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A STUDY ON LIVER FUNCTION IN THE BACKGROUND OF NEWLY DIAGNOSED THYROTOXICOSIS

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ABSTRACT

Introduction: There is a number of pathological, epidemiological, molecular basis which could establish an association between the liver dysfunction and thyrotoxicosis. Thyrotoxicosis is defined as the state of thyroid hormone excess while Hyperthyroidism is the result of excessive thyroid function.

Aims: Assessment of liver function in the background of newly diagnosed thyrotoxicosis, comparison between liver function and different types of thyrotoxicosis and co-relation of clinical activity score (CAS) and liver function test (LFT) in Graves" disease.

Materials and Methods: The present study was a Institution based Cross-sectional study. This Study was conducted from 18 months (From 1st January, 2020 to 30th June, 2021) at Department of General Medicine, endocrinology outdoor of Calcutta National Medical College and Hospital, Kolkata.

Result: Chi-square (χ^2) test showed that there was significant association between level of total bilirubin and types of thyrotoxicosis of the patients (p=0.0059).High level of total bilirubin was prevalent in significantly higher proportion among the patients with Multinodular Goitre (100.0%) as compared to other types of thyrotoxicosis (p<0.01)

Conclusion: In conclusion, the results of our study suggest that thyrotoxicosis is associated with abnormal liver biochemical tests in about two-third of the presenting cases and the most commonly elevated parameters are ALT and AST followed by ALP levels. Therefore, patients presenting with unexplained hepatic abnormalities require evaluation of the thyroid function.

Keywords: Thyroid hormone, Thyrotoxicosis and Hyperthyroidism.

INTRODUCTION

There is a number of pathological, epidemiological, molecular basis which could establish an association between the liver dysfunction and thyrotoxicosis. Thyrotoxicosis is defined as the state of thyroid hormone excess while Hyperthyroidism is the result of excessive thyroid function.[1,2] Thyrotoxicosis can affect multiple organ system including cardiovascular, nervous, gastrointestinal, and hepatic systems. The thyroid hormones are glucuronidated and sulfated within the liver and subsequently excreted into bile; in addition these hormones maintain the metabolism of bilirubin by playing a role in the enzymatic ativity of glucuronyltransferase and by regulating the of ligandin, a major organic anion binding protein.[3] There are several

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mechanism of liver dysfunction in the background of thyrotoxicosis including hyperthyroidism, increased TSHR-Ab, hypoxia due to increased arterio-venous oxygen difference in splanchnic bed, liver damage due to heart failure or due to anti-thyroid drugs.

CAUSES OF THYROTOXICOSIS:

A) Primary hyperthyroidism: graves" disease, toxic multinodular goiter, toxic adenoma, functioning thyroid carcinoma metastasis, activating mutation of the TSH receptors, struma ovarii, Iodine excess(Jod-Basedow Phenomenon)

B) Thyrotoxicosis without hyperthyroidism: subacute thyroiditis, silent thyroiditis, thyrotoxicosis factitia, amiodarone induced, radiation induced thyroid destruction.

C) Secondary hyperthyroidism: TSH secreting pituitary adenoma, thyroid hormone resistance syndrome, chorionic gonadotropin secreting tumor, gestational thyrotoxicosis.

Graves´ disease is the commonest one among the causes of hyperthyroidism, around 70-80%. Hepatic dysfunction was first described in hyperthyroidism patient by Habeshon in 1874.

CLINICAL ACTIVITY SCORE (CAS) IN GRAVES" DISEASE: (one point is given for each sign. The sum of points defines the activity score. [4]

1) Spontaneous retrobulbar pain
2) Pain on attempted up or down gaze
3) Redness of the eyelids
4) Redness of the conjunctivae
5) Swelling of the eyelids
6) Inflammation of the caruncle and/or plica
7) Conjunctival edema.

• CAS – 3 or more out of 7 indicates active ophthalmopathy

MATERIALS AND METHODS

Study Design: Institution based Cross-sectional study.

Study Setting: The study will be conducted in the Department of General Medicine, endocrinology outdoor of Calcutta National Medical College and Hospital, Kolkata.

Place of Study: Calcutta National Medical College & Hospital.

Period of Study: 18 months (From 1st January, 2020 to 30th June,2021)

Study Population: Patients will be recruited from the Endocrine OPD and indoor patients of Dept. of General Medicine of CNMCH.

Sample size: 35 patients fulfilling the inclusion criteria.

Inclusion Criteria:

Thyrotoxicosis patients of recently diagnosed only

Exclusion Criteria: The following groups of patients were excluded from this study after detailed history taking, clinical examination and investigations because of the confounding factors which will interfere with the results.-

1) HBSAG, Anti-HCV, HIV 1 & 2—reactive patients
2) Chronic alcoholic

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3) On anti-thyroid drug

RESULT AND DISCUSSION

The present study was a Institution based Cross-sectional study. This Study was conducted from 18 months (From 1st January, 2020 to 30th June, 2021) at Department of General Medicine, endocrinology outdoor of Calcutta National Medical College and Hospital, Kolkata.

In our study we found that proportion of patients (28.6%) were higher with age between 50 – 59 years, however, proportion of patients was more or less equally distributed over ages ($Z=0.47;p=0.63$). Thus in this study thyrotoxicosis was more or less evenly distributed over age. In our study the age range was 20-59 years.

In one study (15) the age range was 19-77 years. In another study (19) the age range was 20-60 years.

We found the ratio of male and female (Male: Female) was 1.0:1.7. Test of proportion showed that proportion of females (62.9%) was significantly higher than that of males (37.1%) ($Z=3.67;p<0.001$) in our study.

In one study (16) there was female preponderance of 74%.

In our study, the serum T3 of total population was 273.77±63.10 ng/dl. In our study, the serum fT4 of total population was 2.68±0.68 ng/dl.

In our study, the serum TSH of total population was 0.05±0.06 uIU/ml. In one study (15) the mean TSH was 0.1±0.05 uIU/ml.

In our study, the serum total bilirubin of total population was 0.91±0.33 mg/dl.

In our study, the serum AST of total population was 50.31±33.29 U/L. In our study, the serum ALT of total population was 52.03±41.24 U/L.

In our study, the serum albumin of total population was 4.13±0.46 mg/dl. study, 17.1% of the patients had high level of total bilirubin, and 45.7% patients had high AST & ALT levels, 25.7% of the patient had high ALP level and 5.7 % of the patients had high protein & albumin level.

In one study (14) it has been found that 47 of 65 (72%) patients of thyrotoxicosis had atleast one abnormal LFT. 31 % patient had high total bilirubin, 66 % had high ALP, 23 % had high AST, and 22 % had high ALT values.

In some studies (10, 23, 24, 25), the reported prevalence varies from 15 to 76% with ALP elevation being the most common.

In our study 100% of the patients had high fT4 & low TSH level while 91.4% of the patients having high T3 level.

We found, out of 35 patients, 26(74.3%) of them were found to be suffering from Graves disease, 7(20%) from thyroiditis, and 2(5.7%) from multinodular goitre.

In one study (16) Graves' 52%; toxic goitre 19%, autoimmune thyroiditis 2%; unclear in 6%.

We found that the three types of thyrotoxicosis were more or less equally distributed over ages of the patients.

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We found that 50% of patients with Graves disease had high AST, ALT, while 100 % of multinodular goiter patients had high AST, ALT and 14.3 % of thyroiditis patients had high AST,ALT level. But because of only 2 patients of multinodular goiters in our study, it did not actually reflect the LFT function in the population.

But Gurlek A et al found that 26 out of the 43 patients had at least one liver biochemical abnormality at initial evaluation. Serum ALT, AST, ALP, GGT elevations above the upper limits of normal were observed in 10, 6, 19, 6 patients respectively. None of the patients had elevated total bilirubin.[5]

High level of total bilirubin, ALP was prevalent in significantly higher proportion among the patients with Multinodular Goitre (100.0%) as compared to other types of thyrotoxicosis ($p<0.01$). But because of only 2 patients of multinodular goiters in our study, it did not actually reflect the ALP function in the population.

Level of protein and albumin was more or less equally distributed among the types of thyrotoxicosis.

In our study we found that out of 26 Graves disease patients, 12 (46.2%) patients had active eye disease.

In one study (22), it has been found that they had active eye disease of 28% in Graves disease patients.

In our study we first time found that ALT and AST level increased proportionally with increase to CAS (clinical activity score) in Graves disease but ALP levels was not related not increase in CAS in Graves disease. We could not found similar study regarding relation between liver function abnormality and Clinical activity score in Graves disease.

In our study we found that 62.8 % patients had at least one LFT parameters abnormality.

In one study (15), they found that 60.46 % had at least one liver biochemical abnormality.

Fong TL et al found that hepatomegaly and/or splenomegaly were noted in 15 of 19 patients with hyperthyroidism and congestive heart failure as compared to 6 of 18 patients with uncomplicated hyperthyroidism and 3 of 6 patients with hyperthyroidism and concomitant unrelated liver disease. Serum aminotransferase levels greater than 250 IU/L were noted only 1 of 37 patients without unrelated liver disease[6]

Kubota S et al found that 23 untreated Graves"s disease patients and 14 untreated painless thyroiditis patients were found to have at least one liver function test abnormality[7]

CONCLUSION

- In conclusion, the results of our study suggest that thyrotoxicosis is associated with abnormal liver biochemical tests in about two-third of the presenting cases and the most commonly elevated parameters are ALT and AST followed by ALP levels. Therefore, patients presenting with unexplained hepatic abnormalities require evaluation of the thyroid function.
- Our study also suggests that increase in CAS (clinical activity score) in Graves' disease is associated with increase in liver enzymes particularly AST and ALT.

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Table 1: Diagnostic distribution of the patients

Diagnosis	Number	%
Graves disease	26	74.3%
Multinodular Goitre	2	5.7%
Thyroiditis	7	20.0%
Total	35	100.0%

Table 2: Association between Level of albumin and type of thyrotoxicosis

Level of albumin	Type of thyrotoxicosis			TOTAL
	Graves disease	Multinodular Goitre	Thyroiditis	
Low	2	0	1	3
Row %	66.7	0.0	33.3	100.0
Col %	7.7	0.0	14.3	8.6
High	2	0	0	2
Row %	100.0	0.0	0.0	100.0
Col %	7.7	0.0	0.0	5.7
Normal	22	2	6	30
Row %	73.3	6.7	20.0	100.0

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Col %	84.6	100.0	85.7	85.7
TOTAL	26	2	7	35
Row %	74.3	5.7	20.0	100.0
Col %	100.0	100.0	100.0	100.0

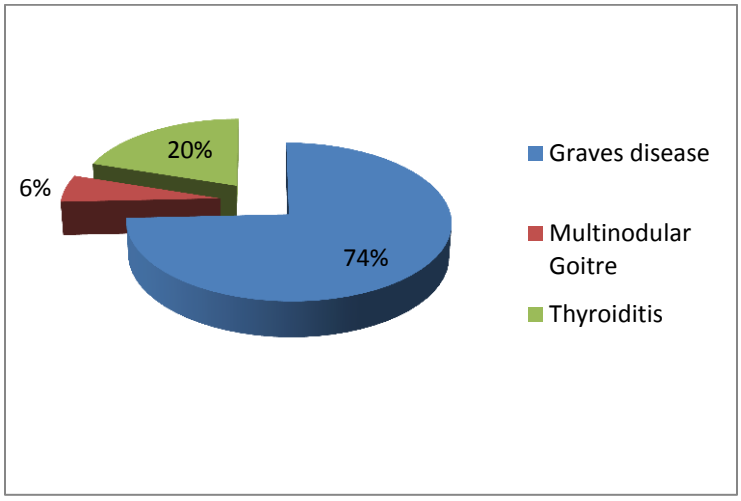

Figure 1: Diagnostic distribution of the patients

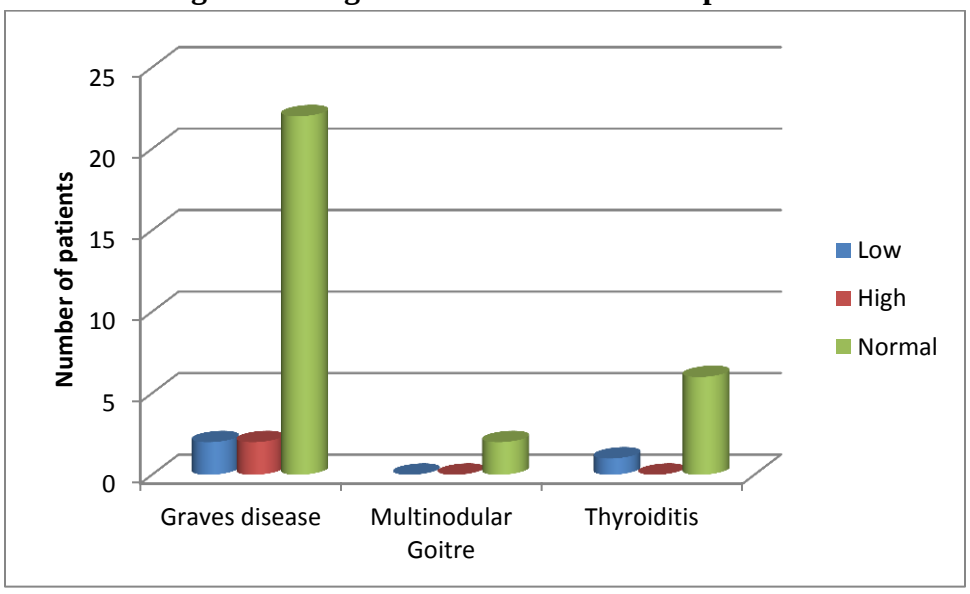

Figure 2: Association between Level of albumin and type of thyrotoxicosis