Skeletal maturity of the hand in an East African group from Sudan

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Abstract

Objectives: Studies of skeletal maturity from Africa indicate a delay, reflected in a negative relative skeletal age (RSA). This study aims to evaluate the influence of age, socioeconomic status (SES) and nutritional status on skeletal maturation in a large sample of children from North Sudan.

Materials: The sample consisted 665 males and 1018 females from 3-25 years from Khartoum. Height, weight, age of menarche and, SES were recorded of patients attending for dental treatment.

Methods: Skeletal age was assigned from hand-wrist radiographs using the Greulich-Pyle (GP) atlas (1952). RSA (difference between skeletal and chronological ages) was compared in groups divided by age, sex, height-for-age and body-mass-index z scores, and SES. Spearman’s correlation and student t-test was used to compare groups.

Results: Delayed skeletal age was noted across all age in boys. In girls, a delay was observed between ages 6-10, while advancement occurred between ages 13–18. Maturity was delayed in low height groups (p < .05) and low SES groups. RSA was negatively associated with HAZ in low SES males (R = −0.27, p < .001) and low SES females (R = −0.32, p < .001).

Conclusions: There were statistically significant skeletal delays in North Sudanese males and most pre-menarche females, low height and low SES groups. Post-menarche females were advanced relative to males and GP references. Low SES impacts were statistically correlated to skeletal delay.

KEYWORDS
bone age, hand-wrist, socioeconomic status, undernutrition

1 INTRODUCTION

Skeletal age provides a useful biological marker in a child’s trajectory toward maturity. Developmental age has important clinical, legal and forensic applications as well as the legal establishment of approximate chronological age in growing children in both healthy and diseased individuals.

Skeletal age is a sensitive parameter and can be affected by genetic and environmental factors (Tanner, Healy, Goldstein, & Cameron, 2001). These include ethnic origin (Koc, Karaoglanoglu, Erdogan, Kosecik, & Cesur, 2001; Mora, Boechat, Pietka, Huang, & Gilsanz, 2001; Wenzel, Droschl, & Melsen, 1984), sex, race, secular trends, nutrition, socioeconomic status, systemic diseases, congenital and endocrinology disease (Hawley, Rousham, Norris, Pettifor, & Cameron, 2009).

Relative skeletal age (RSA), representing the difference between skeletal and chronological ages (SA-CA), is useful to compare individuals or groups to reference populations. Delayed or advanced maturation in one child or group reflects a combination of associated genetic and environmental factors, including long term nourishment and social conditions. For example, poor nutrition and low socioeconomic status are known to cause delayed maturation in many populations (Chan, Chang, & Hsu, 1961; Cole & Cole, 1992; Frisancho, Garn, & Ascoli, 1970; Garn, Sandusky, Rosen, & Trowbridge, 1973; Greulich, 1951). Numerous methods and references exist to estimate skeletal age and relative maturity from developing hand-wrist bones (Gilsanz and Ratib,
2005; Greulich and Pyle, 1959; Poland, 1898; Pyle, 1971; de Roo and Schröder, 1976; Tanner and Whitehouse, 1962; Thiemann, Nitz, Schmeling, Reisinger, & Kleiber, 2006; Todd, 1937). Among these, the most widely used is the Greulich and Pyle (GP) radiographic atlas of skeletal development of the hand and wrist (Greulich & Pyle, 1959). The GP Atlas is a series of X-rays representing skeletal ages of growing American children from Ohio (USA) in the 1930s and 1940s described to have middle to high socioeconomic status from birth to 19 years (males) and birth to 18 years (females). Assessing maturity using atlas based methods have been criticized as they may hide environmental impact due to the high variability between different hand and wrist bones. An additional major limitation of the GP atlas is that it does not investigate children to full maturity but to age 18 years in females and 19 years in males. These ages might not necessarily translate to full maturity (Cole, 2015).

The applicability of the GP standards in non-Caucasian population is not universally accepted, as there is evidence that skeletal development varies between groups (Chariot & Denis, 2013; Lewis, Lavy, & Harrison, 2002; Mansourvar et al., 2014; Mohammed et al., 2015; Zhang, Sayre, Vachon, Liu, & Huang, 2009). There is considerable debate as to how much environmental effects contribute to the large variation in timing for normal and stressed groups, and how much variation derives from genetic or other biological factors (Schmeling et al., 2000). Only two studies on skeletal maturity in Africa allow direct comparison between groups with different nutrition, social status and ethnicity (Lewis et al., 2002; Mackay, 1952). Both these studies note that males are more delayed than females and a possible explanation is the higher impact of environmental stress on males compared to females (Lewis et al., 2002). The magnitude of the delay in skeletal maturity in these studies from East and South Africa (Lewis et al., 2002; Mackay, 1952) was approximately 1.67 years (SD, 2). Males and females were both delayed and the sequence of hand bone maturity was shown to follow the same patterns of skeletal development. However, males were reported to experience more delays when environmental stress was high. West Africans are delayed by approximately 16 months relative to the GP atlas (Weiner & Thambipillai, 1952). The causes of delayed skeletal maturity in East Africans relative to the GP atlas are not clear and not fully explained by poor nutrition despite this being a major contributor (Lewis et al., 2002; Schmeling, Reisinger, Geserick, & Olze, 2006).

High environmental stress and under-nutrition have a negative impact on other biological markers, such as puberty and menarche, as well as skeletal development (Thomas, Renaud, Benefice, de Meeus, & Guegan, 2001). A delay in skeletal age and age at menarche are thought to be correlated in some African populations (Attallah, 1978; Attallah, Matta, & El-Mankoushi, 1983; Ekisawa, D’Hulst, & Ghersquiére, 1986; Pasquet et al., 1999; Thomas et al., 2001). Children from other underprivileged populations in Nepal also showed a similar delay to Africans (Fleshman, 2000). Other studies have demonstrated that relative maturity was significantly advanced in both American, Australian and Portuguese males and females in modern samples than their historic predecessors (Duren, Nahhas, & Sherwood, 2015; Freitas et al., 2011; Ranjitkar, Lin, Macdonald, Taylor, & Townsend, 2006). Other investigators showed similar bone maturity trends between American black and white males and females in different age groups (Johnston, 1963; Loder et al., 1993), or a delay in these groups compared with Hispanic and Asian children (Zhang et al., 2009). Schmeling et al. (2000) argues that delays in maturity are due to the environmental stress and can be quantified. They suggest that population based reference standards should be produced to account for local variability in timing, which are linked to environmental factors.

Despite the difficulties in translating skeletal age to chronological age, a major use of the GP Atlas is to estimate maturity and birth age. Several authors recommend national references be established to enable accurate maturity assessment in specific populations (Cox, 1997; Lewis et al., 2002) but none exists in Africa.

The aim of this study was to investigate skeletal maturity in a group of children from East Africa. We also explore the applicability of the GP atlas in this group and report on the impact of socio-economic status and reduced height for age z scores on hand-wrist skeletal maturity and age at menarche.

2 | MATERIALS AND METHODS

The study was conducted at the dental hospital of the Khartoum Centre for Research and Medical Training in Sudan between 2008 and 2016. Ethical approval was granted by the Ethics committee at the Centre prior to the study (January 11, 2010). The sample consisted of North Sudanese subjects living in Khartoum aged from 3–23 years (665 females, 1018 males). Inclusion criteria were healthy status and a documented date of birth. Birth registration has been mandatory in Sudan since the 1970s. Verbal and written consent was obtained from study subjects and parents of minors.

On attending the centre, medical history and date of birth were recorded. Height to the nearest centimeter and weight to the nearest 0.1 kg were measured using calibrated scales and stadiometer (Seca, Hamburg, Germany). Anthropometric measurements were assessed with no shoes and light clothes.

A radiograph of the left hand was obtained (CS8100, Carestream, USA) and is illustrated in Figure 1. Each radiograph was assigned a skeletal age from the GP atlas by one calibrated examiner (Nihal Abdelaazeem). Descriptive statistics were calculated including the means and standard deviations of the chronological and skeletal ages and the difference compared to zero for each age category. Statistical analysis was carried out if the age group contained at least 10 individuals.

Height for age and BMI z scores were calculated using WHO Anthro and Anthro Plus: WHO, version 3.2.2 (available from: www. who.int/childgrowth/software/). As the group is skewed toward low height and undernutrition, a - 1 cutoff z score was used to compare groups. Height and weight data were not available for all individuals due to practical difficulties conducting clinical research in this part of the world. These included a lack of continuity of retaining medically trained staff, a lack of basic amenities such as continuous electricity and water and safety due to the civil war. The subset of the total
sample for whom height, weight and SES data were recorded was 487 males and 627 females.

Individuals were assigned to either a low or high SES based on insurance category (insurance is available only for families on low income as defined by the Department of Social Affairs, Ministry of Health) and type of school attended. Government school are usually attended by children with insurance. Privately funded schools were attended by children from higher income parents. Preschool children were defined by insurance, address and attendance at privately funded kindergartens. Individuals who had finished school (age 16) were defined by insurance, address and attendance at privately funded colleges.

The Spearman rank order correlation coefficient was applied to measure the association between relative maturity indicators (the difference between skeletal age and chronologic age, SA-CA) and SES, HA and BMI z scores indicating nutritional status. SPSS, Release Version 17.0 (© SPSS, Inc., 2009, Chicago IL) was used to analyze data.

A trained medical nurse recorded the recall age of menarche to the nearest month in 124 females aged 10 to 16 years and this was confirmed by the mother. Age of menarche was not available for all girls and those younger than 10 and older than 16 were excluded, as well as girls attending without their mothers or when the exact month could not be recalled. The cultural and religious traditions, the lack of sanitation and high level of female circumcision put extra emphasis on the reliability of the recollection of this female milestone. Mean age at menarche was calculated from the 124 females.

3 | RESULTS

The age and sex distributed is illustrated in Figure 2 showing relatively larger numbers of older females.

Kappa value to assess intra-examiner agreement was 0.86 for skeletal age (examiner Nihal Abdelazeem). The radiographs were assessed one month apart and Kappa indicates excellent agreement (Landis & Koch, 1977).

The mean age of menarche in females (N = 124) was 12.75 years (SD, 1.19; Minimum 9.74; Maximum 15.82).

![FIGURE 1](image1.png) Radiographic image of a 14-year old female showing hand-wrist bones

![FIGURE 2](image2.png) Age distribution of North Sudanese males and females
<table>
<thead>
<tr>
<th>Age group</th>
<th>N</th>
<th>Stature</th>
<th>Weight</th>
<th>BMI</th>
<th>HAZ Mean (SD)</th>
<th>BMIZ Mean (SD)</th>
<th>SA-CA Mean (SD)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>3–3.99</td>
<td>18</td>
<td>94.72</td>
<td>18.77</td>
<td>24.16</td>
<td>1.80 (0.63)</td>
<td>−0.01 (1.75)</td>
<td>2.80 (0.70)</td>
<td>3.05 (0.29) NS</td>
</tr>
<tr>
<td>4–4.99</td>
<td>20</td>
<td>104.13</td>
<td>16.89</td>
<td>15.66</td>
<td>0.12 (1.46)</td>
<td>0.13 (1.25)</td>
<td>4.00 (1.13)</td>
<td>4.51 (0.28) &lt;.05</td>
</tr>
<tr>
<td>5–5.99</td>
<td>29</td>
<td>111.19</td>
<td>19.17</td>
<td>15.43</td>
<td>0.16 (0.10)</td>
<td>0.03 (1.52)</td>
<td>4.00 (1.09)</td>
<td>5.71 (0.32) &lt;.05</td>
</tr>
<tr>
<td>6–6.99</td>
<td>40</td>
<td>121.12</td>
<td>22.02</td>
<td>14.91</td>
<td>−0.32 (1.51)</td>
<td>−0.09 (1.15)</td>
<td>5.51 (0.96)</td>
<td>6.57 (0.28) &lt;.05</td>
</tr>
<tr>
<td>7–7.99</td>
<td>39</td>
<td>121.88</td>
<td>22.48</td>
<td>15.15</td>
<td>−0.29 (0.96)</td>
<td>−0.31 (1.28)</td>
<td>5.78 (1.20)</td>
<td>7.43 (0.29) &lt;.05</td>
</tr>
<tr>
<td>8–8.99</td>
<td>42</td>
<td>130.19</td>
<td>26.43</td>
<td>15.69</td>
<td>−0.26 (0.84)</td>
<td>−0.13 (0.90)</td>
<td>7.13 (0.85)</td>
<td>8.57 (25) &lt;.01</td>
</tr>
<tr>
<td>9–9.99</td>
<td>28</td>
<td>133.62</td>
<td>29.50</td>
<td>16.46</td>
<td>−0.19 (0.93)</td>
<td>−0.38 (1.07)</td>
<td>7.94 (1.03)</td>
<td>9.49 (0.26) &lt;.01</td>
</tr>
<tr>
<td>10–10.99</td>
<td>25</td>
<td>139.38</td>
<td>30.61</td>
<td>15.81</td>
<td>−0.57 (0.78)</td>
<td>−0.21 (1.01)</td>
<td>9.32 (1.42)</td>
<td>10.42 (0.30) &lt;.05</td>
</tr>
<tr>
<td>11–11.99</td>
<td>34</td>
<td>142.77</td>
<td>34.57</td>
<td>16.83</td>
<td>−0.44 (0.96)</td>
<td>−0.39 (1.06)</td>
<td>9.79 (1.12)</td>
<td>11.52 (0.31) &lt;.05</td>
</tr>
<tr>
<td>12–12.99</td>
<td>32</td>
<td>147.11</td>
<td>37.71</td>
<td>17.35</td>
<td>−0.49 (0.93)</td>
<td>−0.69 (1.11)</td>
<td>11.20 (1.78)</td>
<td>12.35 (0.29) &lt;.05</td>
</tr>
<tr>
<td>13–13.99</td>
<td>35</td>
<td>150.15</td>
<td>35.45</td>
<td>15.68</td>
<td>−1.32 (0.84)</td>
<td>1.00 (1.07)</td>
<td>11.83 (1.24)</td>
<td>13.49 (0.36) &lt;.05</td>
</tr>
<tr>
<td>14–14.99</td>
<td>30</td>
<td>157.72</td>
<td>47.62</td>
<td>18.97</td>
<td>0.41 (1.12)</td>
<td>−0.79 (1.18)</td>
<td>13.35 (1.19)</td>
<td>14.46 (0.32) &lt;.05</td>
</tr>
<tr>
<td>15–15.99</td>
<td>24</td>
<td>162.92</td>
<td>54.22</td>
<td>20.10</td>
<td>−0.32 (1.41)</td>
<td>−0.52 (0.87)</td>
<td>14.13 (2.17)</td>
<td>15.50 (0.34) &lt;.05</td>
</tr>
<tr>
<td>16–16.99</td>
<td>28</td>
<td>171.48</td>
<td>55.78</td>
<td>18.98</td>
<td>−0.68 (0.88)</td>
<td>−0.10 (0.82)</td>
<td>15.94 (1.59)</td>
<td>16.45 (0.30) &lt;.05</td>
</tr>
<tr>
<td>17–17.99</td>
<td>27</td>
<td>170.59</td>
<td>61.59</td>
<td>21.25</td>
<td>−0.17 (0.89)</td>
<td>−0.67 (0.91)</td>
<td>17.54 (0.88)</td>
<td>17.52 (0.30) &lt;.05</td>
</tr>
<tr>
<td>18–18.99</td>
<td>36</td>
<td>172.05</td>
<td>59.25</td>
<td>20.09</td>
<td>−0.68 (1.21)</td>
<td>−0.47 (0.94)</td>
<td>17.70 (0.87)</td>
<td>18.51 (0.27) &lt;.05</td>
</tr>
</tbody>
</table>

N = number per age group, BMI = body mass index, HAZ = height for age z score; BMIZ = body mass index z score; SA = chronological age; SA−CA = skeletal age; standard deviations, NS, non-significant, <.001 and <.05, significant at the 0.001 and 0.05 level respectively (2-tailed).
TABLE 3 Spearman correlation between height for age and BMI for age z scores and the relative skeletal age (SA-CA) among males and females from North Sudan

<table>
<thead>
<tr>
<th>Group</th>
<th>Males (N = 665)</th>
<th>Females (N = 1018)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>R p</td>
<td></td>
</tr>
<tr>
<td>HAZ</td>
<td>0.27 &lt; .05</td>
<td>0.32 &lt; .05</td>
</tr>
<tr>
<td>BMIZ</td>
<td>0.27 &lt; .05</td>
<td>0.33 &lt; .05</td>
</tr>
</tbody>
</table>

p, significance level (2-tailed); CA, chronological age; SA, skeletal age; HAZ, height for age z score; BMIZ, body mass index for age z score.

Tables 1 and 2 show results of height, weight, HAZ, BMIZ, SA, CA and SA-CA for each age group for males and females respectively. Skeletal age was delayed by a mean of 1.56 years (SD, 1.61) in males and 0.97 (SD, 2.20) in females compared to the GP atlas (p < .05). The delay was uniform across age in males but females younger than 11 years of age were significantly delayed by a mean of 1.37 years (SD, 1.26). Post-menarche females were advanced by 0.71 years (SD, 1.55).

Table 3 shows a statistically significant positive correlation (p < .05) between height for age (R = .27 males, R = .32 females), BMIZ and relative skeletal age (R = .27 males, R = .33). Males had HAZ mean of −0.13 (SD, 1.07) and BMIZ mean of −0.23 (SD, 1.20) while females had HAZ mean of −0.11 (SD, 0.99) and BMIZ mean of −0.04 (SD, 1.02) indicating the group was skewed toward under-nutrition. This demonstrates the overall association between chronic malnutrition and delayed maturity in both males and females.

Tables 4 and 5 show that the delay in skeletal maturity in males was greater in the low height group (1.63, SD 1.37) compared with the control (0.91, SD 1.40). In females, the delay was similar between the groups. The low SES group was significantly more delayed in skeletal age than the high SES group in males. Skeletal age differed significantly between low and high SES in females (p < .05). Interestingly, in high SES females skeletal age was not delayed (0.35, SD 1.66) whereas in the low SES group a delay was noted (0.51, SD 1.74).

4 | DISCUSSION

The study presents hand wrist maturity data for a group of children and young adults from Northern Sudan and demonstrates that skeletal maturity from age 3 onwards was delayed in males and pre-menarche females similar to those reported in children from Malawi (Lewis et al., 2002; Mackay, 1952). Both studies from Malawi demonstrated statistically significant delays in East African children and attribute the delays to nutritional deficit assessed by measuring BMI, height and weight. Loder et al. found that African American girls were more mature than other ethnic groups (Loder et al., 1993). Our study showed that males and pre-pubertal females were delayed compared to GP references while post menarche females were advanced relative to GP references. This suggests that the GP atlas should be used with care for the purposes of assessing maturity in groups of African ancestry.

Our finding of a delay in skeletal age in males compared with females is in agreement with Cole et al. (2015) in South Africa. This is contrast to an earlier study that reported a similar delay in males and females in a deprived population in Central America (Frisancho et al., 1970). That study reported an improvement in relative skeletal maturity with age in both males and females (Frisancho et al., 1970) whereas we noted this in females only. In our study, relative skeletal maturity improved in post menarche females and maturity was advanced suggesting an altered response of this group to extreme nutritional stress and low socio-economic status.

Height for age and BMI z scores for age were below world standards in the high SES group. The correlation between nutritional status and relative skeletal age was evident in low SES in females but there were no significant correlations in the high SES group. This suggests that low SES has less overall impact on the skeletal maturity of post menarche girls. Males in the low SES group were delayed.

Low socioeconomic status was negatively correlated to delayed skeletal maturity. There was a statically significant negative correlation between chronological age and skeletal age in the low SES male and female groups, however the two are invariably linked and further investigation is required. This is in agreement with a previous study that reported that skeletal maturity was more affected in males than females in adverse conditions (Cole et al., 2015).

A strength of our study is that it complies with the AGFAD recommendations of adequate sample size, with uniform age groups and known ethnic origin. The age of subjects was accurate and analysis was separate for males and females. The time of the examination and examined features are clear. We also include details on the methods and the reference population regarding genetic/geographic origin and outline socioeconomic status and state of health (Schmeling et al., 2001, 2006, 2008).
addition, our sample extended well beyond the last age illustrated in the GP atlas to full maturity.

The pathway toward maturity is affected by a multitude of environmental factors and may act disproportionately on skeletal systems. We found that skeletal maturity is not affected equally across age in males and females under extreme environmental stress and females showed a protective mechanism post menarche.

An interesting finding from our study is the strong association between delayed skeletal maturity and SES for only some age groups. A clearer understanding of the effects of poor nutritional and SES on skeletal maturity in East African populations needs to be established before using the GP atlas to assess maturity. The link between undernutrition and socioeconomic status is complex and establishing trends in relative skeletal maturity is problematic. The distinct effects of independent stressors on skeletal age are a challenge to quantify across age due to the plasticity of human growth. Nutritional parameters are easier to establish than SES in child populations and one study reports that low and middle SES children were significantly delayed compared to high SES children (Bogin & MacVean, 1983). Similarly, girls were advanced to boys across age (Bogin & MacVean, 1983).

A limitation of our study was the cross-sectional design and the lack of very young children. The relationship between the delays in boys and pre-menarche girls and the critical periods in prenatal life and early child development could not be investigated as our minimum age was 3 years. Another limitation of this atlas method of skeletal bone age is that it hides possible bone specific changes that may be present. A further limitation in our study was the relatively undernourished group to measure the state of health and disease. Sudan is one of the poorest countries in the world with a long history of internal conflict and displacement (Yagoob & Ting, 2016). Sudan is characterized by extreme environmental and socioeconomic pressure yet do not seem to exhibit delay. Our results are marginally later than black females from South Africa with a median of 12.4 years (Cole & Cole, 1992; Cole et al., 2015). Our results of the recall age at menarche (12.75 years) is earlier than previously reported values using status quo methods of contemporary Sudanese girls of 13.93 years (Elsheikh & Ali Mohammed, 2011) and 13.35 years for the well-off females; 13.85 years for the middle class and 14.06 years for the poor females (Attalah et al., 1983). The age at menarche can be influenced by genetics, ethnicity, SES and undernutrition (Henneberg & Louw, 1995; Thomas et al., 2001). One reason for the early onset of menarche in our study is that the sample represented an urban population reflecting better nutrition and SES. Despite the fact that puberty is a complex biological stage, global advances in age of menarche have been observed (Okasha, McCarron, McEwen, & Smith, 2001). Improved nutrition and social conditions have been cited as major factors in lower menarche ages.

These findings suggest that skeletal maturity in groups is more sensitive to the aggregate of poor environmental factors than the singular effect of under-nutrition. Many programs in sub-Saharan Africa are aimed at alleviating undernutrition with little impact on socioeconomic status and further investigation of these groups will help evaluate the relationship between socioeconomic status and the adverse skeletal maturity.

5 | CONCLUSIONS

We show a delay in skeletal maturity in this group in Khartoum, with exception of post-menarche females. Poor nutrition and low SES were strongly associated with delay. Low SES had less impact in post-menarche females than males and young females. Despite similar ethnic, geographic and well defined environmental parameters, our study showed that skeletal delay is not uniform across all ages. These findings suggest that the GP atlas be interpreted with care in groups from Africa.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest, financial or personal relations with other organizations or people who may influence the study findings appropriately.
References


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