

Thyroid Function Abnormalities among Hospital Patients of Hilly Nepal

Raj Krishna Dangol,^a Priya Lanjekar,^a Chandrasekhar Pulipati^a

ABSTRACT:

Introduction: Thyroid dysfunction stands as the second most common endocrine disease after diabetes mellitus. National reports on its prevalence are meagre. Hence, the study was conducted with the objective of exploring the prevalence of thyroid dysfunction among hospital patients of hilly region of Nepal. **Methods:** A hospital based, retrospective, analytical study was conducted in the department of biochemistry, Lumbini Medical College Teaching Hospital (LMCTH) from 15th February 2017 to 30th April 2017. The hospital records of patients from March 2014 to mid-February 2017 with suspected thyroid dysfunction and presented from different departments of hospital were reviewed. Data was entered in Excel 2007 and analysis was done with Statistical Package for Social Sciences (SPSS-21). Necessary descriptive and inferential statistical analysis was done. *P* value less than 0.05 was regarded as statistically significant. **Results:** Out of 3136 subjects, 601 (19.2%) were male and 2535 (80.8%) were female with F:M ratio of 4.2:1. Female were more likely to be suspected of thyroid dysfunction. Mean age of male was 39.28 years (*SD* = 19.01) and that of female was 39.60 years (*SD* = 14.63). Prevalence of thyroid dysfunction was 23.31%. Correlation of log₁₀ TSH with age showed a significant relation (*r* = -0.05, *p* = 0.003). Age group and thyroid function category among female patients was found to be statistically significant (*p* = 0.01). **Conclusion:** The prevalence of thyroid dysfunction was high in Tansen region, a hilly mid-west Nepal. Female above 40 yrs (post reproductive age) and male above 60 yrs (elderly group) were more prone to thyroid disorders. Also, the study revealed that younger people are more likely to be euthyroid whereas as age advances, people are likely to be either hypothyroid or hyperthyroid. These findings can be a guide for elaborative research in thyroid disorder in future.

Keywords: hyperthyroidism • hypothyroidism • thyroid diseases • thyroid function tests • thyroid hormones

INTRODUCTION:

Among the endocrine diseases, thyroid dysfunctions are the second most common, being next only to diabetes mellitus. It may manifest ranging from hyperthyroidism to hypothyroidism depending on the level of thyroid hormones in the blood. Dietary Iodine deficiency is an important underlying cause of thyroid disorder, especially in hilly region.[1,2]

The frequency of thyroid disorders varies in different countries. The national study for prevalence of thyroid dysfunction in Nepal was not conducted, to the best of our knowledge. However, numerous studies from different parts of Nepal have reported different prevalence.

The present study was planned to explore the prevalence of thyroid dysfunction in different age and sex in population visiting Lumbini Medical College Teaching hospital which mainly covers hilly districts of Nepal.

METHODS:

This was a hospital based, retrospective, analytical study conducted in the department of biochemistry, Lumbini Medical College Teaching Hospital (LMCTH) from 15th February 2017 to 30th April 2017. We reviewed the hospital records from

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March 2014 to mid-February 2017 of the populations presenting to various departments of the hospital and were suspected of having thyroid dysfunction. Duplication involved in the follow up was excluded. The study was approved by institutional review committee of LMCTH.

Thyroid Function Test:

Blood samples in the fasting state were collected with aseptic precautions. After centrifugation at optimum speed, sera were separated and then stored at 4°C until the assay. Assays of T₃, T₄ and TSH were performed by chemiluminescent immunoassay using the kits and procedure from Acculite using high affinity specific conjugated and immobilized antibody in excess. The immobilization was achieved by the interaction of streptavidin and exogenously added biotinylated monoclonal antibody coupled to the test sample. Following antigen-antibody reaction, soluble sandwich complex formation and enzymatic conversion of substrate to the product, light was generated which was proportionate to the concentration of test sample.

The following were the reference ranges for normal T₃, T₄ and TSH as per the kit suppliers:

- Serum T₃: 0.5 to 1.9 ng/ml
- Serum T₄: 4.5 to 11.6 µg/ml
- Serum TSH: 0.3 to 5.1 µIU/ml

The subjects were categorized according to measurements of serum TSH and total thyroid hormone concentrations as in Table 1.

Data regarding age, sex, and hormone level were collected using Excel 2007, analysis was done with Statistical Package for Social Sciences (SPSS-21) for windows (SPSS Inc.; Chicago, IL, USA). Data were presented as percentage, frequency, mean, and standard deviation. Correlation was done between two scale data, Chi-square test was used to analyze the relationship between categorical data,

Table 1: Categorization of study subjects based on thyroid function test.

Category	Criteria
Euthyroid	Normal serum TSH with normal T ₃ and T ₄
Subclinical hypothyroid	serum TSH >5.1 µIU/ml and normal T ₄
Hypothyroid	Serum TSH >5.1 µ IU/ml and total T ₄ < 4.5 µg/dl)
Hyperthyroid	Serum TSH < 0.3 µ IU/ml

t-test was done to compare mean of two groups and ANOVA test were used to observe the relationship between mean of more than two groups. *P* value <0.05 was considered as statistically significant.

RESULTS:

There were a total of 3136 subjects who were suspected of thyroid dysfunction and advised for thyroid function test. Of this, 601 (19.2%) were male and 2535 (80.8%) were female with F:M ratio of 4.2:1. Assuming equal distribution of gender coming to our hospital, the difference in proportion of gender was statistically significant ($\chi^2[N=3136, df=1] = 1192.7, p < 0.001$). Female were more likely to be suspected of thyroid disorder.

Mean age of male was 39.28 years (*SD* = 19.01) and that of female was 39.60 years (*SD* = 14.63). This difference of age among gender was not statistically significant ($t = -0.38, df = 776.7, p = 0.7$).

Among 3136 subjects, 731 (23.31%) had abnormal thyroid function; thus, the prevalence of thyroid dysfunction was 23.31% among the hospital patients who were suspected of having the condition (Table 2).

Among the patients with abnormal thyroid function, 17.4% ($n = 127, N = 731$) were male and

Table 2: Frequency of thyroid function category among study population

Category	<i>n</i>	%
Euthyroid	2405	76.7
Subclinical hypothyroidism	313	10
Hyperthyroidism	306	9.8
Overt hypothyroidism	112	3.6
Total	3136	100

82.6% ($n = 604$) were female. The F:M ratio among the subjects with abnormal thyroid function was 4.76:1. This difference in proportion of gender ($F = 82.6\%, M = 17.4\%$) when compared to that among suspected of having abnormal thyroid function ($F = 80.8\%, M = 19.2\%$) was not significant ($\chi^2[N=731, df=1] = 0.004, p = 0.985$).

The TSH value among the population was not normally distributed (Fig: 1). When it was transformed to $\log_{10}$ of TSH, the values were near normally distributed (Fig: 2). Correlation of $\log_{10}$ TSH with age showed a significant relation ($r = -0.05, p = 0.003$). With advancing age, $\log_{10}$ TSH was likely to decrease (Fig: 3).

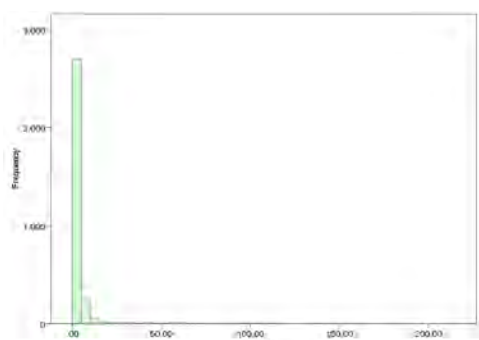


Fig 1: Distribution of serum TSH which is right skewed

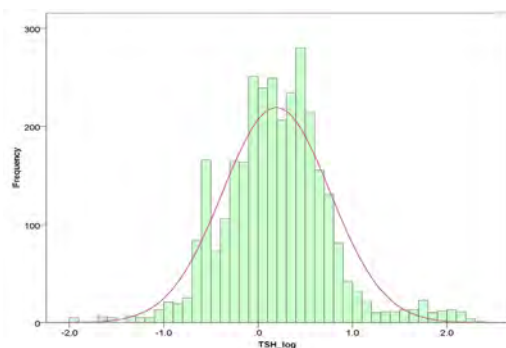


Fig 2: Distribution of $\log_{10}$ TSH which is near normally distributed.

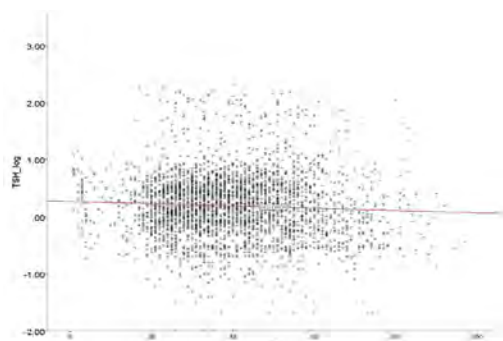


Fig 3: Correlation between age and $\log_{10}$ TSH of the study subjects showing a negative correlation

Mean age of subjects according to thyroid function test category is shown in Table 3. This difference in mean age was significant by Anova test ($F = 10.7$, $df = 3$, $p < 0.001$). Post-hoc analysis showed a significant difference of mean age between euthyroid and overt hypothyroid individuals ($p = 0.02$), and euthyroid and hyperthyroid individuals ($p < 0.001$), but not between other groups. This shows that younger people are more likely to be euthyroid whereas as age advances, people are likely to be either hypothyroid or hyperthyroid.

Occurrence of thyroid function category in both gender is shown in Table 4. The difference in the rate between two gender was not statistically significant ($X^2[df=3, N=3136] = 4.1$, $p = 0.25$).

Table 3: Mean age of subjects according to thyroid function test category

Thyroid function test category	n	Mean (Yrs)	SD
Euthyroid	2405	38.73	15.28
Subclinical hypothyroid	313	40.82	16.63
Overt hypothyroid	112	43.08	13.65
Hyperthyroid	306	43.26	16.55

Table 4: Thyroid function category in both gender

Gender	Euthyroid	Subclinical hypothyroid	Hyperthyroid	Overt hypothyroid
Male	474	61	51	15
n (%)	(78.9)	(10.1)	(8.5)	(2.5)
Female	1931	252	255	97
n (%)	(76.2)	(9.9)	(10)	(3.8)

$$X^2 = 4.1, N = 3136, df = 3, p = 0.25$$

Patients were divided into clinically appropriate age groups to see the relationship of various thyroid dysfunction with those age groups in both gender. Females were divided into three age group; up to 20 years, 21 to 40 years, and more than 40 years on basis of pre-reproductive age, reproductive age, and post-reproductive age respectively. Males were divided into three age group; up to 30 years, 31 to 60 years, and more than 60 years to indicate young, adults, and elderly people respectively.

Relationship between age group and thyroid function category among female patients is shown in Table 5. There was a statistically significant relation by Chi-square test. Post-hoc analysis showed only the cell in euthyroid above 40 years of age was significant. Thus, with increasing age, chance of being euthyroid decreases significantly in female.

Relationship between age group and thyroid function category among male patients is shown in Table 6. There was no significant relation by Chi-square test.

Table 5: Relationship between age group and thyroid function category among female

Age (Yrs)	Euthyroid	Overt hypothyroid	Subclinical hypothyroid	Hyperthyroid
< 21	135	4	14	11
n (%)	(82.3)	(2.4)	(8.5)	(6.7)
21-40	985	40	112	116
n (%)	(78.6)	(3.2)	(8.9)	(9.3)
>40	811	53	126	128
n (%)	(72.5)*	(4.7)	(11.3)	(11.4)

$$X^2 = 16.7, df = 6, N = 2535, p = 0.01, * = \text{significant cell}$$

Table 6: Relationship between age group and thyroid function category among male

Age (yrs)	Euthyroid	Overt hypo- thyroid	Subclinical hypothyroid	Hyper- thyroid
< 31 n (%)	174 (83.7)	3 (1.4)	19 (9.1)	12 (5.8)
31-60 n (%)	235 (78.1)	11 (3.7)	28 (9.3)	27 (9)
>60 n (%)	65 (70.7)	1 (1.1)	14 (15.2)	12 (13)

$$\chi^2 = 11.6, df = 6, N = 601, p = 0.7$$

DISCUSSION:

The prevalence of thyroid dysfunction depends on many factors including the method of assay, ranges of serum values defining hypo and hyperthyroidism and the age, gender and also ethnicity of the individuals used in the study. When the studies are undertaken without keeping these variables in mind the value of the study becomes limited. The present study showed an overall 23.31% prevalence of thyroid dysfunctions among the population of mid-western hilly Nepal who came to hospital for various reason and were suspected of having thyroid dysfunction. Similar study conducted in other parts of Nepal found various results. Baral N et al. found that 30% of populations among the hospital patients were affected from thyroid disorder in eastern part of Nepal.[3] Aryal M et al.[4] recorded 25% in Kavre, Mahato RV et al.[5] reported 29% in central (Kathmandu) Nepal, Yadav RK et al.[6] observed 17.42% in Pokhara, and Yadav NK et al.[7] found 33.66% in far-western part of Nepal. This variation may be due to ethnic, geographic, and environment factors including iodine intake status as mentioned in other studies.[1,2] Iodine deficiency may be an important factor in the hilly areas. Though government of Nepal has made a mandatory provision for iodine fortification in salt, still iodine concentration are simply not high enough to maintain thyroid hormone production due to lack of knowledge in proper use of iodized salt. Further, chronic stimulation of thyroid may leads to thyroid nodularity and autonomy.[8]

As 80.83% of the study subjects were female, they constituted 82.62% of the total population with thyroid dysfunction. When gender wise prevalence is considered, 21.13% among male and 23.82% among female were found, which indicates almost similar prevalence of thyroid dysfunction among the male and female. Similar result is also reported by Baral N

et al.[3] and Jailkhani R et al.[9]

In this study, the prevalence of total hypothyroidism was 13.55% (9.98% subclinical and 3.57% overt hypothyroidism). It was also supported by Bhutia SC et al. on their hospital based study carried out in Gangtok of Sikkim, India, which reported 13.5% hypothyroidism with 10.0% subclinical and 3.5% overt hypothyroidism.[10] A report from Pokhara which is near to our study location, also found similar result with 12.76% hypothyroidism.[6]

We found more than 80 percent of population affected were female indicating females were more susceptible for thyroid dysfunction. The thyroid disorders are more common in female than male. [10,11,12] It may due to hormonal change, such as during or after pregnancy or after menopause. Sex hormones, especially estrogen and prolactin, have an important role in modulating the immune system and may impact autoimmune disease. A study conducted by Unnikrishnan AG et al. in different cities of India found females and older age were significantly associated with hypothyroidism and most of them had positive for anti-thyroid peroxidase (TPO) antibodies indicating the autoimmune etiology.[13] Serum TSH concentrations decrease even in normal individuals with increase in age due to decreased pituitary function. In addition, there is also a shift in the circadian rhythm of TSH secretion with a peak occurring one to 1.5 hours earlier in the elderly. In some studies an increase in TSH was found with increase in age which might be due to the inclusion of women with thyroid antibodies and /or subclinical hypothyroidism. The age dependent increase of prevalence of positive antithyroperoxidase (anti-TPO) and anti-thyroglobulin (Anti-Tg) antibodies, especially in females over 60 years have been reported. [14]

Hyperthyroidism was detected in 9.76% in the present study which was comparable to Aryal M et al.[4] A hospital based study carried out by Yadav NK et al in far western region of Nepal, found 24.8% of hyperthyroidism which is much higher than our finding.[7] Another study conducted by Mahato et al. in central region of Nepal and Yadav RK et al. in western region of Nepal, reported the prevalence of 4% and 4.66% of hyperthyroidism respectively which is much lower than in the present study.[5,6]

In present study, the mean age of patients with thyroid dysfunction was found 42.18 yrs ($SD = 16.2$). It was in concordance with the result of Das A. et al. in which the abnormal thyroid function

is common above age of 40 yrs.[15] The American Thyroid Association also recommends that adult be screened for thyroid dysfunction by measurement of the serum thyrotropin concentration, beginning at age 35 yrs and every 5 yrs thereafter.[16]

When age-wise prevalence of thyroid dysfunction was considered, 51.3% of total study populations with thyroid dysfunction were in age group of more than 40 yrs and 42.4% in age group 21-40 yrs. This study showed the incidence of thyroid dysfunction to be much higher among adults. Among female, several studies have reported higher incidence of thyroid dysfunction in reproductive age which is contrast to our study.[9,17,18] Our study revealed the higher frequency of thyroid dysfunction in more than 40 yrs which is in accordance with other studies.[15,19]

This study has limitations of being hospital based, it cannot represent general population, and

the inability to assay auto antibodies. Further, we did a total T_3 and T_4 along with TSH. The study could have been strengthened if free T_3 , free T_4 , thyroid binding globulin, and antibodies were included in stratifying thyroid dysfunction.

CONCLUSION:

The present study revealed that the prevalence of thyroid dysfunction were high in Tansen region, a hilly mid-west Nepal. Thyroid dysfunction is common in female more than 40 yrs of age (post reproductive age) and male more than 60 yrs (elderly group). This can be used as a baseline data for further studies in future.

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