Original Article

Assessment of thyroid hormones in full-term neonates with late-onset sepsis

Dhananjay Singh[1], Amit Agrawal[2], Jyotsna Shrivastava[3]

From [1]Senior Resident, [2]Associate Professor, [3]Professor and HOD, Department of Pediatrics, Gandhi Medical College and Kamla Nehru Hospital, Bhopal, Madhya Pradesh, India

ABSTRACT

Background: Neonatal sepsis is a clinical syndrome characterized by signs and symptoms of infection with or without bacteremia in neonatal age. The previous studies found that there might be an association between thyroid hormone profile and outcomes in patients with late-onset of sepsis (LOS). **Objective:** The objective of the study was to assess the thyroid hormone levels in full-term neonates with late-onset sepsis. **Materials and Methods:** This analytical prospective cohort study was conducted in the neonatal intensive care unit of a tertiary care teaching institution in Central India. Full-term neonates, with culture-proven LOS, were taken as the study population. Estimation of thyroid hormones (thyroid-stimulating hormone [TSH], T3, T4, fT3, and fT4) among full-term neonates with LOS was assessed and correlated before and after antibiotic therapy. **Results:** A total of 195 full-term neonates were included in the study. Mean values of TSH, T3, T4, fT3, and fT4 before antibiotic therapy were 5.29±2.11 µg/ml, 94.4±44.4 ng/dl, 7.25±2.72 µg/dl, 1.84±0.9 pg/ml, and 1.43±0.458 µg/dl, respectively, and after antibiotic therapy, the values reach to 9.19±1.63 µg/ml, 185.3±44.53 ng/dl, 13.29±10.24 µg/dl, 3.60±0.89 pg/ml, and 2.54±052 µg/dl, respectively. A significant ($p<0.0001$) improvement in TSH, T3, T4, fT3, and fT4 after antibiotic therapy was found. *S. aureus* (15.39%) and *Streptococcus* (15.39%) were found to be the most common organisms for LOS. **Conclusion:** Our study showed a significant improvement in TSH, T3, T4, fT3, and fT4 after antibiotic therapy among full-term neonates with LOS. Due to this correlation, thyroid profile can assist in treating newborns with LOS.

Key words: Antibiotics, Late-onset sepsis, Neonate, Thyroid profile

Neonatal sepsis is a clinical syndrome characterized by signs and symptoms of infection with or without bacteremia in neonatal age. The incidence of neonatal sepsis in India is 38 per 1000 live births according to the data obtained from the National Neonatal Perinatal Database [1]. It is classified into two types depending on the time of onset of symptoms: Early onset of sepsis (EOS) which presents within the first 72 h of life and late onset of sepsis (LOS) that occurs after 72 h of life [2].

Many neuroendocrine changes take place during critical illness; however, reports of these changes in neonatal sepsis are limited. Thyroid hormones play an important role in the adaptation of metabolic function to stress, regulation of the metabolic homeostasis, and critical illness. Although the exact cause of alteration of thyroid hormones during sepsis is not known, it has been hypothesized that the immune system cells can affect systemic thyroid hormone activity. This activity may be attributed to the complex pathophysiological interplay between thyroid-stimulating hormone (TSH) and the immune system [3,4]. The various lymphokines and monokines factors act as a marker in sepsis and can influence the hypothalamic-pituitary-thyroid axis modulating thyroid hormone levels [3,5].

Multiple studies have been performed in the recent past showing correlation of sepsis and thyroid hormones [6-12]. A study conducted by Kurt *et al*. showed a significant change in thyroid hormone levels before and after the treatment of neonatal sepsis with antibiotics [6]. Joosten *et al*. performed a study on children with meningococcal sepsis found that the children who do not survive meningococcal sepsis have an impaired adrenal response, altered thyroid hormones, and below normal reference values of T4, T3, rT3, and TSH levels [7].

The majority of the previous studies present in the literature have correlated LOS with T3, T4 hormone levels, or assay only, but in our study, we have included TSH, T3, and T4 along with fT3, and fT4 which are highly sensitive in the detection of thyroid hormone levels. Hence, the present study was conducted to find the relationship between thyroid profile and development of neonatal LOS in full-term neonates.

MATERIALS AND METHODS

This analytical prospective study was carried out in the neonatal intensive care unit of the Department of Pediatric

Access this article online	
Received - 23 June 2021 Initial Review - 27 June 2021 Accepted - 30 June 2021	Quick Response code
DOI: 10.32677/IJCH.2021.v08.i06.006	

Correspondence to: Dr. Amit Agrawal, Department of Pediatrics, Gandhi Medical College and Kamla Nehru Hospital, Bhopal, Madhya Pradesh, India. E-mail: agrawaldramit@yahoo.co.in

Medicine, Gandhi Medical College, Bhopal, over 12 months from May 2017 to April 2018. The approval was obtained from the Institutional Ethical Committee of Gandhi Medical College, Bhopal, before the start of the study. After explaining the nature, procedure, and purpose of the study, written consent was obtained from the parents/legal guardians of the neonates.

The cases included full-term neonates (gestational age >37 completed weeks) admitted with LOS between 72 h and 28 days of life. Criteria for sepsis were neonates having positive septic screening. The various components of the septic screen included total leukocyte count (TLC) <4000/mm^3 and >24,000/mm^3, absolute neutrophil count <1800/mm^3, immature to the total neutrophil ratio (IT ratio) >0.2, elevated microerythrocyte sedimentation rate, and C-reactive protein (CRP) RP >6 mg/dl and/or neonates had any of body fluid culture positive (blood, cerebrospinal fluid, urine, etc.). All pre-term and post-term neonates, neonates with EOS, major congenital anomaly, birth asphyxia, and with a history of maternal thyroid hormone dysfunction were excluded from the study. Flowchart describes the protocol followed during the study (Fig. 1).

The sample size was calculated using the formula: $n=(z\alpha)^2 p(1-p)/d^2$, where, Zα is the confidence level at 95% (Zα=1.96 for 95% CI) CI, p is the population proportion (p=13.5, taken from the previous studies), and d is the margin of error (5%). Based on the formula, a sample size of 195 was taken for the present study.

The data obtained from the subjects were recorded in a pre-structured pro forma. Maternal data including maternal age, religion, socioeconomic status, last menstrual period, risk factors, and drug intake were obtained from the mother/legal guardians of the baby, and the medical records of the mother. A detailed natal and postnatal history including age at admission, gestational age, gender, type of feeding, pre-lacteal feeds, and presenting complaints of the neonates was also obtained. A thorough physical examination and systemic examination findings were noted for all the recruited neonates. The gestational age was assessed from the last menstrual period and the New Ballard score.

Relevant investigations were sent for all the neonates as per the hospital policy including hemoglobin, TLC, differential leucocyte count, CRP, blood culture, electrolytes, and random blood sugar. Other investigations such as chest X-ray, lumbar puncture, urine routine and microscopy, urine for fungal hyphae, urine culture, and arterial blood gas analysis were done when required. In all the included neonates, blood samples for septic profile and thyroid profile were taken before starting antibiotic therapy. Repeat thyroid profile was done 14 days after antibiotic therapy. Levels of T3, T4, TSH, fT3, and fT4 were compared in newborns before and after antibiotic therapy. All newborns were managed according to standard treatment guidelines [13].

The blood samples collected in the test tube were centrifuged; serum thus obtained was used to estimate T3, T4, and TSH. They were estimated by the chemiluminescence method (using the Immulite 1000 Immunoassay System-Siemens). The samples were sent to the laboratory for the estimation of serum TSH, T3, T4, fT3, and fT4, which was done by DPC IMMULITE chemiluminescent immunoassay [14]. Neonates who found to be hypothyroid were excluded from the study and treated for the hypothyroidism.

Statistical Analysis

The data obtained were entered into MS Excel spreadsheet; the results were expressed in mean±standard deviation (SD) for

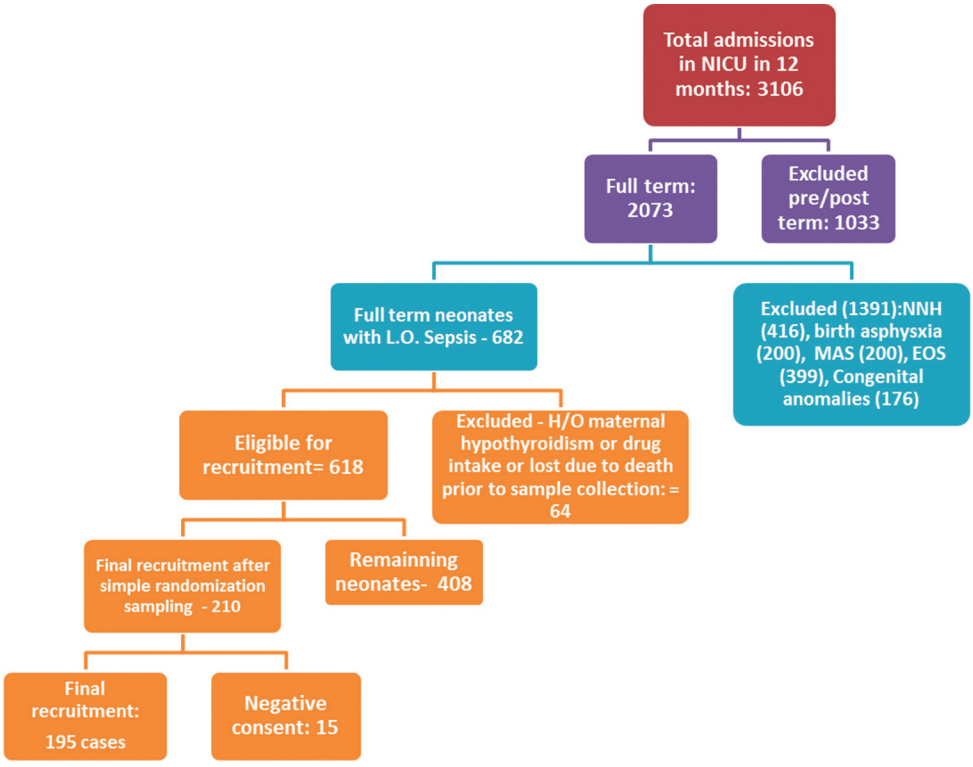

Figure 1: Flowchart describing the protocol followed during the study

continuous variables and as a percent (%) for categorical data. Observations were statistically analyzed using GraphPad Prism version 7.0. Unpaired and paired t-tests were used to denote statistical significance and $p<0.05$ was considered statistically significant.

RESULTS

A total of 195 cases were enrolled, out of which, 51.2% were male and 48.8% were female. Most of the neonates (35.9%) were between 7 and 10 days of age and most of them (67.7%) had birth weight between 1.5 and 2.5 kg. Out of total cases, 40% were on exclusive breastfeed (EBF). The age of most of the mothers (50.2%) was between 20 and 25 years and the percentages of neonates born with institutional delivery and home delivery were 67% and 33%, respectively. The maximum numbers of the patients presented with a chief complaint of refusal to feed or poor feeding (32.3%). The demographic variables of the neonates and their mothers are shown in Table 1.

Table 1: Demographic variables of the neonates and their mothers (n=195)

Variables	total (n=195)	%
Age		
3–7 days	49	25.1
7–10 days	70	35.9
10–15 days	18	9.2
>15 days	58	29.8
Gender		
Males	100	51.2
Females	95	48.8
Birth weight		
<1.5 kg	3	1.5
1.5–2.5 kg	132	67.7
More than 2.5 kg	60	30.8
Type of feeding		
Exclusive breastfeed (EBF)	78	40.00
Mixed feed	83	42.56
Top feed	34	17.44
Maternal age		
<20 years	75	38.46
20–25 years	98	50.26
>25 years	22	11.28
Mode of delivery		
Institutional delivery	142	67
Home delivery	53	33
Presenting complaints		
Abdominal distension	22	11.28
Convulsion	25	12.82
Excessive crying	21	10.77
Fever	13	6.67
Not excepting feeds	63	32.31
Dullness	15	7.69
Respiratory distress	36	18.46

The thyroid profile was performed before antibiotic therapy in all 195 subjects. Due to the death of 25 neonates under the study before completion of 14 days of antibiotic therapy, only 170 neonates could be followed up for TFT after antibiotic therapy. The mean values of TSH, T3, T4, fT3, and fT4 before starting antibiotic therapy were 5.29±2.11 µg/ml, 94.4±44.4 ng/dl, 7.25±2.72 µg/dl, 1.84±0.9 pg/ml, and 1.43±0.458 µg/dl, respectively. After completion of antibiotic therapy, the values were 9.19±1.63 µg/ml, 185.3±44.53 ng/dl, 13.29±10.24 µg/dl, 3.60±0.89 pg/ml, and 2.54±052 µg/dl, respectively. The p-value for all hormones was <0.0001; hence, the difference between the mean thyroid indices before and after antibiotic treatment was statistically significant (Table 2).

Blood culture was done for all the patients. *Staphylococcus aureus* (15.39%) and *Streptococcus* (15.39%) were found to be the most common organisms for LOS. It was found that 43 (22%) septic organisms were culture negative. Two cases (1.03%) were positive for fungal sepsis (Table 3). The mean thyroid indices were also compared between culture-positive and culture-negative groups. The mean values (TSH, T3, T4, fT3, and fT4) for culture-positive neonates group were 5.21±2.18 µg/ml, 92.93±43.82 ng/dl, 7.18±2.71 µg/dl, 1.81±0.9 pg/ml, and 1.42±0.45 µg/dl, respectively, while for culture-negative neonatal septic subjects group, the mean values of TSH, T3, T4, fT3, and fT4 were 5.56±1.82 µg/ml, 99.83±46.43 ng/dl, 7.51±2.79 µg/dl, 1.94±0.91 pg/ml, and 1.48±0.47 µg/dl, respectively. We observed no statistical significance between both the groups (Table 4).

DISCUSSION

The present study was conducted to investigate the relationship between thyroid profile (TSH, T3, T4, fT3, and fT4) and LOS in the 195 full-term neonates. Neonates presenting with EOS were excluded from the study to rule out the impact of maternal/perinatal factors on the development of sepsis.

There are two biologically active thyroid hormones: Thyroxine (T4) and 3,5,3'-triiodothyronine (T3) [5]. In normal fetuses, concentrations of TSH, thyroxine-binding globulin, and thyroid hormones increase progressively during intrauterine life. A surge in the serum TSH is seen at 30 min after delivery (up to 60–70 µU/L). Within 1–7 days of the newborn, the concentration of TSH reaches 1–39 µU/ml which dropped to 0.5–6.5 µU/ml between 8 and 28 days. In the 1st postnatal week, the T4 serum levels reach concentrations (9–22 µg/dl) that are higher than at any other time of life as between 8 and 28 days, the concentration dropped to 8.2–17 µg/dl. The levels of T3 are in the range of 36–316 ng/dl within a week of delivery which can rise till 105–346 ng/dl in between 8 and 28 days. In between 1 and 7 days of newborn, the concentration of FT3 and FT4 is 1.3–6.1 pg/ml and 2.2–5.3 ng/dL which reaches to 2.2–8 pg/ml and 0.9–2.3 ng/dL at 8–28 days of newborn, respectively [2,4,3,14].

In the present study, a maximum number of cases belonged to the category of low birth weight (LBW) babies, that is, 1.5–2.5 kg (67.69%). The higher prevalence of LBW babies in the study group can be explained as LBW is a known risk

Table 2: Statistical calculation outcomes for the values of thyroid hormone levels before and after the commencement of antibiotic therapy

Thyroid profile	Before antibiotics (n=195)			After antibiotics (n=170)			p-value (Paired t-test)
	Mean	Range	SD	Mean	Range	SD	
TSH (µg/ml)	5.29	0.4–8.9	2.11	9.19	4.6–12.5	1.63	p<0.0001
T3 (ng/dl)	94.4	4.2–181	44.4	185.30	114.4–260.5	44.53	p<0.0001
T4 (µg/dl)	7.25	2.1–12.6	2.72	13.19	6.4–105	10.24	p<0.0001
fT3 (pg/ml)	1.84	0.5–4.8	0.9	3.60	1.6–5.5	0.89	p<0.0001
fT4 (µg/dl)	1.43	0.4–2.3	0.458	2.54	1.1–3.4	0.52	p<0.0001

TSH: Thyroid-stimulating hormone

Table 3: Distribution of the study population detected with various species during body fluid culture of children and their respective percentages

Results	Body fluid culture for species	Number of children	Percentage
Positive	*Acinetobacter*	6	3.08
	Candida	2	1.03
	Cons	28	14.36
	Escherichia coli	27	13.85
	Klebsiella	12	6.15
	Micrococcus	2	1.03
	Pseudomonas	3	1.54
	Staphylococcus aureus	30	15.39
	Streptococcus	30	15.39
	Staphylococcus epidermidis	12	6.15
Negative		43	22.05
Total		195	100.00

factor for the development of sepsis. We found an increase number of institutional delivery (67%) of neonates which can be correlated with the increased awareness and better health transport facilities in the community. The percentages of institutional deliveries and home deliveries in Madhya Pradesh as per the National Family Health Survey (NFHS-4) were 80.8 and 2.3%, respectively [15], which is almost similar to the findings of our study. Out of total cases, 42.56% were on EBF, while a higher number of cases (57.5%) were either on top feed or mixed feed which are known risk factors for the development of sepsis, whereas, in Madhya Pradesh as per the NFHS-4, 58.2% infants were on EBF [15].

In our study, we found that there is a significant (p<0.0001) improvement in TSH, T3, T4, fT3, and fT4 after antibiotic therapy. A prospective cohort study conducted by Kurt *et al*. on 292 newborns found that serum total T_3 and total T_4 levels of septic newborns were significantly less as compared to those of healthy newborns at the onset and serum total T_4 level was increased significantly after antibiotic therapy. They suggested a significant change in thyroid hormone levels after the treatment of neonatal sepsis [6]. In a similar study, Das *et al*. studied 49 neonates (8–28 days) for serum cortisol, total T3, total T4, and TSH levels at diagnosis and at discharge following recovery. They found a low level of total T3 and T4 in neonates with sepsis and level was normalized following treatment. However, the mean serum TSH level was in the normal range both at admission and at discharge [9].

Schonberger *et al*. observed a transient hypothyroidism in 12% of the neonates admitted to the neonatal intensive care with various problems such as sepsis, prematurity, and respiratory distress [10]. According to Hagag *et al*., neonates with sepsis have higher serum cortisol and hepcidin and significantly lower free T3 and free T4 than that of healthy neonates. They claim that these findings can be used as a marker in the diagnosis of sepsis for a better prognosis [11]. A study done by Silva *et al*. on a small study population of term newborn babies with sepsis, low T3 syndrome was observed in 50% cases, while T3-T4 syndrome was observed in 100% of study subjects. The four out of six newborns with fungal sepsis progressed to septic shock [12]. Neonates with fungal sepsis were also included in our study. Kadivar *et al*. in their study found that neonates with <34 weeks had significantly lower thyroxine levels (7.15±2.56; p=0.03) than others [16]. Therefore, in our study, pre-term and post-term neonates were excluded from the study to alleviate the effect of gestational age.

The mechanism behind this relationship between sepsis and alteration of thyroid hormones is not clear; however, many theories have tried to elucidate the mechanism leading to the hormonal change in newborns with sepsis. One hypothesis proposed that the lower metabolism rate of the body is responsible for this relationship [17]; whereas, another theory suggests that a decrease in the activity of 5'-monodeiodinase, which converts T4 to T3, may also be involved as an underlying mechanism of a low T3 level [18]. Since in sepsis patients, iodine is used as a halide ion, some theories also believed that the low levels of thyroid hormones may be responsible for the activation of the phagocytic system of neutrophils [19-21]. Fabris *et al*. hypothesized that several inflammatory cytokines, such as interleukin (IL)1, IL6, and tumor necrosis factor-α, suppress the thyroid function at different levels through direct or indirect pathways [22].

IL-1 is found to be a major cytokine stimulating the hypothalamopituitary adrenal axis that leads to an increase in glucocorticoid levels [23]. These cytokines also act on the hypothalamopituitary thyroid axis and inhibit the TSH secretion, biosynthesis, and release of thyroid hormone and thyroid growth [24]. In sepsis, the increase in the production of pro-inflammatory cytokines is more pronounced than that in other

Table 4: Comparing mean thyroid indices between culture-positive and culture-negative groups

Thyroid profile	Culture positive (n=152)			Culture negative (n=43)			Unpaired t-test
	Mean	Range	Sd	Mean	Range	Sd	p-value
TSH (µg/ml)	5.21	0.4–8.9	2.18	5.56	1.2–8.2	1.82	p=0.3327
T3 (ng/dl)	92.93	4.2–180.5	43.82	99.83	25.8–166.8	46.43	p=0.3696
T4 (µg/dl)	7.18	2.1–12.6	2.71	7.51	2.6–11.5	2.79	p=0.4860
fT3 (pg/ml)	1.81	0.5–4.8	0.90	1.94	0.5–4.5	0.91	p=0.3833
fT4 (µg/dl)	1.42	0.4–2.3	0.45	1.48	0.5–2.2	0.47	p=0.4060

TSH: Thyroid-stimulating hormone

types of critical illness. Fabris *et al*. found that the thyroid-immune interactions exist and analyzed the possible integration between pituitary-thyroid hormones and immune factors that help in the development and maintenance of immune efficiency [22]. The severity of illness influences every aspect of thyroid hormone in the body, from the control of secretion to the delivery, metabolism, and ultimate action. This has led to the terminology known as "Sick Euthyroid Syndrome" which is characterized by a significant decrease in serum tri-iodothyronine (T3), slight decrease in serum thyroxin (T4), increase in reverse T3 level, and no significant change in TSH [25].

We have tried our best to depict the relationship between thyroid hormone with LOS among full-term neonates but despite our efforts, several limitations are present in our study. First, we have not investigated the maternal thyroid profile. The maternal thyroid status was assessed based on history and drug intake, so we could not assess exact maternal thyroid status. Second, the use of thyroxin in sepsis is still debatable as our study is not an interventional study; hence, more randomized controlled trials are recommended to assess the usefulness of the thyroxin replacement therapy in neonatal sepsis. Finally, larger sample size and serial TSH monitoring are required to establish the clear prognostic significance of the thyroid profile.

CONCLUSION

Our study suggested a significant improvement in TSH, T3, T4, fT3, and fT4 after antibiotic therapy in full-term neonates with LOS. Hence, based on our observation, we suggest that there is a correlation of thyroid profile with a prognosis of illness but since this is not an interventional study, more clinical trials overcoming the above-mentioned limitations are recommended.

REFERENCES

1. National Neonatal Perinatal Data Base on Neonatal Sepsis; 2020. Available from: https://www.newbornwhocc.org/pdf/nnpd_report_2002-03.pdf. [Last accessed on 2020 May 06].
2. Puopolo KM, Cloherty JP, Eichenwald EC, Lieberman E. Bacterial and fungal infections. Manual Neonatal Care 2012;7:624-55.
3. Williams CB, Eisenstein ME, Cole FS. Immunology and infection. In: Gleason CA, Devaskar SU, editors. Avery's Text Book Diseases of Newborn. 9th ed. Amsterdam, Netherlands: Elsevier; 2012. p. 992-1017.
4. Donohue JE, Yu S. Hypothalamic-pituitary-adrenal response to critical illness. In: Shaffner DH, Nichols DG, editors. Rogers Textbook of Pediatrics Intensive Care. 5th ed. Philadelphia, PA: Lippincott Williams and Wilkins; 2015. p. 1326-47.
5. Csaba G, Pallinger E. Thyrotropic hormone (TSH) regulation of triiodothyronine (T(3)) concentration in immune cells. Inflamm Res J 2009;58:151-4.
6. Kurt A, Aygun AD, Sengul I, Sen Y, Kurt AN, Ustundag B. Serum thyroid hormones levels are significantly decreased in septic neonates with poor outcome. J Endocrinol Invest 2011;34:e92-6.
7. Joosten KF, de Kleijn ED, Westerterp M, de Hoog M, Eijck FC, Hop WC, *et al*. Endocrine and metabolic responses in children with meningoccocal sepsis: Striking differences between survivors and non-survivors. J Clin Endocrinol Metab 2000;85:3746-53.
8. Meyer S, Schuetz P, Wieland M, Nusbaumer C, Mueller B, Christ-Crain M. Low triiodothyronine syndrome: A prognostic marker for outcome in sepsis? Endocrine 2011;39:167-74.
9. Das BK, Agarwal P, Agarwal JK, Mishra OP. Serum cortisol and thyroid hormone levels in neonates with sepsis. Indian J Pediatr 2002;69:663-5.
10. Schonberger W, Grimm W, Gempp W, Dinkel E. Transient Hypothyroidism associated with prematurity, sepsis and respiratory distress. Eur J Pediatr 1979;132:85-92.
11. Hagag A, Elfarargy MS, Lyonis R, Al-Ashmawy GM. Diagnostic value of assessment of serum cortisol, hepcidin and thyroid hormone levels in neonates with late onset sepsis. Infect Disord Drug Targets 2021;21:248-56.
12. Silva MH, Araujo MC, Diniz EM, Ceccon ME, Carvalho WB. Thyroid abnormalities in term infants with fungal sepsis. Rev Assoc Med Bras (1992) 2016;62:561-7.
13. National Neonatology Forum Guidelines on Management of Neonatal Sepsis; 2020. http://www.nnfpublication.org. [Last accessed on 2020 May 06].
14. Markus B, Colinus K; Thyroid gland and thyroid hormones. In: Mark A, editor. Sperlings Pediatrics Endocrinology. 4th ed. Amsterdam, Netherlands: Elsevier; 2014. p. 1167-79.
15. Ministry of Health and Family Welfare. National Family Health Survey-4 by Ministry of Health and Family Welfare (NFHS-4) 2015-2016. Madhya Pradesh: Ministry of Health and Family Welfare MP Fact Sheath, No. 1-4.
16. Kadivar M, Parsaei R, Setoudeh A. The relationship between thyroxine level and short term clinical outcome among sick newborn infant. Acta Med Iran 2011;49:93-9.
17. Kaptein EM, Garieb DA, Spencer GA, Wheeler WS, Nicoloff JT. Thyroxine metabolism in the low thyroxine state of critical nonthyroidal illnesses. J Clin Endocrinol Metab 1981;53:764-71.
18. Santini F, Chopra IJ. A radioimmunoassay of the rat Type I iodothyronine 5'-monodeiodinase. Endocrinology 1992;131:2521-6.
19. Klebanoff SJ. Myeloperoxidase-halide-hydrogen peroxide antibacterial system. J Bacteriol 1968;95:2131-8.
20. Migler R, DeChatelet LR, Bass DA. Human eosinophilic peroxidase: Role in bactericidal activity. Blood 1978;51:445-56.
21. Klebanoff SJ, Rosen H. The role of myeloperoxidase in the microbicidal activity of polymorphonuclear leukocytes. Ciba Found Symp 1978;65:263-84.
22. Fabris N, Mocchegiani E, Provinciali M. Pituitary-thyroid axis and immune system: A reciprocal neuroendocrine-immune interaction. Horm Res 1995;43:2938.
23. Blalock JE. A molecular basis for bidirectional communication between the immune and neuroendocrine systems. Physiol Rev 1989;69:1-32.

24. Enomoto T, Sugawa H, Kosugi S, Inoue D, Mori T, Imura H. Prolonged effects of recombinant human interleukin-1 alpha on mouse thyroid function. Endocrinology 1990;127:2322-7.
25. Marieke D, Koen F, Visser TJ, Hop WC, de Rijke YB, Hazelzet JA, *et al*. Euthyroid sick syndrome in meningococcal sepsis: The impact of peripheral thyroid hormone metabolism and binding proteins. J Clin Endocrinol Metab 2005;90:5613-20.

Funding: None; Conflicts of Interest: None Stated.

How to cite this article: Singh D, Agrawal A, Shrivastava J. Assessment of thyroid hormones in full-term neonates with late-onset sepsis. Indian J Child Health. 2021; 8(6):225-230.