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The profile of thyroid disorders in patients attending a tertiary care hospital in Pokhara, Nepal

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Abstract

Background: The profile of thyroid disorder has been reported with limited evidence in Nepal. The aim of this study was to examine the profile and incidence of different types of thyroid disorder in patients attending a hospital appointment in Western Nepal and identify factors associated with it.

Method: This was a hospital-based study. A total of 1000 patients attending the department of medicine at Gandaki Medical College, Teaching Hospital and Diabetes, Thyroid and Endocrinology Care Centre, Pokhara for thyroid examination were recruited. Thyroid disorders were classified as hypothyroidism, hyperthyroidism, T4-thyrotoxicosis including their sub types where applicable. **Results:** Nearly 33% of the participants were found to have some form of thyroid disorders. Majority of the patients with thyroid disorder were females (87%). Hypothyroidism was found to be the most common type of thyroid disorder (57.5%) followed by hyperthyroidism (37.5%) and secondary hyperthyroidism (5.0%). BMI was found to be independently associated with hyperthyroidism on regression model. **Conclusion:** Hypothyroidism was found to be the most common thyroid disorder followed by hyperthyroidism. The findings highlight that thyroid disorder is a significant clinical burden and a major public health concern in Western Nepal. The findings also emphasize a need to roll out thyroid screening programmes in the general population so that this condition can be identified and treated early.

Key Words: Hypothyroidism, Hyperthyroidism, Thyroid Disorder

INTRODUCTION

It is a widely known fact that thyroid gland produces two hormones, namely triiodothyronine (T3) and thyroxine (T4)¹, which are essential for our health and wellbeing; they play a vital role in growth, neuronal development, reproduction, and regulation of energy metabolism in our body². The activities of our thyroid gland is regulated by Thyroid Stimulating Hormone (TSH) which is produced by the anterior pituitary gland. British Thyroid Foundation³ has outlined the normal levels of these thyroid hormones as following; TSH 0.4-4.0 milliunits per litre, FT4 9.0-25.0 picomoles per litre, FT3 3.5-7.8 picomoles per litre. However, the units and cut off criteria vary widely between

different countries and clinical practices.

Hypothyroidism and hyperthyroidism are the two most common types of thyroid disorders reported in the literature^{4,5}. In hypothyroidism, the thyroid gland is underactive, as a consequence of which it cannot produce enough hormones. Usually increased TSH level and decreased T4/T3 level indicates that thyroid gland may be under-active. Hypothyroidism is often caused by the Hashimoto's disease⁶, which is also called chronic autoimmune lymphocytic thyroiditis. Fatigue, memory problems, constipation, depression, weight gain, weakness, slow heart rate are some of the common symptoms associated with hypothyroidism. In contrary, in hyperthyroidism the thyroid gland is overactive and produces excessive hormones; increased T4/T3 and decreased TSH levels indicate that thyroid gland may be overactive. Graves' disease is the

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most common cause of hyperthyroidism⁷, affecting about 70% of people with an overactive thyroid gland. Restlessness, nervousness, racing heart, irritability, increased sweating, shaking, anxiety, trouble sleeping are some of the common symptoms associated with hyperthyroidism.

Other types of thyroid-related disorders include T4 thyrotoxicosis (increased level of T4 hormone, TSH of normal level), sub-clinical hyperthyroidism (decreased TSH level, T4/T3 of normal level), sub-clinical hypothyroidism (increased TSH level, T4/T3 normal level), secondary hypothyroidism (decreased TSH, T4, T3 hormone levels), and secondary hyperthyroidism (decreased TSH, T4, T3 levels).

Prevalence of thyroid disorder is a much debated research topic. Inconsistency across studies in the definition of thyroid disorder, participant selection criteria, environmental and geographical factors, and different techniques and criteria used for assessment of thyroid functions are some of the major factors identified to contribute towards this debate⁷. This is further complicated by social stigmas and lack of awareness associated with thyroid disorders due to which people may feel hesitant to visit a doctor specially in countries where health literacy rate is lower⁸. It is possible that prevalence of thyroid disorder in the literature is often underestimated.

A recent study from Australia reported the prevalence of 0.3% for both clinical and subclinical hyperthyroidism in general population⁹. In 2002, United States National Health and Nutrition Examination Survey (NHANES III) found the prevalence of hyperthyroidism and subclinical hyperthyroidism in general population to be 0.5% and 0.7%, respectively¹⁰. A meta-analysis of studies from European countries showed the mean prevalence rate of 0.75% for males and females combined and an incidence rate of 51 cases of thyroid disorder per 100,000 per year¹¹. A UK-based longitudinal study found an incidence of thyroid disorder of 80 cases per 100,000 women per year¹².

Also, a higher prevalence of hyperthyroidism has been found in iodine-deficient countries¹³.

In Nepal the profile of thyroid disorder has been reported with limited evidence. A recent study by Gupta et al¹⁴ found the prevalence of thyroid disorder in Achham district hospital to be 17.11% (range, 14%-o 20%), of which hypothyroidism was most common followed by hyperthyroidism. Also females were found to disproportionately have higher prevalence of thyroid disorder compared to men (14.7% vs. 2.4%). Another study from Eastern Nepal showed that chronic iodine deficiency persisted in a small fraction of pregnant women, and that the mild thyroid dysfunction was also common in these women¹⁵. Khatiwada et al¹⁶ reported that thyroid dysfunction was widely common co-morbid condition (38.6%) in patients with chronic kidney disease. Another study showed that 3.2% of the school age children have thyroid dysfunction in Eastern Nepal¹⁷. To our knowledge there are no studies from Western Nepal that have examined the profile of thyroid disorders, which this study examined. In addition to examining the profile, we also fitted regression models to identify which factors (age, gender, BMI, pulse, blood pressure) were associated with thyroid disorder independently.

METHODS

Study type: This was a hospital-based retrospective study of case-control design. Most of the data were collected at the outpatient department of Gandaki Medical College and Teaching Hospital, Pokhara. The study protocol was approved by the Institutional Review Board of the same institute.

Inclusion criteria: (i). Patients attending the Outpatient Department of Gandaki Medical College and Teaching Hospital and Diabetes, Thyroid and Endocrine Care Centre to be evaluated for the thyroid function tests or thyroid disorders; (ii). Patients able to provide informed consent for taking part in the study

Exclusion criteria: (i). Patients not wanting their

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medical records to be included in the study; (ii). Patients with incomplete data.

In total, 1000 patients examined from May 2016 to April 2018 were recruited retrospectively. Using our previous (unpublished) data, and to attain a power of 80% with a precision error and type 1(α) error of 5% each, the required sample size was calculated to be 965. A slightly greater number ($n=1000$) has been used in this study.

Patients were briefed during their visit that their data could be used to report in scientific journals but they will remain anonymous. All data were handled with applicable ethical guidelines, and followed the tenants of Helsinki Declaration. The reporting follow the Strengthening the Reporting of Observational studies in Epidemiology (STROBE) guidelines¹⁸.

The patient data were collected by reviewing their medical files by the same author (TU), who is also the consultant endocrinologist at, both, the Gandaki Medical College and Teaching Hospital, and the Diabetes, Thyroid, and Endocrinology Care Centre, Pokhara Nepal. The main variables collected were age, T3, T4, TSH, random blood sugar, systolic and diastolic blood pressure, pulse rate and Body Mass Index (BMI) for each participant. Lab tests were done at either one or the other of the two institutes with which the first author (TU) is affiliated to by certified professionals. Data entry was double checked before processing and analyses. FT3 level of 2.27-4.55 picomoles/litre, FT4 level of 0.65-1.74 picomole/litre and TSH level of 0.35-5.29 millinternational units/litre were considered normal levels. The following criteria were used to classify thyroid disorders: t3,t4 normal and high level of TSH-subclinical hypothyroidism; low TSH with normal t3,t4 levels-subclinical hyperthyroidism; high t4 but normal TSH and t3 levels- thyrotoxicosis; high t4,t3 and TSH levels-secondary hyperthyroidism; low t3, t4, and TSH-secondary hypothyroidism; low t3,t4 but high TSH levels-primary hypothyroidism.

Data were analysed using Statistical Package for the Social Sciences (SPSS, version 24). No data were excluded from the analyses. Data of continuous variables were normally distributed (Levene's test, $p>0.05$). Independent t-tests was used to compare between any two variables between the participant groups (i.e., with thyroid disorder vs. normal). Multiple linear regression models were fitted to identify which of the variables (age, BP, BMI, pulse, etc.) were independently associated with different thyroid disorders.

RESULTS

Mean, standard deviation and standard error for participants with some form of thyroid disorder and normal participants is provided in Table 1. Out of the total 1000 participants, 339 (33.9%) had some form of thyroid disorder. As expected participant groups (normal vs. thyroid disorder) differed significantly in age, T3, T4, TSH and pulse levels ($p\leq 0.02$). Surprisingly, diastolic blood pressure (but not the systolic blood pressure) was also found to differ significantly between the participant groups. Since the aim of the study was to examine the profile of patients with thyroid disorder, the subsequent analyses do not include data from normal participants.

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Table 1. Mean, standard deviation, and standard error for the variables examined for participants with and without thyroid disorders. Comparisons between participant groups were done using independent samples t-tests. * indicates significant p-values.

Variable	Participant group	Mean value	Standard Deviation	Standard Error Mean	p-values
Age (years)	With thyroid disorder	42.93	11.89	0.68	0.02*
	Normals	44.72	12.26	0.50	
T3 (pg/ml)	With thyroid disorder	3.20	1.94	0.12	<0.001*
	Normals	2.95	0.41	0.02	
T4 (ng/dl)	With thyroid disorder	3.83	5.58	0.34	<0.001*
	Normals	1.19	0.33	0.01	
TSH (mlu/ml)	With thyroid disorder	8.07	9.75	0.46	<0.001*
	Normals	2.67	1.39	0.06	
FBS (mg/DL)	With thyroid disorder	105.51	36.05	2.16	0.97
	Normals	106.05	36.86	1.52	
BP:systole	With thyroid disorder	119.17	15.69	0.89	0.4
	Normals	119.92	16.40	0.68	
BP:Diastole	With thyroid disorder	77.11	10.87	0.61	0.04*
	Normals	78.49	9.69	0.40	
Pulse/minute	With thyroid disorder	79.46	8.05	0.46	0.009*
	Normals	78.35	7.70	0.32	
BMI (Kg/m ²)	With thyroid disorder	27.17	4.95	0.28	0.97
	Normals	27.12	4.71	0.19	

Fig.1 provides a pie chart showing the incidence of each type of thyroid disorders.

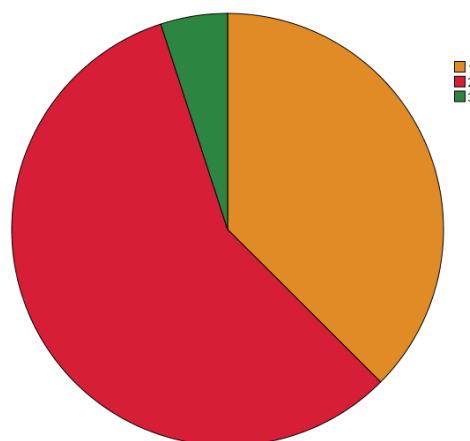


Figure 1. Pie chart showing incidence of different types of thyroid disorder.

1=Hyperthyroidism 2=Hypothyroidism 3=secondary hyperthyroidism.

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Hypothyroidism was found to be most prevalent, wherein primary hypothyroidism and subclinical hypothyroidism (not shown separately in the pie chart) together accounted for 57.5% of the total cases of thyroid disorder. There is a wealth of evidence to suggest that hypothyroidism is the most common type of thyroid disorder. Hyperthyroidism was found in 37.5% of the participants of which 21.8% had presented with clinical findings suggestive of thyrotoxicosis. Secondary hyperthyroidism was the least common type of thyroid disorder identified (5.0%).

Next, we examined which of the variables such as age, BMI, pulse, BP, and FBS for independently predicted hypothyroidism ($n=195$), hyperthyroidism ($n = 127$) and secondary hyperthyroidism ($n = 17$) by using multiple regression models in SPSS. Overall, the regression model did not statistically significantly predict hypothyroidism, $F(6, 188) = 1.31, p = 0.25, R^2 = 0.04$. None of these variables studied added statistically significantly to the prediction of hypothyroidism. Also, the regression model did not statistically significantly predict hyperthyroidism, $F(6, 120) = 0.99, p = 0.43, R^2 = 0.05$. None of the variables except BMI ($p=0.05$) added statistically significantly to the prediction of hyperthyroidism. For secondary hyperthyroidism, although the regression model overall statistically significantly predicted the condition, $F(6,16) = 3.40, p = 0.04, R^2 = 0.67$, none of the variables studied individually added statistically significantly to the prediction of secondary hyperthyroidism except diastolic BP ($p = 0.01$). The results suggest that measurements of BMI and diastolic BP are important parameters in predicting patients at risk of developing thyroid disorders (in particular in those with hyperthyroidism and secondary hyperthyroidism respectively) and may be considered adjunctive entities in screening for thyroid diseases.

¹As female gender is widely known as an independent risk factors of thyroid disorder we did not use that variable to fit regression models.

DISCUSSION

In this study we examined the profile of different types of thyroid disorders encountered in patients attending a tertiary care practice in Western region of Nepal (Pokhara and surrounding places). Consistent with the literature we also found that hypothyroidism was the most prevalent thyroid disorder. In the general population various studies have shown the prevalence of hypothyroidism to be as high as 10%¹⁹⁻²¹. The worldwide prevalence of hypothyroidism in various studies shows a very significant variation and current prevalence ranges from 1% to 20% for sub-clinical and 1-2% for overt hypothyroidism²⁴. Although hypothyroidism is very common endocrine problem, but frequency and severity of the symptoms vary between individuals. Sign and symptoms reflect the numerous organ systems affected by thyroid hormones but not a single clinical manifestation specially indicates thyroid dysfunction²⁵. In our study majority of the subjects are females which indicates this is the disease of the females which is also supported by other studies²⁶. The prevalence of hypothyroidism in our study was followed by hyperthyroidism and secondary hyperthyroidism. Nearly 87% of those with thyroid disorder were females. Using the regression models we showed that pulse and BMI are significant parameters associated with hyperthyroidism. When compared with normal participants (i.e., those without thyroid disorders) participants with thyroid disorders were found to differ significantly not just in the level of thyroid hormones and TSH, but also in age, diastolic blood pressure and pulse rates. Indeed it has been reported that that patients with thyroid disorders have abnormal pulse rates²².

Following limitations of our study should be noted; data were collected from patients attending a tertiary care hospital/centre so that our results may not be representative of the general population. Also, patients whose thyroid hormone levels were normal may have been on medication previously as a result of which their blood tests may have revealed normal T3, T4 or TSH levels, and hence were classified as normal. Also we did not examine

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life style factors such as the effect of smoking and co-morbid conditions like diabetes and depression. Smoking has been linked with thyroid disorder²³. Nonetheless, our findings highlight that thyroid disorder is a significant clinical burden and a major public health concern in Western Nepal, thereby warranting a need to roll out thyroid screening programmes in the general population so that this condition can be identified and treated early. Our findings also suggest BMI which is easily measurable in the community may be useful additional tools for screening patients with thyroid disorders, particularly hyperthyroidism.

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