IJN
Iranian Journal of Neonatology
http://ijn.mums.ac.ir

Open Access
Original Article

Newborn Thyroid-Stimulating Hormone Dynamicity as per the Antenatal and Perinatal Factors

Patel Suprava[1], Padhi Phalguni[2], Naik Tripty[2], Rachita Nanda[1*], Mohapatra Eli[1], Sarita Agrawal[3]

1. Department of Biochemistry, All India Institute of Medical Sciences, Raipur, Chhattisgarh, India
2. Department of Pediatrics, All India Institute of Medical Sciences, Raipur, Chhattisgarh, India
3. Department of Obstertrics and Gynaecology, All India Institute of Medical Sciences, Raipur, Chhattisgarh, India

ABSTRACT

Background: Recent surge in the diagnoses of congenital hypothyroidism (CH) has necessitated the measurement of newborn TSH levels and understanding of the way various antenatal and perinatal factors influence its dynamicity.
It is a cross-sectional study on newborns delivered or admitted to the All India Institute of Medical Sciences Raipur (AIIMS Raipur), Chhattisgarh, India.
Methods: Dried blood spot analysis of newborn thyroid-stimulating hormone (nTSH) was carried out on 1,216 newborns after ethical clearance. The TSH levels were presented in percentage to determine the distribution in the study population. The mean values were compared within the groups categorized under each variable. The newborns' variables in this study included birth weight, Ponderal index, and neonatal complications. The studied maternal variables included antenatal visits, maternal age, gestational age, anemia, and mode of delivery.
Results: The mean (standard error of the mean) for nTSH was obtained at 3.37 (0.12) mIU/L and 97% of newborns were below 8 mIU/L. Mean nTSH was significantly high in mothers older than 30 years (P=0.019) and those with anemia during the antenatal period (P<0.001). It was significantly raised in babies with complications (P=0.004). Besides, higher values were also observed in low birth weight babies and those with low Ponderal Index. Higher nTSH was observed among newborns born to mothers with a thyroid disorder, those delivered prematurely and/or by cesarean section, and those with no antenatal visits.
Conclusion: It is highly essential to take a precautionary note on the antenatal status of mothers in terms of advanced age, premature delivery, associated maternal diseases, mode of delivery, newborn's birth weight, and complications which are supposed to influence the dynamicity of thyroid hormones in newborns and result in CH.

Keywords: Dried blood spot, Maternal disease, Percentile, Sick newborn, TSH range

Introduction

Regarding the recent rising trend of inborn errors of metabolic disorders (IEM), especially congenital hypothyroidism (CH), newborn screening (NBS) has become of prime importance in neonatal medicine. Estimation of newborns' thyroid-stimulating hormone (nTSH) using dried blood spot (DBS) sample is gaining its position as one of the principal components in diagnostic panels of neonatal health assessment. A nationwide registry is still lacking in India to provide the actual prevalence of CH, determine the effectiveness of disease surveillance, and identify the etiological factors for CH. The morphological dysgenesis of the thyroid gland is the common cause of CH to date, whereas other inherited or genetic defects pertaining to hormone synthesis and utilization are relatively rare (1). Many genetic mutations, such as THOX2 (for thyroid oxidase), DUOX2, DUOXA2 (for thyroid peroxidase), PAX8, and others are still under investigation and may be attributed to persistent CH. Other than these un-modifiable risk factors, studies have reported the influence of modifiable risk factors on CH (1–3). Some studies have pointed out the effect of maternal factors, such as advanced age, increased parity, associated thyroid

* *Corresponding author*: Rachita Nanda, Department of Biochemistry, All India Institute of Medical Sciences, Aipur, Chhattisgarh. Tel: 8518881763; Email: dr.rachitananda@aiimsraipur.edu.in

Please cite this paper as:
Suprava P, Phalguni P, Tripty T, Rachita N, Eli M, Sarita A. Newborn Thyroid-Stimulating Hormone Dynamicity as per the Antenatal and Perinatal Factors. Iranian Journal of Neonatology. 2021 Jul: 12(3). DOI: 10.22038/ijn.2021.52430.1937

disorders, gestational diabetes mellitus (GDM), gestational hypertension, pre-eclampsia, anemia, premature delivery, and cesarean section (CS) mode of delivery on CH; however, these factors' influence on nTSH has not been well characterized yet (2, 4–6). Advanced age and CS mode of delivery have become increasingly common in India irrespective of parity. (7,8). The former is common among the urban population, whereas the latter is common in rural communities. Moreover, low birth weight (LBW) and neonatal complications are quite common in India and have an influence on thyroid status (9-10). As a tertiary center, the institute in the present study attends to both rural and urban populations, complicated and uncomplicated pregnancies, and healthy and sick children. Therefore, the combination of these features provided a unique opportunity to explore the impact of these factors on nTSH levels using the DBS sample which is a universally accepted approach for the NBS. The study aimed to present an analytical view regarding the percentile distribution of the nTSH among the study population and the influence of antenatal and perinatal study variables on nTSH.

Methods

In total, 1,216 newborns were enrolled for the cross-sectional study conducted in the Department of Biochemistry and Department of Pediatrics in AIIMS Raipur, Chhattisgarh, India. The study was approved by the Ethical Committee of AIIMS Raipur, India. The newborns were either delivered or admitted to the AIIMS Raipur, India, and were selected for the study through the purposive sampling method after the informed consent was obtained from the parents or the legal guardians. The parents were allowed enough time to peruse the information brochure and ask their questions regarding the benefits of NBS. Babies with a history of receiving blood transfusions were excluded from the study.

A sampling of the babies was carried out within 48 h of the birth through the heel prick method. With all the necessary aseptic measures, two spots of capillary blood were collected on Whatman 903 paper. The Filter paper was air-dried at room temperature for 3-4 h and then placed in a plastic zipper pouch prior to sending it to the laboratory for quantitative analysis.

The DBS was analyzed for the estimation of TSH using fluoroimmunoassay kits (Labsystems Diagnostics Oy, VANTAA, Finland). The cut-off limit for screening positive for TSH was 10mIU/L. Newborns with TSH values above 10 mIU/L were considered screening positive and were recalled for confirmatory testing. Blood was collected in vacutainer without anticoagulant, and confirmatory testing was performed for serum TSH and T4 levels through chemiluminescence method using automated chemiluminescence immunoanalyzer (Advia Centaur XP immunoassay system, Siemens Healthineers, USA). The biological reference intervals (as per kit insert) for TSH and T4were were 0.51–4.3 μIU/L and 0.76–1.7 ng/dL, respectively. The babies with positive confirmatory results were immediately called for counseling, treatment, and monitoring.

The newborns' variables considered for the study were birth weight, Ponderal Index, neonatal complications, and TSH levels. The maternal variables under study were age, frequency of antenatal care (ANC) visits, parity, gestational age at the time of delivery, any associated medical or surgical history during the antenatal period, anemia, and mode of delivery. The newborns and the mothers were ranked or categorized into different groups for the comparison of the mean TSH and prediction of the trend of TSH values. The characteristics of the groups have been presented in the respective tables.

Statistical analysis

The data analysis was performed using SPSS software (version 20). The quantitative variables, such as birth weight, length, head circumference, Ponderal Index, TSH levels, maternal age, gestational age, and maternal hemoglobin were calculated for 5^{th}, 10^{th}, 25^{th}, 50^{th}, $75^{th,}$ and 95^{th} percentiles along with the frequency of observations under each percentile. The nTSH values were not normally distributed; therefore, they were transformed for normalization only for mean comparison analysis. The prevalence and percentiles were based on non-normalized distribution to obtain the actual percentage. The variables were transformed for rank types or categorized according to the approximation of rank groups and the mean TSH value was compared within the groups using analysis of variance (ANOVA). A p-value less than 0.05 ($P<0.05$) was considered statistically significant.

Results

In total, 1,216 newborns were enrolled for the study and were screened for nTSH through DBS samples taken within 48 h of birth.

The percentile distribution of study variables

In this study, nTSH of DBS ranged from 0.2 to

88 mIU/L. Moreover, the mean (standard error of the mean [SEM]) was obtained at 3.37 (0.12) mIU/L with a median of 3.0 mIU/L. In addition, the mean (SE) of normalized nTSH data was estimated at 3.5 (0.1) mIU/L with a median of 4.4 mIU/L. However, non-normalized data were considered for the presentation of frequency percentages and percentile distribution. The mean of each percentile of nTSH is presented in Figure 1. Based on the assessments, nTSH in 97% and 25% of the cases were below 8 mIU/L and below 2 mIU/L, respectively. The percentile values of the various quantitative variables of newborns and their mothers are tabulated in Table1. The birth weight of infants ranged from 680 g to 4.0 Kg. The mean weight in each percentile was lower in females compared to males.

The mean length was 31 cm (28-59 am) and the head circumference was obtained at 19 (21-40) cm. Moreover, Ponderal Index was obtained at 12.04 (0.98-13.03). In addition, the ranges of ANC visits, maternal age, gestational age, parity, and maternal hemoglobin were between 0 and 5; 18 and 38 years; 28 and 47 weeks; 1 and 6 issues, and 6 and 14 Gm/dL.

The comparison of mean TSH value between the groups

Figures 2-7 present the trend of mean nTSH value in different groups as ranked in the

Table 1. The percentile based mean values of the neonatal and maternal variables

Variables	5th	10th	25th	50th	75th	95th
Birth weight (Kg)	1.6	1.9	2.43	2.8	3.13	3.5
Length (cm)	41	42	45	48	51	55
Head circumference (cm)	25	26	30	33	35	38
Pondrel index	1.8	1.95	2.2	2.4	2.6	3.1
Maternal age (in years)	21	22	25	29	32	35
Gestational age (in weeks)	33	35	37	38	40	43
Maternal hemoglobin (Gm/dL)	9.1	9.6	10.7	11.6	12.3	13.1

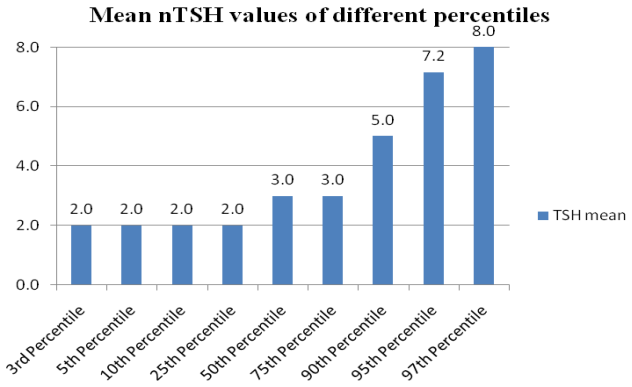

Figure1. The mean nTSH values on the basis of percentiles

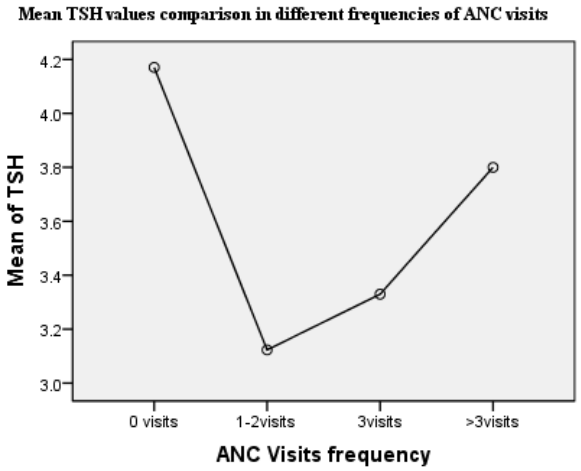

Figure 2. Comparison of mean nTSH values in different frequencies of ANC visits

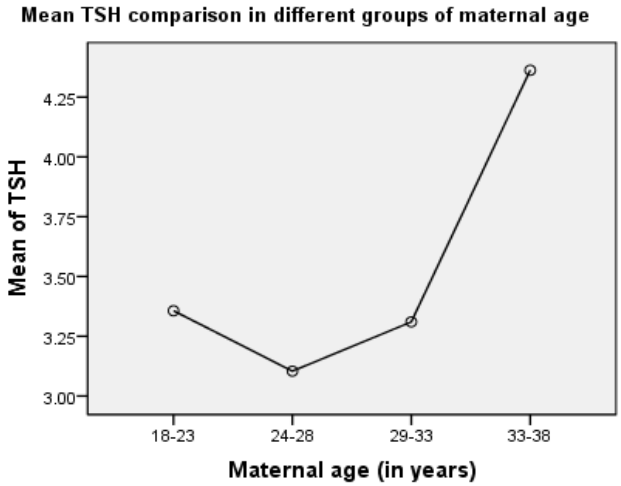

Figure 3. Comparison of mean nTSH values in different maternal age groups

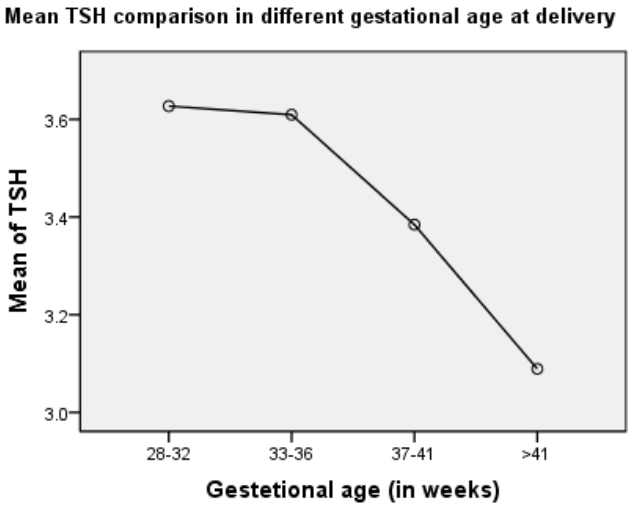

Figure 4. Comparison of mean nTSH values at different gestational age

maternal variables. It was found to be the highest in mothers with no ANC visits (P=0.2). A significantly rising trend was observed with the increase in maternal age (P=0.019). Prematurely delivered newborns (delivered before the 37th weeks of gestation is completed) depicted higher mean nTSH levels (P=0.6). The nTSH levels were highest in mothers with associated thyroid disorders (P=0.9) and those with anemia and hemoglobin levels less than 11 Gm/dL (P<0.001). The mean nTSH showed a rising trend from mild and moderate anemia to severe anemia. Higher values were also reported for babies delivered by CS compared to those delivered normally (NVD).

The nTSH levels as shown in Figure 8 were found to be increased in LBW babies (below 2.5Kg) and those with birth weight above 3.5Kg (P=0.25). Elevated levels of nTSH were also reported for babies with low Ponderal Index (P=0.8, Figure 9). The nTSH level, as shown in Figure 10, was significantly raised in neonates with complications compared to those without complications (P=0.004)

The percentile-based observed frequency of study population

$Table_{suppl}1$ presents the percentile-based frequency distribution of study variables among the study population for better understanding. Compared to Table1, it can be observed that the birth weight in 50% of the newborns ranged from 2.43 Kg to 3.13 Kg. The Ponderal Index in 816 (67.1%) babies ranged from 25th percentile (2.2) to 95th percentile (3.1). Moreover, 19 neonates in the study population were reported positive for nTSH screening, out of whom four babies were confirmed for CH. The neonatal and maternal factors of these 19 screening positive

cases are presented in Table 2. Almost 54% of the mothers were in the age range of 25-32 years. Gestational age at or below 37 weeks was evident in the 25th percentile, and nearly 25% of mothers had hemoglobin levels below 10.7 Gm/dL.

Table 2. Details of neonatal and maternal factors in babies with higher nTSH values

nTSH	Age	ANC visits	Parity	Gestational age	ANC history	Anemia status	Mode of delivery	Gender	Birth weight	Ponderal Index	Neonatal complication
17.6	33-38	3	2	33-36	Thyroid related	Mild to moderate	LSCS	F	1.91-2.43	1.5-2.5	Yes
13.5	33-38	3	2	37-41	No	Mild to moderate	NVD	M	3.14-3.5	>3.5	Yes
14.4	24-28	0	3	37-41	No	Mild to moderate	LSCS	F	2.81-3.13	1.5-2.5	Yes
12	29-33	3	2	37-41	No	Mild to moderate	LSCS	M	3.14-3.5	>2.5-3.5	No
11	29-33	3	2	37-41	Thyroid related With GDM	Mild to moderate	LSCS	F	>3.5	>3.5	No
17	18-23	0	1	33-36	No	Mild to moderate	LSCS	M	3.14-3.5	>2.5-3.5	Yes
21	33-38	3	2	37-41	No	Mild to moderate	LSCS	M	1.91-2.43	1.5-2.5	No
38*	33-38	0	1	33-36	No	Severe	LSCS	M	2.44-2.8	>2.5-3.5	Yes
15	33-38	3	2	28-32	Pre-eclampsia	Mild to moderate	LSCS	F	<1.6	1.5-2.5	Yes
11	29-33	>3	2	37-41	Thyroid related	Mild to moderate	NVD	M	2.81-3.13	>2.5-3.5	No
14	18-23	3	2	28-32	Thyroid related	Severe	LSCS	M	1.6-1.9	>2.5-3.5	Yes
11.3	18-23	0	1	37-41	No	Mild to moderate	NVD	F	1.91-2.43	1.5-2.5	No
11	29-33	3	1	>41	No	Mild to moderate	LSCS	F	>3.5	1.5-2.5	No
87.8*	33-38	0	1	37-41	No	Mild to moderate	NVD	M	2.44-2.8	1.5-2.5	Yes (thyroid dys-hormonogenesis)
13.8	24-28	3	2	28-32	No	Severe	LSCS	F	1.6-1.9	1.5-2.5	Yes
77*	33-38	1-2	2	37-41	Thyroid related	Mild to moderate	LSCS	F	1.91-2.43	>2.5-3.5	No
44*	33-38	3	4	37-41	No	Mild to moderate	LSCS	F	>3.5	1.5-2.5	Yes (thyroid dys-hormonogenesis)
12	29-33	3	2	>41	Thyroid related	Mild to moderate	LSCS	M	2.81-3.13	>2.5-3.5	No
11	18-23	0	1	33-36	No	Mild to moderate	LSCS	F	1.91-2.43	>2.5-3.5	No

*Confirmed for CH

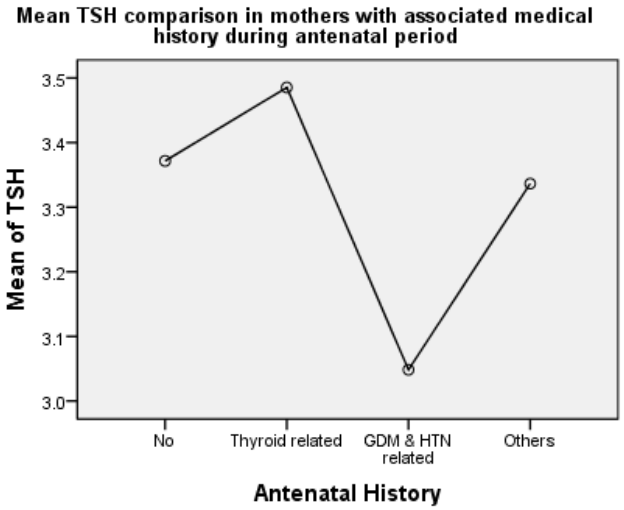

Figure 5. Comparison of mean nTSH values in babies of mothers with associated antenatal history

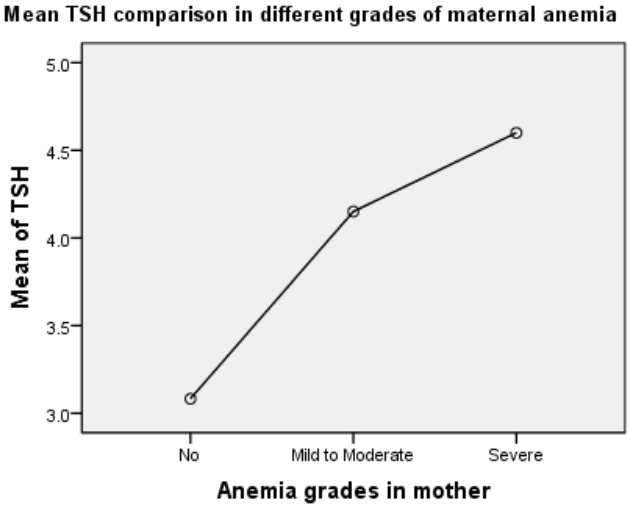

Figure 6. Comparison of mean nTSH values in the babies of mothers with different grades of anemia

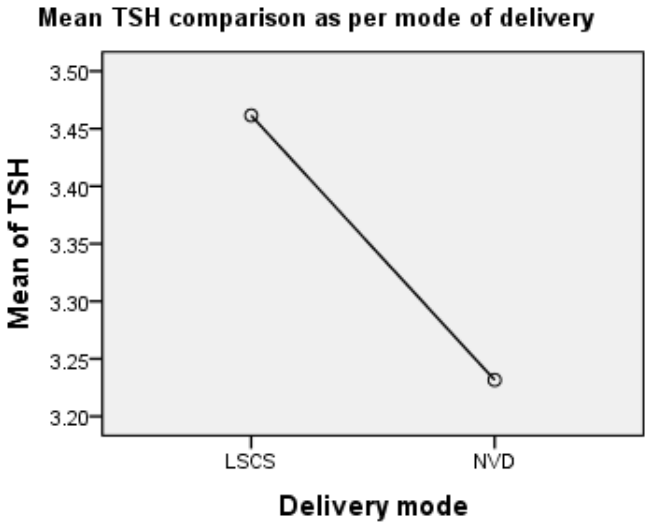

Figure 7. Comparison of mean nTSH values in mothers with different modes of delivery

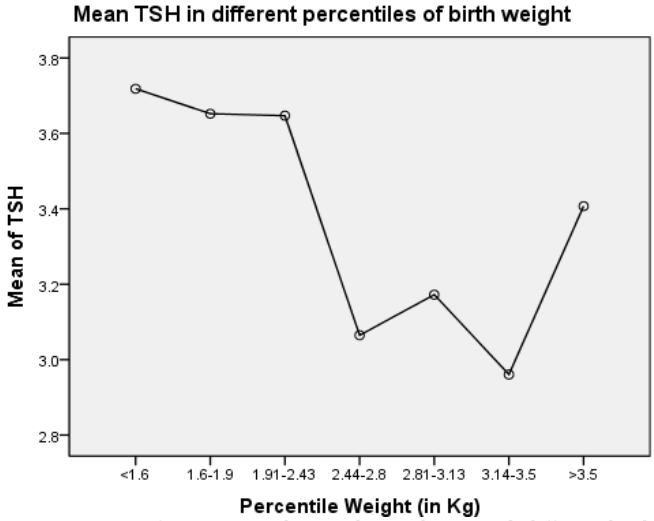

Figure 8. Comparison of mean TSH values in the newborns with different birth weight

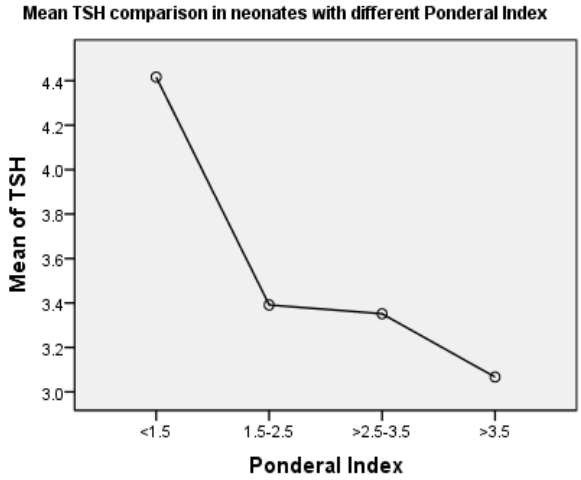

Figure 9. Comparison of mean TSH values in newborns with different Ponderal Index

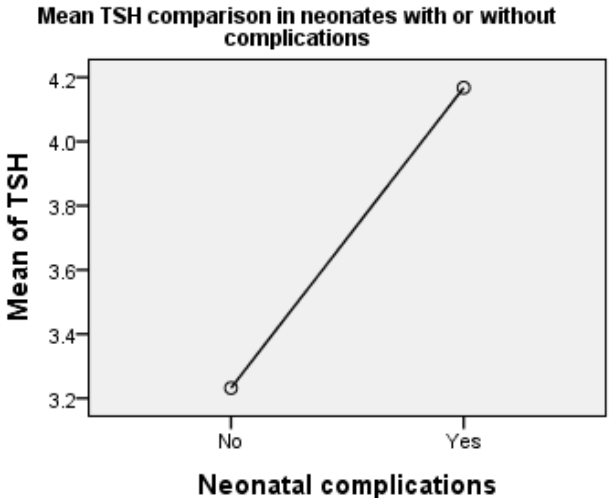

Figure 10. Comparison of mean TSH values in newborns with and without complications

Discussion

The NBS is of paramount importance in day-to-day clinical practice in neonatal health. However, few studies reflect the nTSH distribution in the study population. The observed mean (SE) of DBS nTSH was obtained at 3.37(0.12) mIU/L (Figure1) which was lower than 5.23 (0.3) mIU/L reported by Sheikhbahaei et al. measured in serum samples of 246 healthy term neonates using enzyme-linked immunosorbent assay (ELISA) method (11). The difference in means can be attributed to the specimen of analysis and the methodology used in both studies. The mean values and percentile results (25^{th}-75^{th}:2.0-3.0) (Table1) obtained in the present study were almost comparable to those obtained in the study conducted by Yu et al. that documented mean nTSH of 2.39mIU/L (P25-P75:1.37-3.93) for DBS samples of 437,342 newborns who were screened using time-resolved fluoroimmunoassay method (12).

An overall frequency of LBW was 27.5% (n=335) and 25.2% (n=306) of the birth weight of newborns in the present study and was below 3^{rd} percentile according to the weight-for-age chart for both genders prepared by World Health Organization (WHO) (13). Such high frequency of LBW could be an outcome effect of maternal anemia since more than 50% of mothers with LBW babies were anemic and 27% of them had associated medical conditions, such as thyroid disorders, GDM, hypertension, and pre-eclampsia. These findings were consistent with those of various other studies conducted in India (14–16). Maternal thyroid diseases and some other medical conditions alter the thyroid status in a fetus and neonatal period of infants and result in high nTSH in these babies, which

explains the finding of high nTSH in LBW newborns (9-10,17). An increase in the mean value of birth weight above 3.5 Kg was observed as well. A mild rise in nTSH level of overweight babies has been documented in few studies that could be explained by thyroid hormone resistance and mutation in TSH receptors associated with obesity (18-19). Serial estimation of the parameter would delineate the overall trend of hormone level status in these newborns.

Few studies have documented the impact of maternal factors on thyroid parameters. Such various antenatal and perinatal factors as maternal parity, ANC visits, age, anemia, associated medical conditions, and mode of delivery can influence TSH level (1-2). A significant difference in the level of nTSH was observed in association with maternal age factor and anemia (P=0.019 and P=<0.001) (Figures 3 and 6). Though not significant, nTSH values in babies also reflect a rising trend in the case of infants born to mothers with no ANC visits, premature deliveries, associated thyroid-related issues, and CS deliveries (Figures 2, 4, 5,7). These results were in line with the study conducted by Fan et al. Their study reported low thyroid hormones (FT3) in the cord blood in mothers with advanced age. The effect might be an indirect influence since few studies have implicated an association between advanced maternal age with neonatal subclinical hypothyroidism (SCH) or CH (2, 20), and few other studies reported no significant association between these two factors (1, 21). Nearly 23.8% of mothers aged more than 30 years had a history of thyroid disorders; however, this rate was 17% in younger mothers. It is worth mentioning that the highest TSH values were found in babies born to mothers with thyroid disorders (Figure 4). It should be noted that autoimmune conditions increase the chances of transient CH (3). Studies have depicted neonatal TSH rise in neonates born to hypothyroid mothers and suggested that maternal and newborn anti-thyroperoxidase titer should also be estimated since they might be clinically relevant in such cases (3,12). Based on the obtained results mothers of 31.6% of the newborns with raised nTSH were diagnosed with hypothyroidism. The present study lacks the evidence of titers since it was not estimated in newborns and that all mothers did not have the reports for the same. The recall rate for confirmatory testing was also higher in these newborns as reflected in above-mentioned studies. In total, four babies were diagnosed with congenital hypothyroidism after the performance of confirmatory testing which is indicative of a prevalence of 3.3 per 1000 live births. The prevalence of CH reported in India varied from 3:1000, 3:430, 1:476 to 1.6:1000 and 1:1221 (9, 22–25). One out of these four infants had maternal hypothyroidism indicating a frequency percentage of 24% that was quite high. Thyroid dyshormonogenesis was diagnosed in two of these four infants, according to a thyroid uptake study. It was not possible to trace the fourth case due to the paucity of information . It is reported that two-thirds of the cases of CH could be due to thyroid dysgenesis resulting from genetic mutations in genes encoding for thyroid peroxidase (DUOX2, DUOXA2), pendrin defect, thyroglobulin defect, iodotyrosine deiodinase, transporters, and receptors (12, 26). Maternal iodine deficiency is also quite common in India that has shown to be associated with transient CH. Fetal exposure to antithyroid drugs, transfer of maternal antibodies, and fetal exposure to iodine excess are all known contributory factors (26). One study also revealed a lower intelligence quotient (IQ) in children born to mothers over 30 years old (27). This observation is indicative of the fact that advanced age might influence thyroid development in a fetus. Even the chances for associated medical conditions, such as thyroid disorders, GDM, preeclampsia, and other disorders would be higher with advanced age. The mean TSH was also higher in babies delivered by mothers who had no ANC visits and those who underwent CS. Studies have documented that complicated pregnancies associated with no ANC visit usually result in prolonged labor or assisted labor induction and often end up with CS (28). Although not approved by enough studies, prolonged or obstructed labor cause hypoxic changes that induce D3 deiodinase activity which in turn inactivates peripheral T3 and converts it into inactive T2 (29). Stress conditions play a role in lowering the level of negative acute-phase proteins, such as albumin, transthyretin, and thyroid-binding globulin (TBG) as the transporters for thyroid hormones (30). Low levels of transporter proteins can also lower the total thyroid hormones and alters thyroid function tests. This could also be an explanatory finding for the significantly elevated TSH level observed in newborns with some complications who were enrolled for the present study. Even gestational anemia could also have an altered implication on maternal and neonatal thyroid profile (4). The

TSH values in the newborns of anemic mothers were significantly higher compared to those with non-anemic mothers. The mean nTSH was significantly different in the different grades of anemia (P<0.001). Anemia might influence the maternal thyroid profile that can indirectly alter thyroid hormones in newborns. Iron deficiency is also implicated with altered thyroid peroxidase activity through an unknown mechanism. Whether anemia is a cause or effect of thyroid disorder is still under investigation.

Female newborns, premature newborns, and the term newborns with low ponderal index depicted a non-significant rise in nTSH values in screening. The results of the present study revealed a decreasing trend of nTSH values with an increase in gestational weeks. This finding is consistent with those of previous studies that reported higher TSH levels in premature babies (17,31,32). Thyroid hormone secretion in fetuses increases at mid-gestational age and shows an exponential rise as the gestational weeks advance, with a maximum surge at birth. Preterm neonates may not have a mature hypothalamic-pituitary-thyroid axis which leads to low thyroid levels and high TSH levels (2, 33). Low Ponderal Index as seen in small gestational babies or preterm babies explained the cause for an elevated level of nTSH in these groups of newborns (34).

Limitations

Regarding the limitations of the present study, one can refer to the fact that this was a single-center hospital-based study with very minimal sample size. The laboratory findings were based on the cut-off values as recommended by the kit brochure; however, nationwide lab data are required to formulate a normalized reference range for the population. Moreover, repeated measurements of thyroid hormones, which could have reflected the hormone dynamicity more accurately in the postnatal period, were not carried out after 6 to 8 weeks. Eventually, a better comparison would have been possible provided free T3 and T4 in the newborns were estimated as well.

Conclusion

A significant increase in neonatal TSH was observed in neonates born to mothers of advanced age and those with anemia. The TSH level was raised in babies with neonatal complications. Therefore, it is a challenge to understand the dynamicity of thyroid hormone in the neonatal period as influenced by various antenatal, perinatal and neonatal factors. Statistical interpretations in various studies carried different implications which might lead to erroneous inferences. However, an error-free study design with a larger sample size in the community is essentially required to derive an actual lab reference range and to establish the relationship between neonatal thyroid hormones and the associated factors. It is important to take a cautionary note on mothers and babies of advanced age, prematurely delivered infants, associated maternal diseases, modes of delivery, LBW babies, and neonatal complications.

Acknowledgments

None.

Funding

The study was funded by the All India Institute of Medical Sciences, Raipur, Chhattisgarh, India.

Conflicts of interest

Authors declare that they have no conflict of interest regarding the publication of the present study.

References

1. Medda E, Olivieri A, Stazi MA, Grandolfo ME, Fazzini C, Baserga M, et al. Risk factors for congenital hypothyroidism: results of a population case-control study (1997–2003). Eur J Endocrinol. 2005; 153(6):765-73.
2. Fan P, Luo ZC, Tang N, Wang W, Liu Z, Zhang J, et al. Advanced maternal age, mode of delivery, and thyroid hormone levels in Chinese newborns. Front Endocrinol. 2020; 10:913.
3. Ozdemir H, Akman I, Coskun S, Demirel U, Turan S, Bereket A, et al. Maternal thyroid dysfunction and neonatal thyroid problems. Int J Endocrinol. 2013; 2013:987843.
4. Yang Y, Hou Y, Wang H, Gao X, Wang X, Li J, et al. Maternal thyroid dysfunction and gestational anemia risk: meta-analysis and new data. Front Endocrinol. 2020; 11:201.
5. Zhou J, Luo J, Zhao H, Wang J, Lin F, Zhang H, et al. Risk factors of 125 cases of neonatal congenital hypothyroidism during perinatal period. Zhonghua Liu Xing Bing Xue Za Zhi. 2015; 36(7):747-51.
6. Ryckman KK, Spracklen CN, Dagle JM, Murray JC. Maternal factors and complications of preterm birth associated with neonatal thyroid stimulating hormone. J Pediatr Endocrinol Metab. 2014; 27(9-10):929-38.
7. Pawde AA, Kulkarni MP, Unni J. Pregnancy in women aged 35 years and above: a prospective observational study. J Obstet Gynaecol India. 2015; 65(2):93-6.

8. Singh P, Hashmi G, Swain PK. High prevalence of cesarean section births in private sector health facilities- analysis of district level household survey-4 (DLHS-4) of India. BMC Public Health. 2018; 18(1):613.
9. Lakshminarayana SG, Sadanandan NP, Mehaboob AK, Gopaliah LR. Effect of maternal and neonatal factors on cord blood thyroid stimulating hormone. Indian J Endocrinol Metab. 2016; 20(3):317-23.
10. Herbstman J, Apelberg BJ, Witter FR, Panny S, Goldman LR. Maternal, infant, and delivery factors associated with neonatal thyroid hormone status. Thyroid. 2008; 18(1):67-76.
11. Sheikhbahaei S, Mahdaviani B, Abdollahi A, Nayeri F. Serum thyroid stimulating hormone, total and free T4 during the neonatal period: Establishing regional reference intervals. Indian J Endocrinol Metab. 2014; 18(1):39-43.
12. Yu B, Long W, Yang Y, Wang Y, Jiang L, Cai Z, et al. Newborn screening and molecular profile of congenital hypothyroidism in a Chinese population. Front Genet. 2018; 9:509.
13. World Health Organization. Low birth weight. Geneva: World Health Organization; 2011.
14. Apoorva MS, Thomas V, Kiranmai B. A cross sectional study on socio-demographic and maternal factors associated with low birth weight babies among institutional deliveries in a tertiary care hospital, Hyderabad, Telangana. Int J Community Med Public Health. 2018; 5(11):4901-4.
15. Bhattacharjya H, Das S, Ghosh D. Proportion of low birth weight and related factors in a tertiary care institute of Tripura. Int J Med Public Health. 2015; 5(1):10-3.
16. Rajashree K, Prashanth HL, Revathy R. Study on the factors associated with low birth weight among newborns delivered in a tertiary-care hospital, Shimoga, Karnataka. Int J Med Sci Public Health. 2015; 4(9):1287-90.
17. Mao H, Yang R, Liu Z. Correlation of congenital hypothyroidism with birth weight and gestational age in newborn infants. Zhejiang Da Xue Xue Bao Yi Xue Ban. 2007; 36(4):378-81.
18. Vigone MC, Capalbo D, Weber G, Salerno M. Mild hypothyroidism in childhood: who, when, and how should be treated? J Endocr Soc. 2018; 2(9):1024-39.
19. Niranjan U, Wright NP. Should we treat subclinical hypothyroidism in obese children? BMJ. 2016; 352:i941.
20. Rezaeian S, Poorolajal J, Moghimbegi A, Esmailnasab N. Risk factors of congenital hypothyroidism using propensity score: a matched case-control study. J Res Health Sci. 2013; 13(2):151-6.
21. Diéguez M, Herrero A, Avello N, Suárez P, Delgado E, Menéndez E. Prevalence of thyroid dysfunction in women in early pregnancy: does it increase with maternal age? Clin Endocrinol. 2016; 84(1):121-6.
22. Raj S, Baburaj S, George J, Abraham B, Singh S. Cord blood TSH level variations in newborn – experience from a rural Centre in southern India. J Clin Diagn Res. 2014; 8(7):PC18-20.
23. Rama Devi AR, Naushad SM. Newborn screening in India. Indian J Pediatr. 2004; 71(2):157-60.
24. Sundararaman PG. Neonatal thyroid dysfunction-lessons from Indian experience. Thyroid Res Pract. 2013; 10(4):7.
25. Gopalakrishnan V, Joshi K, Phadke S, Dabadghao P, Agarwal M, Das V, et al. Newborn screening for congenital hypothyroidism, galactosemia and biotinidase deficiency in Uttar Pradesh, India. Indian Pediatr. 2014; 51(9):701-5.
26. Rastogi MV, LaFranchi SH. Congenital hypothyroidism. Orphanet J Rare Dis. 2010; 5:17.
27. Myrskylä M, Silventoinen K, Tynelius P, Rasmussen F. Is later better or worse? Association of advanced parental age with offspring cognitive ability among half a million young Swedish men. Am J Epidemiol. 2013; 177(7):649-55.
28. Raatikainen K, Heiskanen N, Heinonen S. Under-attending free antenatal care is associated with adverse pregnancy outcomes. BMC Public Health. 2007; 7(1):268.
29. Drigo RA, Fonseca TL, Werneck-de-Castro JPS, Bianco AC. Role of the type 2 iodothyronine deiodinase (D2) in the control of thyroid hormone signaling. Biochim Biophys Acta. 2013; 1830(7): 3956-64.
30. Rabah SA, Gowan IL, Pagnin M, Osman N, Richardson SJ. Thyroid hormone distributor proteins during development in vertebrates. Front Endocrinol. 2019; 10:506.
31. Kaluarachchi D, Allen D, Eickhoff J, Dawe S, Baker M. Thyroid-stimulating hormone reference ranges for preterm infants. Pediatrics. 2019; 144(2): e20190290.
32. Liu C, Wang K, Guo J, Chen J, Chen M, Xie Z, et al. Small for gestational age is a risk factor for thyroid dysfunction in preterm newborns. BMC Pediatrics. 2020; 20(1):179.
33. Forhead AJ, Fowden AL. Thyroid hormones in fetal growth and prepartum maturation. J Endocrinol. 2014; 221(3):R87-103.
34. Roje D, Banovic I, Ivo B, Tadin I, Ivica T, Vucinović M, et al. Gestational age--the most important factor of neonatal ponderal index. Yonsei Med J. 2004; 45(2):273-80.