Study of Proportion and Pattern of Sick Euthyroid Syndrome in Patients with Sepsis in Intensive Care Unit of a Tertiary Care Hospital in South Kerala

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ABSTRACT

BACKGROUND

Patients with critical illness can have changes in thyroid hormone metabolism along with changes within the hypothalamus-pituitary-thyroid axis, even though there is no previous history of thyroid disease. Such changes have been named as "Sick Euthyroid Syndrome" or "Non-Thyroidal Illness Syndrome (NTIS)". Such alterations in thyroid function can be seen in patients with sepsis and they are known to affect the prognosis of the disease. The most common abnormality in sick euthyroid syndrome is low serum T3. This study aims to find the proportion and pattern of sick euthyroid syndrome in patients with sepsis.

METHODS

This was a hospital based cross sectional study done in the Department of Internal Medicine in a tertiary care centre in south Kerala. 100 patients with diagnosis of sepsis were selected based on American College of Chest Physician / Society of Critical Care Medicine 2001 Consensus Conference definitions, and included in the study. Serum levels of total T3, total T4 and TSH were measured and the proportion of patients with various abnormalities in thyroid hormone levels and the pattern of abnormalities were analysed.

RESULTS

The mean age of study group was 67.9 years (with standard deviation of 7.184). Female to male ratio was 1.08:1. Proportion of sick euthyroid syndrome in patients with sepsis was 71 %. Low T3 was seen in 69 % patients, low T4 in 11 % and low TSH in 11 %. TSH was above reference range in 3 % patients. The most common pattern of sick euthyroid syndrome was low T3 with normal T4 and TSH in 54 % patients. Low T3 with low T4 and normal TSH was seen in 6 % patients; low T3, T4, TSH in 5 % patients; low T3, elevated TSH, normal T4 in 3 % patients; low TSH with normal T3 and T4 in 2 % patients and low T3, low TSH and normal T4 in 1 % patients.

CONCLUSIONS

Proportion of sick euthyroid syndrome in sepsis was 71 % and the most common pattern was low T3 with normal T4 and TSH seen in 54 % patients.

KEYWORDS

Sick Euthyroid Syndrome, T3, T4, TSH

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BACKGROUND

Thyroid hormones plays a vital role in the adaptation of metabolic needs to critical illness and stress. The hypothalamic pituitary thyroid axis is controlled by an endocrine feedback system. Thyrotropin-releasing hormone (TRH) released from the hypothalamus act on the anterior pituitary to secrete thyroid-stimulating hormone (TSH). In turn, TSH stimulates the thyroid gland to release thyroid hormones. The prohormone thyroxine (T4) is converted in peripheral tissues to the active hormone triiodothyronine (T3).[2] The euthyroid sick syndrome or non-thyroidal illness syndrome refers to alterations in the levels of thyroid hormones which occur in most of acute or chronic illness which is not due to intrinsic dysfunction of thyroid gland or hypothalamic pituitary axis. The term euthyroid sick syndrome was introduced in 1982 by Wartofsky and Bunnan to describe a range of thyroid abnormalities associated with non-thyroidal illness. The term was coined thinking that patients with systemic illness are clinically euthyroid. But there is emerging evidence to suggest that these patients may have acquired transient central hypothyroidism. Euthyroid sick syndrome (ESS) and non-thyroidal illness syndrome are terms used alternatively in the literature.

Changes in thyroid hormone metabolism in critical illnesses is primarily related to the severity of underlying illness. Such alterations in thyroid function are marked in patients with sepsis. Sepsis is a significant problem in critically ill patients. It is the leading cause of mortality in non-coronary intensive care units. Euthyroid sick syndrome has also been well described in patients with renal failure,[5] liver disease,[6] in elderly sick,[7] after stress or surgery,[8] and after ingestion of drugs like corticosteroids,[9] amiodarone,[10] and propranolol.[11]

The most common finding in euthyroid sick syndrome is a decrease in T3, which occurs in even the mildest forms of euthyroid sick syndrome. Hence the condition is also known as low T3 syndrome. Patients with moderate to severe illness may also show abnormalities in TSH and T4. Low triiodothyronine (T3) in critical illness is postulated to be due to increased deiodination of T4 to reverse T3 (rT3), rather than to T3, and increased catabolism of T3 to 3,3-diiodothyronine (T2).[12,13,14] As the severity of illness increases, a decrease in total and free T4, and a decrease in TSH can be observed. Decrease in plasma thyroxine binding globulin (TBG) or transthyretin along with accumulation of substances that lower the plasma thyroid-hormone binding capacity also is considered to be significant for the aforementioned changes in thyroid hormone levels during critical illness. For most of the patients, thyroid function abnormalities observed during critical illness are transient and don't have an intrinsic thyroid disease. It remains unresolved whether these patients with euthyroid sick syndrome need to be treated. Available data do not provide clear evidence of benefit.[15] The changes in thyroid function during critical illness may be protective in that it prevents excessive tissue catabolism.[16] It seems to be a complex mix of physiologic adaptation and pathologic response to acute illness.[15] The implications of abnormal thyroid function observed in various illness are, (1) In patients admitted to the hospital especially with critical illness in the ICU, unless there is compelling indication thyroid function should not be tested as it will be difficult to interpret the results. (2) It is difficult to distinguish untreated primary hypothyroidism from euthyroid sick syndrome in the ICU considering the high prevalence of sick euthyroid syndrome in the ICU.[2] (3) The abnormalities in thyroid function tests observed in critical illness has relation to the severity of illness. Most of the studies of sick euthyroid syndrome are Western and there are few Indian studies which have examined this issue in our intensive care units. The pattern of abnormalities that are seen in Sick euthyroid syndrome is little different in our country where iodine deficiency is higher in some areas.

The aim of the study was to (1) To study the proportion of sick euthyroid syndrome in patients with sepsis admitted to medical intensive care unit, in a tertiary care center. (2) To study the pattern of sick euthyroid syndrome in patients with sepsis.

METHODS

Our study was a hospital based cross sectional study conducted among patients admitted to the medical intensive care unit of Government Medical College Hospital, Trivandrum, South Kerala, for a period of one year. 100 patients with diagnosis of sepsis were included in the study. It was based on levels of T3 hormones between sepsis patients having favourable and unfavourable outcomes. The mean T3 and standard deviation (SD) of T3 levels to diagnose non-thyroidal illness syndrome among patients with and without sepsis were taken into consideration for calculating sample size. From the study it was observed that mean SD of T3 levels among unfavourable outcome is 30.40 + - 13.40 and among favourable outcome is 52.5 + - 19.60. Substituting this the sample size was calculated based on difference between means between the two groups, using precision of 5 %, desired confidence level 95 % and accounting 20 % for attrition, it was estimated to be 87 rounded off to 100 patients.

Inclusion Criteria

All patients > 18 years of age admitted to medical intensive care unit with diagnosis of sepsis based on the 2001 definition by International Sepsis Definitions Conference.

Exclusion Criteria

All patients aged < 18 years, known case of pre-existing thyroid illnesses, patients on drugs known to alter thyroid function and previous endocrine disorders.

Study Variables

Outcome variable - Presence or absence of sick euthyroid syndrome measured by total T3, total T4 and TSH.

Statistical Analysis

Statistical analysis was done using the Statistical Package for the Social Sciences (SPSS). Descriptive statistics was applied to describe the baseline quantitative variables like age, sex, laboratory parameters and thyroid hormone levels. Using mean and standard deviation, all continuous variables like age, sex, sepsis and T3, T4 etc. were expressed in frequency and percentage. The proportion and pattern of sick euthyroid syndrome in sepsis patients was expressed in percentage and frequency.

RESULTS

The study was conducted in 100 patients with age more than 18 years. The number of patients were more in the age group of 60 to 69 years (42 %) (Table 1). The mean age of study group was 67.9 years (with standard deviation of 7.184). 52 % of the patients were females. Regarding sensorium of sepsis patients 52 % were drowsy and 27 % were stuporous (Table 2). About 50 % of patients had pallor and 37 % had icterus. Oedema was seen in 52 % of patients. Low TSH was seen in 8 % of patients, and TSH was above reference range in 3 % patients (Figure 1). Low T3 was seen in 69 % patients and low T4 in 11 %. Proportion of sick euthyroid syndrome in patients with sepsis was 71 % (Figure 2). The most common pattern of sick euthyroid syndrome was low T3 with normal T4 and TSH in 54 % patients. Low T3 with low T4 and normal TSH was seen in 6 % patients; low T3, T4 and TSH in 5 % patients; low T3, elevated TSH, normal T4 in 3 % patients; low TSH with normal T3 and T4 in 2 % patients and low T3, low TSH and normal T4 in 1 % patients. (Table 3)

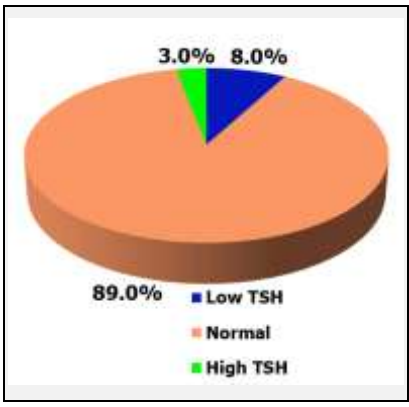

Figure 1. Distribution of Serum TSH Levels

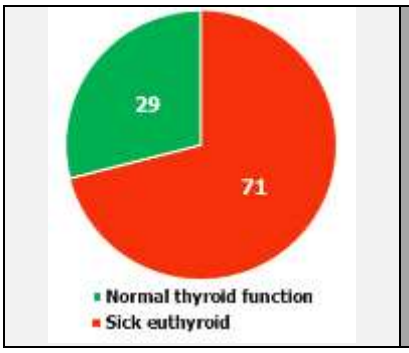

Figure 2. Proportion of Patients with Sick Euthyroid Syndrome

Age in Years	Frequency	Percentage
< 50	1	1.0
50 – 59	12	12.0
60 – 69	42	42.0
70 – 79	40	40.0
≥ 80	5	5.0
Total	**100**	**100.0**

Table 1. Age Distribution

Sensorium	Frequency	Percent
Alert	20	20.0
Drowsy	52	52.0
Stuporous	27	27.0
Semi coma	1	1.0
Total	**100**	**100.0**

Table 2. Sensorium of the Patient

Pattern of Sick Euthyroid Syndrome	Percentage
Low T3, and Normal T4, TSH	54 %
Normal T3, T4, TSH	29 %
Low T3, T4 and Normal TSH	6 %
Low T3, T4, TSH	5 %
Low T3, Normal T4 and Elevated TSH	3 %
Normal T3, T4 and Low TSH	2 %
Low T3, TSH and Normal T4	1 %

Table 3. Pattern of Sick Euthyroid Syndrome

DISCUSSION

Our study was a hospital based cross sectional study conducted among the patients admitted to MICU, in a tertiary care centre in Trivandrum. 100 consecutive patients with a diagnosis of sepsis based on 2001 International Sepsis Definitions Conference sponsored by the Society of Critical Care Medicine SCCM, The European Society of Intensive Care Medicine (ESICM), The American College of Chest Physicians (ACCP), the American Thoracic Society (ATS), and the Surgical Infection Society (SIS). The mean age of study population was 67.9 years (standard deviation - 7.184) of which 52 % of patients were females. 50 % of study population were unemployed, 42 % were involved in unskilled and 8 % in semiskilled labour. 81 % patients were from rural and the rest from urban areas. In this study, 69 % had low T3, 11 % had low T3 and T4, 5 % had low T3, T4 and TSH, 2 % had low T4 alone, and 11 % patients had abnormality of TSH, giving an overall prevalence of sick euthyroid syndrome at 71 %.

This was in line with the study conducted by Zargar et al. which yielded a prevalence of 67 % at admission and 70.5 % at 3 weeks.[17] A study conducted by Loh et al. showed a prevalence of sick euthyroid syndrome to be 84 %, which was slightly higher than ours.[18] Low T3 was the most common abnormality in our patients, which was seen in 69 % patients. This is similar to previous published studies: In the study by Kumar et al. low T3 was seen in 61 % patients. Hosny et al. found that 48.8 % patients had low free T3 below the reference range on admission and 61.3 % patients had low values on day 5. Even though the values were lower than the corresponding values in our study on the day of admission, values on day 5 were comparable to ours. They also observed that the mean level of free triiodothyronine (FT3) was significantly lower in patients with septic shock and severe sepsis as compared to patients with sepsis. Meyer et al. observed that 65 % patients had low T3 on admission and 58 % had low T3 on day 2 and 57 % had low T3 on the day of discharge or death. Loh et al. observed that

low T3 was seen in 67 % critically ill patients admitted to the MICU. The study by Bello et al. yielded a higher prevalence of low T3 in 78.7 % patients. The proportion of low T3 in the study by Bermudez et al. was 70 %.[19,20,21,22,23]

2 % patients had low T4 alone which was similar to study by Zargar et al. which showed low T4 alone in 1 % patients. 11 % of our study subjects had low serum T4. This was similar to the study by Kumar et al. in which 14 % had low T4. The values were higher than ours in studies by Hosny et al. (33.8 % at admission and 31.2 % at day 5), Meyer et al. (24 %), Loh et al. (24 %).

11 % patients in our study had abnormality of TSH, which was similar to studies by Zargar et al. and Ray et al. In their studies abnormalities of TSH was seen in 13.4 % and 15.5 % patients respectively.[17,24] Low TSH was seen in 3 % of our patients which was lower than similar published studies. In the study by Kumar et al. 7 % patients had low serum TSH while Hosny et al. observed that 27.5 % patients had low serum TSH at admission and 23.8 % had low serum TSH at day 5.[19,20] 11 % patients had low T3-low T4. This was comparable to study by Zargar et al. which yielded a prevalence of 13.1 %. But the study by Ray et al. observed that 30.3 % of their study population had low T3-low T4 which was higher than our values.[24]

The most common pattern of sick euthyroid syndrome was low T3, normal T4, normal TSH seen in 54 % patients. There are not many studies which have analysed such pattern combinations in sick euthyroid syndrome. Other patterns of sick euthyroid syndrome in our study were 6 % patients with low T3, T4 and normal TSH; 5 % with low T3, T4 and TSH; low T3, normal T4, elevated TSH in 3 %; normal T3, T4, low TSH in 2 %; low T3, normal T4, low TSH in 1 % patients.

Our study was consistent with the pattern of sick euthyroid syndrome published in literature with low T3 dominating the clinical picture. And various studies have reiterated the importance of low T3 in critical illness and its relationship with prognosis of the disease.

The limitations of the study are, it is observational in nature and was done in a heterogeneous population of patients as the underlying cause for sepsis was diverse. Thyroid parameters were assessed only once during the ICU stay. So, the pattern of fall or rise during the course of disease was not assessed.

CONCLUSIONS

Proportion of sick euthyroid syndrome in sepsis was 71 %. The most common abnormality in thyroid function was low T3, which was seen in 69 % patients. The most common pattern of sick euthyroid syndrome was low T3, normal T4 and normal TSH in 54 % patients.

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