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PREVALENCE AND INCIDENCE OF CONGENITAL HYPOTHYROIDISM IN NEONATES IN TERTIARY CARE CENTRE IN CENTRAL INDIA

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ABSTRACT **Background:** Congenital hypothyroidism is one of the most common disrupters of endocrine and metabolism, that is most important preventable cause of mental and physical disabilities. Clinical features are often lacking at birth even up to the first few weeks or months of life. Diagnosis based on clinical features is difficult at birth without biochemical screening, resulting in delayed initiation of therapy and irreversible brain damage in the affected children. Screening during birth can help in early diagnosis and treatment. Knowledge of the country-specific prevalence of the disease can guide in establishing a universal screening program, thus improving the outcomes of affected children by timely intervention. This study aimed to describe and investigate the prevalence and incidence of CH in Central India by Cord blood screening method. **Material & Methods:** A prospective observational study was conducted for a period of 9 months in the Department of Paediatrics, Index Medical College Hospital & Research Center, Indore after valid approval from Institutional ethics committee on neonates who qualified the inclusion criteria. The screening was conducted on 200 babies delivered at a tertiary care hospital, at Index Medical College Hospital & Research Center, Indore, both by normal vaginal delivery or Caesarean section were included in the study. Cord blood samples was collected on Post neonatal day 1 of these new born and sent for serum thyroid Stimulating hormone (TSH) estimation by IRMA method and followed up. Prevalence was calculated by percentage. **Results:** Out of 200 neonates assessed 6 newborns detected to have serum TSH more than 20 µIU/ml, were further investigated with complete thyroid profile and out of these only one newborn detected to have congenital hypothyroidism eventually with incidence rate of 1:200. **Conclusion:** Early diagnosis of CH with an efficient and accurate screening method which can decrease the risks of developmental delay, mental retardation, and delayed physiological development.

KEYWORDS : Congenital hypothyroidism, New born screening, Cord blood, TSH levels

INTRODUCTION

Congenital hypothyroidism (CH) is a common endocrine disease in newborns and affects approximately 1 in 2000 to 4000 live births with an incidence of 1:2500-2800 live births in India.[1,2] Recent epidemiologic studies reported an exponential increase in the incidence in Western countries, reasons being unclear.[3,4] Multiple contributory factors may be associated, including ethnicity, environmental factors, characteristics of birth and pregnancy, and screening programs.[5–8] As per the reports from most screening programs females showed a higher preponderance with female-to-male ratio for CH being nearly 2:1.[3,7]

Congenital hypothyroidism (CH) is one of the commonest causes of preventable mental retardation. Delays in diagnosis and treatment of CH may cause impairment in neurological development and intelligence quotient (IQ).[9] Retrospective clinical studies showed that less than half were diagnosed by three months and approximately two-thirds by one year of age.[10,11]

According to estimates from the International Atomic Energy Agency (IAEA), 50,000 newborns in South East Asia are at risk of CH each year. As reported by Rose and Brown et al., (2006) although routine newborn CH screening has been practised for more than 40 years in developed countries, developing countries have recently addressed this issue in the last 10 years due to difficulties associated with their healthcare systems.[12]

In the era before new-born screening, less than half of the cases of severe hypothyroidism were recognized in the first month of life. At birth, the clinical signs and symptoms of congenital hypothyroidism are usually absent or so nonspecific or subtle that the majority of infants look completely normal. The development of features of hypothyroidism will depend upon the type of the defect, the age of onset and the duration and severity of the thyroid hormone deficiency. Since irreversible damage to the central nervous system may take place even before the clinical manifestations suggest the diagnosis, the early detection and treatment is critical to the mental development. If picked up early and treated well, children with congenital hypothyroidism lead a normal life with no sequalae.[13,14]

With increasing age, these neonates would have deficient growth and delayed development. By a certain age, they would exhibit the obvious physical and facial characteristics of cretinism. A majority of patients with severe, untreated hypothyroidism had IQs below 80, which led to serious mental disability. The majority of these infants eventually found themselves in institutional care. When given the proper thyroxine therapy, most congenitally hypothyroid babies grow and develop normally in all other areas. CH screening is not, however, performed on a regular basis because to numerous logistical issues.

There is a paucity of literature highlighting the prevalence and clinical-etiological profile of thyroid disorders and especially hypothyroidism in pediatric age group in a developing country like India. Thyroid hormones are unique in view of their important role in fetal and early neonatal brain development and also having actions on growth and development during the first two decades of life. The adverse effects of deprivation of thyroid hormone on the rapidly growing infantile brain have prompted the need for neonatal screening for congenital hypothyroidism and also identify other causes leading to hypothyroidism thus promoting an early intervention.

But in the absence of similar services in India, many cases of hypothyroidism remain unrecognized and may cause havoc in the developing brain. The findings of this study underscore the need to adopt strategies to evaluate children from our community for disorders of thyroid gland. Further, under ideal protocol neonatal screening for CH is done by blood sample collection for TSH estimation on Post neonatal Day 3 but in the present study we did the screening through Cord blood sampling which was done on Post neonatal day 1 thus increasing the accuracy of the results and also decreasing the patient attrition. Another reason for choosing PND 1 over PND 3 in the present study was most of post neonatal child did not stay in the hospital till Day 3 due to economic status and family issues. Further, the babies who were reported positive by cord blood samples on day 1 were invited for a reconfirmation on PND3 to check accuracy and efficacy of the test done on post neonatal day 1.

In advent of same, the present prospective observational study was planned and conducted to determine the prevalence and incidence of congenital hypothyroidism using serum thyroid Stimulating hormone (TSH) estimation by IRMA method.

MATERIAL & METHOD

This Prospective Observational study was carried out in the Department of Paediatrics, Index Medical College Hospital & Research Center, Indore for a period of 9 months i.e., 10th May 2022 to January 2023, on 200 infants delivered consecutively at a tertiary care hospital at Index Medical College Hospital & Research Center, Indore, both by normal vaginal delivery or Caesarean section were included in the study. Cord blood samples of these new born were collected on Post

neonatal day 1 (PND-1) and sent for serum thyroid Stimulating hormone (TSH) estimation by IRMA method and followed up. Prevalence was calculated by percentage. The study was conducted after obtaining approval from the Institutional Ethics Committee and written informed consent from the patient's parents or guardian.

Inclusion Criteria:
- Full term healthy Newborn born at tertiary care hospital irrespective of Vaginal or LSCS.
- Children whose parents gave consent for the study

Exclusion Criteria
- Children whose parents refuse to give consent
- Preterm delivered newborns
- Neonates whose mothers who were known cases of hypo or hyperthyroidism or on any drugs were excluded from the study.

Method:
After obtaining written informed consent from the parents of the infants, umbilical cord blood collection was done on Day 1 of Post neonatal day and they were advised to come for follow up. Parents were told about the implication of an abnormal result and they were assured early treatment and follow up if required in future.

Mixed cord blood sample from umbilical artery and vein was obtained on PND 1 in a sterile container for TSH estimation by IRMA method at the time of delivery. Types of outcome measures was in form of raised TSH (TSH>20 µIU/ml) or normal TSH (TSH< 20 µIU/ml). Babies detected to have elevated cord blood TSH were recalled for complete thyroid profile and were clinically examined by a pediatrician.

Statistical Analysis
Especially designed pre-structured proforma was used for collecting the data. The data was also entered to master chart. The raw data was entered into the computer database. Statistical software, SPSS version 20.0 was used for statistical analysis. Prevalence of an outcome variable along with 95% confidence limits was calculated.

RESULTS
200 freshly collected cord blood samples were sent to Radioimmunoassays (RIAs) laboratory for TSH estimation by IRMA method. Total umbilical cord blood TSH level are depicted in Table 1. 64.5% patients i.e., 129 had Cord blood TSH level in range of 4-15.99 followed by 30% which had <4. 6 patients had Cord blood TSH level more than 20 µIU/ml.

Amongst the total of 200 infants, 46.5% (93) patients were Primigravida whereas 53.5% (107) were multigravida in the study group with ratio of 1:1.15. (Graph 1). The birth weight range of cohort was between 2.5 to 4.2 kg. The male to female ratio was 52:48 (1.08:1) (Graph 2).

A total of 6 infants were detected to have TSH value more than 20 µIU/ml. The percentage of detection of raised TSH was 3%. Of these 6 neonates 03 were detected to have TSH value between 20-24.99 µIU/ml. One neonate detected to have a TSH of 28 µIU/ml and another with TSH of 33 µIU/ml. The highest level of TSH detected in this study was 52 µIU/ml and this baby was detected to have congenital hypothyroidism eventually. These 6 neonates were followed up with full thyroid profile (Table 2).

In this subgroup ratio of male to female was 4:2 and birth weight ranged between 2.58-3.80 (Table 3). Of the 93 primigravida, 03 neonates (3.2%) had TSH value more than 20 µIU/ml and out of 107 multigravida, 03 (2.8%) had TSH value more than 20 µIU/ml. P value calculated for primigravida and multigravida was 0.821.

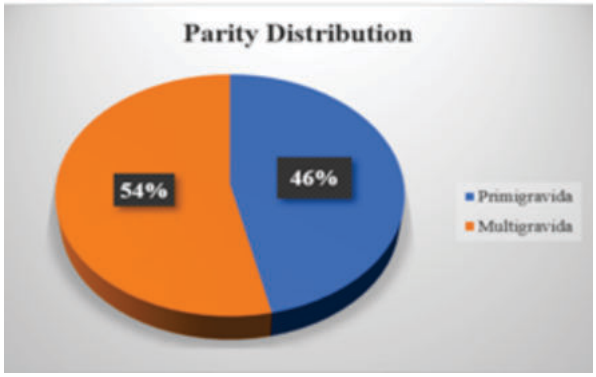
Out of 104 male neonates only 04 (3.8%) had TSH value more than 20 µIU/ml and out of 96 female neonates only 02 (2%) had TSH value more than 20 µIU/ml. However, P value calculated for male and female neonates was 0.102 and thus not significant. The significance value (combined) for gestation age (Table 4), birth weight and maternal age (Table 5) for TSH more than 20 µIU/ml was 0.095, 0.724 and 0.578 respectively.

Mean and standard deviation for age, gestation age and birth weight are depicted in (Table 6). Normal thyroid function parameters for neonate aged 2 to 4 weeks given in (Table 7)

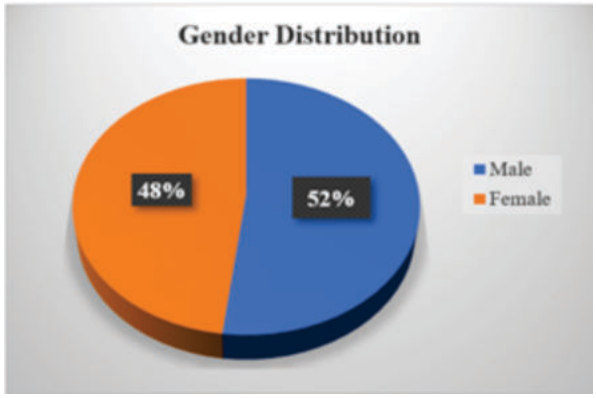
Table1: Umbilical cord blood TSH levels

Cord blood TSH level(ulu/ml)	No of samples n=200	%
<4	60	30
4-15.99	129	64.5
16-19.99	5	2.5
20-24.99	3	1.5
25-29.99	1	0.5
30-34.99	1	0.5
52	1	0.5

Mean=7.88 Standard deviation=4.35



Graph 1: Parity wise case distribution



Graph 2: Sex wise distribution of case

Table 2: Follow up T3 T4 TSH And Free T4 Done Between 2 To 4 Weeks Of Age

T3 (ng/dl)	T4 (ug/dl)	TSH (mIu/l)	Free T4 (ng/dl)
202	8.5	4.0	1.4
163	7.1	3.6	1.2
213	13.1	4.7	0.98
107	7.8	6.1	2.1
268	11.3	7.7	1.7
109	9.1	5.5	1.3
62	2.6	5.3	0.4
212	9.9	4.1	1.92
176	8.7	4.6	1.88
177	12.9	8.1	1.0
203	11.1	6.4	1.6
125	11.9	4.8	4

Table 3: Weight Wise Distribution Of Samples

Weight (in kg)	No. of samples
2.5-2.99	140 (70%)
3.0-3.49	44 (22%)
3.5-3.99	15 (7.5%)
4 and above	1 (0.5%)

Table 4: Gestation Age Wise Distribution Of Cases

Gestational age in weeks	No. of Cases	%
37-37.6%	12	6%
38-38.6%	76	38%
39-39.6%	106	53%
40-41%	6	3%

Mean=39.07 Standard deviation=0.52

Table 5: Age Wise Distribution Of Cases

Age (yrs)	No. of cases
Between 20-30	188
31 & above	12

Table 6: Mean And Standard Deviation For Age Gestation Age And Birth Weight

TSH (mIU/l)		Age (yrs)	Gestation age (week)	Birth wt. (Kg)
<20	Number	194	194	194
	Mean	25.45	39.446	2.9654
	SD	3.167	11.3158	0.34567
20 and above	Number	6	6	6
	Mean	25.82	39.302	3.0264
	SD	3.579	0.2768	0.35868
Total	Number	200	200	200
	Mean	25.43	39.448	2.980
	SD	3.180	11.2476	0.34596

Table 7: Normal Thyroid Function Parameters In Infants Aged 2 To 6 Weeks

Serum constituents	Concentration
T3	100-300 (ng/dl)
T4	6.5-16.3 (ug/dl)
Free T4	0.9-2.2 (ng/dl)
TSH	1.7-9.1 (mIU/l)

DISCUSSION

Since the previous two decades, congenital hypothyroidism (CH) screening has been more common. Due to a number of issues, including cost, a dearth of widely accessible trustworthy laboratories, and the absence of baseline population data, we have been unable to deploy it in India. The ease of use and accessibility of cord blood TSH as a screening tool make it an attractive proposition.

In a study done by **Fuse, et al.**[15] he had reported that mixed cord blood is a good ans sensitive sampling technique for neonatal screening for CH. Similarly, **Walfish**[16] concluded that cord blood TSH had a better sensitivity, specificity and accuracy as compared to cord or filter paper T4 at 3-5 days of age. In our study the mean value of cord blood TSH was 7.86 ± 4.35 µIU/ml in the 200 new-borns screened, which was lower when compared to **Feleke, et al.**[17] who observed a value of 9.6 ± 7.8 mIU/L in 4206 new-borns screened. Our TSH values were lower than found by **Feleke et al**[17] **and Khadilkar et al**[18] who, in a study of 203 neonates reported a mean cord TSH value of 12.3 ± 4.9 µIU/ml.

The recall rate in the present study was 1.5% which was in concurrence with the large study of **Wu et al**.[19] whose large cohort 11,000 neonates had a recall rate of 2.27%.

Normal cord TSH values show a wide range of 1- 38.9 µIU/ml[20], and we in the present study used a cut-off of 20 µIU/ml, but had we opted for a higher cut-off of 25, 30 for recall purposes, our recall rates would have fallen to 0.03 and 0.02% respectively. In the present study only only one neonate out of 200 was reported to have CH, giving an incidence of 1 in 200, which is way higher than the world figure of 1 in 4000[21], but other Indian data too have quoted higher incidences as 1 in 248[22] and 1 in 1700[23] and a recent Iranian study found an incidence of 1 in 914[24]. Probably geographic and ethnic differences are responsible and of course, this cohort of 200 samples is too small to assess incidence.

Our figures have shown a comparable trend as with the normative data for cord blood TSH values as reported by various workers across the globe. We conclude that we may safely use the widely used cut off cord blood TSH value of >20 µIU/ml for purposes of recall for retesting, though from logistic angles a cut off value of >30 or >40 may be used. Still even larger population-based studies may be done to achieve more credible guidelines, more so to gauge the incidence and epidemiology of CH in our country.

The only limitations of the present study were a small sample size and the data was primarily collected in a single setup. A larger scale study is indicated for better accurate results for a national level reference data.

CONCLUSION

Early detection and treatment of congenital hypothyroidism can prevent intellectually impaired children and raise IQ along with normal physical development. Neonatal patients need to be examined as quickly as possible, typically within 48 hours after being notified, in a paediatric facility with the necessary equipment. Congenital hypothyroidism in babies requires counselling because the parents are inevitably highly anxious about the future. Parents require assurances on the good prognosis and the probability that their child would develop into a normal, healthy adult with traditional level of intelligence.

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Conflict Of Interest: None

Ethical approval: Approved by Institutional Ethics Committee

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