







**Table 4:** Correlation of outcome with sr. free T4 level of patients

Free T4(ng/dl)	Expired	Normal	Total
<0.86	3(37.5%)	5	8
0.86 – 1.76	6 (40%)	9	15
>1.76	9(52.9%)	8	17
Total	18	22	40
p value = 0.682			

**Table 5:** Correlation of outcome with sr. TSH level of patients

Sr. TSH( $\mu$ IU/ml)	Expired	Normal	Total
<0.34	6 (46.2%)	7	13
0.34 – 4.25	7(36.5%)	12	19
>4.25	5(62.5%)	3	8
Total	18	22	40
p value = 0.471			

In the study RBS and Sr. Insulin level of patients also did not predict the mortality outcome in ICU Table 6 and Table 7 respectively. The p value observed was non significant (>0.05). It was seen that out of 24 patients having high level of sr. insulin 13 (54.2%) patients succumbed to death.

**Table 6:** Correlation of outcome RBS level of patients.

RBS (mg/dl)	Expired	Normal	Total
<70	2(50%)	2	4
70 – 125	4(36.4%)	7	11
>125	12(48%)	13	25
Total	18	22	40
p value = 0.793			

**Table 7:** Correlation of outcome with sr. insulin level of patients

Sr. Insulin( $\mu$ IU/ml)	Expired	Normal	Total
<0.7	1(25%)	3	4
0.7 – 9	3 (27.3%)	8	11
>9	13(54.2%)	11	24
Total	18	22	40
p value = 0.241			

A total of 23 patients had an APACHE II scoring of more than 14 out of which 14(60.9%) patients succumbed to death, Table 8 with a significant p value.

**Table 8:** Correlation of outcome with APACHE II score of patients.

APACHE II	Expired	Normal	Total
$\leq 14$	4(23.5%)	13	17
>14	14(60.9%)	9	23
Total	18	22	40
p value = 0.019* (significant p=<0.05)			

Correlating the two significant parameters of Free T3 and APACHE II, out of 30 patients who had a low Free T3 level 22 patients also had an APACHE II score of >14, reducing the p value further significantly to 0.002, Table 9.

**Table 9:** Correlation of Free T3 with APACHE II score of patients.

APACHE II	T3 (<2.4pg/ml)	T3(2.4- 4.2pg/ml)	Total
$\leq 14$	8(47.1%)	9(52.9%)	17
>14	22(95.5%)	1(4.3%)	23
Total	18	22	40
p value = 0.002* (significant p=<0.05)			

The comparison of the parameters studied where compared among the 2 group of patients, the survivors and the non-survivors. The data analyzed is given in, Table 10. It was found that free T3 and APACHE II had a significant p values.

**Table 10:** Comparison of the mean values of study parameters among patients

Parameters	Expired	Normal	t	degree of freedom	P
Free T3	0.87 $\pm$ 0.65	1.84 $\pm$ 1.18	3.273	38	0.002*
Free T4	4.64 $\pm$ 5.21	2.44 $\pm$ 2.62	1.625	38	0.117
Sr. TSH	2.68 $\pm$ 4.05	1.65 $\pm$ 2.03	0.993	38	0.331
RBS	148.27 $\pm$ 66.10	147.9 $\pm$ 65.03	0.018	38	0.986
Sr. Insulin	34.51 $\pm$ 59.88	20.18 $\pm$ 20.56	1.051	38	0.300
APACHE II	20 $\pm$ 6.85	14 $\pm$ 8.96	2.280	38	0.028*
* = p value <0.05 is significant					

## 5. Discussion

In this study of patients admitted to ICU survival prediction was not related to demographic details of the patient as a whole like age and sex. As these factors were comparable in most of the study participants of this study the age and sex of the patients were not found to be confounding factors in this study. This is the strong point of the study as our subjects had a matched population in the comparison groups. Age and sex plays a significant role in outcomes especially

the extremes of age, but this effect was not a player in our study.

Our study demonstrated that low T3 is an important marker of the severity of the illness and predicts mortality in ICU, as 17 (56.7%) out of 30 patients having serum free T3 less than 2.4 succumbed to their illness. The same was not seen with low T4, low TSH or when any of these were combined with low T3. Our study showed low T3 (56.7%) is the commonest abnormality followed by low TSH (46.2%) and low T4 (37.5%). Previous study from pediatric ICU patients from Mumbai, showed low T3 in 80%, low T4 in 50 % and low TSH in 6.7% [26]., conducted among 30 critically ill children and control of less than 12years age admitted in pediatric ICU. Two samples were collected from all patients, first during admission and second during at the time of discharge from ICU or death. This study showed that mean T3 and T4 levels were significantly lower in critically ill children than control. The combination of low T3 and T4 together increased the mortality risk by 30 times. Our study differs in the study population (adults), no. of study sample (single sample at admission only), and lack of control group from previous study explaining the discrepancy in observed data [26].

Our study did not establish any relation between RBS, Serum Insulin in predicting the mortality of ICU patients. The outcome in serum glucose level was variable amongst survivors and non survivors. This may be attributed to the small sample size of the study. Even though not statistically significant serum insulin level, we did find that out of 24 patients having high level of serum insulin (>9 $\mu$ IU/ml), 13 (54.2%) patients succumbed to their illness, hence pointing towards increased mortality rate in patient with high insulin

level. In a prospective randomized control trial study conducted on 1200 ICU patients in Belgium; it was found that although length of stay in the ICU could not be predicted on admission, among 433 patients who stayed in the ICU for less than three days, mortality was greater among those receiving intensive insulin therapies. In contrast, among 767 patients who stayed in the ICU for three or more days, in-hospital mortality in the 386 who received intensive insulin therapy was reduced from 52.5 to 43.0 percent ( $P=0.009$ ) and morbidity was also reduced [27]. So it can be stated that intensive insulin therapy significantly reduced morbidity but not mortality among all patients in the medical ICU [28].

Our study also did establish the relationship between APACHE II scoring and outcome of the patient, as a score of  $> 14$  was found to be a bad prognostic marker in 14(60.9%) patients out of 23 patients. This is in agreement with a recent study done on 5815 intensive care admission from 13 different hospitals showing an increasing score (range 0-71) was closely correlated with the subsequent risk of hospital death [29]. We also studied the influence of addition of free T3 to APACHE II and found that if taken together they were more accurate in prediction of the outcome [30].

The limitations in our study were firstly the small sample size. It was calculated based on the admission frequency in ICU of the hospital and considering the time frequency of the study (2months). Although the results obtained were statistically significant in parameters like free T3 and APACHE II scoring but outcomes related to other parameters could have been significant in a larger study sample because in our study those parameters were variable amongst survivors and non-survivors. This study can be a reference to future studies based on similar hypothesis, with a larger sample size where a universal dictum can be made based on the hormonal correlation of the ICU patients. Secondly we could not relate other hormones like cortisol, which also plays an important part in deciding the outcomes of ICU patients because of the cost restrain.

## 6. Conclusions

To conclude, our study points that in critical illness hormones plays a very important role in outcome of ICU patients. This study suggested that low serum free T3 is an important marker to correlate with the outcome of patients admitted in ICU. A scoring of  $>14$  on APACHE II grading scale also is an indication of poorer outcome in ICU patients. Addition of APACHE II scoring to serum free T3 increases the prediction capacity of APACHE II scoring. This study also concludes that free serum T3 is a better prognostic marker than glycemic status of the patient (RBS, and serum insulin).

## 7. Acknowledgements

The authors express their sincere appreciation to the Indian Council Of Medical Research (ICMR), and the KLE University, Belgavi, for funding the research. We are also thankful to the Basic Science Laboratory, KLE University

for their assistance in storing and processing the samples. We are also thankful to the patients admitted in ICU of KLES Dr. Prabhakar Kore Hospital for their cooperation throughout the study.

## References

- [1] Laura C. Robertson, Mohammed Al-Haddad, Anaesthesia and Intensive Care Medicine Vol. 14, issue 1, pages 11-14 January 2013, Recognising the critically ill patient. P II: S1472-0299(12)00266-4, copyright 2013 Elsevier Ltd.
- [2] Longo, Fauci, Kasper et al. Harrison's Principles of Internal Medicine, 18th edition, vol. 2. McGraw-Hill Companies, Inc., United States of America.
- [3] Henry M. Kronenberg, Shlomo Melmed, Kenneth S. Polonsky, P. Reed Larsen. Williams Textbook of Endocrinology, 11th edition, chapter: Glucose homeostasis and hypoglycaemia, page 1503. Copyright Elsevier Ltd.
- [4] Sahana PK, Ghosh A, Mukhopadhyay P, Pandit K, Chowdhury BK, Choudhury S. A study on endocrine changes in patients in intensive care unit. *J Indian Med Assoc* 2008; 106: 362-364.
- [5] Economidou F., Douka E., Tzanela M., Nanas S., Kotanidou A. Thyroid function during critical illness, 2011 April-June, 10(2):117-24, Pubmed id: 21724536, <http://www.ncbi.nlm.nih.gov/pubmed/21724536>, Athens.
- [6] 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.
- [7] Van den Berghe G, de Zegher F, Baxter RC, Veldhuis JD, Wouters P, Schetz M, et al. Neuroendocrinology of prolonged critical illness : Effects of exogenous thyrotropin -releasing hormone and its combination with growth hormone secretagogues. *J Clin Endocrinol Metab* 1998; 83:309-19.
- [8] Brent GA, Hershman JM. Thyroxine therapy in patients with severe nonthyroidal illness and low serum thyroxine concentration . *J Clin Endocrinol Metab* 1986;63: 1-8.
- [9] Peeters RP, Wouters PJ, van Toor H, Kaptein E, Visser TJ, Van den Berghe G. Serum 3,30,50- triiodothyronine (rT3) and 3,5,30- triiodothyronine/rT3 are prognostic markers in critically ill patients and are associated with post-mortem tissue deiodinase activities. *J clin Endocrinol Metab* 2005;90:4559-65.
- [10] 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; 245:43-5.
- [11] Lim DJ, Herring MK, Leef KH, Getchell J, Bartoshesky LE, Paul DA. Hypothyroxinemia in mechanically ventilated term infants is associated with increased use of rescue therapy. *Pediatrics* 2005; 115:406-10.
- [12] Jyoti C. Suvarna, Chandrashekar N. Fande. Serum Thyroid hormone profile in critically ill children . *Indian Journal of Pediatrics* 2009;76 (12): 1217-1221.
- [13] 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.

- [14] Ture M, Memis D, Kurt I, Pamukcu Z, 2005 Predictive value of thyroid hormones on the first day in adult respiratory distress syndrome patients admitted to ICU: comparison with SOFA and APACHE II scores. Ann Saudi Med 25: 466-472.
- [15] Chinga – Alayo E, Villena J, Evans AT, Zimic M, 2005 Thyroid hormone levels improve the prediction of mortality among patients admitted to the ICU. Intensive Care Med 31: 1356-1361.
- [16] Rothwell PM, Lawler PG, 1995 Prediction of outcome in Intensive Care patients using endocrine parameters. Crit Care Med 23: 78-83.
- [17] Chiolerio R, Lemarchand T, Schutz Y, et al, 1988 Plasma pituitary hormone levels in severe trauma with or without head injury . J Trauma 28:1368-1374.
- [18] Schilling JU, Zimmermann T, Albrecht S, Zwipp H, Saeger HD, 1999 Low-T3-Syndrom bei Polytrauma patienten – Phänomen oder wichtiger pathogenetischer Faktor? Med Klin (Munich) 94: Suppl 3 : 66-69.
- [19] Mocchegiani E, Imberti R, Testasecca D, Zandri M, Santarelli L, Fabris N, 1995 Thyroid and thymic endocrine function and survival in severely traumatised patients with or without head injury. Intensive Care Med 21: 334-341.
- [20] Hackl JM, Gottardis M, Wieser C, et al, 1991 Endocrine abnormalities in severe traumatic brain injury – a cue to prognosis in severe craniocerebral trauma? Intensive Care Med 17 : 25-29.
- [21] Kumar KH, Kapoor U, Kalia R, Chandra NA, Singh P, Nangia R. Low triiodothyronine predicts mortality in critically ill patients; Indian Journal of Endocrinology and Metab 2013; 17:285-8.
- [22] 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.
- [23] Douglas B. Coursin, Michael J. Murray . How sweet is euglycemia in critically ill patients? Mayo Clinic Proceedings, Volume 78, Issue 12, December 2003, Pages 1460-1462.
- [24] Quynh N. Hoang, Margaret A. Pisani, Silvio Inzucchi, Buqu Hu, Shyoko Honiden. (2014) The prevalence of undiagnosed diabetes mellitus and the association of baseline glycemic control on mortality in the intensive care unit: A prospective observational study. *Journal of Critical Care* 29, 1052-1056
- [25] Cao FT, Zhenq ZQ. The changes in insulin sensitivity under stress and its clinical significance in the critically ill patients. PMID:18687177; 2008 Aug; 20(8):482-5.
- [26] Suvarna JC, Fande CN. Serum thyroid hormone profile in critically ill children. Indian J Pediatr 2009; 76:1217-
- [27] Yamada K, Milbrandt EB, Moore J. Intensive insulin therapy in the medical ICU – not so sweet? Intensive Crit Care 2007, 11:311.
- [28] Van den Berghe G, Wilmer A, Hermans G, Meersseman W, Wouters PJ, Milants I, Van Wijngaerden E, Bobbaers H, Bouillon R: Intensive insulin therapy in the medical ICU. N.Engl.J.Med 2006; 354: 449-61 [1].
- [29] Knaus, William A. , Draper, Elizabeth A., Wagner, Douglas P., Zimmerman, Jack E. APACHE II: A

severity of disease classification system. Critical Care Medicine : October 1995- Volume 13 , Issue 10.

- [30] Bermudez F, Surks MI, Oppenheimer JH. High incidence of decreased serum triiodothyronine concentration in patients with non-thyroidal disease. J Clin Endocrinol Metab 1975;41:27-40

### Author Profile



**Mr. Prince Agarwal** :He is now perusing MBBS, final year (III/IV), from Jawaharlal Nehru Medical College, KLE University, Belgaum , Karnataka, India



**Dr. Madhav Prabhu** : He received his MBBS and MD in (General Medicine) degree from Rajiv Gandhi University of Health Science. He is now an associate professor in Department of General Medicine , Jawaharlal Nehru Medical College, Belgavi, Karnataka, India



**Mr. M. D. Mallapur** : He is now an assistant professor of biostatistics, Jawaharlal Nehru Medical College, Belgavi, Karnataka.