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## Incidence of congenital hypothyroidism and associated congenital anomalies at VSS Medical College & Hospital, Burla

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### Abstract

**Background:** The worldwide incidence of CH ranges from 1 in 3000 to 1 in 4000 live newborn. However, varied incidence has been found from state, regional, and national screening programs.

**Objective:** to know the incidence of Congenital Hypothyroidism and associated congenital anomalies in this part of the country, which is necessary to understand the burden of congenital hypothyroidism to the society.

**Setting:** Primary serum TSH measurement in screening neonates with backup thyroxine (T<sub>4</sub>) determination in infants with high TSH levels (>20mIU/L). TSH and FT<sub>4</sub> were estimated by Chemi Luminescence Immuno Assay (CLIA) method using reagent moonblind, INC.

**Result:** Serum TSH of screened neonates ranged between 0.16mIU/L and 80.32mIU/L, Mean  $\pm$  SD of sTSH being 5.80 $\pm$ 3.96mIU/L. Out of 2212 screened newborns, 9 newborns had sTSH value >20mIU/L. out of 9 recalled newborns, 3 had persistently elevated sTSH >20mIU/L. Making incidence of Congenital hypothyroidism of 1:737 in our study. In a study carried out at Israel found 15.6% cases of Congenital Hypothyroidism were associated with congenital anomalies majority being cardiac anomalies.

**Conclusion:** In our study we found a higher incidence of 1 in 737, when compared to estimated national incidence of congenital hypothyroidism. Our study reported significant number of neonates with sTSH value >10mIU/L indicating iodine deficiency prevalent in this part of country.

**Keywords:** Congenital hypothyroidism, congenital anomalies, iodine deficiency, thyroid hormone

### Introduction

Congenital hypothyroidism (CH) is defined as deficiency of thyroid hormone at birth. Congenital hypothyroidism is one of the most common preventable Etiologies of mental retardation. Age of diagnosis and severity of mental retardation due to underlying hypothyroidism have inverse relationship. Congenital hypothyroidism may be classified as permanent or transient and this in turn determines the requirement of duration of therapy<sup>[1, 2]</sup>. The worldwide incidence of CH ranges from 1 in 3000 to 1 in 4000 live newborn<sup>[1, 3, 4]</sup>. However, varied incidence has been found from state, regional, and national screening programs. Studies reveal that the incidence varies by geographic distribution. In few states of India incidence is as high as 1:300-600 in newborn infants have found<sup>[1, 4]</sup>.

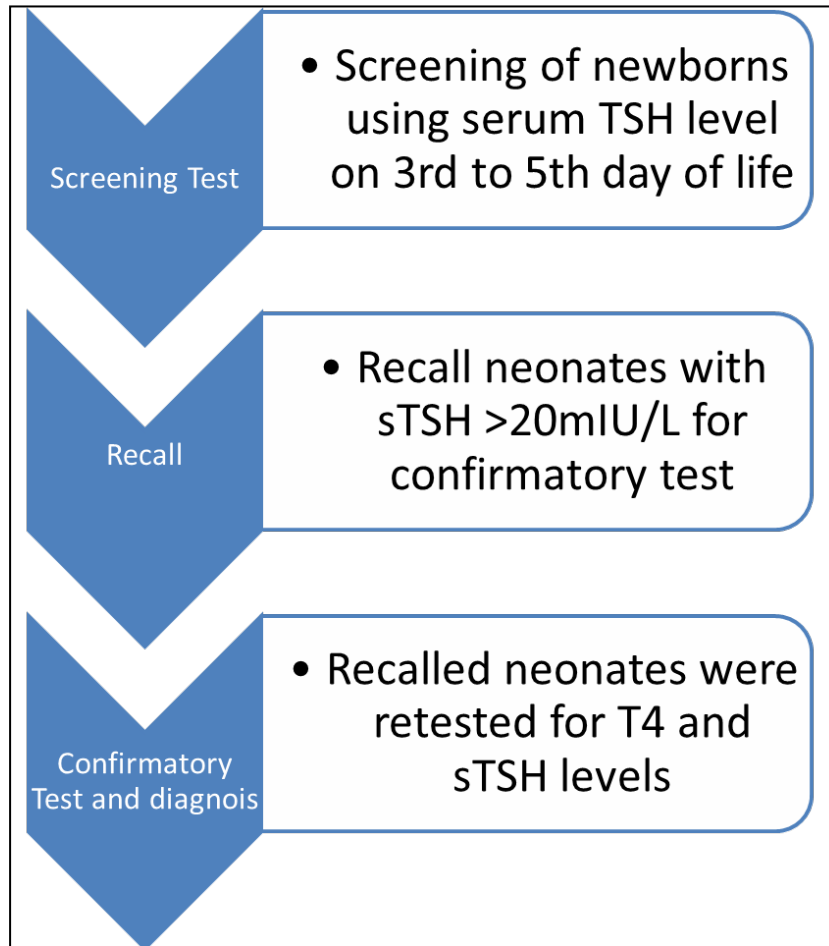
Congenital Hypothyroidism often asymptomatic or present with subtle manifestations at birth. Most often hypothyroidism in the newborn period is underdiagnosed, and delay in diagnosis leads to the most severe effect of Congenital Hypothyroidism, Mental Retardation (MR), dictating the importance of Newborn Screening<sup>[5, 6]</sup>.

Newborn screening (NS) for CH is one of the major achievement of Preventive and Social Medicine. The problem of CH and its ill effects has been addressed in developed countries by the introduction of NS since 1972, but many of the developing countries still are deficient in NS programs for CH. In India, such programs are yet to be introduced and implemented as such no definite incidence and hence no burden of this disorder is known<sup>[7]</sup>.

This study focuses and aims at evaluating the feasibility of thyroid screening program, to know the incidence of Congenital Hypothyroidism and associated congenital anomalies in this part of the country, which is necessary to understand the burden of congenital hypothyroidism to the society.

**Materials & Methods:** Our study was an observational study done for duration of 2 years from December 2013 to November 2015 at VIMSAR, Burla, Sambalpur, Odisha. A total of 2212 newborns attending the well neonatal clinic and normal newborn born at VIMSAR were included in the study after using inclusion and exclusion criteria. Institutional Ethical Committee clearance was sought for conducting the study. Neonates apart from exclusion criteria were involved in congenital hypothyroid screening program on 3<sup>rd</sup> to 5<sup>th</sup> day of life after obtaining an informed consent from either of the parents. Detailed history, examination of

newborn and short questionnaire was used for screening. In our study most widely accepted screening strategy was used- primary serum TSH measurement in screening neonates with backup thyroxine (T<sub>4</sub>) determination in infants with high TSH levels (>20mIU/L). Newborns with elevated serum TSH level were recalled for repeat testing at a gap of a week time duration to newborn follow up clinic for confirmatory test (serum T<sub>4</sub> and TSH levels measurements) by Chemi Luminescence Immuno Assay (CLIA) method using reagent moonblind, INC.



**Result:** An observational study was carried during the time duration of 2 years, from December 2013- November 2015. There were 1633(74%) males and 579(26%) females, giving a study population male to female ratio 2.8:1.

Out of 2212. Only 9 neonates recalled neonates, there were 7(77.8%) males and 2(22.2%) females and male to female ratio in recalled newborns is 3.5:1.

**Gestation age:** Neonates involved in study were of average gestation age of 36.8 weeks, and Mean±SD of gestation age being 36.88±2.11. However average gestational age in recalled neonates was 35.8 weeks Table 1.

**Table 1:** Gestation age of Recalled Neonates

Gestation age	Number of newborns	Percentage
<32	0	0
32- 36weeks+6 days	9	100%
37- 41weeks+6 days	0	0
>42	0	0

**Serum TSH:** Serum TSH of screened neonates ranged

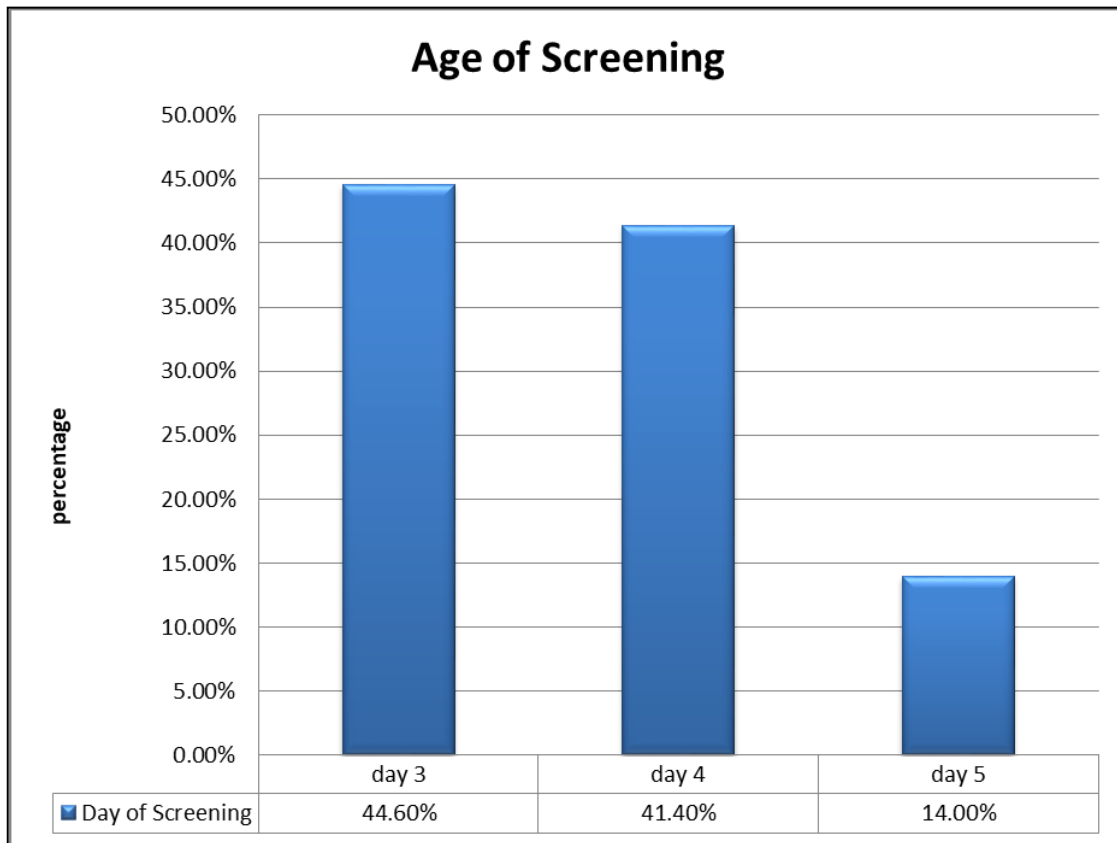
between 0.16 mIU/L and 80.32 mIU/L, Mean±SD of sTSH being 5.80±3.96mIU/L. Mean±SD sTSH in screened female newborns was 5.69±2.8mIU/L and male newborns was 5.63 (SD=3.9) mIU/L.

**Recall Rate:** Out of 2212 screened newborns, 9 newborns had sTSH value >20mIU/L, who were recalled for confirmatory test, giving a recall rate of 0.4%. 99.6% were <20mIU/L and 0.4% were >20mIU/L. 4.1% of screened population had sTSH value >10mIU/L. Indicating mild iodine deficiency in the screened newborns. Table2

**Table 2:** sTSH value <10mIU/L, Iodine deficiency

sTSH (mIU/L)	Newborns	percentage
<10	2122	95.9%
>10	90	4.1%

**Age of screening:** Age of screening ranged from 3 to 5 days of life, Mean age of screening being 3.69 (SD = 0.70) days of life (Figure 1).



**Age of recall:** screened newborns with sTSH >20mIU/L were recalled after 7 days of initial screening, day of patients attending OPD varied from day10 to day 27 of life and mean being 14.6 (SD = 5.95) days of life.

**Incidence of CH:** Out of 9 recalled newborns, 3 had persistently elevated sTSH >20mIU/L. Making incidence of Congenital hypothyroidism of 1:737 in our study.

- Sex ratio: male: female: 2:1.
- Ethnicity: all belonging to Hindu ethnicity.
- Mode of Delivery: 2 by vaginal and 1 by LSCS.
- Birth weight: ranging from 1.6 to 2.5kg, average being 2.1kg.
- Maternal age: maximum being 35years and minimum being 27years. 29.6years being average maternal age.
- Gestational age: all belonging to near term gestational age group.

**Congenital anomalies/syndromes:** We found syndromes like anal atresia, down syndrome, CTEV, cleft lip &/ palate, collodion baby, diaphragmatic hernia, hydrocephalus, rhizomelic chondrodysplasia punctata, meningocele, undiagnosed syndromic baby. Table 3

**Table 3:** Syndromes in screened newborns

Syndromes	Number of cases
Anal atresia	3
Down syndrome	3
CTEV	6
Cleft lip &/palate	4
Collodion baby	1
Diaphragmatic hernia	1
Hydrocephalus	1
Rhizomelic Chondrodysplasia punctata	1
Meningocele	1
Undiagnosed syndrome	1

**Discussion:** In our study out of 3 newborns were diagnosed to have Congenital Hypothyroidism out of 2212 screened newborns, in which 2 were male and 1 was female, indicating male preponderance with male to female ratio 2:1, this finding is supported by few studies carried out previously which reports male to female ratio with male preponderance like Anjum *et al.* [8] (1.1:1), Anastasovska *et al.* [9] (1.6:1).

**TSH:** In our study we could not perform T4 level along with TSH for neonatal screening due to high cost. This would not detect Central Hypothyroidism, a rare cause and not precisely able to differentiate between true or physiological rise in TSH. However, since Neonatal screening for CH is recommended by the 5th day of the child’s life at the latest. Therefore, we believe that we have performed the screening between 3th day and 5th day of life mean age of screening being 3.69 (SD = 0.70) days of life; thus rise in sTSH in the present study might be true.

**Mean TSH:** In our study we obtained mean TSH value of 5.80±3.96mIU/L which was quite comparable to mean TSH value obtained by a study carried out by Manglik *et al.* [4] in Kolkata (6.13±5.29 mIU/L) but lower than that reported by Singh *et al.* [5], in Manipur (8.833±7.059 mIU/L) and Raj *et al.* [11] at Trivandrum in Kerala (12.88 mIU/dL). This difference in mean TSH values within different regions of India may be explained by differential iodine sufficiency/insufficiency prevalent in different regions of India. Anjum *et al.* [8], reported mean TSH value of 5.6±5.1 mIU/L (Pakistan) which is quite similar to our findings but lower than that reported by Yousef *et al.* [12], 8.61±2.66 mIU/L (Fayoum) and Feleke *et al.* [13], 9.6±7.8mIU/L (Ethopia). This difference in mean TSH values in different studies carried out in different regions across the globe can be accountable to differences in the geographical distributions, ethnicity and iodine insufficiency across the globe.

In our study the sTSH value ranged from 0.16 mIU/L to 80.32 mIU/L. Mean sTSH of female newborns and male newborns was comparable 5.69 (SD=2.8) mIU/L and 5.63(SD=3.9) mIU/L respectively similar to that of study done by Gupta *et al.* [14] and Raj *et al.* [11], where mean TSH of both female and male newborns were similar.

**Recall rate:** Our recall rate for repeat testing was 0.40% (9/2212) which is comparable with a large scale, 5-year prospective study from Thailand with a sample size of 35,390 neonates which had a recall rate of 0.43%. The recall rate in other studies were 0.18% (Anastasvska *et al.* [9], 0.22% (Yousef *et al.* [12]), 1.83% (Manglik *et al.* [4]), 31.9% (Raj *et al.* [11]).

**Age of recall:** The timing of diagnosis, treatment, and monitoring of treatment are crucial in ensuring the best neurodevelopmental outcome in patients with CH. However no guidelines have been laid down regarding recall timings. Since there is an inverse relationship between the age of diagnosis/treatment and intelligence quotient (IQ) [15], we recalled screened newborns with higher sTSH value >20mIU/L, for confirmatory test depending on day of initial TSH assessment, with a gap of 7 days.

**Incidence:** The incidence of CH among neonates in Odisha has not been separately evaluated before. In our study we screened newborns attending our tertiary care centre from different districts of Western Odisha residing in and around Burla (Dist. Sambalpur) giving the incidence of 1:737 live births. Our study incidence is much higher than the world figure of 1 in 4000 and also higher than the estimated incidence of India which is 1:2500-2800, but other Indian data have observed higher incidences of 1 in 248 and 1 in 1700 in separate studies, from different regions of India [33, 34].

Our study incidence was closer to the incidence reported by Manglik *et al.* [4] from neighbouring state West Bengal, which was 1:600. This similarity in incidence may be accounted to the fact that West Bengal and Odisha, being neighbouring states shares almost similar geographical condition, ethnic group, food habits and genetic makeup, which all are main determining factors for developing hypothyroidism in a neonate. A quite similar incidence was found in other studies conducted by Sundararaman [16] in Chennai and Sanghvi *et al.* [17] in Kerala, where incidence were 1:625 and 1:476 respectively.

**Gestational age, prematurity and sTSH:** Thyroid gland function develops and matures during fetal life, with production of serum thyroxine (T4) concentrations beginning around 12 weeks gestation and increasing to term. [18]. Thus hypothyroidism is common in preterm infants. Multiple factors influence thyroid function in preterm infants other than immaturity of the hypothalamic-pituitary-thyroid axis/immaturity of thyroid hormonal regulation and increased demand for thyroid hormone by certain diseases of preterm infants (not congenital abnormalities of the thyroid gland), immature thyroid hormone synthesis or metabolism, and increased survival rate of a growing number of preterm babies, also insufficient or excessive iodine intakes also influence preterm thyroid function [19].

**sTSH and Maternal age:** In our study we found a Positive ( $r=0.049$ ) and Significant ( $p<0.05$ ) correlation between sTSH and Maternal Age, similar to the findings that of study conducted by Raj *et al.* [11], from Kerala and Zhou *et al.* [20], from china. Advanced maternal age may increase the possibility of new mutations in genes encoding some

transcription factors associated with thyroid gland development [21]. However a study conducted by Gupta *et al.* [22], from Haryana observed no such correlations between sTSH and maternal age.

**Iodine sufficiency:** Along with urinary iodine concentrations, it has been proposed that neonatal TSH concentrations are a good indicator of the prevalence of iodine deficiency disorders in populations [9]. World Health Organization (WHO), United Nations International Children's Emergency Fund (UNICEF) and the International Council for Control of Iodine Deficiency Disorders (ICCIDD) included neonatal TSH as one of the indicators for assessing iodine deficiency disorders (IDD) and their control.

**Congenital Anomalies:** In a study carried out at Israel found 15.6% cases of Congenital Hypothyroidism were associated with congenital anomalies majority being cardiac anomalies [23]. A study from a series of infants identified with congenital hypothyroidism there is an increased incidence of extra thyroid abnormalities [24] and another study reported that congenital hypothyroidism was associated with various forms of co-occurring congenital anomalies. DS was the most frequently observed congenital anomaly. Following Down syndrome, congenital heart defect and DDH were the next most common defects occurring among Congenital Hypothyroidism infants [25].

Present study is first of its own kind in this part of country, which would help in assessment of incidence of congenital hypothyroidism and feasibility of implementation of newborn screening program for Congenital Hypothyroidism. We excluded premature newborns (<32 weeks), very low birth weight and sick newborns who exhibit transient hypothyroidism due to immature/defective hormone regulation which would have resulted in high number of false positive results. Age of screening was between 3th to 5th days of life preventing false positive results and was not beyond 7th day thereby preventing delayed diagnosis of congenital hypothyroidism. We used widely used safe cut off sTSH value >20mIU/L for recall purpose in order to prevent missing out cases of mild to moderate CH which are quite well picked up by lower cut off like. Fortunately no dropouts were observed in our study making 100% recall success and retesting of all screening positive cases. None of the studied newborn mother was on anti-thyroid drug making the study free of drug induced neonatal hypothyroidism. Using sTSH value we were able to elicit the degree of iodine deficiency prevalent here as described by WHO.

**Conclusion:** In our study we found a higher incidence of 1 in 737, when compared to estimated national incidence of congenital hypothyroidism. Our study reported significant number of neonates with sTSH value >10mIU/L indicating iodine deficiency prevalent in this part of country. Education and awareness about Iodine deficiency and Iodine Deficiency Disorders (IDD) to susceptible population and thereby encourage intake of adequate Iodine in food. Larger and nationwide integrated study need to be done to estimate the burden and morbidity of congenital hypothyroidism in society both at regional and national level. Thus this can provide suitable planning and implementation of screening program at both national and regional level as necessary and credible screening guidelines must be laid, more so to gauge the incidence and epidemiology of CH in our country.



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