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Newborn Screening for Congenital Hypothyroidism in India is Still Overdue

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Abstract

Deficient in the production of thyroid hormone or any defect in thyroid hormone receptor activity can lead on to hypothyroidism. Congenital hypothyroidism (CH) is one of the most common preventable causes of mental retardation in children. In our study all the babies were screened by intravenous blood samples collected between 48-96 hours of age and identified 3 babies with CH. Along with CH screening, necessary investigations done were blood grouping and serum bilirubin as a standard hospital policy. The TSH was measured by Electrochemiluminescence immuneassay method. Newborn screening for congenital hypothyroidism (CH) by intravenous blood TSH screening in our institute has been effective as a screening tool. From our study, there is no doubt that CH screening fits into the criteria of the diseases that needs to be screened in India, as the incidence in our study of nearly 1:1050 is high and should not be ignored.

Keywords: Thyroid; Hormone; Infant; Congenital.

Introduction

Thyroid hormone plays an important role in the development and maturation of the fetal brain. Deficient in the production of thyroid hormone or any defect in thyroid hormone receptor activity can lead on to hypothyroidism. Congenital hypothyroidism (CH) is one of the most common preventable causes of mental retardation in children [1].

The worldwide incidence is 1:3000-4000 live births.[2] 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 age [3]. 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 own [4].

Newborn screening programs should be confirmed by finding an elevated serum TSH and low T4 or free T4 level [4]. Other diagnostic tests, such as thyroid radionuclide uptake and scan, thyroid sonography, or serum thyroglobulin determination may help pinpoint the underlying etiology, if not possible treatment should be started. Aetiological workup can be done after 2-3 yrs.

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 disease [4]. 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 [5-10].

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 [10,11]. 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 [10,11].

Screening the newborn for presence or absence of

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functioning thyroid tissues is clinically important as functioning thyroid tissues have better neuro-psychologic prognoses than those without [12,13]. Despite the crushing evidence of high incidence of CH, India continues to await a plausible universal screening program.

Materials and Methods

Source of Data

A hospital based observational study was performed on term neonates fulfilling inclusion criteria over a period of one year and 9 months at department of Paediatrics, Sangameshwar and Basaveshwar Teaching general hospital attached to Mahadevappa Rampure Medical College,Kalaburagi from December 2014 to September 2016.

Method of Collection of Data

In our study all the babies were screened by intravenous blood samples collected between 48-96 hours of age and identified 3 babies with CH. Along with CH screening, necessary investigations done were blood grouping and serum bilirubin as a standard hospital policy. The TSH was measured by Electrochemiluminescence immuneassay method. With values greater than 20 micIU/L whole blood was reported as abnormal and requiring follow up. Primary TSH, back up T4method: TSH is measured first, and T4 is measured only if TSH is >20 mu/L. Abnormal values on screening was confirmed by a repeat venous sample using age appropriate cut-offs of more than 20 mIU/L. We initiated treatment after drawing the infants sample if TSH >20 mIU/L or T4 is low. For intermediate screening values of TSH, with normal T4 (if available), the treatment was initiated only after confirmation of diagnosis based on the blood report.

Selection Criteria of the Patients

Inclusion Criteria

In the present study all babies born at Basaveshwar teaching general hospital & Sangameshwar teaching general hospital, Kalaburagi were screened for congenital hypothyroidism.

Exclusion Criteria

Newborns needing NICU admission, birth asphyxia, congenital anamolies, preterms.

Statistical Analysis

Keeping in view the aims and objectives of the study, the different variables were identified. The code book as per the requirements of the study was prepared. Data was subjected to univariate, bivariate analysis using Chi-Square Test, large sample Z test & unpaired t test. Data was fed and processed using Statistical Package for Social Scientist (SPSS) Version 16.0.

Results

Table 1: Distribution of neonates according to level of serum TSH

Sr. TSH	No. of Study Samples	%	Congenital Hypothyroidism Cases	%
<1	1027	32.62	0	0.0
1.01-5.0	1853	58.82	0	0.0
5.01-10.0	226	7.18	0	0.0
10.01-15.0	30	0.96	0	0.0
15.01-20.0	04	0.18	0	0.0
>20	05	0.16	3	100.0
Total	3150	100.0	3	100.0

In the present study, majority of the babies (58.82%) had serum TSH values between 1.01 and 5.0 µIU/ml, TSH values ranged less than 1 µIU/ml in 1027 babies (32.62%), 226 babies (7.18%) had TSH values between 5.01 and 10.0 µIU/ml, TSH values were between 10.01 and 15.01 µIU/ml in 30 babies (0.96%), 4 babies showed TSH values between 15.01 and 20.0 µIU/ml and in 5 babies the TSH values were more than 20 µIU/ml.

Out of 3150 babies screened, maximum number of babies 2018 (64.1%) belonged to the age group of 3-4 days, followed by 964 babies (30.6%) in the age group 1-2 days, 113 babies (3.6%) in the age group 5-6 days and 55 babies (1.7%) were more than 7 days old. There was no statistical significance difference of age among males and females neonates. Out of 3150 babies included 1618 (51.4%) were males and 1532 (48.6%) were female babies and the male to female ratio was 1.05:1. Male to female sex ratio of congenital

hypothyroidism cases was 2:1. There is no statistical significance difference of sex in the incidence of congenital hypothyroidism. Present study reveals the incidence of congenital hypothyroidism with 0.95 for every 1000 neonatal cases and the ratio of CH cases is 1: 1050. Maximum number of congenital hypothyroidism cases (66.7%) were in age group of 3-4 days followed by one case was more than 7 days old. The mean serum TSH level was very high (145.5) in the age group of 3-4 days as compare to higher age group of greater than 7 days showing mean serum TSH of 20.1 in congenital hypothyroidism cases. Out of 3150 babies, 1599 (50.8%) were delivered through normal vaginal delivery and 1551 (49.2%) by lower segment caesarean section. All the three cases of congenital hypothyroidism were delivered by LSCS. In the present study 25 mothers had history of recurrent abortions, but none of the mothers of congenital hypothyroidism cases showed history of illness. In the present study, 176 mothers complained of poor feeding in their babies and 30 mothers complained of excessive sleeping. 83 babies (2.63%) showed prolonged jaundice, 50 babies (1.59%) had constipation, 19 babies had open posterior fontanel 2 babies (0.06%) each had hoarse cry and hypothermia respectively and only one baby (0.03%) had hypotonia. In the present study, majority of the babies (58.82%) had serum TSH values between 1.01 and 5.0 μIU/ml, TSH values ranged less than 1 μIU/ml in 1027 babies (32.62%), 226 babies (7.18%) had TSH values between 5.01 and 10.0 μIU/ml, TSH values were between 10.01 and 15.01 μIU/ml in 30 babies (0.96%), 4 babies showed TSH values between 15.01 and 20.0 μIU/ml and in 5 babies the TSH values were more than 20 μIU/ml. Mean serum TSH value of CH cases was found to be 104.23±58.3 which has statistically significant p value.

Discussion

The world has progressed a long way since the first pilot screening programs started in Quebec and Pittsburgh in 1974. At present, screening programs are well established in North America, Europe, Japan, Australia and some parts of U.K[14,15,16]. Maternal T4 plays a role in fetal development especially that of the brain, before the synthesis of fetal thyroid hormone begins. The fetus of a hypothyroid mother may be at risk for neurologic injury, and a hypothyroid fetus may be partially protected by maternal T4 until delivery. The amount of T4 that crosses the placenta is not sufficient to interfere with a diagnosis of congenital hypothyroidism in the neonate [18].

If fetal hypothyroidism develops, untoward effects may be demonstrated in certain organ systems especially in central nervous system & skeletal system. However most infants at birth appear physically normal. Serum thyroxine (T4) levels in the cord blood of athyroid fetuses approximate one third of maternal levels [1]. In addition, studies in animal models of hypothyroidism demonstrate increased levels of brain iodothyroninedeiodinase, the enzyme which converts T4 to T3. In the hypothyroid fetus, this increased enzyme acting on T4 of maternal origin is sufficient to produce near normal fetal brain T3 concentrations [2].

Screening for congenital hypothyroidism (CH) has for long been considered an appropriate approach to prevent long term morbidity[18,19,20]. The relative absence of clinical features makes diagnosis of congenital hypothyroidism in the early neonatal period, virtually impossible. The preventable morbidity of this condition makes it mandatory for us to detect and institute therapy for congenital hypothyroidism at the earliest [18].

Congenital hypothyroidism accounted for 0.09% of the 3150 newborn babies screened from December 2014 to September 2016, showing an incidence of 1 in 1050. Sanghvi et al, Dussault et al, Al-Jurayyan et al, Devi and Naushad and Hulse et al in their studies observed an incidence of 2.1 per 1000 [21], 1 in 7,000 [22], 1 in 3292 [23], 1 in 1700 [24] and 1 in 3363 births respectively[25]. Maximum number of babies 2018 (64.1%) belonged to the age group of 3-4 days. No genetic and definite association with any illness is seen in our study. In a study by Dorreh et al, 79.9% of neonates were 3-5 days old, 18.9% of the neonates were aged between 5-21 days and 1.1% babies aged more than 21 days [26]. Male to female sex ratio of congenital hypothyroidism cases was 2:1. Dorreh et al and Zeinalzadeh et al reported male to female ratio of 1.05:1 and 1.4:1[26,27]. In all the 3 cases (100%) with congenital hypothyroidism, mothers complained of poor feeding and excessive sleeping in their babies. 2 cases (66.7%) had constipation and one patient (33.3%) had hoarse cry, hypothermia and open posterior fontanel was observed in one patient (33.3%). In a study by Lowrey et al observed difficulty in feeding in 83% of infants, respiratory distress in 30.6% abnormal dryness of skin in 32.6%, constipation in 32.6% patients and prolonged jaundice were observed in 12.2% [28]. In a study by Hulse et al, out of 87 444 babies, 9 babies (35%) had feeding problems, 10 babies (38%) were jaundiced after 10 days, constipation was observed in 7 babies (27%) and hoarse cry in 5 (19%). Umbilical hernia was present in 9 babies (35%), macroglossia in

4(15%), large fontanel was observed in 6 (23%); and hypotonia in 4 (15%). No signs were observed in 7 cases (27%) [25].

In the present study, the mean serum TSH level was very high (145.5) in the age group of 3-4 days as compare to higher age group of greater than 7 days, showing mean serum TSH of 20.1 in congenital hypothyroidism cases. We had only 2 false positives, with an intermediate result in the range of 30 micIU/L whole blood. Confirmed CH cases had TSH values greater than 100 micIU/L. These are acceptable performance metrics showing clear demarcation between false positive and positive result. In a study done by Ilamaran et al in Tamilnadu, a total of 785 healthy term neonates were screened at birth with cord blood TSH. Elevated TSH of more than 20mIU/L was noted in 22 neonates (2.8%). Six of these 22 neonates recalled had elevated TSH and low fT4 on retesting.

Follow up of these neonates revealed transient CH in 5 of them and permanent CH in one. The incidence of CH in their study was 1:785 [29]. In a study by Delange et al, 14 of 1805 newborns showed high TSH levels, but later only 3 cases were subsequently confirmed and were diagnosed as primary congenital hypothyroidism. In their study, one case showed TSH value more than50 μIU/ml and 2 cases with TSH 27μIU/ ml and 50μIU/ ml respectively [20]. A study done by Kishore et al in Cloudnine Hospitals, Bangalore, all babies born were screened for Congenital Hypothyroidism accounting for nearly 19,800 samples. Blood was collected from these babies between 36 to 48 hours. 32 of the 19,800 samples for CHT screening were positive, of which 19 samples contained a blood spot TSH concentration more than 100 μIU/ml of whole blood, eight a TSH concentration between 50 and 100 μIU/ml of whole blood, and five a concentration between 12 and 50 μIU/ml of whole blood.

Once a result was reported as abnormal, repeat TSH along with T4 and T3 were checked as per the protocol to confirm the result. If their TSH was high, the baby was subjected to radionuclide scan for thyroid [30]. Universal neonatal screening has been acknowledged as the most effective method to prevent the severe developmental and physical morbidities associated with congenital hypothyroidism [31]. Only 35% world newborn population are screened and the major hit are the third world population, So clinicians here should recognize the disorder early [4,32]. On detecting congenital hypothyroidism, treatment was commenced within first month of life which makes prognosis for intellectual development better.

Conclusion

Newborn screening for congenital hypothyroidism (CH) by intravenous blood TSH screening in our institute has been effective as a screening tool. From our study, there is no doubt that CH screening fits into the criteria of the diseases that needs to be screened in India, as the incidence in our study of nearly 1:1050 is high and should not be ignored. Despite being a well recognized clinical entity, universal screening for CH is yet to become incorporated in routine neonatal care in India.

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