Section: Biochemistry

Original Research Article

TREND OF THYROID HORMONES IN PEDIATRIC TO GERIATRIC SPECTRUM

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ABSTRACT

Background: Thyroid hormones play a vital role in growth, metabolism, and maintenance of physiological homeostasis throughout life. Age-related alterations in thyroid function may influence the interpretation of thyroid function tests and clinical decision-making. This study aimed to evaluate age-related trends in serum free triiodothyronine (FT3), free thyroxine (FT4), and thyroid-stimulating hormone (TSH) from the pediatric to geriatric age groups. **Materials and Methods:** A retrospective cross-sectional study was conducted on 210 individuals aged 10–90 years who underwent thyroid function testing at a tertiary care hospital. Participants were categorized into pediatric, adolescent, young adult, middle-aged, and elderly groups. Demographic details and serum FT3, FT4, and TSH levels measured using a fully automated chemiluminescent immunoassay (CLIA) analyzer were retrieved from laboratory records. Descriptive statistics were used to summarize the data. As the variables were not normally distributed, Spearman's rank correlation analysis was performed to evaluate the association between age and thyroid hormone levels as well as the interrelationships among FT3, FT4, and TSH. A p value <0.05 was considered statistically significant. **Results:** The mean age of the participants was 38.60 ± 15.26 years. Young adults constituted the largest proportion of the study population (48.1%), and females predominated (86.2%). Age demonstrated a weak but statistically significant negative correlation with FT3 levels ($r = -0.217$, $p = 0.002$), indicating a gradual decline in FT3 with advancing age. No significant association was observed between age and FT4 ($r = 0.085$, $p = 0.226$) or TSH ($r = 0.019$, $p = 0.784$). FT3 showed a significant positive correlation with FT4 ($r = 0.327$, $p < 0.001$), while both FT3 ($r = -0.224$, $p = 0.001$) and FT4 ($r = -0.359$, $p < 0.001$) demonstrated significant inverse correlations with TSH, consistent with physiological hypothalamic-pituitary-thyroid axis regulation. **Conclusion:** Advancing age was associated with a modest decline in serum FT3 concentrations, whereas FT4 and TSH levels remained relatively stable across the lifespan. The observed hormonal interrelationships reflected normal thyroid feedback physiology. These findings highlight the importance of considering age-related physiological variations when interpreting thyroid function tests and support the need for population-specific age-related reference data to improve diagnostic accuracy and clinical management.

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INTRODUCTION

Thyroid hormones are crucial for regulating growth, development, metabolism, thermogenesis, and maintaining homeostasis throughout an individual's life. They have a significant physiological impact during early development, energy metabolism, and adaptation to various environments.[1] The hypothalamic-pituitary-thyroid (HPT) axis experiences significant physiological transformations from infancy through to old age, affecting the secretion and levels of thyrotropinor thyroid-stimulating hormone, (TSH), triiodothyronine (T3), and thyroxine (T4). These hormones play a crucial role in normal neurocognitive development in childhood, metabolic regulation in adulthood, and the maintenance of physiological functions in older individuals.[2] Age-related differences in thyroid function have gained more attention recently. In the neonatal and pediatric stages, thyroid hormones play a vital role in physical growth and the development of the central nervous system. Hormone levels tend to stabilize in adulthood, but as individuals age, there are notable changes in thyroid physiology, which encompass variations in hormone production, metabolism, peripheral conversion, and pituitary sensitivity.[3] Numerous studies have indicated that serum TSH levels tend to rise with age, accompanied by a decrease in circulating T3 levels in older adults, whereas T4 levels generally remain fairly constant.

Interpreting thyroid function tests in various age groups presents difficulties, as reference intervals set for adults may not truly represent the physiological changes that occur during childhood or as one age.[4] Nonetheless, the extent and clinical importance of these alterations continue to be topics of active discussion. Thyroid disorders are intricate and influenced by multiple factors, and misreading age-related hormonal variations may result in either overdiagnosis or underdiagnosis of thyroid dysfunction, especially among pediatric and geriatric groups.[5]

The diagnosis of thyroid disease relies on evaluating symptoms and signs associated with the condition, alongside measuring the circulating levels of TSH, T3, and T4. Therefore, it is crucial to establish age-specific trends in thyroid hormone levels to enhance diagnostic precision and inform suitable clinical management. While many studies have investigated thyroid function within particular age groups, there is a scarcity of thorough analyses that explore the trends of thyroid hormones throughout the entire lifespan, from pediatric to geriatric populations. Additionally, factors such as demographics, genetics, nutrition, and the environment can affect thyroid hormone levels, highlighting the need for data specific to different populations. Consequently, this study was conducted to assess the trends in serum TSH, free T3 (FT3), and free T4 (FT4) levels among various age groups, from children to the elderly. Gaining insight into these hormonal patterns related to age may aid in establishing age-specific reference ranges and improve the clinical assessment of thyroid function tests throughout an individual's life.

MATERIALS AND METHODS

This study was a retrospective study conducted on 210 participants in the age range of 10-90years to analyse the levels of TSH, T3 and T4 levels across different age groups ranging from pediatric and geriatric individuals. The study was conducted in the department of Biochemistry of Government Medical College The study was conducted following approval from the Institutional Ethics Committee and was in accordance to institutional and global ethical guidelines.

Study design and setting

A retrospective cross-sectional study was conducted in the Department of Pathology at a tertiary care teaching hospital. Thyroid function test (TFT) records of patients who underwent thyroid hormone analysis during the study period were retrieved from the laboratory database and hospital medical records.

Study population

The study included 210 participants aged 10–90 years who underwent thyroid function testing. Patients were categorized into five age groups: pediatric (<13 years), adolescent (13–18 years), young adult (19–39 years), middle-aged adult (40–59 years), and elderly (≥60 years) to evaluate age-related trends in thyroid hormone levels.Patients aged 10 years and above who underwent thyroid function testing and had a complete thyroid hormone profile, including serum triiodothyronine (T3), thyroxine (T4), and thyroid-stimulating hormone (TSH), along with complete demographic information (age and sex), were included in the study. Patients with incomplete laboratory or demographic records, missing values for T3, T4, TSH, or age, and duplicate patient records were excluded from the analysis.

Data collection

Demographic variables including age and sex, along with laboratory parameters comprising serum T3, T4, and TSH levels, were extracted from the laboratory information system. Data were anonymized before statistical analysis to maintain patient confidentiality.

Laboratory analysis

Serum concentrations of free triiodothyronine (FT3), free thyroxine (FT4), and thyroid-stimulating hormone (TSH) were measured in the central clinical laboratory using a fully automated chemiluminescent immunoassay (CLIA)-based analyzer according to the manufacturer's instructions. Routine internal quality control procedures were followed throughout the study period to ensure analytical accuracy and precision. The laboratory reference ranges used for interpretation were 2.3–4.2 pg/mL for FT3, 0.89–1.76 ng/dL for FT4, and 0.55–4.78 µIU/mL for TSH. Thyroid function status was interpreted based on these assay-specific reference ranges in conjunction

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with the combined FT3, FT4, and TSH results, in accordance with standard clinical diagnostic criteria. The data obtained were analyzed using Spearman's correlation as there was asymmetrical distribution of data in this study. It is a non-parametric method which does not require normally distributed variables and is less sensitive to outliers was therefore chosen for statistical analysis. A two tailed p value <0.05 was considered statistically significant.

RESULTS

A retrospective cross-sectional study was conducted to evaluate the trends in thyroid hormone levels across different age groups ranging from the pediatric to geriatric population. The levels of TSH, T3 and T4 were obtained from the laboratory of a private hospital over a period of 7 months from July 2025 to January 2026. The participants of the study ranged from 10-90yrs involving both males and females. This study included individuals from pediatric and geriatric age groups and the mean and median age was38years with ages ranging from 10 to 90 years. The 95% confidence interval (CI) for the mean age (36.52–40.68 years) suggests a reliable estimate of the average age of the study population.

The majority of participants were young adults (19–40 years), while the pediatric age group represented the smallest proportion of the study population. The study population was predominantly composed of young adults, accounting for 101 (48.1%) participants, followed by middle-aged adults with 74 (35.2%) participants. Elderly individuals constituted 19 (9.0%) of the study population, while adolescents accounted for 14 (6.7%) participants. The pediatric age group was the least represented, comprising only 2 (1.0%) participants. (Chart 1) Overall, more than four-fifths (83.3%) of the study population belonged to the young adult and middle-aged groups, indicating that the cohort was primarily composed of adults.

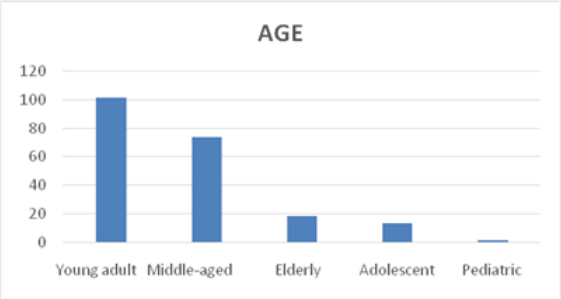


Chart 1: Bar graph showing age wise distribution of participants

Among the 210 participants, 181 (86.2%) were female and 29 (13.8%) were male, indicating a marked female predominance in the study population. (Chart 2) This distribution suggests that the study cohort was predominantly composed of females, with a female-to-male ratio of approximately 6.2:1.

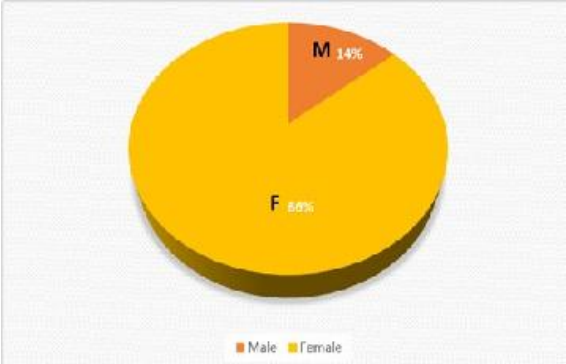


Chart 2: Pie chart showing gender distribution

The mean serum T3 concentration was 2.97 ± 0.84, with a median of 2.88, indicating a relatively symmetric distribution with moderate inter-individual variability. Similarly, the mean serum T4 concentration was 1.18 ± 0.34, with a median of 1.17, suggesting a fairly uniform distribution and comparatively lower variability among participants. In contrast, serum TSH levels exhibited considerable variability, with a mean of 4.12 ± 7.02 and a median of 2.34. The marked difference between the mean and median, together with the broad range of values (0.00–67.57), indicates a positively skewed distribution, reflecting the presence of a small number of participants with markedly elevated TSH concentrations. [Table 1]

Table 1: Descriptive Analysis of Age and Serum Thyroid Hormone Levels in this Study

	Mean±SD	Median (IQR)	Min	Max	95% CI
Age	38.60 ± 15.26	38.00 (26-49)	10	90	36.52 to 40.68
T3	2.97 ± 0.84	2.88 (2.54-3.20)	0.81	9.32	2.86 to 3.09
T4	1.18 ± 0.34	1.17 (1.00-1.32)	0.39	3.78	1.14 to 1.23
TSH	4.12 ± 7.02	2.34 (1.08-4.72)	0.0	67.57	3.16 to 5.07

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Spearman's correlation was used to measure the strength and direction of association between age and thyroid hormone T3, T4 and TSH along with interrelationship among thyroid hormones. The correlation analysis demonstrated a weak but significant inverse association between age and serum T3 levels, whereas no significant correlations were observed between age and serum T4 or TSH levels. Serum T3 exhibited a significant positive correlation with T4 and a weak negative correlation with TSH. Furthermore, T4 showed a moderate negative correlation with TSH, reflecting the physiological negative feedback regulation of the hypothalamic–pituitary–thyroid axis. Overall, these findings suggest that T3 levels decline modestly with advancing age, while T4 remains relatively stable, and the expected interrelationships among thyroid hormones and TSH are preserved. [Table 2]

Table 2: Spearman's Correlation Analysis Among Age, Free T3, Free T4, and TSH Levels

	n	Spearman's"r"	P value	Significance
Age vs T3	210	-0.217	0.002	Weak negative; statistically significant
Age vs T4	210	0.085	0.226	Very weak positive, not significant
Age vs TSH	210	0.019	0.784	Negligible positive correlation; not statistically significant
T3 vs T4	210	0.327	<0.001	Weak – moderate positive; statistically significant
T3 vs TSH	210	-0.224	0.001	Weak negative; statistically significant
T4 vs TSH	210	-0.359	<0.001	Moderate negative, statistically significant

DISCUSSION

The thyroid gland is largely developed by the 7th week of gestation; however, the formation of follicles and the synthesis of thyroid hormones do not begin until the 10th to 12th week.[6] TSH, T3 and T4 can be detected in fetal blood 11-12weeks onwards, physiological thyroid hormone is secreted by 2nd semester, fetal HPT axis matures by 18-20weeks gestation and maturation continues throughout third trimester. Prior to this maturation maternal T4 which cross placental barrier helps in normal development.[7] Thyroid hormonesensure key physiological roles in early development, energy metabolism, reproduction and acclimation of different environments.[8]Under normal physiological conditions, the intact hypothalamic-pituitary-thyroid (HPT) axis maintains stable circulating levels of thyroid hormones (THs) and energy homeostasis. In hyperthyroidism, elevated TH levels induce a hypermetabolic state, which is marked by an increase in resting energy expenditure, weight loss, lower cholesterol levels, heightened lipolysis, and enhanced gluconeogenesis. In contrast, hypothyroidism leads to a decrease in TH levels, resulting in a hypometabolic state characterized by decreased resting energy expenditure, weight gain, elevated cholesterol levels, diminished lipolysis, and reduced gluconeogenesis.[9] TSH and thyroid hormone levels vary throughout a person's life. They are at their highest during early life and noticeably decrease during puberty. In adults, these levels tend to remain fairly stable, even with some fluctuations. After birth, the circulating levels of thyroid hormones reach their peak to help the body adjust to the new environment through thermogenesis. Most countries have established neonatal screening programs to identify congenital hypothyroidism.[10] Upon examining the discrepancies in TSH, T3, and T4 levels, additional diagnostic evaluations are required to determine the root cause of the disease process. These evaluations should encompass thyroid imaging and the detection of specific autoantibodies. More than 95% of thoroughly screened individuals who do not have thyroid disease or autoantibodies exhibit TSH levels below 2.5 mIU/L, indicating that the existing thyroid reference ranges must be revised.[12] Fluctuations in TSH and thyroid hormone levels are influenced by factors such as age, ethnicity, and pregnancy, with age being a significant factor. Symptoms like tiredness, fatigue, and those associated with aging are not reliable indicators of hypothyroidism.[13] Elevated TSH levels can indicate normal aging, suggesting that slight increases in TSH may not warrant treatment, and that levothyroxine dosages should decrease as one ages. In contrast, children and adolescents need higher doses of levothyroxine compared to adults. The aim of the current study is to analyze the age-related trends of serum TSH, Free T3, and Free T4 levels from pediatric to geriatric age groups and compare thyroid function across the lifespan.

The levels of serum T3 were found to be inconsistent across various age demographics. In the pediatric group, free T3 levels were at their peak, but these levels tended to decrease from adolescence into adulthood, with notable inter-individual differences in the older populations. Analysis using Spearman's correlation indicated a weak negative statistically significant relationship between age and serum T3 levels. The decline in serum T3 levels as age increases is in line with the physiological changes in thyroid hormone metabolism that occur with aging. Aging leads to a decrease in the peripheral conversion of thyroxine (T4) into the biologically active triiodothyronine (T3), due to a reduction in the activity of type I 5′-deiodinase.[1] The observed decrease in free T3 levels with age aligns with its function as the active effector molecule of the HPT axis, which also shows diminished activity as individuals age.Similarly, Lawton et al 2024 reported that serum T3 levels gradually decline with advancing age and are associated with longevity and demographic characteristics, reflecting reduced hypothalamic pituitary thyroid axis activity in older

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individuals.[14] As a result, the levels of circulating T3 generally decline progressively with age, even in those without clear thyroid disorders. Nevertheless, the weak strength of the correlation indicates that factors beyond age, such as nutritional status, systemic diseases, medications, and individual metabolic differences, significantly influence serum T3 levels.[15] This study was conducted to examine the age-related patterns of serum thyroid hormones (free T3, free T4, and TSH) throughout the lifespan, from childhood to old age, in order to compare thyroid function across various age groups.

Serum free T3 levels exhibited variations related to age, with the pediatric population showing the highest concentrations, followed by a gradual decrease from adolescence into adulthood. Significant inter-individual variability was observed, especially among older participants. Spearman's correlation analysis indicated a weak yet statistically significant negative correlation between age and free T3 levels, suggesting that serum T3 levels decline as age increases. This finding aligns with the physiological impacts of aging on thyroid hormone metabolism. The aging process is linked to a reduced peripheral conversion of thyroxine (T4) into the biologically active triiodothyronine (T3), attributed to decreased activity of type I 5′-deiodinase, which leads to lower circulating T3 levels despite relatively stable thyroid hormone secretion.[1]

Serum free T4 levels remained relatively stable across the pediatric, adolescent, young adult, and middle-aged groups, with slightly higher values observed in the elderly population. Spearman's correlation analysis demonstrated no significant association between age and free T4 levels, indicating that circulating thyroxine concentrations remain largely preserved throughout life. This finding supports previous reports suggesting that thyroid hormone production is maintained through compensatory homeostatic mechanisms despite advancing age.[16] The preservation of serum free T4 concentrations, despite declining free T3 levels, supports the concept that aging predominantly affects peripheral conversion of T4 to T3 rather than thyroidal hormone secretion itself. Reduced deiodinase-mediated conversion of T4 to T3 has been proposed as one of the principal mechanisms underlying age-related changes in thyroid hormone metabolism.[17]

Serum TSH levels exhibited variation across age groups, with the lowest concentrations observed among young adults (19–39 years) and the highest levels recorded in the elderly population, followed by the middle-aged group. Although Spearman's correlation demonstrated a weak positive relationship between age and TSH, this association was not statistically significant. Therefore, while there was a tendency for TSH concentrations to increase with advancing age, the present study did not demonstrate a significant age-dependent increase in serum TSH levels. Previous population-based studies have consistently reported that the upper limit of the TSH reference range increases with age, whereas the lower limit remains relatively unchanged.[18] Variations in TSH reference intervals have also been attributed to environmental and demographic factors such as iodine intake, smoking status, seasonal variation, ambient temperature, sex, and ethnicity.[19] The absence of a significant association of TSH in the present study may be explained by the heterogeneous nature of the study population, inclusion of participants with diverse clinical conditions, and the wide inter-individual variability of TSH values. Furthermore, TSH secretion is influenced by multiple physiological and pathological factors, which may obscure a direct relationship with chronological age.

Correlation analysis between thyroid hormones T3 and T4 demonstrated a weak-to-moderate positive correlation. This relationship is physiologically expected because T3 is predominantly generated through peripheral deiodination of T4. Consequently, individuals with higher circulating free T4 concentrations generally exhibit higher free T3 levels, reflecting the physiological dependence of peripheral T3 production on the availability of its precursor, T4.[20] Conversely, both free T3 and free T4 demonstrated inverse correlations with TSH concentrations. A weak but statistically significant negative correlation was observed between free T3 and TSH, whereas free T4 and TSH exhibited a moderate negative correlation. These findings are consistent with the well-established negative feedback regulation of the hypothalamic-pituitary-thyroid axis, whereby increasing circulating thyroid hormone concentrations suppress pituitary TSH secretion, while declining hormone levels stimulate TSH release.[21] The stronger inverse correlation observed between free T4 and TSH compared with free T3 and TSH may reflect the predominant role of circulating T4 in pituitary feedback regulation. The anterior pituitary expresses high levels of type 2 iodothyronine deiodinase (D2), which converts circulating T4 to the biologically active T3 intracellularly. This locally generated T3 binds to thyroid hormone receptors in pituitary thyrotrophs and suppresses TSH gene transcription and secretion, making serum TSH more closely related to circulating free T4 concentrations than to circulating free T3.[22]

Overall, the findings of the present study suggest that aging is associated with a gradual decline in serum free T3 concentrations, whereas free T4 levels remain relatively stable across the lifespan. Although TSH levels tended to increase with age, this trend did not reach statistical significance in the study population. The observed hormonal correlations are consistent with established physiological mechanisms governing thyroid hormone synthesis, peripheral metabolism, and hypothalamic-pituitary-thyroid axis regulation. These findings provide further evidence that age-related changes in thyroid function predominantly involve alterations in peripheral thyroid hormone metabolism rather than impairment of thyroid hormone production.

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CONCLUSION

The present study demonstrated that advancing age is associated with a modest but significant decline in serum free T3 levels, whereas free T4 and TSH concentrations remain relatively stable across the pediatric to geriatric age spectrum. The positive correlation between free T3 and free T4 and the inverse correlations of both hormones with TSH were consistent with the physiological regulation of the hypothalamic–pituitary–thyroid (HPT) axis. These findings suggest that age-related changes in thyroid function are primarily related to alterations in peripheral thyroid hormone metabolism rather than impaired thyroid hormone secretion. Understanding these physiological variations is important for the accurate interpretation of thyroid function tests and may help improve age-appropriate diagnosis and clinical management of thyroid disorders. Further large-scale, population-based studies are warranted to establish age-specific reference intervals for thyroid hormones.

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