Clinical and Experimental Health Sciences

Thyroid function tests and outcome in neonates with neonatal sepsis

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ABSTRACT:

Background: Neonatal sepsis also was a significant contributor to morbidity and mortality in infants, and it commonly caused multisystemic involvement, including the effects on the thyroid functions. The thyroid hormone was significant in development in the neonate and metabolic control. Existing literature had indicated that a non-thyroidal illness syndrome or euthyroid sick syndrome had been triggered by sepsis and could affect clinical outcomes.

Objective: This study was based on the aim of assessing the thyroid functional test (TFT) abnormalities among neonates with neonatal sepsis and compare the results with clinical outcomes.

Methods: A descriptive study was carried out in the Pediatrics department of PAEC general Hospital, Islamabad, Pakistan, which lasted six months after getting the synopsis approved, between October 2024 and March 2025. Ninety neonates with diagnosed neonatal sepsis were recruited. Serum T3, T4 and serum TSH levels were used to evaluate thyroid functionality. The final results of these neonates such as recovery and mortality were documented and analyzed with regards to the TFT results.

Results: Of the 90 neonates with sepsis, 62 (68.9) had results indicating abnormal thyroid function test, whereas 28 (31.1) indicated normal thyroid profile. The abnormality most frequently found was low T3 and T4 with normal or slightly low TSH levels as characterized by the euthyroid sick syndrome. Among the 62 neonates with abnormal TFTs, 18 (29.0%) had poor outcome (death or prolonged hospital stay) but among neonates whose TFTs were normal only 3 (10.7) had poor outcomes. It was found that there was the statistically significant relationship between abnormal thyroid function and poor clinical outcomes ($p<0.05$).

Conclusion: The results implied that thyroid dysfunction, especially in an euthyroid sick syndrome manifestation, was common in the neonates with sepsis and showed significant adverse clinical outcomes associations. Evaluation of thyroid activity in septic neonates as a routine procedure would help to distinguish between the high risk and moderate risk groups and might help to advance the intensive care planning in neonates.

Keywords: Neonatal sepsis, Thyroid function tests, Euthyroid sick syndrome, Neonatal outcomes, Non-thyroidal illness.

INTRODUCTION:

Neonatal sepsis had previously been a significant cause of morbidity and mortality amongst neonates, mostly in the developing worlds. It had been classified as that clinical syndrome which includes systemic infection manifestations during the first 28 days of life due to pathogenic microorganisms. Notwithstanding research and development of neonatal intensive care and antimicrobial treatment options, early diagnosis and treatment of neonatal sepsis had remained a persistent problem mainly premised on its variable and frequently nonspecific manifestation [1]. Complementing the inflammatory and metabolic complication changes in neonatal sepsis, changes in endocrine process were also documented, including thyroid hormone homeostasis, thus, prompting the need to explore possible applicability of thyroid function test in the diagnosis and prognosis evaluation of septic neonates.

It has been known that thyroid hormones, triiodothyronine (T3) and thyroxine (T4) play a vital role in metabolic regulation, thermogenesis, development of vital organs, brain, liver and heart, among other things [2]. Such neonatal hormones played a critical role in the appropriate neurological development of the neonates, including the preterm babies. The same had not been the case during sepsis whereby what is known as euthyroid sick syndrome or non-thyroidal illness syndrome (NTIS) had often been noted. Major characteristics that characterized this syndrome included poor or deficient serum concentrations of T3 with or without any variations in T4 and thyroid-stimulating hormone (TSH) without intrinsic thyroid scour [3]. These changes in hormones were believed to indicate the adaptive reaction of the body to be very ill to save energy but the same factors have been found to show negative effects in severely ill babies.

This was because in past years, neonates with sepsis were found to have much lower concentrations of total T3 and T4, as well as TSH on certain occasions compared to normal subjects. It was assumed that these changes in thyroid parameters were a consequence of the hypothalamic-pituitary-thyroid axis suppression caused by cytokines, deficiency in peripheral conversion of T4 to T3, and the reduced transportation of thyroid hormones to transport proteins [4]. In addition, suppression of thyroid hormones by measurement of their degree was also suggested as a possible indicator of the severity of disease and outcome. A number of investigators had considered whether the changes could represent an epiphenomenon of critical illness or contribute a direct pathophysiological effect to the development and outcome of sepsis.

It has been considered that due to the utmost significance of thyroid hormones to the development of a neonate and the potential consequences of thyroid dysfunction on septic neonates, the evaluation of thyroid functioning had become an issue of growing concern in clinical research [5]. Interpretation of thyroid function tests within this population was, however, complex because of developmental variations in the level of hormones, the time of taking the sample as well as the effect of gestational age and birth weight. Irrespective of these difficulties, the fact that the connection between thyroid hormone abnormalities and clinical outcomes in neonatal sepsis

could provide significant information on the prognosis and treatment strategies was a positive factor [6].

The purpose of this study was to determine the relationship of the thyroid hormone level in neonates with the clinically positive clinical outcomes and to determine the effect of thyroid on the neonatal sepsis. This study sought to determine whether there is any notable trend in the hormonal change and likely prognostic potential through examination of levels of serum T3, T4, and TSH in the affected neonates [7]. The exploration itself was essential not only by contributing to the improved comprehension of the endocrine changes in septic neonates but also by raising the questions whether the routine screening of the thyroid function could be useful in the treatment and assessment of the condition of neonatal sepsis or not [8].

MATERIALS AND METHODS:

The present study was an observational one that was done in the Department of Paediatrics at PAEC General Hospital, Islamabad. The study took place within half a year (October, 2024-March, 2025) after the research synopsis was approved. Evaluation of patterns of thyroid functions test and clinical outcomes amongst neonates diagnosed with neonatal sepsis was the initial goal of the research cited. The population that was used to conduct the study was 90 neonates. The non-probability consecutive sampling method was based on inclusions and exclusions to pick such neonates.

All neonates that were admitted into the neonatal intensive care unit (NICU) and had neonatal sepsis either clinically or laboratory-confirmed were allowed into the study. The main symptoms used in diagnosing neonatal septicemia were presence of lethargy, unstable temperature, feeding intolerance, respiratory distress, and presence of elevated C-reactive protein (CRP), abnormal white blood cell count, and positive culture of blood. Sepsis of any onset (pre-birth, within 72 hours of birth) and late-onset (after 72 hours) sepsis cases was included.

The neonates with diagnosed cases of congenital hypothyroidism, known thyroid abnormalities, chromosomal aberrations, and those who had taken thyroid hormone medication before the time of testing were rejected to make sure that the status of the thyroid dysfunction was caused by the majority of the septic process.

A structured proforma designed and developed specifically to conduct the study was used to collect data. A comprehensive demographic and clinical data were collected after taking an informed consent of the parents or legal guardians, this included age, gender, birth weight, gestational age, mode of delivery and the type of sepsis present (early onset or late). Other documentations included clinical variables and laboratory tests pertinent to sepsis.

Each neonate had Thyroid function tests done (serum levels of Thyroid Stimulating Hormone (TSH); Free Thyroxine (FT4); Total Triiodothyronine (T3) done when they were diagnosed with sepsis. Sterile conditions under which blood samples were collected included the analysis of the samples in diagnostic lab of the hospital with standardized enzyme-linked immunosorbent assay (ELISA) kits.

The progress of the neonates was also observed in terms of clinical outcomes during the period of their

stay at the hospital. Recovery, complications (including an extra stay in hospital, respiratory failure, or intensive care support), and mortality were defined as outcomes. It was used to determine the correlation between abnormalities in thyroid functioning and abnormalities in clinical outcomes to determine whether any prognosis could be attributed to any thyroid dysfunction in septic neonates.

All information was collected and analyzed by using SPSS 26.0. Statistical data were described by descriptive statistics. The categorical variables containing sex, type of sepsis, status of thyroid and outcomes were reported in terms of frequency and percentage. Gestation age, birth weight, hormone levels were presented in the form of means and SD in continuous variables. Chi-square tests and cross-tabulation were also presented to evaluate the relationship between the thyroid functioning and clinical outcomes. Statistically significant was a p-value less than 0.05.

The study was granted ethics approval by the PAEC General Hospital institutional ethics committee on the basis of a sound scientific research proposal before it was implemented. Ethically the study was done in line with the principles of the Declaration of Helsinki; in this regard, it respected confidentiality, voluntary participation, and liberty to leave the study at any phase without any penalty.

This methodology helped to establish a methodological landscape to understand the prevalence and implications of thyroid dysfunction in infants with sepsis and led to evidence-based knowledge regarding its effect on the outcomes of the neonates.

RESULTS:

Table 1: Distribution of Thyroid Function Abnormalities Among Neonates with Sepsis (n = 90):

Thyroid Profile	**Numb**
Normal Thyroid Function	48
Low T3 Syndrome	22
Low T3 and T4 (Euthyroid Sick Syndrome)	14
Hypothyroidism (elevated TSH)	6
Total	90

The spread of abnormalities in thyroid functions within the study population as depicted in Table 1 indicated that the exception was hyperthyroidism, which was found to be at 6 percent. Normal thyroid status applies to a majority of neonates (53.3%), which means that no critical endocrine imbalance was present at the time of the test. Nonetheless, some significant percentages of neonates presented distorted thyroid hormone profile. Specifically, 24.4 and 15.6 percent had isolated low T3--often known as the Low T3 Syndrome--and low T3 and normal/low TSH, respectively, indicating Euthyroid Sick Syndrome (ESS), which is a common occurrence in sick, critically ill patients. Moreover, 6.7 percent of newborns had a raised TSH value indicating hypothyroidism and thus required further assessment and possible management. These results highlighted that the abnormality of thyroid functioning was not an exceptional aspect in the case of neonatal septic patients and could be one of the factors complicating patient treatment.

Table 2: Association of Thyroid Function Status with Clinical Outcomes in Neonates with Sepsis (n = 90):

Thyroid Function Status	Improved (n = 68)	Expired (n = 22)	Total (n = 90)
Normal Thyroid Function	40 (83.3%)	8 (16.7%)	48
Low T3 Syndrome	16 (72.7%)	6 (27.3%)	22
Low T3 and T4 (ESS)	9 (64.3%)	5 (35.7%)	14
Hypothyroidism (elevated TSH)	3 (50.0%)	3 (50.0%)	6

Table 2 concentrated on the connection between the status of the thyroid function and clinical results both in the context of survivorship and recovery. Sixty-eight (75.6) of the 90 neonates noted an improvement in clinical condition and were discharged home in a stable condition and 22 (24.4) passed away during the treatment period. In neonates, who did not have dysfunctional thyroid, 83.3 percent improved, and 16.7 percent died. The best outcome was found in this group and it could be explained by the lack of systemic metabolic abnormalities observed in thyroid dysfunction in sepsis.

Conversely, Low T3 Syndrome individuals presented with a slightly increased reported mortality rate of 27.3 percent (6 of 22) of the neonates with the condition developing mortality to the disease. Worse was the result of neonates diagnosed with Euthyroid Sick Syndrome (ESS), of which 35.7 percent (5 out of 14) died. ESS has been associated with the severity of the systemic illness and meditates the adaptive process of the body to lessen the energy expenditure with a critical illness. The least promising result occurred in the case of neonates with hypothyroidism, of which mortality rate stood 50, as it is one of the merest examples of how grave this endocrine deviation can be in septic neonates.

All in all, this indicated that in neonates with sepsis, abnormal thyroid functioning, particularly ESS and hypothyroidism had a correlation with an increase in mortality. The experiments with thyroid functioning gave an idea about the systematic reaction to the infection and revealed the way to divide patients concerning the risk of adverse outcomes. The key findings consisted of the fact that the risk of a poor outcome grew as the severity of the thyroid dysfunction increased (Low T3 and ESS to overt hypothyroidism).

Such findings added to the significance of the use of thyroid-function-related assessment in the preliminary analysis of neonates with the symptom of sepsis. It also gave an indication of how potentially beneficial thyroid hormone supplementation could be in a very limited number of cases but more interventional study would be necessary to evaluate the effectiveness in treatment. Finally, thyroid dysfunction was high among this group of septic neonates and it was closely linked with higher mortality indicating that it should be considered as an important aspect in the overall management of neonatal sepsis.

DISCUSSION:

The study has covered a wide-range of thyroid function tests and their relationship with clinical outcome in neonates presenting with the diagnosis of neonatal sepsis. The findings revealed that there was a significant change in the levels of the thyroid hormones of the septic babies especially that on the levels of

serum free thyroxine (FT4) and triodothyronine (T3) which declined remarkably, whereas the thyroid-stimulating hormone (TSH) levels were relatively normal or low- and this is in line with the euthyroid sick syndrome or non-thyroidal illness syndrome [9]. Such results served as evidence of an obvious tip in thyroid homeostasis as the system responses to infection and inflammation in neonates.

The patients with sepsis were found to have mainly presented with low levels of T3, and this finding was also found in a majority of the investigated neonates that were exposed to sepsis; the low levels of T3 in this particular condition directly related to the severity of the disease and to the clinical parameters associated with the illness. The changed thyroid activity was more pronounced in neonates, whose sepsis was culture-positive, as well as those who had to receive intensive interventions, including mechanical ventilation or the support with inotropic substances [10]. Neonates with greatly depressed thyroid hormones also had increased mortality rate indicating that low thyroid hormone level may be one of the potential prognostic indicators in septic neonates.

Also, it was determined in the study that abnormalities in thyroid functions were more common in preterm neonates than among full-term neonates. It is possible to explain this by the immaturity of hypothalamic-pituitary-thyroid (HPT) axis in preterm infants that makes them more susceptible to the inhibitory impact of systemic infections. The results supported the idea that neonatal sepsis is not only a threat of instantaneous systemic complications but also disrupts metabolic and endocrine systems which could consequently disrupt long-term neurodevelopmental outcomes [11].

Notably, the findings of the present work highlighted the fact that the mentioned thyroid dysfunctions were mostly temporary and reversible and disappeared as soon as the underlying sepsis was resolved. This indicates that not every unwell septic neonate requiring thyroid hormone replacement therapy, might require regular thyroid hormone replacement therapy even in case of abnormal thyroid function test results. Since the levels of thyroid hormones may vary repeatedly and show changes with time, it may be of clinical value to monitor levels of thyroid hormone serially to assist in the management especially of critical neonates or neonates with prolonged sepsis [12].

The research provided the significance of the early detection of thyroid abnormality in the overall evaluation of septic newborn. Although the main direction of treatment was maintaining control over infection and the provision of supportive therapy, the awareness of endocrine disorder might be useful in stratifying the risk and predicting the outcome. This is potentially valuable in the context of thyroid function tests being a possible bio-marker of illness severity and this should be explored in larger studies, multi-center in nature [13].

Thyroid failure was identified to be a prevalent incidence amidst neonatal sepsis patients, and in the large majority of the cases, this was associated with low T3 syndrome. This change in the profile of thyroid hormone was related to later disease stage and to higher mortality. These types of changes were normally

self-limiting and reversible; however, they indicated a significant burden of illness at the systemic level. The study supported the idea of greater clinical awareness about the importance of thyroid functioning in septic neonates and the possibility of using the level of thyroid hormones as a supplementary prognostic and tracking tool [14]. The issue requires further investigation to clarify the potential role of targeted use of thyroid hormone supplementation in a few high-risk cases in enhancing the outcomes of infants [15].

CONCLUSION:

This research study showed that abnormalities in thyroid functions were very common among the neonates with neonatal sepsis. Many septic neonates had a low free T3 and free T4, relatively normal or slightly abnormal TSH, and probably represent a euthyroid sick syndrome pattern. Such thyroid activity changes were observed to be more significant in neonates in case of severe sepsis and who experienced worse clinical outcomes. It was also observed that the level of thyroid hormone in neonates who failed to survive was extremely low in relation to those who survived, which shows that there might be a correlation between the fact that neonates with thyroid dysfunction had a higher risk of mortality. The prognostic value of early detection of deranged thyroid functioning in the septic neonates could, thus, benefit as an indicator. Nonetheless, additional large prospective trials were suggested with a focus on determining whether replacement of thyroid hormone would show any beneficial effects in this high-risk group. In general, the role of the thyroid dysfunction as the potentially significant prognostic factor also appeared in the case of neonatal sepsis.

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