

Case Report

Congenital hypothyroidism : Importance of neonatal screening in preventing neurocognitive deficit

Sudhir M Naik¹, Sarika S Naik²

Congenital hypothyroidism is one of the most common preventable causes of mental retardation in children. The prognosis of infants detected by neonatal screening and started on treatment early is excellent, with intelligence quotients similar to sibling or classmate without the disease. Department of ENT, Head and Neck Surgery, KVG Medical College, Sullia. A 15 year old boy came with history of head ache, generalized body ache and lack of concentration in school. He was a case of congenital hypothyroidism and was on irregular treatment for the last 13 years. The patient was advised strictly to continue the oral l-thyroxine 100µg one hour before food and come for regular follow-up. Definite intellectual deterioration is seen if oral l-thyroxine is not started within 50 days of life and the deterioration is irreversible. So in India newborn screening programs should be implemented as a national program as it is very important to diagnose and treat congenital hypothyroidism as soon as possible and to treat it effectively.

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Key words : Hypothyroidism, neonatal screening, l-thyroxine, neurocognitive development.

Thyroid hormone plays a critical role in the development and maturation of the fetal brain¹. Deficient production of thyroid hormone or a defect in thyroid hormone receptor activity can lead on to hypothyroidism¹. Congenital hypothyroidism (CH) is one of the most common preventable causes of mental retardation in children¹. The incidence in India is estimated to be 2.1 per 1000 live births which is at least 8 times higher than what is reported in western literature¹.

CH was defined as TSH more than 20 mIU/L at less than 2 weeks of age or TSH more than 10mIU/L after 2 weeks of age². Clinical features are not present at birth as some maternal thyroid hormone pass trans-placentally and is sufficient till the newborns thyroid starts functioning on its own³. Newborn screening programs should be confirmed by finding an elevated serum TSH and low T4 or free T4 level⁴. Other diagnostic tests, such as thyroid radionuclide uptake and scan, thyroid sonography, or serum thyroglobulin determination may help pinpoint the underlying etiology, although treatment should be started without these tests⁵.

Oral levothyroxine being the drug of choice and the starting dose is 10 to 15 µg/kg/day³. The immediate goals of treatment are to rapidly raise the serum T4 above 130 nmol/L (10 µg/dL) and normalize serum TSH levels³. Frequent biochemical thyroid profiles monitoring in infancy is essential to ensure optimal neurocognitive outcome³. Serum TSH and free T4 should be measured every 1-2 months in the first 6 months of life and every 3-4 months thereafter³. In general, the prognosis of infants detected by screening and started on treatment early is excellent, with intelligence quotients similar to sibling or classmate without the disease³.

Studies show that a lower neurocognitive outcome may occur in those infants started at a later age (>30 days of age), on lower l-thyroxine doses than currently recommended, and in those infants

with more severe hypothyroidism³.

Neonatal screening programs for detection of CH in neonatal period are widespread in the developed countries for the last three decades and are fast gaining momentum in India as well^{6,7}. In most screening programs blood samples are collected at 5-6 days age, but with large number of babies being discharged early, cord blood samples are being used as well^{8,9}.

In India, it is very difficult to call back babies once discharged and an effective health system whereby babies who can be examined at home is practically impossible^{8,9}. Thus cord blood remains a very practical alternative for screening purposes, and thus is the practice in some Asian countries^{8,9}. The Indian Academy of Pediatrics recommends the use of cord blood samples for screening for congenital hypothyroidism¹¹.

CASE REPORT

A 15 year old boy came with history of head ache and generalized bodyache and lack of concentration in school. He was examined in the department of ENT, KVG medical college and was found that he was a case of CH and was on irregular treatment for the last 13 years. Biochemical thyroid profile showed T3- 59ng/dl, T4 - 2.10 µg/dl and TSH -38.39 µIU/ml suggesting hypothyroid status. The patient had stopped taking elthroxin for the past 1 month causing a recurrence of the hypothyroid status.

Sonography of the neck showed both lobes were small in size with mild hypoechoic echotexture. The right lobe was 1.09x0.36x0.98 cm in dimension and the left lobe 0.8x0.67x0.96 cm in dimension. A benign lymph node measuring 5.7x2.7 mm was noted which had a fatty hilum on the left side at level². Major vessels of the neck were normal. The sonography concluded that the overall size of the thyroid was reduced with mild hypoechoic echotexture and benign cervical lymphadenopathy (Fig 1).

Presently the patient did not complain of decreased urine output or passing high colored urine but had constipation. The parents complained of poor school performance less in par with other children of his age. Slurred speech was present but no hoarseness was

Department of ENT, Head & Neck Surgery, KVG Medical College, Sullia, Kurunjibag, Karnataka 574327

¹MBBS, MS (ENT), Associate Professor and Corresponding author

²MBBS, DA, Senior Resident, Department of Anaesthesia

seen. Cold intolerance was present but no history of decreased activities and played well with other children.

Neonatal screening was not done in this patient and clinical diagnosis was missed in him till 2½ years. At the age of 2½ the parents took the baby to clinician with swelling of the face and abdomen of 1 week duration. The swelling and puffiness were uniform throughout his face not localized to the eyes and present only in morning hours. A uniform painless distension of the abdomen was seen of week duration. Reflexes were exaggerated but superficial and babinski reflexes were diminished. Clinical diagnosis of hypothyroidism was done and the investigations showed T3- 0.25ng/ml (0.75-2.4), T4- 0.96µg/dl (4.7-11.1), TSH- 51.90 µIU/ml (0.2-5.0), serum cholesterol -566.0 mg/dl, Hb% - 9.0g/dl, blood urea- 35 mg/dl, serum creatinine - 1.8 mg/dl, total protein- 505 g/ml, serum albumin-2.5 gm/dl, serum globulin- 3.0 g/ml, TC -5000 cells/mm³, DC-neutrophil-40%, eosinophil-2%, lymphocyte- 56%, basophil- 5%, monocytes- 2%.

Peripheral blood smear showed normocytic hypochromic anemia. ECG showing low voltage complexes in all leads. Chest X-ray was within normal limits. X-rays of both the wrists joints showed delayed bone age corresponding to 5 years of age and the present X-ray wrists seems normal (Fig 2). His younger sister and brother were screened for hypothyroidism and found to be normal. In 100µg of elthroxin once orally in the morning one hour before food was started at 2½ years of age warning his parents not to stop the drug at any instance. The patient was advised initial 3 month follow up till 4 years and 6 months follow up till 10 years as literacy in family was low frequent follow were necessary. The patient had regular follow up till 6 years and later became irregular. He consulted with complains of relapse and later was advised to continue l-thyroxine. The patient is seen at 2½ years, 14 years and at 15 years (Fig 3).

DISCUSSION

Congenital hypothyroidism (CH) is defined as thyroid hormone deficiency present at birth¹. Thyroid hormone deficiency at birth is most commonly caused by a problem with thyroid gland development (dysgenesis) or a disorder of thyroid hormone biosynthesis (dys-hormonogenesis)². These disorders result in primary hypothyroidism³.

Secondary or central hypothyroidism at birth results from a deficiency of thyroid stimulating hormone (TSH)³. Congenital hypothyroidism is classified into permanent and transient CH³. Permanent CH refers to a persistent deficiency of thyroid hormone that requires life-long treatment³. Transient CH refers to a temporary deficiency of thyroid hormone, discovered at birth, but then recovering to normal thyroid hormone production³. Recovery to euthyroidism typically occurs in the first few months or years of life³.

Permanent CH can be further classified into permanent primary and secondary (or central) CH; transient primary CH has also been reported³. The underlying etiology of CH typically will determine whether hypothyroidism is permanent or transient, primary, secondary, or peripheral, and whether there is involvement of other organ systems³. Screening a newborn for congenital hypothyroidism is very important as mental retardation can be prevented in



Fig 1 — Sonography of the right and left thyroid lobes showing short dimensions of the thyroid gland



Fig 2 — Sonography of the thyroid and xray of the wrists

85% of the cases with early initiation of thyroxine supplementation therapy before 3 months of age¹². The incidence of the cases have risen from 1:7,000 to 1:10,000 to 1:3,000 to 1:4,000 after the introduction of worldwide newborn screening programs^{13,14}.

The incidence of congenital hypothyroidism in India varies from 1:2500 to 1:2800 live births¹⁵. Universal neonatal screening has been acknowledged as the most effective method to prevent the severe developmental and physical morbidities associated with congenital hypothyroidism¹⁶. However, despite proven benefits, efforts to implement it in India are still in its infancy¹⁶. CH features manifest minimally at birth making it difficult to diagnose on the basis of clinical features alone¹⁶.

Clinical diagnosis is made in only 10% children in the first month of life and 30% in the first 3 months¹⁷. Hence there is a high risk of delayed diagnosis exposing the child to various degrees of developmental delay¹⁷. In view of the high incidence, apparently asymptomatic nature, propensity to cause neuro-developmental delay and residual impairment even with treatment, early detection and treatment of CH would be the most cost effective method to confront this problem³. Despite the crushing evidence of high inci-



Fig 3 — Growth patterns at 2½ years, 14 years and 15 years

dence of CH, India continues to await a plausible universal screening program¹. It is high time we start routine neonatal screening for CH to tackle this preventable cause of mental retardation¹.

As considerable difference in inheritance, prognosis and therapy are present, finding the etiology of the condition is important¹⁸⁻²⁰. Thyroid dysgenesis (aplasia, ectopia, or hypoplasia) amounts to 80%, dysmorphogenesis amounts to 10-15%, pituitary or hypothalamic hypothyroidism, transient hypothyroidism and autoimmune mechanisms less than 5% of cases of CH¹⁸⁻²⁰. Thyroid hormone replacement should be administered to all cases with biochemical confirmation of the diagnosis of hypothyroidism¹⁷. Even, cases of ectopic gland should be treated even if laboratory data reveal borderline or compensated hypothyroidism to prevent complications from enlargement of lingual or sublingual thyroid tissues¹⁹. Screening the newborn for presence or absence of functioning thyroid tissues is clinically important as functioning thyroid tissues have better neuro-psychologic prognoses than those without^{19,20}.

CH due to enzyme defect in thyroxine production follow an autosomal recessive pattern of inheritance hence genetic counseling is required for patients with this disorder¹⁸⁻²⁰. CH could also result from transient abnormality in thyroid gland function, which subsequently recovers²¹. The possible explanations include iodine deficiency, transplacental passage of maternal TSH-binding inhibitory antibodies, and maternal exposure to radioiodine, iodine or antithyroid drugs²¹.

Muir *et al*, in their 50 case study concluded that sonography cannot be an alternative to thyroid scintigraphy to define the cause of CH²⁹. Takashima *et al*, suggested that thyroid scintigraphy is required only in patients with no visibility of the thyroid gland in the normal location and patients with an enlarged gland in the normal anatomic place with ultrasound²². Sonographic analysis has a potential to predict the prognosis of patients with suspected CH²².

The condition is often subtle in presentation and many newborn infants remain undiagnosed at birth^{23,24}. This is due to passage of maternal thyroid hormone across the placenta as it has protective effect on the fetal brain^{25,26}. Even it is reported that the commonest form of CH has some moderately functioning thyroid tissue^{25,26}. As the clinical features developed slowly and the need for early treatment has led to rampant newborn screening programs^{25,26}. Only 35% world newborn population are screened and the major hit are the third world population, so clinicians here should recognize the disorder early^{25,26}.

On initial examination, the most common signs are umbilical hernia, macroglossia and cold or mottled skin^{25,26}. Symptoms are not typical but maternal and pregnancy history is informative^{25,26}. In 20% of cases gestation exceeds 42 weeks^{25,26}. Hoarse cry, constipation, neonatal hyperbilirubinemia more than 3 weeks due to immaturity of hepatic glucuronyl transferase are common features seen^{25,26}.

Thyroid hormone is also important in the formation and maturation of bone^{27,28}. Deficiency leads to a wide posterior fontanel of greater than 5 mm^{27,28}. This, along with persistent jaundice and poor feeding are the most striking clinical features^{27,28}. Common symptoms include decreased activity and increased sleep, feeding difficulty, constipation, and prolonged jaundice. On examination, common signs include myxedematous facies, large fontanels, macroglossia, a distended abdomen with umbilical hernia, and hypotonia⁷. Neurologic examination findings include hypotonia with delayed reflexes²¹. Skin may be cool to touch and mottled in appearance reflecting circulatory compromise²³. X-rays can reveal absent femoral epiphyses in up to 54%²⁹.

CH appears to be associated with an increased risk of congenital malformations³⁰. The prevalence of these extra thyroidal congenital malformations amount to 8.4%, cardiac malformations being more common³⁰. Other associated malformations include spiky hair, cleft palate, neurologic abnormalities and genitourinary malformations³⁰. Also, the incidence of congenital hypothyroidism is increased in patients with Down's Syndrome³¹.

CONCLUSION

On detecting congenital hypothyroidism by neonatal thyroid screening programs treatment should be commenced within first month of life which makes prognosis for intellectual development better. Complete restoration of intellectual performance may not always be possible due to prenatal thyroxine deficiency.

Definite intellectual deterioration is seen if the treatment is not started within 50 days of life and the deterioration is irreversible. So in India newborn screening programs should be implemented as a national program as it is very important to diagnose and treat congenital hypothyroidism as soon as possible and to treat it effectively.

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