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To Study Dissociation of Clinical And laboratory Diagnosis In Hypothyroidism

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Abstract

Aims of the study: To assess the significance of clinical versus biochemical diagnosis of hypothyroidism using a clinical scoring index and to reduce the number of laboratory tests for diagnosing hypothyroidism.

Methodology: The study was undertaken in the department of medicine in collaboration with the department of Biochemistry in Govt. Medical College, Amritsar, Punjab. It was carried out in 100 clinically suspected cases of hypothyroidism with no other concurrent illness and receiving no other medications between age group of 16-80 years were clinically classified as hypothyroid, euthyroid or inconclusive by the diagnostic index of Billewicz. TSH estimation was done using ELISA TSYROKIT TSH (Immunoenzymometric assay) while Serum T₃ and T₄ was done by (Immunoenzymometric assay).

Results: Out of 100 patients, 20 had Billewicz score of >-24. Out of which 13 male (13%) and 7 female (7%) patients, all of whom were euthyroid. Patients with Billewicz score >+19 were 80 out of which 47 male (47%) and 33 female (33%) patients.

Conclusion: The results of present study conclude that clinical scoring index alone cannot establish diagnosis of hypothyroidism. So it is important that clinical based diagnosis is further substantiated by laboratory diagnosis.

Keywords: Hypothyroidism; dissociation

Introduction

Thyroid diseases are common both in general practice as also in specialist endocrine clinic where they account for 85% of non-diabetic consultation. Apart from the patients presenting with altered thyroid

function hyper or hypothyroidism with prevalence of 6 to 10% in general population, goitre is also frequent. Reduced production of thyroid hormone is the central feature of clinical state termed hypothyroidism.^{1,2}

Primary hypothyroidism is the main etiology in approximately 99% of cases of hypothyroidism, with less than 1% being due to TSH deficiency or other causes.

The development of highly sensitive and precise methods for the measurement of total and free thyroid hormones and, mainly, TSH makes the diagnosis of obvious thyroid dysfunction easy. However, using these methods, more and more atypical laboratory constellations can be found, including subclinical forms of hypothyroidism and hyperthyroidism^{3,4,5} as well as various other conditions, such as resistance to thyroid hormones⁶, and many divergent laboratory results due to drugs interfering with hormone metabolism or determination.⁷

Measurement of serum TSH is generally considered the best screening test for thyroid disease. Increased values indicate hypothyroidism. The test is both sensitive and specific. However, its sensitivity causes a dilemma, as some patients are found to have elevated TSH levels, but have normal free thyroxine hormone levels, and may also be asymptomatic.

Downgrading of clinical aspects of hypothyroidism has paralleled the increase in demand for thyroid function tests over the past 20 years. Few authors

believe that a diagnosis of clinical hypothyroidism can be made on the basis of biochemical measurements alone and that signs and symptoms are not important.⁸ Others challenge this statement and maintain that biochemical tests can be misleading and that diagnosis can be made on clinical grounds alone.⁹

Therefore various attempts were made to study the clinic-biochemical spectrum of hypothyroidism and the relative importance of thyroid function tests. The aim of our study was to assess the significance of clinical versus biochemical diagnosis of hypothyroidism using clinical scoring index and optimizing the numbers of laboratory test for prompt diagnosis and initiation of the appropriate treatment.

Materials and Methods

This study was carried out in 100 clinically suspected cases of hypothyroidism with no other concurrent illness and receiving no other medications between age group of 18-60 years. Duration, type of symptoms and clinically detected signs and symptoms were evaluated in all subjects by the diagnostic index of Billewicz.

Billewicz scoring system

Sr. No.	Symptoms	Diagnostic	Weight
		Present	Absent
1	Dry skin	+3	-6
2	Cold intolerance	+4	-5
3	Hoarseness	+5	-6
4	Weight gain	+5	-1
5	Constipation	+2	-1
6	Decreased Sweating	+3	-6
7	Parasthesias	+5	-4
8	Decreased hearing	+2	-0
Signs			
1	Slow movement	+11	-3
2	Coarse skin and hair	+7	-7
3	Cold skin	+3	-2
4	Periorbital Puffiness	+4	-6
5	Bradycardia	+4	-4
6	Slow reflex relaxation	+15	-6

Patients having score $>+19$ are indicative of hypothyroidism clinically and score of >-24 are not indicative of clinical hypothyroidism.(diagnostic index $>+19/<-24$ indicates clinical hypothyroidism).

Exclusion Criteria

Patients with the following history were excluded from the study.

1. Total/Subtotal thyroidectomy
2. Patients on I^{131} treatment,lithium,antithyroid drugs.
3. Graves disease, toxic multinodular goitre, toxic adenoma and carcinoma.
4. Radiation exposure.
5. Gestational hypothyroidism.

Following investigations were carried out in all the patients.

1. Fasting glucose;- Glucose oxidase method
2. Serum T_3 estimation;- Immunoenzymometric assay
3. Serum T_4 estimation:- Immunoenzymometric assay
4. Serum TSH:- Immunoenzymometric assay
5. Hb estimation:- Acid haematin method using Sahli's haemoglobinometer
6. TLC:- Thomas-Zeiss haemocytometer with improved Neubauer counting system.

100 subjects were subjected to serum total T_4 immunoassay, free T_4 index, total T_3 immunoassay,free T_3 index and TSH estimation by microplate immunenzymometric assay (ELISA Microwell's method) available at Biochemistry department.

Normal ranges of T_3,T_4 TSH are:
 TSH- .39-6.16 μ IU/ml
 Total T_4 Immunoassay- 4.4-10.8 μ g/dl
 Total T_3 immunoassay - .52-1.85 ng/dl

Observations

Out of 100 clinically suspected hypothyroid subjects, 80 subjects were found to have diagnostic index of Billewicz ($>+19/<-24$) whereas 20 subjects were found to have Billewicz index >-24 . All clinical subjects were subjected to T_3, T_4 TSH estimation.

The suspected subjects having values of T_4 and T_3 less than the reference ranges and TSH >6.6 - <10 μ IU/ml were labelled as inconclusive whereas patients having TSH >10 μ IU/ml and T_4 less than normal were labelled as suffering from primary hypothyroidism and subject having normal value of T_3,T_4 TSH were labelled as euthyroid.

Table 1 Showing the age and sex distribution of 100 clinically suspected cases of hypothyroidism, 32 males (58.18%) and 27 females (60%) were in age group of 20-40 years. While rest of the patients were in the age group of 40-60 years.

Table 1

Age group	Sex			
	Male		Female	
	No. Of cases	% age	No.of cases	% age
20-40	32	58.18	27	60.00
40-60	23	41.82	18	40.00
total	55	100	45	100

Table 2 Showing the percentage of male and female with Billewicz score of > -24 . Out of which 13 (13%) subjects were males and 7 (7%) subjects were females

while the patients with Billewicz score $> +19$ were 80 out of which 47 (47%) were males and 33 (33%) were females.

TABLE 2

Billewicz Score	Male		Female	
	No. Of cases	%age	No. Of cases	%age
>-24	13	13	7	7
>+19	47	47	33	33

Table 3 showing the mean value of T3, T4 TSH in Euthyroid patients.

24 subjects were found to be having following mean value of T3, T4 TSH. Among 24 subjects, 15 subjects were males and were having mean value of T3

hormone level of $.55 \pm .5$ and mean t4 level of 5.4 ± 2 and TSH level of $.40 \pm 1.1$. out of remaining 9 female subjects (11.25%) they were having mean T3 level in the range of $.65 \pm .25$ and mean T4 value 6.8 ± 1.1 and TSH level of $.4.8 \pm 1.2$ and all the subjects were found to be euthyroid.

TABLE 3

Thyroid profile	Normal range	Male(n=15)	Female (n=9)
T3	.52-1.85 ng/dl	$.55 \pm .25$	$.65 \pm .24$
T4	4.4-10.8 μ g/dl	5.4 ± 2.0	6.8 ± 1.1
TSH	TSH-.39-6.16 μ IU/ml	$.4 \pm 1.1$	4.8 ± 1.2

Table 4 showing the mean value of T3, T4 TSH in Hypothyroid patients.

Out of 20 patients, 11 patients were males with 9 patients females. Among the male patients the mean T3 level were in range of $.55 \pm .25$, T4 level were found to be in the range of $2.4 \pm .5$, whereas TSH level were in the range of 25.5 ± 10 .

In 9 female patients mean T3 level was in the range of $.65 \pm .25$ whereas T4 level in the range of 2.2 ± 0.5 , the mean TSH level in these females were found to be in the range of 26.5 ± 10.5 . It is clear that patients having hypothyroid state all the male and female patients were having decreased T4 hormone level whereas TSH hormone level was increased.

Table 4

Thyroid profile	Normal range	Male(n=11)	Female (n=9)
T3	.52-1.85 ng/dl	$.55 \pm .25$	$.65 \pm .25$
T4	4.4-10.8 μ g/dl	$2.4 \pm .5$	2.2 ± 0.5
TSH	TSH-.39-6.16 μ IU/ml	25.5 ± 10.0	26.5 ± 10.5

Table 5 showing showing the mean value of T3, T4 TSH in patients having inconclusive results.

21 subjects were males whereas 15 subjects were females. The mean T3 level in males was $.55 \pm .25$

and mean T4 level was 5.3 ± 1.8 and TSH level was 8.6 ± 1 .

Similarly in females mean T3 level was $.65 \pm .20$ and T4 level was 6.6 ± 1.2 and TSH level was in range of 7.1 ± 1 .

Table 5

Thyroid profile	Normal range	Male(n=21)	Female (n=15)
T3	.52-1.85 ng/dl	.55± .25	.65±.20
T4	4.4-10.8 µg/dl	5.3±1.8	6.6±1.2
TSH	TSH-.39-6.16 µIU/ml	8.6±1.0	7.1±1.0

Table 6 showing symptoms and signs according to the percentage.

The table shows the concordance between the clinical Billewicz score and biochemical investigations of 100 suspected subjects of hypothyroidism. The table also shows that the main symptoms according to Billewicz

scoring system were dry skin (87%), Hoarseness of voice (84%), Cold intolerance (80%), weight gain (49%), constipation (45%). Whereas main signs were slow reflex relaxation (85%), slow movements (80%), coarse skin and hair (80%) and periorbital puffiness (80%).

Table 6

Sr.No.	Symptoms	No. Of patients With symptoms		Billewicz score		Thyroid profile	
		No.	% age	➤ -24	➤ +19	Normal	Abnormal
1	Dry skin	87	87%	7	80	31	56
2	Cold intolerance	80	80%	0	80	24	56
3	Hoarseness	84	84%	4	80	28	56
4	Weight gain	49	49%	20	29	24	25
5	Constipation	45	45%	13	32	18	27
6	Decreased sweating	87	87%	7	80	31	56
7	Decreased hearing	22	22%	13	9	13	9
8	Paraesthesia	57	57%	6	51	17	40
Signs							
1	Slow movement	80	80%	0	80	24	56
2	Coarse skin and hair	80	80%	0	80	24	56
3	Cold skin	40	40%	17	23	21	19
4	Periorbital puffiness	80	80%	14	66	34	46
5	Bradycardia	41	41%	20	21	20	21
6	Slow reflex relaxation	85	85%	0	85	24	61

Table 7 showing Sensitivity, Specificity, PPV and NPV Derivation

Table 7

Billewicz score	Thyroid profile	
	Normal	Abnormal
>-24	20	0
>+19	60	20

True positive a=20	True Negative c=20
False Positive b=60	False Negative d=0

True Positive -20
True Negative-20
False Positive- 60
False Negative- 0
Sensitivity: $a/a+d \times 100$
Specificity: $c/c+b \times 100$
PPV : $a/a+b \times 100$
NPV : $c/c+d \times 100$
Accuracy : $a+c/a+b+c+d \times 100$

Table 8 showing the Sensitivity and Specificity of Billewicz Scoring System

Billewicz scoring system is highly sensitive (100%) but its specificity is very less (25%) its positive

predictive value is only (25%) whereas negative predictive value is (100%) and accuracy is just only to the tune of (40%).

Table 8

	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value	Accuracy
Billewicz scoring system	100%	25%	25%	100%	40%

Discussion

The results of the present study demonstrate that the modern laboratory tests for thyroid function have completely changed the clinical picture of hypothyroidism.

The classical symptoms and signs are still described as having a high frequency of 90-97%, but they were observed less often in our patients (50-85%).

In our study we found that the main symptoms according to Billewicz scoring system were dry skin (87%), hoarseness of voice (84%), cold intolerance

(80%), weight gain (49%), constipation (45%). Whereas main signs were slow reflex relaxation (85%), slow movements(80%), coarse skin and hair (80%) and periorbital puffiness (80%).

Sampath et al in their study reported that, symptoms most common were generalized weakness 66.6%, weight gain 62.5%. Cold intolerance 33.3% and hoarseness in 4.1% of cases.¹⁰

Among the signs periorbital puffiness was noticed in 25% while bradycardia was observed in 41.6% and delayed ankle jerk in 12.5% of cases.¹⁰

While in large scale Colorado thyroid prevalence study, the most common symptoms were dry skin, cold intolerance and puffed eyes (15-30%).¹¹

In our study out of 100 clinically suspected hypothyroid subjects age range was 18-60 years and percentage of females (41%) and males (59%) and ratio 1.43:1.

Whereas study conducted by Sarita Bajaj et al,¹² the male female ratio was 1:5.8.

In this study, no subject between 18-25 years of age was found to be having any sign and symptoms of hypothyroidism.

When the Billewicz score was applied to 100 subjects who were suspected to be suffering from hypothyroidism, 20 subjects were having Billewicz score of >-24 , out of which 13 were males (13%) and 7 were females (7%). These patients were not suffering from hypothyroidism and upon being subjected to T3, T4, TSH estimation, they were found normal.

Out of remaining 80 patients, 24 were found to be having following mean values of T3,T4,TSH. Among 24 patients, 15 (62.5%) were males and having mean T3 value of $.55 \pm .5$ and mean T4 level 5.4 ± 2 and mean TSH level of 4.2 ± 1 . out of remaining 9 females (11.25%) were having mean T3 levels $.65 \pm .25$ and mean T4 levels 6.8 ± 1.1 and mean TSH levels in the range of 4.8 ± 1.2 . All patients were found to be euthyroid.

Among 80 patients score $>+19$ after being subjected to T3,T4, TSH estimation, 36 subjects were of inconclusive group. Out of these 36 patients (26.25%) were males and 15 were females (18.75%). Mean T3 levels were $.55 \pm .25$, mean T4 levels 5.3 ± 2 and mean TSH levels were 8.6 ± 1 in male patients. Similarly in female patients Mean T3 was $.65 \pm .23$ and T4 6.6 ± 1.2 and TSH were found to be in the range of 7.8 ± 1 .

It is clear from the above mean value of T3,T4, TSH values that T3, T4 hormone levels were within the normal range while the TSH hormone level was in the range of >6.6 - $<10 \mu\text{IU/ml}$. These subjects fell under inconclusive (36%) groups. In study conducted by Sarita Bajaj, the subject who fell under inconclusive group were 29.9%.¹²

Out of 100 subjects whose score was $>+19$, 20 patients (20%) were found to be having hypothyroidism.

In present study, 44% patients were having euthyroid state, 20% were in the range of overt hypothyroidism. While study conducted by Sarita Bajaj the euthyroid subjects were in range of 48.4% and 21.6% were in the range of overt hypothyroidism.

Zulweski et al observed that subclinically hypothyroid patients (n=93), 24% (Billewicz index, 6%) were designated hypothyroid, 29% (Billewicz index, 29%) were euthyroid, and 47% (Billewicz index 65%) were in intermediate range.¹³

In our study T4 hormone level value was decreased in 25% of cases and they were having normal T3 level. While a study conducted by Sampath et al, 18.9% patients were having low T4 level and normal T3 level.¹⁰

In our study the T4 level value was decreased in 25% of the patients and they were having normal T3 value in both male and females whereas TSH levels were increased in both males and females. In a study by Sarita Bajaj et al, 21.6% patients were found to be having decreased T4 and increased TSH i.e hypothyroid state which matches our study.¹²

Our study results match the results of Sarita Bajaj et al and Sampath et al in concluding that clinical parameters alone are insufficient in establishing diagnosis of hypothyroidism and biochemical tests should be a routine criterion for establishing the diagnosis of hypothyroidism.

The Billewicz clinical scoring system, when applied to Large scale Colorado health study population and to this present study, identified persons more likely to be hypothyroid. Although efficacy of this clinical scoring index still is much less than that of serum TSH measurement, symptom score may prove a useful adjunct in the diagnosis of hypothyroidism. Symptom scores may enhance the cost effectiveness of thyroid testing.

From the present study, It is evident that clinical parameters alone are insufficient in establishing a diagnosis of hypothyroidism and are often misleading, thus biochemical confirmation is a mandatory in establishing the unequivocal diagnosis of overt hypothyroidism. This is in accordance with the American Academy of Clinical Endocrinologists guidelines which state that appropriate laboratory evaluation with a sensitive TSH test should always be used as the standard criterion for confirming the diagnosis.¹⁴

Conclusion

Present study concludes that although the Billewicz scoring index is highly sensitive but is non specific. Interpretation of the diagnosis of hypothyroidism on the basis of this index remains elusive until confirmed with the biochemical investigation. So thyroid profile is mandatory to establish the diagnosis of hypothyroidism. Same conclusion was derived from various studies on Dissociation in clinical and laboratory diagnosis in hypothyroidism.¹¹

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References

- Grozinsky-Glasbergs, Frasser A, Nahshoni E, Weizman A, Leibovici L. 'Thyroxine triiodothyronine combination therapy versus thyroxine monotherapy of clinical hypothyroidism: meta-analysis of randomized controlled trials'. *J Clin Endocrinol Metab.* 2006; 19.
- Weetman AP. Hypothyroidism: screening and subclinical disease. *BMJ* 1997;314: 1175.
- Fredlund BO, Olsson SB. Long QT interval and ventricular tachycardia of "torsade de point" type in hypothyroidism. *Acta Med Scand.* 1983;213:231-35.
- Keating FR, Parkin TW, Selby JB, Dickinson LS. Treatment heart disease associated with myxedema. *Prog Cardiovasc dis.* 1961; 3: 364-81.
- Vanderump MPJ, Ahlquist JAO, Franklyn JA, Clayton RN. Consensus statement for good practice and audit measures in the management of hypothyroidism and hyperthyroidism. *BMJ* 1996; 313: 539-44.
- Danese MD, Power NR, Sawin CT, Ladenson PW. Screening for mild thyroid failure at the periodic health examination: a decision and cost-effectiveness analysis. *JAMA* 1996; 276: 285-92.
- Rae P, Farrar J, Beckett F, Toft A. Assessment of thyroid status in elderly people *BMJ* 1993; 307: 177-80.
- Gomberg-Maitleind M, Freshman WH. Thyroid hormone and cardiovascular disease. *Am Heart J* 1998; 135: 187-96.
- Klein I, Ojamaa K. The cardiovascular system in hypothyroidism. In Braverman LE, Utiger RD, eds. *Werner and Ingbar's the thyroid: a fundamental and clinical text.* 8th ed. Philadelphia: Lippincott Williams and Wilkins 2000: 777-82.
- Sampath W, Singh P, Somani B, Arora MM, Batra HS, Harith AK et al. Study of clinicobiochemical spectrum of hypothyroidism. *MJAI* 2007; 63:233-236.
- Canaris GJ, Manowitz NR, Mayor G, Ridgway EC. The Colorado Thyroid Disease Prevalence Study. *Archives of internal Medicine* 2000; 160: 526-534.
- Bajaj S, Sharma GP, Kumar D, Mehrotra R. Dissociation in clinical and laboratory diagnosis in hypothyroidism. *JAPI* 2005; 53:15-18.
- Zulewski H, Muller B, Exer P. Estimation of tissue hypothyroidism by a new clinical score: evaluation of patients with various grades of hypothyroidism and controls. *J Clin Endocrinol Metab.* 1997; 82: 771-776.
- Surks ML, Chopra IJ, Mariash CN, Nicoloff JT, Solomon DH. American Association of Clinical Endocrinologists Medical Guidelines for Clinical Practice For the Evaluation and Treatment of Hyperthyroidism and Hypothyroidism. *Endocrine Practice*, 2002; 8:6.

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