Re-vised Wayne′s Thyrotoxicosis Diagnostic Index for Clinical Diagnosis of Hyperthyroidism

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Abstract:

Background: Thyrotoxicosis denotes thyroid hormone excess from any cause. Hyperthyroidism specifically refers to endogenous thyroid gland over-activity most commonly caused by grave′s disease, toxic multi-nodular goiter, or toxic adenoma. Signs and symptoms vary between people and during pregnancy. This study attempt to help our hyperthyroid patients to circumvent the cost of thyroid function tests, a relatively heavy financial burden for the average Iraqi citizen now a days, also when thyroid function tests results are at variance with clinical suspicion.

Aim: To design a protocol for clinical diagnosis of hyperthyroidism utilizing the Wayne′s Thyrotoxicosis Diagnostic Index (WTDI) as a base line.

Material and Methods: This study was conducted on 100 thyrotoxic patients diagnosed by hormonal assay and 100 clinically euthyroid subjects of similar sex and age, attending Kirkuk General Hospital and private clinic over a period of two years from June 2012 -- June 2014 .We took a history and physical examination pertinent to hyperthyroidism for each patient and each subject including all component of the WTDI .The main outcome measures obtained both patients and subjects measured using sensitivity, specificity ,and predictive values of each symptom and sign. The WTDI was utilized for assessing the clinical findings of patient and subject.

Result: Two symptoms and ten physical signs, including two new signs that were not part of WTDI-the velvety skin and the wide pulse pressure, attained confirmatory value in ruling -in the diagnosis of hyperthyroidism. Two symptoms and four signs did attain a confirmatory value in ruling - out diagnosis when absent. Both hot hands and tachycardia reached rule-in and rule -out states. 95 of the 100 patients entered the thyrotoxicosis zone of the WTDI by attaining more than or equal to 19 points. By offering two points and one point to the velvety skin and the wide pulse pressure respectively, all the 100 patients attained more than or equal to 19 points. The highest score attained by any of the 100 subjects was 14 points; the mentioned addition would at most bring the highest score among subjects to 17 points; less than the diagnostic score of WTDI.

Conclusions: WTDI with minor modification is worth adopting for diagnosing thyrotoxicosis and on follow up re-assessment of patient during medical treatment when a patient could not bear the cost of the thyroid function tests with the possible exception of some patients like pregnant women who may need a more elaborated evaluation.

Key words: Hyperthyroidism, Goiter, Koilonchia.

Introduction:

Thyrotoxicosis denotes thyroid hormon excess from any cause [(1)]. Hyperthyroidism specifically refers to endogenous thyroid gland over-activity most commonly cased by grave′s disease, toxic multinodular goiter, or toxic adenoma [(1)]. In fact geographical distribution of thyrotoxicosis coincides with areas of high incidence of endemic goiter. No surprise, thyrotoxicosis appears prevalent in our locality [(2)].

The standard confirmatory procedure for the clinical diagnosis of a hyperthyroid state nowadays is thyroid function tests,

specifically: plasma TSH as the single first choice, usually with plasma free thyroxine (T4) and triiodothyronine (T3) [3]. Undoubtedly, these tests are of extreme help to the clinician in the suspicious relatively mild hyperthyroid case and in the elderly population [4]. However, the present economical circumstances in Iraq, makes sending for thyroid function tests a rather heavy financial burden for the average citizen, we may add that several factors, other than thyroid disorders, can affect results of these tests [5, 6]. They might lead the unwary clinician who relies too much on laboratory results to err in diagnosing thyrotoxicosis when it does not exist. Furthermore, at least one thyroid disorder resistance to thyroid hormone has led to the mistaken diagnosis of hyperthyroidism when the clinical evaluation was not taken seriously into consideration [7]. On the other hand, many hyperthyroid patients are too obvious clinically to warrant laboratory confirmation especially in young age [8]. Therefore, and particularly because of the mentioned economical factor, we planned to conduct a careful clinical evaluation of recently hormonally diagnosed hyperthyroid patients aiming at attaining a clinical approach to diagnosis, particularly, for the present circumstances.

A clinical index for the diagnosis of hyperthyroidism was first developed by Crooks et al in 1959 [9, 25]. Wayne in 1960 presented his famous thyrotoxicosis diagnostic index WTDI [10]. The WTDI depends on clinical evaluation, where each of the included 19 symptoms and signs was given a score ranging from -5 TO +5 points. A total score of (+ 19) or more was considered diagnostic of hyperthyroidism, 12 -18 as equivocal, and 11 or less as exclusive of hyperthyroid state [10]. The WTDI was described as being of great value to clinicians, making their diagnosis more objective [3, 11]. We also noticed that some commonly encountered physical signs like the velvety texture of the skin, [12, 13] and the wide pulse pressure [13, 14], were not included in the WTDI. Nevertheless, up to 1987, the WTDI was still retained with minimal modifications for clinical diagnosis [14]. Lastly, we thought this occasion could help to obtain a rough estimate of the shares of the different pathogenetic factors in causing hyperthyroidism in our locality.

Materials and Methods:

In this study 100 patients attending the outpatient clinic in Kirkuk General Hospital and private clinic over a period of two years from June 2012 -- June 2014. Inclusion of the patient depended on clinical suspicion of hyperthyroidism supported by, at least, positivity of two of the following tests: TSH, free T4, free T3. All patients had their hyperthyroid state either an initial episode or as recent relapse after attaining remission by drug therapy. One hundred apparently clinically euthyroid subjects among visitors of outpatient clinic in Kirkuk General Hospital and private clinic, were included as a control group during the period of 2012 - 2014. They were selected to match with the age and sex of the patients and evaluated in the same way.

Each patient and control was subjected to a clinical evaluation as shown in table (1). Admittedly, most of the interrogation was on binary basis, few were on tertiary one, e.g. weight loss -- weight gain -- No weight change or preferring cold --preferring heat -- indifference to temperature.

For borderline or doutful finding, a second opinion was regularly sought mostly from the same clinic. After neck inspection, the thyroid gland was assessed by palpation. As an exophthalmometer was lacking, search for exophthalmos depended on use of a suitable ruler applied perpendicularly at the outer border of the bony orbital margin and by tangential look, the prominence of the corneal surface beyond the outer orbital margin was recorded in millimeters. Measurements exceeding twenty millimeters were considered as abnormal (exophthalmos): 20 mm or less were considered within normal range [15]. Tachycardia for the purpose of this study was a heart rate of 100 beats/ minute or more [16]. A pulse pressures more than 60mmhg was considered a raised pulse pressure; 60 mmHg was considered the upper limit of normal pulse pressure [16].

The texture of the skin was assessed by gentle palpation of the skin on the inner aspect of the arm, because of easy accessibility; even though the upper thorax and the inner thigh are suitable alternatives [15].

Examination for proximal myopathy was assessed by asking each patient to rise from squatting position [16]. Hyperkinesia was assessed while obtaining history by observing the patient whether she or he cannot sit still, shifts position frequently, movement are quick, jerky, exaggerated and often purposeless [11]. Tremor was examined with the patient eyes closed and outstretched separated fingers [16].

For each symptom and sign, the followings were computed; sensitivity, specificity, negative predictive value, positive predictive value, and the overall diagnostic accuracy [17]. For each patient and control, the sum of the 19 Clinical features of WTDI as calculated for allocation in its appropriat range :< 11, 12--18, ≥ 19.

Results:

Table (1) shows the frequency of symptoms and signs for the 100 thyrotoxic patients (sensitivity) and the 100 apparently euthyroid controls (1-specficity). In addition, both the negative and positive predictive values of each clinical feature are projected. All symptoms, excluding hyper-defaecation, and all signs but the last three in the list (pulse pressure, velvety skin and koilonychia) constitute what was originally included in WTDI.

Table (2) represent the degree of diagnostic accuracy of each clinical feature mentioned in table (1) rearranged from the most accurate (or valid) down to the least. WTDI scoring is shown besides each relevant clinical manifestation. It can be noted that some discrepancy is evident between the diagnostic weights of the two diagnostic parameters: accuracy versus WTDI. It is worth saying that both the velvety texture of the skin and the wide pulse pressure fell in the upper half of the list, whereas some highly specific manifestations like exophthalmos and atrial fibrillation fell near the bottom of the list.

Table (3A) shows the clinical features that confirm (Rule-In) the diagnosis of hyyperthyroidism where as B shows those that refute (Rule--out) the diagnosis when absent.

The clinical state of the thyroid gland of the hyperthyroid patient is presented in Table (4) separately for each sex. Among the 81 patients with goiter, diffuse enlargement was the most common where as single nodule proved the lest common. All patients with exophthalmos had diffuse enlargement of the thyroid.

Table (1): Frequency of 23 symptoms and signs in 100 hyperthyroid patients (sensitivity) and 100 euthyroid subjects (1-specificity) and their predictive values.

Symptoms	Hyperthyroid Sensitivity	Euthyroid 1-specificity	Specificity	Negative predictive value	Positive predictive value
Nervousness	91	32	68	89	74
Increased sweating	89	10	90	90	90
Heat intolerance	73	36	64	71	67
Palpitation	98	26	74	98	79
Breathlessness	98	16	84	98	86
Weakness	55	14	86	66	80
Weight loss	66	14	86	72	83
Increased appetite	53	32	68	60	63
Hyperdefaecation	45	0	100	65	100
Signs					
Goiter	81	8	92	83	91
Thyroid bruit	59	0	100	71	100
Exophthalmos	8	0	100	52	100
Lid retraction	58	0	100	71	100
Lid lag	39	0	100	63	100
Hyperkinesis	56	0	100	70	100
Tremor	94	19	81	94	84
Hands-moist -hot	100 100	26 0	74 100	100 100	80 100
Tachycardia >100/min	91	5	95	92	95
Atrial fibrillation	22	5	95	55	82
Velvety skin	69	0	100	77	100
Wide pulse pressure .>60mmHg	79	8	92	82	91
Koilonychia	29	8	92	57	79

Table (2): List of the studied clinical features according to the degree of overall diagnostic accuracy (true positive and true negative/ all true and false positive and negative) and WTDI scoring rates.

No	Clinical finding	Overall accuracy	WTDI Score	
			present	absent
1	Hot hads	100	+2	
2	Tachycardia (≥ 100/min)	93	+3	--3
3	Breathlessness	91	+1	
4	Increased sweating	89.5	+3	
5	Tremor	87.5	+1	
6	Moist hands	87	+1	
7	Goiter	86.5	+3	--3
8	Palpitations	86	+2	
9	Wide pulse pressure(≥60mmHg)	85.5		
10	Velvety skin texture	84.5		
11	Thyroid bruit	79.5*	+2	--2
12	Nervousness	79.5*	+2	
13	Lid retraction	79	+2	
14	Hyperkiness	78	+4	
15	Weight loss	76	+3	--3
16	Hyperdefaecation	72.5		
17	Weakness	70.5	+2	
18	Lid Lag	69.5	+1	
19	Heat intolerance	68.5	+5	--5
20	Koilonychia	60.5*		
21	Increased appetite	60.5*	+3	--3
22	Atrial fibrillation	58.5	+4	
23	Exophthalmos	54	+2	

*Signs were considered superior to symptoms when the degree of overall diagnostic accuracy is equal for a sign and a symptom.

Table (3A): symptoms and signs that confirm (Rule-in) the diagnosis of hyperthyroidism when present (specificity > 90; positive predictive value >90).

Symptoms	Signs
1.Increased sweating 2.Hyperdefaecation	1.Hot hands 2.Tachycardia 3.Goitre 4.Wide pulse pressure 5.Velvety skin texture 6.Thyroid bruit 7.Lid retraction 8.Hyperkiness 9.Lid lag 10.Exophthalmos

Table (3B): Symptoms and signs that refute (Rule - out) the diagnosis of hyperthyroidism when absent (sensitivity > 90; negative predicitive value >90).

Symptoms	Signs
1. Breathlessness 2.Palpitations	1. Hot hands 2. tachycardia 3,Tremor 4. Moist hands

Table (4): State of the thyroid among one hundred thyrotoxic patients.

Type of goiter	No. of patient	Women	Men	Women: men
Diffuse	50	41	9	4.6 : 1
Multinodular	20	15	5	3 : 1
Single nodule	11	11	0	-------
No goiter	19	14	5	2.8: 1
Total	100	81	19	

Wayne Index

Symptoms in order of importance	*Points if present*	*Points if absent*
Heat intolerance (cold preference)	5	
Heat preference	-5	
Appetite--increasesd	3	
Weight--decreased	-3	
Excessive sweating	3	
Palpitations	2	
Fatgue	2	
Nervousness	2	
Dyspnoea	1	
Signs,in order of importace		
Hyperkinetic movement	4	
Atrial fibrillation	4	
Thyromegaly	3	--3
Tachycardia	3	
Bruit	2	--2
Exophthalmos	2	
Hot hands	2	
Lid retraction	2	
Lid lag	1	
Moist hands	1	
Tremors	1	

*Total score ≥ 19 = toxic.
*11-18 = equivocal.
*<11 = euthyroid.

Discussion:

On looking at tables (1, 2) and particularly table (3), amodern epidemiologist would conclude that the combined absence of hot hands and tachycardia will exclude (Rule-out) where as their presence confirms (Rule-in) the diagnosis of hyperthyroidism. This is a reminder of the old practice, especially among surgeons, where a normal sleeping pulse was taken for granted as exclusive of hyperthyroid state especially for the sake of anaesthesia and surgery. Tachycardia might be a reflection of anxiety due to the associated vasoconstriction leads to cool hands. Hot hands are a feature of several hyperdynamic states including, anaemia, pregnancy and thiamine deficiency [18]. We would guess that the mentioned epidemiological conclusion is valid on condition that other causes of hyperdynamic states have been excluded.

Our inclusion of two signs that were missed in WTDI and other indices [14, 17], appears valid and worthwhile, we mean the wide pulse pressure and the velvety skin texture. Both signs fell in the upper half of the list in the table (2) and attained confirmatory (Rule-in) value for the diagnosis of hyperthyroidism table (3-A).

A sizable degree of discrepancy between the powers of the two diagnostic parameters shown in table (2) is evident, notably concerning heat intolerance. Heat intolerance came nineteenth among twenty three items in it is power of accuracy in diagnosis, yet it held the strongest power among the 19 items of WTDI. This discrepancy, we believe, might partly be due the difference between Iraqi and British weather. A possibly more important reason is the fact that evaluation of our control subjects was conducted during the exceptionally hot summer of 2012-2013. We now suggest that in the hot days of the summer we better ask about the like and dislike of heat during the previous winter because a large proportion of normal citizens are likely to state heat intolerance when such a question is asked during summer , not to recall exceptionally hot summer of 2012-2013 .

This snag concerning the undoubtedly salient symptom of heat intolerance hindered the tendency to try and develop a different diagnostic approach, like suggesting CRITERIA for the diagnosis of hyperthyroidism.

Now on applying the WTDI on the overall symptoms and signs of the studied patients and subjects, (95%) of the proved thyrotoxic patients fell within the hyperthyroid range (a score of >19 points).The remaining five patients scored between 16 and 18 points but had additional physical signs that were missing in WTDI . The velvety texture of the skin in all these five patients and wide pulse pressure (≥60 mmHg) in four of them .On offering a humble score of plus two points to the velvety skin and plus one point to wide pulse pressure, all the five patients enter the hyperthyroid range of WTDI: ≥ 19 points. We have to mention that the highest score attained among the clinically euthyroid subjects was 14points. Thus none of these subjects could attain the thyrotoxicosis range.

As for the nails, contrary to what is found in the literature, onycholysis was encountered in only one of the one hundred hyperthyroid patients, but we noticed twenty nine patients displaying koilonychia in its wider term- thinness, brittleness and/ or spooning.Koilonychia

is a manifestation of nutritional deficiency. Although coined with iron deficiency, it appears that sulphur containing amino acids (notably cystine) deficiency is another important cause [19]. It may surprise the unwary when facing such a result, but we have to realize that a sizable sector of Iraqi citizens was under poor socioeconomic states from 2003--2012 that contributed to the prevalence of many nutritional deficiencies. Furthermore, hyperthyroid patients are a particularly susceptible group to nutritional deficiency conditioned mainly by their high metabolic rate [20].

Atrial fibrillation appeared as expected , more common in elderly patients with mean age 58.7, while eye signs occurred more frequently in young patients in conformity with the results obtained by Steil and HAIES [21].

Lastly, as for the aetiology of hyperthyroidism, the clinical evaluation revealed fifty patients with diffuse goiter presumbly grave′s disease; the eight patient s that had exophthalmos all fell within the diffuse goiter as to support our presumption. Twenty of the hyperthyroid patients had multi-nodular goiter and again, we assume that a multi-nodular goiter was the cause of the hyperthyroid state. Likewise, we had eleven of the hyperthyroid patients who appear to have a single nodule, presumably toxic adenoma. In western countries Grave′s disease and toxic multi-nodular goiter are the more common etiological causes [22]. In the UK Hall, reported that only (5%) of cases of hyperthyroidism were due to multi-nodular goiter [23]. In Jordan, multi-nodular goiter was found to be the most common causes (73%); Grave′s disease was the second most common cause (16%) and was ascribed to the fact that Jordan is not an endemic goiterous area [24]. The Jordanian figures widely differed from our results where Grave′s disease look the largest share by our, and we have no clear cut explanation for this difference at the present time.

Conclusion:

We conclude that WDTI with minor modification remains a useful tool to circumvent the need for thyroid function tests, as when dealing with a patient who finds these tests a heavy financial burden. Actually, a sizable sector of Iraqi citizens are such during the years 2003--2012 .Admittedly some patients have to be evaluated with caution as, for example, pregnant women who have a hyperdynamic circulatory state because of the pregnancy which can cause positivity of more than one sign and symptom of hyperthyroidism .

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