

Alteration in Thyrotropin Stimulation in Infants below One Year of Age

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ABSTRACT: Thyroid stimulating hormone also known as TSH or thyrotrophin is a peptide hormone synthesized and secreted by the thyrotroph cells of anterior pituitary. It is a glycoprotein in nature and its molecular weight is approximately 30,000Da. It serves as the most useful physiological marker of thyroid hormone action. The present study was undertaken to determine the alteration in thyrotropin stimulation in infants below 1 year of age. This retrospective study was conducted at Clinical Laboratory in north Malabar region of Kerala, over a period of six months from October 2016 to April 2017. Out of 100 samples tested by Immunofluorescence method, 37 children were found to have thyroid function abnormalities. 11 samples having increased and 26 having elevated TSH concentration. From the total of 100 subjects 63 cases were within the normal limits.

KEYWORDS: Thyroid stimulating hormone, glycoprotein, Immunofluorescence, hypothyroidism.

I. INTRODUCTION

Thyroid hormone is essential for the growth and maturation of many target tissues, including the brain and skeleton. As a result, abnormalities of thyroid gland function in infancy and childhood result not only in the metabolic consequences of thyroid dysfunction seen in adult patients, but in unique effects on the growth and /or maturation of these thyroid hormone-dependent tissues as well. In most instances, there are critical windows of time for thyroid hormone-dependent development and so the specific clinical consequence of thyroid dysfunction depends on the age of the infant or child. In the newborn infant, thyroid function is influenced by the neonate's own thyroid gland and by the transplacental passage from the mother of factors that affect the foetal thyroid gland [1].

Optimal functioning of thyroid gland is essential at all stages of life, including pregnancy and foetal development. Sufficient evidence is available showing that thyroid dysfunction during pregnancy can affect the maternal outcome as well the neuropsychological development of foetus. Since the reported prevalence of thyroid disorders during pregnancy ranges from 2 to 5% in pregnant women, it is important that these are detected early for timely intervention. Physiological changes such as haemodilution, increased serum thyroxine-binding globulin and increased human chorionic gonadotrophin especially in the first trimester could affect functioning of thyroid gland and interpretation of thyroid function tests [2].

Congenital hypothyroidism is the most serious cause of an elevated TSH in a newborn. If left untreated, congenital hypothyroidism leads to developmental delay and mental retardation; however, with early treatment, intellectual outcomes are greatly improved. Today more than 70% of the babies worldwide are born in areas without an organized screening program. New insights about genetic causes, screening strategies and treatment of congenital hypothyroidism are reported. Hyperthyroidism in newborns is usually a transient consequence of transplacental passage of TSH receptor stimulating antibodies. Hypothyroidism can be detected in infants born to hyperthyroid mothers, due to transplacental passage of TSH receptor antibodies or hypothalamic-pituitary suppression. In childhood and adolescence autoimmune thyroid disease (AITD) as chronic lymphocytic thyroiditis and Graves' disease account for the main cause of hypothyroidism and hyperthyroidism, respectively. Incidence of AITD increase from infancy to adolescence [1].

Thyroid stimulating hormone also known as TSH or thyrotrophin is a peptide hormone synthesized and secreted by the thyrotroph cells of anterior pituitary. It is a glycoprotein in nature and its molecular weight is approximately

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30,000Da. Glycosylation helps in the stability of the molecule so that it can function properly. TSH production is controlled by thyrotrophin releasing hormone (TRH). It is a tri peptide, which is manufactured in the hypothalamus and transported to the anterior pituitary gland where it increases TSH production and release.

TSH is tropic to thyroid gland influences its activities. There are glycoprotein receptors on the thyroid cell membrane which bind to the receptor binding site on b subunit of TSH. The complex then activates adenylate cyclase which catalyses the formation of cAMP which acts as the second messenger for most TSH actions as follows. TSH stimulates the thyroid acinar cells to secrete thyroid hormones thyroxine (T₄) and tri-iodothyronine (T₃). It stimulates all the steps that is, iodine uptake, synthesis and release of thyroid hormones. Thus plays a pivotal role in the control of thyroid axis. It serves as the most useful physiological marker of thyroid hormone action. TSH increases the synthesis of proteins, nucleic acids and phospholipids in the thyroid gland. It stimulates glycolysis, TCA cycle and HMP shunt. It activates adipose tissue lipase to enhance the release of fatty acids (liposis). TSH also stimulates the metabolism of membrane lipids and this mechanism is probably related to the increased size of thyroid gland. TSH surge immediately after birth. Peaking at 30 minutes at 25 to 160 μ IU/L, values decline back to cord blood concentration by 3 days and reach adult values in the first week of life. There are no significant sex or race differences.

Thyroid Stimulating Hormone(TSH) is the most common immunochemistry test done in a clinical biochemistry laboratory. TSH level altered in many diseased conditions such as immune disorders, iodine deficiency and nodular goitre or due to alterations in the regulation by hypothalamus. Serum concentration of TSH reflects integrated action of thyroid hormones. Thus the measurement of TSH is more reliable in the diagnosis of the thyroid gland dysfunction than is the measurement of thyroid hormone concentration themselves. Pituitary TSH is exquisitely sensitive to circulating thyroid hormone concentration. Because of the circadian fashion in the secretion of TSH, its level varies throughout the day, with early-morning values greater than later ones and is accentuated by sleep deprivation, strenuous exercise or working during the night or evening shifts.

According to the guidelines of the American Thyroid Association (2012), "serum thyrotropin (TSH) is the single best screening test for primary thyroid dysfunction for the vast majority of outpatient clinical situations" [3]. Measurement of TSH is the best initial screening test for the presence of primary hypothyroidism. If the TSH is elevated, then evaluation of the free T₄ will distinguish whether the child has subclinical (normal free T₄) or overt (low free T₄) hypothyroidism. Measurement of TSH, on the other hand, is not helpful in central hypothyroidism.

The most common causes of primary hypothyroidism are iodine deficiency and autoimmune thyroid disease. The diagnosis of primary hypothyroidism is based on a low level of thyroid hormones in association with a high TSH level. Thyroid hormone actions are very important, and even the correction of mild thyroid dysfunction can have a positive impact on health. In many cases, hypothyroidism is suspected early, but sometimes it is diagnosed only when obvious symptoms and signs occur, e.g. goitre, weight gain, cold intolerance, or constipation[4].

II. RELATED WORK

A study conducted by Emilio et al (2015) in Italy, concluded that Iodine intake modulates the pattern of thyroid diseases, and iodine supplementation is associated with an increased frequency of thyroid autoimmunity. Thyroid autoimmunity is associated with an increased risk of PTC (papillary thyroid cancer) however, different factors should be taken into account when evaluating this association. They pointed out Thyroid function may also affect the frequency of PTC, the risk of cancer increasing with serum TSH levels[5].

Another study from China, Weiping Teng et al, reported that although iodine supplementation should be implemented to prevent and treat iodine deficiency disorders, supplementation should be maintained at a safe level. Levels that are more than adequate (median urinary iodine excretion, 200 to 299 μ g per liter) or excessive (median urinary iodine excretion, >300 μ g per liter) do not appear to be safe, especially for susceptible populations with either potential autoimmune thyroid diseases or iodine deficiency[6].

As per the survey conducted by the National Nutrition Monitoring Board (NNMB) in 2000-2001 in rural areas of Kerala, Tamil Nadu, Karnataka, Andhra Pradesh, Maharashtra, Madhya Pradesh, Orissa and West Bengal, the overall prevalence of total goitre rate (TGR) among six to twelve year old children was about 4 percent. The prevalence of goitre was highest in Maharashtra (11.9%) and West Bengal (9%)[7].

The present study was undertaken to determine the alteration in thyrotrophin stimulation in infants below 1 year of age. This retrospective study was conducted at Clinical Laboratory in north Malabar region of Kerala, over a period of

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six months from October 2016 to March 2017. During this period, a total of 100 subjects aged below 1 year of both sex were included.

III. METHODOLOGY

The 3ml of blood samples were collected under aseptic condition and allowed to clot, serum was separated and subjected to TSH assay. Immunofluorescence method (VIDAS Biomerieux, France) was used for estimation of serum TSH. Depending on the normal reference range of TSH, the age group of infants was categorised to 1 day to 7 days, 1 week to 2 week, 2 week to 4 month and 5 month to 12 months.

IV. RESULTS

Among the 100 subjects tested, 9 samples were from the age group between 1 day to 7 days, in which 8 subjects were within the normal range. Only 1 samples shows increased TSH level. Table 1 reveals the age distribution of TSH level in infants below 1 year. 16 samples were received from the age group between 1 week to 2 week. Among them 8 subjects was within the normal value. 5 samples had elevated and 3 samples shows reduced level of TSH. Majority of the samples were from the age group of 2 week to 4 months. A total of 66 samples of children were subjected from this age group. In the present study it was observed that 39 children were within the normal reference range under this age group. Whereas 6 subject's shows increased TSH and 21 samples had decreased concentration of TSH. In our study only 9 samples received from 5 to 12 months. Remarkably 8 subject was within the normal range and 1 samples had elevated TSH. Repeated the test for sharply elevated or declined TSH concentration and that test also revealed the same.

SI No	Age group	Number of samples	Increased TSH	Decreased TSH	Normal
1	1 day to 7 days	09	01	0	08
2	1 week to 2 week	16	03	05	08
3	2 week to 4 months	66	06	21	39
4	5 months to 12 months	09	01	0	08
5	Total	100	11	26	63

Table 1 represent the age distribution of TSH level in Infants below 1 year.

out of 100 samples tested by Immunofluorescence method, 37 infants were found to have thyroid function abnormalities. The value is greater than normal TSH value suspect's hypothyroidism and the value is less than normal TSH value suspect's hyperthyroidism. 11 samples having hypothyroidism and 26 having hyperthyroidism. From the total of 100 subjects 63 cases were within the normal limits. Table 2 represents sex distribution of TSH level in infants below 1 year of age. Among the patients suspected with Hypothyroidism (TSH greater than normal) 27% were males (3) and remaining 73% were females (8). While in the case of suspected Hyperthyroidism (TSH less than normal), 62% were males (16) and 38% (10) were females.

SI No	Sex	High TSH	Low TSH	Normal TSH
1	Male	03	16	32
2	Female	08	10	31
3	Total	11	26	63

Table 2 : Sex distribution of TSH level in infants below 1 year of age

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V. DISCUSSION

Knowledge of foetal thyroid development is of value when managing pregnancies in women with current or previous thyroid disorders (mainly Graves' disease), as maternal status may influence placental metabolism and foetal thyroid function. Transplacental transfer of maternal TRAb (thyrotropin receptor antibodies) may induce foetal thyrotoxicosis, leading to an increased risk of intrauterine death, neonatal mortality and craniostenosis. In addition, the anti thyroid drugs taken by these mothers cross the placenta and block foetal thyroid hormonogenesis, thus affecting skeletal and neurological development [8].

The remarkable result emerge from this retrospective study was there is an alteration in thyrotropin infants below 1 year of age. 11 samples having hypothyroidism and 26 having hyperthyroidism. To date no work regarding TSH concentration among has been published in this north Malabar region of Kerala. One limitation of our study was the sample size, which was too small. A large sample would be able to make more accurate predictions.

Brahmbhatt S R et al [9] (2001) from Gujarat, reported that the prevalence of hypothyroidism was about 7% and iodine deficiency continues to be a problem, as more than 20% of the population had a very low median urinary iodine of <50 µg/l. Another study conducted by Marwaha RK et al from Cochin (2010) [10] revealed that the occurrence of hypothyroidism was only 3.9%. But our study shows 11% of hypothyroidism among infants below 1 year of age. This study doesn't correlate with the findings of Brahmbhatt et al that the iodine deficiency leads to hypothyroidism, but suspects that children who suffer from hypothyroidism may do so as a result of the deficiency of iodine. An immature hypothalamic-pituitary-thyroid axis and postnatal depletion of thyroxine stores by the end of the first week, administration of drugs (dopamine, steroids) and iodine exposure may all lead to thyroid insufficiency in newborns [11].

The high levels of TSH in children may due to mothers with preeclampsia, placental insufficiency or foetal hypoxia which in turn triggers higher TSH levels in the neonate. The variation in the TSH value (High/Low) depends on the various factors such as immunological deficiencies, disease of the thyroid gland, abnormal production in TRH (thyroid releasing hormone) level, iodine deficiency and age of the children. Despite the successful implementation of National Iodine Deficiency Disease Control programme in India, thyroid function abnormalities are still prevalent in many part of the country. The epidemiological significance of elevated TSH in infants below 1 year of age vary with in the geographical area as well as thyroid dysfunction of mother. Many cases of hypothyroidism and hyperthyroidism remain un recognized in India. However, further studies has to be done to know their role as emerging threat for healthy life.

VI. CONCLUSION

In conclusion, there is significant alteration in thyrotropin stimulation in infants below one year of age (37%) in North malabar region of kerala. Since the sample size was too small to predict more accurate value of TSH, further studies has to be done in this region. But thyroid abnormalities may lead to serious neurological disorders and affect the mental development also. So early detection of thyroid dysfunction through neonatal screening has inevitable role in the prevention of neurological disorders and thus it become a mandatory test during the neonatal period or childhood.

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