Prevalence of Subclinical Hyperthyroid Disease In Population of Central Nepal and Its Association With Age and Gender A Hospital-Based Study

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Abstract

Background: Subclinical hyperthyroidism is an increasingly recognized entity that is defined as normal serum free thyroxine and free triiodothyronine levels with thyroid-stimulating hormone level suppressed below the normal range and usually undetectable. Subclinical hyperthyroidism may be related only in part to Graves' disease or multi nodular goitre. The burden of thyroid disease in the general population is enormous. Here, we critically study the prevalence of subclinical hyperthyroid disease in the population of Central Nepal.

Materials and Methods: The study was carried out at National Medical College and Teaching Hospital, Birgunj, Nepal Anthropometric data were collected including thyroid function profile (free T3 and free T4).

Results: Of the 680 patients in the study group, 165 were males and 515 were females, ranging from 21 to 60 years of age. Status of euthyroid, overt hyperthyroid, subclinical hyperthyroid, and low free T3 & T4 levels were seen in 70.74%, 12.65%, 10.44%, and 6.18% respectively in cases. The prevalence of subclinical thyroid disease was found to be 10.44%, with 2.4% in males and 8.04% in females; and being more prevalent in age group 21-40 years age compared to other age groups ($p<0.05$).

Conclusion: The prevalence of subclinical hypethyroidism amongst the suspected cases was 10.44 % which is much higher compared to the other parts of the world, with higher prevalence seen in females as compared to males. The reason(s) for such a high prevalence of hyperthyroidism in central Nepal needs to be studied further.

Keywords : Subclinical hyperthyroidism, free T3, free T4, central Nepal

Introduction

Thyroid disease is a common disorder previously thought to affect 1–2% of the United Kingdom adult population and its prevalence is affect ed by several factors such as age [1] (Tunbridge et al., 1977). The epidemiology of thyroid disease and thyroid dysfunction remains unclear, especially when compared with other endocrine disorders [2] (Flynn et al., 2004), affecting about 300 million people worldwide and over half are presumed to be unaware of their condition [3] (Peter, 2009), and is also a major health problem of Nepal with prevalence of nearly 30% of the population affected in eastern region of Nepal alone (Baral et al., 2002). However, the prevalence and pattern of hyperthyroidism depend on ethnic, geographic, and environmental factors including iodine intake status [3,4,5] (Baral et al., 2002; Peter, 2009; Aminorroaya et al., 2009).

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Subclinical hyperthyroidism is an increasingly recognized entity that is defined as a normal serum free thyroxine and free triiodothyronine levels with a thyroid-stimulating hormone level suppressed below the normal range and usually undetectable [6] (Diene et al., 2002). The pathophysiology of subclinical hyperthyroidism relates to the sensitivity of the pituitary gland to respond to minor elevations in serum freeT3 and freeT4 levels. Although these vels remain within the normal range, minimal increase in these thyroxine and triiodothyronine are sufficient, not only to decrease the serum TSH level by several logarithms (from about 1.0 μU per mL (1.0 mU per L) to less than 0.01 μU per mL (0.01 mU per L]), but also to induce abnormalities in several organs, including the heart and bones [6] (Diane et al., 2002). There is a varying degree of reports of hyperthyroidism across the globe, particularly in Asian regions. A study by Akhtar et al reported 5.1% hyperthyroidism and 5.85% subclinical hyperthyroidism in all age groups [7] (Akhtar et al., 2001). An epidemiological survey from Cochin showed 1.6% subclinical and 1.3% overt hyperthyroidism in case subjects [8] (Menon et al., 2009). Another study by Gomez et al reported 58.2% hyperthyroidism (53.1% of which were T4 thyrotoxicosis, 12.5% T3 thyrotoxicosis and 34.4% had subclinical hyperthyroidism) and 8.2% of patients had iodine induced hyperthyroidism [9] (Gomez et al., 1993). In a hospital-based study from Pondicherry, it was found that the prevalence of subclinical and overt hyperthyroidism was 0.6% and 1.2% of subjects respectively [10] (Abraham et al., 2009). Similarly, another hospital-based study from Kavre, Nepal, reported 9% of total hyperthyroidism including both 6% subclinical hyperthyroidism and 3% hyperthyroidism [11] (Aryal et al., 2010); whereas study conducted in Far Western Parts of Nepal, reported 24.8% hyperthyroid disorders, including 14.9% overt hyperthyroidism and 9.9% subclinical hyperthyroidism [12] (Yadav et al., 2012).

Due to the variations in the prevalence of hyperthyroidism including both overt- and subclinical hyperthyroidism, we aimed to study their prevalence in population of Central Nepal. To the best of our knowledge, this is the first study that has investigated the prevalence of subclinical hyperthyroid disease in population of Central Nepal; and its association with age and gender.

Materials and Methods

The study was carried out using data retrieved from the register maintained in the Department of Biochemistry, Central Laboratory Services (CLS) of the National Medical College and Teaching Hospital, Birgunj, Nepal, from July, 2009 to January, 2012. Anthropometric data were collected including thyroid function profile (free T3, and free T4). Serum fT3 and fT4 were assessed in the biochemistry laboratory, Central Laboratory, National Medical College, Birgunj, Nepal, using an Eliscan™ free T3 and free T4, manufactured by RFCL Limited, India. The internal quality control was included in each batch of tests performed.

Statistical analysis

The data collected was analyzed using Excel 2003, R 2.8.0 Statistical Package for the Social Sciences (SPSS) for Windows Version 16.0 (SPSS Inc; Chicago, IL, USA). Data were analyzed using Student's t-test. All the data are mean ± SD. Two-sided $P < 0.05$ was considered to indicate statistical significance.

Results

Of the 680 patients in the study group, 165 were males (24.26%), 515 were females (75.74%).

Table 1: Percentage Distribution of Thyroid Disorders

Table 1. The status of thyroid disorders in the studied population

Cases	Frequency	Percentage (%)
Euthyroidism	481	70.74
Overt Hyperthyroidism	86	12.65
Subclinical Hyperthyroidism	71	10.44
Low fT3 and fT4	42	6.18

Table 2. Comparison of % Prevalence of Subclinical hyperthyroidism in male and female population

Gender	Subclinical Hyperthyroidism (%)
Males	2.4
Females	8.04

Table 2. Shows the variation in % prevalence of subclinical hyperthyroidism in male and female population of Central Nepal. This study showed the prevalence of subclinical hyperthyroidism of 10.44%. Females showed higher prevalence of subclinical hyperthyroidism with 8.04% as compared to males with 2.4% ($p<0.05$).

Table 3. Comparison of Thyroid Hormone Levels in Males and Females

Thyroid Hormones	Males	Females	p Value
fT3	2.25 ± 0.52	4.92 ± 5.13	< 0.05
fT4	1.42 ± 0.26	1.93 ± 1.91	< 0.05

Table 3. Comparison of level of thyroid hormones (free T3 and free T4) in males and females. Serum fT3 and fT4 levels were significantly different in male and females.

Table 4. Comparison of Thyroid Hormone Levels Among Different Thyroid Disorders

Thyroid Hormones	Euthyroidism	Overt Hyperthyroidism	Subclinical Hyperthyroidism
fT3	2.31 ± 1.26	16.14 ± 4.09	1.98 ± 1.28
fT4	1.26 ± 0.51	5.09 ± 0.42	1.76 ± 0.27

Table 5. Comparison of Thyroid Hormone Level among Different Age Groups

Thyroid Hormones	0 - 20 Years	21 - 40 Years	41 - 60 Years	> 60 Years
fT3	3.13 ± 4.01	4.19 ± 4.97	3.98 ± 5.09	3.96 ± 3.51
fT4	1.86 ± 1.19	2.23 ± 1.68	1.76 ± 1.57	1.56 ± 1.29

Table 5. Comparison of serum free T3 and free T4 levels among different age groups. The serum free T3 and free T4 levels showed variation in different age groups. Serum free T3 and free T4 levels in age groups between 21 - 40 years were found to be significantly increased as compared to 0 - 20 years, 41 -60 years, and > 60 years age group (all $p<0.05$).

Discussion

Thyroid disorder is the major health problem associated with endocrine abnormalities worldwide. Our study showed 23.09% prevalence of total hyperthyroidism including both overt hyperthyroidism (12.65%) and subclinical hyperthyroidism (10.44%) in population of Central Nepal. Our study is in accordance with another study by Yadav et al, a hospital-based study done in eastern part of Nepal which showed 24.8% hyperthyroidism including 14.9% overt hyperthyroidism and 9.9% subclinical hyperthyroidism (Yadav et al., 2012).

The present study showed higher prevalence of hyperthyroidism in females as compared to males. This also corroborates with the study conducted by Mark et al who showed higher prevalence of subclinical hyperthyroidism in females compared to males (Mark et al., 2011). Similarly, in the Whickham survey cohort, the mean annual incidence of hyperthyroidism in women was 0.8 per 1000 with no new cases detected in men [14] (Vanderpump et al., 1995). Other cohort studies provide comparable incidence data, which suggess that many cases of hyperthyroidism remain undiagnosed in the community unless routine testing is undertaken [14] (Vanderpump, 2005). In the large population study in Tayside, Scotland, 620 incident cases of hyperthyroidism were identified with an incidence rate of 0.77/1000 per year (95% CI): 0.70–0.84) in women and 0.14/1000 per year (95% CI: 0.12–0.18)

in men [2] (Flynn et al., 2004). The incidence rate showed that women were affected two to eight times more than men across the age range. Recent further analysis suggested that the incidence of thyrotoxicosis was increasing in women but not in men between 1997 and 2001 [16] (Leese et al., 2008). However, contrasting result have been showed by Baral et al. [4] (2002) , where they reported equal proportion of thyroid dysfunction in male and female (Baral et al., 2002) [4]. Therefore, other factors, such as sex hormones and genetic differences, may have an influence on the free T3 and freeT4 findings.

Our results also showed higher free T3 and free T4 levels in 21 – 40 years [17] age group as compared to other age groups. This result is similar to the NHANES III study which showed the prevalence being highest in those subjects aged 20–39 years (Hollowell et al., 2002). Also, the peak age-specific incidence of Graves' disease was between 20 and 49 years in two studies [18] (Zimmerman, 2009). However, this result is in contrast to the one conducted by Yadav et al who showed insignificant increase in free T3 and free T4 levels in all age groups [12] (Yadav et al., 2012).

Hence, from our study, we can conclude that the people residing in Central Parts of Nepal have higher risk for hyperthyroid disorders, with higher prevalence being in females as compared to males.

To the best of our knowledge, this is the first study that has investigated the prevalence of subclinical hyperthyroidism in population of Central Nepal; and its association with age and gender. Since the strengths of this study were modest, their clinical significance remains to be determined in prospective studies related to risk of cardiovascular disease and bone loss. A limitation of this study is that it has a cross-sectional design; implicating cause-and-effect relationship cannot be discerned. Also, since it was a hospital-based study, the prevalence of thyroid dysfunction may not be applicable to the general population. However, we believe that its strength is due to the greater number of subjects of this study.

Recommendation

Further studies are required to characterize the reasons for this high prevalence of subclinical hyperthyroidism in population of Central Nepal. Extensive field-based countrywide epidemiological studies are necessary to provide accurate data about thyroid dysfunction in the community. Also, the people are required to be educated regarding the thyroid dysfunction cause and prevention methods to minimize the occurrence of thyroid disorders. Since, the analysis of a low TSH level and subclinical hyperthyroidism raises the controversial issue of screening, there should be recommendation about serum TSH concentration screening be instituted at age 35 years in both men and women and be repeated every five years [19] (Ladenson et al., 2000); and of course, if symptoms develop or if risk factors are present (e.g., thyroid antibodies), more frequent testing may be in order (Helfand et al., 1998) [20].

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