Analysis of Factors Associated with Thyroid Dysfunction: A Hospital Based Study

Risal P,[1] Adhikari B,[2] Shrestha R,[2] Manandhar S,[2] Bhatt RD,[1] Hada M[1]

[1]Department of Clinical Biochemistry,

[2]Department of Natural Science-Human Biology,

Kathmandu University School of Medical Sciences

Dhulikhel, Kavre, Nepal.

Corresponding Author

Prabodh Risal

Department of Clinical Biochemistry

Kathmandu University School of Medical Sciences

Dhulikhel, Kavre, Nepal.

E-mail: prabodh07@hotmail.com

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ABSTRACT

Background

Thyroid dysfunction (TD) is one of the major public health concerns in Nepal. This study intends to identify factors in association with thyroid dysfunction and its hospital based prevalence.

Objective

To determine hospital-based prevalence of thyroid dysfunction and to identify and analyze factors in association with thyroid dysfunction.

Method

A retroprospective cross-sectional study was conducted among patients attending Dhulikhel Hospital-Kathmandu University Hospital (DH,KUH) from January to December, 2015 with prospective part carried out from July to December 2015 in the patients visiting Dhulikhel hospital for health check-up and requested for Thyroid Function Tests (TFTs). Thyroid Function Tests of 1530 subjects were performed in the biochemistry laboratory and semi-structured questionnaire were introduced to 312 participants with convenient sampling method and their anthropometric measurements were taken. Chi-square test, Pearson's correlation and student-t test were used as a measure to analyze factors.

Result

Out of total 1530 subjects, 35.3% were having thyroid dysfunction with the prevalence of overt hyperthyroidism, subclinical hyperthyroidism, overt hypothyroidism and subclinical hypothyroidism to be 2.5%, 2.4%, 5.6% and 24.8% respectively. The distribution of thyroid dysfunction was preponderant among females and among older age. The prevalence of thyroid dysfunction was highest among Terai/Madhesi (40.0%) and lowest among Newars (28.5%) with higher fraction of hypothyroidism in each ethnic group. There were significant correlation between Thyroid Stimulating Hormone (TSH) with waist-hip ratio ($p<0.05$) and weight (kg) with free thyroxine (fT4) ($p<0.05$). Direct pesticide exposure ($p<0.05$) was significantly associated with hypothyroidism. The serum fT4 was significantly different ($p<0.05$) among vegetarian and non-vegetarian whereas TSH and free triiodothyronine (fT3) were not significantly different. Smoking, alcoholism, dietary food habits, diabetes and hypertension were not significantly associated with thyroid dysfunction.

Conclusion

Thyroid dysfunction was highly prevalent among participants with higher proportion of subclinical hypothyroidism. Besides, direct pesticide exposure found to be factor in association with hypothyroidism, this study could not find significance relation with other established risk factors.

KEY WORDS

Hyperthyroidism, Hypothyroidism, Thyroid dysfunction, Thyroid function test

INTRODUCTION

Thyroid dysfunction (TD) is defined as the graded phenomenon with abnormal serum Thyroid Stimulating Hormone (TSH) level with normal or abnormal thyroid hormones (Triiodothyronine-T_3 and Thyroxine-T_4.[1] It is a common endocrine disorder and one of the major public health concerns in the world. TD can be either hyperthyroidism (subclinical and overt) or hypothyroidism (subclinical and overt) based on TFTs. About 300 million people are affected by TD in the world and half of which are expected to be unaware of it.[2] Hospital based studies performed in different parts of Nepal shows higher prevalence of TD ranging from 25 to 34%.[3-5] Female and elderly age people are at higher risk of TD.[2-3] All forms of TD affect females more than men and older age people more than younger.[2-3,6]

Thyroid dysfunction depends on status of iodine intake and dietary factor.[2] Excess or deficiency of iodine in diet leads to hypothyroidism.[7] In context of Nepal, 18% of the population have iodine deficiency.[8] Therefore, Nepalese people are at high risk hypothyroidism. Soya beans and its products, vegetables from brassica family, cruciferous vegetables, peach, turnip, spinach, rutabaga, carrot and plant tuber possess goitrogens that have marked effect on thyroid function.[9-10]

Use of pesticide in agriculture is increasing rapidly in Nepal.[11] It could be the reason behind higher prevalence of TD in Nepal, because different studies showed that pesticide exposure interfered thyroid function.[12,13]

A study among Nepalese Diabetes Mellitus Patients showed smoking, family history and female gender as associated risk factor with TD.[14] However Study of factor associated with TD among Nepalese population is still limited. Hence, the primary objective of this study was to analyze and identify different factors in association with TD. We also aimed to determine distribution of TD among the studied population. The findings of this study will help to design a community oriented strategy for prevention and management of TD.

METHODS

A retroprospective, cross-sectional study was conducted among the patients attending Dhulikhel Hospital, Kathmandu University Hospital (DH, KUH) from January to December 2015 with prospective part carried out from July to December 2015 for health check-up and who were requested for Thyroid Function Tests (TFTs). In the prospective study, semi-structured questionnaire were introduced to 312 patients and their anthropometric measurements (Height, Weight, Waist Circumference, and Hip Circumference) were taken to evaluate the factors in association with thyroid dysfunction. Informed consent was taken from patients before introducing semi-structured questionnaire and anthropometric measurement. Blood was collected from median cubital vein by phlebotomist using aseptic technique in a vacutainer. The blood sample was then processed in the clinical biochemistry laboratory for TFTs using Chemiluminescence ImmunoAssay (CLIA) technique (LIAISON, DiaSorin, Italy) following standard protocol according to the manufacturer. Free thyroxine (fT_4), free triiodothyronine (fT_3) and TSH were measured during TFTs. Ethnicity of subjects were classified to determine ethnicity wise distribution of TD based on Population Monograph of Nepal, 2014.[15]

Patients below twenty and above eighty years of age and pregnant women because of physiologically abnormal thyroid function, patient with thyroidectomy, patients taking anti thyroid drugs or thyroid hormones were excluded from this study. Ethical clearance was taken from institutional review committee of (DH, KUH) and privacy of all participants was maintained.

Classification of Thyroid Dysfunction: Classification of TD was done based on result of TFTs. The reference range of fT_4, fT_3 and TSH were 0.8-1.7 ng/dL, 2.2-4.2 pg/mL and 0.3-3.6 mIU/L respectively. The subjects whose fT_4, fT_3 and TSH fall within given range were considered as normal (euthyroidism). Those with abnormal fT_4, fT_3 and TSH were further classified into four types: overt hypothyroidism (elevated TSH and low T_4), subclinical hypothyroidism (elevated TSH and normal fT_4 and fT_3), subclinical hyperthyroidism (low TSH and normal fT_4 and fT_3) and overt hyperthyroidism (low TSH and elevated fT_4 and fT_3).

Due to missing information in the questionaries only 288 samples were used for data analysis. Data analysis was performed using Microsoft excel 2010 and SPSS version 20.0. Chi-square test, Pearson's correlation and student t-test were used to assess factors associated with TD in univariate analysis.

RESULTS

Out of 1530 patients, 1110 (72.5%) were female and 420 (27.5%) were male. Among them 540 (35.3%) people had thyroid dysfunction and 990 (64.7%) were euthyroid. The distribution of hyperthyroidism (including subclinical and overt hyperthyroidism) was 74 (4.8%) and that of hypothyroidism (including subclinical and overt hypothyroidism) was 466 (30.5%) people. The distribution of overt hyperthyroidism, subclinical hyperthyroidism, overt hypothyroidism and subclinical hypothyroidism were 2.5%, 2.4%, 5.6% and 24.8% respectively.

As shown in the figure 1. the distribution of TD was found to be higher among Terai/Madhesi followed by Hill-Chhetri and Hill-Brahmin and lower among Newars followed by Hill-Dalits.

Table 2 shows that pesticide exposure was found to be significantly associated with hypothyroidism. Beside this

Table 1. Characteristics of participants enrolled in the study

Characteristics	Number (%)
Age group	
20-29	106(36.8)
30-39	76(26.4)
40-49	72(25)
50-59	23(7.9)
60 and above	11(3.9)
Gender	
Female	88(30.5)
Male	200(69.5)
Smoking status	
Non-smoker	245(85)
Smoker	43(15)
Alcohol	
No	218(75.7)
Yes	70(24.3)
Pesticide Exposure	
Not exposed	200(69.5)
Exposed	88(30.5)
Diet	
Non-vegetarian	248(86.1)
Vegetarian	40(13.9)
Goitrogenic vegetable intake	
Never	38(13.2)
Occasional	196(68)
Frequent	54(18.8)
Cooking oil	
Mustard oil	148(51.4)
Other	140(48.6)

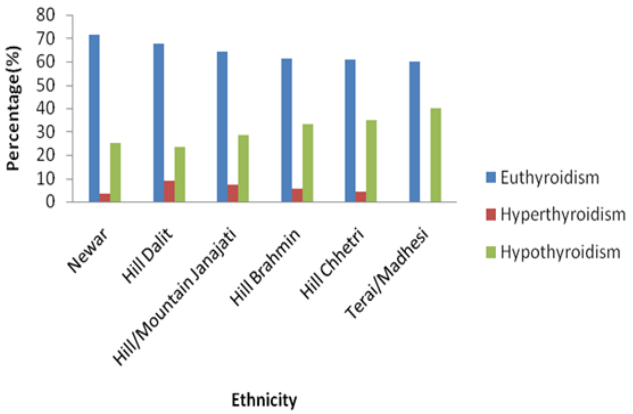

Figure 1. Ethnicity wise distribution of Thyroid Dysfunction

Table 2. Analysis of factors associated with Hypothyroidism

Factors		Total N=288 n	Euthyroidism N=172 n(%)	Hypothyroidism N=116 n(%)	p value
Smoking	Non smoker	245	147 (60.0)	98 (40.0)	0.819
	Smoker	43	25 (58.1)	18 (41.9)	
Alcohol	No	218	126 (57.8)	92 (42.2)	0.240
	Yes	70	46 (65.7)	24 (34.3)	
Pesticide exposure	Not exposed	200	131 (65.5)	69 (34.5)	0.003
	Exposed	88	41(46.6)	47 (53.4)	
Diet	Non-Vegetarian	248	153(61.7)	95(38.3)	0.089
	Vegetarian	40	19(47.5)	21(52.5)	
Goitrogenic vegetable intake	Never	38	23 (60.5)	15 (39.5)	0.421
	Occasional	196	121 (61.7)	75 (38.3)	
	Frequent	54	28 (51.9)	26 (48.1)	
Cooking Oil	Mustard oil	148	92 (62.2)	56 (37.8)	0.385
	Other	140	80 (57.1)	60 (42.9)	
Diabetes mellitus	Absent	264	160 (60.6)	104 (39.4)	0.164
	Present	22	10 (45.5)	12 (54.5)	
Hypertension	Absent	234	142 (60.7)	92 (39.3)	0.489
	Present	54	30 (55.6)	24 (44.4)	

Table 3. Comparison of Biomedical Parameters-TSH, fT_4 and fT_3 among different factors

Factors		Thyroid Hormones		
		TSH (mIU/L) ± SE	fT_4 (ng/dL) ± SE	fT_3 (pg/mL) ±S
Gender	Male	4.38±0.41	1.06±0.575	3.09±0.05
	Female	4.56±0.23	1.04±0.01	3.04±0.04
	P	0.709	0.339	0.458
Direct pesticide exposure	Yes	3.35±0.29	1.03±0.67	3.32±0.39
	No	3.75±0.45	1.04±0.04	2.95±0.12
	P	0.586	0.877	0.226
Diet	vegetarian	3.64±0.47	1.00±0.03	2.91±0.11
	Non vegetarian	3.79±0.33	1.12±0.04	3.17±0.14
	P	0.858	0.015	0.459

none of the other factors were found to be significantly associated with hypothyroidism. Similarly none of factors were found to be significantly associated with hyperthyroidism.

Table 3 shows comparison of different biochemical parameters among different factors. TSH, fT_3 and fT_4 levels were not significantly different in between male and female when student-t test was applied. However, the mean level of TSH was higher and thyroid hormones were slightly lower among females. Similarly, the level of TSH and fT_3 were not significantly different among vegetarian and non-vegetarian subjects whereas level of fT_4 was significantly different among them (p=0.015).

Our study revealed that there were significant correlation between TSH with waist-hip ratio (r=0.147, p<0.05) and weight (kg) with fT_4 (r=-0.149, p<0.05) whereas there was

no significant correlation between BMI and TSH, fT_4 or fT_3.

And finally 99.4% subjects of our study were found to use iodized salt and almost every people use iodized salt during cooking.

DISCUSSION

The prevalence of TD was found to be higher compared to the previous study done in DH-KUH (35.3% vs. 25%).[3] This suggests that after an interval of 5 years, TD might be increasing by 10%. Similarly, compared to the prevalence reported by other hospital based study in Nepal, our finding is higher which may be due to higher sensitivity of methodology (CLIA instead of ELISA) used for TFTs in this study.[4-5]

Our study revealed that the prevalence of hypothyroidism was higher than hyperthyroidism. Which was similar to the findings made by various hospital based studies of Nepal.[3-5] Studies indicate that Nepalese people are at higher risk of hypothyroidism due to the iodine deficiency.[7,8]

According to our present study, almost 99.4% people were using iodized salt which contradict that an iodine deficiency is not the reason behind hypothyroidism. But almost every people added iodized salts during cooking which results in excessive loss of iodine resulting in iodine deficiency and increasing risk to hypothyroidism. This reason is supported by a study showing that the iodine loss depends on cooking methods and time of addition of iodized salts during cooking.[16]

This study also found the prevalence of hyperthyroidism and hypothyroidism were not significantly different among males and females. Our finding was similar with Baral et al.[4] Contrasting with the findings of Aryal et al. and Tunbridge et al.[3,6] This difference among studies conducted within Nepal and abroad might be due to the biases resulting from selection of patients attending hospital as a study population.

In our present study, distribution of TD was found to be higher among Terai/Madhesi followed by Hill-Chhetri and Hill-Brahmin and lower among Newars followed by Hill/Mountain-Janajati. The distribution of hypothyroidism is much higher in each ethnic group in comparison to hyperthyroidism. Our study showed that 40.0% of subjects within Terai caste and 35.7% within hill caste had TD which means TD is nearly equal in both terai and hill caste which was contrasting with a study in eastern Nepal, which showed that the ratio of TD for hill caste and terai caste to be 1:4.[4] It might be due to very few sample size of patients from terai caste in our study.

In this study, level of fT_4 was not significantly different among smoker and non-smoker. This is similar to different studies that showed that smoking results in no change in T_4 level and was contrasting with the few other studies which reported that smoking results in slight rise in T_4 level.[17-20] Similarly, our study showed that TSH level didn't significantly vary among smoker and non-smoker which was concordant with a study done by Karakaya et al. and Eden et al.[18,19] And was contrasting with the findings made by few other studies that report TSH level decreases with smoking.[17-19] Furthermore, fT_3 level was not significantly different among smoker and non-smoker. This was contrast with the study done by Hegedus et al. and Karakaya et al.[18,21] It indicates TD might be independent of smoking. In this study diabetes and dyslipidemia was identified on the basis of past medical report so there is chance of classification bias that might have resulted in negative finding association with those factors.

The level of TSH, fT_4 and fT_3 was found to be unchanged despite the direct exposure to pesticides and is similar to the findings in different studies.[13,22] But, is different with some other studies which showed TSH level increase and fT_3 level decrease on exposure to pesticides.[12,23] However, chi square test performed to find out the association of pesticide exposure to TD in this study revealed that hypothyroidism is significantly associated with direct pesticide exposure.

This study found no correlation between BMI and TSH, which is similar to a finding in a study done by Manji et al. but is different with the study done by Knudsen et al.[24,25] Although BMI did not correlate with TSH, waist hip ratio was found to be significantly correlated with TSH ($p < 0.05$). Our present study found negative correlation between weight and serum fT_4 ($p<0.05$) which support the fact that increasing fT_4 increase body metabolism resulting in reduction of weight.

This study found that vegetarian diet affects the level of fT_4 but not TSH and fT_3. Chi square test performed to determine association between vegetarian and non-vegetarian diet with hypothyroidism or hyperthyroidism showed no significant association between them. It shows that having vegetarian or non-vegetarian diet slightly alters fT_4 level but do not results in hypothyroidism or hyperthyroidism. Similarly, chi-square test performed to find out association between intake of goitrogenic vegetables and TD showed no significant association. It might be due to consumption of least amount of seasonal goitrogenic vegetables per day.

In this study participants were not asked about the pesticides they spray and amount of pesticide exposed were not assessed. Many other factors analyzed in this study are the factor associated with Hypothyroidism. Here, Association doesn't mean that they are risk factors. A factor precedes the TD or vice versa can't be determined with this type of cross-sectional study so we can't say any variable being studied as risk factor. Moreover, this study could not find any significance relation with the established risk

factors, therefore it was not possible to see odds ratio and since chi-square test itself does not gives any conclusion, larger population based study is required for identifying and reporting the independent risk predictors.

CONCLUSION

TD was highly prevalent among participants with higher proportion of subclinical hypothyroidism. Besides, direct pesticide exposure found to be factor in association with hypothyroidism, this study could not find any significance relation with other established risk factors. Since this study is a hospital based study it does not represent entire population of the region so further population based studies including urinary iodine measurement should be performed to find out risk factors associated with TD among Nepalese population.

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