Study on Clinical and Laboratory Profile of Patients with Primary Hyperthyroidism

M. Sai Krishna[1], L. Uma Pradeepa[2], Swetha Ambati[3], Sriram Ravintula[4]

ABSTRACT

Introduction: Thyroid hormones regulate numerous metabolic processes. Therefore, any alteration in their synthesis or function has important health implications. Aims: Study done on clinical and laboratory profile of patients with primary hyperthyroidism**.**

Material and methods: Descriptive and cross-sectional Study done amongst the in-patients with a proven Primary Hyperthyroidism. 60 Patients with newly diagnosed Primary Hyperthyroidism above the age of 18 years. Diagnostic hormone levels i.e. increased SERUM T3,T4 levels with decreased TSH levels.

Results: out of 60 patients of Hyperthyroidism, 60% were Grave's disease, 28.3% were Toxic multinodular goiter and 1.7% was toxic solitary nodule. Majority of TSH values were less than 0.01. In all most all cases both T3 and T4 were elevated (predominantly T4). There was no difference in T3, T4 and TSH values among the three common causes of Hyperthyroidism. Wayne's clinical Diagnostic index had good correlation with T3 (p value of 0.024), T4 and TSH. When the Wayne's index was high, T3 & T4 were also high and TSH was low.

Conclusion: Wayne's clinical index correlate quite well with the thyroid function tests particularly raised T3 and the score could be a useful tool for follow up of hyperthyroid patients.

Keywords: Clinical and Laboratory Profile, Primary Hyperthyroidism

INTRODUCTION

The term Primary Hyperthyroidism and thyrotoxicosis are often used almost synonymously. However, in the strict definition of the term they are not the same. Primary hyperthyroidism implies excess hormone production by the thyroid gland. Thyrotoxicosis on the other hand is a more general term that refer to state of hormone excess and includes conditions which cause primary hyperthyroidism plus conditions like thyroiditis where there is a transient increase in hormone release and others like secondary hyperthyroidism.[1,2,3]

Grave's disease is globally the most common cause of primary hyperthyroidism. This study was done see if other conditions like Toxic Multinodular Goiter and Toxic adenoma were important contributors in this part of the world. The clinical and laboratory profile of these patients were assessed and an attempt made to see if they differed in any major way to presentation elsewhere.

MATERIAL AND METHODS

Descriptive and cross-sectional study was done amongst the in-patients with a proven Primary Hyperthyroidism patients.

Inclusion Criteria: Patients with newly diagnosed Primary Hyperthyroidism above the age of 18 years. Diagnostic hormone levels i.e. increased SERUM T3,T4 levels with decreased TSH levels.

Exclusion Criteria: Drug induced Hyperthyroidism, Patients who are critically ill with a probable clinical picture of Sick Euthyroid Syndrome, secondary hyperthyroidism.

A detailed history, physical examination and Wayne's clinical diagnostic scoring were recorded in all cases. Lab investigations, Serum T3,T4 and TSH were measured by enzyme Immunoassay. CBP, ESR and ECG were done. Thyroid scan was done in all patients.

individuals screened with results of TSH, free T3 and/or free T4 from a third-level health care institution of Medellin, of any sex and age, residents from Medellin, and with clinical suspicion of alterations in thyroid function were included. Ninety-six reports with incomplete or illogical information for TSH were excluded.

Data collection

A secondary information source based on clinical laboratory records with patient identification data, age, sex, date of test and test results was used. With those data an excel file was made with the variables registered by the clinical laboratory: age, sex, type of test and its result.

Thyroid profile determination

Measurements of TSH, free T4 and free T3 hormones were done in the automated system. For the determination of TSH, a third-generation immune assay with a sensibility of 0.008 mIU/L and a linearity limit of 150 mIU/L was used. Free T4 and T3 concentrations were determined using competitive immune assays. The assay for the quantification of free T4

[1]Assistant Professor, Department of General Medicine: Chalmeda Anand Rao Institute of Medical Sciences, Karimnagar, [2]Fellow in pain, Department of Anaesthesia and Pain, Yashoda Hospital, Secunderabad, Telangana, [3]MICU Specialist, Department of Anaesthesia, Niloufer Hospital, Hyderabad, Telangana, [4]Junior Consultant, Department of Anaesthesia, KIMS Hospital, Secunderabad, Telangana, India.

Corresponding author: Dr L. Uma Pradeepa, Fellow in Pain, Department of Anaesthesia and Pain, Yashoda Hospital, Secunderabad, Telangana, India.

How to cite this article: M. Sai Krishna, L. Uma Pradeepa, Swetha Ambati, Sriram Ravintula. Study on Clinical and Laboratory Profile of Patients with Primary Hyperthyroidism. International Journal of Contemporary Medical Research 2019;6(9):I1-I6.

DOI: http://dx.doi.org/10.21276/ijcmr.2019.6.9.43

Symptoms of Recent Onset and/or Increased Severity	Present		Signs	Present Score	Absent Score
	Score	Score			
Dyspnoea on effort	+1		Palpable thyroid	+3	-3
Palpitations	+2		Bruit over thyroid	+2	-2
Tiredness	+2		Exophthalmos	+2	
Preference for heat (irrespective of duration		-5	Lid retraction	+2	
Preference for cold	+5		Lid lag	+1	
Indifferent to temperature	0		Hyperkinetic movements	+4	-2
Excessive sweating	+3		Fine finger tremor	+1	
Nervousness	+2		Hands		
Appetite Increased	+3		Hot	+2	-2
Appetite Decreased		-3	Moist	+1	-1
Weight Increased		-3	Casual Pulse rate:		
Weight Decreased	+3		Atrial fibrillation		
			Regular rates:		
			80 per minute		-3
			80 to 90 per minute	0	
			90 per minute	+3	

had an analytical sensibility of 0,1 ng/dL and a linearity limit of 12 ng/dL.

Wayne's Clinical Diagnostic Index

Symptoms score + sign score = Diagnostic Index

Index under 11 = Non – Toxic

11 – 19 = Equivocal

Over 19 = Toxic

Variables such as age, sex and age group were described by summary measures and frequency, respectively. The general prevalence of thyroid disorders and specific prevalences according to sex and age group were estimated with their respective confidence intervals of 95%. Analysis were done in SPSS 24 with significance of 0.05.

RESULTS

Sixty newly detected cases of primary hyperthyroidism who were in-patients were studied.

The majority of patients were aged between 30-50 years (55%) followed by patients aged between 50-70 years. Out of 60 patients studied, 42 were females and 18 were males, giving a percentage of 70% and 30% respectively and a male to female ratio of 2.3:1 (table-1).

Shortest symptomatic period before diagnosis – 40 days. Four patients presented with thyroid swelling of more than 2 years duration, however their duration of thyrotoxic symptoms were less (table-2).

The commonest symptom observed in our study was weight loss (98.3%). Palpitations (96.7%) were the second most

Age group	Number of patients	Percentage
<30	10	16.7
30-40	19	31.7
40-50	14	23.3
50-60	14	23.3
>60	3	5.0
Total	60	100
Sex		
Male	18	30.0
Female	42	70.0
Total	60	100.0
Comorbidity		
NII	43	71.7
CCF	1	1.7
DM	2	3.3
HTN	9	15.0
DM,HTN	3	1.7
IHD,DM	1	1.7
MVP+MR	1	1.7
Total	60	100.0

Table-1: Demographic distribution

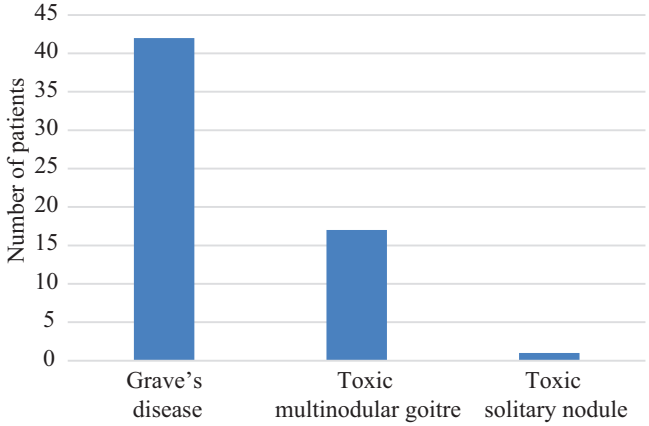

Figure-1: Types of hyperthyroidism

Duration	Number of patients	Percentage
0-1 month	18	30%
1-2 months	10	16.6%
2-3 months	13	21.6%
3-4 months	4	6.3%
4-5 months	3	5%
5-6 months	Nil	Nil
6 months-1 yr	7	11.6%
1-2 years	Nil	Nil
2 years	4	6.3%

Table-2: Duration of symptoms before diagnosis

common symptom. Commonest complaint of the illness in these patients was weight loss (table-3).

Three patients in our study showed haemoglobin value between 7-10 gm%.

General symptoms	Number of patients	Percentage
Fatigue	39	65%
Weight loss	59	98.3%
Heat intolerance	45	75%
Neuromuscular		
Irritability, Nervousness	46	76.7%
Muscular weakness	12	20%
Psychosis	4	6.7%
Dermatological		
Warm extremities	45	75%
Increased sweating	56	93.3%
Gastrointestinal		
Increased Appetite	52	86.7%
Anorexia	1	1.7%
Increased stool frequency	19	31.7%
Cardio respiratory		
Exertional chest paid	2	3.3%
Palpitations	58	96.7%
Breathlessness	11	18.3%
Reproductive		
Amenorrhoea/oligomenorrhoea	13	21.7%
Infertility	Nil	Nil
Pressure symptoms		
Dysphagia	6	10%
Hoarseness of voice	3	5%
Chief complaint		
Neck swelling	53	88.3%
Weight loss	59	98.3%
Palpitations	58	96.7%
Increased appetite	52	86.7%

Table-3: Symptoms and complaints:

Findings	Number of patients	Percentage
Pallor	23	38.3%
Ankle edema	12	20%
Clubbing	Nil	Nil
Lymphadenopathy	Nil	Nil
Warm and moist skin	49	81.7%
Thyroid swelling	53	88.3%
Thyroid bruit	30	50.1%
Tremors	58	96.7%
Pretibial myxoedema	Nil	Nil
Increased pulse pressure	23	38.3%
Pulse rate		
<80	3	5.0
80-90	9	15.0
90-100	23	38.3
>100	25	41.7
Total	60	100.0
Proximal myopathy	12	20%
Eye signs	17	28.3%

Table-4: General Examination

Out of 60 patients 52 Patients had normal Chest X ray, 7 patients showed evidence of cardiomegaly. Among these 5 – Toxic multinodular goiter, 2-Grave's disease.

Out of 60 patients, 35 patients had sinus tachycardia, 4 patients had atrial fibrillations and 3 patients had LVH (table-5).

In our study, majority of TSH values were less than 0.01. In all most all cases both T3 and T4 were elevated (predominantly

Haemoglobin	Number of patients	Percentage
7-10	3	5.0
10-13.5	42	70.0
>13.5	15	25.0
Total	60	100.0
Chest X ray evaluation:		
Cardiomegaly	7	11.7
WNL	52	86.7
ECG evaluation		
Atrial Fibrillation	4	6.7
Normal Sinus Rhythm	18	30.0
Normal Sinus Rhythm, Left Ventricular Hypertrophy.	2	3.3
Sinus Tachycardia	35	58.3
Sinus Tachycardia + Left Ventricular Hypertrophy	1	1.7
Total	60	100.0

Table-5: Results of laboratory profile.

TSH (IU/L)	Number of patients	Percentage
<0.01	36	60%
0.01-0.1	24	40%
T3 (ng/mL)		
2-5	32	53.4%
>5	28	46.6%
T4(Microg/dL)		
<12	2	3.3%
12-18	23	38.3%
18-24	22	36.7%
>24	13	217%

Table-6: Thyroid function test

Clinical score	Frequency	Percent
11-19	10	16.7
20-29	37	61.7
30-39	13	21.7
Total	60	100.0
Minimum score obtained – 15: Maximum score obtained – 38		

Table-7: Correlation with Wayne's clinical index: Wayne's Clinical scoring

Wayne's Index	T3	T4	TSH
R	.291	.174	-.156
P	0.024 sig.	.184	.034
N	60	60	60
r – correlation coefficient, p – p value, N – number			

Table-8: Correlations in present study

T4). There was no difference in T3, T4 and TSH values among the three common causes of Hyperthyroidism (table-6).

In this study, out of 60 patients, 42 were Grave's disease. Grave's disease was taken as the etiology when there was a uniform increase in thyroid uptake with suppressed TSH.17 were Toxic multi nodular goiter, and 1 was Toxic solitary nodule, giving a percentage of 70%,28% and 2% respectively (figure-1).

In our study, a score of more than 19 was obtained in 50 patients. Wayne's clinical diagnostic index had good correlation with T3 (p value of (0.024). T4 and TSH. When the Wayne's index was high, Te & T4 were also high and TSH was low (table-7).

In our study a score of more than 19 was obtained in 50 patients. Wayne's clinical Diagnostic index had good correlation with T3 (p value of 0.024), T4 and TSH. When the Wayne's index was high, T3 & T4 were also high and TSH was low (table-8).

DISCUSSION

This study was conducted on 60 patients of Primary Hyperthyroidism, to determine the common presenting clinical features and laboratory findings. The age of the patients included in this study ranged from 18 years and above. The majority of patients were aged between 30-50 years (55%) followed by patients aged between 50-70 years. Majority of Grave's disease in this study manifested by the age of 40 years, while no patients developed Toxic multinodular goiter and Toxic solitary nodule before 40 years of age. This correlates with the data from earlier studies. Zarger A H et al[4] in their study on 203 patients of hyperthyroidism stated that, the mean age of Hyperthyroidism was 39.98 ± 14.4 years. The majority of the patients with toxic multinodular goiter were aged above 40 years, where as the peak incidence of Grave's disease was between 20-40 years.

In the present study, females were 70% and males were 30%, with a female to male ration of 2.3:1. Although the female prevalence was slightly less than the many previous studies, the fact that a significant number of admissions tend to be made could explain this phenomena. However, even here there is a clear preponderance of females as shown.

Micheal M Kaplan[5] in his study on 120 patients of Hyperthyroidism reported that, women are affected 4-5 times more commonly than men. Joll[6] after reviewing the published data from all over the world, found a ratio of 4.4-8.2:1. The average ratio is about 4.5:1.

Type of hyperthyroidism

In the present study, out of 60 patients of Hyperthyroidism, 60% were Grave's disease, 28.3% were Toxic multinodular goiter and 1.7% was toxic solitary nodule. All these studies are consistent with observation that the Grave's disease is the most common cause of Hyperthyroidism. Micheal M Kaplan[5] in his study on 120 patients of Hyperthyroidism reported Grave's disease, Toxic multinodular goiter and Toxic solitary nodule in 85.8%., 5.8% and 3.3% of cases respectively.

Zarger A H et al[4] in their study on 203 patients of Hyperthyroidism stated that, Grave's disease is the most common cause of hyperthyroidism contributing 63.1% of cases, where as Toxic multinodular goiter and Toxic solitary nodule contributing for 23.1%, 12.3% of cases respectively.

Duration of symptoms

Most of the patients (43.3%) were diagnosed around 6 months in the present study. Shortest symptomatic period before the diagnosis was 30 days. Sidney C Werner[7] study duration of symptoms in Hyperthyroidism can be as brief as a few days or be a matter of 25 years or more. Not infrequently, the patient is unaware of illness and comes to the physician only because of pressure from family.

Mode of presentation

The commonest symptom observed in our study was weight loss (98.3%). Palpitations (96.7%) were the second most common symptom. In the study done by Williams R H et al[8], weight loss and palpitations were seen in 85%, 89% cases respectively. In a study done by Spaluding S W et al[9] weight loss was seen in 85% of patients and palpitations in 89% of cases. In the same study, nervousness was the most common symptom in 97.5% of cases. But our study showed a prevalence of 76.7%.

Other common symptoms observed in our study were sweating (93.3%), increased appetite (86.7%), hot skin (75%), fatigue (65%), diarrhoea (31.7%) amenorrhea (21.7%), and muscle weakness (20%). These results correlated with various western studies and an Indian studies.[10]

In our study, Diarrhoea was observed in 31.7% of patients. In majority of cases, there is an increased stool frequency rather than true diarrhoea. Brown R B et al[11] reported that, true diarrhoea was seen in 25% cases of Hyperthyroidism and history of increased frequency of stools may be seen in additional 30% cases.

In our study, 6 patients were presented with dysphagia. Majority of these patients had a larger goiter various other symptoms observed in this study were correlated with different western studies.

Co-morbidities

In our study, 5 patients were having coexisting type 2 Diabetes mellitus. Symptoms of uncontrolled Diabetes may be exacerbated by coexistent Hyperthyroidism. Usually there will be increased incidence of type 1 diabetes in patients with Grave's disease. Larson P R et al[12] mention that autoimmune diseases like Type 1 diabetes, pernicious anaemia, myasthenia gravis, adrenal atrophy, Systemic lupus erythematosus, Sjogren's syndrome and rheumatoid arthritis are not infrequently associated with Grave's disease.

Hyperthyroidism makes the patient symptomatic or worsens pre-existing Ischemic heart disease. It can also precipitate heart failure in a patient with heart disease, which is refractory to drugs. In our study, one patient had ischemic heart disease and one patient had heart failure along with hyperthyroidism. One patient had Mitral valve prolapsed in the present study. Channick BJ et al[13] reported increased prevalence of mitral valve prolapsed in hyperthyroid patients compared to normal individuals.

Examination Findings

The commonest signs observed in this study group were thyroid swelling (88.3%) and tremors (96.6%). Williams RH et al[8] observed goiter and tremors in 100%, 97% of cases respectively.

Warm moist skin was observed in 49 patients (81.7%) in our study. Spaulding SW et al[9] reported warm moist skin in 76% of cases where as William R H et al in 97% of cases.

Thyroid bruit was observed in 30 cases (50.1%) in this study. William R H et al[8] observed this in 77% of cases. In the Spaulding SW et al[9] study, it was also reported in 77% of cases.

Eye signs were noted in 17 cases (40.4%) in this study. Most of the eye signs were observed in cases of Grave's disease. In William R H et al[8] study, 71% cases had eye signs.

Other common signs observed in this study were increased pulse pressure (38.3%) and proximal myopathy (20%). Ankle edema was observed in 12 patients (20%). No patient had pretibial myxoedema. Jameson JL et al[14] reported that pretibial myxoedema is rare, occurs in 5% of patients with Grave's disease.

Evaluation of pulse rate

In this study, 25 patients (41.7%) had pulse rate more than 100 beats per minute. Where as in 48 patients (79%) pulse rate was more than 90. In Von-Olshausen K et al[15] study, pulse rate exceeding 100 beats per minute was observed in 40% of patients with Hyperthyroidism.

Correlation of laboratory findings

Hemoglobin: Three patients in our study showed haemoglobin value between 7-10 gm%. Out of which one had documented evidence of iron deficiency anaemia and in other two patients showed features of anaemia of chronic disease. In Hyperthyroidism, plasma volume is often more increased than red cell mass. This probably reflects the mild anaemia frequently seen in hyperthyroidism which improves with antithyroid therapy alone. Larson PR et al[12] reported pernicious anaemia in 3% of patients with Grave's disease. This study did not reveal any patients to suggest features of a pernicious anaemia.

T3, T4 and TSH: In our study, majority of TSH values were less than 0.01. In all most all cases both T3 and T4 were elevated (predominantly T4). There was no difference in T3, T4 and TSH values among the three common causes of Hyperthyroidism. Zargar A H et al[4] in their study on 203 subjects of hyperthyroidism, did not find any significant difference among the three common causes of hyperthyroidism.

Chest X ray evaluation: In the present study, Cardiomegaly was seen in 7 patients (11.7%). Out of which 5 were Toxic Multinodular goiter and 2 were Grave's disease. Zargar A H et al[4] in their study on 203 subjects of hyperthyroidism reported cardiomegaly in 9.8% of cases, where it is common with Toxic multinodular goiter (27.6%) followed by Toxic solitary nodule (8%) and Grave's disease (3.9%). The higher prevalence of cardiomegaly in those with Toxic multinodular goiter probably reflects the older age of this group of patients and their consequent increased risk for problems like IHD.

Evaluation of ECG: In our study, 35 (58.3%) patients had sinus tachycardia and 4 cases (6.7%) had atrial fibrillation. Atrial fibrillation was seen 2 cases (11.7%) of Toxic MNG and 2 cases (4.6%) of Grave's disease. In our study of Zargar A H et al[4], atrial fibrillation was noted in 4.6% cases of Grave's disease, 14.8% cases of Toxic Multinodular goiter and 20% cases of Toxic solitary nodule. High incidence of atrial fibrillation in Toxic MNG and Toxic Solitary nodule can be explained by delayed onset of disease in these individuals.

Correlation with Wayne's clinical index: In our study a score of more than 19 was obtained in 50 patients. Wayne's clinical Diagnostic index had good correlation with T3 (p value of 0.024), T4 and TSH. When the Wayne's index was high, T3 & T4 were also high and TSH was low. This suggests that the Wayne's scoring system is a potentially useful clinical tool to decide the presence of Thyrotoxicosis. It would be a potentially useful tool in the follow up of thyrotoxic patients on therapy as it could decrease the number of times hormone assays are done at follow up. This is relevant as in general tests for thyroid hormone tend to be expensive.

CONCLUSION

Hyperthyroidism is common in women in the third and fourth decades. Therefore when these individuals come with symptoms of palpitations and weight loss, the index of suspicion needs to be high and appropriate testing indicated. Most patients present with symptoms of weeks to months particularly when retrospectively looked at, older patients therefore more often present with complications like atrial fibrillation and heart failure. Grave's disease is the most common cause (60%) of Primary Hyperthyroidism even in Indian setting. The most common presentation of Primary Hyperthyroidism is with goiter. Weight loss and palpitations in various combinations. The presence of this triad should considerably raise the suspicion of the condition. Wayne's clinical index correlate quite well with the thyroid function tests particularly raised T3 and the score could be a useful tool for follow up of hyperthyroid patients.

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Source of Support: Nil; **Conflict of Interest:** None

Submitted: 06-08-2019; **Accepted:** 22-08-2019; **Published:** 28-09-2019