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Original Research Article

A Prospective Observational Assessment of the Emerging Role of a Newborn Screening Program for Congenital Hypothyroidism

Jeetendra Mahato[1], Vivek Kumar[2], Gopal Shankar Sahani[3]

[1]Assistant professor, Department of Pediatrics, SKMCH, Muzaffarpur, Bihar, India
[2]Senior Resident, Department of Pediatrics, SKMCH, Muzaffarpur, Bihar, India
[3]Associate professor and HOD, Department of Pediatrics, SKMCH, Muzaffarpur, Bihar, India

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Corresponding author: Dr.Gopal Shankar Sahani
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Abstract

Aim: To evaluate the incidence & screening of neonates for congenital hypothyroidism for timely diagnosis and integral psychomotor development.

Material & Methods: This was a prospective study carried out in the Department of Pediatrics, SKMCH, Muzaffarpur, Bihar, India, over a period of two years. All live newborn gestational age > 34weeks delivered and out born delivered with an age of fewer than five days.

Results: A total of 1281 babies were enrolled, but 800 were an eligible candidate for the study period. Of the total eligible neonates, 651 were term babies and 149 were preterm babies with more than 34 weeks. Neonatal thyroid-stimulating hormone was estimated in all 783 neonates out of whom 4 cases were positive for CH, 14 cases had initially high values between 10-19 μIU/L.

Conclusion: Timely diagnosis and treatment of CH are important in order to prevent its consequences. NBS is the need of the hour for early diagnosis of CH, which is simple, fast as well as cost-effective.

Keywords: Congenital Hypothyroidism, Neonate, Thyroid hormone

Introduction

Congenital hypothyroidism (CH) is a heterogeneous entity. At birth, most countries effectively screen for primary CH by thyrotropin (TSH) determination [1]. However, this approach misses central CH (CCH), which is caused by disorders of the hypothalamic-hypophyseal system and characterized by impaired TSH production, resulting in low circulating thyroid hormones in combination with low, inappropriately normal, or slightly elevated TSH levels [2].

Although CCH was previously assumed as a rare, mild, and non-relevant disorder, nowadays its spectrum includes an important risk of morbidity, especially when severe cases remain untreated [3, 4].

The main underlying cause of CCH is combined congenital pituitary hormone

deficiency (CCPHD), mostly associated with growth hormone (GH) and adrenocorticotropin (ACTH) deficiencies. This may result in recurrent hypoglycemia and acute adrenal insufficiency with impairment of growth and neurodevelopment [2, 5, 6].

Symptoms of congenital hypothyroidism are initially nondescript; however, the maternal and pregnancy history may provide some clues. In twenty percent, gestation extends beyond forty-two weeks [7].On initial examination, the most common signs are umbilical hernia, macroglossia and cold or mottled skin [8]. Thyroid hormone is also important in the formation and maturation of bone [9, 10].This can lead to a wide posterior fontanel of greater than 5 mm.

Congenital hypothyroidism may be permanent (thyroid aplasia, hypoplasia, ectopia or dyshormonogenesis) or transient (due to maternal blocking antibodies, iodine excess or deficiency, or some types of dyshormonogenesis [11]. Central hypothyroidism is caused by dysfunction of hypothalamic or pituitary control of the thyroid axis that leads to inadequate production and/or bioactivity of TSH. Congenital hypothyroidism of central origin is rare. Permanent CH required lifelong treatment and monitoring whereas, transient CH shows normal thyroid hormone production after the first few months. TSH screening is more sensitive for diagnosis, while T4 is more specific.

This study is an attempt to evaluate the incidence & screening of neonates for congenital hypothyroidism for timely diagnosis and integral psychomotor development.

Material & methods:

This was a prospective study carried out in the Department of Pediatrics, SKMCH, Muzaffarpur, Bihar, India, over a period of two years. A total of 1281 babies were enrolled, but 800 were an eligible candidate for the study period. Before sampling well written informed consent was taken from either of the parents.

Inclusion criteria: All newborns with a gestational age of 34 weeks or more delivered in the hospital during the study period were included in the study.

Exclusion criteria: Preterm neonates with gestational age less than 34 weeks, blood transfusion prior to sampling, refusal of informed consent and out born babies with age more than 5 days were excluded from the study.

Methodology

All live newborn gestational age > 34weeks delivered and out born delivered with an age of fewer than five days. The study was approved by the institutional ethics committee. A well written informed consent was taken from all of the participants after explaining the details, benefits, and risks to them.

The blood sample was taken in a sterile container under aseptic precautions, between 3-5 days of life to minimize the false positive high TSH values due to the physiological neonatal surge that elevates TSH level and causes T4, T3 changes in 1-2 days. In cases with a healthy newborn baby, sampling was done between 3-5 days.

Detailed antenatal history, parity, medical history, thyroid status, and community were recorded on a predesigned proforma. Details of the baby were recorded on a separate proforma. TSH was estimated within 24 h by chemiluminescence Immunoassay (kit supplied by Roche E411). Newborn with TSH value more than 20μ IU/L were labeled as a case of congenital Hypothyroidism and whose values were between 10-20 μIU/L were followed up with repeat TSH level after weeks.

Interpretation of screening test: Venous TSH >20 mIU/L (serum units) is taken as the cut-off for postnatal screen samples after 48-72 hours of age is to be taken as positive newborn TSH between 10- 20 mIU/L were taken for a second TSH sample at 7 to 10 days of age.

All the data were analyzed by descriptive statistics and expressed in terms of percentage and tabulated form. The analysis was done on Microsoft Excel 2013**.**

Results:

A total of 1281 babies were enrolled, but 800 were an eligible candidate for the study period. Those, not eligible candidates received a blood transfusion, death within 3 days, left against medical advice (LAMA) or shifted to other hospitals and nonconsenting of parents for the study.

Numbers of term deliveries were 651 and preterm deliveries were 149, with 488 (61%) males and 312 (39%) female babies. Of the total eligible neonates, 651 were term babies and 149 were preterm babies with more than 34 weeks (Table 1).

Neonatal thyroid-stimulating hormone was estimated in all 783 neonates out of which 4 cases were positive for CH, 14 cases had initially high values between 10-19 μIU/L which were later on repeat testing after two weeks were found to be in normal limits.

(Table 2).

Table-1: Demographic profile from the study. (N=800)

Variable	Number	Percentage
Mother's age (Years)		
=18-25	401	50.13
26-30	300	37.5
>30	99	12.38
Sex		
Male	488	61
Female	312	39
Gestational age (Weeks)		
34-<37 weeks (Preterm)	149	18.63
=37 weeks (Term)	651	81.38
Birth weight (Kg)		
<2.5 kg	242	30.25
=2.5 kg and above	558	69.75
Mode of delivery		
LSCS	482	60.25
Normal	270	33.75
Maternal history of hypothyroidism	48	6

Table-2: TSH value among Neonates.

Variable	TSH value at 48-72hrs	TSH value after 14days
TSH < 10mIU/L	783	Normal

TSH 10-20mIU/L	14	Normal
TSH >20mIU/L	03	Higher

Discussion:

Neonatal screening programs are an invaluable public health tool. Created to detect certain congenital diseases, they aim at modifying their deleterious natural course. They started in the early 1960s and progressively expanded with new determinations to accurately identify and treat metabolic, neurological, and endocrine diseases. Nevertheless, their use in the approach to new diseases should be based on updated information on the disorder, its prevalence, natural course if undetected, available tools for detection, and treatment and cost benefits. [12]. CCH encompasses a group of rare diseases that frequently remains unrecognized during the neonatal period.

Infants who have serum T4 concentrations below 10 μg/dL in the first year of life accompanied by serum TSH concentrations above 15 mU/L have been shown to have lower IQ's than infants whose serum T4 concentrations are above 10 μg/dL [13]. Also, higher doses of l-thyroxine have been associated with higher intelligence quotients at 7 and 8 years of life, especially in the areas of verbal memory and verbal comprehension [14]. Thirdly, variations in serum T4 and TSH during the first year of life have been correlated with changes in mental development index and verbal intelligence quotient [13, 15].

Babies who received active intervention in the form of resuscitation and LSCS for fetal distress were expected to have raised TSH levels as a response to the stress that they had endured due to the procedures. Thus raised TSH in these neonates has to be interpreted in that context. The incidence of consanguinity is very common in India and varies from 1 % in the northern region to 30% in Karnataka [16]. Thus, the incidence of expression of autosomal recessive CH is raised in these geographic regions.

The male to female ratio in the present study was 1:1 while 1.2:1 was in Japan [17] in Bosnia [18] and 1.8:1 in Saudia Arabia [19]. However, some studies did not find any significant differences in mean TSH level according to sex [20-21] Out of the two babies who were diagnosed CH both were male. [22]

Conclusion:

Timely diagnosis and treatment of CH are important in order to prevent its consequences. NBS is the need of the hour for early diagnosis of CH, which is simple, fast as well as cost-effective. Although universal newborn screening is implemented in developed countries; our country has still not implemented this universally.

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