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Research Article

Study of Thyroxine (T4) and Thyroid Stimulating Hormone (TSH) Levels in Newborns to Find a Correlation between T4 and TSH Levels with Birth Weight

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Abstract: Early detection and treatment of congenital hypothyroidism can prevent mental retardation in early life. Since less than 5% of infants are diagnosed on clinical grounds, therefore the estimation of serum T4 and TSH levels are of paramount significance as early detection and treatment of congenital hypothyroidism in the first month of life might obviate neurological deficiencies in these infants. The present study was conducted on newborns over a period of one year, with an aim to find a correlation between T4 and TSH levels with birth weight of new borns using ELISA technique. It was found that the mean serum T4 decreased with decrease in birth weight and mean serum TSH increased with decrease in birth weight significantly.
Keywords: Thyroxine, TSH, New born, Birth weight, Hypothyroidism, Congenital mental retardation.

INTRODUCTION

The first anatomical description of ductless glands as a group was given in 1766 by Haller who mentioned the thyroid, thymus and spleen as glands, which did not have ducts and hence emptied their secretion directly into the veins. The morphological evidence of internal secretion was first offered in 1836 by king who showed that some of the colloid if the thyroid gland passed into the lymphatics and from there into the circulation.

A better understanding of the complex glandular interrelations was attained with the demonstration that anterior lobe of the pituitary produces several hormones, the combination of which accounts for a variety of physiological effects upon the rest of the endocrine.

Originally classified amongst salivary glands, the thyroid gland received its name from Wharton in 1956 as a descriptive term referring to its square shape. The glandular nature of this organ however remained unrecognized and it was supposed to be engaged in the regulation of blood supply of the brain.

The true significance of the thyroid was understood only after Schieff performed thyroidectomies on dogs with fatal outcome, and successful transplantation was achieved later in a woman who had developed myxedema after thyroidectomy.

Congenital hypothyroidism is the most common cause of preventable mental retardation. It has been shown that when hypothyroid infants are treated before the age of three months, 70% have an I.Q above 85; whereas when treatment is delayed for 3 to 7 months, 85% have definite mental deficiency [1].

80-90% cases of primary congenital hypothyroidism are due to developmental defects of the thyroid gland (thyroid dysgenesis). This includes absence of thyroid gland (atyriosis) or arrested migration of the thyroid gland in the sublingual area (ectopic thyroid) and functional defects in one of the steps involved in the biosynthesis of thyroid hormone (thyroid dyshormonogenesis) which occurs in 10-20 % cases [2].

Since less than 5% of infants are diagnosed on clinical grounds, therefore the estimation of serum T4 and TSH levels are of paramount significance as early detection and treatment of congenital hypothyroidism in

the first month of life might obviate neurological deficiencies in these infants [3].

The ideal time for assessment of T4 and TSH levels in new born is 3-5 days after birth to avoid physiological changes in hormone levels during first 3 days of life [4].

It is ideal to screen all newborns by both T4 and TSH measurements. Various methods such as chemiluminescence radioimmunoassay (RIA) and Enzyme Linked Immunosorbent Assay (ELISA) are used for doing thyroid profile in new born. Out of these ELISA technique is very quick, relatively inexpensive and less cumbersome than RIA technique [5].

Some screening programmes may use cord blood for screening, although TSH levels in cord blood are affected by perinatal factors. The American Academy of Pediatrics recommends that thyroid functions should be repeated during infancy when there is:

- Clinical suspicion of hypothyroidism.
- History of thyroid disease during pregnancy.
- Family history of thyroid dyshormonogenesis.
- Infants with Downs syndrome [6].

With starting of screening programmes for congenital hypothyroidism, several authors have reported transient impairment in neonatal thyroid functions in goiter endemic regions. Anti-thyroid drugs cross the placenta and are excreted in breast milk. As stated, transplacental passage of propylthiouracil (PTU) and excretion into breast milk are less than methimazole (MMI). A detailed clinical examination of new born along with history of drug intake in mother helps in making diagnosis of congenital hypothyroidism [7, 8].

Data on congenital hypothyroidism in india is still scanty because of various reasons. This fact prompted us to undertake this study.

MATERIAL AND METHODS

In the present study all newborns, healthy as well as sick admitted in nursery/ obstetric ward were included in the study.

Inclusion criteria

All the newborns-term, preterm, healthy as well as sick admitted in nursery/ obstetric ward.

Exclusion criteria

Newborns who died within 72 hours of birth were excluded.

A detailed history was taken and was recorded on a prepared proforma related to the obstetric history of the mother-prenatal, natal and postnatal along with age, sex of the child, gestational age, birth weight, clinical features, general physical and systemic examination, laboratory investigations and the outcome of the presenting illness if any, after obtaining the informed consent of the guardian.

Laboratory investigations

The following investigations were carried out in all the newborns after 72 hours of birth and upto 28 days of life.

- Serum T4
- Serum TSH

Method used for estimation of serum T4 and TSH

The method used for estimation of T4 and TSH was Enzyme Linked Immunosorbent Assay (ELISA) technique [9, 10].

Explanation of ELISA procedure

ELISA method is a second generation assay which provides the means for discrimination in the hyperthyroid-euthyroid range. The functional sensitivity of the one hour procedure is 0.195 micro IU /ml [11].

Reference values

Serum TSH:

Preterm: 28-36 weeks (1st week of life): 0.7-27.0 m lU/L

Term infants: Birth to 4 days : 1-38.9 m lU/L

2-20 Weeks : 1.7-9.1 m lU/L

Serum Thyroxine (free T4):

New Born Infants (upto 3 days): 2-4.9 ng/dl

Infants (>3 days) : 0.9-2.6 ng/dl

Pre-pubertal children : 0.8-2.2 ng/dl

RESULTS

Thyroid status in relation to birth weight

The mean value of T4 concentration in babies weighing above 2.5 kg was 1.73 + - 0.16 ng/dl and in low birth weight babies weighing less than 2.5 kg was 1.33 + - 0.29 ng/dl. The mean value of TSH concentration in babies weighing above 2.5 kg was 6.75 + - 0.42 micro IU/ mL and in low birth weight babies weighing less than 2.5 kg was 7.51 + - 0.64 micro IU/mL

Table 1: Thyroid status in relation to birth weight

Birth weight	No. of cases	%	Serum T4 (ng/dl)	Serum TSH (micro IU/ mL)
< 2.5 kg	181	32.37	1.33 + - 0.29	7.51 + - 0.64
2.5 kg or more	378	67.63	1.73 + - 0.16	6.75 + - 0.42
p-value			p<0.001	p<0.001

Table 1 shows the incidence of low birth weight infants was 32.3% and this table shows that correlation between birth weight and serum T4 and TSH statistically highly significant ($p<0.001$).

DISCUSSION

In the present study, out of 559 newborns, 181 newborns were low birth weight infants measuring <2500 g giving an incidence of 32.8 %. The present study revealed significant increase in serum T4 with increase in birth weight but serum TSH levels showed a significant negative correlation with the birth weight.

A study done in 1979 also reported a positive correlation birth weight and serum T4 and negative correlation between birth weight and serum TSH [12].

Elevated serum TSH level in neonates indicates insufficient supply of thyroid hormone to the developing brain. International organizations such as World Health Organization and United Nations Children′s Fund have included neonatal TSH as one of the indicators for assessing iodine deficiency disorders [13, 14].

Detection of Congenital Hypothyroidism by newborn screening program relies on the immunoassay measurement of different combinations of thyroid hormones. Total T4 is not the same as free T4. Free T4 is the more accurate reading of thyroid hormone. Free T4 measures the free, unbound thyroxine T4 levels in blood and generally is lowered in hypothyroidism. However, many newborn screening programs, including those in Australasia, perform a single TSH test as it is simple and there is relatively low false positive rate compared with combined strategies. This strategy will not detect central hypothyroidism and low birth weight and premature babies are a potential source of false negative screens due to hypothalamic immaturity and thus require a second sample [15, 16].

A study was done on 385,000 newborns over a period of 2 years and found 19 cases of congenital hypothyroidism with permanent brain damage. This emphasizes the importance of neonatal screening program and implementation of timely treatment [17].

The measurement of serum concentration of thyrotropin (TSH), a glycoprotein with a molecular weight of 28,000 daltons and secreted from the anterior pituitary, is generally regarded as the most sensitive indicator available for the diagnosis of primary and secondary hypothyroidism [18].

In present study, out of 559 cases, 18 mothers had history of maternal hypothyroidism and were taking eltroxin. The value of T4 and TSH in such infants did not show any significant difference as placenta imposes a relative barrier to the thyroid hormones and is impermeable to TSH so that the foetal hypothalamic-pituitary-thyroid system develops autonomously of the maternal system.

Out of 559 cases, one baby had transient hypothyroxinemia. This is more common in low birth weight infants with or without prematurity, especially if they are sick but may occur in normal newborns occasionally. In this case baby had history of meconium aspiration along with birth asphyxia. The value of serum T4 was below the normal range whereas seum TSH was within normal limits. These values were repeated at six weeks which came out to be within normal limits. Transient hypothyroxinemia does not cause significant ill effects on the development of the new born, hence routine supplementation may not be required, although they need to be followed up closely.

CONCLUSION

Thus to conclude, in the present study, in comparison with birth weight the mean serum T4 decreased with decrease in birth weight and mean serum TSH increased with decrease in birth weight significantly.

To prevent the development of cretinism, most of the developed countries have now initiated neonatal screening programmes for early detection and treatment of hypothyroidism at birth.

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