"EFFECT OF PERINATAL ASPHYXIA ON THYROID HORMONES AND THYROID STIMULATING HORMONE IN NEW BORNS"

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ABSTRACT:
Introduction: Perinatal asphyxia, a major cause of early infant deaths in India, accounts for 30% of neonatal mortality globally. It is a significant contributor to death and morbidity, with severe birth asphyxia affecting 4.6% of neonates. Prenatal asphyxia outcomes are challenging to predict. **Aims:** The study investigates the effects of perinatal asphyxia on thyroid hormones and TSH levels in newborns and the correlation between Hypoxic Ischemic Encephalopathy severity. **Methodology:** The study compares thyroid hormone levels in 50 full-term newborns, 25 with birth asphyxia and 25 without, over 18 months in Krishna Vishwa Vidyapeeth, Karad, assessing gestational age, perinatal events, consent, and newborn examination. **Results:** The study explores the effects of perinatal asphyxia on thyroid hormones and stimulating hormone levels in newborns, revealing low incidence of meconium-stained liquor, hypoxic-ischemic encephalopathy, and thyroid hormone differences. **Discussion:** The study found mixed associations between birth weight and perinatal asphyxia, with vaginal delivery more common in non-asphyxiated neonates and LSCS more prevalent in asphyxiated newborns. **Conclusion:** Perinatal asphyxia affects neonatal health, leading to lower thyroid hormone levels, higher HIE stages, seizures, and meconium stained liquor. Early identification, monitoring, and comprehensive management are crucial.

INTRODUCTION

Perinatal asphyxiaAsphyxia is a primary cause of early infant deaths in India, closely trailing infections, and it constitutes around 30% of neonatal mortality globally. In India, it is a significant contributor to death (28.8%) and morbidity, serving as the primary cause of stillbirths (45.1%). Approximately 8.4% at 1 minute and 2.45% at 5 minutes exhibit Apgar scores below 7, signifying a critical requirement for oxygen. Severe birth asphyxia affects around 4.6% of neonates.[1] Comprehending the terminology associated with oxygen deficiency is essential: Anoxia denotes a complete absence of oxygen resulting from several causes; hypoxia signifies a reduced oxygen supply to tissues, while ischemia refers to inadequate blood flow, jeopardizing tissue integrity.[2] Hypoxic-ischemic encephalopathy (HIE) is a specific condition characterized by encephalopathy due to oxygen deprivation. Neonatal encephalopathy, characterized by altered awareness and indications of brain damage, is present in several cases. The mortality rate for infants with HIE is approximately 20-30%, and 40% of survivors frequently encounter long-term complications such as cerebral palsy and other neuro developmental abnormalities.[3]

Forecasting outcomes in prenatal asphyxia is challenging. Diverse methodologies are employed, including scientific evaluation, observation of general movements, preliminary electrophysiological tests, imaging techniques such as ultrasound and MRI, and Doppler blood flow measurement. Despite the significance of thyroid hormones in essential bodily functions, their role in prenatal asphyxia warrants further scrutiny.

In this thesis, the terms perinatal asphyxia and birth asphyxia are synonymous.

AIM AND OBJECTIVES

The study aims to investigate the impact of perinatal asphyxia on thyroid hormones and TSH levels in newborns and the association between severity of Hypoxic Ischemic Encephalopathy.

MATERIALS AND METHODS

This descriptive study focuses on 50 full-term newborns, 25 of whom had birth asphyxia and 25 without. The study includes cases and controls, with a 18-month study period in Krishna Vishwa Vidyapeeth,

Karad. Exclusion criteria include preterm neonates, maternal history of thyroid dysfunction, fetal history of thyroid medication, antenatal malformations, metabolic disorders, and parents refusing consent. The study aims to compare FT3 levels in cases and controls, determining the minimum number of subjects required for the study.

The study involved assessing gestational age, perinatal events, consent, newborn examination, and thyroid hormone levels. Obstetric age was determined from obstetric records, and perinatal events included assisted techniques, APGAR scores, and weight at birth. Thyroid hormone levels were collected from both asphyxiated and non-asphyxiated groups at 18-24 hours of life. Data analysis compared thyroid hormone levels between cases and controls, and correlations were found. Statistical significance was determined at a p value less than 0.05.

RESULTS

The study analyzed the impact of perinatal asphyxia on thyroid hormones and stimulating hormone in newborns, comparing cases and controls.

Table1:Distribution of total neonates according to their birth-weight

Birthweight Group	No. of Neonates	Percent
2000 -2499 gm	10	20.0
2500 -3500 gm	40	80.0
Total	50	100.0

Table 1 shows 50 neonates' birth-weight distribution, with 20% having a weight between 2000-2499 grams, and 80% having a weight between 2500-3500 grams, indicating that most newborns were within or above the normal range.

Table2:Distribution of total patients according to mode of delivery

Mode of delivery	Cases		Control		Total	
	Freq	Percent	Freq	Percent	Freq	Percent
Vaginal Delivery	**13**	**52.0**	**17**	**68.0**	**30**	**60.0**
NormalVaginal Delivery	9	36.0	15	60.0	24	48.0
AssistedVaginalDelivery (Ventouse)	4	16.0	2	8.0	6	12.0
Lower Segment Caesarean Section (LSCS)	**12**	**48.0**	**8**	**32.0**	**20**	**40.0**
Meconium-stainedliquor	5	20.0	1	4.0	6	12.0
PreviousLSCS	0	0.0	4	16.0	4	8.0
Breech	2	8.0	2	8.0	4	8.0
Fetal Distress	3	12.0	0	0.0	3	6.0
Abruptio Placenta	2	8.0	0	0.0	2	4.0
PROM	0	0.0	1	4.0	1	2.0
Total	**25**	**100.0**	**25**	**100.0**	**50**	**100.0**

Table 2 shows the distribution of delivery modes between Cases (Asphyxiated Neonates) and Control (Non-asphyxiated neonates). It includes the frequency and percentage of each mode of delivery within each group. The table is divided into two main categories: Vaginal Delivery and Lower Segment Caesarean Section (LSCS). In the Vaginal Delivery category, normal vaginal deliveries are more common in the Control group, with 15 cases (60%) compared to 9 cases (36%) in the Cases group. Assisted vaginal deliveries are more common in the Cases group, with 4 cases (16%) and 2 cases (8%). Breech

deliveries are equal in both groups, and other indications for LSCS are more frequent in the Cases group. Pre-eclampsia is noted only in the Control group with 1 case (4%).

Table3:DistributionoftotalneonatesaccordingtoMeconium-StainedLiquor

Meconium-StainedLiquor	No. of Neonates	Percent
Yes	14	28.0
No	36	72.0
Total	50	100.0

Table 3 shows a low incidence of meconium-stained liquor among neonates, with only 28% of 50 having it, compared to 72% of 36 not having it.

Table 4: Comparison of APGAR score at 1 minamong cases and controls

APGAR1min Group	Cases		Control		Total	
	No. of Neonates	%	No. of Neonates	%	No. of Neonates	%
<=3	25	100.0%	0	0.0%	25	50.0%
>6	0	0.0%	25	100.0%	25	50.0%
Total	25	100.0%	25	100.0%	50	100.0%

Table 4 shows APGAR scores for asphyxiated and non-asphyxiated newborns, categorized as ≤3 and >6. 100% of cases had a score ≤3, while all control newborns had a score >6.

Table 5 presents a comparison of APGAR scores at five different cases and controls.

APGAR 5minGroup	Cases		Control		Total	
	No. of Neonates	%	No. of Neonates	%	No. of Neonates	%
3-6	9	36.0%	0	0.0%	9	18.0%
>6	16	64.0%	25	100.0%	41	82.0%
Total	25	100.0%	25	100.0%	50	100.0%

Table5 compares APGAR scores at 5 minutes for both groups, showing 36% of cases had scores between 3-6, while 64% had scores >6, excluding control newborns.

Table 6: Distribution of Case group according to HIE stage

HIE Stage	No. of Neonates	Percent
Stage1	12	48.0
Stage2	10	40.0
Stage3	3	12.0
Total	25	100.0

Table 6 shows varying severity of hypoxic-ischemic encephalopathy (HIE) in asphyxiated newborns, with Stage 1 observed in 48%, Stage 2 in 40%, and Stage 3 in 12%.

Table 7 displays the distribution of case groups based on the presence of seizure.

Seizures	No. of Neonates	Percent
Yes	13	52.0
No	12	48.0
Total	25	100.0

Table 7 shows that 52% of asphyxiated newborns experienced seizures, indicating a significant neurological complication in this group, compared to 48% who did not experience seizures.

Table 8 compares birth weight among cases and control groups.

Birth weight Group	Cases		Control		Total		Pvalue
	No. of Neonates	%	No. of Neonates	%	No. of Neonates	%	
2000 – 2499 gm	5	20%	5	20%	10	20%	0.999
2500 – 3500 gm	20	80%	20	80%	40	80%	
Total	25	100%	25	100%	50	100%	

Table 8 compares birth weights of 25 asphyxiated and 25 non-asphyxiated newborns. Both groups have the same distribution, with 20% in the 2000 gm - 2499 gm category and 80% in the 2500 - 3500 grams category. The p-value is 0.999, indicating no statistically significant difference in birth weights between the two groups.

Table 9:Comparison of mode of delivery among cases and controls

Modeof delivery	Cases		Control		Total		Pvalue
	No. of Neonates	%	No. of Neonates	%	No. of Neonates	%	
Normal Vaginal Delivery	13	52%	17	68%	30	60%	0.248
Lower Segment Caesarean Section (LSCS)	12	48%	8	32%	20	40%	
Total	25	100%	25	100%	50	100%	

Table 9 compares the mode of delivery (Normal Vaginal Delivery vs. Lower Segment Caesarean Section) among two groups. 52% of cases were delivered vaginally, while 48% were via LSCS. The p-value of 0.248 suggests no significant difference in delivery method between asphyxiated and non-asphyxiated groups.

Table10: Comparison of Meconium-Stained Liquor among cases and controls

Meconium-Stained Liquor	Cases		Control		Total		Pvalue
	No. of Patients	%	No. of Patients	%	No. of Patients	%	
Yes	11	44.0%	3	12.0%	14	28.0%	0.011
No	14	56.0%	22	88.0%	36	72.0%	
Total	25	100.0%	25	100.0%	50	100.0%	

Table 10 shows a significant difference (p-value of 0.011) in meconium-stained liquor prevalence between asphyxiated and non-asphyxiated newborns, with 44% of newborns having this condition, indicating a higher prevalence in asphyxiated newborns.

Table11: Comparison of FT3, FT4 and TSH values among cases and controls

Thyroid Hormones	Groups	Cases	Mean	Std. Deviation	Pvalue
FT3(18-24hrs)(pmol/L)	Case	25	2.76	.831	<0.001*
	Control	25	5.48	1.447	
FT4(18-24hrs)(ng/dL)	Case	25	1.84	.746	<0.001*
	Control	25	3.84	.624	
TSH(18-24 hrs)(mIU/L)	Case	25	3.32	1.030	<0.001*
	Control	25	8.55	1.1	

Table 11 compares thyroid hormone levels in asphyxiated and non-asphyxiated newborns. The mean values for FT3, FT4, and TSH are significantly lower in asphyxiated newborns, suggesting thyroid dysfunction associated with asphyxia. The p-values for all comparisons are less than 0.001, indicating significant differences between the two groups.

Table12:Comparison of FT3, FT4 and TSH values according to HIE stages among cases

Thyroid Hormones	HIEStage	N	Mean	Std. Deviation	Pvalue
FT3(18-24hrs) (pmol/L)	Stage1	12	3.25	0.75	0.002*
	Stage2	10	2.50	0.53	
	Stage3	3	1.67	0.58	
FT4(18-24hrs)	Stage1	12	2.33	0.49	<0.001*
	Stage2	10	1.60	0.52	

(ng/dL)	Stage3	3	0.67	0.58	
TSH(18-24hrs) (mIU/L)	Stage1	12	3.92	0.51	<0.001*
	Stage2	10	3.30	0.48	
	Stage3	3	1.00	0.00	

Table 12 reveals significant differences in thyroid hormone levels among asphyxiated newborns categorized by hypoxic-ischemic encephalopathy (HIE) stages. Lower stages have higher hormone levels, suggesting more severe thyroid dysfunction in higher HIE stages, as indicated by the p-values.

Table 13: Comparison of FT3, FT4 and TSH values in cases according to presence of seizures

Thyroid Hormones	Seizures	N	Mean
FT3(18-24hrs) (pmol/L)	Yes	13	2.31
	No	12	3.25
FT4(18-24hrs) (ng/dL)	Yes	13	1.38
	No	12	2.33
TSH(18-24hrs)(mIU/L)	Yes	13	2.77
	No	12	3.92

Table 13 shows that asphyxiated newborns with seizures have lower mean thyroid hormone levels (FT3, FT4, and TSH), suggesting a more severe metabolic disturbance in these neonates, as evidenced by the lower levels compared to those without seizures.

DISCUSSION

The study aimed to investigate the impact of perinatal asphyxia on thyroid hormones and thyroid stimulating hormone in newborns, comparing asphyxiated and non-asphyxiated neonates.

The study found mixed results on the association between birth weight and perinatal asphyxia in newborns. While some studies found no significant association, others found higher incidence of low birth weight in asphyxiated infants. Other studies, such as Lee et al. (2021) and Patel et al. (2018), highlighted the complexity of factors influencing birth weight and asphyxia. [4,5]

Our study's lack of significant differences may be due to controlled selection, ensuring matched birth weights, while variability in other studies may be due to maternal health, prenatal care quality, and genetic factors.

The study found that vaginal delivery is more common in non-asphyxiated neonates, while LSCS is more prevalent in asphyxiated newborns. However, the difference was not statistically significant. This aligns with previous research that found no significant impact of delivery mode on perinatal asphyxia incidence. The similarity in delivery modes suggests that perinatal asphyxia may not be directly influenced by delivery type, but could be attributed to variations in clinical practices and emergency response protocols in different healthcare settings.[6,7]

A study found that asphyxiated newborns had significantly lower APGAR scores at 1 minute compared to non-asphyxiated newborns. This is consistent with previous studies, as low APGAR scores indicate perinatal asphyxia severity. These findings are crucial for identifying newborns needing urgent resuscitation and intervention, as they reflect compromised respiratory and cardiovascular function immediately post-birth. [8,9]

Asphyxiated newborns still have significantly lower APGAR scores at 5 minutes compared to controls, highlighting the sustained impact of perinatal asphyxia on neonatal vitality. This persistent lower scores suggest that the effects of asphyxia extend beyond immediate birth, indicating prolonged recovery time

for affected newborns. This highlights the need for continuous monitoring and support for asphyxiated infants. [10,11]

Meconium-stained liquor is more prevalent in asphyxiated newborns, according to various studies. However, no significant association was found, suggesting environmental and maternal health influences. Meconium-stained liquor is a sign of fetal distress and often associated with hypoxia. Differences in findings may be due to differences in diagnostic criteria and maternal factors like prenatal care and nutrition. [12,13]

The study found significant differences in thyroid hormone levels (FT3, FT4) and TSH levels between asphyxiated and non-asphyxiated newborns, with asphyxiated newborns showing lower levels. This aligns with previous studies by Kumar et al.[14] (2021), Zhang et al.[15] (2020), Davis et al.[16] (2019), and Taylor et al. [17](2017). Asphyxia or hypoxia in newborns can lead to thyroid dysfunction through several mechanisms.

Firstly, hypoxia impairs cellular metabolism and energy production, leading to oxidative stress and damage to thyroid follicular cells responsible for producing thyroid hormones. This damage can result in decreased synthesis and secretion of thyroid hormones.

Secondly, the stress response triggered by hypoxia induces the release of stress hormones, such as cortisol, which can inhibit the hypothalamic-pituitary- thyroid (HPT) axis. This can suppress the release of thyrotropin-releasing hormone (TRH) and thyroid-stimulating hormone (TSH), reducing thyroid hormone production.

Finally, hypoxia can disrupt the regulation of iodine uptake by the thyroid gland, leading to decreased hormone synthesis. Hypoxia-induced ischemia and reperfusion injury can cause inflammation and damage to thyroid tissues, exacerbating dysfunction.

These hormonal alterations underscore the need for endocrine evaluation and intervention in affected infants. Variations in findings could be due to differences in the severity of asphyxia and timing of hormone measurements.

The study reveals a significant correlation between the stages of hypoxic-ischemic encephalopathy (HIE) and thyroid hormone levels in newborns. Lower HIE stages are associated with higher thyroid hormone levels, while more severe HIE stages correspond to a greater degree of thyroid dysfunction, characterized by reduced hormone levels. This inverse relationship between HIE severity and thyroid function is crucial for understanding the pathophysiological mechanisms underlying HIE and its impact on the endocrine system. Severe hypoxia and ischemia lead to oxidative stress and damage to thyroid follicular cells, which are essential for thyroid hormone synthesis. Severe hypoxia can also disrupt the regulation of iodine uptake, critical for thyroid hormone synthesis. The inflammation and tissue damage resulting from ischemia-reperfusion injury further exacerbate thyroid dysfunction in severe HIE cases. The study underscores the significant physiological and biochemical impact of perinatal asphyxia on newborns, emphasizing the need for early identification, comprehensive monitoring, and targeted interventions to improve neonatal outcomes.[18,19]

CONCLUSION

Perinatal asphyxia significantly impacts neonatal health, with lower thyroid hormone levels and higher HIE stages in asphyxiated newborns. This leads to high seizures and meconium stained liquor. Early identification, vigilant monitoring, and comprehensive management are crucial for improving health outcomes and mitigating long-term effects. The study provides insights for enhancing clinical care strategies for newborns affected by perinatal asphyxia.

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