



Original Article

Study of Thyroid Profile in Patients with Sepsis

Authors

A. Pal¹, N. Jain², M. Patidar³

¹Assistant Professor, Department of Medicine N.S.C.B Medical College Jabalpur

²Assistant Professor, Department of Medicine N.S.C.B Medical College Jabalpur

³RMO, Department of Medicine N.S.C.B Medical College Jabalpur

Abstract

Background: *Thyroid hormone abnormalities are frequently encountered in patients with sepsis, sepsis is important cause of death in developing countries. The aim of study is to analyze thyroid profile in sepsis patients at admission and evaluate the prognostic role of thyroid dysfunction in sepsis patients.*

Method: *In prospective observational study, thyroid hormone levels (FT3, FT4, TSH) measured in 75 in-patients with sepsis. Serum thyroid level measured by chemiluminescent assay at the time of admission. Sepsis patients further divided into survivors and non-survivors.*

Observation and Results: *Thyroid profile was assessed in 75 sepsis inpatients, low FT3 (56%) was the commonest abnormality observed, followed by low FT4 (10.67%) and high TSH (10.67%) followed by low TSH (8%).*

-Non survivors have low mean FT3 (1.56 ± 0.77) than survivors (2.31 ± 0.65) which was statistically significant ($p < 0.0001$). Significant positive correlation observed between serum FT3 and serum albumin ($p=0.002$, $r=0.36$)

Conclusion: *low level of FT3 has positive correlation with decrease survival in sepsis patients. FT3 may be used as predictor of mortality. Serum FT3 and serum albumin have positive correlation.*

Introduction

The metabolic responses to sepsis involve every organ and tissue of the body and yet, surprisingly, little is known about the underlying mechanisms. During sepsis and other critical illnesses, the state of stress results in hyper metabolism, increased energy expenditure, hyperglycemia and muscle loss^{1,2}.

Critical illness is often associated with alterations in thyroid hormone concentrations in patients with no previous intrinsic thyroid disease³⁻⁵. Euthyroid Sick Syndrome (ESS) is the commonest endocrine

change seen in critically ill patients⁶. It is described as abnormalities in circulating thyroid hormone levels without pre-existing hypothalamic pituitary or thyroid gland dysfunction in the setting of a Non-Thyroidal Illness (NTI)⁷.

ESS is characterized by low triiodothyronine (T3), low or normal thyroxine (T4) and normal Thyroid Stimulating Hormone (TSH). Three patterns are described in ESS; Type 1 or low T3 syndrome (seen in moderately sick patients), type 2 or low T4 syndrome (low T3 and T4, seen in very sick patients and associated with poor prognosis) and

type 3 or low TSH syndrome. These probably reflect different stages on a continuum and severity of illness⁸. The most common thyroid hormonal change reported in critically ill patients is reduced serum T3 level. Under normal circumstances 100% of T4 and 10-20% of T3 are directly secreted by the thyroid gland. 5'-deiodinase causes peripheral mono de iodination of T4 contributing to 80-90% of T3 and also increases the clearance of the inactive isomer reverse T3 (rT3) (which is derived by the action of 5'-deiodinase on T4)⁹. Critical illness decreases 5'-deiodinase activity, thereby, decreasing T4 to T3 conversion and rT3 clearance⁸. Increased metabolic clearance of T4 in critical illness further diverts T4 to form the inactive isomer rT3^{10,11}. Thus, T3 decreases and rT3 increases¹².

Several mechanisms can contribute to the inhibition of 5'-monodeiodination and therefore to the low serum T3 concentration in critically ill patients with non thyroidal illness: 1) Exogenous glucocorticoid therapy¹³ 2) Circulating inhibitors of deiodinase activity, such as free (non-esterified) fatty acids¹⁴. 3) Treatment with drugs that inhibit 5'-monodeiodinase activity, such as amiodarone and high doses of propranolol 4) Cytokines (such as tumor necrosis factor, interferon- alpha, NF-kB and interleukin-6)¹⁵⁻¹⁷. As the severity of illness progresses, there is gradual development of a more complex syndrome associated with low T3 and low T4 levels that may correlate with the bad prognosis¹⁸.

Material and Methods

The present study is carrying out from Department of Medicine, Netaji Subhash Chandra Bose Medical College & Hospital, Jabalpur (M.P.) INDIA. In prospective observational study, thyroid hormone levels (FT3, FT4, TSH) measured in 75 in-patients with sepsis. All the patients with sepsis or septic shock who are willing to be part of the study were included. Patients with Known Thyroid Disease, Patient with history of intake of drugs altering thyroid function were excluded from study.

-Blood sample will be drawn from sepsis patients at admission and sent for thyroid evaluation. thyroid hormone levels (FT3, FT4, TSH) measured in 75 in-patients with sepsis. Serum thyroid level measured by chemiluminescent assay at the time of admission. Sepsis patients further divided into survivors and non-survivors. The normal reference range for thyroid hormones in our laboratory is as follows: fT3 (2.1-4.4pg/ml), fT4 (0.8-2.7ng/dl) and TSH (0.5-5 µIU/ml). Any deviation from the normal range is considered to be abnormal (low or elevated).

Discussion

Critical illness or sepsis is a major cause of mortality and morbidity and is a global health burden. Early recognition, efficient decision making and rapid initiation of therapy can prove to be lifesaving in such patients. present study is the conducted for the prognostic value of thyroid hormones dysfunction in 75 sepsis inpatients.

1) in our study Thyroid profile was assessed in 30 female(40%) and 45 male(60%) . in study Kiran Bhat et al¹⁹ (2016) Thyroid profile was assessed in 340 inpatients. Out of these 249 (73.2%) were females and 91 (26.8%) were males.

2) in our study Non survivors have low mean FT3 (1.56 ± 0.77pg/ml) than survivors (2.31 ± 0.65pg/ml) which was statistically significant (p <0.0001). in study Mohamed Hosny et al (2015)²⁰ Non survivors have low mean FT3 (1.9 ± 0.89pg/ml) than survivors (2.9 ± 1.03 pg/ml) which was statistically significant (p <0.001).

3) in our study out of 75 patients ,survivors included 47 patients (62.67%)and non survivors included 28 patients (37.33%). In study Mohamed Hosn et al (2015)²⁰ out of 80 patients survivors included 41 patients(51.25%) and non survivors included 39 patients(52%).

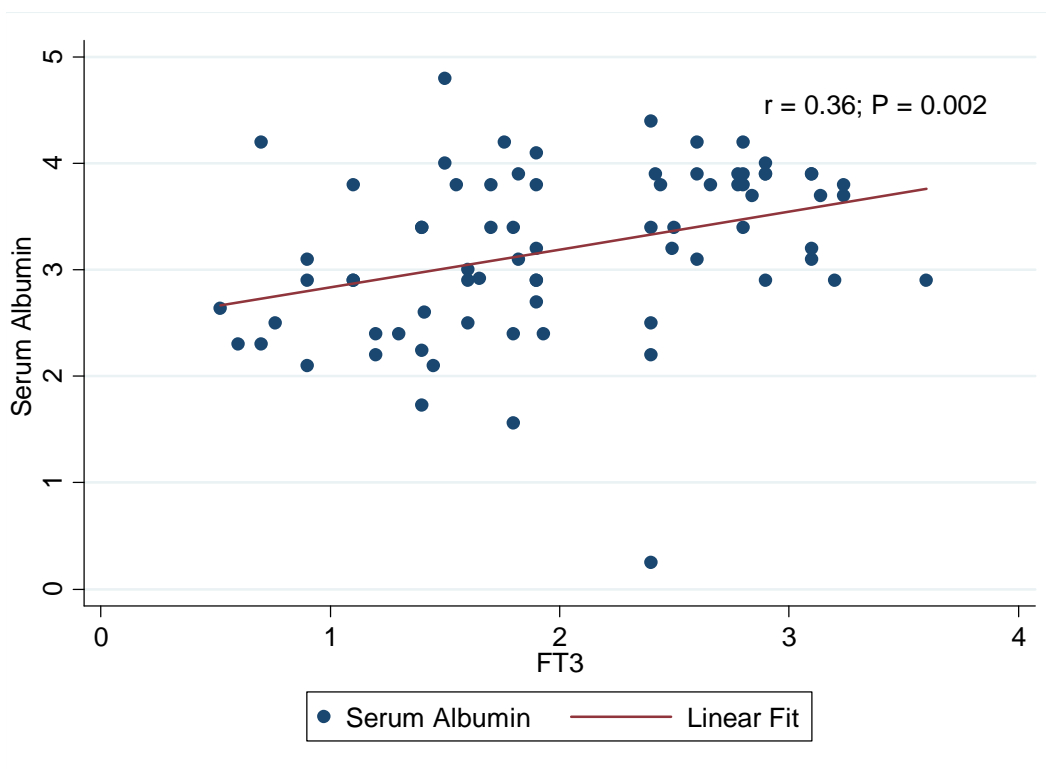
4) in our study 75 sepsis inpatients, low FT3 (56%) was the commonest abnormality observed, followed by low FT4 (10.67%) and high TSH (10.67%) followed by low TSH (8%). In Study Kiran Bhat et al(2016)¹⁹ low fT3 (50%) was the commonest abnormality followed by high TSH

(12.4%), low TSH (8.8%) and low FT4 (4.7%) concentration.

5) we found that FT3 was the most powerful predictor of ICU mortality among the complete thyroid indicators (FT3, FT4, TSH). Among the thyroid hormone indicators, FT3 was the only independent predictor of ICU mortality. In study Feilong Wang et al(2012)²¹, they found that FT3 was the most powerful and only independent predictor of ICU mortality among the complete thyroid panel of indicators.

6) in our study 75 patients were included in the study with mean age $42.44 \pm$ years .A total of 45 patients were included in the study Dr. Desai Vidya Sripad et al (2015)²² with mean age 70 ± 15 years,

7) in our study Significant positive correlation observed between serum FT3 and serum albumin ($p=0.002, r=0.36$).In study Dr. Desai vidya sripad et al (2015)²² no Significant positive correlation observed between serum FT3 and serum albumin ($p<0.85, r=0.19$)



Linear Fit Scatter plot showing correlation between serum albumin and FT3

Conclusion

- Thyroid profile was assessed in 75 sepsis inpatients, low FT3 (56%) was the commonest abnormality observed, followed by low FT4 (10.67%) and high TSH (10.67%) followed by low TSH (8%).
- Non survivors have low mean FT3 (1.56 ± 0.77) than survivors (2.31 ± 0.65) which was statistically significant ($p < 0.0001$). Significant positive correlation observed between serum FT3 and serum albumin ($p=0.002, r=0.36$)

- Low level of FT3 has positive correlation with decrease survival in sepsis patients. FT3 may be used as predictor of mortality. Further more studies required with large no of cases to find relation between low FT3 and mortality so it can be taken as prognostic marker in sepsis related critical illness and further studies are required to correlate with other critical illness and relation with thyroid function test(TFT).

References

1. Plank LD, Connolly AB, Hill GL. Sequential changes in the metabolic

- response in severely septic patients during the first 23 days after onset of peritonitis. *Ann Surg* 1998; 228: 146-158.
2. Fong Y, Marono MA, Moldawer LL. The acute splanchnic and peripheral tissue metabolic response to endotoxin in humans. *J Clin Invest* 1990; 85: 1896-1904.
 3. Farwell AP. Sick euthyroid syndrome in the intensive care unit. In: Irwin RS, Rippe JM, (eds), *Irwin and Rippe's Intensive Care Medicine*, Philadelphia, PA: Lippincott Williams & Wilkins, 2003; pp: 1205-1216.
 4. DeGroot LJ. Non-thyroidal illness syndrome is functional central hypothyroidism, and if severe, hormone replacement is appropriate in light of present knowledge. *J Endocrinol Invest* 2003; 26: 1163-1170.
 5. Adler SM, Wartofsky L. The nonthyroidal illness syndrome. *Endocrinol Metab Clin North Am* 2007; 36: 657-672.
 6. Sahana PK, Ghosh A, Mukhopadhyay P, Pandit K, Chowdhury BK, Chowdhury S. A study on endocrine changes in patients in intensive care unit. *J Indian Med Assoc* 2008; 106: 362-364
 7. Haas NA, Camphausen CK, Kececioglu D. Clinical review: Thyroid hormone replacement in children after cardiac surgery: is it worth a try? *Crit Care* 2006; 10: 213.
 8. Vasa FR, Molitch ME. Endocrine problems in the chronically ill patient. *Clin Chest Med* 2001; 22: 193-208
 9. Zucker AR, Chernow B, Fields AI, Hung W, Burman KD. Thyroid function in critically ill children. Clinical and lab observations 1985; 107: 552-554.
 10. Chopra IJ, Hershman JM, Pardridge WM, Nicoloff JT. Thyroid function in nonthyroidal illness. *Ann Intern Med* 1983; 98: 946-957.
 11. Chopra IJ, Chopra U, Smith SR, Reza M, Solomon DH. Reciprocal changes in serum concentrations of 3, 3, 5-triiodothyronine (T3) in systemic illness. *J Clin Endocrinol Metab* 1975; 41: 1043-1049.
 12. Kaptein EM, Weiner JM, Robinson WJ, Wheeler WS, Nicoloff JT. Relationship of altered thyroid hormone indices to survival in non-thyroidal illness. *Clin Endocrinol* 1982; 16: 565-574.
 13. Chopra IJ, Williams DE, Orgiazzi J, Solomon DH. 1975 Opposite effects of dexamethasone on serum concentrations of 3,3',5'triiodothyronine (reverse T3) and 3,3'5'-triiodothyronine (T3). *J Clin Endocrinol Metab* 1975; 41: 911-920.
 14. Chopra IJ, Huang TS, Beredo A, Solomon DH, ChuaTeco GN, Mead JF. Evidence for an inhibitor of extrathyroidal conversion of thyroxine to 3,5,3'-triiodothyronine in sera Assessment of thyroid function in critically ill patients *Biomed Res- India* 2016 Volume 27 Issue 2 451 of patients with nonthyroidal illnesses. *J Clin Endocrinol Metab* 1985; 60: 666-672.
 15. Van der Poll T, Romijn JA, Wiersinga WM, Sauerwein HP. Tumor necrosis factor: a putative mediator of the sick euthyroid syndrome in man. *J Clin Endocrinol Metab* 1990; 71: 1567-1572
 16. Stouthard JM, van der Poll T, Endert E. Effects of acute and chronic interleukin-6 administration on thyroid hormone metabolism in humans. *J Clin Endocrinol Metab* 1994; 79: 1342-1346.
 17. Corssmit EP, Heyligenberg R, Endert E, Sauerwein HP, Romijn JA. Acute effects of interferon-alpha administration on thyroid hormone metabolism in healthy men. *J Clin Endocrinol Metab* 1995; 80: 3140-3144.
 18. .Slag MF, Morley JE, Elson MK, Crowson TW, Nettle FQ, Shafer RB.

Hypothyroxinemia in critically ill patients as a predictor of high mortality. JAMA 1981; 245: 43-45

19. Kiran Bhat1*, Sumita Sharma1 , Kapil Sharma1 , RK Singh2: Assessment of thyroid function in critically ill patients Biomedical Research 2016; 27 (2):
20. Mohamed Hosny RaniaRashad Doaa Atef Nashwa Abed: Predictive value of thyroid hormone assessment in septic patients in comparison with C-reactive protein. The Egyptian Journal of Critical Care Medicine Volume 3, Issues 2–3, August–December 2015
21. Feilong Wang,#1 Wenzhi Pan,#2 Hairong Wang,#1 Shuyun Wang,1 Shuming Pan, 1 and Junbo Ge 2: Relationship between thyroid function and ICU mortality: a prospective observation study Published online 2012 Jan 19. doi: 10.1186/cc11151
22. Dr. Desai Vidya Sripad, Dr.N.V.S. Chowdary, Dr.V.Sivaprabodh, Dr.Ravi Shekharal :Relationship between Free T3 and ICU Mortality: A Prospective Observation. international Journal of Scientific and Research Publications, Volume 5, Issue 1, January 2015 1 ISSN 2250-3153.