiac dysfunction or adverse cardiac end points (including atherosclerotic disease and cardiovascular mortality) [10], elevation in total and low-density lipoprotein cholesterol [11], systemic or neuropsychiatric symptoms [12] and progression to overt symptomatic hypothyroidism [13].

Approximately 4% of community-based patients per year, who are found to have subclinical hypothyroidism, are estimated to progress to

overt hypothyroidism [13, 14]. Subclinical hyperthyroidism may also be associated with adverse cardiac end points [15, 16] including atrial fibrillation [17], cardiac dysfunction, systemic and circulatory disease mortality [18], neuropsychiatric symptoms [19], [20], reduced bone mineral density and fractures [23], [24].
The evidence supporting the progression of subclinical hyperthyroidism to overt hyperthyroidism lacks consensus, as the available studies tend to be small, with study populations having significant heterogeneity [14], [23],[24],[25],[26].

The prevalence of thyroid dysfunction in U.K is high in the elderly population (13.8%), especially in elderly women (17.9%) [24]. Estimates of the prevalence of subclinical thyroid dysfunction in elderly populations differ substantially and vary according to ethnic groups, dietary iodine intake and the prevalence of antithyroid antibodies [27],[28],[29],[30]. The prevalence of subclinical hypothyroidism has been estimated in European and American populations of elderly ambulatory participants, to vary 5-fold from 1.4% in rural Sweden [31] to 7.8% in the Framingham Heart Study [25]. Subclinical hypothyroidism appears to be more common in females (7–18%) than in males (2–15%) [27, 30, 33] and the Whickham survey (British survey of adults of all ages) demonstrated an increasing prevalence with age in women, reaching 18% in those aged 74 yrs and older, as compared to a relatively stable 2–5% in males regardless of age [34].

Because of the high prevalence of thyroid dysfunction in patients over 60 years of age, the American Association of Clinical Endocrinologists (AACE) has recommended screening for this disorder in older women [34].

Iran is now not an iodine deficiency area, but thyroid dysfunction is one of the major health issues in our country [35]. The prevalence of thyroid dysfunction in elderly women in the community has neither been documented nor established in recent years. The aim of this community-based survey was to investigate the prevalence of thyroid dysfunction in elderly women aged 60 yrs or older.

Materials and Methods
Subjects And Methods

The subjects of this study were enrolled as participants of a community-based survey which was carried out from August 2007 to April 2008 in Tabriz, the capital city of East Azerbaijan, a north-western province of Iran. A sample of 1150 subjects was drawn by using a simple random method from a sampling frame constructed from the records of the mentioned local household registry. The selected subjects were approached either directly or by letter after the exclusion of nonresponse subjects; finally, 1000 (89.6%) subjects were included in our study. The design of this research was approved by the Research Ethics Committee of Tabriz University (Medical Sciences). Personal details on past and present thyroid disorders were obtained by a questionnaire and a general physical examination. The recently prescribed drugs were noted. Following written consent, a blood sample was taken. Fasting blood samples were drawn from the ante cubital vein. Sera were separated after 10 minutes of clotting at room temperature and 10 minutes of centrifugation at 3000rpm. Serum samples were stored at -20 °C prior to their analysis. Tests of thyroid function including those to check TSH concentration in all subjects, free T4 concentration, free T3 concentration and levels of anti-microsomal antibodies, were conducted in patients with abnormal TSH. Serum FT4 and FT3 levels were measured in the same specimens for which tests for the measurement of TSH levels were done. Patients with a clear biochemical evidence of thyrotoxicosis or hypothyroidism (most of whom had symptoms of thyroid dysfunction) were then treated appropriately.

Assays

Sera TSH, FreeT4, FreeT3 and anti-microsomal antibody levels were measured using a fully automated chemiluminescent immunoassay (Liaison, DiaSorin, Saluggia VC, Italy). The coefficients of variation percent were 7.9, 6.2 and 8.3 for TSH, FT4, and FT3, respectively.

The laboratory reference range was 0.3 to 4.5 mU/L for TSH, 0.8 to 1.9 ng/dl for free T4 and 2.2 to 4.2 pg/ml for free T3.

Statistical Analysis

Analyses were undertaken using SPSS (version 14). The results are summarized using Mean ± SD & N (%). Chi square, Fisher Exact test and

Pearson correlation coefficients were calculated to evaluate the association between variables. A probability of <0/05 was considered to be statistically significant. Adjustment to normal distribution was tested by the Kolmogorov – Smirnov test.

Results

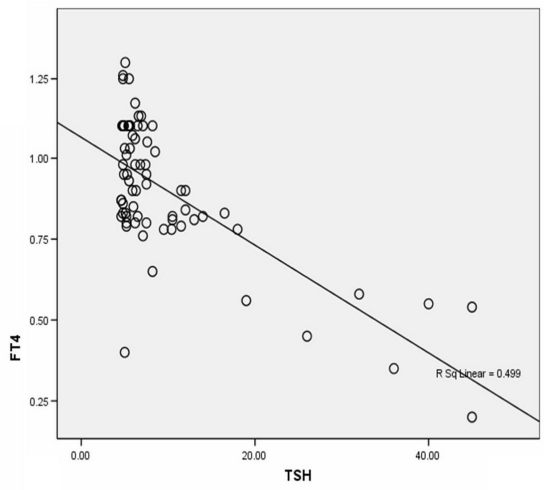
The overall serum TSH levels were 1.77 ± 0.94 mU/liter. Eight hundred and seventy three (87.3) subjects were euthyroid, as indicated by their serum TSH concentrations. One hundred and twenty seven (12.7) subjects had either high or low TSH levels. Seventy-three of them had high TSH and 54 had low TSH values. Prevalence of individuals with low, normal, and high TSH values are given in [Table/Fig 1] with regards to different age strata (60-64, 65-69, 70-74, 75-79, and 80+). There was no correlation between age strata and TSH levels (χ^2 =6.87, df = 8, P = 0.55).

(Table/Fig 1) TSH values in the study group. Results are shown for subjects, divided according to age and TSH concentrations (mU/liter).

AGE	TSH n(1000)			Total
	<0.3	>4.5	0.3 - 4.5	
60-65	32	41	554	627
	5.1%	6.5%	88.4%	100.0%
65-69	12	13	154	179
	6.7%	7.3%	86.0%	100.0%
70-74	6	9	110	125
	4.8%	7.2%	88.0%	100.0%
75-79	3	7	37	47
	6.4%	14.9%	78.7%	100.0%
>80	1	3	18	22
	4.5%	13.6%	81.8%	100.0%
Total	54	73	873	1000
	5.4%	7.3%	87.3%	100.0%

χ^2 = 6.87,df = 8 p = 0.55

Seventy-three subjects (mean age 65.8 ± 6.9 years) had high serum TSH levels. Serum TSH values in this group ranged from 4.6 to104 mU/liter (mean serum TSH, 10.16± 10.30 mU/liter). Serum TSH values strongly correlated with FT4 levels in this group (r = – 0.50, n = 73, p = <0.0005) [Table/Fig 3]. Fifteen subjects had serum FT4 levels below the normal range and 58 were within the normal range. The prevalence of overt hypothyroidism was 1.5% (mean serum TSH, 25.1 ± 2.55 mU/liter) and prevalence of subclinical hypothyroidism was 5.8%. The 54 subjects (mean age 64.5±5.1 years) had low serum TSH levels (range: 0.02 to 0.29 mU/liter; mean serum TSH, 0.067±0.045 mU/liter). Twelve subjects with low TSH (mean serum TSH, 0.06±0.04) had low FT4 levels. One subject had elevated serum FT3 levels with low TSH and normal FT4 levels; 41 subjects with low TSH levels had normal FT4 and FT3 levels. The prevalence of overt hyperthyroidism, subclinical hyperthyroidism and T3 toxicosis were 1.2%, 4.1%and 0.1%, respectively. The anti-microsomal antibody titer was measured in all patients with high TSH levels. A high titer of antibody was present in 60.8% of the patients with high TSH concentrations (88.8% of those with TSH concentrations over 10 mU/liter and in 51% of those with TSH over 4.5 mU/liter and less than or equal to10 mU/liter) Fisher Exact test showed that this difference was significant (χ^2 =8.29, df = 1, P = 0.004).



(Table/Fig 3)The clearly inverse correlation between serum TSH and FT4 was found in high TSH group.

Discussion

The present study has confirmed the markedly high prevalence of thyroid dysfunction in elderly women.

[Table/Fig 2] summarizes the data from previous similar studies. It is notable that each of these studies revealed a similar prevalence of elevated TSH values to that found in the present report, with the exception of Falkenberg et al. (1983)[31] and Chuang et al.(1998) [36] whose found that the prevalence of hypothyroidism was about 2 % and 3%, respectively. The low incidence of hypothyroidism in these two studies might be related to high iodine consumption in the subjects who were studied in Taiwan, as indicated by their high urinary iodine excretion and probably, the use of the low sensitivity TSH assay in the Falkenberg study.

(Table/Fig 2) Summary of the major findings of the present and previous studies of the prevalence of thyroid dysfunction

Reference mU/liter	Age of Subjects	Sex (%)	Number of Subjects	Elevated TSH In female	%
Nystrom [40] et al,(1981)	60+	F 100	222	8.6	(>8)
Falkenberg [31] et al,(1983)	60+	F 100	1442	2.27	(>7)
Sawin [32] et al,(1985)	60+	M 41 F 59	2139	13.6	(>5)
Parie [24] et al,(1991)	60+	M 41 F 59	1210	11.6	(>5)
Chuang [36] et al,(1998)	65+	M 57 F 43	917	3	(>4.65)
Wilson [41] et al, (2006)	65+	M 49 F 51	5960	4	(>5.5)
Present study	60+	F 100	1000	7.3	(>4.5)

Few studies have investigated the prevalence of TSH concentrations below the normal range, although Parle et al. (1991) [24] and Chuang et al. (1998) [36], by using a TSH assay with increased sensitivity, found a level of prevalence in their study, which was similar to our results (6.3%, 4.3% respectively).

In the current study, in subjects with high TSH levels, the TSH values were inversely related to the free T4 values. The results were compatible to the findings of other similar studies [24],[36], [37]. It suggested that elevated TSH values directly reflected on impaired thyroid hormone production. Previous studies have shown that individuals with TSH values above 10 mU/liter could progress to overt hypothyroidism [24], [37], [38]. Furthermore, the follow-up of subjects with high TSH values was important to diagnose the progression of their disease to overt thyroid failure. Nevertheless, the risk of progression to thyrotoxicosis in those with low TSH values appeared to be slight [24].

We found that serum TSH levels did not vary with age. This result was in agreement with other reports [8].

A high prevalence of thyroid autoantibodies (73.3%) was found in patients with overt hypothyroidism. This indicated that autoimmune disease was the major causes of hypothyroidism in elderly populations of Iranian women, in agreement with other studies [8],[36],[39].

In conclusion, we have shown that thyroid dysfunction is common in elderly women; it may often go undetected and may be associated with adverse health outcomes that can be avoided by the measurement of serum TSH levels. High titers of antithyroid antibodies were found in 60.6% of the patients with high TSH levels. This result indicates that autoimmune disease is still the major cause of hypothyroidism in aged people.

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