Original Article

ISSN (O): 2347-3363; ISSN (P): 2347-3355

Association between Thyroid Profile and Serum Bilirubin Levels in Term Neonates on Day 3 of Life

Prahlad Kadambi[1], **MA Ramprakash**[2], **Gandi Soujanya**[1], **L Sushanth Prabhath Reddy**[1]

[1]Post-Graduate Student, Department of Paediatrics, Meenakshi Medical College Hospital and Research Centre, Kanchipuram, Tamil Nadu, India, [2]Assistant Professor, Department of Paediatrics, Meenakshi Medical College Hospital and Research Centre, Kanchipuram, Tamil Nadu, India.

Abstract

Background: Neonatal indirect hyperbilirubinemia is a common clinical scenario that manifests as jaundice in the first week of life. Studies have shown that the physiological peak of serum bilirubin (SBR) levels is highest at 72 hours of life as a result of which SBR is measured at 72 hours of life routinely. The American Academy of Pediatricians (AAP) recommends routine screening for congenital hypothyroidism within the first week of life for all neonates. In common practice, both parameters are assessed simultaneously at 72 hours of life. This study aims to correlate thyroid Profile and serum bilirubin levels assessed in term neonates at 72 hours of life. **Subjects and Methods:** Our retrospective study included 105 term neonates born through cesarean-section at MMCHRI, Kanchipuram; between August 2018 and August 2019. Pre-term, neonates born to eclamptic, pre-eclamptic, diabetic, hypothyroid, Rh-incompatible mothers were excluded from the study. The data collected included Birth Weight, Gestational Age, Thyroid Profile (T3, T4, TSH), SBR (Total and Direct). Data were analyzed using SPSS v16. **Results:** The mean gestational age of the study population was 268.05±6.25 days, and mean birth weight was 2.997±0.36 kgs. The mean serum levels of total bilirubin were 11.36±3.52 mg/dl. The mean serum fT3, fT4, TSH levels were 8.17±23.2 pg/ml, 2.16±1.68 ng/dl and 4.07±3.4 mIU/ml respectively. A positive association was noted between serum TSH and total serum bilirubin (r= 0.176, p = 0.067) but not statistically significant. **Conclusion:** Our study has not shown a significant association between serum TSH and SBRT in term neonates. However, the simultaneous assessment remains practical in practice.

Keywords: Neonatal hyperbilirubinemia, Congenital hypothyroidism, Screening

Corresponding Author: Prahlad Kadambi, Post-Graduate Student, Department of Paediatrics, Meenakshi Medical College Hospital and Research Centre, Kanchipuram, Tamil Nadu, India.
E-mail: Prahlad.kadambi@gmail.com

Received: 11 May 2020 **Revised: 3 June 2020** **Accepted: 9 June 2020** **Published: 9 July 2020**

Introduction

Neonatal indirect hyperbilirubinemia (NNH) is a common clinical scenario manifesting as jaundice in the first week of life.[1] NNH manifests with physical findings such as yellowish discoloration of the skin and sclera in newborns is due to accumulation of unconjugated bilirubin. However, unconjugated hyperbilirubinemia usually reflects a normal physiological phenomenon in most neonates.[2] Studies have shown that the physiological peak of serum bilirubin (SBR) levels is highest at 72 hours of life as a result of which SBR is routinely measured at 72 hours of life in practice.[3] The prevalence of neonatal hyperbilirubinemia is 55.2%.[4] Phototherapy is an effective methodology to treat NNH which prevents complications such as Bilirubin encephalopathy and kernicterus.[5]

Congenital Hypothyroidism (CH) is the most common cause of preventable mental retardation.[6] The American Academy of Pediatricians (AAP) recommends routine screening for CH within the first week of life for all neonates to assist in early diagnosis.[7] If diagnosed within the first few weeks after birth, the neurodevelopmental sequelae have a good outcome. Infants with CH are at an increased risk of developing congenital anomalies such as pulmonary stenosis, atrial septal defect, and ventricular septal defect.

CH is a well-known cause of prolonged unconjugated hyperbilirubinemia and appears to be associated with the delayed maturation of hepatic uridine diphosphate glucosyltransferase (UDPGT) enzyme activity. Since thyroid hormones act on almost all tissues of the body and influence enzyme concentration and activity, the metabolism of substrates, vitamins and mineral salts, basal metabolism, or calorigenesis; they also stimulate oxygen consumption and act in other endocrine

systems. [8]

While it is important to test for both NNH and CH, it is only the natural practical choice to test for both simultaneously to avoid multiple pricks to the neonate. In common practice, both parameters are assessed simultaneously at 72 hours of life.

A study done by Baljinder Singh Et al, [9] in 2003 attempted to establish a cause and effect relationship between iodine deficiency and jaundice. Another study done by Kayıran et al, [10] in 2010 could not establish a correlation between serum bilirubin levels and thyroid hormones. However, there are limited studies that have studied the relationship between serum bilirubin levels and Thyroid profile in neonates.

Objective

This study aims to correlate thyroid Profile and serum bilirubin levels assessed in term neonates at 72 hours of life.

Subjects and Methods

The study followed the principles of the Helsinki Declaration and ethical committee approval was obtained. The study was designed as a retrospective study included 105 term neonates born through cesarean-section at Meenakshi Medical College Hospital and Research Institute, Kanchipuram between August 2018 and August 2019. Pre-term neonates; neonates born to eclamptic, pre-eclamptic, diabetic, hypothyroid, Rh-incompatible mothers were excluded from the study to rule out confounding factors. Data were collected from the archives of the Medical Records Department. The data collected included birth weight, gestational age, Thyroid Profile (T3, T4, TSH), SBR (Total and Direct). Data were analyzed using SPSS v16. Statistical tests used were Descriptive statistics and Pearson's Correlation Test.

Results

Out of the 105 neonates included in the study, 55 were male and 50 were female. The mean gestational age of the study population was 268.05±6.25 days and mean birth weight was 2.997±0.36 kgs. 96 out of the 105 neonates were appropriate for gestational age (AGA), 7 were small for gestational age (SGA) and 2 were large for gestational age (LGA). The mean total Serum bilirubin level was 11.36 ±3.52 mg/dl. The mean serum fT3 level was 8.17±23.2 pg/ml. The mean serum fT4 level was 2.16±1.68 ng/dl. The mean TSH level was 4.07±3.4 mIU/ml. These findings are summarized in [Table 1]

A positive association was noted between serum TSH and total serum bilirubin (r= 0.176, p = 0.067). This association was not statistically significant. A positive association was noted between fT3and total serum bilirubin (r= 0.06, p = 0.144) but was not found to be statistically significant. No association was noted between fT4 and total serum bilirubin (r= 0.024, p = 0.227).

Table 1: Characteristics of the Study Population

Parameter	Mean ± SD
Gestational Age (days)	268.05 ±6.25
Birth Weight (kgs)	2.997±0.36
Total Bilirubin (mg/dl)	11.36 ±3.52
Direct Bilirubin (mg/dl)	0.47 ± 0.199
fT3 (pg/ml)	8.17 ±23.2
fT4 (ng/dl)	2.16 ±1.68
TSH (mIU/ml)	4.07 ±3.4

12 out of the 105 neonates (11.4%) had TSB values above the phototherapy range as per the AAP Nomogram.

2 neonates had abnormal Thyroid profiles and the laboratory parameters of these neonates were as given below in [Table 2]

[Figure 1] depicts the correlation between TSB and TSH graphically.

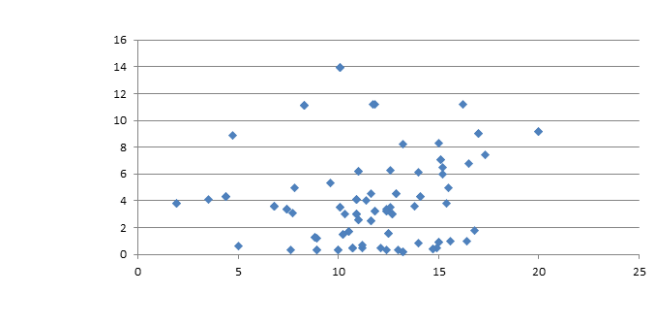

Figure 1: Graphical Correlation between TSB and TSH

Discussion

Our study included 105 term neonates and excluded pre-term neonates and neonates with additional risk factors because they act as confounding factors in the relationship between NNH and CH. 96 out of the 105 neonates were appropriate for gestational age (AGA), 7 were small for gestational age (SGA) and 2 were large for gestational age (LGA). This finding can be explained because high-risk neonates were excluded and are in line with what is considered to be expected. 12 out of the 105 neonates (11.4%) had TSB values above the phototherapy range as per the AAP Nomogram. These neonates were treated by phototherapy as per the guidelines prescribed by the American Academy of Paediatricians (AAP). The mean serum fT3 level was 8.17±23.2 pg/ml. The mean serum fT4 level was

Table 2: Tabular column of laboratory parameters of neonates with abnormal thyroid profile

	T3 (pg/ml)	T4 (ng/dl)	TSH (mIU /ml)	Total Serum Bilirubin (mg/dl)	Direct Bilirubin (mg/dl)
Normal Expected	1.4-4.2	0.8-2	<10.0	<15.0	<0.5
Neonate 1	109.1	8.1	13.93	10.1	0.3
Neonate 2	2	1.7	11.2	16.2	0.5

2.16±1.68 ng/dl. The mean TSH level was 4.07±3.4 mIU/ml. As a whole, the study population was at low risk of CH and the mean values of the thyroid profile fell within normal limits. This is probably because the study population comprised of term neonates with no additional risk factors.

Out of the two neonates who had abnormal thyroid profiles, one neonate had Total serum bilirubin above the phototherapy range. This neonate (Neonate-2 as referred in Table 2) received phototherapy for 24 hours.

The other neonate (Neonate-1) had normal Total serum bilirubin which was below the phototherapy range.

The findings in our study are similar to that of Baljinder Singh et al and Kayıran et al as we could not establish a relationship between thyroid profile and serum bilirubin at 72 hours of life.[9,10]

These results suggest that while simultaneous measurement of T4, TSH, and bilirubin levels is a useful clinical tool for screening, there is no significant clinical correlation between these parameters in healthy term neonates. We can speculate that clinical conditions like neonatal jaundice resulting from thyroid hormone levels as in CH will depend on the degree and duration and will affect all tissues to a lower or greater extent including bilirubin metabolism. Since the early neonatal period is dynamic and influenced by several factors,[11] further studies are needed with a larger sample size to establish the correlation of thyroid hormones and bilirubin levels in the first days of hypothalamic-pituitary-thyroid axis maturation.

Conclusion

Our study has not shown a significant association between serum TSH and Total Serum Bilirubin in term neonates. However, the simultaneous assessment remains practical in practice.

References

1. Olusanya BO, Osibanjo FB, Slusher TM. Risk Factors for Severe Neonatal Hyperbilirubinemia in Low and Middle-Income Countries: A Systematic Review and Meta-Analysis. PLOS One. 2015;10(2):e0117229–e0117229. Available from: https://dx.doi.org/10.1371/journal.pone.0117229.
2. Mishra S, Agarwal R, Deorari AK, Paul VK. Jaundice in the newborns. Indian J Pediatr. 2008;75(2):157–63. Available from: https://dx.doi.org/10.1007/s12098-008-0024-7.
3. Gartner LM, sun Lee K, Vaisman S, Lane D, Zarafu I. Development of bilirubin transport and metabolismin the newborn rhesus monkey. J Pediatr. 1977;90(4):513–531. Available from: https://dx.doi.org/10.1016/s0022-3476(77)80360-0.
4. Bhutani VK, Zipursky A, Blencowe H, Khanna R, Sgro M, Ebbesen F, et al. Neonatal hyperbilirubinemia and Rhesus disease of the newborn: incidence and impairment estimates for 2010 at regional and global levels. Pediatr Res. 2013;74(S1):86–100. Available from: https://dx.doi.org/10.1038/pr.2013.208.
5. Das S, van Landeghem F. Clinicopathological Spectrum of Bilirubin Encephalopathy/Kernicterus. Diagnostic. 2019;9(1):24–24. Available from: https://dx.doi.org/10.3390/diagnostics9010024.
6. Rastogi MV, LaFranchi SH. Congenital hypothyroidism OJRD. . Orphanet J Rare Dis. 2010;17(5):1750–1772. Available from: https://dx.doi.org/10.1186/1750-1172-5-17.
7. Desai MP, Sharma R, Riaz I, Sudhanshu S, Parikh R, Bhatia V. Newborn Screening for Congenital Hypothyroidism: Recommended Guidelines. Indian J Pediatr. 2018;85(6):440–447. Available from: https://dx.doi.org/10.1007/s12098-017-2575-y.
8. Mullur R, Liu YY, Brent GA. Thyroid Hormone Regulation of Metabolism. Physiol Rev. 2014;94(2):355–382. Available from: https://dx.doi.org/10.1152/physrev.00030.2013.
9. Singh B, Ezhilarasan R, Kumar P, Narang A. Neonatal hyperbilirubinemia and its association with thyroid hormone levels and urinary iodine excretion. . Indian J Pediatr. 2003;70:311–315. Available from: https://dx.doi.org/10.1007/BF02723587.
10. Kayıran SM, Gürakan B. Correlation of Third Day TSH and Thyroxine Values with Bilirubin Levels Detected by a Neonatal Screening System. Med J Bakirköy. 2010;6:117–120.
11. Gregory KE, LaPlante RD, Shan G, Kumar DV, Gregas M. Mode of Birth Influences Preterm Infant Intestinal Colonization with Bacteroides Over the Early Neonatal Period. Adv Neonatal Care. 2015;15(6):386–393. Available from: https://dx.doi.org/10.1097/ANC.0000000000000237.

How to cite this article: Kadambi P, Ramprakash MA, Soujanya G, Reddy LSP. Association between Thyroid Profile and Serum Bilirubin Levels in Term Neonates on Day 3 of Life. Asian J. Clin. Pediatr. Neonatol. 2020;8(2):42-45.

DOI: dx.doi.org/10.47009/ajcpn.2020.8.2.8

Source of Support: Nil, **Conflict of Interest:** None declared.