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Original Research Article

Thyroid symptom scoring index: an auxiliary guide to thyroid function tests: a prospective comparative study from a general hospital in South India

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ABSTRACT

Background: Thyroid disease has myriad manifestations. Thyroid stimulating hormone (TSH) and a paired determination of TSH and freeT4 would add to find out the degree of dysfunction with overutilization of thyroid function tests (TFT's) as the symptoms are being overseen in the recent days. The objectives of the present study were to validate the clinical symptom scoring index for thyroid disorders using TSH and FT4.
Methods: The clinical symptom scoring index consisting of 20 parameters was given to 110 patients presenting to our outpatient department with new onset thyroid-related complaints from June2018 to Spetemer2018. They were subjected to TFT (TSH and free T4) and classified accordingly. Statistical analysis was done and receiver operator curves (ROC) plotted.
Results: The mean TSH for the 3 groups (hypothyroid, hyperthyroid and euthyroid) were 13.65, 0.31 and 1.7 mIu/ml respectively (normal value: NV-0.25-5). Mean FT4 were 0.58, 5.01 and 1.28 ng/dl respectively (normal value 0.82-1.51). Most frequent findings in biochemical hyperthyroidism were easy tremors (100%), tiredness (90%), palpitations (93%) and weight loss (75.6%). The clinical symptom scoring index had a sensitivity of 85% and accuracy rate of 86.76% with area under the curve (AUC) 0.865 on ROC analysis for the detection of hyperthyroidism. It had a 100% sensitivity and AUC 0.65 for hypothyroidism.
Conclusions: The symptom scoring index for thyroid disorders was found to have good specificity, negative predictive value (NPV) and accuracy rate when correlated with TSH and FT4 for the detection of hyperthyroidism. In the developing countries, these score indices can aid as auxiliary diagnostic tools, reducing the load on referral centers.

Keywords: Thyroid symptom scoring index, TFT, FT4

INTRODUCTION

Thyroid disease has myriad manifestations. Thyroid stimulating hormone (TSH) is the single best test to triage thyroid dysfunction. A paired determination of TSH and freeT3/FT4 would add to the quantification of degree of dysfunction.[1] Various scoring indices such as Wayne's index for hyperthyroidism, Billewicz scoring for hypothyroidism have been tried and tested in the past.[2] Caceres et al was the 1st to device UST (University of St. Thomas) scoring index for the entire gamut of thyroid disease and reevaluated the same. None of these questionnaires have been more valuable than the conventional biochemical tests neither have they been made with the intention of replacing these tests. They may be utilized in reducing the number of tests and in post treatment follow up.[2] Hypothyroidism symptoms, which are frequently vague at presentation have

decreased the likelihood of biochemical tests if subjected to symptom scoring.[3-5] There is overutilization of thyroid function tests (TFT's) as the symptoms are being overseen in the recent days. Hence, the need to validate the symptom scoring against the present-day biochemical tests for utilization in resource constraint settings.

Objective

The objective of the present study was to validate the clinical symptom scoring index for thyroid disorders using TSH and FT4.

METHODS

This prospective comparative study was conducted from June 2018 to September 2018 over a duration of three months. Institutional ethical committee approval and patient consents were obtained. A minimum of 100 patients were planned to be recruited in the study by analyzing the prevalence of various thyroid related complaints and presentations in our outpatient department and a statistical power of 80%. The clinical symptom scoring index consisting 20 parameters was given to 110 patients presenting to the outpatient department with various new onset thyroid-related complaints, classified into hyperthyroid, hypothyroid and euthyroid groups. Scoring index was given in the local language and was validated by experts. Signs and symptoms were given a particular score which was then categorized into 3 groups-hyperthyroid >10, euthyroid 0-10 and hypothyroid <0. Sample size was calculated with 50% prevalence and 95% confidence level (alpha- 0.05) and 20% relative precision from an average of three years out patient department census, and was found to be a minimum of 100 patients. Inclusion criteria included patients with thyroid related complaints aged more than 18 years. We excluded pregnant patients, patients with psychiatric disease and patients on drugs that effect TFT. After subjecting the study group to these criteria, the study population was 101. They were then subjected to TFT (TSH and free T4) and classified accordingly. Euthyroidism was defined as a state of normal thyroid function, documented biochemically by normal TSH and thyroxine levels. Overt hypothyroidism is a form of thyroid dysfunction in which there is under-activity of the gland, manifested biochemically by an elevated TSH and decreased thyroxine level. Overt hyperthyroidism is a form of thyroid dysfunction in which there is over-activity of the gland, manifested biochemically by a decreased TSH and increased thyroxine level. Normal TSH falls within the assay reference range of 0.5 to 4.8 mIU/ml. Normal FT4 falls within the assay reference range of 0.9 to 1.8 ng/dl. TFT was done with Biomerieux mini vidas analyzer, VIDAS thyroid panel based on enzyme linked immunoassay technique. Statically analyses were done and sensitivity, specificity, ANOVA multivariate analysis and receiver operator curves (ROC) curves plotted with IBM.SPSS 23.0 and Microsoft Excel sheet.

RESULTS

Our study had a female preponderance with profile of patients and their demographic details described in Figure 1 and Table 2. Clinical and biochemical correlation has been tabulated in Table 1.

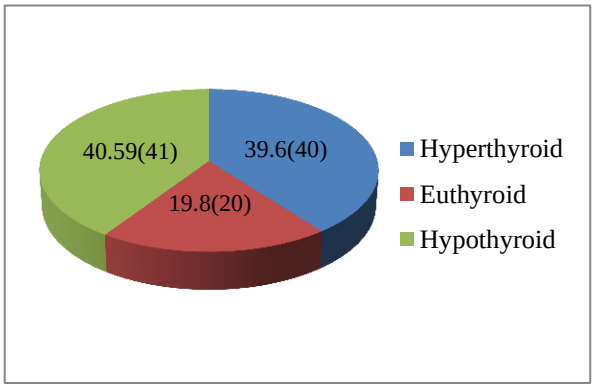

Figure 1: Profile of patients.

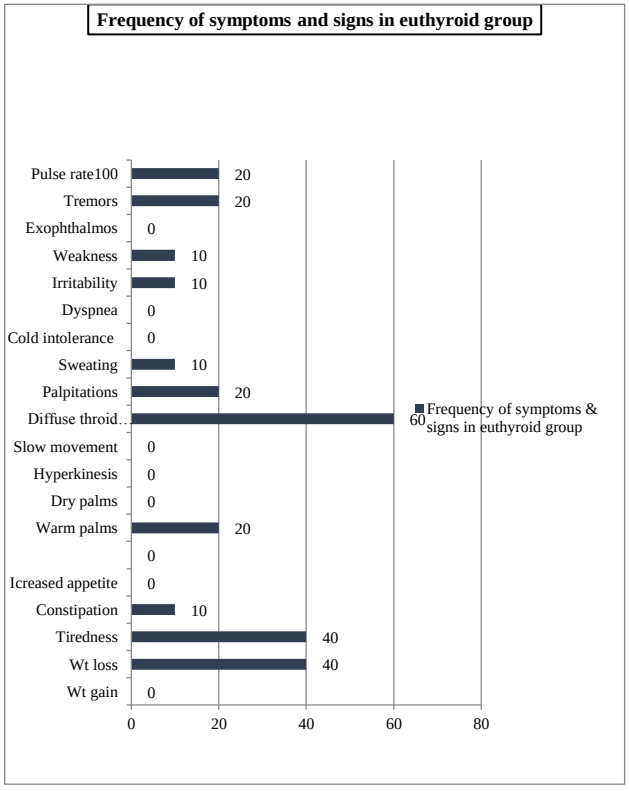

Figure 2: Frequency of symptoms in hyperthyroidism.

Most frequent findings in biochemical hyperthyroidism were easy tremors (100%), tiredness (90%), palpitations (93%) and weight loss (75.6%) (Figure 2).

Euthyroid group had diffuse thyroid enlargement (60%) and tiredness (40%) as frequent complaints (Table 3). In the hypothyroid group: constipation (48%) and weight gain (25%) were frequent symptoms with a significance of p=0.08 (Figure 3).

Table 1: Distribution of patients according to clinical score and biochemical status.

Clinical score/biochemical status (p=0.005)	Hyperthyroid (n=43)	Euthyroid (n=46)	Hypothyroid (n=12)
Hyperthyroid (>10)	37	4	0
Euthyroid (0-1)	6	14	0
Hypothyroid (<0)	0	28	12

Table 2: Demographic characteristics.

Parameters	Hyperthyroid	Euthyroid	Hypothyroid
Age in years	39.66±12.93	34.95±11.68	32.78±14.84
Male	5	10	6
Female	35	10	35
TSH	0.31±0.87	1.7±1.59	13.65±24.98
FT4	5.01	1.28	0.58

The clinical symptom scoring index had sensitivity, specificity, accuracy rate and area under the curve (AUC) for the detection of hyperthyroidism as described in Figure 4 and Table 4.

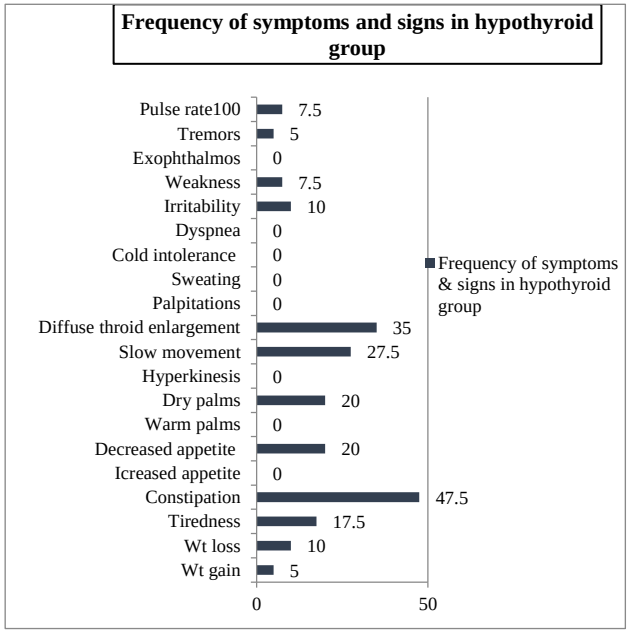

Figure 3: Frequency of symptoms in hypothyroidism.

Table 3: Frequency of findings in euthyroidism.

Euthyroid	Frequency (%)	P value
Easy tiredness	40	-
Thyroid enlargement	60	0.082
Irritability	10	0.085
Weakness	10	0.395

Hence the symptom scores were more accurate for diagnosis of hyperthyroidism. Clinical scoring for euthyroid patients had a sensitivity, specificity and AUC as shown in the Figure 5. Symptom scoring index was less accurate for detection of hypothyroidism and euthyroidism with AUC being 0.65 and 0.56 respectively (Figure 6 and Table 5).

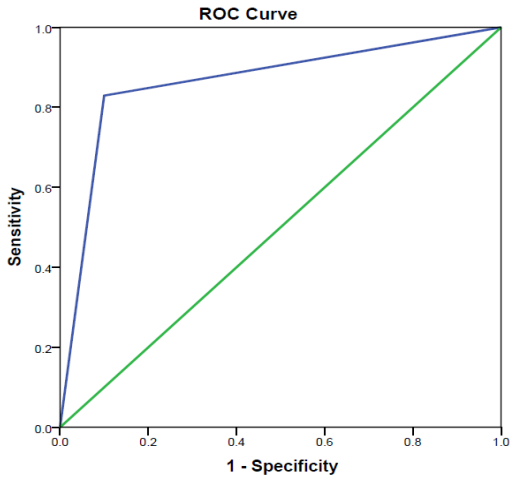

Figure 4: ROC of clinical scoring for hyperthyroidism (AUC: 0.865, CI: 0.784-0.945).

Table 4: Statistics in hyperthyroidism.

Hyperthyroidism	Our study
Sensitivity	85
Specificity	88.52
PPV	82.93
NPV	90
Accuracy	86.76

Table 5: Statistics of hypothyroidism.

Hypothyroidism	Our study
Sensitivity	100
Specificity	68.54
PPV	30
NPV	100
Accuracy	84.27

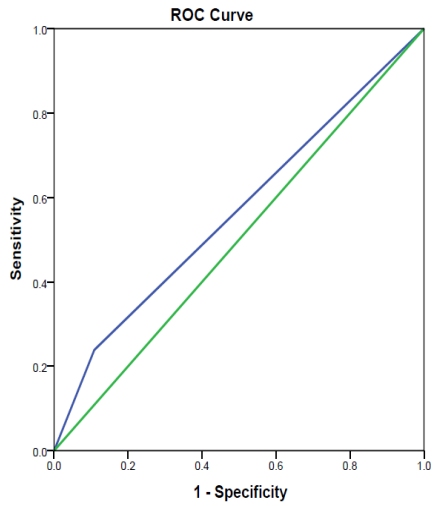

Figure 5: ROC of clinical scoring in euthyroid patients.

AUC: 0.565, CI: 0.452-0.679.

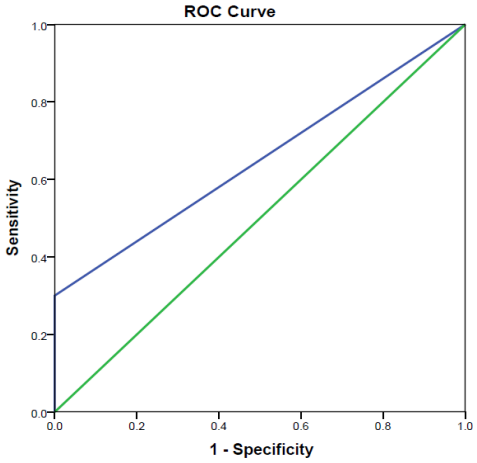

Figure 6: ROC of clinical scoring in hypothyroidism.

AUC: 0.65; CI: 0.535-0.765.

DISCUSSION

In our short term prospective comparative study, we tried to study if we could reduce the load of biochemical tests by resorting to assessment of symptom scores in our patients. This study was done with an intent to review the importance of symptom scores in evaluating and categorizing those patients with numerous vague complaints. A mildly elevated TSH by 0.5 above normal can result in undue stress, subjecting these patients to unnecessary medications. Those with specific complaints suggesting hyper function or hypo functioning gland were further subjected to biochemical tests and classified accordingly. In this study, the most frequent symptoms in biochemical hyperthyroidism were tiredness (90%), palpitations (93%) and weight loss (75.6%) and sign was easy tremors (100%) with similarity to Galia et al; In the euthyroid group nonspecific findings like diffuse thyroid enlargement (60%) and tiredness (40%) were seen more frequently; and in the hypothyroid group: constipation (48%) and weight gain (25%) were noted which was comparable to Galia et al showing constipation and weight gain in 44% of patients.[1,8] The distribution of symptoms were widely different among all three groups. Nazarpour et al studied hypothyroid patients validating Billewicz scoring with constipation and weight gain in 17% and 5% of patients while Canaris et al saw similar prevalence of constipation.[2,6]

In a study by Biondi et al, the severity of symptoms in hypothyroidism was related to disease severity, duration of the disease and the sensitivity of the patient to thyroid hormone.[3,7] The scoring index was found to be useful in detecting hyperthyroidism in the study population with good negative predictive value (NPV) and accuracy.[9-11] There was a significant female preponderance noted in our study similar to others by Caceres et al (90 females).[6] Some modifications of the scoring index were employed in the study with less importance given to hyperkinetic or sluggish movements which were nonspecific in our study. A score of more than 10 was considered hyperthyroidism with a specificity of 89%, NPV of 90% and accuracy of 86% which was comparable to Caceres et al.[1,6] Another Korean study also proved that the scoring index was useful in predicting thyrotoxicosis.[4] Whereas, a score of less than 0 was considered hypothyroid with 100% NPV and accuracy of 84% with an AUC of just 0.65. Caceres et al had an accuracy of 92% with the hypothyroidism scores and Galia et al had a NPV of 90% which was different from our study. Our results showed that the scoring could not accurately detect those patients with hypothyroidism though Billewicz scoring has been repeatedly validated for the same.[2,6,12] On the other hand, a study from Denver suggested they correlated with TFTs.[3] Another multicentric study showed similar findings.[5] Similarly, the AUC for euthyroid scores was only 0.56, which suggested that the scoring index could not accurately predict euthyroidism. A good symptom scoring index can accurately predict thyroid dysfunction, helping us in further research, though it cannot replace the conventional biochemical tests.[13-15]

CONCLUSION

Symptom scoring index has been repeatedly validated against TSH and FT4. This Symptom scoring index for thyroid disorders was found to have good specificity, NPV and accuracy rate when correlated with TSH and FT4 for the detection of hyperthyroidism. Traditional symptom scores cannot replace supersensitive TFT's. In the developing countries, with very minimal resources, these score indices can aid as auxiliary diagnostic tools, thus reducing the load on referral centers, avoiding unnecessary tests for vague complaints. Nonspecific symptoms could not be accounted for in our study, as it was institution based and not population based. The results cannot be applied to those patients who are on follow up with antithyroid drugs or thyroxine. Another

limitation of this study is that the data was drawn from a largely iodine sufficient region.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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