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EVALUATION OF THYROID PROFILE OF TERM AND PRETERM NEONATES AT 1ST AND 4TH WEEK AFTER BIRTH: A HOSPITAL BASED OBSERVATIONAL STUDY.

Nematology

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ABSTRACT

Objective: To evaluate the thyroid profile(T4,FT4 and TSH) in term and preterm neonates at 1st week after birth and during follow up at 4th week.
Material and Method: This prospective observational hospital based study was conducted with 30 term(>37 completed week) and 30 preterm neonates(from 28 to 36 week 6days) with exclusion criteria of maternal thyroid disease or neonates with co-morbidity or significant congenital anomalies. Serum T4,FT4 and TSH level were measured at 1st week and 4th week of postnatal age and results are analysed statistically.
Results: We found TSH was elevated more in preterm than in term neonates in the 1st week, which decreased in both the groups at the 4th week . T4 and FT4 were significantly higher in the term neonates than in preterm in the 1st week. During follow up in the 4th week, T4 and FT4 decreases in term and increases in preterm so that the FT4 level almost matches in both the group at the end of 1st month.
Conclusion: Our study shows that T4, FT4 and TSH has a significant relationship with gestational age. Premature infants are born with higher levels of TSH and lower levels of FT4 and T4 than term, which almost normalizes at 4th week.

KEYWORDS

Thyroid profile, Term, Preterm, Neonate.

INTRODUCTION.

Thyroid hormones are essential for growth and neurodevelopement of a neonate and growing infant. Because of the delayed maturation of the hypothalamic-pituitary-thyroid axis in preterm infants, thyroid dysfunction is frequently encountered in a preterm baby.

During foetal life, the thyroid gland starts producing thyroxine (T4) and triiodothyronine (T3) from about 12 weeks gestation, the levels of which increase upto term[1]. Throughout gestation, maternal T4 crosses the placenta in limited amounts, but in the first trimester, this plays a critical role in central nervous system development of the foetus[2]. From mid-gestation, hypothalamic expression of thyrotrophin releasing hormone (TRH), pituitary production of thyroid stimulating hormone (TSH), and thyroidal production of T4 rise steadily until 36 weeks gestation[3].

In babies born at more than 30 weeks gestation, T4 and free T4 levels increase over the next six to eight weeks to levels comparable to those of babies born at term[4]. However, in the preterm baby born at less than 30 weeks gestation and with very low birth weight (< 1500 g), the TSH and T4 surges are limited and there is often a fall in T4 in the first one to two weeks after birth, and transient hypothyroxinaemia is common[5]. The more preterm the baby the more pronounced is this hypothyroxinaemia. Although there is an increase in the incidence of transient primary hypothyroidism in these babies with high TSH level ,but this hypothyroxinaemia is often associated with a normal TSH level.

The reason for this hypothyroxinaemia is multifactorial , including the loss of the maternal T4 contribution, immaturity of the hypothalamic-pituitary axis with reduced hypothalamic TRH production and secretion, an immature response of the thyroid gland to TSH, an inefficient capacity of the follicular cell of the thyroid to organify iodine and a low capacity to convert T4 into active T3. Iodine balance is negative in the first few weeks after birth in these very low birth weight babies, suggesting an inability to augment thyroidal iodine uptake and increase T4 secretion[6].

Hence, when a baby is born preterm, the level of T4 is lower than that of term babies and correlates with gestational age and birth weight. Despite low levels of T4 and T3, TSH elevation is often delayed in preterm infants.. This hypothyroxinaemia of prematurity is mostly physiological[7]. So in this study we have tried to compare the level of T4,FT4 and TSH in term and preterm babies in the 1st and 4th week to see any significant difference between the two groups.

MATERIAL AND METHOD:

This hospital-based prospective observational analytical study was conducted in the sick newborn care unit (SNCU) of a district medical college of West Bengal from March 2020 to August 2020. All neonates admitted during this period were evaluated clinically and with necessary investigation and after that 30 term and 30 preterm neonates were selected by simple random sampling after applying the following inclusion and exclusion criteria.

Inclusion Criteria: 1.Preterm infants born at > 28 weeks to 36weeks 6 days of estimated gestational age and 2.Term neonates born ≥ 37 completed weeks of gestational age.

Exclusion Criteria:1.newborns with maternal thyroid disease,2. with significant congenital anomalies,3. with other comorbid conditions such as birth asphyxia, sepsis, respiratory distress syndrome (RDS), patent ductus arteriosus (PDA), intra ventricular haemorrhage (IVH), necrotizing enterocolitis (NEC), bronchopulmonary dysplasia (BPD). Blood sample for TSH, T4 and FT4 was collected in the 1st week preferably between day 3 and 5 and again repeated at 4th week of post-natal life in both the term and preterm groups. Data was analysed by MedCalc statistical software where we have done comparison of mean analysis with $p<0.05$ as statistically significant.

RESULTS:

In this study among the 30 neonates chosen in the term group, 16 were male and 14 were female. While in the 30 neonates of the preterm group, 17 were male and 13 were Female. The average birth weight in the preterm Group (1716.67±237.7 gm) was significantly lower than the average birth weight in the term Group (2465±429.76 gm). ($p<0.001$)

Table 1 Thyroid profile of term neonates

	1st week	4th week	p-Value
TSH(mU/L)	5.92±0.75	3.72±0.53	<0.0001
T4(mcg/dL)	11.95±0.88	10.68±1.23	<0.0001
FT4(ng/dl)	2.11±0.24	1.62±0.29	<0.0001

Table 1 shows that TSH, T4 and FT4 level in term babies are significantly higher in1st week in comparison to 4th week(p-value<0.0001).

Table 2 Thyroid profile of preterm neonates

	1st week	4th week	p-Value
TSH(mU/L)	8.25±4.27	6.28±2.46	0.033
T4(mcg/dL)	6.01±1.75	7.08±1.62	0.017
FT4(ng/dl)	1.41±0.67	1.54±0.53	0.408

Table 2 shows that there is significantly low value of T4 and high TSH in preterm babies in 1st week in comparison to 4th week (p-Value<0.05).Difference of FT4 between 1st and 4th week is not statistically significant.

Table 3 Comparison of thyroid profile of term and preterm at 1st week

	Term	Preterm	p-Value
TSH(mU/L)	5.92±0.75	8.25±4.27	0.0047
T4(mcg/dL)	11.95±0.88	6.01±1.75	<0.0001
FT4(ng/dl)	2.11±0.24	1.41±0.67	<0.0001

Table3 shows that T4 and FT4 are significantly low and TSH significantly high in preterm babies in comparison to term in 1st week (p-Value<0.05).

Table 4 Comparison of thyroid profile of term and preterm at 4th week

	Term	Preterm	p-Value
TSH(mU/L)	3.72±0.53	6.28±2.46	<0.0001
T4(mcg/dL)	10.68±1.23	7.08±1.62	<0.0001
FT4(ng/dl)	1.62±0.29	1.54±0.53	0.47

Table4 shows that T4 is significantly high and TSH low in term babies in comparison to preterm in 4th week (p-Value<0.05). But the difference of FT4 in term and preterm is not statistically significant at the end of 4th week.

DISCUSSION

As preterm infants are born before the maturation of hypothalamic-pituitary-thyroid axis, the normal feedback mechanisms that regulate thyroid hormone production remain immature.

The incidence of this hypothyroxinaemia of prematurity is inversely correlated with gestational age.

In our study we have found that TSH was elevated more in preterm than in term neonates in the 1st week and decreased in both the groups at the 4th week during follow-up. However the TSH level was still higher in the preterm than in the term neonates in the 4th week. T4 and FT4 was significantly higher in the term neonates than in preterm in the 1st week. During follow up in the 4th week, T4 and FT4 decreases in term and increases in preterm so that the FT4 level almost matches in both the group at the end of 1st month. Various other studies on thyroid profile in term and preterm neonates shows almost similar results.

Kapelari K et al in their study found that the variance for TSH, FT4 and T4 was greatest in the first month of life and became narrower with increasing age[8]. Clark SJ et al. in their study of 120 infants born between 25 and 36 weeks of Gestation found that free thyroxine did not correlate with gestational age, but there was a statistically significant correlation of thyrotropin with gestation[9]. Wassenaer V et al. found that smaller and more immature preterm infants have significantly lower FT4 levels than more mature preterm infants or term infants[10]. Delayed TSH elevation has also been associated with low birth weight.

Torkaman M et al. concluded that gestational age was the only factor which affect the FT4 changes over two weeks follow-up although the differences between baseline and follow-up amount of TSH were not significantly influenced by gestational age[11]. However, the adjusted TSH and FT4 serum level changes during follow-up were significantly different between the patients with congenital hypothyroidism and normal preterm.

Zdraveska N et al. in their study concluded that thyroid hormones vary with gestational age, and their levels vary between term and preterm infants[12]. Preterm new-borns are prone to thyroid dysfunction which is now more frequently observed with the advances of neonatal care and improved survival of extremely premature infants.

Our study was not devoid of limitations. The sample size was small and involved a single centre. We have taken only the neonates without co-morbidity and excluded the non-thyroid illness syndrome related hypothyroxinemia of prematurity[13]. Multi centric study with a larger study population is warranted before a more specific pattern of difference is established in thyroid profile between term and preterm neonates.

CONCLUSION

From our study we conclude that TSH, FT4 and T4 level has a significant relationship with gestational age. Premature infants are born with higher levels of TSH and lower levels of FT4 and T4 than term. This altered thyroid profile of preterm has almost normalized and matches with the term babies at around 4th week in our study. So at least two thyroid function tests are recommended at 1st and 4th week of postnatal life to differentiate between physiological hypothyroxin aemia of prematurity or congenital hypothyroidism and neonates with abnormal thyroid profile even at 4th week may warrant further evaluation and management.

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