peripheral metabolism of T4 may be the cause of these differences, since they found low levels of T3 in association with normal levels of of rT3. The pattern of alterations found in the arterial blood of asphyxiated group suggests the occurance of central hypothyroidism, in which low level of thyroid hormones are secondary to low concentrations of TSH.

Saleh[19] found highly statistically significant decrease (P< 0.001) of T3, FT4& TSH after 18 to 24 hrs in HIE patients than control suggesting the occurance of central hypothyroidism, in which low level of thyroid hormones were secondary to low concentrations of TSH.

Pirrone et.al[21] found T3 concentration was significantly lower at day 4, day 5, day 6, and day 7 compared with day1 (P< 0.05), and T4 concentration was significantly higher at birth than at all other time points (P< 0.01).

It is evident that in this study, TSH, T3, T4 and FT3 levels in the newborns with HIE, were normal at birth but it decreases significantly after (18 to 24) hours suggesting the occurrence of central hypothyroidism, in which low levels of thyroid hormones are secondary to low concentrations of TSH. The results of this study showed abnormal thyroid function tests in the absence of clinical signs of thyroid disease similar to that found in patients with non thyroidal illness syndrome in the previous studies Pereira and Procianoy[18]& Saleh.[19]

Conclusion:

Serum concentrations of TSH, T4, T3, FT3 and FT4 are lower in asphyxiated newborns than in normal newborns between 18 and 24 hours of life; this suggests central hypothyroidism secondary to asphyxia.

References:

1. Gonzalez FF, Miller SP. Does perinatal asphyxia impair cognitive function without cerebral palsy? **Arch Dis Child Fetal Neonatal** Ed (2006); 91(6): F454- F459.
2. Marlow N, Rose AS, Rands CE, Draper ES. Neuropsychological and educational problems at school age associated with neonatal encephalopathy. **Arch Dis Child Fetal Neonatal** Ed (2005); 90(5): F380- F387.
3. Van Handel M, Swaab H, De Vries LS, Jongmans MJ. Long- term cognitive and behavioral consequences of neonatal encephalopathy following perinatal asphyxia: a review. **Eur J Pediatr** 2007; 166(7): 645- 654.
4. Low JA, Lindsay BG, Derrick EJ. Threshold of metabolic acidosis associated with newborn complications. **Am J ObstetGynecol** (1997); 177(6): 1391- 1394.
5. Lawn JE, Cousens S, Zupan J. 4 Million neonatal deaths: when? Where? Why? **Lancet** (2005); 365(9462): 891- 900.
6. Paul VK. Neonatal morbidity: report of the National Neonatal and Perinatal Database. **Indian Pediatr** (1999); 36(2): 167- 169.
7. Scher M. Brain disorders of the fetus and the neonate. In Fanaroff AA, Fanaroff JM (eds) **Care of the high risk Neonate**. Elservier Saunders 6th edition (2013):489- 90.
8. Chan S and Kilby MD (2000). Thyroid hormone and central nervous system development. **J Endocrinol**; 165:1.
9. Brown RS (2001). **The thyroid gland: Clinical Pediatric Endocrinology, Brook CGD**, Hindmarsh PC (eds.), 4th ed, W. B Saunders, Philadelphia, pp: 288.
10. Moreno M, Lambardi A, Beneduce L, et.al. (2002). Are the effects of T3 on resting metabolic rate in euthyroid rates entirely caused by T3 itself?. **Endocrinol**; 143:504.
11. Franklin R and O'Grady C (1985). Neonatal thyroid function: effects of non thyroidal illness. **J Pediatr**; 107:599.
12. Borges M, Lanes R, Moret LA, et.al. (1985). Effect of asphyxia on free thyroid hormone levels in full term newborns. **Pediatr Res**; 19:1305.
13. Stockigt JR (1996): Guidelines for diagnosis and monitoring of thyroid disease: non thyroidal illness. **Clin Chem**; 42:188.
14. Sarnat, H. B., M. S. Sarnat, (1976). Neonatal encephalopathy following fetal distress: a clinical and electroencephalographic study. **Arch Neurol J.,** 33: 696- 705.
15. Shah PS and Perlman M (2006). Birth asphyxia and multiorgan dysfunction. **Rec adv ped**; 23:113.
16. Baberi I, Calabro MP and Cordaro S (1999). Myocardial ischemia in neonates with perinatal asphyxia. Electrocardiographic, echocardio-graphic and enzymatic correlations. **Eur J Pediatr**; 158: 742.
17. Selway, L. D. (2010). State of the science: hypoxic ischemic encephalo-pathy and hypothermic intervention for neonates. **Adv Neonatal Care J.,** 10(2): 60- 6.
18. Pereira DN and Procianoy RS (2003). Effect of perinatal asphyxia on thyroid stimulating hormone levels. **Acta Pediatr**; 92:339.
19. Saleh MI (2006). Thyroid functions in newborns with HIE. Thesis submitted for partial fulfillment of **master degree** in pediatrics, undersupervision of Al- Rashidy of, Tawfik PH, Awadalla MM, Faculty of Medicine, Ain Shams University, pp: 85.

Table (2) Thyroid hormonal study in group A& B in cord blood sample

Cord Samples	Group A (No= 30)(Mean±SD)	Group B (No= 20)(Mean±SD)	Significance P Value	
C- TSH (µu/ml)	18.4± 9.8	15.7± 6.9	t= 1.2	P>0.05
C- T3 (ng/ml)	1.5±0.4	1.3±0.7	t= 1.3	P>0.05
C- T4 (µg/dl)	11.4± 1.9	10.4± 3.9	t= 1.1	P>0.05
C- FT3 (Pmol/L)	4.67± 1.7	4.6± 2.8	t= 0.15	P>0.05
C- FT4 (Pmol/L)	19.9± 2.1	17.4± 7	t= 1.6	P>0.05

<0.05* significant

Table (3) shows highly statistically significant decrease of (18- 24) hours TSH, T3, T4, FT3& FT4 in group A than group B.

Table (3) Thyroid hormonal study in group A& B in 18- 24 hours blood sample:

18- 24 Hours Samples	Group A (No= 30)(Mean±SD)	Group B (No= 20)(Mean±SD)	Significance P Value	
TSH (µu/ml)	8.1± 4.6	18.3± 6.4	t=- 6.1	P<0.001*
T3 (ng/ml)	0.86±0.1	3.1± 0.96	t= 10.4	P<0.001*
T4 (µg/dl)	9.4± 1.5	14.8± 4.3	t= 5.4	P<0.001*
FT3 (Pmol/L)	3.3± 1.3	7.3± 3.05	t=- 5.6	P<0.001*
FT4 (Pmol/L)	21± 3.7	27.6± 5.9	t= -4.4	P<0.001*

<0.05* significant

Table (4) Shows Highly Statistically Significant Decrease In TSH, T3, T4 and FT3 in (18- 24) hrs Samples Than Cord Samples In Group A.

Table (4) Changes Occurred In Thyroid Hormones Of 18- 24 Hrs Samples Than Cord Samples In Studied Group A:

Thyroid Hormones	Mean±SD	Significance P Value	
Cord TSH (µu/ml)	18.4± 9.8	t= ٧-.99	P<0.001*
18- 24hrs TSH (µu/ml)	8.1± 4.6		
Cord T3 (ng/ml)	1.5± 0.4	t= 9.3	P<0.001*
18- 24hrs T3 (ng/ml)	0.9± 0.1		
Cord T4 (µg/dl)	11.4± 1.9	t= 7.5	P<0.001*
18- 24hrs T4 (µg/dl)	9.4± 1.5		
Cord FT3 (Pmol/L)	4.7± 1.7	t= -3.1	P<0.01*
18- 24hrs FT3 (Pmol/L)	3.3± 1.3		
Cord FT4 (Pmol/L)	19.9± 2.1	t= -1.4	P >0.05
18- 24hrs FT4 (Pmol/L)	20.96± 3.7		

<0.05* significant

Table (5) Shows Highly Statistically Significant Increase in TSH, T3, T4, FT3& FT4 in (18-24) hrs Samples Than Cord Samples in Group B.

Table (5) Changes Occurred In Thyroid Hormones Of 18- 24 Hrs Samples Than Cord Samples In Studied Group B:

Thyroid Hormones	Mean±SD	Significance P Value	
Cord TSH (µu/ml)	15.7±6.9	t= -7.2	P<0.001*
18- 24hrs TSH (µu/ml)	18.33±6.4		
Cord T3 (ng/ml)	1.3±0.7	t= -15.5	P<0.001*
18- 24hrs T3 (ng/ml)	3.1±1		
Cord T4 (µg/dl)	10.4±3.9	t= -14.5	P<0.001*
18- 24hrs T4 (µg/dl)	14.8±4.3		
Cord FT3 (Pmol/L)	4.6±2.8	t= -17.6	P<0.001*
18- 24hrs FT3 (Pmol/L)	7.3±3.1		

Dscussion:

In the current study, there was highly statistically significant increase (P< 0.001) in RR and decrease in BP in HIE patients than control group. Increase in RR in HIE patients was explained by that hypoxaemic or hypovolaemic lung insults can result in delayed pulmonary adaptation to extrauterine life. Delayed clearance of lung fluid, secondary inactivation of surfactant, delayed fall in pulmonary vascular resistance leading to persistence of pulmonary hypertension, and hemorrhagic pulmonary oedema.[15] Decrease in BP in HIE patients was explained by that myocardial hypoperfusion, acidosis and responses from sympathetic nervous system and peripheral vascular receptors lead to hypotension.[16]

In the current study, we assessed thyroid hormones and TSH levels in the cord blood (immediately after birth) and in the arterial blood (between (18- 24) hrs after birth) of asphyxiated and control newborns in order to investigate the effect of asphyxia on those hormone concentrations. Comparing TSH, T3, T4, FT3 and FT4 of HIE patients and control groups at birth from cord blood, we found no significant difference between both groups.

Borges et.al.[12] did not find differences in the concentration of TSH, FT3 and FT4 in the cord blood between HIE cases and control groups. Pereira and Procianoy[18] carried out their study to assess thyroid hormones and TSH levels in the cord blood immediately after birth. They assessed the concentrations of T4, T3, FT4, TSH and rT3 by radioimmunoassay. They found that the mean levels of thyroid hormones and TSH in the umbilical cord blood were similar in both asphyxiated and control groups. Saleh[19] carried out their study to assess thyroid hormones and TSH levels in the cord blood immediately after birth They assessed the concentrations of T3, FT4& TSH. They did not find statistical differences in the concentration of cord blood T3, FT4& TSH between normal and asphyxiated newborns in their study. Rashmi et.al.[20] found that infants with birth asphyxia had significantly higher cord blood TSH levels as compared to control.

The current study revealed that, in the samples collected (18- 24) hours after birth, highly statistically significant (P< 0.001) decreased levels of TSH, T4, T3& FT3 in asphyxiated newborns in whom hormone concentrations failed to increase when compared to cord blood levels and non statistically significant increase (P>0.05) of FT4 in the samples collected (18- 24) hours after birth in asphyxiated newborns when compared to cord blood levels. On the other hand, in the control group highly statistically significant (P< 0.001) increased levels of TSH, T4, T3, FT3 and FT4 were observed, in whom hormone concentrations increase in the samples collected (18- 24) hours after birth when compared to cord blood levels. FT4 increased in case and control groups in the samples collected (18- 24) hours after birth when compared to cord blood levels but was highly statistically significant (P< 0.001) lower in the asphyxiated group. The mean time elapsed until the second collection was similar in both groups, which rules out the possibility of interference of this factor on the hormone levels studied. Low level of thyroid hormones at (18- 24) hours after birth in asphyxiated group were explained by the occurrence of central hypothyroidism secondary to low concentrations of TSH (Pereira and Prociano.[18]

Pereira and Prociano[18] found highly statistically significant decrease (P< 0.001) of TSH, T3, T4 and FT4 in the arterial blood collected 18-24 hours after birth in asphyxiated newborns in comparison to the control group suggesting that alterations in hormone production and in the

Introduction:

Prenatal asphyxia remains a major cause of long- term sensor neural impairments and disabilities;[1][2][3] with an incidence of 1 to 2 per 1000 births in developed countries and up to 5 per 1000 births in developing countries.[4][5][6] The definition of asphyxia implies two overlapping mechanisms: hypoxia or reduced supply of oxygen in the blood; and ischemia or reduced perfusion of blood flow.[7] Thyroid hormones (TH) stimulate growth and development of various tissues including the central nervous system and skeleton.[8] Thyroid hormones may influence the oxygen consumption of the brain in infants but not in adults. TH are essential for CNS differentiation.[9] Thyroid hormone has been recognized as a major regulator of the oxidative metabolism of energy producing substrates by the mitochondria where food stuffs are turned into useful energy in the form of ATP.[10]

However, a study performed with seven asphyxiated newborns during the first 48 hrs of life showed decreased levels of free T4 (FT4) in relation to seven control newborns; suggesting central hypothyroidism secondary to asphyxia.[12]

Low levels of thyroid hormones in non- thyroidal illness have been associated with a poor prognosis and with high mortality rates.[13]

Hypoxic- ischemic encephalopathy was classified as mild if hyper excitability or hypotonic persisted without seizures for at least 24 hours after birth; as moderate if the infant was lethargic and had hypotonic, weak primitive reflexes, and seizures; and as severe if the infant had frequent seizures, apnea, flaccid weakness, or coma.[14]

The aim of this study was is to compare serum concentration of thyroid hormones and TSH of term newborns with and without asphyxia. Also to investigate the association between the severity and mortality of HIE and alterations in thyroid hormone levels. we measured Cord blood samples and arterial blood samples (18- 24) hrs after birth) for Thyroid function tests (TSH, T3, T4, FT3, FT4) in whom hypoxic- ischemic encephalopathy is likely to develop.

Materials And Methods:

This study was a case- control study, carried out in El Galaa teaching hospital Neonatal intensive care unit in the period from October 2019 to May 2020.

- The case group group (A); It includes 30 term newborns exposed to perinatal asphyxia. The age of the patients was the first day of life while their gestational age ranged between (37- 42) weeks.

  Inclusion Criteria: Profound metabolic or mixed acidemia (pH< 7.0) in an umbilical artery blood sample. Persistence of an Apgar score of≤ 3 and≤ 5 at one and five minutes respectively. Requiring bag and mask ventilation for at least one minute immediately after birth. Neonatal neurological problems (eg. Seizures, Coma, Hypotonia).
- The control group group (B): It includes 20 healthy full term neonates with an Apgar score≥ 8 and≥ 9 at one and five minutes, umbilical cord blood pH≥ 7.2 and similar to the case group in birth weight, gestational age, mode of delivery and sex.

After obtaining verbal consents from the parents of Newborns included in the study, each of them was subjected to the following:

1. Clinical assessment:
   a. Thorough medical history of the mother including perinatal history (prenatal, natal and postnatal history), especially to exclude mothers who had used antihypertensive, corticosteroids, thyroid or antithyroid drugs during pregnancy.
   Clinical examination of the neonate: For the case group (group- A):
   - Neurological evaluation following Sarnat and Sarnat's classification. According to Sarnat and Sarnat's group A is classified into 3 subgroups, group A1 (HIE I), group A2 (HIE II) and group A3 (HIE III).
   - Monitoring during the first 24 hrs of life for oxygen saturation, CNS manifestations, urine output and any vascular or cardiovascular manifestations.

   b. Laboratory investigations:
   - Complete blood picture (CBC), C- Reactive protein (CRP). Serum glucose, Serum calcium (Ca+), Kidney function tests& Liver function tests. Serum Na+ and K+ estimation were done. Blood gas analysis of cord blood. Blood gas analysis after (18- 24) hrs of life.
   - Thyroid function tests (TSH, T3, T4, FT3, FT4) were done on cord blood& venous samples (18- 24) hrs after life.

Statistical Analysis:

Data collected were reviewed, coded, entered PC (personal computer), where statistical analysis were carried out using SPSS version XI (statistical package for social science version XI).

Results:

Table (1) Shows The Population Characteristics Of The Two Groups Of Babies: Those Born Hypoxic Ischemic Encephalopathy (Group A) And Normal Babies (Group B). There Is Highly Statistically Significant Increase In RR In Group A (57.8± 10.9) Than Group B (40± 6).

Table (1) Clinical Characteristics Of Studied Neonate Group A (Case Group)& B (Control Group)

Clinical Characteristics		Group A (No= 30) (Mean± SD)	Group B (No= 20) (Mean± SD)	P Value	
Gestational Age (Wks) (Mean± SD)		39± 3.2	38.7± 2.9	t= 0.35	P >0.05
Sex	(Male %)	21(70%)	14 (70%)	-	P>0.05
	(Female %)	9 (30%)	6 (30%)		
Weight (Kg) (Mean± Sd)		2.75±0.6	2.84±0.55	t= 0.6	P >0.05
Length (Cm) (Mean± Sd)		47± 2.65	47.4± 2.6	t= 0.4	P >0.05
Head (Cm) cicumference (Mean± SD)		34.1± 1.9	34.2± 1.7	t= 0.03	P >0.05
Hr (Min)		129.8± 12.9	134.9± 6.6	t= 1.8	P>0.05
Rr (Min)		57.8± 10.9	40±0	t= 8.9	P<0.00*
Temp. °c		36.9±0.2	37±0	t= 0.47	P>0.05
Bp (mmhg)		38.6± 7.3	42.9± 3.6	t= 2.7	P=0.0 1*

<0.05* significant.

Table (2) shows no statistically significant difference in cord TSH (18.4± 9.8), T3 (1.5± 0.4), T4 (11.4± 1.9), FT3 (4.67± 1.7)& FT4 (19.9± 2.1) between group (A)& (B).

A Study of Impact of Perinatal Asphyxia on Thyroid Hormone Levels in Newborns admitted in NICU, Al Galaa Teaching Hospital

Reham S. Abd AlHameed (PhD)

ريهام شاكر عبدالحميد

Summary

Introduction: Perinatal asphyxia causes multiple alterations in the fetus and newborn due to failure in the gas exchange system. Perinatal asphyxia also triggers rapid alterations in the concentration of several hormones. We compare serum concentration of thyroid hormones and TSH of term newborns with and without asphyxia. Also investigate the association between the severity and mortality of HIE and alterations in thyroid hormone levels. We measured Cord blood samples and arterial blood samples (18- 24) hrs after birth for Thyroid function tests (TSH, T3, T4, FT3, FT4) in 20 normal infants and 30 infants who were delivered in El Galaa Teaching hospital and admitted in NICU with asphyxia and developed hypoxic- ischemic encephalopathy.

Results: The study revealed that Serum concentrations of TSH, T4, T3, FT3 and FT4 are lower in asphyxiated newborns than in normal newborns between 18 and 24 hours of life; this suggests central hypothyroidism secondary to asphyxia.

Conclusions: The asphyxiated term newborn infants present altered TSH and thyroid hormone levels.

Keywords: Neonate, Hypoxic- Ischemic encephalopathy, Asphyxia, thyroid hormone level.

دراسة تأثير الاختناق في الفترة المحيطة بالولادة على مستويات هرمون الغدة الدرقية

لحديثي الولادة الذين تم قبولهم في NICU، مستشفى الجلاء التعليمي

مقدمة: يسبب الاختناق في الفترة المحيطة بالولادة تغيرات متعددة في الجنين وحديثي الولادة بسبب فشل في نظام تبادل الغازات. يؤدي الاختناق في الفترة المحيطة بالولادة أيضا إلى تغيرات سريعة في تركيز العديد من الهرمونات. قارنا تركيز مصل هرمونات الغدة الدرقية وTSH لحديثي الولادة المصابين بالاختناق وبدونه. تحقق أيضا من العلاقة بين شدة وموت HIE والتغيرات في مستويات هرمون الغدة الدرقية. قمنا بقياس عينات دم الحبل السري وعينات الدم الشرياني (١٨– ٢٤) ساعة بعد الولادة لاختبارات وظائف الغدة الدرقية (TSH، T3، T4، FT3، FT4) في ٢٠ رضيعا عاديا و٣٠ رضيعا تم ولادتهم في مستشفى الجلاء التعليمي وتم قبولهم NICU مع الاختناق وتطور اعتلال دماغي نقص التأكسج.

النتائج: كشفت الدراسة أن تركيزات المصل من (TSH وT4 وT3 وFT3 وFT4) أقل في الأطفال حديثي الولادة المختنقين مقارنة بالمواليد الجدد الذين تتراوح أعمارهم بين ١٨ و٢٤ ساعة من العمر؛ هذا يشير إلى قصور الغدة الدرقية المركزي الثانوي للاختناق.

الاستنتاجات: المصطلح المختنق للرضع حديثي الولادة يظهرون تغيرا في مستويات هرمون TSH وهرمون الغدة الدرقية، ويفترض أنهم علامات تنبؤية.

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