ORIGINAL ARTICLE

ESTIMATION OF SKELETAL AGE BY GREULICH-PYLE METHOD IN HEALTHY ADOLESCENTS

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ABSTRACT

OBJECTIVE: To assess the Greulich-Pyle method for the determination of skeletal age in healthy adolescents in Karachi using legal document as gold standard proof of the chronologic age. **DESIGN:** Cross-sectional study **METHODOLOGY:** After obtaining approval from the institutional ethics review committee, a convenience sample of healthy boys and girls was recruited from public schools in Karachi, Pakistan. Plain radiographs of wrist and hand were acquired for determination of bone age using Greulich-Pyle atlas. All plain films were interpreted by two experienced radiologists, who were blinded to the actual age of the subjects. Legal documents (that is birth certificate) was used as gold standard for the proof of the chronological age. **RESULTS:** Ninety-nine subjects (52 boys and 47 girls) were included in the study with a median age of 14.1 years. The median bone age estimated by Greulich-Pyle method for the whole sample was 15 years, which was not significantly different ($p>0.05$) from the median chronologic age. However, median bone age estimated for girls under the age of 13 years was significantly different from the median chronologic age ($p<0.01$). **CONCLUSION:** Our study revealed significant discrepancies between chronologic age and bone age in adolescents as estimated by the Greulich-Pyle method.
Keywords: Skeletal age; bone age; chronologic age; Greulich-Pyle method.

Introduction

One of the foremost methods of assessment of skeletal maturation is by the use of radiographic investigations.[1] Such determination of skeletal age has pertinent utility not only in medicolegal cases,[2] but also for making diagnostic and judicious therapeutic decisions in such diverse fields as endocrinology,[3] pediatrics[4] and orthodontics.[5] Numerous methods have been devised to predict accurately the chronologic age of an individual based on radiographic appearances.[6] Greulich-Pyle method is the most popular radiologic method used worldwide for the determination of skeletal age in young individuals.[7] As this method was based upon a sample of healthy white children of Northern America, its applicability to individuals of different ethnicities is questionable.[8] Inaccurate estimation of skeletal age, particular in the adolescent age group has significant implications for social, legal and medico legal purposes.[9] Some preliminary studies raised concerns regarding the use of this method in the Pakistani population.[10,11] However, these studies were based on a hospital-based sample, their applicability to the general population was limited. In this study, our aim was to assess the accuracy of the Greulich-Pyle method for determination of skeletal age in healthy adolescents.

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Materials and Methods

This cross-sectional study was performed after obtaining approval from the Ethics Review Committee (ERC) at a tertiary care hospital in Pakistan. A sample of healthy children was recruited from various schools in Karachi, Pakistan during a period from 1st Jan to 31st Dec 2018. A non-probability, convenience sampling strategy was used. Inclusion criteria for study subjects were healthy boys or girls between the ages of 13 to 18 years, who did not have any known endocrine or genetic diseases. All the children went under a medical check-up by a consultant pediatrician and the child s height and weight were also recorded. Exclusion criteria included absence of documentation of legal age and known medical disease (genetic syndrome, endocrine disorder or growth abnormalities) or history of upper extremity fracture. Informed consent and assent were obtained from the parents (or guardians) and child participating in the study. Funding was received from the University Research Council (URC) for the purpose of this study.

Data was obtained for study subjects through interviews and recorded on a predesigned structured questionnaire. Parents (or guardians) of study subjects were asked to produce legal documents (birth certificate or domicile) as proof of age. Plain radiographs for all subjects were performed in the Department of Radiology. X-ray of the left hand and wrist in postero-anterior projections were acquired using either Q-RAD 50 KW 630 mAs (Shimadzu Medical systems, Japan) or 630 mAs OTC 12S (DEL Medical Systems, United Systems). Standard exposure settings of 54 KVs and 3 mAs were used for all radiographs. Two pediatric radiologists with more than 10 years of experience interpreted plain radiographs and estimated bone age based on the Greulich-Pyle atlas. Data relating to actual (chronologic) age, gender, ethnicity, bone age, weight, height and participation in sports were recorded on the structured pro forma. Statistical Package for Social Sciences (SPSS) version 20.0 was used for statistical analysis. Frequencies were calculated for qualitative variables, while median (inter-quartile range [IQR]) were computed for quantitative variables. Non-parametric Wilcoxon signed ranks test was used for comparison of median bone age and median chronologic age. Pearson product-moment correlation was used to assess the linear correlation between two quantitative variables. Multivariate linear regression for all calculations, a *p*-value of less than 0.05 was considered statistically significant.

Results

A total of 99 children were included in the study with a median age of 14.1 (IQR: 12.3 15.8) years. Boys constituted 52.5% (*n*=52) of the sample and the most common ethnicity was Gujrati. The distribution of boys and girls among the various age groups is shown in (Fig.1). The median weight and height for study subjects were 48 (IQR: 39 59) kg and 157 (IQR: 150.5 165.5) cm respectively with a median BMI of

Characteristics	Frequency (%)
Sex	
Male	52 (52.5%)
Female	47 (47.5%)
Age (median [IQR])	14.1 (12.3–15.8) years
Ethnicity*	
Gujrati	53 (53.5%)
Urdu speaking	25 (25.3)
Memon	4 (4.0%)
Sindhi	2 (2.0%)
Punjabi	1 (1.0%)
Unknown	14 (14.1%)
Weight (median [IQR])	48 (IQR: 39–59) kg
Height (median [IQR])	157 (IQR: 150.5–165.5) cm
BMI	
Less than 18.5 kg/m^2	42 (42.4%)
18.5–22.9 kg/m^2	38 (38.4%)
23–29.9 kg/m^2	18 (18.2%)
30 kg/m^2 or higher	1 (1.0%)
Participation in sports	
Yes	94 (94.9%)
No	5 (5.1%)
History of fracture	
Yes	10 (10.1%)
No	89 (89.9%)

BMI = Body mass index; IQR = interquartile range
* Description of ethnicity was based solely on how subjects described themselves

Table 1: Characteristics of subjects included in our study (*n*=99)

19.2 (IQR: 16.5 22.1) kg/m^2. The weight-for-age and height-for-age for our study sample arerepresented in (Fig.2). Descriptive statistics for our entire study sample are summarized in (Tab.1).

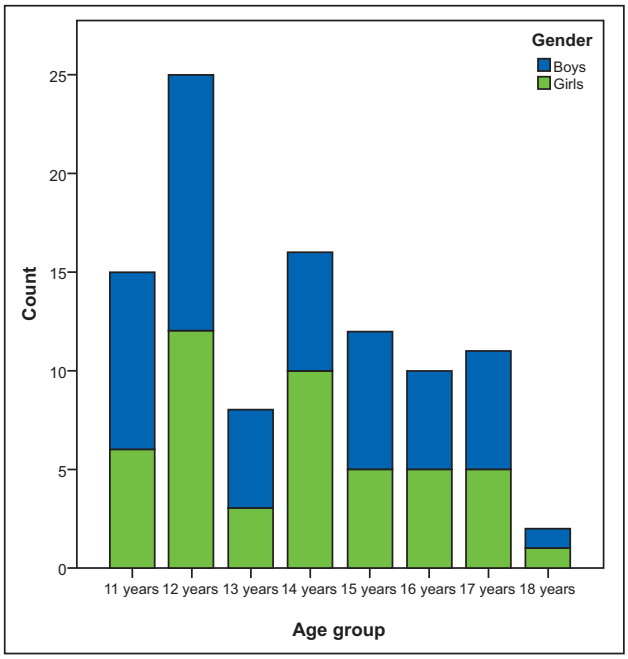
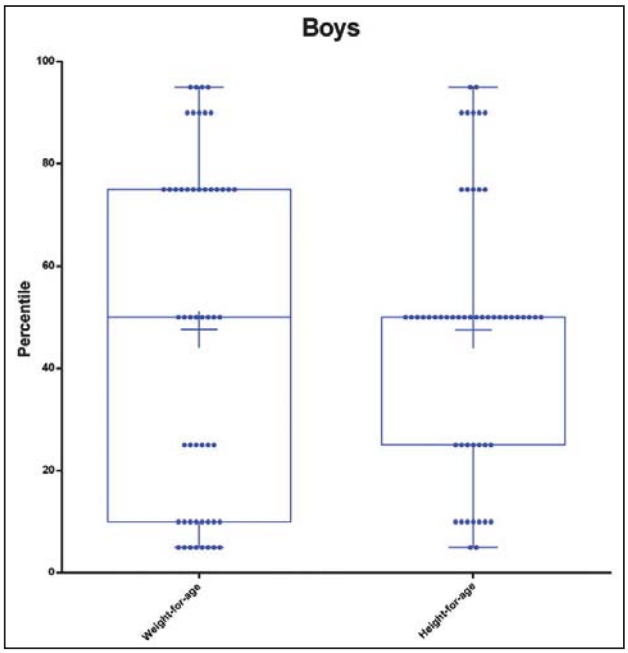


Figure 1: A bar chart depicting a breakdown of the entire sample by age and gender.



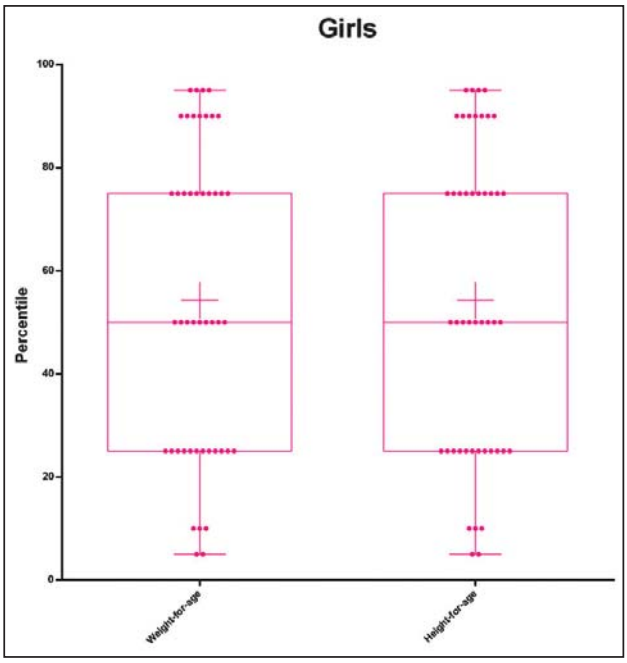


Figure 2: A graph depicting the weight-for-age and height-for-age (percentiles) for boys and girls included in the sample. Individual dots represent a single subject. Plus (+) indicates mean, while boxes represent 95% confidence intervals. Central horizontal lines within the box represent median and lines with bars extending from the box represent ranges of values.

The results of bone age estimation versus actual chronologic age for the whole sample are shown in (Fig.3). There was a strong correlation between chronologic age and bone age (Pearson product-moment correlation coefficient, r=0.858; p<0.001). The median bone age estimated by Greulich-Pyle method for the whole sample was 15 (IQR: 12 17) years which, when compared to the median chronologic age (14.1 [IQR: 12.3 15.8] years) using Wilcoxon signed ranks test, was not significantly different (p>0.05). The difference between bone age and chronologic age (termed age discrepancy) for boys and girls of various age groups is shown in (Fig.4). The median bone age estimated by Greulich-Pyle method for boys (13.8 [IQR: 12.0 16.5] years) was not significantly different from the median chronologic age (13.5 [IQR: 12.3 15.6] years) as assessed using Wilcoxon signed ranks test (p>0.05). However, the median bone age estimated by Greulich-Pyle method for girls (16 [IQR: 13 17] years) was significantly different from the median chronologic age (14.5 [IQR: 12.4 15.8] years) as assessed using Wilcoxon signed ranks test (p<0.05). (Fig.5) shows

bone age and chronologic age for boys and girls aged less than 13 years and those aged greater than or equal to 13 years. A polar plot (Fig.6) was also constructed for both boys and girls to depict the severity of age discrepancy for various age groups.

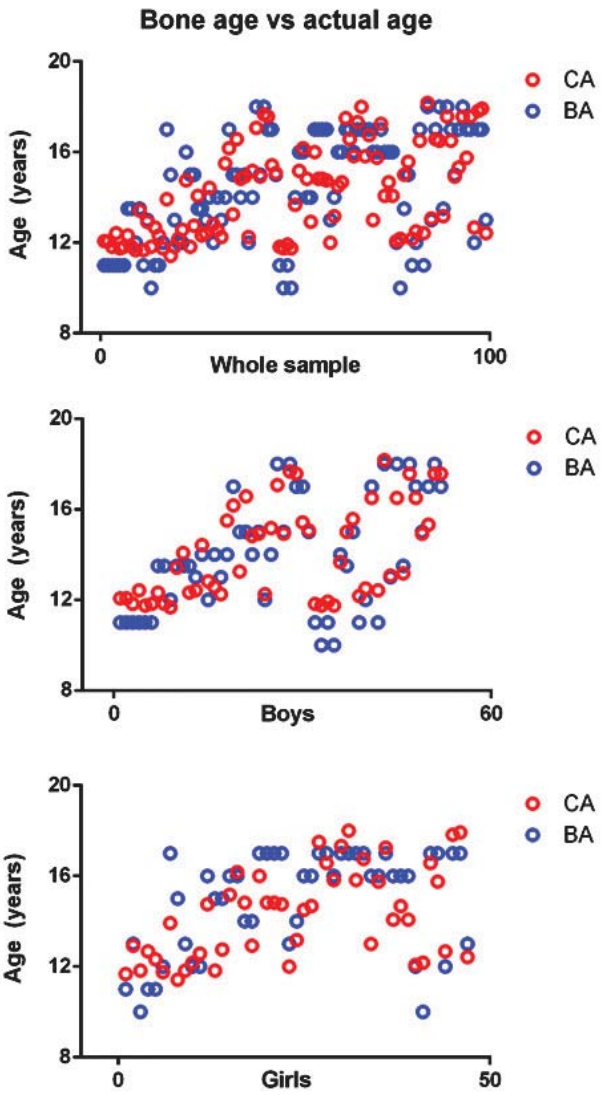


Figure 3: Graphs depicting the distribution of bone age (BA) and chronologic age (CA) for study subjects included in the whole sample. X-axis represents individual study subjects, while Y-axis shows the age in years.

To further assess factors that might account for age discrepancy, we split the dataset into boys and girls who were underweight (BMI < 18.5 kg/m^2) vs those who were not underweight. There was strong correlation between chronologic age and bone age for all

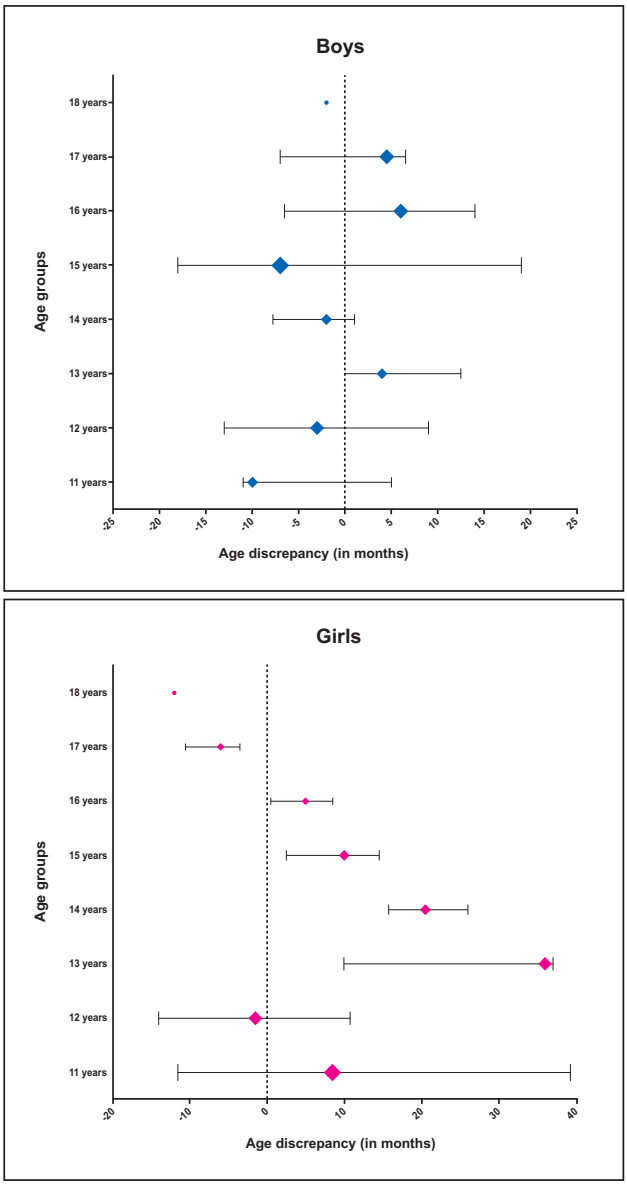


Figure 4: A graph showing the median age discrepancy (i.e. the difference between bone age and actual chronologic age) represented by diamonds with interquartile ranges represented by bars for each age group among boys and girls.

the groups. (Fig.7) shows the age discrepancy for boys and girls who wereunderweight or not underweight. Weconstructed a linear regression model in order to assess the factors affecting age discrepancy. In the multivariate linear regression model, gender (=0.355, p<0.001), height (=0.512, p=0.002)and chronologic age (= -0.346, p=0.007)were found to be independent predictors of age discrepancy. However, given the small sample size, the model had overall poor performance (R^2=0.236).

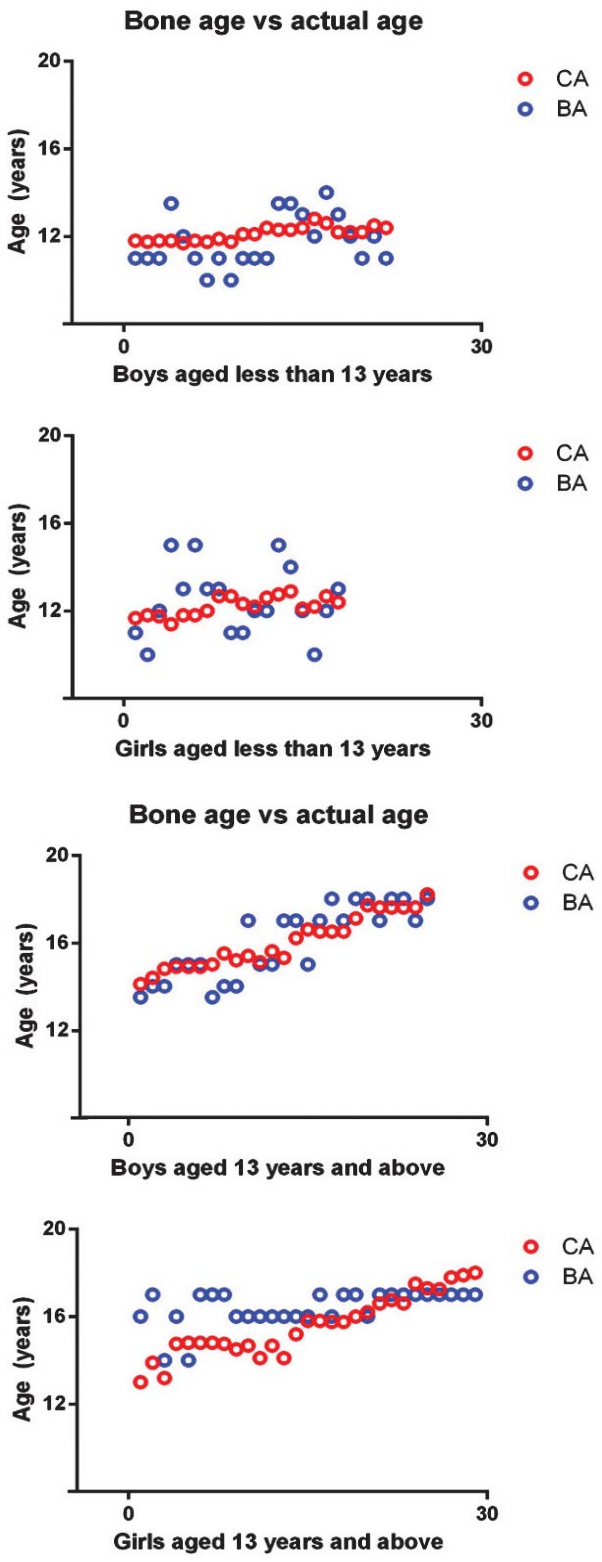


Figure 5: Graphs depicting the distribution of bone age (BA) and chronologic age (CA) for boys and girls below 13 years of age vs those aged 13 years or more. Abscissa represents individual study subjects, while ordinate shows the age in years.

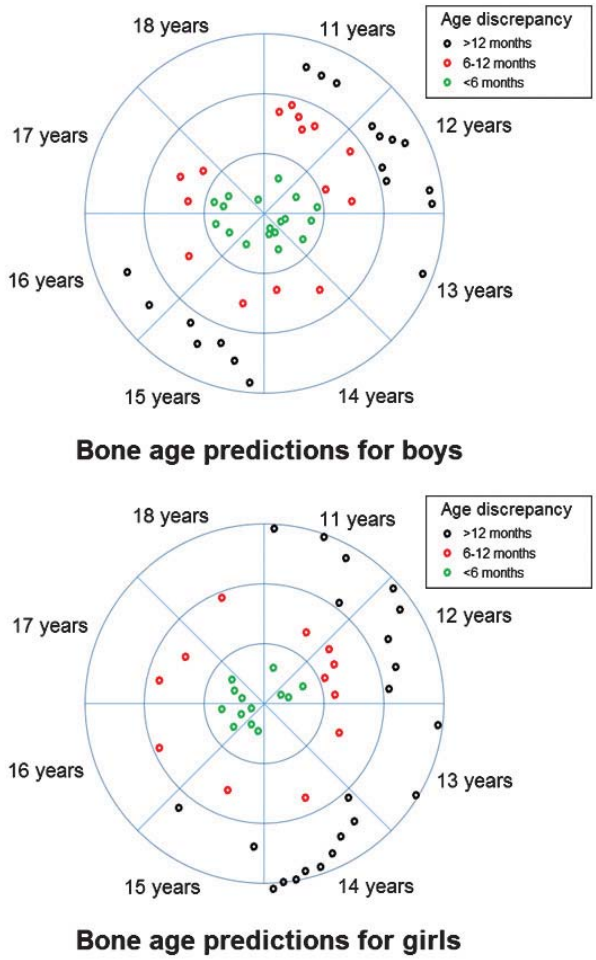


Figure 6: A polar plot depicting the age discrepancy (i.e. the difference between bone age and actual chronologic age) for different age groups among boys and girls. Each circle represents a single study subject and its distance from the center (radius) indicates age discrepancy (i.e. the further from the center, the higher the age discrepancy). Each pie of the chart represents a particular age group.

Discussion

We performed a cross-sectional study of bone age estimation using Greulich-Pyle method in a sample of healthy children in Karachi. Our study revealed that Greulich-Pyle method was not accurate for estimation of bone age in Pakistani children. These results have important implications as Greulich-Pyle method is currently the most commonly employed method for bone age determination in Pakistan.

Greulich-Pyle atlas was developed based on a Caucasian sample of North American children. The

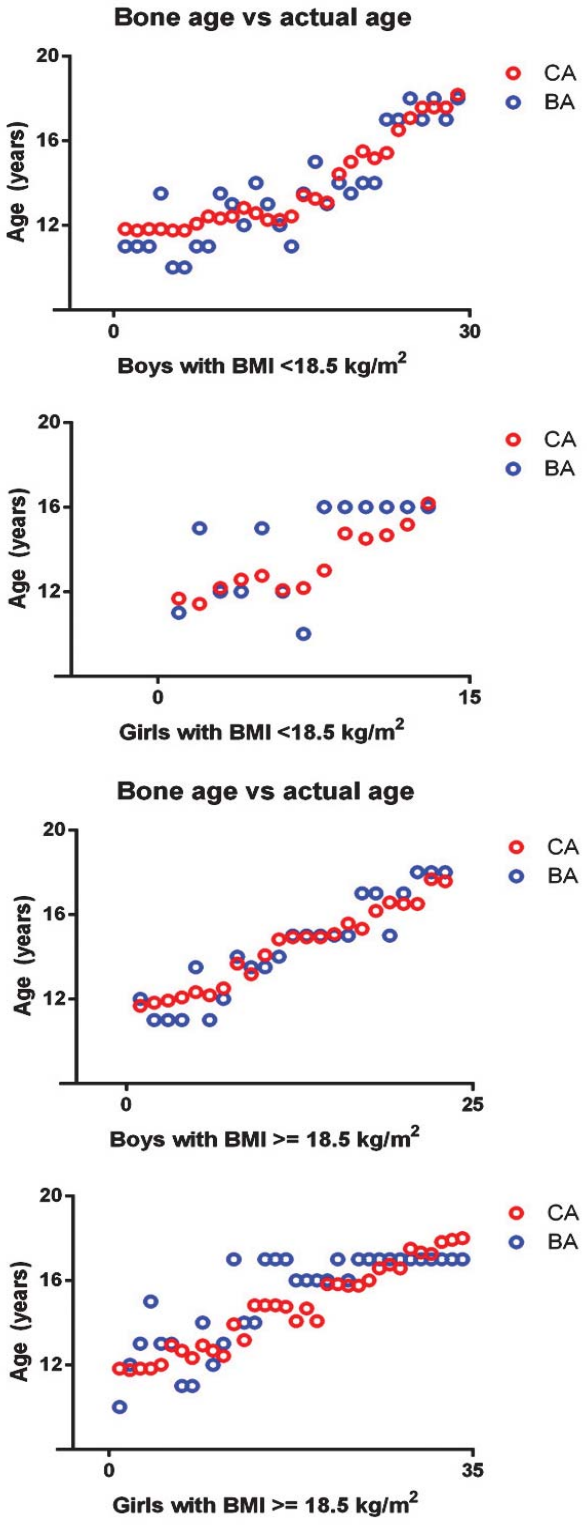


Figure 7: Graphs depicting the distribution of bone age (BA) and chronologic age (CA) for boys and girls who had a body mass index (BMI) of 18.5 kg/m^2 or more vs those who were underweight (i.e. BMI < 18.5 kg/m^2). Abscissa represents individual study subjects, while ordinate shows the age in years.

applicability of this method of bone age estimation to other populations has been critically evaluated in the past. Maggio and colleagues assessed the accuracy of Greulich-Pyle atlas for estimation of bone age in a Western Australian population and concluded that this method of bone age estimation is not suitable for legal purposes.[12] Hackman and Black observed that Greulich-Pyle method consistently over-estimated age in girls up to the age of 13 years and under-estimated age in boys up to the age of 13 years in the Scottish population.[13] Moreover, a systematic review comparing the Greulich-Pyle, Tanner-Whitehouse and Fels methods of bone age estimation found that Greulich-Pyle method was less accurate than the other two methods.[14]

The applicability of Greulich-Pyle method to boys and girls of Asian and African ethnicities has also been intensely debated. Mansourvar and colleagues reported that the Greulich-Pyle method was inaccurate in African and Asian ethnic groups.[15] Asystematic review published in 2019 compared the performance of Greulich-Pyle method in various ethnic groups.[8] The authors pooled the results of 35 studies with a low to medium risk of bias (as assessed using the National Institute for Health and Care Excellence tool)and concluded that the Greulich-Pyle method was not accurate for estimating bone age in African girls and Asian boys.

Data on bone age estimation from Pakistan are relatively limited. Zafar AM et al. in 2010 cautioned against the use of Greulich-Pyle method in the Pakistani population.[10] Awais M et al. in 2014 compared Greulich-Pyle and Girdany-Golden methods for bone age estimation and observed that both methods were inaccurate for estimation of bone age.[11] Taken together, these data strongly suggest that the Greulich-Pyle method of age estimation is unreliable for use in the Pakistani population.

Limitations of our study included a small sample size, which limits evaluations of the accuracy of Greulich-Pyle method in different subgroups (such as different ethnicities and nutritional status) and precluded precise regression analyses. Moreover, we did not perform blood tests for endocrine abnormalities in our study subjects, which could potentially confound the observed results. However, all children included in the study underwent medical check-up by a consultant pediatrician and were found to be healthy.

Despite these limitations, our study has the strength of being the first one done on healthy subjects with legal proof of chronological age. Building on prior work done in this regard in Pakistan, we provide further evidence that Greulich-Pyle atlas is not reliable for estimation of bone age in the Pakistani population. The natural next step to this conclusion is to pursue the development of an indigenous method of bone age estimation that is representative of all ethnicities of our country and is specifically calibrated for use in the Pakistani population.

Conclusion

Our study revealed significant discrepancies between chronologic age and bone age in adolescents as estimated by the Greulich-Pyle method. The Greulich-Pyle atlas does not appear to be reliable for estimation of bone age in the Pakistani population.

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