



To Study the Correlation Between Clinical and Biochemical Profile in Patients with Multinodular Goiter in Central India

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ABSTRACT

Introduction

Dysfunction of the thyroid gland leads to two sets of symptoms those related to the local effect of a mass in the neck and the effects of either an excess or a deficiency of thyroid hormones. Dysfunction of the thyroid gland ranks next only to diabetes mellitus amongst the endocrine diseases. Thyroid-stimulating hormone (TSH) presumably has an important role in the maintenance of thyroid growth and goitrogenesis. In this study a group of patients with multinodular goiter were examined clinically and investigated to find the various correlations.

Methods

This observational study was conducted in 50 consecutive patients who attended department of medicine, M.G.M. Medical College & M.Y. Hospital, Indore, MP, India, from one year of study duration.

Results

The incidence of multi-nodular goiter for hyperthyroidism, hypothyroidism, or euthyroid cases is much more in females as compared to males. Almost all patients with multinodular goiter had goiter on physical exam. Most multinodular hypothyroid patients had sinus bradycardia (80%). Skin changes & edema was in next frequency (40% each). Some patients had delayed ankle reflex & eye signs (20% each). In multinodular hyperthyroid patients sinus tachycardia & tremors (90% each) were commonest physical signs. Eye & Skin changes (45% & 25%) were other signs. The mean serum cholesterol value in hyperthyroid group was 177.4 mg/dl as against 238.2 mg/dl and 180.03 mg/dl in the hypothyroid and euthyroid group. Total serum lipids were 455.3 mg/dl, 577.4mg/dl, and 480.0 mg/dl in all the three groups respectively.

Conclusions

Most of the patients had cardiac involvement in one or the other way as documented by clinical examination electrocardiography or biochemical investigation. There is no correlation between sex and susceptibility for the involvement of cardiovascular system in cases of multinodular goiter. Lipid levels were significantly deranged in hypothyroidism or hyperthyroidism patients.

Keywords: Euthyroid, Hypothyroid, Multinodular goiter

INTRODUCTION

The thyroid gland through its hormones serves as a metabolic thermostat, regulating the level of biochemical activity of most tissues of the body. In general dysfunction of the thyroid gland leads to two sets of symptoms those related to the local effect of a mass in the neck and the effects of either an excess or a deficiency of thyroid hormones. Dysfunction of the thyroid gland ranks next only to diabetes mellitus amongst the endocrine diseases.

The normal thyroid gland is a fairly homogenous structure but nodules often form within its substance. These nodules may be only the growth and fusion of localized colloid-filled follicle or more or less discrete adenomas, or cysts. Nodules larger than 1 cm may be detected clinically by palpation. Careful examination, disclose their presence in at least 4% of the general population. Nodules less than 1 cm in diameter not clinically detectable unless located on

the surface of the gland are much more frequent. The terms adenomatous goiter, on toxic nodular goiter and colloid nodular goiter are used interchangeably as descriptive terms when a multinodular goiter is found.

Multinodular non-toxic goiter is the most prevalent thyroid pathology characterized by unilateral or bilateral thyroid growth with morphologically and/or functionally transformed follicles and euthyroidism. In contrast to the endemic goiter, iodine deficiency is not primary causal factor. Environmental factors such as natural goitrogenic iodine intake, malnutrition, drugs, stress, pollution or infections, constitutional factors such as female gender and several genetic factors, i.e. circulating thyroid growth factors contribute to different degree to the development of nodular thyroid enlargement. Also controversially debated, thyroid-stimulating hormone (TSH) presumably has an important role in the maintenance of thyroid growth and goitrogenesis. The observation that TSH- suppressive treatment may cause a reduction of goiter volume underlines the role of TSH as goitrogen factor. In this study a group of patients with multinodular goiter were examined clinically and investigated to find the various correlations.

MATERIALS AND METHODS

In this observational study 50 individuals from Department of medicine, M.G.M. Medical College & M.Y. Hospital, Indore, MP, India, were taken in the study from February 2016 to October 2017

Group: Cases included of all cases & control subjects was taken and all ethical issues considered.

A written consent of all cases & control subjects was taken and all ethical issues considered.

Inclusion Criteria

50 Diagnosed cases of Multinodular goiter with symptoms and signs of hypothyroidism or hyperthyroidism or no symptoms and signs. Patients with biochemical evidence of hypothyroidism or hyperthyroidism were included.

Exclusion Criteria

Patients suffering from Hypertension, Diabetes Mellitus, Coronary artery disease or other cause of LV dysfunction

Patients with history of chronic alcoholism.

Study Protocol

Following criteria were used for selection of the patients

1. Age: Patients from all age groups were included in this study.
2. Sex: Patients from all age groups were included in this study
3. Therapy : only fresh cases were selected
4. Population: Indian patients of all socio-economic classes, casts and rural and urban habitat were studied.

All the patients of thyroid swelling were subjected to further clinical and laboratory evaluation.

Clinical Profile:

Symptoms pertaining to the cardiovascular & neurovascular system were given importance. They were recorded as follows:

1. Dyspnea: The grade was recorded
2. Chest Pain: The nature, duration location, and associated symptoms like sweating, vomiting, sudden onset breathlessness and syncope were recorded.
3. Palpitation
4. Increased fatigability
5. Symptoms suggestive of congestive cardiac failure were noted, like breathlessness, cough with blood tinged sputum, fever, upper abdominal pain, edema etc.
6. Previous therapy for thyroid disturbance: Medical, surgical or radiological was noted.
7. Personal history: Personal history was recorded with a special reference to sleep habits, appetite and bowel habits.
8. Menstrual and obstetric history: In the female patients, menstrual and obstetric history was given importance. Growth of the children of our patients was enquired. History of hysterectomy, if any, was recorded. The histopathological examination report if available was noted.
9. Family history and social history was recorded.

Physical examination:

On general examination: Following points were noted

1. Appearance : Whether agitated, normal or depressed
2. Height and weight
3. Temperature
4. Carotid thrill or bruit if any
5. Pulse rate, volume, force, tension and rhythm
6. Blood pressure and pulse pressure
7. Swelling of thyroid
8. Nail changes – specifically Plummer's nails.
9. Skin examination: The texture, temperature, colour, hypo or hyperpigmented patches and whether dry or moist.
10. Examination of the hair colour, texture, distribution, and density.
11. Pretibial myxedema
12. Gynaecomastia in males
13. Secondary sexual characteristics in both males and females
14. Myoedema

b) On systemic examination:

- i) Respiratory System:
- ii) Per abdominal examination:
- iii) Cardiovascular system examination
- iv) Central nervous system examination

c) **On the examination of eyes:** following points were noted

- Spastic signs
- Proptosis, eye movements and congestive ophthalmopathy
- Periorbital swelling
- d) **Examination of thyroid:** included the size, symmetry, tenderness, nodularity, pyramidal lobe, consistency, and presence of bruit.

Biochemical Investigations:

1. Hb, WBC count, Platelet count were done in all cases
2. FBS, PPBS, Urine, BUN, serum creatinine, Lipid profile were done in all cases.

Statistical analysis:

Patients were divided in groups on the basis of clinical characteristics. Percentage analysis was used to describe demographic variables and presence of outcome events. The analysis was carried out using SPSS(Statistical Package for Social Science) for windows. ANOVA test was used for calculation of statistical significance. Mean and Standard Deviation was calculated with help of Microsoft Excel Office 2007 version. Probability values are two sided throughout and a P value of <0.05 was considered significant.

RESULTS

As shown in table 1, main symptoms in all euthyroid patients (25) were mass in the neck(84%), dysphagia(44%), and stridor(12%).

Table 1: Including of main symptoms in euthyroid cases

S. No.	Symptoms	No. of Cases	Percentage
1	Mass in neck	21	84%
2	Dysphasia	11	44%
3	Stridor	3	12%

As shown in table 2, out of 5 multi-nodular hypothyroid patients, sinus bradycardia was present in 80% cases. Skin changes & peripheral edema was in next frequency (40% each). Also some patients had delayed ankle reflex & eye signs (20% each).

Table 2: Including of main physical signs in hypothyroid patients

S. No.	Signs	No. of Cases	Percentage
1	Bradycardia	4	80%

2	Eye signs	1	20%
3	Goiter	5	100%
4	Skin changes	2	40%
5	Edema	2	40%
6	Delayed ankle reflex	1	20%
7	Myopathy	-	-

As shown in table 3, out of 20 multi-nodular hyperthyroid patients sinus tachycardia & tremors (90% each) were commonest physical signs. Bruit over thyroid (60%), Hyper-reflexia (50%) Eye & Skin changes (45% & 25%) were other signs.

Table 3: Including of main physical signs in hyperthyroid patients

S. No.	Symptoms	No. of Cases	Percentage
1	Tachycardia	18	90%
2	Goiter	20	100%
3	Tremors	18	90%
4	Bruit over thyroid	12	60%
5	Eye signs	9	45%
6	Skin Changes	5	25%
7	Hyper-reflexia	10	50%

As shown in table 4, the abnormal cardiovascular findings in multi-nodular hypothyroid cases shows, 60% of patients have diastolic hypertension & apex not localized, 20% patients had muffled heart sounds, pulse pressure <40mm Hg & S3.

Table 4: Including of abnormal finding on CVS examination in hypothyroid cases

S. No.	Findings	No. of Cases	Percentage
1	Pulse pressure < 40mm hg	1	20%
2	Diastolic hypertension	3	60%
3	Cardiomegaly	-	-
4	Apex – not localized	3	60%
5	Muffled heart sounds	1	20%
6	Pericardial effusion	-	-
7	S3	1	20%
8	S4	-	-

As shown in table 5, the abnormal cardiovascular findings in multinodular hyperthyroid cases shows loud S1 in 75% cases, hyperdynamic apex and loud S2 in 70% cases, pulse pressure >40 mm Hg in 60% cases, systolic hypertension in 50% cases, diastolic pressure <70mm Hg in 50% cases and cardiomegaly in 45% cases.

Table 5: Incidence of abnormal findings on CVS examination in hyperthyroid cases

S. No.	Findings	No. of cases	Percentages
1.	Pulse pressure >40mm Hg	12	60%
2.	Diastolic pressure<70 mm Hg	10	50%
3.	Systolic Hypertension	10	50%
4.	Cardiomegaly	9	45%
5.	Hyperdynamic apex	14	70%
6.	Loud S1	15	75%
7.	Loud S2	14	70%
8.	Systolic murmur	5	25%
9.	Click	6	30%

As shown in table 6, only 1(5%) patient with hyperthyroidism had serum cholesterol less than 160 mg/dl. 19(95%) patients of hyperthyroidism, 4(80%) patients of hypothyroidism and 25(100%) patients of euthyroidism had value between 160-240 mg/dl with mean of 180.2 mg/ dl, 209.1 mg/dl & 180.3 mg/dl respectively. Only 1(20%) patient of hypothyroidism had value 300mg/dl.

In Serum triglyceride levels, only 1(20%) patient with hyperthyroidism had value more than 200 mg/dl i.e. 218.9 mg/dl. 20 (100%) patients of hyperthyroidism, 4(80%) patients of hypothyroidism and 25(100%) patients of euthyroid cases had value between 150-200 mg/dl with mean of 176.2 mg/ dl, 189.0 mg/dl and 154.7 mg/dl respectively.

In serum HDL levels, only 1(20%) patients with hyperthyroidism had value more than 60 mg/dl i.e. 74.2 mg/dl, 19(95%) patients of hyperthyroidism,

3(60%) patients of hypothyroidism and 22(88%) patients of euthyroid cases had value between 30-60 mg/dl with mean of 40.9 mg/dl, 53.7 mg/dl & 41.4 mg/dl respectively. Only 1(5%) patient of hyperthyroidism, 1(20%) patient of hypothyroidism, and 3(12%) patients of euthyroid cases had value between 30 mg/dl with mean of 28.4 mg/ dl, 29.0mg/dl and 28.5 mg/dl respectively.

The mean lipid parameters are depicted. The mean serum cholesterol value in hyperthyroid group was 177.4 mg/dl as against 238.2 mg/dl and 180.03 mg/dl in the hypothyroid and euthyroid group respectively. The values were 40.4 mg/dl, 53.3 mg/dl, and 40.1 mg/dl for HDL in three groups. The serum triglyceride levels were 176.2 mg/dl, 203.9mg/dl and 154.7 mg/dl respectively in the same groups. Total serum lipids were 455.3 mg/dl, 577.4mg/dl and 480.0 mg/dl in all the three groups respectively.

Table 6: Serum lipid levels in cases studied

Serum Lipid Levels (in mg/dl)		Hypothyroidism			Hyperthyroidism			Euthyroid		
		No.	%	Mean	No.	%	Mean	No.	%	Mean
Cholesterol	<160	-	-	-	1	5	119.1	-	-	-
	160-240	4	80	209.1	19	95	180.2	25	100	180.3

	>240	1	20	300.0	-	-	-	-	-	-
Triglyceride	<150	-	-	-	-	-	-	-	-	-
	150-200	4	80	189.0	20	100	176.2	25	100	154.7
	>200	1	20	218.9	-	-	-	-	-	-
HDL	<30	1	20	29.0	1	5	28.4	3	12	28.5
	30-60	3	60	53.7	19	95	40.9	22	88	41.4
	>60	1	20	74.2	-	-	-	-	-	-

DISCUSSION

This study included 50 cases, out of which 5 were hypothyroid, and 20 were hyperthyroid, and 25 were euthyroid cases.

Mass in neck and slow pulse rate was a striking finding in our patients 4 patients out of 5 i.e. 80% had sinus bradycardia. The slow pulse and lower systolic blood pressure is a likely manifestation of the decreased cardiac output. Disorders of lipid metabolism including elevation in serum cholesterol in hypothyroidism have been clearly identified as significant risk factor for the development of hypertension and atherosclerotic cardiovascular disease. Plasma renin plasma aldosterone and aldosterone production rates are decreased in hypothyroid patients with hypertension thus, the hypertension of myxedema can be classified as low renin state (Klump F et al 1975)².

Diekman MJ et al³ noted have noted a rise in vascular resistance in hypothyroid states. This change in peripheral resistance would be expected in turn to decrease the cardiac output but if the adaptation were not complete the result would be a rise in diastolic blood pressure and elevated mean and diastolic arterial pressures.

On clinical examination 3 patients i.e. 60% were having apex not visualized cardiac enlarged reduced cardiac pulsation and low voltage was first associated with myxedema. The resemblance of this clinical picture to pericardial effusion soon became evident. Signs of cardiovascular involvement were found in abundance in hyperthyroid patients. In multi-nodular hyperthyroid pts., sinus tachycardia & tremors (90% each) were commonest physical signs. Bruit over thyroid (60%), Hyper-reflexia (50%), Eye & Skin changes (45% & 25%) were other signs.

The values for the various lipid parameters when compared statistically with the euthyroid group was found to be significant for total cholesterol, triglycerides and total lipids ($p < 0.05$).

Vierhapper H et al⁴ found serum cholesterol to be significantly higher in both overt and sub-clinical hypothyroidism while serum triglyceride were raised only in overtly hypothyroid patients. In the present study similar results were obtained with respect to the euthyroid group. However in the present study patients were not categorized according to progressive thyroid failure. They also found that HDL levels to remain within the normal range in both sub-clinical and overt hypothyroidism. In the present study also the HDL levels were found to be within the normal range they were higher than those of the euthyroid group.

C.V. Rizos et al⁵ documented significant decrease in serum cholesterol with therapy in severe thyroid dysfunction while the decrease was insignificant in mild dysfunction. There was no significant change in triglyceride values. The HDL cholesterol also did not show much change. The result of present study also show overall increased values for serum cholesterol and total serum lipids. Serum triglycerides however were also found to be elevated. The mean serum HDL-cholesterol concentration in the present study was also found to be at the lower limit of normal (40.4 mg/dl) and it was almost same as the mean value of serum HDL in the euthyroid group (mean 40.1 mg/dl). On comparison the serum HDL cholesterol value of the present study was found to be statistically significant ($p < 0.05$).

All the patients in the present study had serum triglyceride concentrations within the normal range of 150-200 mg/dl with a mean of 176.2 mg/dl. The

mean value in the euthyroid group was 154.7 mg/dl. The values of triglyceride in the present study in patients with hypothyroidism was found to be statistically insignificant ($p>0.05$).

In the present study total serum lipid concentration was within the normal range in 21 patients with a mean of 472.6 mg/dl. 4 patients had the values of S. total lipid less than the normal range with a mean of 370 mg/dl. The present study also documented a similarly total serum lipid level in hypothyroid patients although the levels in both the morbid and euthyroid groups remained within normal limits.

CONCLUSIONS

Most of the patients had cardiac involvement in one or the other way as documented by clinical examination electrocardiography or biochemical investigation. There is no correlation between sex and susceptibility for the involvement of cardiovascular system in cases of multinodular goiter. Lipid levels were significantly deranged in hypothyroidism or hyperthyroidism patients.

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Conflict of interest: Not declared

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