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STUDY OF MATERNAL AND NEONATAL VARIABLES AFFECTING THE THYROID STIMULATING HORMONES LEVELS IN NEONATES

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ABSTRACT

Background and Aim: Thyroid hormones are critical for fetal growth and development, especially of the central nervous system. The primary regulating hormone is thyroid stimulating hormone (TSH). The present study aimed to determine the effect of maternal and neonatal variables on the thyroid-stimulating hormones levels in neonates.

Patients and Methods: This retrospective study was carried out on 856 newborns delivered in Ghurki Trust and Teaching Hospital, Lahore – Pakistan from 6th March 2022 to 5th April 2023. Within 48-72 hours of delivery, all neonates were investigated for neonatal-TSH (n-TSH). TSH was measured using a fuorometric enzyme immunoassay on a dried blood spot. Maternal variables included demographic status, clinical history, and obstetric history. As neonatal factors, anthropometric measures at birth and clinical information were recorded. SPSS version 27 was used for descriptive statistics.

Results: The overall mean maternal age was 29.28±3.84 years. The mean birth weight of neonates was 2720.23±556.98 gram. Mean gestational age was 38.58±2.978 weeks. Overall mean parity and maternal Hb (g/dl) was 1.48±0.95 and 11.48±1.216 respectively. An n-TSH showed a significant connection with maternal age whereas the maternal blood hemoglobin levels showed a significant negative connection. A slight change was observed in TSH levels with neonate's birth weight. Neonates of first order, delivered normally at term or preterm, and need post birth resuscitation had significantly higher TSH levels.

Conclusion: The present study found that neonates of first order, delivered normally at term or preterm, and need post birth resuscitation had significantly higher TSH levels. . However, additional factors may exacerbate the impact, and these aspects should be addressed when evaluating the screening program's results.

Keywords: Thyroid stimulating hormones, Neonates, Maternal factors, Neonatal factors

INTRODUCTION

Fetal development, brain maturation, and neurodevelopment are all associated with thyroid hormones. During pregnancy, hypothyroidism leads to the pregnancy associated with complications such as gestational diabetes, hypertension, adverse neurodevelopmental outcomes, and premature delivery due to the closed relationship of neonatal and maternal thyroid levels [1-3]. Thyroid stimulating hormones are responsible for thyroid hormone synthesis that significantly varies in premature neonates; term neonates had higher TSH levels than preterm [4]. In preterm infants, variation in TSH levels significantly implicates the complications associated with thyroid in later stages of life due to its heritability [5]. Due to the dynamic nature of thyroid stimulating hormone during pregnancy, it varies with changes in circumstances accordingly. TSH is a critical regulatory hormone that governs the sufficient synthesis of thyroid hormones (T3 and T4) in the thyroid gland as well as their active conversion in the periphery. By the time the newborn exhibits signs of thyroid diseases, the levels have become severely disturbed, perhaps resulting in irreparable consequences. It is critical that any modest change in thyroid levels be detected early in order to avoid such clinical irreversibility. As a result, as compared to active thyroid hormones (T3 and T4), neonatal TSH levels are the major goal for screening thyroid-related diseases [6].

Numerous maternal and infant variables have been implicated in the diversity of TSH levels in term and preterm newborns. Gestational age, mode of delivery, infant gender, birth weight, and age at testing are different factors that affect the variation in thyroid stimulating hormone levels [7, 8]. Hypertension, parity, gestational diabetes, and maternal age are various maternal variables associated with thyroid hormone levels of neonates; however, conflicting results have been reported by numerous studies [9-12]. The iodine sufficiency of the population could be monitored by TSH levels of neonates as a marker [13]. Lee et al. [14] found no statistically change in mean TSH levels in blood during the 4th-7th day of life. In Pakistan, there has been very little research on the impact of different variables on TSH levels. This study examined the effects of different maternal and neonatal variables on TSH levels in neonates delivered in a Tertiary Care Hospital.

METHODOLOGY

This retrospective study was carried out on 856 newborns delivered in Ghurki Trust and Teaching Hospital, Lahore – Pakistan from 6th March 2022 to 5th April 2023. Within 48-72 hours of delivery, all neonates were investigated for neonatal-TSH (n-TSH). TSH was measured using a fuorometric enzyme immunoassay on a dried blood spot. Maternal variables included demographic status, clinical history, and obstetric history. As neonatal factors, anthropometric measures at birth and clinical information were recorded. Maternal complications associated with pregnancy such as hypertension and gestational diabetes as well as additional details such as delivery mode (normal or c/section), and labour types (natural or induced) were recorded. Blood samples (2 mL) were extracted with a 5 cc syringe from the umbilical vein of the umbilical cord (15-20 cm long) cut during the baby's delivery in a sterile container. The samples were analyzed on a Cobas analyzer within 4 hours using an electrochemiluminescence immunoassay. Based on kit standards, TSH value 1.00-16.10 IU/mL was considered as normal levels in neonates. Below and above this range were considered as abnormal cases.

SPSS version 27 was used for descriptive statistics. Numerical variables such as birth weight and TSH levels were expressed as mean and standard deviation whereas continuous variables such as mode of delivery, maternal age, order of birth, and maternal complications were described as frequency and percentages. The Chi-square test compared the changes in the TSH levels and their relationship to neonatal and maternal variables. $P < 0.05$ was considered statistically significant.

RESULTS

Of the total 856 neonates, there were 436 (50.9%) male and 420 (49.1%) females. The overall mean maternal age was 29.28±3.84 years. The mean birth weight of neonates was 2720.23±556.98 gram. Mean gestational age was 38.58±2.978 weeks. Overall mean parity and maternal Hb (g/dl) was 1.48±0.95 and 11.48±1.216 respectively. An n-TSH showed a significant connection with maternal

age whereas the maternal blood hemoglobin levels showed a significant negative connection. A slight change was observed in TSH levels with neonate's birth weight. Neonates of first order, delivered normally at term or preterm, and need post birth resuscitation had significantly higher TSH levels. The TSH mean value was 7.79±5.39 µIU/mL with normal range of 1.00 to 16.10 µIU/mL. Demographic and baseline characteristics of patients are shown in Table-I. Table-II represents the effect of neonatal factors on thyroid-stimulating hormones (TSH). Association of maternal age with TSH levels in neonates are shown in Table-III.

Table-I Demographic and baseline characteristics

Variables	**Value [Mean ± SD]**
Gender N (%)	
Male neonates	436 (50.9)
Female neonates	420 (49.1)
Maternal age (years)	29.28±3.84
Birth weight (gram)	2720.23±556.98
Gestational age (weeks)	38.58±2.978
Parity	1.48±0.95
Maternal Hb (g/dl)	11.48±1.216
TSH (µIU/mL)	7.79±5.39

Table-II Effect of neonatal parameters on TSH levels

Neonatal Variables	**N (%)**	**TSH (µIU/mL)**
All neonates	856 (100)	7.79±5.39
Birth Order		
1st order	298 (34.8)	7.98.±6.84
2nd order	282 (32.9)	7.73±4.92
3rd order	276 (32.3)	7.66±4.41
Mode of Delivery		
Normal vaginal delivery	302 (35.3)	7.89±6.50
Elective C/Section	264 (30.8)	7.71±4.79
Emergency C/section	290 (33.9)	7.77±4.88
Birth Weight (gram)		
<2000	32 (3.73)	7.86±5.75
2000-2500	258 (30.1)	7.85±6.23
2500-4000	554 (64.7)	7.68±5.09
>4000	12 (1.40)	7.78±4.49
APGAR score		
<5	18 (2.1)	8.39±7.68
5-7	52 (6.1)	7.89±5.42
>7	786 (91.8)	7.09±3.07
Gender		
Male	436 (50.9)	7.89±5.78
Female	420 (49.1)	7.69±5.0
Resuscitation required		
Routine	814 (95)	7.83±5.41
Beyond initial care	42 (5)	7.75±5.37

Table-III Effect of maternal factors on TSH levels

Maternal variables	**Normal range (1-16.1) N (%)**	**Below normal (<1.0) N (%)**	**Above normal (>16.1) N (%)**	**P-value**
All neonates	792 (92.5)	48 (5.6)	16 (1.9)	0.89
Maternal Age (years)				0.96
18-25	408 (51.5)	25 (52.1)	9 (56.3)	
26-30	356 (44.9)	22 (45.8)	7 (43.8)	
>30	28 (3.5)	1 (2.1)	0 (0)	
Maternal Complications				0.17
Hypertension	98 (12.4)	20 (41.7)	2 (12.5)	
Gestational diabetes	35 (4.4)	3 (6.3)	0 (0)	
Hypothyroidism	9 (1.1)	0 (0)	2 (12.5)	
Both HTN and GD	17 (2.1)	3 (6.3)	0 (0)	
No complications	633 (79.9)	22 (45.8)	12 (75)	

DISCUSSION

The present study mainly focused on the association of maternal and neonatal variables with thyroid stimulating hormones in neonates and found that n-TSH shows a substantial relationship with neonate birth weight, first order neonates, and normal vaginal delivery at term or preterm. In comparison to other parameters, the relationship between TSH and maternal and neonatal demographic characteristics has received less study. Identifying variables that influence TSH variability in babies may aid in understanding the causes of aberrant thyroid levels at birth. The newborn screening data were analyzed to investigate the effect of various maternal and baby variables on the n-TSH of neonates, as hypothesized. This study reveals that various maternal and neonatal factors influence n-TSH. It might be related to the interaction of several other elements for proper thyroid function.

The current investigation duplicated in preterm infants association with maternal and neonatal demographics and TSH that had previously been investigated in term newborns [15]. It has been observed that TSH levels declined from mature to premature neonates. Numerous studies revealed that increasing levels of TSH were significantly associated with decreased birth weight and gestational age [16, 17].

A number of investigations have looked at how maternal demographics (such as parity), maternal exposures (such as smoking), pregnancy problems (such as hypertension), and delivery outcomes (such as delivery type) affect neonatal thyroid hormone levels. One such research assessed the effects of mother and baby demographics and delivery outcomes on TSH levels in cord blood [18]. Another study conducted by Bosch-Gimenez et al. [19] reported that lower levels of TSH have been seen in neonates delivered through cesarean section compared to those at normal vaginal delivery. The current investigation came to a similar result.

In the present study, no significant association of gender with variation in TSH levels were observed, however, previous studies reported TSH levels association with gender [20-22]. Similar to a previous study, first and second order neonates had significantly higher TSH levels [23]. In contrast to the present study, birth weight, which has been proven to have a varied influence on TSH level and neonates with lower gestational age had lower TSH levels [24, 25].

Many prior investigations have found that n-TSH levels rise with gestational age [26, 27]. However, an inverse association has also been documented, and numerous additional investigations [28, 29] found no difference in n-TSH levels with gestational age. One possible reason is that the hypothalamic-pituitary response develops with increasing gestational age. Premature newborns have impaired hypothalamic-pituitary response [30].

In this study, there was a significant negative connection between birth weight and n-TSH level. The results are consistent with those of previous studies [31, 32]. Birth weight had no effect on n-TSH, according to Verma C et al. [33]. Gestational age influences birth weight, length, and head size. Numerous adaptations occur throughout pregnancy. To begin, maternal total or bound thyroid

hormone levels rise with serum thyroid-binding globulin concentration. Second, TSH levels fall in early pregnancy due to poor activation of TSH receptors by human chorionic gonadotropin during the first 12 weeks of pregnancy. Thyroid hormone secretion is therefore promoted, and higher serum free thyroxine (T4) levels restrict hypothalamic thyrotropin-releasing hormone, limiting pituitary TSH output. TSH levels return to baseline in the latter stages of pregnancy and gradually increase in the third trimester due to placental expansion and the generation of placental deiodinase. These physiologic changes should be responsible for the newborn's lower TSH with improved gestation and growth metrics [34].

CONCLUSION

The present study found that n-TSH has significant association with neonate's birth weight, first order neonates, and those delivered by normal vaginal delivery at term or preterm. However, additional factors may exacerbate the impact, and these aspects should be addressed when evaluating the screening program's results.

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