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There are two thyroid hormones with biologic activity in vivo one of them, thyroxine (T₄) is produced only by the thyroid gland. The other 3,5,3‘ - Triiodothyronine (T₃) is produced largely by deiodination of T₄ at extrathyroidal sites and the thyroidal contribution to over all T₃ production is small. The recognition that T₃, the more potent of the two hormones, is produced outside the thyroid gland has changed the way that thyroid hormone production and its regulation must be viewed. Thyroid hormone production is not simply dependent on normal hypothalmic- pitutary - thyroid function.

Under normal circumstances 100% of T₄ and 10-20% of T₃ in the serum is directly secreted by the thyroid gland. The remaining 80% of the T₃ is derived from peripheral monodeiodination of T₄ by the enzyme 5‘deiodinase.

In adults and in children many medical and surgical illnesses lead to sick euthyroid syndrome.

Several studies have correlated both the serum T₄ and T₃ levels with increased mortality in adults but little is known in children especially in infants.

In present study the mean serum T₃ and T₄ levels of both critically ill and severely malnourished patients were significantly lower as compared to that of control group. However it was also seen that the difference in mean values of serum TSH in study and control groups were statistically insignificant in both critically ill patients and severely malnourished patients.

J.N. Carter et al (1974) detected striking abnormality in 75 sick euthyroid patients. There was a highly significant reduction in the mean free serum triiodothyronin levels with most patients having total T₃ levels in the hypothyroid range. The severity of illness correlated well with the reduction in total serum T₃ levels. The mean free serum T₃ concentration was significantly lower than in the control patients. The mean total serum thyroxin levels were also reduced significantly although unlike the total serum T₃ levels they remained with in the normal range. Serum TSH was not increased in any patients which is comparable to our study.

Aaron R. Zucker et al (1985) studied 9 children admitted to the ICU. Approximately 24 hours after admission to the ICU, patients had a mean serum T₄ concentration of 6.4± 1.1 μg/dl (normal 4.2 to 11.8 μg/dl in the age range of patient studied) and mean serum T₃ of 74.4±22.7 ng/dl (normal 80- to 210 ng/dl in the age range of patient studied). Six of nine patients had both serum T₄ and T₃ levels below normal for age despite basal serum TSH levels of < 2.5 μlu/ml (normal <6μlu/ml in the age range of patient studied), which is in concordance with our study.
It can also be inferred from our observation that the patients, in whom the course of the disease was fatal, serum T₃ and T₄ levels were low as compared to patients who were discharged. This shows that there was a marked fall in serum T₃ and serum T₄ values in patients whose illness was severe enough to end in mortality. Our study had 9 patients with T₄<5 µg/dl, and six of them died.

In various studies nadir value of T₄ and T₃ or sequential decrease in the values has been correlated to mortality. Mclarty et al (1975) in a study of 30 patients of myocardial infarction showed a sequential and progressive fall in serum T₃ and T₄ levels from the time of admission reaching abnormally low in all six patients who died in their series.

Eisenberg et al (1980) studied a group of seventy-three patients with in 48 hours of admission to the intensive care unit. They found that nonsurvivors had a greater prevalence of decreased serum total T₃ and T₄ than survivors.

Slag MF et al (1981) measured thyroid function in 86 patients hospitalized in an intensive care unit. They found hypothyroxinemia with normal thyroid stimulating hormone (TSH) levels in 22% of the patients and were associated with a high mortality. There was a high correlation between low T₄ levels and mortality. Their results are comparable to our study.

Kaptein et al (1980) in a study of 195 critically ill medical patients correlated clinical outcomes with the lowest of serial T₄ values as well as other thyroid indices. Mortality was inversely related to nadir serum T₄ concentration. Our study also had 9 patients with T₄<5 µg/dl, and six of them died.
N. Uzel and O. Neyzi (1986) investigated thyroid function in critical illness in infancy. Serum thyroxin (T₄), triiodothyronine (T₃), reverse triiodothyronine (rT₃) and thyroid stimulating hormone (TSH) levels were measured in 13 such patients. Significantly lower initial and subsequent T₄ values were found in the fatal group as compared with the control group. Initial T₃ concentrations both in fatal cases and in patients who recovered were significantly lower than those in the controls. Subsequent T₃ values in the group who recovered showed a relative increase, but in the fatal cases a further decrease in T₃ levels accompanied by a decrease in rT₃ levels to values comparable to those of the controls, was observed in the terminal stage.

Similarly like Uzel & Neyzi, N.K. Anand et al (1994) studied 30 infants with severe acute systemic illness and 30 healthy controls age and sex matched. Their T₃, T₄, and TSH levels were measured at admission and recovery or before death. They found that serum T₃ levels in infants were significantly lower than the controls with normal T₄ and TSH levels at admission. This is contradictory to our study and study conducted by Uzel & Neyzi in context of mean serum T₄ levels. However both serum T₃ and T₄ levels increased with recovery. It was also noticed that T₃ and T₄ values were significantly reduced at or near death when compared with the admission levels.

Graham et al (1973) had studied the thyroid hormone levels in nutritionally normal infants and in infants with marasmus or marasmic kwashiorkor. The T₄ level in the study group was 9.5±0.8 µg/dl, and 4.6±0.4 µg/dl in patients of marasmus and marasmic kwashiorkor respectively, which were lower than the control group (mean
In their study they observed that despite normal TBG serum thyroxin may be decreased in marasmus and during recovery; free thyroxin may be high to low initially and normal or low during recovery; serum TSH was low or normal at both times. Their results of marasmic kwashiorker group of patients are comparable to our study.

Ingenbleek (1986) also reported that there were decreased levels of TT₄, TT₃ and FT₃ in patients of PEM. Values of TT₃, TT⁴ and TSH in patients of PEM were 55±37 ng/dl, 3.5±1.1μg/dl and 5.4μlu/ml respectively and in control group the values of TT₃, TT₄, and TSH were 236± 41ng/dl, 8.4±1.2μg/dl and 8.2±2.7 μlu/ml respectively. FT₄ level was normal or even high in short term PEM contrasting with the decline of FT₄ to hypothyroid range in protracted PEM as result of both thyroid failure and exhaustion of liver thyroxin stores serum TSH level was normal throughout the entire course of therapy.

Turkay's et al (1995) also observed the effect of protein energy malnutrition in children on serum thyroid hormones. Serum TT₄ and TT₃ were all reduced in malnourished group. This decrease in TT₃ was statistically significant (P<0.01) in severe malnutrition. They also reported no change in serum TSH level in the PEM and control group as observed by us. The mean values of T₄,T₃ and TSH in their study group were 8.47±0.21 μg/dl, 139.96±3.19 μg/dl and 2.42±0.07 μlu/ml respectively, and in control group the mean values of T₄, T₃ and TSH were 9.29±0.25μg/dl, 156.87±3.50 ng/dl and 2.28±0.08 μlu/ml respectively, which is in concordance with our study.
Das M.D. et al (1999) observed that, the mean serum triiodothyronin (TT₃) and free T₃ (FT₃) level were significantly lower in malnourished children, where as the total thyroxine (TT₄) and thyroid stimulating hormone (TSH) levels were in the normal range. Their study is not correlated with present study regarding TT₄ levels.

Our study amply demonstrates that protein energy malnutrition has deleterious effect on thyroid function. Various hypotheses have been given by different authors to explain these findings. It may be attributed to impaired thyroidal secretion rate (Ingenbleek et al 1976). Low levels of thyrobinding proteins ( Oppenheimer , 1968; Ingenbleek et al 1974, Pain and Phillips, 1976). Relative iodine deficiency associated high fecal loss and malabsorbiton of iodine ( Ingenbleek and Backers, 1973: ingenbleck & Malvaux , 1974) or abnormal thyrotropin secretion ( Pin stone et al 1973, Vinik et al 1975, Croxson et al 1977).

Low plasma TT₃ concentration may also be brought about by decreased peripheral conversion of TT₄ to TT₃. The majority of T₃ in serum arises from monodeiodination of T₄ rather than from direct thyroid secretion ( Portnay et al 1974). Impaired monodeiodination of thyroxine in the liver has been suggested as a contributory factor to the reduced T₃ levels in malnutrition (Ingenbleek & Beckers, 1975).

Impaired T₄ monodeiodination in liver due to reduced activity of 5' deiodinase system resulting in a decrease in serum T₃ and increase in serum rT₃ concentrations commonly known as “ low T₃ syndrome”. Corticosteroids, which are elevated in stress also inhibit T₃ generation from T₄ by inhibiting the 5- deiodinase system.
Different hypotheses for decrease serum concentration of T₄ as well as T₃ have been given by different researchers viz- decreased thyroid secretion rate, decreased serum concentration of thyrobinding proteins like TBG, TBPA and serum albumin, relative iodine deficiency associated with high fecal loss and malabsorbtion of iodine and abnormal thyrotropin secretion.

Normal TSH level is explained on the basis that as T₄ undergoes intracellular monodeiodination to T₃ at the pituitary level, so central feed back mechanisms are apparently preserved, allowing appropriate adaptation of the thyroid.

The importance of changes in thyroid hormone level with non-thyroidal illness is uncertain. At present there is no evidence that T₄ administration is required in euthyroid sick syndrome. Brent and Hershman (1986) studied effects of thyroxin therapy on patients with severe NTI and low serum thyroxin concentration. Thyroxin administration rapidly normalized serum T₄ concentration but T₃ concentration did not increase. Thyroxin therapy in the said study did not augment thyroid hormone action nor did it improve survival. Decreased conversion of T₄ to T₃ in the periphery has been postulated to be the predominant cause of low T₃ levels in spite of T₄ therapy.

A very significant and an interesting observation of our study which has also been reported by other workers is that though thyroid activity is altered in patients of PEM most of the patients remain euthyroid clinically.

The findings suggested that the altered thyroid profile in critically ill patients and in PEM is perhaps a defense mechanism
against excessive metabolic stimulation and energy consumption. The resultant hypometabolism protects the malnourished child with low calorie reserve from an early death.