Journal of Neonatal Surgery
ISSN(Online): 2226-0439
Vol. 14, Issue 21s (2025)
https://www.jneonatalsurg.com

OPEN ACCESS

Assessment of Bone Age in Pediatric Patient Using X-ray, Thyroid Stimulating Hormones (TSH), and Vitamin D

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Cite this paper as: Oinam Gokulchandra Singh, Ali Aldhebaib, Hosam Shujaa Alharthi, Thittamaranahalli Muguregowda Honnegowda, Abdullah Mones Alamri, Aljawharah Nawaf Alotaibi, Jayachandran Vetrayan, Smily Jesu Priya Victor Paulraj, Mohammed Ziyad Alturki, Turki Ayed Alharthi, Fayaz ul Haq, Winni Philip, (2025). Assessment of Bone Age in Pediatric Patient Using X-ray, Thyroid Stimulating Hormones (TSH), and Vitamin D. *Journal of Neonatal Surgery*, 14 (21s), 603-610.

ABSTRACT

Bone age (BA) assessment is crucial in evaluating skeletal development and diagnosing endocrine and growth disorders in pediatric patients. The Greulich-Pyle (GP) method remains widely used, though artificial intelligence (AI) advancements are enhancing accuracy. Vitamin D and thyroid-stimulating hormone (TSH) also play key roles in bone metabolism, yet their impact on BA remains unclear. This study investigates the bone age assessment using X-ray, Thyroid Stimulating Hormones (TSH), and Vitamin D among the pediatric patients visiting King Abdullah Specialist Children (KASCH), Riyadh, Saudi Arabia

Materials and Methods

A cross-sectional study was conducted at King Abdullah Specialized Children's Hospital (KASCH), Riyadh, Saudi Arabia, utilizing retrospective data from 100 pediatric patients aged between 1-16 years, covering the period from 2019 to 2020. BA was assessed using left-hand radiographs analyzed with the GP method. Vitamin D and TSH levels were measured using serum 25-hydroxy vitamin D [25(OH) D] and electrochemiluminescence immunoassay (ECLIA) test. Pearson and Spearman correlation analyses determined associations between BA, chronological age, vitamin D, and TSH levels.

Results

A strong positive correlation was observed between chronological age and BA ($r = 0.858$, $p = 0.001$), validating the reliability of the GP method. Vitamin D levels exhibited a weak negative correlation with age ($r = -0.261$, $p = 0.031$) and BA ($r = -0.226$, $p = 0.064$), while TSH showed no significant association with either ($p > 0.05$). Most patients (57.4%) had insufficient vitamin D levels, whereas 94% had normal TSH levels.

Conclusion

Chronological age and BA strongly correlate, confirming the GP method's applicability. However, vitamin D and TSH showed limited influence on skeletal maturation, highlighting the need for further research to determine their precise roles in bone development.

Keyword: *Bone age assessment (BA), Greulich-pyle (GP) method, Pediatric skeletal maturation, Radiological age, Thyroid-stimulating hormone (TSH), Vitamin D.*

1. INTRODUCTION

Bone age (BA) signifies an individual's skeletal and biological development. There is a total difference between BA and standard chronological age estimation, which is measured using the date of birth of an individual, which pediatricians and endocrinologists often demand to match with chronological age for diagnosing diseases. Serial estimations are also used to evaluate the effectiveness of medications for these diseases [1]. Hand and wrist radiographs are the most common way to demonstrate bone age in a posterior-anterior (PA) view of the hand and wrist is excellent for obtaining the length of the bone. Also, it can indicate bone-growing results specifically for each age [2]. BA could also be essential because of its practicability in diagnosing genetic diseases and maturity disorders [3]. Several methods, such as Greulich-Pyle (GP), estimate bone age. It is one of the earliest and most used techniques of bone age estimation, and it uses an atlas as a standard for comparing radiographic images of the left hand and wrist [4].

On the other hand, biochemical markers and hormonal factors, such as age-specific reference ranges for thyroid hormones, examine peripheral thyroid metabolism in short children born small for gestational age (SGA), both before and during growth hormone (GH) treatment [5]. Traditionally, bone age has been evaluated using Greulich & Pyle (GP) Atlas and Tanner-Whitehouse (TW) methods, which rely on manually interpreting left-hand radiographs. However, AI-driven approaches now automate and optimize this process. However, it is also essential to acknowledge that AI-based radiographic analyses are not inherently infallible, as their accuracy relies on the quality of the training data and the efficiency of the model's selection and training processes. Therefore, expert evaluation remains crucial in the final assessment [6]. Deep learning models, particularly convolutional neural networks (CNNs), have been employed to analyze radiographs and estimate bone age. These models can extract relevant features from images, reducing the need for manual intervention [7]. The manual assessment of BA using G&P and TW3 is subject to observer variability, as accuracy depends on the assessor's experience and expertise. Automated systems such as BoneXpert have been introduced to minimize this subjectivity, providing a standardized and reproducible alternative for BA determination. While BoneXpert has been validated for use in various populations, its accuracy and applicability to Saudi Arabian children remain unexplored [8]. Additional morphological dental and skeletal methods may also be utilized based on individual case circumstances [9]. However, these standards were developed using data from Western populations, raising concerns about their applicability to children of different ethnic backgrounds, including Koreans; due to this, the Korean Standard Bone Age Chart (KS) was introduced in 1999, based on a large cohort of Korean children, and has since been widely used in clinical practice [10]. Significant differences in bone development across various ethnic groups. It will raise concerns about the applicability of the GP atlas to non-Western populations, including Indian children [11]. While the impact of congenital hypothyroidism on bone development is well-documented, the effects of juvenile hypothyroidism-where thyroid hormone deficiency occurs after birth but during the growth phase-remain less clearly defined. Existing literature on this subject is primarily limited to case reports, and the extent of skeletal recovery following thyroid hormone replacement therapy is not well understood [12]. Advancements in research have also uncovered the genetic basis of thyroid hormone-related skeletal disorders, including mutations in thyroid hormone receptors that lead to resistance to thyroid hormone (RTH). Understanding these genetic disorders provides insights into the broader implications of thyroid hormone signaling on bone metabolism [13]. The prevalence of vitamin D deficiency varies across populations due to differences in geographic location, lifestyle, and dietary habits. In South Korea, concerns regarding vitamin D insufficiency in children have grown, prompting further research into its prevalence and associated risk factors [14]. Despite its importance, vitamin D deficiency has become a global health concern, affecting individuals of all ages due to limited sun exposure, dietary insufficiencies, and lifestyle changes [15].To investigate the association between bone age, vitamin D levels, and thyroid-stimulating hormone (TSH) levels in pediatric patients, evaluating their collective impact on skeletal maturation.

2. MATERIALS AND METHODS

Study Design and Setting

We reviewed a cross-sectional study of bone age estimation from the King Abdullah Specialist Children's Hospital (KASCH), National Guard Health Affairs, Riyadh, Saudi Arabia. Using a sample of N=100, the data was retrospectively extracted from the BESTCare system at the X-ray Unit, Medical Imaging Department, covering the period from 2019 to 2020. The study aims to assess bone age using X-ray imaging of the left hand and wrist and evaluate its correlation with thyroid-stimulating hormone (TSH) and vitamin D levels.

Inclusion Criteria

Children and adolescents aged from 1 to 16 years.

Individuals undergoing routine bone age assessment

Exclusion Criteria

Patients with prior wrist or hand trauma.

Individuals with congenital anomalies affecting the hand or wrist

Data Collection

Bone ages were determined using an X-ray of the left hand and wrist following the Greulich and Pyle (G&P) atlas method. An experienced radiologist analyzed radiological images to compare skeletal maturity with standard reference images. Vitamin D Levels and thyroid Stimulating Hormone (TSH) measurements were done using serum 25-hydroxy vitamin D [25(OH) D] and Electrochemiluminescence immunoassay (ECLIA).

Ethical Considerations

The study obtained approval from the King Abdullah International Medical Research Centre (KAIMRC),

Riyadh, Saudi Arabia, Institutional Review Board (IRB)/Ethics Committee by ethical guidelines.

Statistical Analysis

Data was analyzed using IBM SPSS Statistics for Windows, Version 29 (Released 2023; IBM Corp., Armonk, New York, United States). Using a frequency table, Pearson correlation was used to determine the relationship between age and radiological age, while Spearman's rank correlation was applied to the other variables. Statistical significance was considered at the 5% level. The data for this study was obtained through random sampling from the workstation of designated diagnostic rooms in the X-ray section of the KASCH, Saudi Arabia. The BEST Care system and a data collection sheet were used to review reports and analyze the findings from the sample.

3. RESULTS

Table 1 presents the demographic and clinical characteristics of the study population. A total of 100 patients (57 males [57%] and 43 females [43%]) aged 1 to 16 years were included in this study. It includes gender distribution, with 57% males and 43% females. The mean chronological age and radiological age are both 10 ± 3 years. Most individuals in the sample are between 7 to 13 years old. The number of patients who did the Vitamin D and Thyroid Stimulating Hormone (TSH) tests are 32 (32%) and 92(92%), respectively.

Table 1: Demographic Details of study subjects

Variable	Number (Percentage)
Gender Males Females	 57(57) 43(43)
Actual age in years, Mean ± SD	10 ± 3
Radiological age in years, Mean ± SD	10 ± 3
Vitamin D	40(33, 52.3) [IQR]
Thyroid Stimulating Hormone (TSH)	1.82(1.39, 2.67) [IQR]

Table 2 presents the correlation analysis between age, radiological age, vitamin D (Vit D), and thyroid stimulating hormone (TSH). The relationship between age in years and radiological age shows a strong positive correlation ($r = 0.858$, $p = 0.001$), which is statistically significant. Also, there is a weak negative correlation with vitamin D levels ($r = -0.261$, $p = 0.031$), indicating a significant inverse relationship. However, no significant correlation is observed between age and TSH ($r = -0.055$, $p = 0.606$). Similarly, radiological age shows a weak negative correlation with vitamin D ($r = -0.226$, $p = 0.064$). Moreover, a weak positive correlation with TSH ($r = 0.046$, $p = 0.667$) is not statistically significant. Furthermore, vitamin D and TSH exhibit a weak positive correlation ($r = 0.096$, $p = 0.445$), which is also insignificant. A Pearson correlation was used for the relationship between age and radiological age, while Spearman's rank correlation was applied to the other variables. Statistical significance was considered at the 5% level.

Table 2: Correlation analysis between variables

Variable	Radiological age	Vit D	TSH
Age in years	r= 0.858 p= 0.001*	r= -0.261 p= 0.031*	r= -0.055 p= 0.606
Radiological Age	-	r= -0.226 p= 0.064	r= 0.046 p= 0.667
Vit D	-	-	r= 0.096 p= 0.445

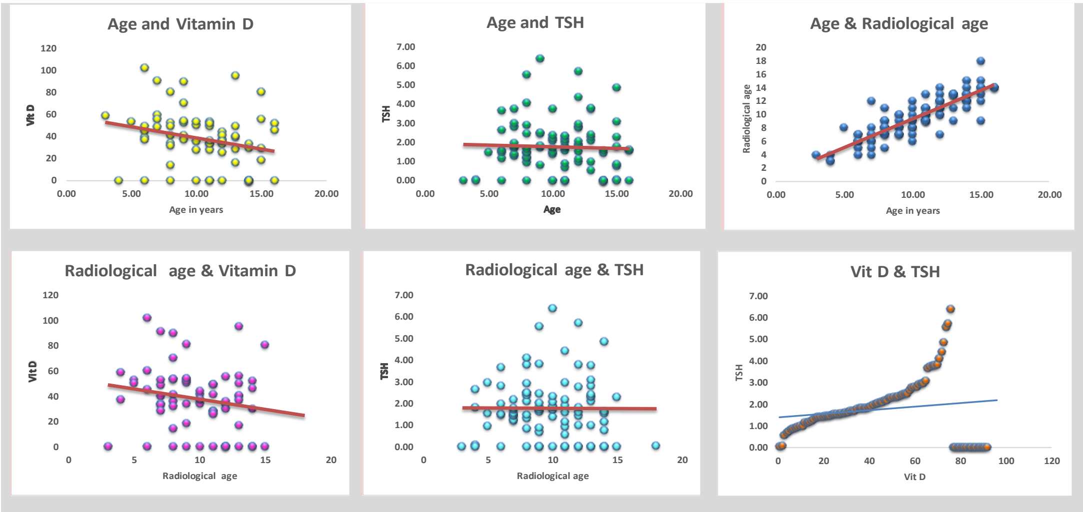
Statistically Significant at 5%

Age in years & Radiological age: Pearson Correlation others: Spearmann Rank Correlation

r is the Correlation Coefficient

The provided set in Figure 1 visualizes correlations between age, radiological age, vitamin D (Vit D), and thyroid-stimulating hormone (TSH). The trend lines in each graph indicate the direction and strength of relationships.

Figure 1: Scatter plot for various correlations



Age and Vitamin D

A negative correlation is evident, as indicated by the downward-sloping trend line. The correlation coefficient from Table 1 is r = -0.261, p = 0.031, suggesting a weak but statistically significant inverse relationship. As age increases, vitamin D levels tend to decrease. This could indicate that older children in the study have lower vitamin D levels, possibly due to dietary factors, reduced sun exposure, or metabolic changes.

Age and TSH

The points appear widely dispersed with no clear trend, and the trend line is almost flat. The correlation coefficient is r = -0.055, p = 0.606, indicating no significant relationship. There is no meaningful association between chronological age and TSH levels, suggesting that thyroid function as measured by TSH remains relatively stable across different ages.

Chronological Age and Radiological Age

A strong positive correlation is visible, as the data points closely follow an upward-sloping trend line. The correlation coefficient is r = 0.858, p = 0.001, indicating a powerful and statistically significant relationship. Radiological age closely aligns with chronological age, meaning bone development progresses with age in this population.

Radiological Age and Vitamin D

A weak negative correlation is observed, with a slightly downward-sloping trend line. The correlation coefficient is r = -0.226, p = 0.064, which is not statistically significant. While there is a slight tendency for individuals with higher radiological age to have lower vitamin D levels, this relationship is not strong enough to be considered meaningful in this dataset.

Radiological Age and TSH

Data points appear scattered, with no strong pattern. The correlation coefficient is r = 0.046, p = 0.667, indicating no significant relationship. There is no notable association between radiological age and TSH, implying that thyroid hormone levels do not strongly influence bone development in this group.

Vitamin D and TSH

The scatter plot shows a non-linear relationship, with a cluster of low TSH values at lower vitamin D Levels and an upward trend at higher vitamin D levels. The correlation coefficient is r = 0.096, p = 0.445, suggesting a weak and non-significant correlation. While the trend suggests a potential relationship at higher vitamin D levels, the overall correlation is weak and not statistically significant, implying that vitamin D levels do not strongly impact TSH levels in this population.

Figure 2 represents the distribution of TSH (Thyroid-Stimulating Hormone) levels among subjects, categorized into normal, borderline, and high ranges. Most subjects (94%) fall within the normal TSH range, indicating overall thyroid function stability in most cases. A small percentage (4.4%) have borderline TSH levels, while 1.1% have high TSH levels, suggesting possible hypothyroidism. It highlights that thyroid dysfunction is present in a minority of subjects.

Figure 2: Classification of TSH (Thyroid-Stimulating Hormone) levels

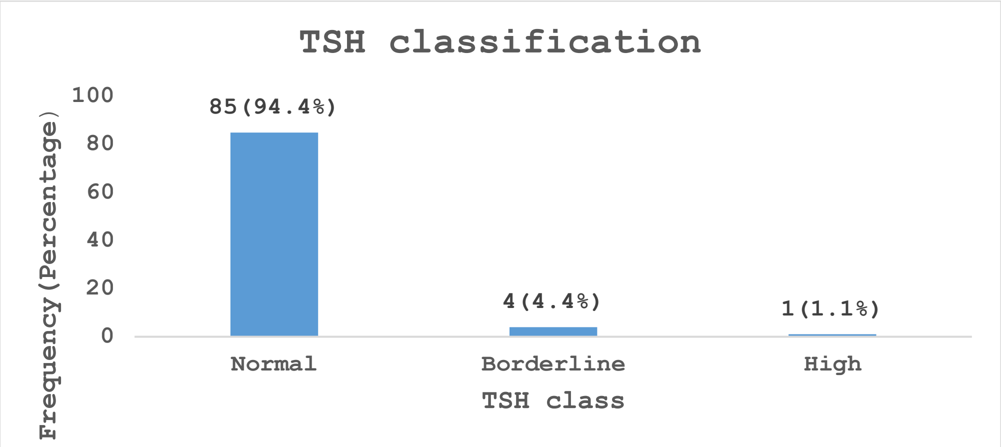


Figure 3 illustrates the classification of Vitamin D levels among subjects, categorized into deficiency, insufficient, adequate, and optimum. Most individuals (57.4%) fall into the insufficient range, indicating that more than half of the subjects fall under this category, which may require intervention. While 22.1% of the subjects have adequate Vitamin D levels, 11.8% are classified as deficient, potentially putting them at risk for health issues related to Vitamin D deficiency, such as bone disorders or weakened immunity. However, only 8.8% of the subjects achieved an optimum level of Vitamin D. The data suggests a prevalent issue of inadequate Vitamin D levels, highlighting the need for monitoring and possible supplementation in a significant portion of the population.

Figure 3: Classification of Vitamin D level for study subjects

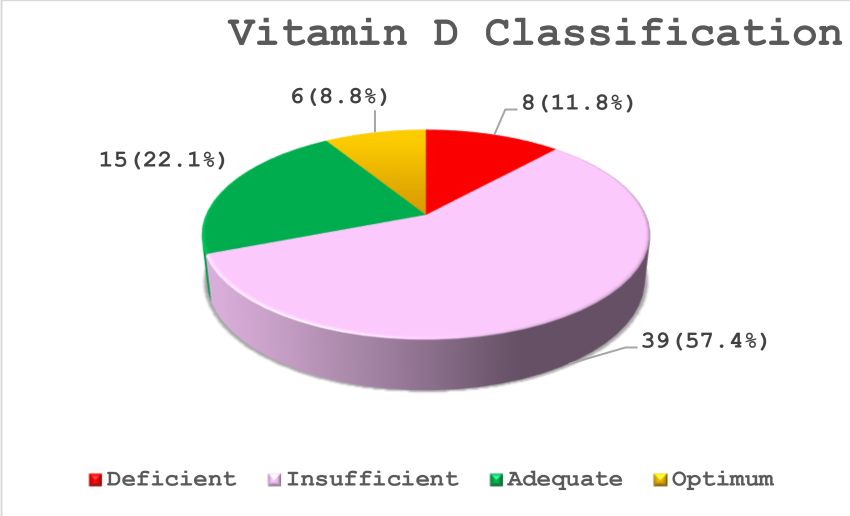
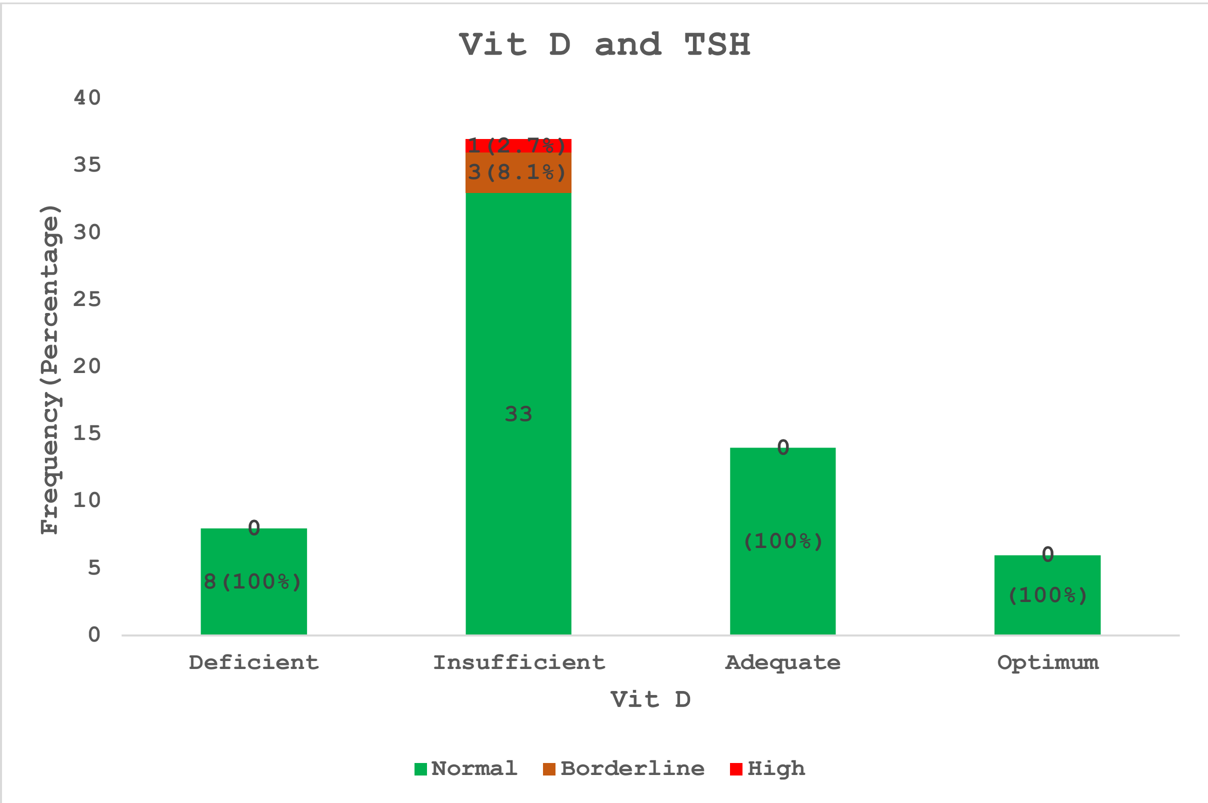


Figure 4 illustrates the distribution of thyroid-stimulating hormone (TSH) levels across different vitamins. D (Vit D) categories (Deficient, Insufficient, Adequate, and Optimum) among study subjects. The frequency is represented as a percentage on the y-axis, while the x-axis categorizes vitamin D levels. The bars are color-coded to indicate different TSH levels. In the Deficient Vitamin D Group, all subjects (100%) in this category have normal TSH levels. No cases of borderline or high TSH are observed. While Insufficient In the vitamin D Group, the majority (33 individuals) have normal TSH levels. A small proportion (3 individuals, 8.1%) exhibit borderline TSH levels. A tiny percentage (1 individual, 2.7%) shows high TSH levels. Similarly, in Adequate and Optimum Vitamin D Groups, all individuals (100%) in both categories have normal TSH levels, with no cases of borderline or high TSH.

Fig 4: Relation between Vit D and TSH for study subjects



4. DISCUSSION

Worldwide studies have reached almost the same results regarding the difference between actual and radiological ages. The results of this study also highlight the importance of bone age assessment in clinical and forensic contexts. In pediatric endocrinology, determining radiological age is crucial for diagnosing growth disorders, monitoring delayed or advanced skeletal maturation, and assessing the effects of hormonal treatments [1]. Additionally, artificial intelligence-based approaches have been explored to enhance traditional bone age assessment methods, showing comparable or improved accuracy over manual GP evaluations [7]. The present study found a strong positive correlation between actual age (AA) and radiological age (RA) using the Greulich-Pyle (GP) method, with Pearson's correlation coefficient $r = 0.858$ ($p = 0.001$), indicating a statistically significant association. It suggests that the GP method effectively aligns radiological age with chronological age, supporting its validity in assessing bone development in pediatric populations. Similar findings have been reported in prior studies, demonstrating the applicability of the GP method in different ethnic and regional populations. For instance, one of the studies evaluated the accuracy of the GP method in Saudi Arabian children and confirmed its reliability for bone age assessment [8]. These findings reinforce the reliability of radiological assessments in tracking skeletal maturity and highlight the continued relevance of the GP method in clinical practice." Additionally, forensic investigations often rely on bone age estimation to verify age in legal cases, particularly for unaccompanied minors and individuals without verifiable identification [9]. Given these critical applications, accurate bone age assessment using wrist and hand X-rays remains essential in medical and legal fields. The GP method remains one of the most widely used approaches in pediatric radiology due to its ability to estimate bone age through standardized atlas comparisons, offering a non-invasive and practical method for evaluating skeletal maturity (10]. Furthermore, studies have demonstrated that while the GP method is generally accurate, there may be variations in its applicability based on ethnic and regional differences. For example, research assessing the use of the GP atlas in Indian and Pakistani children has indicated that the method may sometimes overestimate or underestimate bone age compared to local population standards [11]. The increasing role of AI in radiological assessments suggests that future applications could further refine bone age determination, making the process more standardized and less dependent on manual interpretation. The correlation analysis in this study revealed a weak negative association between radiological age and vitamin D levels ($r = -0.226$, $p = 0.064$) and no significant correlation between radiological age and TSH ($r = 0.046$, $p = 0.667$). These findings align with previous research indicating that while vitamin D plays a role in skeletal maturity, its direct impact on bone age assessment remains limited [16]. Similarly, as measured by TSH levels, thyroid function has been shown to influence bone health without a strong direct correlation to radiological age [13]. One of the studies found that children exhibited significant delays in skeletal maturation; their bone health, as assessed by BHI, was not substantially impaired. The delay in BA was associated with total calorie intake but not with bolus vitamin D supplementation [17]. Overall, the findings of this study reinforce the strong correlation between chronological age and radiological age, supporting the continued use of the GP method for bone age assessment. While newer approaches, such as AI-based models, are emerging, traditional methods remain a cornerstone of skeletal maturity evaluation. Future research should further explore how ethnicity, nutritional status, and hormonal influences affect bone age estimation to enhance the precision and applicability of current assessment techniques. In this study, overall outcomes showed that actual age and radiological ages were closely linked. There is no statistical significance except in a few samples for TSH and Vitamin D. Biochemical markers and hormonal tests evaluate factors that impact growth and skeletal maturation. While they do not directly determine bone age, they offer valuable insights into the biological processes influencing bone development. However, there is an indirect correlation between bone age and these biochemical markers or hormonal tests. The strength of this study aligns with previous international research, reinforcing its credibility and allowing comparisons across different populations. The study examines relationships between radiological age, chronological age, vitamin D levels, and thyroid function (TSH), providing a comprehensive analysis. On the other hand, the limitation of this study was missing values for both TSH and vitamin D tests, leading to inconsistencies in the findings. Limited Vitamin D and TSH Impact, lack of additional biomarkers. This study does not track changes in skeletal maturation over time, which would provide deeper insights into bone development patterns. Only a few studies have explored the relationship between bone age, vitamin D, and TSH levels. Further research is needed to provide empirical evidence.

5. CONCLUSION

These findings indicate that although bone age and chronological age are closely related, further research is needed to understand how bone formation and resorption markers, vitamin D, TSH, and other hormonal tests impact growth and development

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