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Original Research Article

An observational study on the prevalence of congenital hypothyroidism and factors affecting TSH levels in premature babies at tertiary care rural centre

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ABSTRACT

Background: Premature babies, particularly those with very low birth weight (VLBW), are at a higher risk of developing congenital hypothyroidism. The inadequate development of the hypothalamic-pituitary axis in preterm infants contributes to the higher prevalence of this condition in this population. However, the optimal screening and treatment protocols for congenital hypothyroidism in preterm newborns remain unclear.
Methods: This was a hospital-based observational study conducted over a period of 18 months. The study included 150 preterm babies born at the Sri Adichunchanagiri hospital and research centre. Non-probability sampling was used to select the study subjects. Data on demographic and clinical factors were collected from mothers and newborns. Blood samples were collected at day 3 of life to estimate thyroid-stimulating hormone levels. Correlations between TSH levels and various parameters were analyzed using statistical methods.
Results: The study found that the prevalence of congenital hypothyroidism in preterm newborns was 2%. The mean TSH level at day 3 was 7.56 mIU/L, and 9.3% of cases had TSH levels above 20 mIU/l. Significant associations were found between high TSH levels and primiparity, vaginal delivery, and maternal gestational diabetes mellitus. There was an inverse correlation between TSH levels and gestational age, birth weight, and Apgar scores at 1 and 5 minutes.
Conclusions: The study revealed a prevalence of congenital hypothyroidism of 2% in preterm newborns. Risk factors such as primiparity, vaginal delivery, and maternal GDM were associated with high TSH levels. These findings highlight the importance of screening and early detection of congenital hypothyroidism in premature babies to improve outcomes.

Keywords: Congenital hypothyroidism, Preterm babies, Risk factors, TSH levels, Prevalence

INTRODUCTION

The prevalence of congenital hypothyroidism is 1 in 4000 people worldwide. Congenital hypothyroidism is prevalent in India at a rate of 1:2500-2800.[1] The most frequent preventable cause of mental retardation, it is also the most prevalent paediatric endocrine condition. The age at which therapy is started has a significant impact on the outcome. Delaying treatment causes irreversible mental retardation and a variety of cognitive abnormalities, whereas early replacement therapy - starting in the first few weeks of life - has been shown to improve IQ levels. Unfortunately, at this critical age, clinical diagnosis is challenging because neonates do not exhibit many clinical symptoms and indicators of hypothyroidism. The disease is frequently overlooked, which has irreparable negative repercussions on IQ.[2] Congenital hypothyroidism is a condition that meets all the criteria for neonatal screening because it is difficult to diagnose clinically, early treatment and diagnosis have a significant positive impact on outcomes, sensitive diagnostic tests are available, and the cost-benefit ratio is excellent.[2] The first neonatal screening programme

for congenital hypothyroidism was created in Quebec in the middle of the 1970s; this type of screening programme is now carried out in many nations, underscoring the need of early detection and treatment of congenital hypothyroidism.[3] The usual procedures continue to be debatable despite the existence of a sizable body of historical data about screening programmes for congenital hypothyroidism.[4] Indian Academy of Pediatrics recommends the use of cord blood samples for screening for congenital hypothyroidism.[5-7]

Most screening programmes around the world collect blood samples after 72 hours of birth, but because babies are frequently discharged early, cord blood samples are often used as well.[5,6] Premature births are becoming increasingly common, and improvements in neonatal care have increased the survival of preterm newborns who have thyroid dysfunction more frequently than term newborns. Data from various screening programmes showed that due to inadequate hypothalamic-pituitary axis development, preterm and low birth weight (LBW) neonates had a greater rate of CH than normal newborns.[7-10]

It has been estimated that the prevalence of this syndrome is around 1 in 400 instances in very low birth weight (VLBW) newborns with birth weights of less than 1500 g, which is much greater than the prevalence in full-term infants (1 in 4000 cases).[10,11] On behalf of all paediatric endocrinologist associations worldwide, the European Society for Pediatric Endocrinology (ESPE) published updated guidelines on congenital hypothyroidism in 2014 and advised rescreening for the condition in all preterm newborns.[11] The techniques of screening for preterm newborns have also been detailed in other recent guidelines, such as those published in the journals of the Japanese Society for Pediatric Endocrinology and the Indian Society for Pediatric and Adolescent Endocrinology.[12,13] The best way to treat thyroid dysfunction in premature newborns is yet unknown, though. The current study sought to ascertain the prevalence and risk factors of congenital hypothyroidism in preterm infants in light of the aforementioned debate.

METHODS

This is a hospital based observational study conducted in Department of Pediatrics, Adi Chunchanagiri Institute of Medical Science, B. G. Nagara, which is a tertiary care hospital from March 2021 to September 2022 (18 months). Preterm babies born during this study period were included.

Sample size

Consecutive type of non-probability sampling was used for selection of study subjects after taking prior informed consent from the parents. A total of 150 pre-term babies born in our hospital during study period, fulfilling eligibility criteria were included in the study.

Inclusion criteria

Preterm babies <37 completed weeks of gestation, Low birth weight babies (<2500 kg), Very low birth weight babies (<1500 kg), Extremely low birth weight babies (<1000 kg), babies born to hypothyroid mother, babies with congenital heart disease, babies with congenital malformation and anomlies were included.

Exclusion criteria

Term gestation > 37 completed weeks of gestation were excluded.

Procedure

The protocol of the study was accepted by the Ethical Committee of our institute. Informed consent was obtained from either of the parents. Socio-demographic data related to the study was taken from mothers and antenatal and intra partum information was noted from the records. After delivery, newborns were examined in detail for APGAR score, birth weight and any other clinical condition. Clinical data of both mothers and newborns were recorded and entered in a predesigned proforma. About 1 ml of venous blood sample was collected under aseptic precaution at day 3 of life for the estimation of TSH (TSH>20Mu/l). If TSH value was significant according to gestation, again screened after 2 weeks of life. Assay range for TSH was 1.00– 20.00 mIU/l. To identify the factors affecting congenital hypothyroidism- a history about mother with thyroid disorder and on any anti-thyroid drug intake, any congenital anomalies and malformations, advanced maternal age, low birth weight babies, neural tube defects, mode of delivery, GDM mother, were ruled out.

Statistical analysis

Data were statistically described in terms of mean (±SD), frequencies (number of cases) and percentages when appropriate. Comparison of quantitative variables between the study groups was done using unpaired t test for normally distributed data or by Mann Whitney test for non-normally distributed data. For comparing categorical data, Chi square test was performed. Exact test was used instead when the expected frequency is less than 5. A probability value (p value) less than 0.05 was considered statistically significant. All statistical calculations were done using computer programs Microsoft Excel 2021 (Microsoft Corporation, NY, USA) and SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) version 26.

RESULTS

The study groups were analyzed based on various demographic and clinical factors.

Table 1: Distribution of parameters.

Parameter	Distribution (%)
Maternal age (years)	
≤20	16.7
21-25	49.3
26-30	26.0
> 30	8.0
Total	100.0
Mean maternal age (years)	24.7
Parity	
Primi	48.7
Multi	51.3
Maternal hypothyroidism	7.3
Gestational diabetes mellitus (GDM)	4.0
Congenital anomalies	1.3
Mode of delivery	
Vaginal	52.0
LSCS	48.0
Gender distribution	
Female	43.3
Male	56.7
Birth weight (Kg)	
<1.5	1.3
1.5-2.0	12.7
2.0-2.5	56.7
>2.5	29.3
Newborn status	
AGA	89.3
SGA	10.0
LGA	0.7
APGAR Score (1 min)	
<7	9.3

The distribution of study groups according to maternal age revealed that the majority of participants fell within the age range of 21-30 years, accounting for approximately three-fourths (75.3%) of the females in the study. The mean age of the mothers of the study cases was 24.7 years. In terms of parity, the study observed that 48.7% of the mothers were primigravida, while 51.3% were multigravida. This indicates a relatively equal distribution between first-time mothers and those who had previously given birth. The study also examined the presence of specific risk factors among the participants. Maternal hypothyroidism was identified in 7.3% of the cases, gestational diabetes mellitus (GDM) in 4.0% of the cases, and congenital anomalies in 1.3% of the cases. Regarding the mode of delivery, the study found that 52% of the cases were delivered vaginally, while 48% required a cesarean section (LSCS). The gender distribution of the newborns revealed that 56.7% were males, while 43.3% were females. In terms of birth weight, the study observed that the majority of newborns had a birth weight between 2.0-2.5 kg, accounting for 56.7% of the cases. Additionally, 29.3% had a birth weight greater than 2.5 kg, 12.7% fell within the range of 1.5-2.0 kg, and only 1.3% had a birth weight below 1.5 kg.

Table 2: Correlation of blood TSH levels at day 3 with various parameters.

Pearson co-relation matrix: TSH		
Gestational age	R value	-0.26
	P value	0.03
Birth weight	R value	-0.30
	P value	0.02
APGAR at 1 min.	R value	-0.21
	P value	0.04
APGAR at 5 min.	R value	-0.23
	P value	0.35

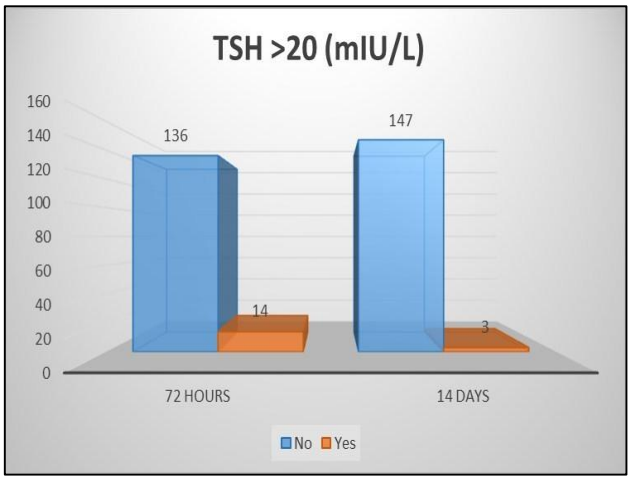

Figure 1: Association of raised TSH levels at day 3 with day 14 TSH levels.

The status of the newborns was categorized as appropriate for gestational age (AGA), small for gestational age (SGA), or large for gestational age (LGA). The study found that the vast majority (89.3%) of the babies were classified as AGA, while 10.0% were categorized as SGA, and only 0.7% fell into the LGA category. The study also assessed the Apgar scores of the newborns, which reflect their overall well-being and vital signs at 1 and 5 minutes after birth. The analysis revealed that 9.3% of the babies had an Apgar score below 7 at 1 minute, while 2% had an Apgar score below 7 at 5 minutes. To summarize, the study examined the distribution of study groups based on the following parameters: maternal age, parity, presence of risk factors (including maternal hypothyroidism, GDM, and congenital anomalies), mode of delivery, gender distribution of newborns, birth weight, newborn status (AGA, SGA, LGA), and Apgar scores at 1 and 5 minutes. These findings provide a comprehensive overview of the characteristics of the study population.

DISCUSSION

Congenital hypothyroidism has a worldwide prevalence of 1 in 4000. In India, the prevalence ranges from 1 in 2500 to 1 in 2800. It is not only the most common pediatric endocrine disorder but also the leading preventable cause of mental retardation.[14] The prevalence of congenital

hypothyroidism is higher in preterm and low-birth-weight (LBW) newborns compared to normal ones. Insufficient development of the hypothalamic–pituitary axis in these infants contributes to the higher rate of congenital hypothyroidism.

In the present study, the researchers aimed to determine the prevalence and risk factors of congenital hypothyroidism in premature babies. The study included 150 preterm babies born at their hospital. Blood samples were collected at day 3 of life to estimate TSH levels. If the TSH value was significant according to gestation, the babies were screened again after 2 weeks of life.

The prevalence of congenital hypothyroidism in the study was observed to be 2% or 20 out of 1000 preterm newborns. Previous studies by Fariba Hemmati et al conducted a retrospective study of congenital hypothyroidism in premature infants of live births.[15] TSH levels in premature infants were measured by heel prick test, and the number of premature newborns with high TSH was 15381, and the prevalence of CH was 2.3%. Dinushan et al conducted a study to determine the incidence of congenital hypothyroidism in preterm infants and to identify associated risk factors. A total of 3137 preterm infants born at 22-31 weeks of gestational age were included in the study. Forty-nine infants were diagnosed with congenital hypothyroidism. The overall incidence of congenital hypothyroidism was 1.56%.[15,16]

The mean blood TSH value in the present study was 7.56 mIU/l, and 9.3% of cases had TSH values over 20 mIU/l at day 3. In a study by Gupta A et al on newborns, neonates having values more than 20 microIU/ml at 72 hours. Manglik et al observed that of babies had their TSH levels above 20mIU/l at 48-72 hours. Mekonnen Y et al. in their study observed that males and females had TSH values between 10-20 mIU/l. Klein et al in a study showed that the TSH levels were more than 20 µU/ml in 15% cases. Factors affecting high blood TSH levels at 48-72 hours were investigated in the study. The researchers found significantly higher TSH levels in babies born to primiparous mothers compared to multiparous mothers. Gupta A et al. also observed higher TSH levels in first order deliveries. Lakshminarayana et al also observed the mean TSH level to be significantly higher in first order neonates. Kumar V et al. also observed primigravida mothers as risk factors for a significantly high TSH level. Similar results were also observed by other authors.[17,18]

The mode of delivery also influenced TSH levels, with significantly higher levels observed in babies born vaginally compared to those delivered via cesarean section. This finding was consistent with studies by Divya Durga et al. who found the highest values with forceps extraction followed by vaginal deliveries and lowest in infants born by elective cesarean section. Lakshminarayana SG et al. also observed the prevalence rate of TSH level >20 µIU/ml to be significantly higher in neonates delivered by assisted vaginal delivery and normal delivery. In another study, Chan et al found that TSH levels were elevated with instrumental and vaginal deliveries but not with elective or emergency LSCS. No significant association was found between blood TSH levels and thyroid status of the newborn. However, mean blood TSH levels were significantly higher in babies born to mothers with gestational diabetes mellitus (GDM). Chan et al. reported higher TSH levels in infants of mothers with gestational diabetes and pregnancy-induced hypertension. Kumar et al also observed GDM as a risk factor for a significantly high TSH level.[19,20]

A significant inverse correlation was observed between TSH levels and gestational age, indicating higher TSH values with decreasing gestational age. Significantly higher TSH levels were observed in low-birth-weight babies (<2.5 kg). Even higher values were observed among very low birth weight babies. Similarly, significantly higher TSH levels were observed in small for gestational age (SGA) babies and those requiring resuscitation. A significant inverse correlation was also observed between blood TSH values and Apgar score at 1 minute. The postnatal surge in TSH levels, common to all newborns, is considered to be mediated through alpha-adrenergic stimulation following cold stress. Perinatal factors such as hypoxia and perinatal stress contribute to increased secretion of catecholamines, which in turn may be responsible for the observed increase in TSH levels in newborns with perinatal complications, low Apgar scores, vaginal delivery, and primiparous mothers.[21] In summary, the present study observed a prevalence of congenital hypothyroidism as 2%. Elevated TSH levels were associated with factors such as primiparity, gestational diabetes mellitus, vaginal mode of delivery, small for gestational age, gestational age, birth weight, need for resuscitation, and low Apgar scores. Therefore, when interpreting elevated TSH values in newborns, it is important to consider these perinatal stress factors and the mode of delivery.

CONCLUSION

The study observed a prevalence of 2% among the preterm babies, highlighting the importance of early screening and detection. Various factors were found to be associated with elevated TSH levels, including primiparity, gestational diabetes mellitus, vaginal delivery, small for gestational age, gestational age, birth weight, need for resuscitation, and low Apgar scores. These findings emphasize the need for careful consideration of perinatal stress factors and mode of delivery when interpreting elevated TSH values in newborns. Early identification and appropriate management of congenital hypothyroidism can help prevent long-term complications and ensure optimal neurodevelopmental outcomes for these infants.

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