

STUDY OF CLINICAL PROFILE OF NON-TOXIC GOITER WITH SPECIAL REFERENCE TO CORRELATION OF PATHOLOGY, LIPID PROFILE AND ANTIBODY LEVELSantanu Saha¹, Somnath Mukherjee², Ayan Basu³, Shuvankar Mukherjee⁴**HOW TO CITE THIS ARTICLE:**

Santanu Saha, Somnath Mukherjee, Ayan Basu, Shuvankar Mukherjee. "Study of Clinical Profile of Non-Toxic Goiter with Special Reference to Correlation of Pathology, Lipid Profile and Antibody Level". Journal of Evolution of Medical and Dental Sciences 2014; Vol. 3, Issue 04, January 27; Page: 827-834, DOI: 10.14260/jemds/2014/1911

ABSTRACT: OBJECTIVE: To evaluate the morphology of non-toxic goiter, the role of auto-immunity and lipid abnormalities in overt and sub-clinical hypothyroid goiter patients. **METHODS:** A descriptive observational study was undertaken amongst goiter patients without thyrotoxic features comprising 50 randomly selected cases within the range of 12-65years. Goiter patients with thyrotoxic features, acute illness and other visceral diseases were excluded. The patients were evaluated with thyroid function tests, USG-thyroid, FNAC-thyroid, anti-TPO and lipid profile after thorough clinical examination. **RESULTS:** In my study, most patients were female (with male: female ratio 1:5.25) and were middle aged (between age group 30-49years). Among all patients 60 % (i.e. 30) patients had Hashimoto's thyroiditis, 24% (i.e. 12) patients had diffuse colloid goiter and 16% (i.e. 8) patients had nodular goiter. 52% (i.e. 26) of all patients and 76.6% (i.e. 23) of Hashimoto's goiter patients were anti-TPO positive. Majority of colloid goiter (i.e. 66.7%) and nodular goiter (50%) patients were euthyroid but majority of Hashimoto's goiter patients were hypothyroid (65.38% overt and 33% sub-clinical). Majority of anti-TPO positive patients were hypothyroid (65.38% overt and 30.62% sub-clinical) and majority of anti-TPO negative patients (66.67%) were euthyroid. Within reference range of TSH, there was a linear increase in total serum cholesterol, LDL-cholesterol, triglyceride and decrease in HDL-cholesterol with increase in TSH. This lipid profile changes are mainly seen in Hashimoto goiter patients. **CONCLUSION:** this study emphasizes the role of auto-immunity in non-toxic goiter patients especially Hashimoto's thyroiditis patients and lipid profile changes in those patients.

KEYWORDS: Non-toxic goiter, Hashimoto's thyroiditis, Auto-immunity.

INTRODUCTION: Dysfunction and anatomic abnormalities of the thyroid are among the most common diseases of the endocrine gland. Goiter refers to any enlargement of thyroid gland¹ Goiter can be classified as diffuse or nodular, non-toxic or toxic (i.e. associated with thyroid hormone overproduction)² and benign or malignant. Biosynthetic defects, iodine deficiency, auto-immune diseases, and nodular diseases can each lead to goiter, though different mechanism.

Biosynthetic defect or iodine deficiency are associated with reduced efficiency of thyroid hormone synthesis, leading to increased TSH, which stimulate thyroid growth as a compensatory mechanism to overcome the block in hormone synthesis. If the underlying disorder is sufficiently severe, the compensatory responses may be inadequate to overcome the impairment in hormone synthesis resulting in goitrous hypothyroidism.

Graves's diseases and Hashimoto thyroiditis are also associated with goiter. In Graves' disease, the goiter results mainly from TSH-R mediated effect of TSI. The goitrous form of Hashimoto thyroiditis occurs because of acquired defect in hormone synthesis, leading to elevated level of TSH

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and its consequent growth effects. Lymphocyte infiltration and immune system induced growth factors also contribute to the thyroid enlargement in Hashimoto thyroiditis³ Because auto-immune process gradually reduces thyroid function, there is a phase of compensation when normal thyroid levels are maintained by a rise in TSH. Though some patients may have minor symptoms, this state is called subclinical hypothyroidism. Lately, unbound T4 level falls and TSH level rises further (usually TSH>10 mIU/L). Symptoms are more readily apparent at this stage which is referred to as clinical / overt hypothyroidism. Anti-TPO antibodies are present in >90% of patients with auto-immune hypothyroidism. TB-II can be found in 10-20% of patients¹ Nodular thyroid disease is common, occurring in about 3-7% of adult when assessed by physical examination and >25% by ultrasound. Thyroid nodule may be solitary or multiple and they may be functional or non-functional.

Hypothyroidism is associated with elevated plasma LDL-C level due primarily to a reduction in hepatic LDL- receptor function and delayed clearance of LDL. Conversely, plasma level of LDL-C is often reduced in the hyperthyroid patients. Hypothyroid patients also frequently have increased level of circulating IDL and some patients with hypothyroidism also have mild hypertriglyceridemia.

In this study non-toxic goiter patients (i.e. without thyroid hormone overproduction) have been evaluated for their probable etiology by FNAC and anti-TPO level (whether autoimmune or diffuse or nodular goiter) and for lipid profile changes in these patients.

MATERIAL AND METHODS: This observational, cross-sectional study was undertaken in the department of General Medicine of Bankura Sammilani Medical College, Bankura over the period from May 2011 to April 2012. Approval was taken from the institutional ethics committee before starting the study. Informed consent was taken from each patient. Patients were selected randomly from medicine OPD and patients admitted in medicine ward. Patients presenting with clinical goiter aged between 12-65 years were screened for TFT and after excluding the hyperthyroid cases, the euthyroid, sub-clinical and overt hypothyroid cases were included in the study. These selected patients were further evaluated with lipid profile (including total cholesterol, LDL-C, HDL-C, triglyceride), serum anti-TPO, USG thyroid, FNAC thyroid. These patients were also evaluated with blood for complete hemogram, FBS & PPBS, serum urea, creatinine, LFT, ECG, and CXR to exclude other co-morbid illness. 50 non-toxic goiter patients were chosen excluding diabetes mellitus, alcoholism, chronic liver disease, renal disease and drug induced dyslipidemia. All the clinical and laboratory data were collected in the pre-designed proforma for the study.

Statistical analysis: Data collected was entered into MS Excel and analyzed by using SPSS 10.

RESULTS: In present study 50 non-toxic goiter patients were taken of whom 8 patients (16%) were male and 42 patients (84%) were female and among all patients 50% patients were in the age group of 30-49yrs. So, in majority of my patients were female with male: female ratio 1:5.25 and maximum patients were middle aged. (table 1).

26 patients (52%) among all non-toxic goiter patients and 23 (i.e.76.6%) among all Hashimoto goiter patients were anti-TPO positive. This study clearly states about the auto-immune etiology of Hashimoto's thyroiditis. (table 2).

Among all non-toxic goiter patients, 16 patients (32%) were euthyroid, 14 patients (28%) were sub-clinical and 20 patients (40%) were overt hypothyroid and among all Hashimoto's goiter patients, 45.35% were overt and 33.3% were sub-clinical hypothyroid, but majority of colloid goiter patients (66.7%) and nodular goiter patients (50%) were euthyroid. (table 2).

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Out of all 26 anti-TPO positive patients, 17 (i.e. 65.38%) were overt and 9 (i.e. 34.62%) were sub-clinical hypothyroid, but among all 24 anti-TPO negative patients, 16(i.e. 66.67%) were euthyroid. (table3).

Among 50 non-toxic goiter patients, mean total cholesterol was 205.06 ± 32.38 , mean total TG was 173.78 ± 35.48 , mean LDL-C was 126.13 ± 20.05 and mean HDL-C was 40.48 ± 3.11 (table 4).

Among 30 Hashimoto's goiter patients, mean total cholesterol was 217.2 ± 33.69 , mean total TG was 189.23 ± 31.12 , mean LDL-C was 132.08 ± 21.36 and mean HDL-C was 39.4 ± 3.11 . (table 4).

Among 12 diffuse colloid goiter patients, mean total cholesterol was 185.0 ± 19.64 , mean total TG was 143.33 ± 29.07 , mean LDL-C was 118.33 ± 15.73 and mean HDL-C was 41.95 ± 3.06 . (table 4).

Among 8 non-toxic nodular goiter patients, mean total cholesterol was 189.62 ± 17.77 , mean total TG was 161.5 ± 27.45 , mean LDL-C was 115.5 ± 10.96 and mean HDL-C was 42.31 ± 1.64 . (table 4).

The above study shows higher total cholesterol, triglyceride, LDL-C and lower HDL-C among Hashimoto's goiter patients in comparison to diffuse colloid goiter or non-toxic nodular goiter patients.

In all 16 patients presenting with euthyroid state (0.4-5mU/L) mean total cholesterol was 173.75 ± 8.01 , mean total TG was 133.31 ± 13.71 , mean LDL-C was 105.78 ± 11.86 and mean HDL-C was 42.90 ± 2.63 . (table 5).

In all 14 patients presenting with sub-clinical hypothyroid state (5-10mU/L) mean total cholesterol was 198.71 ± 30.09 , mean total TG was 180.5 ± 24.20 , mean LDL-C was 121.14 ± 8.49 and mean HDL-C was 41.3 ± 1.48 .(table 5).

In all 20 patients presenting with overt hypothyroid state (> 10 mIU/L) mean total cholesterol was 234.55 ± 16.96 , mean total TG was 201.45 ± 21.34 , mean LDL-C was 145.9 ± 9.57 and mean HDL-C was 37.92 ± 2.25 . (table 5).

This study shows within the reference range of TSH, there was a linear increase in total serum cholesterol, LDL cholesterol, and triglycerides, and a linear decrease in HDL cholesterol with increasing TSH.

DISCUSSION: Goiter usually results from biosynthetic defect or iodine deficiency, auto-immune diseases (like Hashimoto thyroiditis or Graves' disease) or nodular diseases (which can be solitary or multiple and functional or non-functional). Hashimoto's disease is the most common cause of hypothyroidism in areas of the world in which dietary iodine is sufficient and is of auto-immune etiology. Non-toxic goiter is not associated with thyroid hormone overproduction i.e. they are either euthyroid or subclinical/overt hypothyroid.

In present study most of the patients were female (with male: female ratio 1:5.25) and were middle aged (between age group 30-49years). Among total 50 non-toxic goiter patients, 30 patients (60%) had Hashimoto's disease, 12 patients (24%) had diffuse colloid goiter and 8 patients (16%) had nodular goiter. Male: female ratio was 1:6.5 among all Hashimoto's goiter,

According to Framingham's study, the world wide prevalence of non-toxic goiter is 4.6% (male: female=1.5:6.4=1:4.27) and Wickham study displays a 3.2% prevalence (male: female=1.6:6) ⁴, ⁵ According to Santamello B.et al. Study ⁶ on non-toxic goiter in adult population of Genoa, Italy (10yrs of experience) of 1980 patients, 1629(83.63%) were female and 351(16.37%) were male, aged 14-70 yrs. The mean age was 42.6yrs.

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Anti-TPO positivity was seen in 52% of all non-toxic goiter and 76.6% of all Hashimoto's thyroiditis. The AACE consensus paper⁷ reported that auto-antibodies were positive in 95% of patients with Hashimoto's thyroiditis. According to Singh et al⁸ Cytomorphologic study of Hashimoto's thyroiditis and its serologic correlation, overall Ab positivity (anti-TPO/ anti-TG/ both) was seen in 133 cases (88.67%). Anti-TPO was positive in 119 cases (79.3%) and anti-TG was positive in 101(67.3%) patients. While a combination was seen in 87(58%) cases. Harrison's text book of internal medicine also states that anti-TPO antibodies are present in >90% of patients with auto-immune thyroiditis.

Majority of Hashimoto's goiter patients were overt (45.35%) or sub-clinically (33.3%) hypothyroid but majority of colloid goiter patients (66.7%) and nodular goiter patients (50%) were euthyroid. According to Singh et al.⁸ study of Hashimoto's thyroiditis and serological correlation, among Hashimoto's thyroiditis based on thyroid function test, 86 patients (57.3%) were hypothyroid, of these 57(38%) had overt and 29(19.3%) had subclinical hypothyroid. In present study among all 26 anti-TPO positive patients, 17 (i.e. 65.38%) were overt and 9(i.e.34.62%) were sub-clinical hypothyroid, but among all 24 anti-TPO negative patients, 16(i.e. 66.67%) were euthyroid. According to WJ Med Sci, DOSI, vol-I, ⁹ patients who had high TSH, 35.55% had normal anti-TPO but 64.45% had abnormally high anti-TPO and the differences between patients who had normal anti-TPO and patients with high anti-TPO were significant ($p<0.0001$). Bjoro et al., ¹⁰ in a 20-years follow-up study found that positive anti-TPO were strongly correlated to thyroid dysfunction and the prevalence of elevated TSH was nearly 10-fold higher both in females and males with positive anti-TPO compared with subjects with negative anti-TPO. Kontiainen et al., ¹¹ found elevated levels of anti-TPO antibody in 47% of samples with abnormal and in 12% of samples with normal levels of TSH, indicating a meaningful difference ($p<0.001$) and also showed that 61% of patients with hypothyroidism and 26% with hyperthyroidism contained this antibody in their sera ($p<0.001$).

Higher total cholesterol, triglyceride, LDL-C and lower HDL-C were seen more in Hashimoto's goiter in comparison to diffuse colloid goiter or non-toxic nodular goiter patients. Koppers LE et al., Valdemarsson S et al.^{12, 13} showed alterations in thyroid function can have profound effects on plasma lipids, and all patients with significant hyperlipidemia should be screened for hypothyroidism. The classic manifestation of hypothyroidism is an elevation of the plasma LDL-C level (6.5 to 15.5 mm/L [250 to 600 mg/dL]), but this disorder can also be associated with high plasma triglyceride levels. Levels of HDL-C are usually unchanged or slightly lower in hypothyroidism and may be reduced in hyperthyroidism; the later effect may be related to alterations in hepatic lipase activity.¹⁴ The elevations of plasma LDL-C in hypothyroidism are associated with impaired clearance of LDL, ¹⁵ probably reflecting decreased LDL receptor expression.¹⁶ The high LDL-C levels in hypothyroidism are associated with an increased risk of atherosclerosis, ¹⁷ but risk of myocardial infarction is not necessarily increased, ^{17, 18} perhaps because hypothyroidism decreases myocardial oxygen demand. Subclinical hypothyroidism, in which metabolic abnormalities are present without symptoms, can also cause hypercholesterolemia that responds to treatment with thyroid hormone.

Hypothyroidism is also associated with low LPL activity, ¹³ predisposing to increased plasma triglyceride levels. Hyperlipidemia with hypothyroidism may be more marked in those with an underlying genetic susceptibility, ¹⁹ but it responds dramatically to thyroid hormone replacement. In elderly patients with CHD or significant risk factors, thyroid hormone should be replaced cautiously to avoid precipitating ischemic heart disease clinical events.

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Within the reference range of TSH, there was a linear increase in total serum cholesterol, LDL cholesterol, and triglycerides, and a linear decrease in HDL cholesterol with increasing TSH and this was mainly seen in Hashimoto goiter patients. The HUNT Study by Asvold BO et al. Showed within the reference range of TSH, there was a linear and significant (P for trend <0.001) increase in total serum cholesterol, LDL cholesterol, non-HDL cholesterol and triglycerides, and a linear decrease (P for trend <0.001) in HDL cholesterol with increasing TSH. Study by A. Regmi et al.²⁰ in original Article Nepal Med Coll J 2010 showed that There was a positive association between hypothyroidism and TC>200, LDL>130 and TG>200mg/dl; 48.4% of hypothyroid patient had hypercholesterolemia and 32.3% had hypertriglyceridemia. The mean TC, LDL and TG levels were increased progressively with the increase in the serum TSH. It was noteworthy in this study that even a slight increase in serum TSH (between 6.2-10 mIU/L) showed significant increase in serum lipid level.

CONCLUSION: From our study we may conclude that non-toxic goiter may be of multiple etiologies-like auto-immune thyroiditis (Hashimoto's goitre), diffuse colloid goiter or nodular goiter. Hashimoto's thyroiditis are mainly seen in middle-aged female and there is high rate of anti-TPO positivity. Higher values of total-cholesterol, LDL-cholesterol, TG and lower values of HDL-cholesterol are seen in Hashimoto's goiter patients and there is a linear increase in total cholesterol and LDL-cholesterol with increase in serum TSH level.

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		Male	Female	Total
AGE	10-29 years	2	10	12
	30-49years	4	21	25
	>50years	2	11	13
ETIOLOGY	Hashimoto	4	26	30
	Colloid	2	10	12
	Nodular	2	6	8
TSH-level	0.4-5	4	12	16
	5-10	2	12	14
	>10	2	18	20
Anti-TPO	+ve	4	22	26
	-ve	4	20	24

Table-1: Gender wise distribution of non-toxic goitre according to age, etiology TSH-level and Anti-TPO positivity

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		Hashimoto	Colloid	Nodular	Total
Anti-TPO	+ve	23	2	1	26
	-ve	7	10	7	24
TSH-level	0.4-5	4	8	4	16
	5-10	10	2	2	14
	>10	16	2	2	20

Table-2: Distribution of non-toxic goiter with correlation of etiology with anti-TPO positivity and TSH-level

		Anti-TPO +ve	Anti-TPO -ve	Total
TSH level	0.4-5	0	16	16
	5-10	9	5	14
	>10	17	3	20
total		26	24	50

Table 3: Distribution of non-toxic goiter with correlation of anti-TPO positivity and TSH level

	Hashimoto's goiter	Diffuse goiter	Nodular goiter	Total non-toxic goiter
Mean total cholesterol	217.2 ± 32.38	185.0 ± 19.64	189.62 ± 17.77	205.06 ± 32.38
Mean TG	173.78 ± 35.48	143.33 ± 29.07	161.5 ± 27.45	173.78 ± 35.48
Mean LDL-C	126.13 ± 20.05	118.33 ± 15.73	115.5 ± 10.91	126.13 ± 20.05
Mean HDL-C	39.4 ± 3.11	41.95 ± 3.06	42.31 ± 1.64	40.48 ± 3.11

Table 4: Distribution of non-toxic goiter with correlation of different etiologies and lipid profile parameters

	TSH level		
	0.4-5	5-10	>10
Mean total cholesterol	173.75 ± 8.01	198.71 ± 30.90	234.55 ± 16.96
Mean TG	133.31 ± 13.71	108.5 ± 24.20	201.45 ± 21.34
Mean LDL-C	105.78 ± 11.86	121.14 ± 8.49	145.9 ± 9.57
Mean HDL-C	42.90 ± 2.63	41.3 ± 1.48	37.92 ± 2.25

Table 5: Distribution of non-toxic goiter with correlation of TSH-level and lipid profile parameters

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AUTHORS:

1. Santanu Saha
2. Somnath Mukherjee
3. Ayan Basu
4. Shuvankar Mukherjee

PARTICULARS OF CONTRIBUTORS:

1. Assistant Professor, Department of General Medicine, Bankura Sammilani Medical College, Bankura.
2. Senior Resident, Department of General Medicine, RG Kar Medical College, Kolkata.
3. RMO cum Clinical Tutor, Department of Tropical Medicine, School of Tropical Medicine, Kolkata.

4. Assistant Professor, Department of Community Medicine, Calcutta National Medical College, Kolkata.

NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Ayan Basu,
46/27A, Becharam Chatterjee Road,
Behala, Kolkata - 700034, West Bengal.
E-mail: ayanbasustm@gmail.com

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