

## Determination of bone age and its correlation to the chronological age based on the Greulich and Pyle method in Saudi Arabia

### Abstract

**Introduction:** Many clinical indications need the measurement of bone age, including growth and development abnormalities, the timing of corrective procedures in pediatric patients, and the assessment and treatment of specific endocrine conditions. These evaluations are also useful in forensic science. This study aims to compare the bone age of children aged 4 to 18 years old with their chronological age in order to determine whether the Greulich-Pyle (GP) method is trustworthy for Saudi youngsters. **Materials & Methods:** Multiple approaches for determining bone age have been published, but Greulich and Pyle's methodology is the most extensively utilized. This method is based on an inspectional evaluation that compares the radiograph to the pattern described in a 1950 atlas using a sample of North American children aged birth to 18 years for the female sex and up to 19 years for the male sex. It is one of the most commonly utilized procedures for assessing the skeletal age of children and adolescents since it is rapid and quick to perform. It is based on the fact that ossification centers in the hand and wrist bones emerge in a predetermined order. For male and female youngsters, the degree of ossification in various hand and wrist bones is compared to the nearest matching plate on the Greulich & Pyle Atlas.

**Results:** Total 216 patients were included or selected in this study among age group 4-18 years, the sex distribution among them were 148 (68.5%) and 68 (31.5%) were male and female respectively. Chronological age and bone age assessment by GP method among doctors when chronological age was  $135.2 \pm 45.0$  (range, 45-216 months). Chronological age in male and female were  $143.5 \pm 44.0$  and  $116.9 \pm 41.8$  respectively with p value  $<0.001$  which was statistically significant. The bone age were observed in two reading, first reading and second reading after 15 days by two doctors separately and all the finding were recorded almost similar and significant with p value  $<0.001$ . Correlation between Chronological age and Bone age by GP method in both sex observed significant p value  $<0.001$ . Linear regression analysis showed that the bone age and its correlation to the chronological age assessment in first reading in male ( $r=0.761$  and  $p<0.001$ ) and female ( $r=0.889$  and  $p<0.001$ ), in reading after 15 days in male ( $r=0.760$  and  $p<0.001$ ) and female ( $r=0.868$  and  $p<0.001$ )

**Conclusion:** This study indicated that the bone age of children aged 4 to 18 years old should be compared to their chronological age in order to determine whether the Greulich-Pyle (GP) method is reliable for Saudi youngsters.

**Key words:** Bone age, Chronological age, Greulich-Pyle, Correlation,

### Introduction:

Bone age is a common index used in pediatric radiology and endocrinology departments across the world to define bone maturity for medical and non-medical purposes, as well as in forensic medicine for identifying deceased victims and in connection with crimes and accidents.<sup>1-3</sup>

One of the most important factors in identification is age determination. Bone age, as opposed to chronological age, is a good indication for physiological development, detecting

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**Comment [WU2]:** It should be written as per the authors instruction format of journal. No setting, time duration, study type etc are mentioned whether in abstract or in Methodology section

**Comment [WU3]:** Please rephrase. Comparison is not suitable word because this is not comparative study. This is descriptive cross sectional study.

various disorders, and deciding the time of treatment.<sup>4</sup> As ways for establishing a patient's age, Stewart RE and Barber TK list chronological age, biological age, morphologic age, skeletal age, dental age, circumpubertal age, behavioral age, mental age, secondary sexual characteristics, peak height velocity, skeletal maturation, and self-concept age.<sup>5-8</sup> Because of the wide variation in the timing and duration of the pubertal growth spurt and other developmental stages, chronological age is the most obvious and easily determined developmental age, which is simply figured from the child's date of birth. However, chronological age is unreliable for assessing developmental status.<sup>5,9,10</sup>

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The ossification phases of the hand and wrist bones can be used to track bone maturity. This region has a number of ossification centers that work in tandem with the rest of the human body.<sup>11-15</sup> Among the several approaches presented for determining skeletal age using carpal radiographs, the Greulich and Pyle method stands out. Because it is quick and simple to do, it is one of the most often used procedures for estimating the skeletal age of children and adolescents.<sup>15-19</sup> Many studies have evaluated the applicability of the Greulich and Pyle method, and these have been conducted in Central Europe<sup>20</sup>, Italy<sup>21</sup>, USA<sup>22,23</sup>, Turke<sup>24-26</sup>, Denmark<sup>27</sup>, Taiwan<sup>28</sup>, Holland<sup>17</sup>, Pakistan<sup>29</sup> and in Brazil.<sup>11,12</sup>

Gender, dietary, metabolic, genetic, and socioeconomic variables, as well as acute or chronic disorders, including endocrine dysfunction, can all influence bone age.<sup>30</sup> This study aims to compare the bone age of children aged 4 to 18 years old with their chronological age in order to determine whether the Greulich-Pyle (GP) method is trustworthy for Saudi youngsters.

#### **Material and methods:**

A total of 216 participants were targeted. Consent forms were signed by parents and approval was granted by the Ministry of Health in Saudi Arabia, Central IRB log:21-32E. The participants were chosen randomly from the orthopedic clinic during follow-up for any complaint at Majmaah Hospital based on inclusion and exclusion criteria. Subsequently, all participants have undergone radiography of the left wrist and hand (Figure 1).

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Figure 1: Example of left-hand X-ray, PA view

#### Data collection procedure

At the hospital, their height and weight were noted. Two Radiologists, each with more than five years of experience, independently reviewed images. The observers were not aware of the participants' chronological ages. Each evaluator assessed the identical image twice, with at least a 15-day interval between evaluations. To minimize visual fatigue, a maximum of ten images were reviewed every day. Paired student's t-test was used to assess inter-observer reliability, whereas Pearson Correlation was applied to see the relationship between chronological ages and bone ages calculated by Greulich & Pyle Atlas. Greulich–Pyle identified two standard templates: 31 and 27 radiographic pictures in male and female people, respectively, illustrating distinct stages of bone development between the ages of 0 and 18 or 19 years. Thus, gender-specific scans were compared to those produced by patients by first assessing the closest chronological age and then the surrounding standards. As a result, the standard that seemed comparable was initially selected, and then the inspection of each bone segment in an ordered sequence was conducted by assigning the matching bone age to the individual segments, as instructed in the atlas of GP t. It is important to focus on in order to adequately describe bone maturation, an in-depth bone-by-bone investigation is recommended instead of a simple comparison. The date of birth of the participants was obtained from family cards or medical records. The optional documents were chosen by inclusion and exclusion criteria.

#### Inclusion Criteria:

Healthy children with an age limit of 4 – 18 years of the age -of both genders

**Exclusion Criteria:** One or more of the following:

History of systemic diseases for more than one month

Height above 95th percentile for age height below 5th percentile for age

History of chronic systemic diseases or syndromes

History of steroid use

History of left upper limb trauma

History of hospitalization for more than a week

#### Statistical analysis

**Comment [WU6]:** Please mention for the software for data analysis and this should be written after data collection procedure under the heading of **Statistical analysis**. Write for the descriptive statistics like frequency percentage and mean as well

**Comment [WU7]:** Please rephrase

**Sample Size:** The sample size was calculated using the following formula [1] by placing the correlation value of 0.30. The minimum required sample size came out ~~was~~ 158. A p-value of < 0.05 was considered statistically significant.

$$N = \frac{(Z_{1-\alpha/2} + Z_{1-\beta})^2}{\frac{1}{4} \left[ \log_e \left( \frac{1+r}{1-r} \right) \right]^2} + 3$$

Fig. 1: Sample size calculation formula

Where;

The standard normal deviate for  $\alpha = Z_{\alpha} = 2.5758$

The standard normal deviate for  $\beta = Z_{\beta} = 1.2816$

### Results:

A total of 216 patients were included in this study among the age group 4-18 years, the sex distribution among them were 148 (68.5%), and 68 (31.5%) ~~were~~ male and female, respectively shown in table 1. Chronological age and bone age assessment by GP method among doctors when chronological age was  $135.2 \pm 45.0$  (range, 45-216 months). The bone age was similar to those of both doctors in the first reading as well as reading after 15 days shown in table 2. Chronological age in males and females were  $143.5 \pm 44.0$  and  $116.9 \pm 41.8$  respectively, with p-value <0.001, which was statistically significant.

The chronological age was recorded in males (143.5 Months, SD 44.0) and in females (116.9 Months, SD 41.8) with a t-value of 4.195 and p-value <0.001 shown in table 3. In table 3, also the bone age was observed in two readings, first reading, and second reading after 15 days in both sexes (male and female), separately by two doctors separately, and all the findings were recorded almost similar and significant with a p-value <0.001 shown in table 3.

In table 4, Intraclass correlation and reliability analysis of bone age assessment by the two doctors, in the first reading we observed that Intraclass correlation 1.000, 95% Confidence Interval both LB and UB 1.000 with Cronbach's Alpha 1.000 whereas in reading after 15 days Intraclass correlation 0.995, 95% Confidence Interval both LB 0.993 and UB 0.996 with Cronbach's Alpha 0.995.

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Correlation between Chronological age and Bone age by GP method in male first reading and reading after 15 days we recorded Pearson Correlation 0.873 and 0.872 respectively with p-value <0.001 whereas in female first reading and reading after 15 days we recorded Pearson Correlation 0.943 and 0.93 respectively with p-value <0.001 (see table 5).

In figure 2, a positive correlation was observed to exist between bone age and chronological age. It also shows the scatter plot of chronological age against bone age in the male first reading with a line of best fit indicated ( $r=0.761$ ). Whereas Significant Linear regression analysis showed that the bone age and its correlation to the chronological age assessment in the first reading in females ( $r=0.889$ ) shown in figure 3. In figure 4, the scatter plot of bone age against chronological age reading after 15 days with line best fit in male( $r=0.760$ ) and in figure 5 female( $r=0.868$ ).

Table 6 shows the Regression equation for estimation of Chronological age in males by GP method; we recorded in both first reading and reading after 15 days R Square 0.761 and 0.760 respectively with p-value <0.001. In table 7, Regression equation for estimation of Chronological age in females by GP method, we recorded in both first reading and reading after 15 days R Square 0.889 and 0.868 respectively with p-value <0.001

**Table 1: Sex distribution**

Sex	Frequency	Percent
Male	148	68.5
Female	68	31.5
Total	216	100.0

**Table 2: Statistics of Chronological age and bone age assessment by GP method**

Age (months)	N	Mean	Median	Std. Deviation	Min	Max	
Chronological age by months	216	135.2	135.5	45.0	45	216	
Bone age (First Reading)	Doctor 1	216	138.9	150.0	52.9	24	218
	Doctor 2	216	139.0	150.0	53.0	24	216
Bone age (Reading after 15 days)	Doctor 1	216	139.4	150.0	53.2	24	240
	Doctor 2	216	138.6	150.0	52.9	24	218

**Table 3: Comparison of age between sexes**

Age (in months)	Sex	N	Mean	Std. Deviation	t-value	P-value
Chronological age	Male	148	143.5	44.0	4.195	<0.001
	Female	68	116.9	41.8		
Bone age (Doctor 1-1st Reading)	Male	148	147.6	51.4	3.670	<0.001
	Female	68	119.9	51.6		
Bone age (Doctor 2-1st Reading)	Male	148	147.8	51.4	3.692	<0.001
	Female	68	120.0	51.6		
Bone age (Doctor 1-Reading after 15 days)	Male	148	148.1	51.8	3.642	<0.001
	Female	68	120.5	51.8		
Bone age (Doctor 2-Reading after 15 days)	Male	148	147.8	51.4	3.895	<0.001
	Female	68	118.5	51.0		

**Table 4: Intraclass correlation and reliability analysis of bone age assessment by the two doctors**

	Intraclass Correlation	95% Confidence Interval		Cronbach's Alpha
		LB	U B	
<b>1st Reading</b>	1.000	1.000	1.000	1.000
<b>Reading after 15 days</b>	0.995	0.993	0.996	0.995

**Table 5: Correlation between Chronological age and Bone age by GP method.**

Bone Age	Male		Female	
	Pearson Correlation	P-value	Pearson Correlation	P-value
<b>1st Reading</b>	0.873	<0.001	0.943	<0.001
<b>Reading after 15 days</b>	0.872	<0.001	0.931	<0.001

**Figure 2: Scatter plot for Correlation between Chronological age and Bone age by GP method [1<sup>st</sup> Reading-Male]**

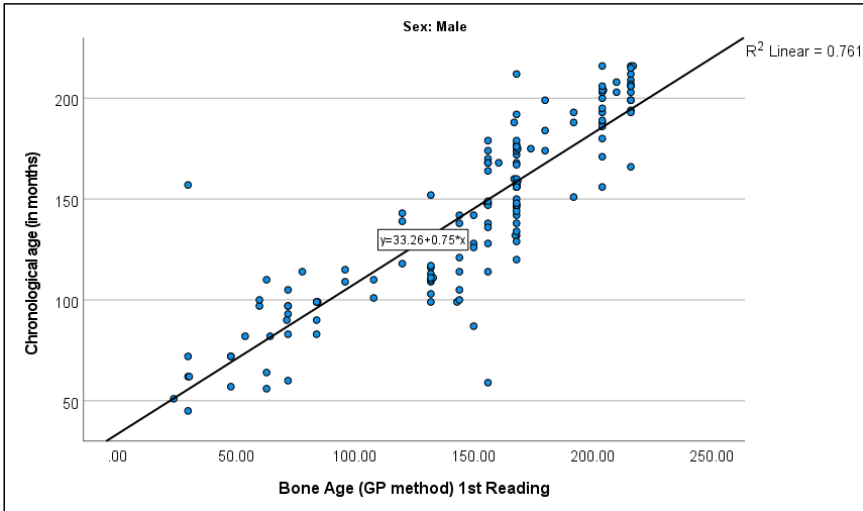


Figure 3: Scatter plot for Correlation between Chronological age and Bone age by GP method [1<sup>st</sup> Reading-Female]



Figure 4: Scatter plot for Correlation between Chronological age and Bone age by GP method [Reading after 15 days-Male]

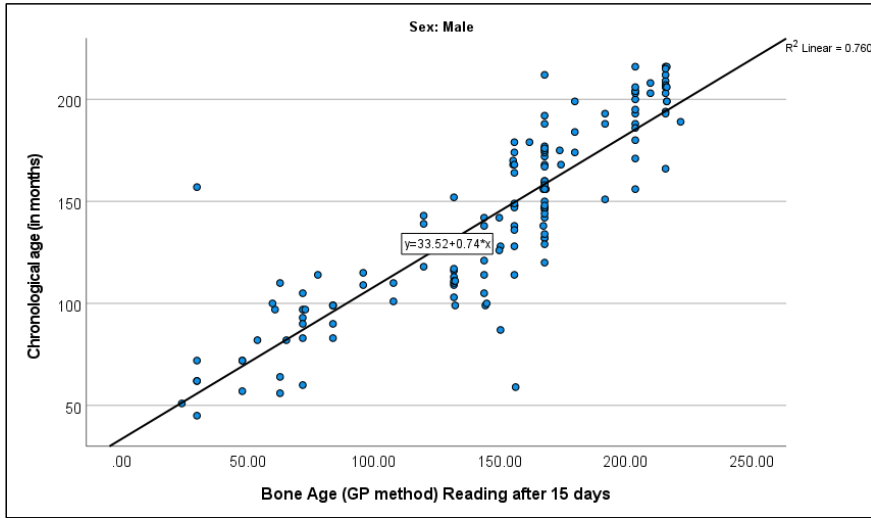


Figure 5: Scatter plot for Correlation between Chronological age and Bone age by GP method [Reading after 15 days-Female]

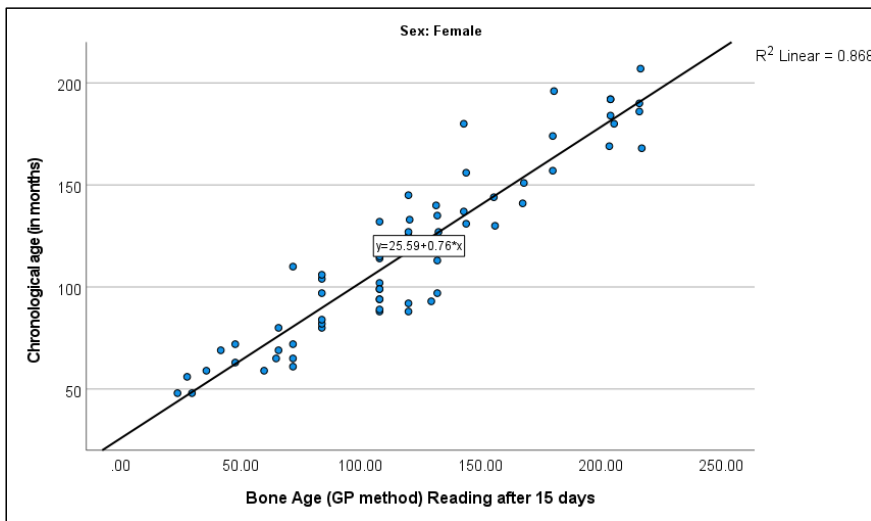


Table 6: Regression equation for estimation of Chronological age by GP method (Male)

Model	Beta	95% C. I for Beta Coefficient		P-value	R Square
		LB	UB		

Model 1	(Constant)	33.26	22.57	43.94	<0.001	0.761
	Bone Age (1st Reading)	0.75	0.68	0.82	<0.001	
Model 2	(Constant)	33.52	22.82	44.21	<0.001	0.760
	Bone Age (Reading after 15 days)	0.74	0.68	0.81	<0.001	

**Table 7: Regression equation for estimation of Chronological age by GP method (Female)**

Model	Beta Coefficient	95% C.I for Beta Coefficient		P-value	R Square	
		LB	UB			
Model 1	(Constant)	25.19	16.53	33.84	<0.001	0.889
	Bone Age (1st Reading)	0.76	0.70	0.83	<0.001	
Model 2	(Constant)	25.59	16.06	35.11	<0.001	0.868
	Bone Age (Reading after 15 days)	0.76	0.69	0.84	<0.001	

### Discussion:

In pediatric endocrinology, orthopedics, forensics, and anthropology, assessing bone age and its link to chronological age is critical for determining whether or not children are growing normally.<sup>31</sup> The goal of this study is to investigate whether the Greulich-Pyle (GP) method is accurate for Saudi children by comparing bone age to chronological age in children aged 4 to 18.

The degree of skeletal growth reflects a subject's level of physiologic maturity. In assessing an adolescent's physical development, bone age has been proven to be just as essential as CA. Furthermore, SA predicts how much additional growth a youngster will achieve.<sup>8</sup> The hand and wrist radiograph, according to Koshy and Tandon, is often utilized for skeletal developmental evaluation, particularly since it comprises many ossification canthers in small regions.<sup>32</sup>

Previous research evaluating bone age assessment employed GP reference criteria derived from clinical records, interpretations from independent reviewers, or both.<sup>33-35</sup> Our study have

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some similarities but different from the ~~previous~~ ~~prior~~ studies in correlation to the chronological age due to paucity of data in this country.

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The current study's findings are consistent with those of prior research by Groell et al., Schmidt et al., and Buken et al.<sup>15,20,26</sup> Bone age was delayed in our study, and the differences were significant for both sexes. The methodology used in this study shown that the difference between bone age and chronological age was statistically significant for both male and female.

In theory, disparities between our results and G&P standards may be explained in part by ethnic differences. Ontell et al. analyzed bone age in children of various ethnicities (599 radiographs of White, Black, Asian, and Hispanic boys and girls) and found that utilizing G&P criteria to estimate bone age requires reservations. Patil et al. discovered that males had higher skeletal retardation than females.<sup>36,23</sup>

The R2 value of 0.88 for the female sex and 0.76 for the male in the current study suggested that the chronological age may predict 88 % and 76 % of the bone age, respectively. For both sexes, this study shows a strong link between bone age and chronological age. The discovered correlation indices were comparable to those observed by other researchers.<sup>11,12,17,24,37</sup>

In this study we observed that the bone age and its correlation to the chronological age were significant. Similar findings were also observed by Vallejo-Bolanos & Espana-Lopez Hegde RJ & Sood PB and Prabhakar et al..<sup>38-40</sup>

### Conclusion:

This study concluded that ~~Compare~~ the bone age with chronological age of children aged 4 - 18 years old in order to recognize whether Greulich-Pyle (GP) method could be reliable for Saudi children. The measurement of bone age is critical for several clinical purposes, including growth and development abnormalities, the timing of corrective operations on juvenile patients, and the assessment and treatment of specific endocrine diseases. These evaluations are also useful in forensic science. Although the reported difference is within the acceptable margins of error established by Greulich and Pyle due to its consistency, it would be smart to adopt new criteria that account for the developmental delay. ~~To define the~~

minimum adult age characterized by complete epiphyseal fusion, new criteria would be necessary.

Comment [WU12]: No need in conclusion

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