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Prevalence and Risk Factors of Subclinical Thyroid Disorders in Al-Baha Region, Saudi Arabia

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Abstract

Background: Subclinical thyroid dysfunction (abnormal thyrotropin level and normal serum-free thyroxine level) is a common health problem all over the world. The epidemiological data of subclinical thyroid disorders are still missing among populations in different region of Saudi Arabia. The aim of this study was to evaluate the prevalence of subclinical thyroid disease and its risk factors among Saudi population in Al-Baha region, the southwestern, Saudi Arabia.

Methods: We reviewed the data of 1000 patients, visiting the central laboratory at Albaha, KSA over the last 8 years, and selected all those who had thyroid function results recorded in their laboratory data (free thyroxine, free triiodothyronine and thyroid-stimulating hormone). We examined the laboratory results of the subjects, to assess prevalence of different subclinical thyroid disturbances, in regards to the laboratory standard results. We also analyzed the relationship between abnormal thyroid results and epidemiological data of the studied population.

Results: Of selected 567 subjects, the prevalence of subclinical thyroid disease was 20.3%. The patterns of thyroid dysfunction were as follows, 79.7% were euthyroid, 15.9% had subclinical hypothyroidism and 4.4% had subclinical hyperthyroidism, based on predefined cutoff values of TSH level. The prevalence of subclinical thyroid disease is common among females (13.2% and 3.7%, in subclinical hypothyroidism and hyperthyroidism respectively).

Conclusion: Subclinical thyroid disease is more prevalent among populations in Al- Baha region, being more prevalent in women than in men. A physician should be aware of screening for subclinical thyroid disease, especially among elderly females with nonspecific symptoms.

Keywords: Subclinical; TSH; FT4; Thyroid disease; Prevalence; Saudi Arabia; Screening

Introduction

Subclinical thyroid disorders are diagnosed by an abnormal serum thyrotropin (TSH) levels with serum free thyroxine concentration (FT4) being within the reference range [1]. The TSH cutoff values for diagnosis of these abnormalities are still debatable issue. Also, there is much debate about the significance of subclinical thyroid disease in terms of potential associations with long-term morbidity and mortality and hence much debate about whether to screen for these abnormalities, and, once identified, whether to treat or monitor [1]. However, the risk of cardiovascular disease is increased among these patients [2,3]. Despite the high prevalence of subclinical thyroid disease (3-12% for subclinical hypothyroidism and 1-6% for subclinical hyperthyroidism [4-9], the subclinical thyroid disease is still underdiagnosed, and neglected chronic health problem [4-9]. The form of this disease depends on age, gender, presence of thyroid autoantibodies, weather, ethnicity and iodine status in different areas [7,10,11].

To date and best our knowledge, the frequency, and types of subclinical thyroid disease were studied in a few researches in Saudi Arabia, but no research was conducted in our region to highlight the prevailing data on subclinical thyroid disease. Thus, the objective of our study was to determine the prevalence and categories of subclinical thyroid disease in Al-Baha region, the southwestern region of Saudi Arabia and its risk factors.

Subjects and Methods

Study design

This retrospective study was conducted at AL-Baha University, we reviewed the files of 1000 patients visiting the central laboratory in Al-Baha, from 2010 to 2017. The inclusion criteria were the availability of FT4, FT3 and TSH results in the patient's record, the age of the patients were above 18 years.

Of 1000 reviewed files, 567 files of population were selected in this study based on the exclusion of those who had known thyroid disorders, pregnant, on androgens or estrogen therapy, showed

biochemical evidence of hyperthyroidism or hypothyroidism, renal failure, and liver cell failure. From the excluded 433 cases, thirteen cases showed evidence of biochemical hypothyroidism and 15 cases showed evidence of biochemical hyperthyroidism.

The following data were collected from the patients' files: demographic features, history of thyroid disease or thyroid medications, FT4, FT3 and TSH levels.

Ethical aspects

The Ethical Research Committee of the Faculty of Medicine of Al-Baha University criteria was met.

Thyroid profile determinations

Serum TSH, FT3 and FT4 were measured by electrochemical-luminescence immunoassay on Cobas e411 (Roche Diagnostics International Ltd. Switzerland) according to the manufacture protocol. Serum FT4 normal reference range is 9.2-23.8 pg mL, FT3 normal reference range is 1.9-4.8 pg/ mL and TSH normal reference range is 0.35-4.5 mU/L with detection sensitivity 0.005 mIU/mL. The intra and interassay coefficient of variation for TSH was 1.4% and 3.4%, respectively.

Criteria for thyroid alterations

Subjects were further categorized according to measurements of serum TSH and FT4 levels [12]:

- Euthyroid: if FT4, FT3 and TSH were normal
- Hypothyroidism: if the TSH was raised together with a decreased FT4
- Hyperthyroidism: if the TSH was low (TSH <0.20 mU/L) with high FT4 and FT3
- Subclinical hypothyroidism if the TSH was high level >4.5 mIU/L with normal FT4
- Subclinical hyperthyroidism: if TSH was low <0.2 with normal FT4

Statistical analysis

Data analysis was done using Statistical Package for Social Sciences (SPSS software version-20). Means and standard deviations were calculated for quantitative data and proportions for categorical variables. To establish the relationship between categorical variables, Chi square testing was used and Independent t-test or ANOVA were used between continuous variables with normal distribution assumed. P-value <0.05 is considered in rejecting the null hypothesis.

Results

Of the 567 study subjects with no history of thyroid disease, 101 (17.8%) were males and 466 (82.2%) were females. The mean age of the studied population was 43 ± 13.9 SD years (range 18–77 years). Of them, the prevalence of subclinical thyroid disease was 20.3%. The patterns of thyroid dysfunction as follows, 452 (79.7%) were euthyroid, 15.9% had subclinical hypothyroidism and 4.4% had subclinical hyperthyroidism, based on predefined cutoff values of TSH level. The prevalence of subclinical thyroid disease is common among females (13.2% and 3.7%, in subclinical hypothyroidism and hyperthyroidism respectively) (Table 1).

	Gender		p
	Male No. (%)	Female No. (%)	
Euthyroidism	82 (14.5%)	370 (65.3%)	
Subclinical hypothyroidism	15 (2.6%)	75 (13.2%)	0.9
Subclinical hyperthyroidism	4 (0.7%)	21 (3.7%)	

Table 1: Prevalence of subclinical thyroid disorders among the studied populations.

There were significant difference between the mean serum TSH and FT4 levels in patient with euthyroidism when compared with patients presented with different subclinical thyroid disorders ($p \leq 0.001$and 0.002 respectively) (Table 2).

	Serum TSH Mean ± SD (range)	Serum FT4 Mean ± SD (range)
Euthyroidism	2.2 ± 1.08 (0.2-4.6)	16.9 ± 2.8 (10.6-25.1)
Subclinical hypothyroidism	7.8 ± 4.6 (4.6-37.2)	16 ± 3.1 (10.2-23)
Subclinical hyperthyroidism	0.0.08 ± 0.04 (0.001-0.1)	18.1 ± 3.4 (12.5-24.5)
P	<0.001	0.002

Table 2: The mean serum TSH and Free T4 among different pattern of subclinical thyroid disorders.

The prevalence of subclinical hypothyroidism among males was 15 (2.6%) and females was 75 (13.2%), while, the prevalence of subclinical hyperthyroidism among males was 4 (0.7%) and among females was 21 (3.7%), of the studied cases with no significant difference (p=0.9) (Table 1).

	Baha	Baljurashi	Qura	Mikhwa	Al-Mandaq	Hajra	Qilwah
Euthyroidism	249	1	25	90	13	15	59
Subclinical hypothyroidism	43	1	5	25	2	1	13
Subclinical hyperthyroidism	9	0	2	7	2	2	3
P	0.4						

Table 3: Distribution of subclinical thyroid disorders among different cities in Al-Baha region.

The distribution of subclinical thyroid disorders in different areas of Al-Baha region are shown in Table 3 and there was no significant difference of thyroid disorders in different areas of Al-Baha region (p=0.4) (Table 3).

Discussion

Subclinical thyroid dysfunction is a common health problem all over the world and its prevalence is increasing in all parts of the world. Age, gender, iodine status, weather, ethnicity, methods and a cutoff value of TSH and the presence of thyroid autoantibodies may affect its prevalence and pattern in different areas. Due to lack of data from different regions of Saudi Arabia about the subclinical thyroid disease, we aimed to evaluate the prevalence of subclinical thyroid disease and its risk factors among Saudi population in Al-Baha region, the southwestern region of Saudi Arabia.

Previous studies used a variety of TSH assays and/or TSH cutoff values. So, the normal reference range for TSH should be standardized. Some defined the normal reference range of TSH as 0.45 to 4.5 mIU/L [10], while in the German study defined it as 0.3 to 3.7 mIU/L, which is quite lower than the previous reported range. This difference may be related to mild iodine-deficiency among German peoples [13]. In many studies, subclinical hypothyroidism is defined as a TSH>4.0 to 6.0 mIU/L with normal FT4 levels [14-16].

As regards, the prevalence and categories of subclinical thyroid disease in Al-Baha region we found that the prevalence of subclinical thyroid disease was 20.3%. Of them, 15.9% had subclinical hypothyroidism (15 males and 75 females) and 4.4% had subclinical hyperthyroidism (4 males and 21 females). These percentages are comparable with those reported in some other studies [5,15,17,18], although they are considerably higher than those reported by others [19-21]. In Riyadh region, Saudi Arabia, Eidan Al Eidan and his colleagues found that, the prevalence of subclinical hypothyroidism was 10.3% and 2.1% had subclinical hyperthyroidism [21]. This difference in prevalence estimates of subclinical hypothyroidism among the previous studies may be related to the ethnic group, TSH assay, cutoff values used, the type of population assessed (e.g. community, hospitalized), and geographical area [14]. The study conducted in 2011 in Libya reported that, the prevalence of subclinical hypothyroidism was 2.3% [8]. However, in Iraq, Basim et al. found that among 103 patients presented with gall bladder stones, 7.8% found to have subclinical hypothyroidism and most of them were showing the female gender predominance with 81.6%. [22]. The higher prevalence of subclinical thyroid disease in our study may be attributed to the type of selected population (peoples visiting the central laboratory in Al-Baha) which may not represent the whole community and this may hamper the generalization of these results and lower cutoff value of TSH used in our study.

To explore the risk factors attributed to high prevalence of subclinical thyroid disease in our study, we found that, the prevalence of subclinical thyroid disease was affected by gender and age. The subclinical thyroid disease was more common among females' vs. males (13.2 vs. 2.6% in subclinical hypothyroidism and 3.7% vs. 0.7 in subclinical hyperthyroidism). These results vs. are in agreement with some previous studies [8,23-25]. Also, subclinical hypothyroidism had been reported to be higher (20%) especially in females above 60 years [25]. The reason for this higher prevalence among female is still vague, and this could be linked to estrogen female hormone, hormone replacement therapy in women (excluded in our study) [18] and a predominance of autoimmune thyroid diseases in women.

Beside gender, age plays an important role as a risk factor for subclinical thyroid disease in several previous studies, especially with advanced age [19]. In this work, the mean age of our population was 43 ± 13.9 SD years (range 18–77 years).

In addition, We did not anticipate comparable prevalence rates in other populations with differing iodine status, in areas with excess iodine supplementations, thyroid function will be decreased through direct effect or immunological variations [20], subclinical hypothyroidism is more prevalent in relatively iodine-rich areas ; 6.1% to 18.0% [15,25,26] compared to 0.9% to 3.8% in iodine-deficient areas [4,27]. In our study the high prevalence of subclinical thyroid disorders may be related to universal usage of iodized salt in Saudi Arabia, However, the iodine status is not studied in our region to ensure sufficient supply of iodinated salts.

The prevalence of subclinical hypothyroidism has been reported to be increased in cold weather [28]. Our data should be typical with other studies conducted in the same geographical area, Al-Bahah is located in the south west of Saudi Arabia and due to its location at 2,500 meters (8,200 ft) above sea level, Al- Baha's climate is moderate in summer and cold in winter. The effect of climate on the TSH level had been studied before, the TSH level increased 1.4-fold during the winter-spring and then return to normal level during the summer-autumn seasons [28]. This TSH levels variation could be explained by adaptive thermogenesis, which is lower in cold weather [29]. This temperature variation should be considered in the interpretation of TSH level and subclinical thyroid disease prevalence in our region. Also, TSH level could be affected by the photoperiod, and this may be linked to melatonin, which play an important role in neuroendocrine pathways in mammals [30].

The association between ethnicity and prevalence of subclinical thyroid disease was investigated before in many studies with controversy, some of these studies reported that, serum TSH concentrations were higher among whites than in blacks [14,27]. However, the prevalence of subclinical hyperthyroidism was higher among blacks than in whites (0.4, vs. 0.1%, respectively) or Mexican Americans (0.3%) [14]. In contrast, Bagchi et al. found the reverse (3.9 vs. 1% in favor the white populations) [26]. In our region most of the populations are not black.

The reported prevalence of subclinical hyperthyroidism is lower than subclinical hypothyroidism which was between 0.2% to 9.7 % (average 2% to 3%) [27]. The National Health and Nutrition Survey (NHANES) in the United States revealed 1.8% of the general population to have low but detectable serum TSH and only

0.7% to have fully suppressed serum TSH (after exclusion of 'exogenous' cases) [14], with similar findings from a population prevalence study in Scotland [31]. Both of these studies revealed a higher prevalence in women and a rise in frequency with age. In this study, the prevalence of subclinical hyperthyroidism was 4.4% and common also among females (3.7%, vs. 0.7 in males). This prevalence is similar to other studies [4,16] and lower than the other reported prevalence [8]. In Libya, the reported prevalence of subclinical hyperthyroidism was 0.84%, and more common in females [32].

The variation in prevalence of subclinical hyperthyroidism between different studies may be explained by different iodine state, age, race and iodine intake within the population, sample size and variation in participants' characteristics could have resulted in different prevalence of subclinical thyroid disease.

The risk factors of subclinical hyperthyroidism are similar to those found in subclinical hypothyroidism [4,15,16], however the major difference in risk factors is the amount of iodine intake; hyperthyroidism is more common in iodine-insufficient areas [11,16].

Conclusion

Subclinical thyroid disease is more prevalent among the studied populations in Al-Baha region, with a higher prevalence in women. A physician should be aware of screening for subclinical thyroid disease, especially among elderly females with non-specific symptoms and once identified, whether to treat or monitor.

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