

**Original Research Article****Incidence of thyroid dysfunction and hypothyroidism induced hypercholesteremia among the patients in Nobel Medical College Teaching Hospital, Biratnagar, Nepal**

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**ABSTRACT**

**Background:** Disorders of thyroid function is very much known to influence the metabolism of lipids associated mostly with increased level of cholesterol in the body. Hypothyroidism has an adverse effect on the serum lipid profile that may be a predisposing factor to the development of atherosclerotic disease, which again contributing to the establishment of cardiovascular disease (CVD).

**Objectives:** To screen the patients suffering from the disorders of thyroid hormone and to elicit the relation of increased total cholesterol level in the blood in case of hypothyroidism.

**Material and Methods:** A total of 762 patients were screened for thyroid dysfunction by estimating free triiodothyronine-3 (fT3), free thyroxine-4 (fT4), Thyroid Stimulating Hormone (TSH) along with the level of total cholesterol in the blood samples collected from those patients attended Nobel Medical College OPD in between 1st March 2013 to 31<sup>st</sup> January 2014 and recruited for this study after Institutional ethical approval. Serum samples from these patients were tested for fT3, fT4 & TSH level by Chemiluminescence Immunoassay (CLIA). The total blood cholesterol was estimated by CHOD/PAP method. Mean value and standard deviation were calculated using Student's two-tailed t-test. Analysis of data was performed using one-way ANOVA. Results are considered statistically significant if  $p \leq 0.05$ .

**Results:** Out of 762 patients, 20.2% were hypothyroid, 15.09% were hyperthyroid and 64.69% were euthyroid. Out of all cases of hypothyroidism, 63.63% of patients were female where as 36.36% were male patients. Similarly, out of the total patients suffering from hyperthyroidism, 70.43% were of female and 29.56% were of male. Total cholesterol level ( $304 \pm 63$ ) was found to be significantly elevated in those blood samples collected from the group having hypothyroidism than those of euthyroid group ( $p=0.05$ ).

**Conclusion:** The present study provides the information about the prevalence of thyroid disorder among the population of Biratnagar, eastern Nepal. It also elicits that the total cholesterol level is highly increased among the patients associated with hypothyroidism, likely to be a potential factor contributing to cardiovascular disease in this group.

**Keywords:** CLIA, Eastern Nepal; Thyroid hormones; Total Cholesterol

**Introduction:**

Thyroid dysfunction is that condition when the serum level of TSH, free triiodothyronine [fT3] and free thyroxine [fT4] are altered when compared to their respective normal values [1]. In the eastern part of Nepal, this disorder is showing as a major health problem affecting the local population there [2]. Thyroid dysfunction is a common endocrine disorder that can affect 5-10% of an individual's life span [3]. Clinical sign and symptoms being often non specific, diagnosis and monitoring of therapy therefore, can only be dependable on the measurement of thyroid hormone and TSH [4,5].

Thyroid function abnormalities with subclinical hypothyroidism or hyperthyroidism are the most common type of thyroid dysfunction [6,7]. Decrease in thyroid activity is mostly seen in hypothyroidism. It results from reduced secretion of both fT4 and fT3 [8]. The decreased level of fT4 and fT3 concentration leading to hypersecretion of TSH by negative feedback inhibition can ultimately lead to increased serum TSH. Hypercholesteremia in hypothyroidism is due to decrease hormone level (fT4 and fT3) and the decreased lipoprotein lipase activity [9]. Abnormalities in lipid metabolism are shown to be more common among the patients with hypothyroidism. It is also thought to be contributing to the increase cardiovascular risk in

them [10]. While studying patients with hypothyroidism, cholesterol level was found to be elevated in their blood [11-13]. The prevalence of hypothyroidism increases with age, and is higher in females than in males [14]. The present study aims to assess the prevalence of thyroid dysfunction according to age and sex and the association of hypothyroidism with lipid abnormalities in the patients of Biratnagar, Nepal

### Material and Methods:

It is a hospital based study carried out in the Department of Biochemistry of the Nobel Medical College Teaching Hospital, Biratnagar, Nepal between 1st March 2013 to 31<sup>st</sup> January 2014. The study was started after getting the approval of the institutional ethical committee.

Blood samples from 762 patients, suspected to be suffering from thyroid disorder, was collected in Clinical Laboratory Services and analyzed for fT3, fT4, TSH and total Cholesterol. Thyroid function test (fT3, fT4, TSH) was done by Chemiluminescence Immunoassay (CLIA). The standard procedure was followed as per manufacturer's instructions for CLIA (Aculite). Reference ranges according to the manufacturer were 2.5 to 3.9 pg/ml, 0.61 to 1.12 ng/dl and 0.34 to 5.0 uIU/ml, respectively for fT3, fT4, and TSH. Total cholesterol in serum was estimated by Erba 300 machine by enzymatic (CHOD/PAP) method using kit supplied by Humans Biomedical pvt. Ltd., India. According to the manufacturer's kit, the desirable total blood cholesterol level was <200mg/dl and it was taken as reference range.

### Statistical Analysis:

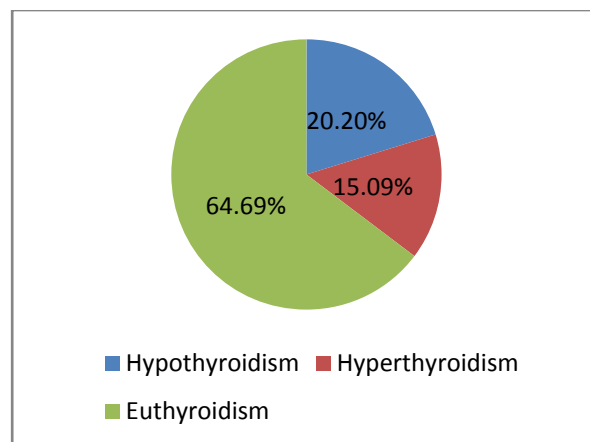
The data on PSA levels were analyzed using nonparametric kruskal-walli's one way analysis of variance by ranks. Mean value and standard deviation were calculated using Student's two-tailed t-test. Analysis of data was performed using a student T-test or one-way ANOVA. Results are considered statistically significant if  $p \leq 0.05$ .

### Results:

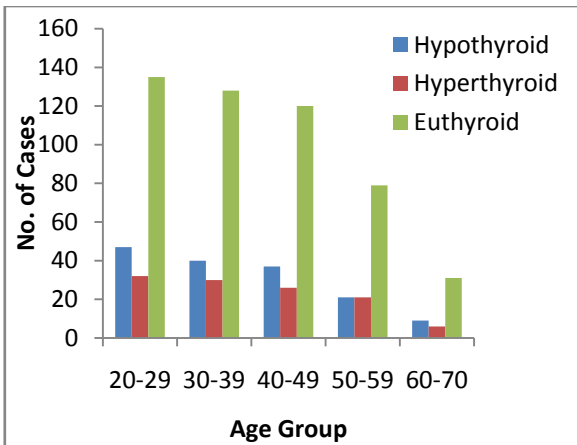
Out of 762 patients, age ranging from 20 years to 70 years, suspected of having thyroid disorder, screened for free T3, Free T4 and TSH, 154 patients (20.2%) were found to be suffering from hypothyroidism, 115 patients (15.09%) were of hyperthyroid and the remaining 493 (64.69%)

were found to be euthyroid as shown in Fig. 1. For a better age wise analysis, we have categorized the patients under five different age groups, i. e. (20-29), (30-39), (40-49), (50-59) and (60-70). Under the age group (20-29), 47 patients were hypothyroid and 32 were hyperthyroid. Similarly, the number of patients suffering from hypothyroidism and hyperthyroidism in other age groups were respectively 40 and 30 for the age group (30-39), 37 and 26 for the age group (40-49), 21 and 21 for the age group (50-59) and lastly, for the age group (60-70), the numbers were 09 and 06 respectively as shown in Fig. 2.

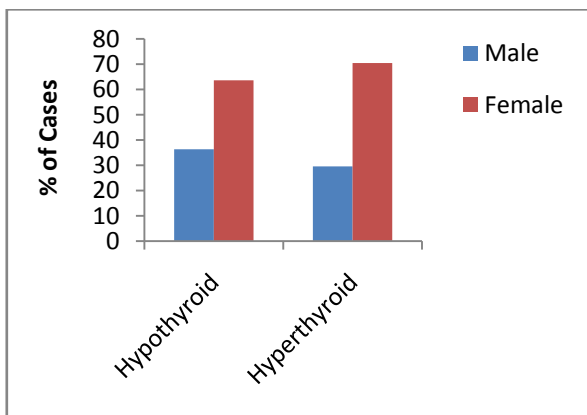
The mean $\pm$ SD value of fT3, fT4 and TSH of hypothyroid patients were 1.6 $\pm$ 0.72 pg/ml, 0.41 $\pm$ 0.18 ng/dl and 32.66 $\pm$ 14.73 uIU/ml respectively. Similarly, the hyperthyroid patients were having mean $\pm$ SD value of fT3, fT4 and TSH as 5.36 $\pm$ 1.29 pg/ml, 2.7 $\pm$ 0.78 ng/dl and 0.25 $\pm$ 0.07 uIU/ml respectively as shown in Table 1. Among all cases of hypothyroidism, 56 (36.36%) patients were male and 98 (63.63%) patients were female where as in the case of hyperthyroidism, 34 (29.56%) were male and 81 (70.43%) were female as shown in Fig. 3. The mean $\pm$ SD value of total cholesterol of hypothyroid patients was (304 $\pm$ 63) mg/dl, which is significantly higher ( $p=0.05$ ) than that of euthyroid patients (176 $\pm$ 54). The hyperthyroid patients were having total cholesterol (182 $\pm$ 41) level within normal range as shown in Fig. 4.



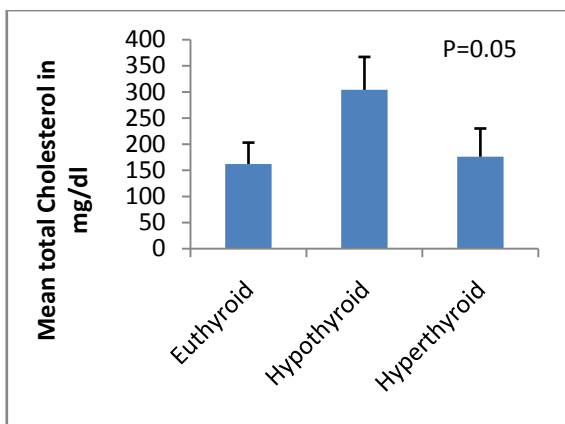
**Figure 1: Prevalence of thyroid dysfunction;** A total of 762 patients were screened for Thyroid dysfunction. Blood samples of these patients were assayed for thyroid function test by CLIA.



**Figure 2: Thyroid dysfunction in different age group of patients;** Patients of age (20-70) were categorized into different age group. Each bar represents the number of cases of hypothyroid, hyperthyroid and euthyroid respectively in the different age group.



**Figure 3: Sex wise distribution of thyroid dysfunction;** Thyroid dysfunction was studied in male and female population. Each bar represents number of cases of male and female in hypothyroid and hyperthyroid group respectively.



**Figure 4: Total cholesterol in the blood samples of the patients;** Total cholesterol was estimated in the blood samples of all patients. Each bar represents Mean±SD of total cholesterol in euthyroid, hypothyroid and hyperthyroid

patients. Statistical significance was compared with euthyroid group by student t test, where  $p = 0.05$ .

	FT3 (pg/ml)	FT4 (ng/dl)	TSH (uIU/ml)
Euthyroid	3.5±1.17	0.9±0.47	3.6±1.85
Hypothyroid	1.6±0.76	0.41±0.18	32.66±14.73
Hyperthyroid	5.36±1.29	2.7±0.78	0.25±0.07

**Table 1: Thyroid function test in blood serum of all patients;** Free T3, Free T4 and TSH were estimated in blood samples of all types of patients. The Mean±SD value of FT3, FT4 and TSH of euthyroid, hypothyroid and hyperthyroid patients.

**Discussion:**

After the analyses of the thyroid profile of 762 patients, suspected of suffering from thyroid dysfunction on the basis of the clinical findings, we got two hundred sixty nine (35.30%) patients showing abnormal profile, in which 20.2% of patients were of hypothyroid and 15.09% of patients were found to be of hyperthyroid. Our findings to those of the cases reported earlier from Dharan, Nepal [2] is almost similar (17.19% cases of hypothyroidism and 13.68% cases of hyperthyroidism). Similarly, the study carried out in Dhulikhel, Nepal, reported 15.4% cases of hypothyroidism and 15.01% cases of hyperthyroidism [15]. The finding in the present study is different from the study carried out in the western countries. In the third National Health and Nutrition Examination Survey (NHANES III), a recent large population-wide survey in the United States, hypothyroidism was found only in 4.6% and hyperthyroidism in 1.3% of the total population [16]. Similarly, in another study carried out in Athens, Greece, the prevalence of hypothyroidism and hyperthyroidism were 5.9% and 10.45% respectively of the total population [17].

Our finding in this present study showed highest percentage of thyroid disorder cases in the age group of 20-29 years with negligible decreases with increase age upto age group 40-49 years. In the last two age groups [50-59 and 60-70], the decrease in the percentage of cases was observed as shown in Fig. 2. Female population showed maximum percentage of hypothyroid and hyperthyroid cases than male population in our result as shown in Fig. 3, which is nearly the same as reported in a study carried out in eastern Nepal by Rohil V *et. al* [26]. In another study carried out in South India revealed thyroid dysfunction as a very common problem there also, in which one

out of every eight young women had thyroid dysfunction [27]. One report from china also showed that females had higher incidence of thyroid dysfunction than males [28]. We have reported the mean±SD value of FT3, FT4 and TSH of hypothyroid and hyperthyroid patients, which is similar to the report from Dhulikhel, Nepal [15]. The report in our study, showing higher percentage of cases of thyroid disorder among female population than male population, also resembles the study carried in Dharan, Nepal [2].

Hypercholesterolaemia is well known potent risk factor of cardiovascular disease. As thyroid hormone is essential for lipid metabolism, its deficiency can elevate the level of cholesterol by increasing LDL and decreasing HDL in blood. The cause of hypercholesterolemia in hypothyroidism is mainly because of decreased activity of LDL-receptors' leading to decreased catabolism of LDL and IDL [19-21]. Hypothyroidism is the second leading cause of high cholesterol, after diet., The liver doesn't function properly and produces excess cholesterol, fatty acids and triglycerides, When thyroid hormone levels drop [18]. Furthermore, the development of atherosclerosis in hypothyroidism is enhanced by some other ways like (i) promoting LDL oxidability [22] (ii) increasing plasma homocysteine levels [23] with its known adverse effect on the cardiovascular system (iii) arterial hypertension [24]. Therefore, only making the effort to reduce the hypercholesterolaemia without looking for the underlying cause of disease could not be a appropriate management. Hence, our study reports a case of hypercholesterolaemia secondary to hypothyroidism to illustrate this point.

Our study showed that the total cholesterol level (mean±SD) of hypothyroid patients was significantly higher ( $P < 0.05$ ) than euthyroid patients. Total cholesterol level of hyperthyroid patients was within the limit as shown in results. Similar findings were reported by Risal P *et. al.* [15]. The findings in our study resembles one study carried out in Brazil, where hypothyroid patients had significantly higher level of cholesterol in the blood than euthyroid patients ( $p = 0.006$ ) [25]. Similarly, the study carried out in Serbia stated that the total cholesterol was statistically significantly higher ( $p < 0.05$ ) in the hypothyroid patients [29].

### Conclusion:

The normative range of serum level of thyroid hormones amongst the population varies according to geographical location. Thus, we have reported the ranges of euthyroid group and also the epidemiology of thyroid dysfunction in this particular area of eastern part of Nepal. Female of age group 20-29, 30-39 and 40-49 were slightly more sufferers of thyroid dysfunction than males in our report. So, we strongly recommend for conducting screening programme for proper identification of the genuine cases of thyroid patients by doing thyroid profile of all the patients starting from the age of 20 years. Our findings suggest that hypercholesterolemia is associated with hypothyroidism that enhances the risk for development of atherosclerosis and coronary artery disease. Generally, cholesterol levels are tested more regularly than their thyroid hormone levels without looking for the link between high cholesterol and underlying hypothyroidism in all dyslipidemic patients. Treating such patients with cholesterol lowering medicines may not be able to solve the real problem. Therefore, for those patients particularly the females within the age group of 20-49 years, should always be recommended for getting their thyroid function test done if the total cholesterol level is found to be higher already.

### Ethical approval:

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

### Informed consent:

Informed consent was obtained from all individual participants included in the study.

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