

MATERNAL HYPOTHYROIDISM AND ITS EFFECTS ON NEONATAL THYROID FUNCTION: A RETROSPECTIVE STUDY

VIJAYALAKSHMI CHANDRASEKHAR¹, KOMAL SAHITHI BARLA¹, SUCHITRA PUSAPATI²,
 VISWA KALYAN KOLLI^{3*}, VENKATA MANASA RONGALA⁴

¹Department of Obstetrics and Gynecology, GITAM Institute of Medical Sciences and Research, GITAM (Deemed to be University), Visakhapatnam, Andhra Pradesh, India. ²Department of Paediatrics, GITAM Institute of Medical Sciences and Research, GITAM (Deemed to be University), Visakhapatnam, Andhra Pradesh, India. ³Department of Biochemistry, GITAM Institute of Medical Sciences and Research, GITAM (Deemed to be University), Visakhapatnam, Andhra Pradesh, India. ⁴Department of Community Medicine, GITAM Institute of Medical Sciences and Research, GITAM (Deemed to be University), Visakhapatnam, Andhra Pradesh, India.

*Corresponding author: Viswa Kalyan Kolli; Email: kolli.kalyan@gmail.com

Received: 06 June 2023, Revised and Accepted: 18 July 2023

ABSTRACT

Objective: The objective of the study is to correlate maternal factors (age, parity, type of delivery, thyroid-stimulating hormone [TSH], and thyroxine [T4] values) and the newborn factors (gestational age, birth weight, and gender) with the TSH and T4 values of the newborn.

Methods: A retrospective observational study was conducted on 90 hypothyroid mothers who were delivered at our Institute between January 2022 and March 2023. The 90 neonates born to these hypothyroid mothers underwent newborn screening tests for thyroid functions (tri-iodothyronine, T4, TSH) after 72 h of birth. These values were statistically analyzed with respect to maternal and fetal parameters.

Results: 7 of the 90 neonates (7.77%) had elevated TSH values, i.e., >10 mIU/L. T4 values were abnormal in 31 neonates (34.4%), i.e., <11 ug/dL or >21.5 ug/dL but had normal TSH values. There was only one case where T4 levels were low and TSH level elevated. The correlation of TSH values with maternal and fetal parameters such as age of mother, parity, gestational age, baby weight, type of delivery, and the gender of the baby was not significant as p-values were all >0.05. There is a weak negative correlation ($r=-0.044$) between maternal TSH and neonatal TSH values which was statistically not significant. However, the maternal TSH and baby weight values are having positive correlation ($r=0.113$).

Conclusion: Our study showed no significant correlation between maternal hypothyroidism and newborn TSH and T4 values which may be due to early antenatal recognition and supplementation with levothyroxine.

Keywords: Maternal hypothyroidism, Newborn screening, Thyroid-stimulating hormone.

© 2023 The Authors. Published by Innovare Academic Sciences Pvt Ltd. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>) DOI: <http://dx.doi.org/10.22159/ajpcr.2023v16i9.48824>. Journal homepage: <https://innovareacademics.in/journals/index.php/ajpcr>

INTRODUCTION

Thyroxine (T4) plays an important role in fetal central nervous system development as it assists in migration, differentiation, and proliferation of neuronal cells [1]. During pregnancy, the fetus depends on maternal thyroid hormone supply for its growth up to the 20th week of gestation before its own thyroid gland starts hormone production [2-4]. This supply of T4 and the T4-binding protein and T4-binding globulin to the growing fetus and the degradation of T4 by placental type 3 iodothyronine deiodinase necessitates an increased production of T4 by the mother during the antenatal period [5]. Diagnosis of both subclinical and overt maternal hypothyroidism is seen in 0.3-2.5% of pregnant women [6,7] and is known to cause adverse pregnancy and neonatal outcomes. Recognition of hypothyroidism early in the antenatal period is important, as supplementation with levothyroxine has been shown to substantially lower the adverse complications [8].

The number of studies on thyroid function tests of neonates born to hypothyroid mothers is very few in India, and this retrospective study has been done to provide an insight into the aspects of neonatal responses to maternal thyroid status [9,10].

METHODS

This retrospective study was conducted at GIMSR Hospital, Rushikonda, Visakhapatnam, Andhra Pradesh. Ethical clearance was obtained from hospital ethics committee GIMSR/Admin/Ethics/Approval/IEC-157/2023 dated 15 Mar 2023.

90 mothers diagnosed with hypothyroidism in the antenatal period and treated with levothyroxine supplements who delivered over a period of 14 months (January 2022-March 2023) and their 90 newborns were enrolled in this study. The data of these 90 hypothyroid mothers were retrieved from medical records and details of maternal age, parity, comorbidities, type of delivery, gestational age of newborn at delivery, birth weight of the baby, and gender of the baby were obtained. The newborn thyroid function tests, tri-iodothyronine, T4, thyroid-stimulating hormone (TSH) values, were collected at newborn

Table 1: The profile of the hypothyroid mothers

Characteristics	Frequency	Percent
Sex		
Female	44	48.9
Male	46	51.1
Total	90	100.0
Gestational age (GA)		
36 weeks-36 weeks+6 days	8	8.9
≥37 weeks	82	91.1
Total	90	100.0
Baby weight		
<2500	17	18.9
2501-3000	35	38.9
3001-3500	25	27.8
>3500	13	14.4
Total	90	100.0

screening 72 h after birth by venous blood sampling and were also retrieved from neonatal digital database.

Statistical analysis of the data was done using SPSS for Windows version 16. Data were represented with mean±SD for quantitative data and frequency with percentage for qualitative data. Chi-square test was used to measure the significance of the association and Pearson's correlation test was done to assess relation. $p < 0.05$ was considered as statistically significant.

Table 2: The profile of the newborn

Characteristics	Frequency	Percent
Mother's age		
18-25	39	43.3
26-35	47	52.2
>35	4	4.4
Total	90	100.0
Gravida		
Primi	35	38.9
Multi	55	61.1
Total	90	100.0
Type of delivery		
Normal	18	20.0
LSCS	72	80.0
Total	90	100.0

RESULTS

A total number of 90 hypothyroid mothers were delivered at our institute between January 2022 and March 2023, and their 90 newborns were enrolled in the study. The profile of the hypothyroid mothers is shown in Table 1 and the profile of the newborn is shown in Table 2.

The reference range of T4 values and TSH value for term infants after 72 h of birth was taken as follows [11]:

T4: 11.0-21.5 ug/dL (Mean: 16.5 ug/dL)

TSH: 1.0-10 mIU/L (Mean: 5.6 mIU/L)

The TSH and T4 values of the neonates are shown in Tables 3 and 4 along with their relationship to maternal and fetal parameters.

Out of the 90 newborns, seven (7.7%) showed elevated TSH values. T4 levels were low in 31 newborns, but when correlated with TSH levels, 30 newborns had normal TSH values. Only 1 newborn had low T4 level and elevated TSH level. The relationship between TSH values and gestational age, age of mother, parity, newborn weight and sex, and type of delivery was not significant as p-values were all > 0.05 . The relationship between maternal and newborn parameters with T4 levels was not significant as p-values were all > 0.05 . Maternal TSH and newborn TSH values are shown in Table 5.

There is a weak negative correlation ($r = -0.044$) between maternal TSH and neonatal TSH values which was statistically not significant.

Table 3: Relationship between newborn TSH levels versus mother and newborns' profile

Parameters	Category	TSH				Total		p-value
		Normal		Abnormal		Count	%	
		Count	%	Count	%			
GA	36 weeks-36 weeks+6 days	7	8.4	1	14.3	8	8.9	0.49
	≥37 weeks	76	91.6	6	85.7	82	91.1	
Age of mother	18-25	37	44.6	2	28.6	39	43.3	0.534
	26-35	42	50.6	5	71.4	47	52.2	
	>35	4	4.8	0	0.0	4	4.4	
Gravida	Primi	33	39.8	2	28.6	35	38.9	0.701
	Multi	50	60.2	5	71.4	55	61.1	
Baby weight	<2500	14	16.9	3	42.9	17	18.9	0.129
	2501-3000	33	39.8	2	28.6	35	38.9	
	3001-3500	25	30.1	0	0.0	25	27.8	
	>3500	11	13.3	2	28.6	13	14.4	
Type of delivery	Normal	15	18.1	3	42.9	18	20.0	0.14
	LSCS	68	81.9	4	57.1	72	80.0	
Sex	Female	39	47.0	5	71.4	44	48.9	0.261
	Male	44	53.0	2	28.6	46	51.1	

$p < 0.05$ is statistically significant. TSH: Thyroid-stimulating hormone

Table 4: Relationship between newborn T4 levels versus mother and newborns' profile

Parameters	Category	T4				Total		p-value
		Normal		Abnormal		Count	%	
		Count	%	Count	%			
GA	36 weeks-36 weeks+6 days	4	6.8	4	12.9	8	8.9	0.44
	≥37 weeks	55	93.2	27	87.1	82	91.1	
Age of mother	18-25	27	45.8	12	38.7	39	43.3	0.696
	26-35	30	50.8	17	54.8	47	52.2	
	>35	2	3.4	2	6.5	4	4.4	
Gravida	Primi	22	37.3	13	41.9	35	38.9	0.82
	Multi	37	62.7	18	58.1	55	61.1	
Baby weight	<2500	11	18.6	6	19.4	17	18.9	0.234
	2501-3000	24	40.7	11	35.5	35	38.9	
	3001-3500	13	22.0	12	38.7	25	27.8	
	>3500	11	18.6	2	6.5	13	14.4	
Type of delivery	Normal	13	22.0	5	16.1	18	20.0	0.599
	LSCS	46	78.0	26	83.9	72	80.0	

GA: Gestational age, T4: Thyroxine

Table 5: Relationship between maternal TSH levels with newborn TSH and newborn weight

Correlation	r-value	p-value
Mother TSH versus baby TSH	-0.044	0.688
Mother TSH versus baby weight	0.113	0.299

TSH: Thyroid-stimulating hormone

However, the maternal TSH and baby weight values are having positive correlation ($r=0.113$).

DISCUSSION

In this study, the prevalence of elevated TSH levels in the newborn, born to hypothyroid mothers, was found to be 7.7% and low T4 levels in 34.3% with normal TSH levels. The relationship between maternal TSH values and TSH values of the newborn was not statistically significant as $p<0.05$. There was no statistically significant association found between maternal TSH values and low birth weight of infants as $p=0.299$ and >0.05 . However, the r value was found to be 0.113 which could suggest a minor significant positive influence of maternal TSH and newborn birth weight.

Studies conducted by Anjum *et al.* [12] and Manglik *et al.* [13] found a significant association between maternal hypothyroidism and congenital hypothyroidism. There was no evidence of hypothyroidism or low birth weight in the neonates in the study done by Shravani *et al.* [14] as the mothers received timely treatment with levothyroxine before 18 weeks of gestation. Garg *et al.* [15] in India found the prevalence of thyrotropinoma in neonates to be 1: 47.

CONCLUSION

This study reveals that early screening of mothers for hypothyroidism in pregnancy and treatment with appropriate dosages of levothyroxine supplements and close follow-up of the neonates born to them by newborn thyroid screening tests will prevent the development of congenital hypothyroidism and associated neurocognitive impairment.

AUTHOR CONTRIBUTIONS

First author Dr. Vijayalakshmi Chandrasekhar Contributed for the conceptual design, research bench work and drafting the manuscript for the study. The second author Dr. Komal Sahithi Barla contributed for the collection of literature. The third author Dr. Suchitra Pusapati contributed for the data collection. The fourth and corresponding author Dr. Viswa Kalyan Kolli contributed for the data pooling and correction of manuscript. The fifth author Ms. Venkata Manasa Rongala contributed for the statistical analysis.

CONFLICTS OF INTEREST

The authors declare no conflict of interest.

FUNDING AND SUPPORT

It is declared that the authors did not receive any financial support or sponsorship for their study.

REFERENCES

- Bernal J. Thyroid hormones and brain development. *Vitam Horm* 2005;71:95-122. doi: 10.1016/S0083-6729(05)71004-9. PMID: 16112266
- Huget-Penner S, Feig DS. Maternal thyroid disease and its effects on the fetus and perinatal outcomes. *Prenat Diagn* 2020;40:1077-1084. doi: 10.1002/pd.5684. PMID: 32181913
- Glinioer D. The regulation of thyroid function in pregnancy: Pathways of endocrine adaptation from physiology to pathology. *Endocr Rev* 1997;18:404-33. doi: 10.1210/edrv.18.3.0300. PMID: 9183570
- Krassas GE, Poppe K, Glinioer D. Thyroid function and human reproductive health. *Endocr Rev* 2010;31:702-55. doi: 10.1210/er.2009-0041. PMID: 20573783
- Schussler GC. The thyroxine-binding proteins. *Thyroid* 2000;10:141-9. doi: 10.1089/thy.2000.10.141. Erratum in: *Thyroid* 2000;10:372. PMID: 10718550
- Khalid AS, Joyce C, O'Donoghue K. Prevalence of subclinical and undiagnosed overt hypothyroidism in a pregnancy loss clinic. *Ir Med J* 2013;106:107-10. PMID: 23691843
- Mahadik K, Choudhary P, Roy PK. Study of thyroid function in pregnancy, its fetomaternal outcome; a prospective observational study. *BMC Pregnancy Childbirth*. 2020;20:769. doi: 10.1186/s12884-020-03448-z. PMID: 33302910; PMCID: PMC7726876
- Pearce EN. Management of hypothyroidism and hypothyroxinemia during pregnancy. *Endocr Pract* 2022;28:711-8. doi: 10.1016/j.eprac.2022.05.004. PMID: 35569735
- Banakar MK, Formosa M. Serum thyroid function tests in neonates of mothers with thyroid disease. *Indian J Pediatr* 2011;78:870-3. doi: 10.1007/s12098-010-0337-1. PMID: 21203866
- Sundaraman PG. Neonatal thyroid dysfunctions-lessons from Indian experience. *Thyroid Res Pract* 2013;10:7-8.
- Sheikhabaei S, Mahdaviyani 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;18:39-43. doi: 10.4103/2230-8210.126528. PMID: 24701428; PMCID: PMC3968730
- Anjum A, Afzal MF, Iqbal SM, Sultan MA, Hanif A. Congenital hypothyroidism in neonates. *Indian J Endocrinol Metab* 2014;18:213-6. doi: 10.4103/2230-8210.129114. PMID: 24741519; PMCID: PMC3987273
- Manglik AK, Chatterjee N, Ghosh G. Umbilical cord blood TSH levels in term neonates: A screening tool for congenital hypothyroidism. *Indian Pediatr* 2005;42:1029-32. PMID: 16269841
- Shravani MR, Tharashree CD, Yashodha HT. Maternal hypothyroidism and neonatal outcome. *Int J Contemp Pediatr* 2018;5:600-4.
- Garg R, Sait H, Jindal A, Juneja M, Gupta S, Thelma BK, *et al.* Factors associated with transient neonatal hyperthyrotropinemia. *Indian J Pediatr* 2020;87:482-3. doi: 10.1007/s12098-019-03095-z. PMID: 31705380