



## The Predictive Power of Low T3 Levels among ICU Patients in a Tertiary Care Hospital of Kerala

Nandu Baby P\*, Ramesh V

Department of Biochemistry, Bharath Institute of Higher Education & Research, Agharam Road, Selaiyur, Chennai – 600 073, Tamil Nadu, India



### Article History:

Received on: 08 Nov 2020

Revised on: 15 Dec 2020

Accepted on: 17 Dec 2020

### Keywords:

Intensive care unit,  
Mortality rate,  
Thyroxine,  
Triiodothyronine

### ABSTRACT

Just a few studies recorded that low thyroid hormones are independent mortality predictors in ICU-admitted patients, indicating the use of thyroid profile in mortality prediction scoring systems. A spectrum of improvements occurs in ICU patients, beginning with low triiodothyronine (T3) accompanied by low thyroxine (T4) and low thyroid-stimulating hormone (TSH) levels. To evaluate whether low T3 levels were responsible for increased mortality among ICU patients in a tertiary care hospital. This is a prospective, observational and interventional study carried on 200 ICU admitted patients aged 30-70 years. The study subjects were categorized into two groups- survivors and non-survivors. Our study results revealed that non-survivors had less T3, less T4, less TSH, more HbA1c indicating that low thyroid levels are playing one of the crucial roles in determining the mortality rate in critically ill patients. Further, we found that the treatment with T4 alone was ineffective while replacement therapy, including T3, proved effective leading to significant clinical improvement. Low T3 syndrome has a significant effect on the mortality rate of critically ill patients. However, a further larger sample of patients should be evaluated to draw more reliable conclusions on Low T3 levels among ICU patients.

### \*Corresponding Author

Name: Nandu Baby P

Phone: +91-9447166067

Email: [nandupremier@gmail.com](mailto:nandupremier@gmail.com)

ISSN: 0975-7538

DOI: <https://doi.org/10.26452/ijrps.v11i4.3941>

Production and Hosted by

IJRPS | [www.ijrps.com](http://www.ijrps.com)

© 2020 | All rights reserved.

### INTRODUCTION

Human body's biochemical response to stress impacts every organ and tissue, but oddly, the fundamental pathogenesis is not known. During stress, sepsis and other essential disorders, the occurrence of hypermetabolism, high energy

intake, hyperglycemia and muscular fatigue can be seen (Plank *et al.*, 1998). Critical illness is usually associated with changes in thyroid levels in patients with no previous thyroid problems (Economidou *et al.*, 2011). Euthyroid Sick Syndrome (ESS) is the most common hormone modification in ICU patients (Nuno, 2020). These range sequential changes suggest differing amounts and disease seriousness (De Groot, 2006). The most prevalent thyroid hormone modification in critically ill patients is reduced serum T3 level (Neto and Zantut-Wittmann, 2016). The acute disease usually decreases 5'-deiodinase behaviour that decreases T4 to T3 conversion. Increased T4 metabolism often diverts T4 into inactive T3. Several other causes can contribute to inhibition of 5'-mono deiodination leading to low serum T3 concentration like therapy with glucocorticoids and drugs which inhibit 5'-mono deiodinase activity like amiodarone and beta-blockers like propranolol and tumor necrosis

factor, interferon-alpha, interleukin-6 (Vanderpas, 2006). Notably, only a few studies evaluated those T3 levels are predictors of mortality in patients admitted to intensive care units (ICU). The prominent evidence from the studies is suggestive of inclusion of the thyroid profile in scoring systems (Djokomoeljanto *et al.*, 2001). There was a series of changes starting with initial low T3 levels followed by low T4 and finally low TSH (Gofton and Young, 2012). Hyperglycemia is also shown as a significant predictor of mortality in intensive care patients (Kumar *et al.*, 2013). In developing countries like India, data on endocrinal parameters in critically ill patients is scarce. Therefore, we sought to evaluate whether the low T3 levels are predicting the mortality rate in ICU admitted patients. Further, we intended to assess whether T4, TSH, HbA1c levels are also playing a role in predicting the mortality rate among critically ill patients in a well-equipped tertiary care centre.

## METHODOLOGY

It was a prospective, observational and interventional study constituting 200 consecutive patients admitted to medical ICU irrespective of the underlying disease and diagnosis in a 400 bedded tertiary care hospital in Kerala. The study was carried out from October 2017 to January 2018. The patients aged below 20 and above 70 years, patients with a known history of thyroid problems, patients taking drugs for thyroid or history of thyroid medication, pregnant and lactating women were excluded from this study. The research met ethical principles of the clinical experimentation committee and the declaration. Institutional Ethical Committee approved this report. Informed consent was also collected from all the study subjects after explaining the details of the study, procedure, risks and benefits involved in the study. During the study, all the patients were followed up and observed by supplementing with both T3 and T4 for improvement of prognosis. The sample of 200 patients was based on the average number of patients admitted to ICU in our tertiary care centre. By systematic random sampling process, we have taken every alternate record of admitted patients from the medical records department (MRD) and ICU department. Patients were chosen in two categories to evaluate every 100 patients. Class 1 – survivors that safely released from hospital and Group 2 – non-survivors – patients who died owing to ICU disease. Fasting venous blood samples were collected on day 1 of admission to ICU from all the patients for hormonal analysis from the ante-cubital vein in a sterile container. In addition to numerous ICU protocol studies, samples were checked for T3,

T4, TSH, and Glycated Hemoglobin (HbA1c). Free T3 and T4 levels were not tested to avoid the variability of these hormones. Standard reference range for thyroid hormones; TSH is 0.3 to 4.6 mIU/L, T3 is 67 to 156 ng/dL and T4 is 4.5 to 11.6 µg/dL.

Any deviation from these normal ranges was considered to be abnormal. Thyroid hormones were estimated by solid-phase competitive chemiluminescence and HbA1c using the high-performance liquid chromatography method. All the clinical data obtained were analyzed by using statistical package for social sciences (SPSS), IBM, USA. (Version7). Student's t-test was used to compare ongoing results. Statistically significant was a p-value <0.05.

## RESULTS AND DISCUSSION

Among 200 study subjects, 78 were females and 122 were males. The mean age of the study population was  $50 \pm 11$  years among survivors and  $52 \pm 10$  years among non-survivors. Age and gender group distribution was mentioned in Figure 1. The average duration of stay in ICU was  $3.3 \pm 3$  days among two groups which were depicted in Figure 2. Cardiovascular diseases were the main reason for admissions into ICU among included subjects (Table 1) There were significant differences between T3, T4, TSH, blood glucose and glycated haemoglobin levels among survivors and non-survivors in the entire study population (Table 2).

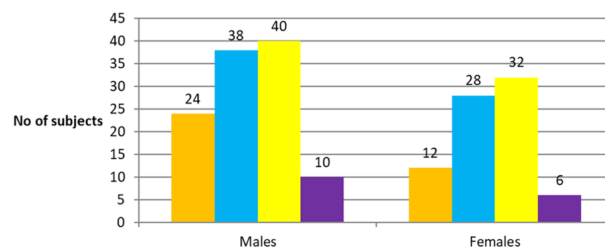


Figure 1: Age and sex distribution of 200 subjects

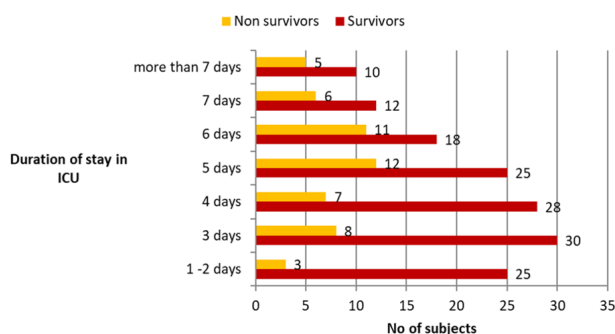


Figure 2: Duration of stay in the hospital among survivors and non-survivors

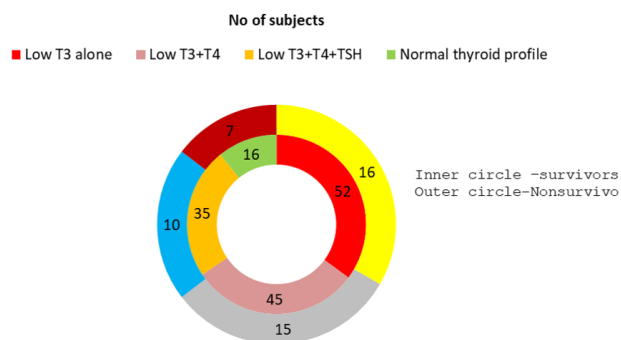
Plasma glucose and HbA1c were high among non-

**Table 1: Etiological distribution of ICU admissions**

S. No.	Cause of ICU admission	No. of subjects
1.	Cardiovascular disorders	65
2.	Infections	43
3.	Gastrointestinal issues	38
4.	Neurological problems	29
5.	Miscellaneous including trauma	25

**Table 2: Parametric distribution pattern among the two groups**

Parameters	Survivors Mean ± SD.	Non-survivors Mean ± SD.	p-Value
HbA1c (%)	5.9±0.9	6.1+1.4	0.23
Venous Glucose (mg/dl)	90+24	120+26	<0.01
T3 (ug/dl)	0.42+0.23	0.23+0.11	<0.01
T4 (ug/dl)	7.5+2.6	4.2+1.5	<0.01
TSH (miu/ml)	1.24+0.21	0.90+0.48	<0.01



**Figure 3: Thyroid profile distribution pattern**

survivor patients when compared to the survivor group. We observed the levels of T4, TSH was comparatively low in the non-survivor group. However, the differences in T4, TSH, and HbA1C and blood glucose were not statistically significant between both the groups. In our study, we observed deficient T3 levels in the non-survivor group of patients when compared to a survivor group indicating that T3 plays a significant role in determining the mortality rate. We observed a statistically significant difference with T3 levels between the two groups was (p-value < 0.05). The distribution of thyroid abnormalities in our study subjects was shown in Figure 3. Low T3 level alone is more prominent among both survivors and non-survivors when compared to combined low T3+T4 and combined low T3+T4+TSH.

Variations in the levels of thyroid hormone among critically ill patients are more common. However, thyroid dysfunction and exacerbation of disease severity and mortality in Intensive Care Unit (ICU)

are still inconclusive. The findings of our study depicted that low T3 is an essential marker in determining mortality rate in ICU patients. Whereas, this effect was not observed with the combined low T4 and low TSH levels along with low T3. Other hormonal parameters, like HbA1C and blood glucose, revealed no significance among survivors and non-survivors. Interestingly, we found low T3 (34%) is the most joint abnormality followed by low T4 +low T3, followed by low T3+T4+TSH. Contrary to our results, some study reported low T3 in 80% of pediatric ICU patients in Mumbai (Suvarna and Fande, 2009). These differences might be to a different type of sample, sample size and lack of the control group explaining the discrepancy in observed data. A survey conducted in Japan population and proved that age-related rise in TSH is probably due to increasing autoimmunity, environmental, and genetic factors (Leng and Razvi, 2019). From our study groups, age-related TSH elevation was not observed, and it may be due to selection bias of critically ill patients. Thus, TSH has no significance in predicting the risk of mortality in ICU patients. HbA1c describes the average 3-month glucose concentration. In ICU patients, hyperglycemia can be viewed as one of the indirect indicators of extreme stress (Ukleja, 2010). Further; our results did not show any difference in outcomes based on HbA1c and blood glucose levels. In his study evaluated free T3, T4, and T4 index and these parameters were more accurate than conventional T3, T4 levels which tend to change under varying conditions. It is one of our study limitations for not evaluating free T3, T4 levels due to lack of feasibility. The other limitations of this study are being a

single-centre study with small sample size. In addition to this, the lack of a control group that would have strengthened the results. (Oral Sessions, 2008)

## CONCLUSION

Our study findings showed that low T3 is a significant survival marker for critically ill ICU patients. Low T4 and TSH levels had no predictability on mortality. Also, HbA1c and blood glucose differed little between survivors and non-survivors. To draw further precise results, more trials with a significant number of patients in different facilities relative to the control group must be performed.

## Funding Support

The authors declare that they have no funding support for this study.

## Conflict of Interest

The authors declare that they have no conflict of interest for this study.

## REFERENCES

- De Groot, L. J. 2006. Non-Thyroidal Illness Syndrome is a Manifestation of Hypothalamic-Pituitary Dysfunction, and in View of Current Evidence, Should be Treated with Appropriate Replacement Therapies. *Critical Care Clinics*, 22(1):57-86.
- Djokomoeljanto, R., Soeatmadji, D. W., Davis, J. 2001. Endocrine Diseases. Drug Benefits and Risks. page 751.
- Economidou, F., Douka, E., Tzanela, M., Nanas, S., Kotanidou, A. 2011. Thyroid function during critical illness. *Hormones*, 10(2):117-124.
- Gofton, T. E., Young, G. B. 2012. Sepsis-associated encephalopathy. *Nature Reviews Neurology*, 8(10):557-566.
- Kumar, K. V. S., Kapoor, U., Kalia, R., Chandra, N. S. A., Singh, P., Nangia, R. 2013. Low triiodothyronine predicts mortality in critically ill patients. *Indian Journal of Endocrinology and Metabolism*, 17(2):285.
- Leng, O., Razvi, S. 2019. Hypothyroidism in the older population. *Thyroid Research*, 12(1):1-10.
- Neto, A. M., Zantut-Wittmann, D. E. 2016. Abnormalities of Thyroid Hormone Metabolism during Systemic Illness: The Low T3 Syndrome in Different Clinical Settings. *International Journal of Endocrinology*, 2016:1-9.
- Nuno, B. N. 2020. Euthyroid sick syndrome in paediatric and adult patients requiring extracorporeal circulatory support and the role of thyroid hormone supplementation: A Review. *Perfusion*, page

0267659120914136.

Oral Sessions 2008. Cerebrovascular Disease. *Small Vessel Disease*, 25(Supple 1):1-192.

Plank, L. D., Connolly, A. B., Hill, G. L. 1998. Sequential Changes in the Metabolic Response in Severely Septic Patients During the First 23 Days After the Onset of Peritonitis. *Annals of Surgery*, 228(2):146-158.

Suvarna, J. C., Fande, C. N. 2009. Serum thyroid hormone profile in critically III children. *The Indian Journal of Pediatrics*, 76(12):1217-1221.

Ukleja, A. 2010. Altered GI motility in critically ill patients: current understanding of pathophysiology, clinical impact, and diagnostic approach. *Nutrition in Clinical Practice*, 25(1):16-25.

Vanderpas, J. 2006. Nutritional Epidemiology and Thyroid Hormone Metabolism. *Annual Review of Nutrition*, 26(1):293-322.