

Prevalence and impact of thyroid disorders based on TSH level among patients visiting tertiary care hospital of South Western Nepal

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ABSTRACT

The clinical judgment for a patient to undergo medication with hypothyroidism and hyperthyroidism is very crucial because it is associated with a constellation of signs and symptoms and is cumbersome to control thyroid disorders. Hence, the prevalence of population based on clinical decision level of TSH at 6.2-10 mIU/l and 10.1-15 mIU/l for proper management of sub-clinical hypothyroidism as well as decision level of TSH <0.1 mIU/l for proper management of sub-clinical hyperthyroidism is projected in this study. This is a cross sectional study carried out in the Department of Biochemistry, Universal College of Medical Sciences Teaching Hospital, Bhairahawa, Nepal from January 2011 to January 2013 for the period of two years. A total of 3109 who visited OPD with suspected thyroid disorders viz a viz hypothyroidism, hyperthyroidism or to rule out thyroid disorders got their thyroid function test. Serum TSH and fT_3/fT_4 estimations were carried out by competitive ELISA method and Sandwich double antibody ELISA method respectively. Out of the 3109 study subjects (male: 23.7% (n=738) and female: 76.3% (n=2371) who visited UCMSTH with chief complaints of thyroid or related diseases, the sub-clinical hypothyroidism was found in 25.98% (n=808), overt hypothyroidism was found in 10.38% (n=323), sub-clinical hyperthyroidism in 2.02% (n=63), overt hyperthyroidism in 1.99% (n=62) and euthyroidism in 59.63% (n=1853). The analysis of scatter diagram between TSH versus fT_4 with decision level of TSH at 10.1-15 mIU/L and with fT_4 more than lower limit of 0.8 ng/dl have prevalence 265 (20.38%) comprising (M:57 (4.53%) and F: 208 (16.56%). Similarly, The TSH level between 6.2-10 mIU/L and with fT_4 more than lower limit of 0.8 ng/dl with frequency 501 (39.88%) comprising (M:116 (9.23%) and F:385 (30.65%). The analysis of scatter diagram between TSH versus fT_4 with decision level of TSH level >0.1 mIU/l and fT_4 level <2 ng/ml have prevalence 77(6.13%) (M: 11 (0.87%) and F: 66 (5.27%). Our study revealed there is still many patients with small increase in TSH level and are not clearly defined for undertaking drug regimen. Moreover, our paper highlight the high prevalence of hypothyroidism among reproductive age group commonly found in female who are in child bearing age and has to undergo thyroid function test time to time.

Keywords: Prevalence, Thyroid Disorders, TSH, South Western Nepal

INTRODUCTION

Thyroid disorders are amidst the most prevalent medical conditions worldwide with 1.6 billion people are at risk and 2.2 billion people are affected with iodine deficiency throughout the world including the United States of America.¹ It has been shown to be the most common endocrine disorders in eastern region, central and far western region of Nepal. There are fundamental limitations in the epidemiological study of thyroid dysfunctions in relation to selection criteria of sample used, explanation of overt and subclinical hypothyroidism, and the influence of age, sex, genetic and environmental factors and various techniques used for the measurement of thyroid hormones.² Besides all these limitations population at particular risk tend to be remote and live in mountainous areas in South East Asia, Latin America and central Africa. Almost one-third of the world's population lives in area of iodine

deficiency.³ Nepal is an endemic area with regard to iodine deficiency and nutritional iodine deficiency are thought to be prevalent in all Himalayan, Sub Himalayan and Terai regions of Nepal.⁴

Increase in serum concentration of Thyroid Stimulating Hormone (TSH) is an early and sensitive indicator of decreased thyroid reserve and in conjunction with decreased free thyroxin (fT_4) is diagnostic of primary overt hypothyroidism.⁵ The term subclinical hypothyroidism is used to describe patients with elevated TSH concentration but with normal levels of T_4 , T_3 and fT_4 . Despite the clinical sensitivity of TSH, a TSH-centered strategy has two primary limitations. First, it assumes that hypothalamic-pituitary function is intact and normal. Second, it assumes that the patient is stable i.e. the patient had no recent therapy for hyper- or hypothyroidism.⁶ If either of these criteria is not met, the serum TSH result can be misleading. In these instances,

to confirm the presence of thyroid dysfunction, in addition to measuring TSH, measurement of free T_4 (fT_4) may be helpful. In 2004, the 13-member expert panel led by Surks published their findings in the January issue of JAMA and recommended TSH reference limits of 0.4-4.5 $\mu\text{U/mL}$ (0.4-4.5 mU/L) and that patients with TSH ranges from 4.5-10.0 mU/L not be routinely treated.⁷ The 2002 American Association of Clinical Endocrinologists (AAACE) guidelines recommend treatment of those with TSH > 10.0 $\mu\text{U/mL}$ (10.0 mU/L) or those with goiter and positive thyroperoxidase antibody (TPOAb) whose TSH is between 4.5-10.0 $\mu\text{U/mL}$ (4.5-10.0 mU/L).⁸ TSH should be used to monitor patients receiving thyroid hormone replacement therapy as well as those treated with hormone to suppress malignant thyroid disease.⁹ At least 6 weeks is needed before retesting TSH following a change in the dose of L-thyroxine.

Overt hyperthyroidism patients have decreased TSH level with increased levels of fT_3 & fT_4 . Subclinical hyperthyroidism is defined as low TSH (<0.1 mU/L) with normal levels of fT_4 & fT_3 without any signs or symptoms of hyperthyroidism.¹⁰ Detection of subclinical hyperthyroidism is particularly important in patients who are over 60 as they have increased risk of atrial fibrillation, increased cardiovascular mortality and osteoporosis.¹¹

We believe this study could be milestone in getting nationwide prevalence and also help the patients to improve their disease state by monitoring and control strategies by assessing their thyroid function based on TSH level.

MATERIALS AND METHODS

This cross sectional study was carried out in the Department of Biochemistry, Universal College of Medical Sciences Teaching Hospital (UCMSTH), Bhairahawa, Nepal from January 2011 to January 2013. UCMSTH is a tertiary care hospital situated at South Western Nepal (SWN) and provides health services to people from different districts of Lumbini zone and adjoining areas of Uttar Pradesh, India. A total of 3109 patients who visited the hospital with suspected thyroid disorders viz a viz hypothyroidism, hyperthyroidism or for screening of thyroid disorders got their thyroid function test done were included in this study. The study protocol was duly approved by the ethical committee of the UCMSTH.

Data Collection: Demographical variables were collected from patient's requisition form sent with blood samples. fT_3 , fT_4 and TSH level were estimated in the Department of Biochemistry by Enzyme Linked Immuno Sorbent Assay (ELISA) method. Serum was separated from blood samples and stored at -20°C until analysis. Serum fT_3 and fT_4 estimation were carried out by competitive ELISA method using commercially supplied

reagents (Human, Germany) and concentrations were expressed in pg/ml and ng/dl respectively. Similarly, estimation of serum TSH level was carried out by Sandwich or double antibody coated ELISA method by aforementioned kit and expressed in mU/L. Washing steps were performed in ELISA washer (Erba, Germany) and reading was taken in ELISA reader (Erba, Germany).

Diagnostic Criteria of thyroid disorders: Patients were diagnosed into different categories according to normal reference range of euthyroid state of the patient as given in the protocol as fT_3 (1.4-4.2 pg/ml), fT_4 (0.8-2.0 ng/dl) and TSH (0.3-6.2 mU/L). The patients having relevant clinical features with low fT_3 and fT_4 level and increased TSH level (>15.0 mU/L) are diagnosed as overt hypothyroidism. The subclinical hypothyroid patients are diagnosed as having normal fT_3/fT_4 and high TSH level (6.2-15.0 mU/L). Similarly, patients with relevant clinical features having high fT_3/fT_4 and low TSH (<0.1 mU/L) are diagnosed as overt hyperthyroidism. The subclinical hyperthyroidism patients have normal fT_3/fT_4 and low TSH level (<0.1 mU/L). The decision level of TSH was taken at two places in scatter diagram one at 10.1-15 mU/L and another at 6.2-10 mU/L with fT_4 at lower limit of normal 0.8 ng/dl for hypothyroid patients to see the actual population under appropriate treatment and other whose treatment might be obscured due to such value of TSH. Moreover, the decision level of TSH was taken at >0.1 mU/L with fT_4 at upper limit of normal <2 ng/dl for hyperthyroid patients to see the distribution of population.

STATISTICAL ANALYSIS

The information and data were entered into the Excel data sheet and then analyzed by Statistical Package for Social Sciences (SPSS version 17.0). Data were represented as percentage, frequency and mean \pm standard deviation. Statistical significance was calculated using One-Way ANOVA, Scatter plot and Pearson's correlation and p values ≤ 0.05 (two tailed) were considered significant.

RESULTS

Out of the 3109 study subjects (male: 23.7% (n=738) and female: 76.3% (n=2371)) the sub-clinical hypothyroidism was found in 25.98% (n=808), overt hypothyroidism in 10.38% (n=323), sub-clinical hyperthyroidism in 2.02% (n=63), overt hyperthyroidism in 1.99% (n=62) and euthyroidism in 59.63% (n=1853). Among hypothyroid patients (n=1131), diagnosis of overt hypothyroidism (n=323) is solely on the basis of their fT_3 (1.18 \pm 0.04 pg/ml), fT_4 (0.64 \pm 0.01 ng/dl) and TSH (27.87 \pm 1.65 mU/L). The sub-clinical hypothyroidism (n=808) were diagnosed with normal level of fT_4 (2.28 \pm 0.10 pg/ml), fT_3 (1.06 \pm 0.03 ng/dl) and high level of TSH (11.03 \pm 0.56 mU/L). Among hyperthyroid patients (n=125), diagnosis of overt hyperthyroidism (n=62) is solely on the basis of their fT_3 (4.84 \pm 0.13 pg/ml), fT_4

Table 1: Comparison of thyroid hormone level among various thyroid dysfunctions

Thyroid status	Number (%)	fT ₃ (pg/ml)	fT ₄ (ng/dl)	TSH (mU/L)
Euthyroidism	1853 (59.60%)	2.54 ± 0.09	1.21 ± 0.05	3.2 ± 0.16
Sub-Hypothyroidism	808 (25.98%)	2.28 ± 0.10	1.06 ± 0.03	11.03 ± 0.56
Overt- Hypothyroidism	323 (10.38%)	1.18 ± 0.04	0.64 ± 0.01	27.87 ± 1.65
Sub-Hyperthyroidism	63 (2.02%)	2.90 ± 0.08	1.39 ± 0.04	0.16 ± 0.06
Overt-Hyperthyroidism	62 (1.99%)	4.84 ± 0.13	2.37 ± 0.08	0.13 ± 0.07

(2.37±0.08 ng/dl) and TSH (0.13±0.07 mU/L). The sub-clinical hyperthyroidism (n=63) were diagnosed with normal fT₃ (2.90 ± 0.08 pg/ml), fT₄ (1.39 ± 0.04 ng/dl) and low level of TSH (0.16± 0.06mU/L) as shown in (Table 1) The mean and SD of fT₃, fT₄ and TSH levels in different categories of thyroid disorders was significantly different (p<0.05).

Age wise stratification of the data revealed that the prevalence of thyroid disorders was relatively higher in the reproductive age group of 21-40 years representing total 52.78% (n= 663) out of which (male: 5.25% (n=66) and female: 29.37% (n=369) in subclinical hypothyroid, (male : 1.91% (n=24) and female: 11.22% (n=141) in overt hypothyroid, (male: 0.39% (n=5) and female: 1.99% (n=26) in subclinical hyperthyroid, (male: 0.23% (n=3) and female: 2.38% (n=30) in overt hyperthyroid as shown in Table 2. The affected age group 21-40 year is followed by 41-60 year representing 31.13% (n=391).

The analysis of scatter diagram is shown in Figure 1 between TSH and fT₄ with decision level of TSH at 10.1-15.0 mU/L and 6.2-10.0 mU/L. The patients with TSH level in between 10.1-15.0 mU/L in lower left quadrant with fT₄ less than lower limit of 0.8 ng/dl can be under treatment but patients in lower right quadrant with fT₄ more than lower limit of 0.8 ng/dl whose

prevalence is 265 (20.38%) comprises (M:57 (4.53%) and F: 208 (16.56%) and TSH & fT₄ levels (12.14 ± 0.13 mU/L) & (1.00 ± 0.03 ng/dl) respectively are under dilemma to undergo treatment of hypothyroidism. Similarly, the TSH level in between 6.2-10.0 mU/L with fT₄ more than lower limit of 0.8 ng/dl falling under lower right quadrant with frequency 501 (39.88%) comprises (M:116 (9.23%) and F:385 (30.65%) and TSH & fT₄ levels (8.05 ± 0.10 mU/L) & (1.04 ± 0.03 ng/dl) respectively are also in question mark for their treatment of hypothyroidism. The observation of TSH >15.0 mU/L and fT₄ <0.8 ng/dl revealed that the left upper quadrant hypothyroid patients are getting medication without any clinical dilemma. Similarly, the patients falling in right upper quadrant with TSH >15.0 mU/L but normal fT₄ level in between 0.8-2 ng/dl undergoing treatment for hypothyroidism.

The analysis of scatter diagram as shown in Figure 2 between TSH and fT₄ at decision level of TSH 0.1 mU/L. The TSH level >0.1 mU/L with fT₄ level <2 ng/ml falling on left upper quadrant with prevalence 77(6.13%) (M: 11 (0.87%) and F: 66 (5.27%) and TSH & fT₄ levels (0.10 ± 0.04 mU/L) and (1.91±0.08 ng/dl) respectively are under question mark for treatment of hyperthyroidism because of its obscure nature created by TSH and fT₄ level. fT₄ more than upper limit of normal i.e. 2 ng/dl revealed that the right lower quadrant hyperthyroid patients are getting

Table 2: Age and Sex wise distribution of various thyroid dysfunctions

Variables		Sub-Hypo Thyroidism (n=808)	Overt- Hypothyroidism (n=323)	Sub-Hyper Thyroidism (n=63)	Overt- Hyperthyroidism (n=62)	Total Thyroid disorder (n=1256)
0-20 yrs	M	31 (2.46%)	3 (0.23%)	0 (0.00%)	0 (0.00%)	34 (2.70%)
	F	44 (3.50%)	19 (1.51%)	1 (0.07%)	0 (0.00%)	64 (5.09%)
	Total	75 (5.97%)	22 (1.75%)	1 (0.07%)	0 (0.00%)	98 (7.80%)
21-40 yrs	M	66 (5.25%)	24 (1.91%)	5 (0.39%)	3 (0.23%)	98 (7.80%)
	F	369 (29.37%)	141 (11.22%)	25 (1.99%)	30 (2.38%)	565 (44.98%)
	Total	435 (34.63%)	165 (13.13%)	30 (2.38%)	33 (2.62%)	663 (52.78%)
41-60 yrs	M	55 (4.37%)	20 (1.59%)	6 (0.47%)	3 (0.23%)	84 (6.68%)
	F	188 (14.96%)	81 (6.44%)	16 (1.27%)	22 (1.75%)	307 (24.44%)
	Total	243 (19.34%)	101 (8.04%)	22 (1.75%)	25 (1.99%)	391 (31.13%)
>60 yrs	M	28 (2.22%)	18 (1.43%)	2 (0.15%)	2 (0.15%)	50 (3.98%)
	F	27 (2.14%)	17 (1.35%)	8 (0.63%)	2 (0.15%)	54 (4.29%)
	Total	55 (4.37%)	35 (2.78%)	10 (0.79%)	4 (0.31%)	104 (8.28%)

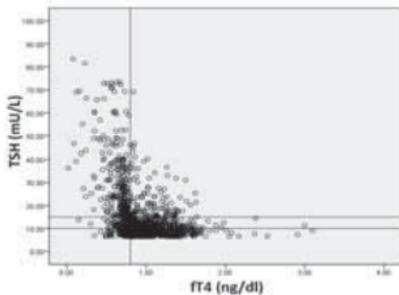


Fig. 1: Scatter plot between TSH and FT_4 among hypothyroid patients at clinical decision level of TSH (6.2-10.0 mU/L) [n=501 (M=116, F=385), mean \pm SD of TSH (mU/L) and FT_4 (ng/dl) are (8.05 \pm 0.10) & (1.04 \pm 0.03) respectively as shown in the right lower quadrant] and (10.1-15.0 mU/L) [n=265 (M=57, F=208), mean \pm SD of TSH (mU/L) and FT_4 (ng/dl) are (12.14 \pm 0.13) & (1.00 \pm 0.03) respectively as shown in the right upper quadrant and at lower normal level of FT_4].

medication without any clinical dilemma. Similarly, the patients falling in left lower quadrant with TSH < 0.1 mU/L but normal FT_4 level in between 0.8-2 ng/dl undergoing treatment of hyperthyroidism.

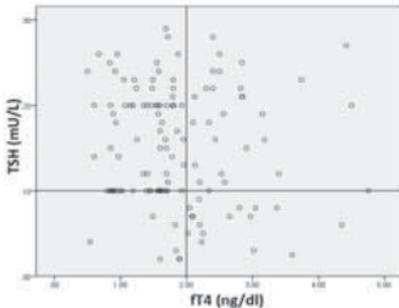


Fig. 2: Scatter plot between TSH and FT_4 among hyperthyroid patients at clinical decision level of TSH > 0.1 mU/L and high normal level of FT_4 , < 2 ng/dl [n=77 (M=11, F=66) and mean \pm SD of TSH (mU/L) and FT_4 (ng/dl) is (0.1 \pm 0.04) & (1.91 \pm 0.08) respectively as shown in the left upper quadrant].

DISCUSSION

Several studies have reported a high prevalence of thyroid disorders based on different geographical location, socio-demographical variation, ramification of thyroid status, physiological, biochemical changes and dietary evaluation for thyroid status. Many studies under different set up have revealed nearly 30% of population was suffering from thyroid dysfunction in eastern part¹², 25% dysfunction in population of Kavre, Nepal¹³ and 33.66% in far western region of Nepal.¹⁴ Our study has found that the prevalence of thyroid disorder among all age group was 40.39% which comprises

of 25.98% of sub-clinical hypothyroidism, 10.38% of overt hypothyroidism, followed by 2.2% sub-clinical hyperthyroidism and 1.99% of overt hyperthyroidism. Similar study conducted by Aryal M et al in Dhulikhel of Nepal has shown overall hypothyroidism case 16%, comprising 8% subclinical hypothyroidism and 8% overt hypothyroidism followed by 6% sub clinical hyperthyroidism and 3% overt hyperthyroidism.¹³ The prevalence of hypothyroidism in this study was 36.37% which is higher as compared to study by Baral N et al¹² and Jha et al¹⁵ as 13.68% and 17.19% respectively. This difference might exist as it reflects the sample employed consisting of total population or hospitalized patients. Similarly there might be geographical, environmental or genetic factors playing role in such difference.¹⁶ Goitrogens in the diet such as thiocyanate in incompletely cooked cassava or thioglucosides in brassica vegetables can explain some of the differences of endemic goiter in areas with similar degrees of iodine deficiency.

The prevalence of thyroid disorders in the reproductive age group of 21-40 years of age was highest 52.78% which is in congregation to result shown by NK Yadav et al¹⁴ and Baral N et al¹². In all age groups female were more affected than male. This might reflect female are more susceptible to autoimmune disorder than male and playing key role in hypothyroidism. The age group 41-50 years with prevalence of 31.13% come on second and followed by >60 years with prevalence of 8.25%. This trend of thyroid disorder in reproductive age group followed by elderly age group show the havoc created by thyroid problem to economically sustain it. This is more vulnerable to child bearing and pregnant women falling under reproductive age groups. Hence American Thyroid Association recommends the screening for those women to be started as early as 20 years and every 5 years thereafter rather than 35 years.

Subclinical hypothyroidism is also one of the important conditions affecting maximum population. Although patients have subtle finding, including alteration in lipid metabolism, cardiac, gastrointestinal, neuropsychiatric and reproductive abnormalities and increase likelihood of goiter.^{17,18} Similarly, subclinical hyperthyroidism has been shown to affect the health of untreated patients adversely. Appropriate laboratory evaluation is critical to establish the diagnosis and cause of hypothyroidism and hyperthyroidism in the most cost effective way. The most valuable test is a sensitive measurement of TSH level. Hence we have designed the decision level of TSH at two points in scatter diagram, one at (10.1-15.0 mU/L) and another at (6.2-10.0 mU/L) to see prevalence of patients which might be devoid of getting actual treatment. At decision level of TSH (10.1-15.0 mU/L) with lower limit of normal 0.8 ng/dl, high TSH (12.14 \pm 0.13 mU/L) and normal FT_4 (1.00 \pm 0.03 ng/dl) has been observed with the prevalence of 20.38%. Similarly, at decision level of TSH between (6.2-10.0 mU/L) and FT_4 at lower limit of normal i.e. 0.8 ng/dl, high TSH (8.05 \pm 0.1 mU/L) and normal FT_4 (1.04 \pm 0.03 ng/dl) was

observed with the prevalence of 39.89%. These patients should not be treated at instance because of its obscure nature created by sensitive TSH as well as fT_4 level. Only patients in left upper most quadrant and few from right upper quadrant in scatter plot are rationalized for getting effective treatment for hypothyroidism. The TSH level >10 mIU/l or in patients with TSH levels between (6.2-10.0 mIU/L) in conjunction with goiter or positive TPOAb or both only should undergo treatment.⁸ At this context, evidence does not support the routine universal screening for subclinical hypothyroidism or recommend for the treatment of subclinical hypothyroidism.^{19, 20, 21, 22}

Hence these patients are at a highest rate of progression of subclinical hypothyroidism patients getting converted into overt hypothyroidism.²³ Moreover, the decision level of TSH at 0.1 mIU/L and fT_4 at upper limit of normal i.e.2 ng/dl with low TSH (0.10 ± 0.04 mIU/L) and fT_4 (1.91 ± 0.08 ng/dl), the prevalence was 6.13%. Only patients with right lower quadrant and few from right upper quadrant in scatter plot are rationalized for getting effective treatment. It has been suggested that prolonged subclinical hyperthyroidism may be associated with decreased bone mineral density, cardiac effect and progression to overt hyperthyroidism.^{24, 25}

The increase in prevalence of thyroid disorders with subtle increase in TSH level clearly indicates likelihood increase in the prevalence of overt hypothyroidism. It is therefore necessary to generate public awareness campaign among Nepalese population about risk of dietary iodine deficiency, autoimmune disorders and various other associated consequences of thyroid disorders.

Our study revealed the high prevalence of hypothyroid patients in which sub clinical hypothyroid is large in population and these patients are at high risk. There are still many patients with small increase in TSH level and are not clearly defined for undertaking drug regimen which can develop constellation of symptoms to the patient related with thyroid problem. Moreover, our study highlights the high prevalence among reproductive age group commonly found in female who are in child bearing age and should undergo thyroid function test at regular interval.

ACKNOWLEDGEMENT:

The authors would like to thank Prof. V.K Pahwa, CEO and Prof. Anand Kumar, Principal, Universal College of Medical Sciences, Bhairahawa, Nepal for their constant bolster and encouragement to carry out this study. Authors are also thankful to Mr. Dewesh Kumar Thakur and Narayan Prasad Guragain, Clinical Laboratory Technician, Universal College of Medical Sciences, Bhairahawa, Nepal for their continuous help in analysis of blood samples and data collection for this study.

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