

Relationship between Free T3 and ICU Mortality: A Prospective Observation.

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Abstract- Low T3 syndrome is emerging as the most sensitive independent predictor of short term survival and is associated with adverse outcome in ICU patients. This study was conducted to assess the prognostic value of the complete thyroid indicators in unselected ICU patients. **MATERIALS AND METHODS:** Patients admitted in ICU and without known thyroid diseases were included in the study, Blood samples were analysed for Free T3, Free T4, Total T3, Total T4 and TSH and were compared with APACHE Score, Hemoglobin, ESR, Serum Lactate Dehydrogenase, Serum Albumin and eGFR. **RESULTS:** There was a statistically significant positive correlation between FreeT3 and TT3 with ($r= 0.44$; $p< 0.001$); statically significant positive correlation between FT3 and TT4 with ($r=0.52$; $p< 0.0001$); FT3 and LDH also showed a significant negative correlation with ($r= -0.40$; $p< 0.05$); FT3 and eGFR ($r=-0.068$; $p<0.63$); FT3 and Albumin ($r=0.19$, $p<0.85$); FT3 and APACHE score negative correlation ($r=-0.34$, $p<0.001$). There was a statically significant positive correlation between FreeT4 and TT4 with ($r= 0.48$; $p< 0.0003$); statically significant positive correlation between FT4 and TT4 with ($r=0.70$; $p< 0.00001$); FT4 and TSH ($r=- 0.027$ $p< 0.85$); FT4 and LDH also showed a significant negative correlation with ($r= -0.40$; $p< 0.006$); FT4 and eGFR ($r=-0.327$; $p<0.02$); FT4 and Albumin ($r=0.20$, $p<0.14$); FT4 and APACHE score negative correlation ($r=-0.45$, $p<0.001$)

Index Terms- APACHE II SCORE, Free T3, Free T4, ICU Mortality, Low T3 Syndrome.

I. INTRODUCTION

During critical illness, changes in circulating hormone levels is a common phenomenon. The alteration in Thyroid hormones is Non thyroidal illness syndrome (NTIS), it is characterized by low serum level of free T3 and Total T3 high levels of reverse T3 accompanied by normal or low levels of T4 and TSH (1). The prevalence of NTIS is 11-18% in non-selected hospitalized patients and increases upto 65% to 70 % in ICU (2). Controversy still exists on whether NTIS is a adaptive response to illness and induces a maladaptive response of thyroid hormones (3). Many studies have confirmed the association between NTIS and adverse outcome in patients with sepsis, multiple trauma, acute respiratory distress syndrome and unselected ICU cases etc (4,5,6,7). The study was taken upto understand the role of complete pannel of thyroid function levels in ICU patients and compare them with other traditional

predictors of mortality the APACHE scores, LDH, eGFR, Hb% and ESR (8,9).

II. REVIEW OF LITERATURE

Low T3 syndrome is emerging as the most sensitive independent predictor of short term survival. Non thyroidal illness syndrome (NTIS) is associated with adverse outcome. The incidence of NTIS is 11-18% in non-selected hospitalized patients and goes upto 60-70% among patients admitted in intensive care units. The pathology underlying the NTIS is explained by three main modes. 1) An imbalance between the activity of type I and type II deiodinase mediated by inflammatory cytokines. 2) A decreased hypothalamus and pituitary sensibility to thyroid hormones mediated by stress induced hormones and cytokines. 3) A reduced T4 binding protein and cellular uptake (10,11). All the above three mechanisms are involved and progressively involved in patients with critical illness. Previous studies suggest a significant association between NTIS and acute renal failure, New York Heart association classification heart failure and metastasized cancer disease. Although there are studies indicating 50% probability of death when serum T4 levels are less than 4 µgm/dl but there are few studies on role of free T3 as a sole predictor of ICU mortality. The present was taken to understand the whether low T3 syndrome itself acts as a sole predictor of ICU mortality (12,13,14,15). So we took up a study to understand the alteration in thyroid function test in acutely ill patients admitted in ICU. Also the study aims to compare these hormones with other acute inflammation indices.

III. MATERIAL AND METHODS

The study was done in NRIMC and GH, by department of Biochemistry. The study involved adult patients admitted in ICU. Exclusion criteria was 1) age younger than 18 years. 2) History of any thyroid disorders. 3) Thyroid nodule on clinical examination. 4) Pregnancy or pregnancy within previous 6 months. 5) patient on any hormonal therapy. Sample was collected taking all aseptic precautions and was collected in redcap vacutainer, was allowed to clot and centrifuged at 3000 rpm for 10 minutes. Serum was separated and analyzed on Centaur CP using CLIA method for T3, T4, TSH, FT3, FT4, S.Lactate dehydrogenase was analyzed on Randox Daytona, S.Creatine and S.Albumin were analysed on Dade Dimension. Estimated Glomerular filtration rate (eGFR) was calculated by using the abbreviated Modification of Diet in Renal study equation. Statistical analysis was done between all the parameters

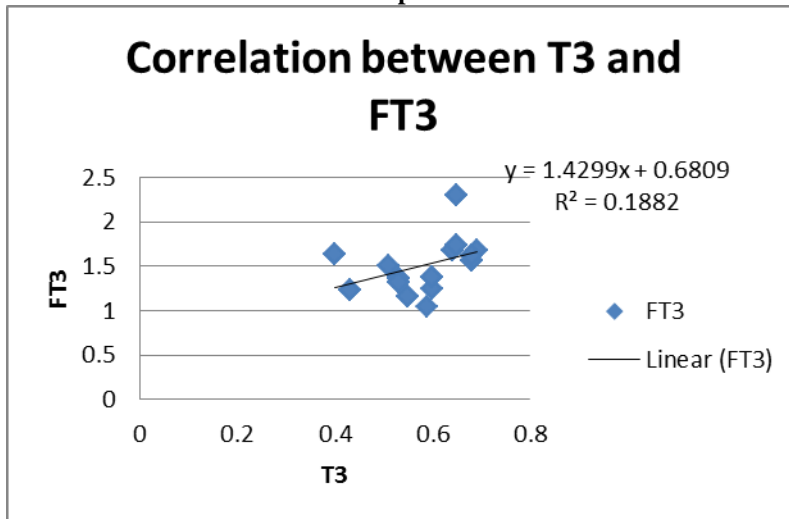
and with APACHE (Acute Physiology and Chronic Health Evaluation II score). Appropriate Calibrations and QC protocols were followed before analyzing the samples.

IV. RESULTS

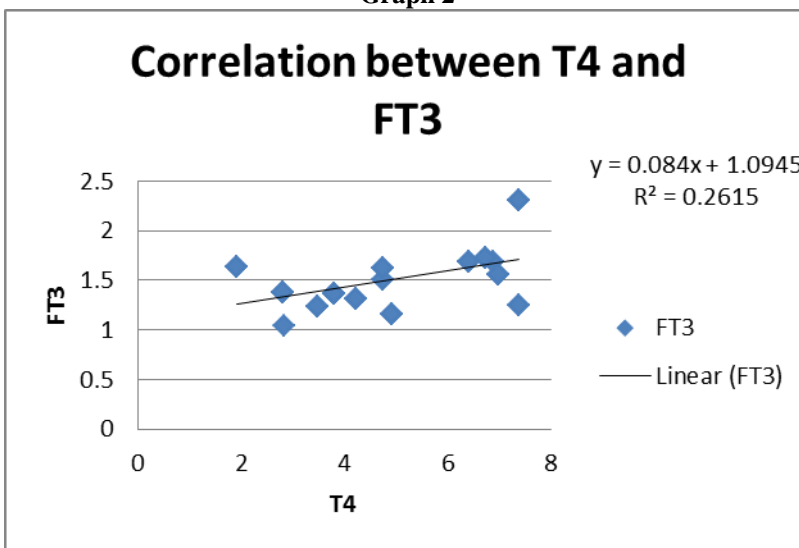
Normal ranges in our laboratory were: FT3 (2.02- 4.40pg/dl); FT4 (0.932 - 1.71 ng/dl); TSH (0.27 -4.20 μ iu / ml) TT3(0.846 -2.02 ng/ml); TT4(5.13- 14.06 ug/dl);LDH(230-460 u/l);Albumin (3.4-5.0 gm/dl); Creatinine (0.6-1.3 mg/dl);ESR (upto 10 mm/first hour) . A total of 45 patients were included in the

study with mean age 70 ± 15 years, There was a stastically significant positive correlation between FreeT3 and TT3 with ($r= 0.44$; $p < 0.001$) ;statically significant positive correlation between FT3 and TT4 with ($r=0.52$; $p < 0.0001$);FT3 and TSH ($r= 0.02$ $p < 0.85$);FT3 and LDH also showed a significant negative correlation with ($r= -0.40$; $p < 0.05$) ;FT3 and eGFR ($r=-0.068$; $p < 0.63$);FT3and Albumin ($r=0.19$, $p < 0.85$); FT3 and APACHE score negative correlation ($r=-0.34$, $p < 0.001$).As shown in Graph 1 and Graph 2.

Graph 1:



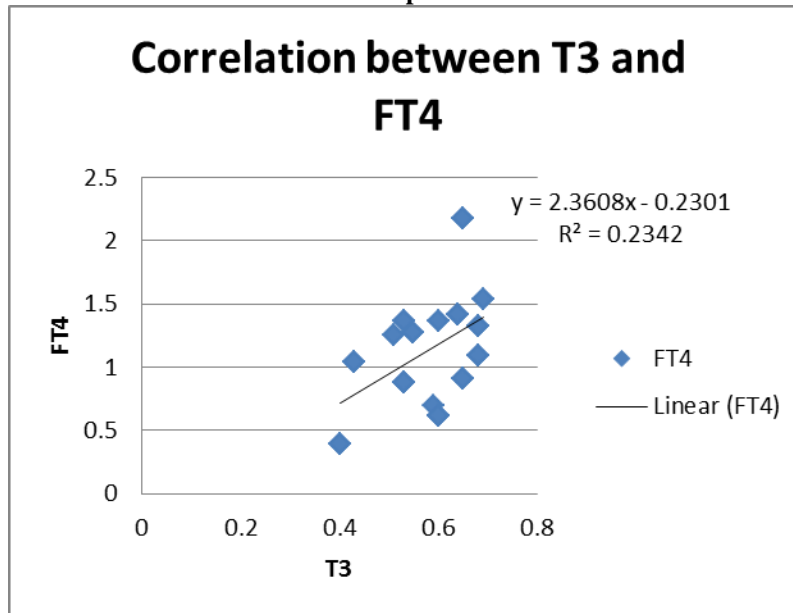
Graph 2



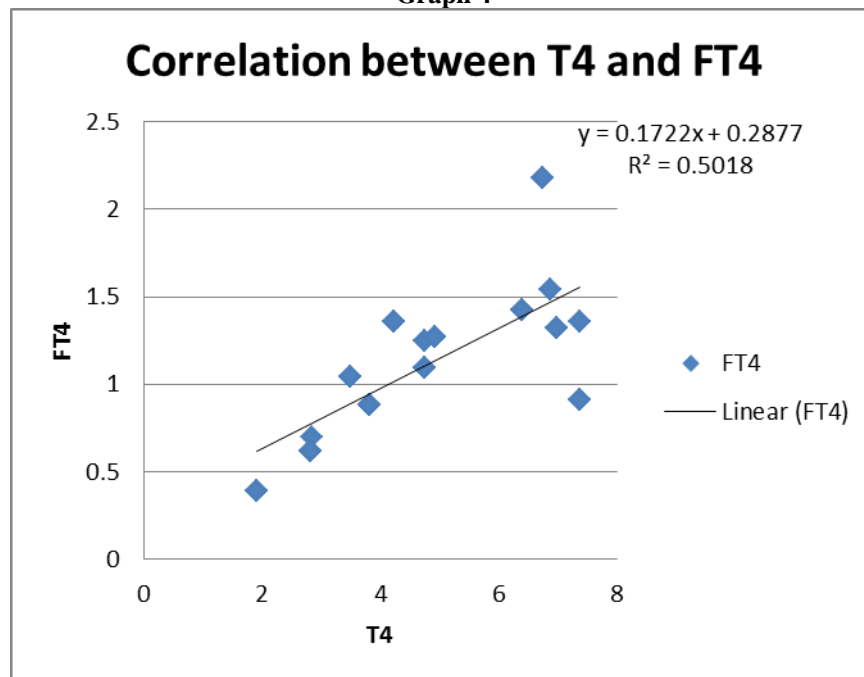
There was a stastically significant positive correlation between FreeT4 and TT4 with ($r= 0.48$; $p < 0.0003$) ;statically significant positive correlation between FT4 and TT4 with ($r=0.70$; $p < 0.00001$);FT4 and TSH ($r=- 0.027$ $p < 0.85$);FT4 and

LDH also showed a significant negative correlation with ($r= - 0.40$; $p < 0.006$) ; FT4 and eGFR ($r=-0.327$; $p < 0.02$);FT4 and Albumin($r=0.20$, $p < 0.14$);FT4 and APACHE score negative correlation ($r=-0.45$, $p < 0.001$).As shown in Graph 3 and Graph 4.

Graph 3



Graph 4



V. CONCLUSION

Overall our study supports the hypothesis of pivotal role of Low T3 syndrome as a very important prognostic factor of short term survival in ICU patients. We found that FT3 and FT4 as the most powerful and independent factor of ICU mortality among the complete thyroid panel of indicators. The cumulative death rate was significantly higher in patients with low T3 syndrome as compared to those without (18%). A significant association was found between patients death rate, Low T3 syndrome and APACHE II and other inflammation indices. The strength of the study is it excluded patients with underlying thyroid disorders. Out of the total thyroid profile FT3 and FT4 have a

more significant association and also are strong predicting factors. In conclusion, our results confirm that low T3 syndrome is very common in ICU acutely ill patients, emerging as the most sensitive independent predictor of ICU mortality.

REFERENCES

- [1] Adler SM, Wartofsky I. The non-thyroidal illness syndrome. *Endocrinol Metab Clin N Am* 2007;36:657-72.
- [2] Chopra IJ. Euthyroid sick syndrome: is it a misnomer? *Clin Endocrinol Metab* 1997;82:329-34.
- [3] De Groot LJ. Non-thyroidal illness syndrome is a manifestation of hypothalamic-pituitary dysfunction and in view of current evidence should

be treated with appropriate replacement therapies. Crit Care Clin 2006;22:57-86.

- [4] Mangas-Rojas a, Garica-Rojas Jf, Barba Chacon A, et al. Changes in the hypophyseal-thyroid axis and their prognostic value in sepsis. Rev Clin Esp 1990;187:395-398.
- [5] Angelousi AG, Karageorgopoulos DE, Kapaskelis AM, Falagas ME: Association between thyroid function tests at baseline and the outcome of patients with sepsis or septic shock: a systematic review. Eur J Endocrinol 2011;164:147-155.
- [6] Ilias I, Stamoulis K et al: Contribution of endocrine parameters in predicting outcome of multiple trauma patients in an intensive care unit.
- [7] Ture M, Memis D et al: Predictive value of thyroid hormones on the first day in adult respiratory syndrome patients admitted to ICU: comparison with SOFA and APACHE II scores. Ann Saudi Med 2005;25:466-472.
- [8] Rothwell PM, Lawler PG: Predictor of outcome in intensive care patients using endocrine parameters. Crit Care Med 1995;23:78-83.
- [9] Sharshar T, Bastuji-Garin S, Polito A, De Jonghe B, et al: Hormonal status in protracted critical illness.
- [10] Feilong Wang, Wenzhi Pan: Relationship between thyroid function and ICU mortality: a prospective observation study. Critical Care 2012;16:R11.
- [11] Sara Togini, Franseca Marchini: Non-thyroidal illness syndrome and short term survival in a hospitalized older population: Oxford Journal Medicine Age and Ageing, 2009; 39:46-50.
- [12] Docter R, Krenning EP, de Jong M, Hennemann G: The Sick euthyroid Syndrome: Changes in thyroid hormone serum parameters and hormone metabolism: Clin Endocrinol (Oxf) 1993;39:499-518.
- [13] Rothwell PM, Lawler PG: Prediction of outcome in intensive care patients using endocrine parameters. Crit Care Med 1995;23:78-83.
- [14] Slag MF, Morley JE, Elson MK, Crowson TW, Nuttall FQ, Shafer RB: Hypothyroxinemia in critically ill patients as a predictor of high mortality. JAMA 1981; 245:43-45.
- [15] Rossoni S, Cossi S, Marenaoni A et al, Low T3 syndrome and outcome in elderly hospitalized geriatric patients. J Endocrinol Invest 2002; 25:73-74.

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