DISTORTED THYROID HORMONE STATUS IN HOSPITALIZED AND AMBULATORY SICK PATIENTS

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ABSTRACT

Objective: *To review all the thyroid test results of the hospitalized and ambulatory sick patients whom blood sample were sent for thyroid function tests to pathology lab and to evaluate non interpretable thyroid test results reported at Pathology department LRH during a period of one year.*

Material and Methods: *This is a retrospective study of thyroid test results performed at pathology department PGMI/LRH Peshawar from April 2007 to April 2008. More than 2000 blood samples were received during the period mentioned for thyroid function tests. All the tests were performed on the instrument immulite using chemiluminecent assays. Thyroid test panel was included TT4, TT3 and TSH. Estimation of thyrotrophin was performed by using 3rd generation assay. Results of the neonates and children have not been included because of incomplete requisition forms lacking relevant clinical details specially age of the patient.*

Results: *A total of 1457 adults patients test results were searched for thyroid dysfunction. Out of the total 1066 were female and 391 male. Test results were interpreted according to NACB guidelines. Distorted hormone status was observed in 117 individuals which is 8 % of the total thyroid function test reports.*

Conclusion: *This fact should be realized that some thyroid tests are inherently non interpretable in severely sick patients and those who are receiving various medication. Therefore the assessment of thyroid function in ill patients are best to be postponed until the illness has resolved except when a diagnosis should affect patient outcome.*

Key words: *Nonthyroidal illness syndrome (NTIS), Sick Euthyroid Syndrome (SES), Total T3 (TT3), Free T3 (FT3) Total T4 (TT4) Free T4 (FT4), Thyroid Stimulating Hormone (TSH).*

INTRODUCTION

Many non thyroidal disorders are accompanied by abnormality of thyroid function tests defined as non thyroidal illness syndrome (NTIS) are characterized by reduction in serum TT3, FT3, and elevation of reverse T3 (r-T3) with subnormal thyroxin (T4) level.[1]

The term Euthyroid Sick Syndrome (ESS) was used by Wartofsky and Bunan in 1982 to describe thyroid abnormalities in euthyroid patients with systemic illness.[2] Non thyroidal illness syndrome (NTIS) and low T4 syndrome (LTS) are the other alternate terms in use. NTIS is frequently accompanied by alteration in circulating thyroid hormone concentration despite majority of the patients remains clinically euthyroid but some of them may be hypothyroid.[3-6]

Low TT3 & FT3 have been observed at early stages of the non thyroidal disease in most of the hospitalized patients and as the severity of the illness increases serum TT4 falls either due to binding protein abnormalities or due to the presence of T4 binding inhibitors in the circulation.[7-10]

The presently available FT4 methods used by most of the clinical laboratories lack diagnostic specificity as these are affected by intravenous heparin and free fatty acids (FFA) and consequently generate spuriously low or high values in seriously ill patients. Therefore an abnormal FT4 tests in the setting of seriously ill patient is unreliable. It is therefore wise to confirm any abnormal FT4 result in serious somatic disease by TT4 measurement. If both (TT4 & FT4) are

THYROID FUNCTION TEST RESULTS OF THE YEAR 2007 – 08

(Data arranged in descending order with percentage)

Status	Total Number	Percentage
Euthyroid	1071	73
Hyperthyroidism	156	10.70
Discordant results	117	8.03
Hypothyroidism	94	6.45
T3 Thyrotoxicosis	12	0.82
Central Hypothyrodism	7	0.48
Grand Total	1457	99.98

Table 1

abnormal in the same direction a thyroid condition may be present. In case TT4 and FT4 are discordant it is more likely the result of an ailment or medication.[11-12]

Medication can cause both in vivo and in vitro effects on thyroid tests and this may lead to misinterpretation of laboratory results and inappropriate diagnosis. Estrogen, Glucocorticoid, Dopamine, Propranolol, Iodide, Amiodarone, Lithium and alpha interferon all are having in vivo effects on the thyroid function test while IV heparin administration and indole acetic acid are reported for causing in vitro effects.[13-14]

Serum TSH concentration remains normal in NTI cases provided that the patients are not receiving drugs like dopamine or glucocorticoid as both the drugs inhibit TSH secretion and even mask the raised TSH level of hypothyroidism in sick hospitalized patient. Therefore TSH in the absence of these drugs is the more reliable test for NTI individuals. However a transient fall in serum TSH in the range of 0.02 – 0.3 mIU/L in the acute stage of NTI followed by a mild elevation during the recovery phase has been observed.[15]

In hospitalized setting sick hyperthyroid patient with extremely low level of TSH (< 0.02 mIU/L) can be easily differentiated from a patient of NTI having transient mild TSH suppression by using 3rd generation TSH assay with a functional sensitivity of < 0.02 mIU/L. Sick hypothyroid patients typically demonstrates the combination of low T4 and elevated TSH (> 20 mIU/L). Therefore minor elevation in TSH during the recovery phase are less diagnostic for the diagnosis of hypothyroidism in the hospitalized patients.[16]

It is clear from a large body of evidence collected over more then two decades that the diagnosis of thyroid dysfunction in the presence of severe NTI is not simple and needs to be interpreted with considerable care. However in general it is best to avoid thyroid testing in hospitalized patient if it all possible.

MATERIAL AND METHODS

This is a retrospective study of thyroid test results performed at pathology department PGMI/LRH Peshawar from April 2007 to April 2008. More than 2000 blood samples were received during the period mentioned for thyroid function tests. All the tests were performed on the instrument immulite using chemiluminecent assays. Thyroid test panel was included TT4, TT3 and TSH. Estimation of thyrotrophin was performed by using 3rd generation assay. Results of the neonates and children have not been included because of incomplete requisition forms lacking relevant clinical details specially age of the patient.

RESULTS

We received more than 2000 tests for thyroid studies from indoor and out door patients department of LRH in the year 2007-2008. All the tests were performed on Immulite USA using chemiluminecent technique of immunometric assay (IMA) which is gaining popularity over the RIA method because it offers the practical advantage of (a) Shorter incubation time (b) An extended dynamic range for assay and (c) More stable labeled antibody reagent. Total T4 and T3 estimations were performed by the DPC Reagents USA. Measurement of serum TSH was performed

DISTRIBUTION OF THE THYROID TEST RESULTS

Disease status	Hyperthyroidsim		Hypothyroidism		Euthyriod
		T3 thyrotoxicosis	Primary	Central	
Female	127	09	63	04	776
Male	29	03	31	03	295
Total	156	12	94	07	1071
F/M ratio	4 : 1	3 : 1	2 : 1	3 : 1	26 : 1
Percentage	10.7	0.82	6.45	0.48	73.5

Table 2

DISCORDANT RESULTS SHOWING DISEQUILIBRIUM BETWEEN TT4/TT3 AND TSH

	Male	Female	Total	%
Ambulatory	15	38	53	3.6
Hospitalized	15	49	64	4.39
Grand Total	30	87	117	8.03

Table 3

using the third generation TSH assay. Test results were interpreted according to NACB guidelines. Thyroid results of all the adults patients are presented here. Results of the neonates and children have not been included because of incomplete requisition forms lacking relevant clinical details and age of the patient. Laboratory data is summarized in the following tables.

DISCUSSION

Diagnostic confusion results when discordant thyroid test results are reported in nonthyroidal illness. The prevalence of one or more abnormalities of thyroid function test in patients with acute medical illness has been reported from 40 % to 70 %.[17-18]

The presented one year data of our lab reports showing about 8 % discordant results we have observed extreme reduction in TT3 levels. Low T3 state in NTI has been ascribed to a block in the 5 deiodinases that convert T4 to biologically active T3 in peripheral tissue this conversion is inhibited in acute and chronic nutritional problem, poorly controlled diabetes mellitus and by drugs such as hydrocorticone and beta blockers.[19] We have also observed extreme reduction in TT4 level. This declining concentration of TT4 in NTIS may be caused by decreased in serum concentration of TBG or by the presence of circulating inhibitor and drugs.

Serum TSH concentration are usually normal but may be mildly or moderately depressed in the acute phase of NTI or slightly elevated during recovery from the critical illness. Serum TSH in most of our cases were either normal or mildly depressed. In a very few cases it was slightly elevated. TSH anomalies may be related to the effect of endogenous or exogenous hormones, altered nutrition or altered biological activity of immunoreactive TSH.[20] For hospitalized patients TSH + T4 (FT4 or TT4) is the most useful test combination to detect thyroid dysfunction in a sick hospitalized patient. However it is more appropriate to use a widened TSH reference interval (10.05-10.0 miU/L). A low normal TSH level in the presence of a low TT4 and TT3 may reflect central hypothyroidism as a result of prolonged illness. We have reported only seven cases of central hypothyroidism.

Thyroid dysfunction occurs in both sexes but women are afflicted more often than men as it is evident from the data presented. Laboratory testing of thyroid hormones is used to diagnose and document the presence of thyroid disease. As an accurate measurement of the thyroid hormones is important for the proper diagnosis of thyroid gland dysfunction a familiarity with normal Physiology and Pathophysiology is also important if these tests are to be properly used and selected. Moreover patients clinical status and drug history help in the proper interpretation of the test results.

CONCLUSION

It is prudent not to rely solely on thyroid function tests in the setting of NTI and a combination of tests should be considered and for that the clinical staff should develop an active collaboration with the laboratory staff in order to select thyroid tests with the most appropriate characteristic to serve the patient population in question.

Drugs and other interferences can affect the interpretation of more than 10% of laboratory results in general and thyroid testing is no exception.

Discordant thyroid results are often encountered both in clinical and laboratory practice. These discordant thyroid test results need to be interpreted with considerable care.

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