ORIGINAL RESEARCH

A study on incidence of congenital hypothyroidism in new born babies at a tertiarycare hospital

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ABSTRACT
The clinical features of congenital hypothyroidism are often subtle and many newborn infants remain undiagnosed at birth. This is due in part to passage of maternal thyroid hormone across the placenta providing a protective effect, especially to the fetal brain and masking the clinical signs. Also, even the most common forms of CH have some moderately functioning residual thyroid tissue making clinical diagnosis difficult. TSH was estimated within 24 hours by electrochemiluminescence immunoassay 'ECLIA' on elecsys 2010 analyser. All babies wherein the cord TSH was found to be over 20mIU/L were intimated within 24hrs of the test. A second venous blood sample from these babies for serum T4 and TSH estimation was collected between 2- 4 day of life. Of the 1037 neonates whose cord blood samples were analyzed 32 neonates had TSH values more than 20 mIU /L. On re estimation of TSH and T4 values more than 72 hrs later all cases who were found to have higher TSH values in cord blood had age appropriate TSH and T4 values. 23 neonates whose cord samples could not be collected during delivery or samples were hemolysed, serum TSH from venous samples collected after 72 hrs of life were found to be normal.

Key words: Incidence, congenital hypothyroidism, new born babies

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INTRODUCTION

Congenital hypothyroidism is the most common congenital endocrine disorder in childhood and also is one of the most common preventable causes of mental retardation. 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 literature.[1]

The clinical features of congenital hypothyroidism are often subtle and many newborn infants remain undiagnosed at birth. This is due in part to passage of maternal thyroid hormone across the placenta providing a protective effect, especially to the fetal brain and masking the clinical signs. Also, even the most common forms of CH have some moderately functioning residual thyroid tissue making clinical diagnosis difficult. Within few weeks of birth as hypothyroxinemia progresses clinical signs and symptoms of hypothyroidism become more obvious and put neonatal brain at risk of irreversible injury.[2]

After making diagnosis, if the treatment is started within in a few weeks of birth, neurodevelopmental outcome is generally normal. Because of this danger, it is important to start treatment as soon as possible after birth. For all the above reasons, screening has become the best way to detect infants with CH.[3]

Pilot screening programs were first developed in Quebec, Canada and Pittsburgh, Pennsylvania in1974. In India the incidence of congenital hypothyroidism is around 1:1700 births, in one study done in Kochi the incidence was 1:1000 births. In western literature the incidence is around 1:4000 births. Despite the overwhelming evidence of high prevalence of CH in India, there is no universal screening program for neonatal hypothyroidism. [4]

This study aims to estimate the prevalence in the region and highlight the need neonatal screening program.

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METHODOLOGY

SAMPLE SIZE: Prospective observational study sampled over 1 year 5 months.
STUDY DESIGN: Prospective observational study.

STUDY POPULATION

SUBJECTS: All babies born in Command hospital, Eastern Command will be includedfor the study in the selected time-frame.
INCLUSION CRITERIA: All babies born in Command hospital, Eastern Command will be included for the study and continued for 18 consecutive months.
EXCLUSION CRITERIA: Prematurity less than 32 weeks and severe perinatal asphyxia requiring extensive resuscitation.
STUDY TOOLS: Case records, Laboratory data.

METHODOLOGY

A prospective study of all consecutively delivered newborns was conducted. Umbilical cord mixed blood samples were collected in a sterile and EDTA container, drawn from placental side of the umbilical cord incised while severing it at the time of birth

The mother's age, parity, comorbid conditions like diabetes, PIH, hypothyroidism, any previous history of child/themselves with G6PD deficiency, unexplained anemia, jaundice requiring exchange transfusion was recorded. The type of medications given to the mother till birth of the baby was recorded. At birth, the babies weight, gender, apgar, congenital abnormalities, were noted.
TSH was estimated within 24 hours by electrochemiluminescence immunoassay 'ECLIA' on elecsys 2010 analyser. All babies wherein the cord TSH was found to be over 20mIU/L were intimated within 24hrs of the test. A second venous blood sample from these babies for serum T4 and TSH estimation was collected between 2- 4 day of life.

RESULTS

GDM was the most common maternal comorbidity noted followed by PIHand Hypothyroidism. Of the hypothyroid mothers two were found to have anti-TPO antibodies. Other common comorbidites like anemia and UTI were not taken into account.

Table 1: Comorbid Factor

Comorbid Factor	Frequency	Percentage
PIH	59	5.6
GDM	166	16.0
Hypothyroid	65	6.2
Others	23	2.2

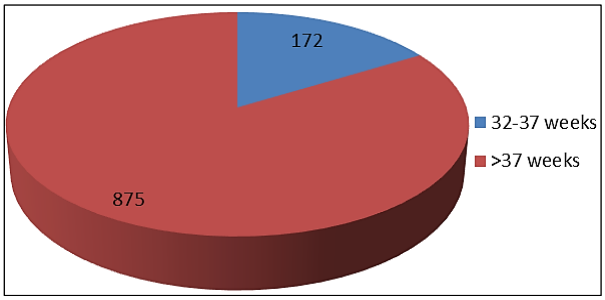

Fig 1: Gestational Age

The average gestational age was 38.2 weeks. The longest POG was 41 weeks 1 day. 172(16.5%) of cases were between 32 to 37 weeks of gestation, and the rest were more than 37 weeks of gestation.

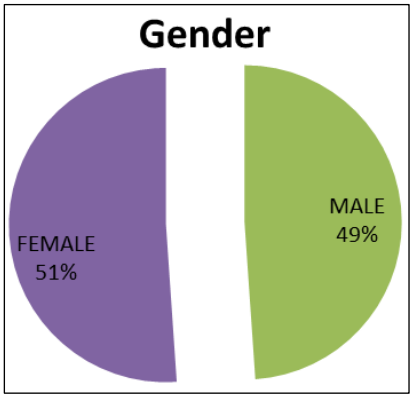

Fig 2: Gender of Neonate

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THE MALE: Female ratio was 0.93. There were 7 pairs of twins and one triplet.

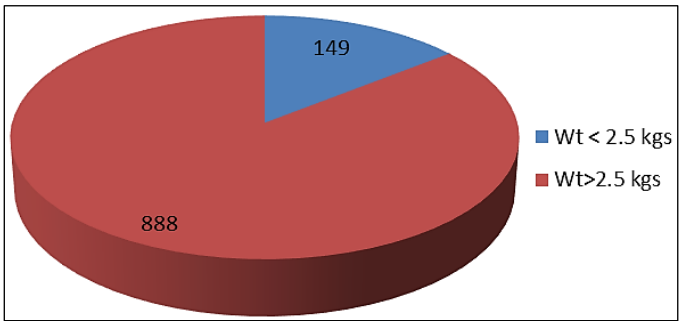

Fig 3: Distribution of Birth Weight

The average birth weight was 2.93 kgs. The highest recorded was 4.22 kgs and lowest was 1.7kgs.

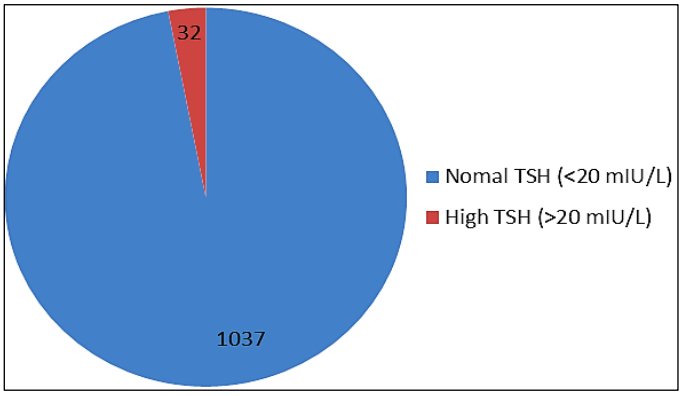

Fig 4: Cord Blood TSH levels

Table 2: Cord Blood TSH

Parameter		No of Patients N=1037	Cord Blood TSH		P Value
			TSH <20	TSH>20	
Sample type	Umbilical	1014	982	32	
	Venous	55	55	0	
Gestational Week	32-37 weeks	144 (13.8)	168	4	0.26
	>37 weeks	875(84.3)	847	28	
Birth weight	1.5-2.49 kgs	149(14.3)	145	4	0.482
	> 2.5 kgs	888(85.6)	860	28	
Maternal age	<20 yrs	53(5.11)	49	4	0.868
	21-25 yrs	354(34.1)	343	11	
	26-30 yrs	426(41.0)	416	10	
	31-35 yrs	169(16.29)	163	6	
	>36 yrs	35(3.3)	34	1	
Maternal comorbidites	GDM	166(16.0)	163	3	0.98
	Hypothyroid	65(6.2)	62	3	
	GDM with hypothyroidism	26(2.5)	25	1	
	Others	74(7.1)	72	2	
	Non diseased	732(70.5)	708	24	
Neonatal Comorbidites	NNJ	65(15.9)	60	5	0.9847
	Mild Birth Asphyxia	15(1.4)	14	1	
	TTNB/RDS	19(1.8)	17	2	
	Others	30(2.8)	30	0	
	No illness	808(77.9)	784	24	

Of the 1037 neonates whose cord blood samples were analyzed 32 neonates had TSH values more than 20 mIU /L. On re estimation of TSH and T4 values more than 72 hrs later all caseswho were found to have

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higher TSH values in cord blood had age appropriate TSH and T4 values. 23 neonates whose cord samples could not be collected during delivery or samples were hemolysed, serum TSH from venous samples collected after 72 hrs of life were foundto be normal. Maximum TSH value obtained was 69.4 mIU/L and minimum was 0.67 mIU/L. Mean was 8.4 and S.D-5.9.

DISCUSSION

Thyroid hormones are necessary for normal development of the human fetal brain and the maturation of other organs. Insufficient production of thyroid hormones during the fetal and neonatal period may result in serious complications and the central nervous system is affected most. It plays an important role for myelination and for normal neuronal connections.[62] Cord blood TSH screening for CH is a simple and accessible procedure. Previous studies have shown a transient TSH surge in the first 24–48 hours of life.However, the measurement of cord serum TSH for CH screening is well established.Walfish *et al.*[5] suggested that cord TSH had a better specificity and sensitivity as compared with cord or filter paper T4 at 3-5 days of age. Fuse *et al*. showed that cord serum is a good sampling technique for screening CH.Mahachoklertwattana*et al*.[6] showed that, if TSH is measured for screening CH, samples should be obtained from the umbilical cord of infants.In India, Singapore, Japan and Ethiopia, cord serum TSH levels have been used for neonatal screening for CH because of the difficulty of calling neonates back.

Newer TSH assay techniques, such as the enzyme-linked immunoassays, chemiluminescent assays and fluoroimmunoassays offer the advantages of using non-radioactive labels and greater sensitivity with the potential for better separation between normal and abnormal TSH concentrations. Thus, many screening programs are considering switching to a primary TSH approach. A majority of European and Japanese programs favor screening by means of primary TSH measurements, supplemented by T4 determinations for those infants with elevated TSH values.

The neonatal serum FT4 levels rapidly increase after delivery to the maximum level at 1 day of age. Thereafter, they decline to a steady state level within 2-4 weeks. After a transient TSH surge in the first 24-48 hrs of life, neonatal serum TSH levels decline and the level at 1-3 days of age is similar to that of the cord serum[66].It changes little after 3 days of age. Therefore, for those infants with initial cord blood TSH > 20mIU/L a repeat blood sample should be obtained after >48 hours. However, the trend towards early discharge of infants and mothers presents problems with this approach. This would result in an unacceptably high recall rate for this group of infants unless the TSH cut off was adjusted for age. Experience using newer assays in a primary TSH screening approach, in a population of infants discharged early,is necessary to determine the effects on recall rates and the possibility of any false-negative test results.

Incidence rates vary by race or ethnicity. Among Asian Indians, 1:1,200; Hispanic, 1:1,600; Asian (Chinese and Vietnamese), 1:2,380; non-Hispanic White, 1:3,533; and non-Hispanic Black, 1:11,000[51].Incidence was higher in preterm, low birth weight babies: more than 2500 grams, 1:1843; 1500-2500g,1:851; and less than 1500 grams, 1:396. Harris and Pass [7] reported a 23% increase in babies born weighing less than 1500 grams. In this study there were no confirmed cases of CH when screened by cord blood TSH estimation. This may be due to a low prevalence in the population and a relatively smaller sample size compared to other studies.

In the United States, the recall rate after primary TSH screening is approximately 0.05%. In the study conducted by Azizi and colleagues in Tehran and Damavand using cord blood samples for screening of CH, a recall rate of 1.06% was obtained with a TSH cut off level of more than 20mIU/L,[6] whereas in Esfahan, the recall rate was approximately 2.2% after primary screening for serum TSH levels using the same Cut off limit of 20mIU/L. These varying recall rates for different TSH cut off levels may be because of several factors, such as the use of T4 or TSH level or both for screening, differences in sample-collection methods and analysis procedures in different laboratories, and differences in recall criteria, which are related to the cultural, regional, and social factors of a country.[8]The recall rates in other countries, after primary TSH level assessment in neonates aged 3-5 days, may vary from 0.2% to 3.3%. The recall rates with TSH cut off of more than 20mIU/L were 0.16% in the Philippines, 0.35% in Austria, 0.3% in Greece, 0.28-0.29% in Hungary, 2.3% in Turkey, and 3.3% in Estonia.

In contrast, studies conducted in Italy, the recall rate measured on the basis of T4 levels was 2.5%, while that measured on the basis of both T4 and TSH levels was 0.11%.[9]

In this study, using only primary cord blood TSH for screening congenital hypothyroidism we had a recall rate of 6.23%. If the cut off is raised to 40 mIU/L we would have a recall rate of 0.6%. Therefore, the laboratory screening methods and TSH cut off level need to be revised to ensure more specific and sensitive CH screening. Recent studies have shown a high prevalence of CH and high patient recall rate after primary screening, which was in line with the results of previous studies in Iran.

Although environmental and genetic variations in addition to the low cut off TSH level may be responsible for the high recall rate, a nationwide study is necessary to clarify the reasons for the high incidence of CH. Future studies should also be able to clarify why small changes in TSH cut off levels during screening lead to substantial changes in the number of neonates with undetected CH.

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The downside to lowering TSH cut offs is an increase in recall of infants with false-positive tests. Each screening program needs to work out its own test cut off, weighing increased detection of mild cases *vs.* harm from recall of normal infants. In our opinion, until there is good evidence of no intellectual impairment, we can come down on the side of detection and treatment of these milder cases. The study of a birth cohort in Southern Spain revealed an impaired mental development at 4 years of age in children with higher neonatal TSH levels compared with children with lower neonatal TSH levels within the normal reference range. These findings indicate that a more thorough screening for neonatal thyroid deficiency is required to prevent long-term developmental effects. Further research is warranted into the influence on neurodevelopment of marginally altered TSH concentrations in newborns[10]. The high recall rate in this study can be attributed to the low cut off for cord blood TSH.

CONCLUSION

The latest guidelines from the United States have also raised the Primary TSH cut off to 100mIU/L if screened on the first day. It was also noted in this study that if we had raised the cut off from 20-40mIU/L we would have a recall rate of 0.46% which is line with the global recall rates. Hence going forward it will be prudent to raise the cord blood TSH cut off to 40mIU/L which will reduce the recall rate and increase the sensitivity and specificity of the program.

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