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Original Research Paper

Pediatrics

THE ROLE OF THYROID HORMONE IN NEONATES WITH SEPSIS

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ABSTRACT

Background: Present study was conducted to examine the role of thyroid hormone in neonates with sepsis and to find out prognostic value.

Methodology: Total 70 cases and 70 controls were taken. Neonates with gestational age more than 37 weeks, body weight more than 2500 grams or without congenital abnormalities were include. Newborns born to mothers having thyroid disease or on thyroid supplements; Neonates with congenital abnormalities and who gave Refusal for consent were exclude. The samples was used to monitor the levels of FT3,FT4,TSH and CRP with other investigations and thyroid hormone profile will estimate after the third day of life.

Results: We found that in case group mean T3 is 1.98 (0.55) pg/ml, mean T4 is 1.85 (0.50) ng/ml and mean TSH is 3.25 (1.17) μIU/mL whereas in control group mean T3 is 3.00 (0.56) pg/ml, mean T4 is 2.76 (0.16) ng/ml and mean TSH is 5.88 (0.85) μ IU/mL. All T3 ,T4 ,and TSH having p value $p<0.001$ (significant) therefore there is significantly lower serum level of FT3, FT4, and TSH in neonates in sepsis as compared to control having all p value of $P<0.001$ (S).

Conclusion: our study suggests that low levels of FT3 and FT4 at baseline correlates closely with poor outcome in neonates with sepsis or septic shock and favor the existence of an association between lower FT3 and FT4 with worse outcome.

KEYWORDS : Neonatal sepsis, FT3, FT4, TSH

INTRODUCTION

Bacterial infection in the newborn account for a considerable morbidity and mortality, as the newborn especially the premature are prone to serious infections by organisms and partly because the signs of these infections may be absent or minimal and are hard to detect2. Neonatal sepsis is characterized by signs and symptoms of infection with or without accompanying bacteremia in the first month of life[1].

Neonatal sepsis is responsible for about 30-50% of the total neonatal deaths in developing countries[2,3]. It is estimated that up to 20% of neonates develop sepsis and approximately 1% die due to sepsis related causes[3].

Neonatal sepsis is the response of neonates to any kind of infections. It can be early or late in onset[4]. In early onset, maximum cases are observed within 24 hours of life. The infection can be contracted from the mother via trans-placental route, ascending infection, during passage through an infected birth canal, or exposure to infected blood at delivery[5]. Late onset sepsis usually presents after 72 hours of age. The source of infection in LOS is either nosocomial (hospital-acquired) or community-acquired and neonates usually present with septicemia, pneumonia or meningitis[6,7].

As a result of this, antibiotics are often started on the slightest clinical suspicions of sepsis. This approach is effective in fighting against the acute infections, but increases the risks of antibiotics induced side effects and the emergence of drug resistant organisms in neonatal units[8,9].

Inability to adequately exclude the diagnosis of neonatal sepsis can result in unnecessary and prolonged exposure of the newborn to antibiotics. Thus, laboratory tests that assist the clinician in diagnosis of infection in neonates have considerable relevance[10].

Epidemiological studies have shown alterations in thyroid hormones levels in hospitalized patients. These alterations are more commonly observed in those with increased age or critical illness[11]. Few studies in critically ill children showed an association of decreased levels of TT3 and TT4 with mortality [12,13]. In another study by Anand et al, no significant changes were observed in thyroid indices with CRP 27 Very few studies have been reported in neonates. To date it is also unclear whether newborns respond in the same way as adults during critical illness.

Therefore, in this study we aimed at assessing the thyroid hormone levels in neonates with sepsis and to find out prognostic value.

MATHERIAL AND METHODS

Present observational Study was conducted in department of pediatrics S.M.S Medical College, Jaipur, Rajasthan over a period of one year. Inclusion criteria: Neonates with gestational age more than 37 weeks, body weight more than 2500 grams or without congenital abnormalities. Exclusion criteria: Newborns born to mothers having thyroid disease or on thyroid supplements; Neonates with congenital abnormalities and who gave Refusal for consent.Sample size is calculated at 95% confidence level, alpha error of. 05 assuming FT3 level of 3.99 pg/ml and 1.98 pg/ml among the control group and septic neonates respectively as per the reference article (thyroid hormone dysfunction and CRP levels in neonates with sepsis). The 5 ml venous blood samples was used to monitor the levels of FT3, FT4,TSH and CRP with other investigations and thyroid hormone profile will estimate after the third day of life.

RESULTS

In present study mean age of cases was 2.04 (1.18) days and that of control was 2.33 (1.18). Maximum number of subjects were falling in age group 1-4 days of life. There were 52 males and 18 females in cases and 51 males and 19 females in controls. Thus, Male subjects out number female subjects. Mean weight of cases was 2.65 (0.13) kg and that of controls was 2.81 (0.14) kg

Table: 1 Distribution of Vitals and CBC parameters

	Cases		Controls		P-value
	Mean	SD	Mean	SD	
HR (beats per minute)	140	8.74	128.8	3.5	<0.001
RR (breaths per minute)	48.17	8.70	40.17	3.67	<0.001
TLC(per microliter)	18568.86	3728.92	9302.71	1091.27	<0.001
Platelet (Lakh/microliter)	1.46	0.16	1.76	0.19	<0.001

In our study we found a statistically significant difference in vital and CBC parameters among cases and controls (Table:1). There were more tachycardia and more tachypnea observed in cases as compared to controls. And, also Leukocytosis and thrombocytopenia more in cases as compared to controls.

On blood culture and urine culture analysis we found that out of 70 cases 32 culture were sterile,17 culture positive of staphylococcus ,8 culture positive of coagulase negative ,8 culture positive of pseudomonas and 1 culture positive of Escherichia coli so maximum number of infected organism found to be staphylococcus (Fig: 1).

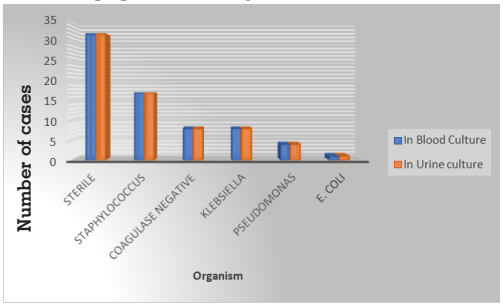

Fig: 1 culture of Blood and Urine

Table: 2 shows Comparison of FT3, FT4 and TSH level in study group. We found that in case group mean T3 is 1.98 (0.55) pg/ml, mean T4 is 1.85 (0.50) ng/ml and mean TSH is 3.25 (1.17) IU/mL whereas in control group mean T3 is 3.00 (0.56) pg/ml, mean T4 is 2.76 (0.16) ng/ml and mean TSH is 5.88 (0.85) IU/mL. All T3 ,T4 ,and TSH having p value p<0.001 (significant) therefore there is significantly lower serum level of FT3, FT4, and TSH in neonates in sepsis as compared to control having all p value of P<0.001 (S).

Table: 2 Comparison of FT3, FT4 and TSH level in study group

Groups	Number	T3 (pg/mL)		T4 (ng/dL)		TSH (μIU/mL)	
		Mean	SD	Mean	SD	Mean	SD
Case	70	1.98	0.55	1.85	0.5	3.25	1.17
Control	70	3	0.56	2.76	0.16	5.88	0.85
P value		P<0.001 (S)		P<0.001 (S)		P<0.001 (S)	

Fig: 2 shows distribution of cases according to their outcomes. Out of total 70 cases 33 cases (47.14%) were survivor and 24 cases (34.28%) were non survivor and 13 cases (18.57%) were septic shock survivor group. Therefore maximum number of cases were found to be survivor.

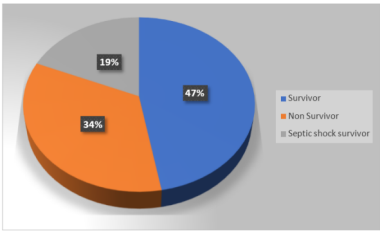

Fig: 2 distribution of cases according to ourcome.

Table: 3 shows comparison of T3, T4, and TSH in non-survivor, sepsis survivor, and septic shock survivor. The mean T3 in non-survivor , sepsis survivor and septic shock survivor is

1.78 pg/ml, 2.16 pg/ml and 1.89 pg/ml respectively. The mean T4 in non-survivor, sepsis survivor and septic shock survivor is 1.60 ng/ml,1.99 ng/ml, and 1.82 ng/ml respectively. The mean TSH in non-survivor, sepsis survivor and septic shock survivor is 4.25 μ IU/ml, 4.03 μ IU/mL and 4.13 μ IU/mL respectively

Non-survivor group had statistically significantly lower FT3, and FT4 levels compared to sepsis survivor. No significant difference was observed in FT3and FT4 values between septic shock survivor and non-survivor group. No significant difference was also observed in FT3 and FT4 values between septic survivor and non-survivor group. No significant difference was also seen in TSH levels in sepsis survivor and septic shock survivor compared to non-survivors.

Table 3 - Comparison of T3, T4, and TSH in non-survivor, sepsis survivor,and septic shock survivor

Sub Groups of Cases	No. of cases	T3 (pg/mL)		T4 (ng/dL)		TSH (μ IU/mL)	
		Mean	SD	Mean	SD	Mean	SD
Non Survivor	24	1.78*	0.59	1.60*	0.61	4.25#	0.87
Sepsis Survivor	33	2.16*	0.49	1.99*	0.40	4.03#	0.34
Septic shock survivor	13	1.89#	0.49	1.82#	0.33	4.13#	0.38

* significant # non-significant

DISCUSSION

The present study was conducted at SPMCHI, department of pediatrics, SMS medical college, Jaipur. It was a hospital based, observational, analytical, cross sectional type of study. The study comprised of total 140 subjects out of which 70 were cases and 70 were control groups. Septic screen profile and thyroid hormones levels profile were done in all the patients after admission

Aims and objectives of this study were to study prognostic value of thyroid hormones levels in neonates with sepsis of gestational age more than 37 weeks, body weight more than 2500 grams or without any congenital abnormalities

A written consent from patients or available guardian was taken before enrollment in this study. FT3, FT4 and TSH values are lower in cases as compared to controls. Non survivor group had statistically significantly lower FT3, and FT4 levels compared to sepsis survivor. No significant difference was observed in FT3and FT4 values between septic shock survivor and non survivor group. No significant difference was also observed in FT3 and FT4 values between septic survivor and non survivor group. No significant difference was also seen in TSH levels in sepsis survivor and septic shock survivor compared to non survivors.

In our study, out of total 140(70 cases +70 controls) maximum no of patients were between age group of 1-4 days. Mean age in cases is 2.04 days and mean age in control is 2.33 days. Our results were in accordance with observations made by Chacko b et al (2005)[14]

Hornik CP et al (2012)[15] also reported that maximum number of cases were of early onset.

In our study mean weight of cases group were lesser than control group, the mean value of weight in cases is 2.65 kg and mean value of weight in controls is 2.81. In our study male subjects out number female subjects that is 74 % in cases and 72% in control. out of 70 cases 52 were male and 18 were female whereas out of total 70 controls 51 were male and 19 were female.

In our study in case group the mean value of heart rate is 140 beats per minute with standard deviation 8.74 whereas in control group mean value of heart rate is 128.80 beats per minute with standard deviation 3.50 having p value of p<0.001 (significant). In our study in case group the mean value of respiratory rate is 48.17 breaths per minute whereas in control group mean value of respiratory rate is 40.17 breaths per minute. Therefore, More tachycardia and more tachypnea observed in cases as compared to controls.

In our study there is increase leucocytosis in cases as compared control group and there is decrease platelet count as compared to control group. Both are significant difference (p value
<0.001).

Stempniewicz et al (1995)[16] did a study to estimate usefulness of morphological blood tests for screening of neonatal infections. The following criteria s were used for estimation: TLC, total PMN count, total immature PMN count, total thrombocyte count, I:T ratio and I:M ratio. They examined 143 newborns admitted to the Neonatal Pathology Clinic in Zabrze, Poland in first week of life, divided into three groups: with sepsis, with suspicion of sepsis and without sepsis. They obtained sensitivity of 54.35% for sepsis, 50% for suspicion of sepsis and 52.70% for both groups (sepsis and suspected sepsis) and specificity for sepsis as 98.55%. They considered that Hematologic scoring system (HSS) is helpful in early diagnostics of neonatal bacterial infections.

Similar studies was observed Rodwellet al (1998)[17] studied 287 neonates for any predisposing perinatal factors or clinical suspicion of sepsis. Hematologic findings and complete blood cell count criteria were evaluated as screening tests for neonatal sepsis. From the data obtained, a hematologic scoring system (HSS) was formulated that assigns a score of 1 for each of seven findings: abnormal TLC, abnormal total polymorpho-nuclear (PMN) count, elevated immature PMN count, elevated immature to total PMN (I:T) ratio, elevated immature to maturePMN(I:M) ratio, platelet count less than or equal to 150,000/mm3 and pronounced degenerative changes in PMNs. There were 298 evaluations for sepsis (243 in the first 24 hours of life and 55 between days 2 and day 30). Twenty-six of 27 (96%) infants with sepsis and all 23 infants with probable infection had scores greater than or equal to 3, compared with 35 of 248 (14%) noninfected infants. The likelihood of sepsis with scores greater than or equal to 3 was 31% and this value differed with both gestational and postnatal ages (34% v/s 8% in preterm and term infants less than 24 hours of age and 65% thereafter). The higher the score, the greater was the likelihood of sepsis. With score less than or equal to 2, the likelihood of sepsis was 1%.

In our study out of 70 cases maximum number of infected organism found to be staphylococcus.

Similar study was observed by Sarkar et al (2006)[13] did a study to determine the need for multiple site blood cultures in the evaluation of neonatal sepsis and concluded that two site blood cultures for the initial evaluation of neonatal sepsis do not have a better yield in pathogen detection. Sepsis in neonates can be detected with sufficient accuracy with a single site blood culture with blood volume of>1 ml.

In our study there is significantly lower serum levels of FT3 and FT4 and TSH in neonates with sepsis compared to age-matched non-septic controls. In our study in case group mean value of T3 is 1.98 pg/ml with standard deviation 0.55, mean value of T4 is 1.85 ng/ml with standard deviation 0.50 and mean value of TSH is 3.25 μ IU/mL with standard deviation 1.17 whereas in control group mean value of T3 is 3.00 pg/ml with standard deviation 0.56 ,mean value of T4 is 2.76 ng/ml with standard deviation 0.16 and mean value of TSH is 5.88 μ IU/mL with standard deviation 0.85 all T3 ,T4 ,and TSH having p value p<0.001 (significant) therefore There is significantly lower serum level of FT3, FT4, and TSH in neonates in sepsis as compared to control having all p value of P<0.001 (S).

Thyroid hormones are important for the metabolic adaptations of the body in times of stress and critical illness. Alterations in the hypothalamic –pituitary thyroid axis suggest a prognostic role of thyroid hormones in neonates with sepsis and septic shock.

In a study by Kurt a et al (2011)[18] serum TT3 and TT4 levels of septic newborns were significantly decreased at the onset while serum TT4 levels increased after the antibiotictreatment. To the best of our knowledge, this report is the first study to compare thyroid hormone levels in a large number of septic newborns and a healthy group. Their findings suggest that before and after treatment of neonatal sepsis a significant change is realized in thyroid hormone levels.

Borkowski et al (2005)[19] have shown that decreased levels of FT3 and TSH were associated with poor prognosis in patients with septic shock.

In another similar study, Lodha et al (2007)[20] suggested that thyroid function derangement in children was not an important factor contributing to severity of septic shock. They found lower levels of TT3, TT4, FT3, FT4 and TSH in children with septic shock compared to sepsis group.

Yildizas et al (2004)[21] observed that the levels of TT3, TT4, FT3, FT4 were markedly lower in non-survivors groups as compared to survivors .these changes in the hypothalamo-pituitary – thyroid axis may suggest a possible prognostic value of thyroid hormones levels in children with sepsis and septic shock.

Shikha Sharma et al (2013)[22] also conducted a study on forty neonates with sepsis were included in the study as cases. Neonates with gestational age less than 37 weeks, body weight less than 2,500 grams or with congenital abnormalities were excluded from the study. Septic neonates were further divided into sepsis survivors (n = 19), shock-survivors (n = 9) and non- survivors. Forty full term neonates without sepsis served as controls. Thyroid hormones and CRP were estimated by chemiluminescent immunometric assay and immunoturbidimetric assay respectively. The FT3 and FT4 hormones levels were significantly decreased (P < 0.001) in neonates with sepsis as compared to controls. No significant difference was observed in TSH levels.

Non survivors had lower FT3 and FT4 levels (P < 0.05) compared to sepsis survivor group. There was also a significant negative correlation between CRP and FT3 level in non-survivor group (r = -0.60; P = 0.02) and septic shock survivor group (r = -0.78; P = 0.006). Low levels of FT3 and elevation in CRP correlate closely with decreased survival in septic neonates.

CONCLUSION:

To conclude our study on neonates with sepsis suggests that low levels of FT3 and FT4 at baseline correlates closely with poor outcome in neonates with sepsis or septic shock and favour the existence of an association between lower FT3 and FT4 with worse outcome.

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