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Case study

Precarious adolescence: Adolescent rickets and anterior sacral angulation in two Dutch skeletal collections from the 18th–19th centuries

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ABSTRACT

Objective: This project aims to provide an objective approach to suggesting cases of adolescent rickets using the presence of anterior sacral angulation and interglobular dentine.
Materials: Sacra from 49 individuals from Hattem and 150 individuals from Middenbeemster, and second and third molars from five individuals from Hattem were analyzed. Both sites date to the 17th to 19th centuries.
Methods: The sacra were visually assessed for sacral angulation and measured to quantify anterior sacral angulation. The sampled molars were thin sectioned to look for the presence of interglobular dentine.
Results: Metric analysis determined that seven individuals had significantly anteriorly angled sacra. Three of the five individuals with sampled molars had interglobular dentine formed during adolescence.
Conclusions: Adolescent rickets may be associated with anterior sacral angulation.
Significance: Anterior sacral angulation may help identify possible cases of adolescent rickets in archaeological human remains.
Limitations: The small sample size for the molars prevented the identification of more individuals with interglobular dentine present during adolescence. Several individuals with visibly angled sacra were unmeasurable due to post-mortem damage and lacked molars.
Suggestions for further research: Research on a larger sample would allow us to understand better the association between anterior sacral angulation and adolescent rickets.

1. Introduction

Rickets is the inadequate endochondral mineralization of newly deposited osteoid and reduced apoptosis of columnar cartilage (Brickley et al., 2020a: 93; Tiosano and Hochberg, 2009). Clinicians have observed rickets to occur throughout childhood and adolescence; however, to date, paleopathological investigation has centered on infants and children (Mays and Brickley, 2018). Anterior sacral angulation has been observed in both historical clinical cases of adolescent rickets (Maxwell and Miles, 1925; Hess, 1930; Maxwell, 1935), as well as in archaeological cases (Molleson and Cox, 1993; D'Ortenzio et al., 2016). In contrast to normal sacral curvature, observed by Abitbol (1989), anterior sacral angulation occurs when the angulation exceeds the normal range for the population being assessed. This paper presents the first systematic evaluation of sacral angulation as a potential marker for adolescent rickets in archaeological skeletal remains. Moncrieff et al. (1973) noted a correlation between the occurrence of rickets and the timing of both the infant and adolescent growth spurts. The high demand for phosphate and calcium needed for bone formation during these periods of rapid growth, paired with a lack of adequate dermal and dietary vitamin D required for calcium and phosphate synthesis (Holick et al., 2011), puts individuals at an increased risk for developing rickets. The prevalence of skeletal disease reflects rates of growth and bone remodeling (Moncrieff et al. 1973); clinically, most cases of rickets occur during infancy (0–23 months), and early adolescence (12–15 years) (Cesur et al., 2011).

Vitamin D deficiency affects the body's ability to mineralize osteoid, with the greatest effects in actively growing skeletal regions. In the most

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clinical cases of adolescent rickets, diagnoses are made based on radiographs of the wrists, knees, and ankles (Agarwal and Gulati, 2009; Al Jurayyan et al., 2012). Changes such as swelling and pain in the wrists, knees, and ankles; genu valgum (inward angulation) or genu varum (outward bowing) at the knees have been observed (Agarwal and Gulati, 2009; Narchi et al., 2001; Puri et al., 2008; Snapper, 1943). Newly deposited osteoid is inadequately mineralized during periods of vitamin D deficiency, making the actively fusing sacral vertebrae more susceptible to the mechanical pressures of sitting and standing. The result can be an anterior angulation of the sacrum. Since sacral vertebrae are actively fusing during adolescence (Broome et al. 1998), angulation occurring during this period of growth and development has a higher likelihood of being preserved in later life. Anterior angulation of the sacrum was observed in adolescents in clinical cases of rickets by Maxwell and Miles (1925) and Hess (1930), but severe cases of adolescent rickets are rarely observed today, likely due to earlier medical intervention.

Interglobular dentine (IDG), too, provides an important source of information, as it forms when there is defective mineralization of dentine. Mineralization occurs when the organic matrix is replaced by crystals composed of calcium salts (calcospherites), which fuse and form a homogenous matrix (D'Ortenzio et al., 2018). Similar to skeletal disease, when an individual is deficient in vitamin D, the calcospherites making up the dentine are unable to fuse adequately, leaving permanently visible bands of inadequately mineralized dentine (Brickley et al., 2020b). Teeth grow at consistent rates; therefore, it is possible to determine the approximate age which an individual with IGD experienced a period of vitamin D deficiency based on the position of IGD within the tooth (Brickley et al., 2020b; D'Ortenzio et al., 2016).

Despite clinical recognition of changes related to rickets occurring in adolescence, they are rarely recognized in paleopathology. Anterior sacral angulation between the second and third sacral vertebrae has, however, been recorded in human remains from the Spitalfields crypt, London (Molleson and Cox, 1993), and an individual from the Saint-Matthew archaeological site in Quebec (D'Ortenzio et al., 2016); interglobular dentine (IGD) was also recorded in the second and third molars of this individual. The combination of the onset of new social roles, such as agricultural work, working in domestic service, leaving home for work in cities, and marriage for older adolescents (Kok, 1997; van Cruyningen, 2005; van Poppel and Nelissen, 1999), as well as rapid growth occurring during puberty, makes early adolescence a crucial age at which to study vitamin D deficiency in archaeological populations.

By evaluating the skeletal changes in the sacrum associated with adolescent rickets and the presence or absence of IGD in two historical skeletal assemblages, this research aims to provide an objective approach to identify possible cases of adolescent rickets. We then focus on an individual with a significantly angled sacrum ($z = 1.5$) to better understand the factors that influence the development of adolescent rickets, the effects of the condition throughout the life-course, and to gain insight into the socio-cultural factors contributing to the development of rickets.

2. Materials and methods

2.1. Materials

The material used in this study comes from two Dutch skeletal assemblages from the municipalities of Middenbeemster (MB11) and Hattem (HT15) dating from the 17th to the 19th centuries, with the latest burials from Middenbeemster dating to 1866 and from Hattem dating to 1829 (Hakvoort, 2013; Veselka and Klomp, 2019). Individuals were included in this research if they were older than nine years of age and had fused or partially fused sacra. The minimum age of nine was chosen in order to capture individuals beginning their growth spurts early. The population sample was comprised of 150 individuals from Middenbeemster and 49 individuals from Hattem (Table 1).

Estimations of sex and age made in previous work were used to keep this research consistent with existing findings (see Lemmers et al., 2013 for Middenbeemster; and Veselka, 2018 for Hattem). The age categories used also reflect those used in previous research. Documentary sources allowed for known age and sex to be determined for some individuals buried after 1829 (van Spelde and Hoogland, 2018), of which twenty-two were included in this research. Sex was estimated by scoring morphological features on the cranium, mandible, pelvis, and sacrum using methods outlined by the Workshop for European Anthropologists (WEA, 1980) (see Lemmers et al., 2013: 36 and Veselka, 2018). Metric evaluation was undertaken using measurements of the humerus, femur, mandible, clavicle, and scapula using methods by Stewart (1979), Steyn and İşcan (1999), McCormick et al. (1991), and Bainbridge and Genoves Tarazaga (1956). Dental development and epiphyseal fusion were the primary techniques used to estimate age at death in subadults (Veselka, 2018; Veselka et al., 2019). The degree of age-related changes of the pubic symphysis and auricular surface, cranial fusion, sternal rib end growth, and fusion of late fusing bones were used to estimate age in adults (Lemmers et al., 2013: 37; Veselka, 2018). Further details regarding age estimation can be found in Section 1 of the Supplemental Materials.

Histological analysis of molars for interglobular dentine could only be conducted on individuals from Hattem. Samples were not collected from the Middenbeemster collection as efforts were being made to maintain the current level of preservation of the sample. Second and third molars were selected, as these teeth form during adolescence. Individuals with molars showing signs of post-depositional damage, wear, or carious lesions were excluded, as such changes can impact the observation of IGD (D'Ortenzio et al., 2018). Many individuals from Hattem had caries, thus limiting the pool of possible samples with sacral angulation to HT15S012 and HT15S018. In addition to the two individuals with sacral angulation, we also sampled three individuals with no sacral angulation to serve as controls. We aimed to keep the number of controls close to the number of sampled cases. In total, three second molars and four third molars were sampled from five individuals. Assessing IGD in individuals with sacral angulation allows us to associate the presence of vitamin D deficiency during adolescence. The absence of IGD during adolescence in individuals without sacral

Table 1
Age and sex distribution of skeletal assemblage.

Age (years)	Hattem			Middenbeemster			Total
	Male	Female	Unknown	Male	Female	Unknown	
9–12	0 (0 %)	0 (0 %)	0 (0 %)	0 (0 %)	1 (0.5 %)	0 (0 %)	1 (0.5 %)
13–17	0 (0 %)	0 (0 %)	0 (0 %)	0 (0 %)	0 (0 %)	4 (2.0 %)	4 (2.0 %)
18–25	5 (2.5 %)	1 (0.5 %)	0 (0 %)	8 (4.0 %)	7 (3.5 %)	5 (2.5 %)	26 (13.1 %)
26–35	6 (3.0 %)	5 (2.5 %)	0 (0 %)	15 (7.5 %)	20 (10.1 %)	0 (0 %)	46 (23.1 %)
36–49	20 (10.1 %)	7 (3.5 %)	0 (0 %)	25 (12.6 %)	19 (9.5 %)	1 (0.5 %)	72 (36.2 %)
50+	1 (0.5 %)	4 (2.0 %)	0 (0 %)	27 (13.6 %)	15 (7.5 %)	0 (0 %)	47 (23.6 %)
18+	0 (0 %)	0 (0 %)	0 (0 %)	1 (0.5 %)	2 (1.0 %)	0 (0 %)	3 (1.5 %)
Total	32 (16.1 %)	17 (8.5 %)	0 (0 %)	76 (38.2 %)	64 (32.2 %)	10 (5.0 %)	199 (100 %)

Note: Adults who could not be assigned a specific age category are listed as 18+.

angulation allows us to further confirm the association between sacral angulation and vitamin D deficiency.

2.2. Recording of sacral shape changes

Visual assessment of shape differences and metric analysis were used to identify individuals with anteriorly angled sacra. Sacra were viewed laterally and evaluated for anterior angulation. For individuals with sacra that were not fully fused or broken, this assessment was made by holding the sacral vertebrae together. Angulation of the sacrum was marked as present if the sacrum appeared to be more angled than the population norm following a gross visual assessment, after which the sacra were measured.

Anterior angulation of the sacrum was evaluated metrically in undamaged and fully fused sacra by calculating the pelvic incidence using methods adapted from Abola et al. (2018) (Fig. 1). The pelvic incidence was calculated by subtracting the straight length of the sacrum, measured using sliding calipers (Fig. 1a) from the curved length of the sacrum, measured using a measuring tape placed against the ventral surface (Fig. 1b) (Abola et al., 2018). Both measurements were taken from the sacral promontory to the bottom of the fourth sacral vertebra (Fig. 1). The fourth and fifth sacral vertebrae fuse between the ages of 5 and 15 years, while the third and fourth sacral vertebrae fuse between the ages of 7 and 15 years (Broome et al., 1998), so by only measuring to the fourth sacral vertebrae, we are more likely to capture fusion occurring during adolescence.

Z-scores were calculated for the sacral angle measurement using Excel (version 16.39). Z-scores were considered significantly larger than the population mean if the score was equal to or larger than $z = 1.5$. The z-scores were calculated by sex to account for sexual dimorphism in size difference. The Interclass Correlation Coefficient (ICC) was used to assess the agreement between measurements taken by the same observer (ML) and external observers.

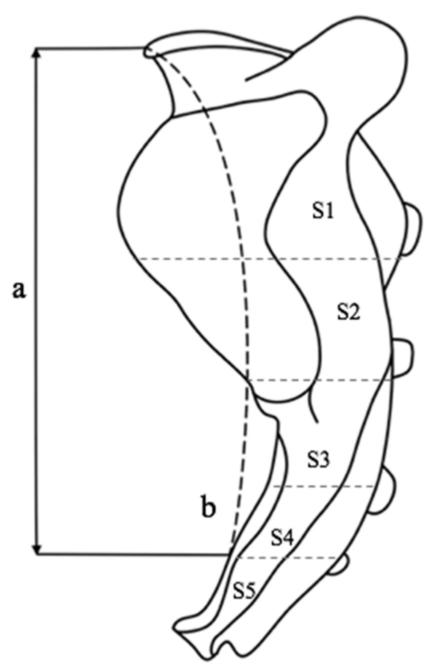

Fig. 1. Measurements used to calculate the pelvic incidence derived from Abola et al. (2018). Measurement a) represents the straight length (sacral promontory to the fused S4/S5 joint), while b) (broken line) represents the curved length.

2.3. Teeth sampled for interglobular dentine

Following methods outlined by De Boer et al. (2013), the molars were embedded in Araldite2020 resin and sliced to a thickness of 700 μm using an IsoMet1000 precision saw. The thin sections were ground first using sandpaper with a grit of P220, and hand polished with sandpaper with a grit of P1200. The sections were then stained for 8 min using Mayer's haematoxylin, and mounted using a glass slide and Entalan® The histological slides were imaged using a ZEISS Axioscope 5 at 50x total magnification. IGD was scored as present, absent, or unobservable and was determined to be present when clear systemic bands of mineralization defects were recorded following dentine layers across the tooth. The IGD was graded using methods defined by D'Ortenzio et al. (2016), whereby grade 1 IGD covers less than 25 % of the dentine band, grade 2 IGD covers 25–50 % of the dentine band, and grade 3 IGD covers more than 75 % of the dentine band. The age that the IGD occurred at was determined using the diagram presented in Fig. 3 of Brickley et al. (2020b).

3. Results

Data for individuals with angled sacra are shown in Table 2. The strength of agreement for all measurements was very good (intra-observer: 0.953–0.998; inter-observer scores: 0.903–0.966). Both of the individuals sampled associated with angulation of their sacra had IGD present in early adolescence (HT15S018, HT15S012) (Fig. 2). Individual number HT15S012 also had IGD spanning throughout adolescence and into early adulthood (8–10 years to 18–25 years) (Fig. 2). Of the three control individuals, HT15S130 had IGD present in early adolescence and early childhood (2.5, 3.5, and 10–11 years) (Veselka et al., 2019 and Table 3), HT15S093 had IGD present in early childhood (5 years), and HT15S0177 had no IGD present. Of the two individuals with IGD during adolescence and macroscopically angled sacra, only one could be measured (HT15S012, pictured in Fig. 3). The sacrum belonging to individual HT15S018 was not fully fused; however, the angle was evaluated by holding the sacrum together.

Upon analysis, it was clear that the macroscopic evaluation over-diagnosed sacral angulation and was thus inaccurate. Of the 30 individuals with macroscopically angled sacra and calculated z-scores, only six (20 %) were significantly more angled than the population norm (see Section 2, Table 2.1 in Supplemental Materials). One additional individual (MB11S476) had a z-score indicating a significantly angled sacrum, which was undetected macroscopically. The total prevalence of significantly angled sacra calculated using the methods by Abola et al. (2018) in the sampled population was 7/199 (13.9 %).

4. Discussion

While the sample size used in this research is small, the presence of statistically significant sacral angulation in an individual with IGD present during adolescence suggests that anterior angulation of the sacrum can be considered as a potential marker for adolescent rickets. Using a biological approach (Mays, 2018) in which clinical reports of sacral angulation in adolescent rickets (Hess, 1930; Maxwell and Miles, 1925; Maxwell, 1935) are considered alongside underlying biological mechanisms, this suggestion seems plausible. The sacral vertebrae are actively fusing throughout adolescence and require adequate levels of vitamin D to mineralize. If adequate vitamin D is absent during fusion, the vertebrae are more susceptible to mechanical pressures, causing them to angle anteriorly. When the vitamin D levels are restored, the sacrum fuses, resulting in the angulation being preserved into adulthood, as seen in Fig. 4. The sample used here is, however, too small to provide complete information on the exact mechanisms involved, but it does provide a sound basis for further work. The prevalence of adolescent rickets at Middenbeemster and Hattem (7/199; 13.9 %), diagnosed using sacral angulation, was noted by Veselka and Klomp (2019) and

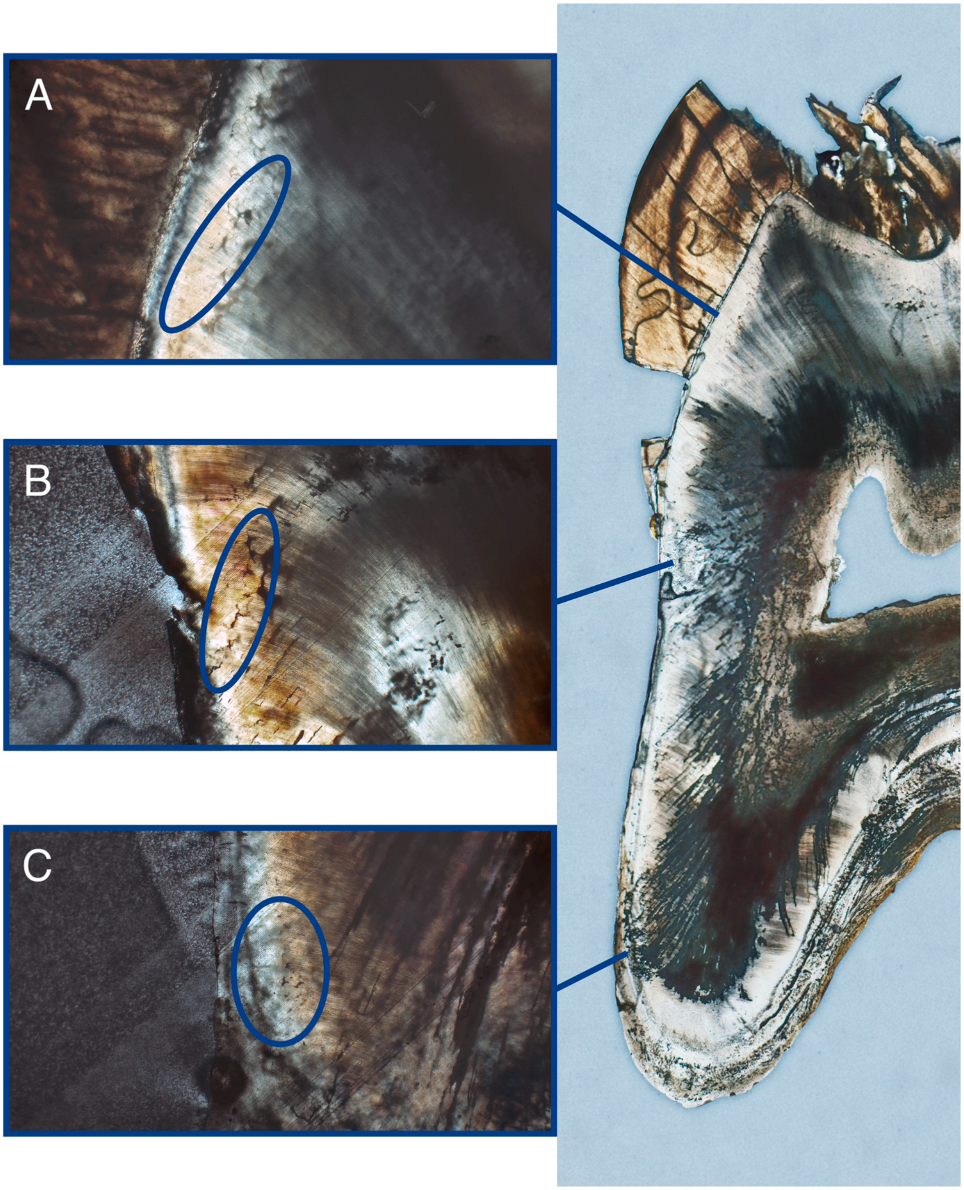

Fig. 2. Episodes of interglobular dentine (IGD) for individual HT15S012. Only three of the six episodes of IGD are pictured in images A through C. Episodes of IGD were graded using methods by D'Ortenzio et al. (2016) and aged using methods by Brickley et al. (2020b). Fig. 2A shows IGD below the enamel, was scored at grades 1–2, and occurred at ages 10–12 years. Fig. 2B shows IGD at the cementoenamel junction, was scored at grades 1–2, and occurred at ages 11–12 years. Fig. 2C shows IGD at the root, was scored at grade 1, and occurred between the ages 18–25 years. Fig. 2C displays polishing slightly further than the other images in order to clarify the IGD.

Veselka et al. (2021) as lower than the presence of residual childhood rickets (50/288; 17.4 %) and active childhood rickets (15/97; 15.5 %). No cases of osteomalacia were recorded in adults from Middenbeemster (Veselka et al., 2018).

4.1. Differential diagnosis

In addition to occurring in cases of rickets, sacral angulation can also occur as a result of osteomalacia or fracture. Brickley et al. (2005) reported anterior angulation of the sacrum in adults with osteomalacia (see discussion in Brickley and Mays, 2019). Rachitic changes to the sacrum are more likely to cause angulation between the vertebral bodies, where the active bone growth takes places (Lockau et al., 2019) rather than within the bodies. However, it is sometimes difficult to detect where angulation occurred, and it may not be possible to distinguish between rickets and osteomalacia (inadequate mineralization of bone on previously formed surfaces). While sacral angulation due to traumatic fracture is possible, a recent literature review of pediatric trauma cases revealed that fractures to the sacrum resulting in anterior angulation were very rare and would likely show other signs of fracture (Hart et al., 2004). Larger body size has also been hypothesized to cause sacral angulation (Krenn et al. (2022). However, Krenn et al. (2022) acknowledge that sacral angulation may also be due to rickets. In our sample, no evidence of traumatic injury was found. As both rickets and osteomalacia are caused by vitamin D deficiency (Mays and Brickley, 2018), it is likely that most cases of sacral angulation identified will represent vitamin D deficiency occurring during adolescence, thus filling a gap in our understanding of the effects of this deficiency through the life-course.

4.2. Sacral angle and vitamin D deficiency

The difficulties in distinguishing between pathological changes and normal variation upon visual analysis have been discussed in work by Brickley et al. (2018). There is an increase in anterior sacral angulation during normal growth and development, with supine posture and the actions of the erector spinae and levator ani muscles contributing to the angle (Abitbol, 1989; Abola et al. 2018). Normal changes in sacral curvature taking place during adolescence is to be expected, particularly as the sacrum is not fully fused until early adulthood (Broome et al., 1998). It should be noted, however, that Abola et al. (2018) were not investigating the potential pathological causes for sacral angulation.

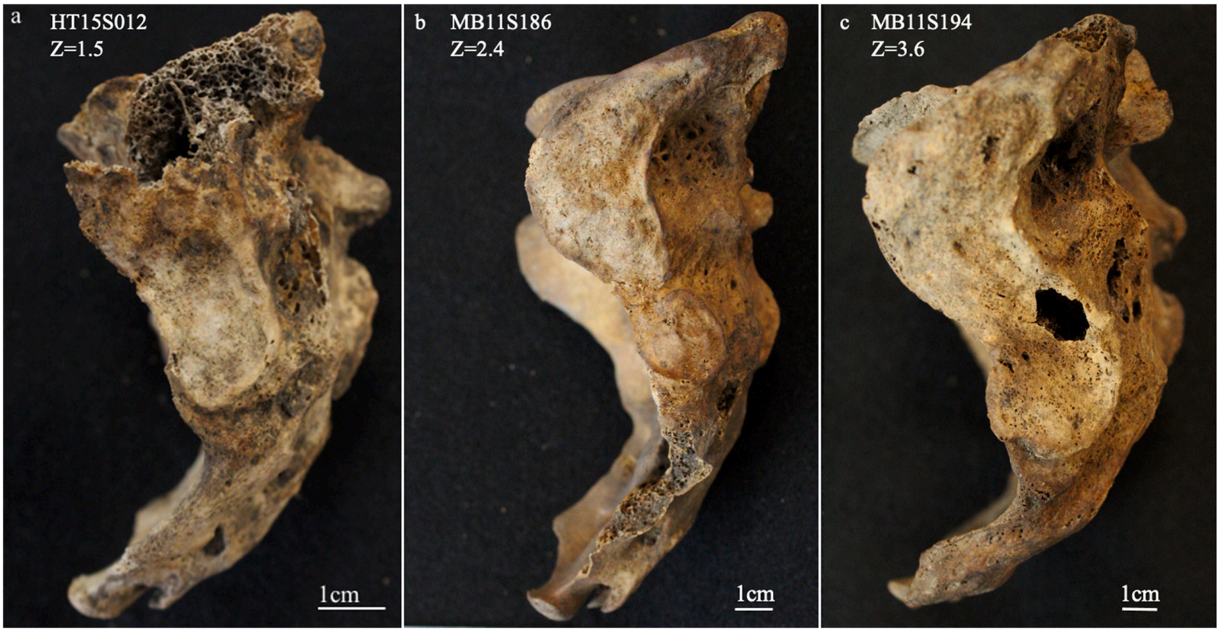

Fig. 3. Lateral view of angled sacra for individuals HT15S012 (z = 1.5), MB11S186 (z = 2.4), and MB11S194 (z = 3.6).

Table 2
Individuals with significantly angled sacra.

Individual	Sex	Age	Abnormal Macroscopic Sacral Angle	Sacral Angle Measurement Z-Score
HT15S012	F	36–49	P	1.5
HT15S090	F	50+	P	3.2
MB11S186	M	36–49	P	2.4
MB11S194	M	50+	P	3.6
MB11S216	F	36–49	P	1.9
MB11S240	M	36–49	P	3.5
MB11S476	F	31	A	3.6

Legend: F = female; M = male; N. = number; P = present; A = absent.

Table 3
Thin section results.

Individual	Sex	Age	Tooth Sampled	N. Episodes of IGD	Age of IGD episode(s) (in years)	Grade
HT15S012	F	36–49	LM_3	6	8–10; 10–12; 11–12; 12–16; 17–20; 18–25	1–2; 1–2; 1–2; 1–2; 2; 1
HT15S018	M	18–25	LM_3	2	8–10; 10–12	2; 2
HT15S077	M	26–35	RM^2; RM^3	0; 0	N/A	N/A
HT15S093	F	26–35	LM_2	1	5	1–2
HT15S130	M	18–25	RM_2; RM_3	2; 2	RM_2: 2.5; 3.5; RM_3: 10–11 (both)	RM_2: 2; 1; RM_3: 1 (both)

Legend: IGD = interglobular dentine; F = female; M = male; N = number; N/A = not applicable.
Note: The grades of IGD are listed in the same order as the age of the IGD episode. The IGD was graded using methods by D'Ortenzio et al. (2016) and age using methods by Brickley et al. (2020b).

Fig. 4. Angled sacrum from individual number MB11S278 from the Middenbeemster collection. Z-scores were not possible for MB11S278 due to post depositional damage.

In our study, the measurements of the sacral angle and use of z-scores by sex allow for normal variation of sacral curvature to be established, and for individuals with significantly abnormally angled sacra to be revealed. By calculating z-scores, individuals who are significantly different from the rest of the skeletal assemblage were identified. Individuals with sacral angulation z-scores larger than $z = 1.5$ have sacra more significantly anteriorly angled than the population norm. These individuals may have been affected by vitamin D deficiency occurring during adolescence, which may have accentuated the normal increase in sacral angulation during growth. Sacral angulation was not present in one individual with IGD in early adolescence (10–11 years) and therefore, it is possible that this angulation forms more readily in older adolescents, or that the period of vitamin D deficiency experienced by this individual was not severe enough to result in skeletal changes.

It was also noted in our study that some sacra recorded as angled based on macroscopic analysis fell within the normal range of variation for their sex when the z-scores for the sacral angle were calculated (See Table 2.1 in Section 2 of the Supplemental Materials). Since the fourth and fifth sacral vertebrae begin to fuse at age five (Broome et al., 1998), it is possible that angulation in this region was observed but too minimal to be captured metrically. Some individuals with visibly angled sacra that were unmeasurable may indeed have been significantly angled. It is also possible that some individuals with angled sacra experienced vitamin D deficiency as children, not as adolescents, which may have contributed slightly to the overall anterior angulation of the sacrum. The more marked growth in adolescence than the preceding middle childhood period (Moncrieff et al., 1973) means most angulation recorded will be linked to adolescent rickets. However, by only considering individuals with sacral angulation z-scores above 1.5, we are selecting individuals with significant sacral angulation. Individuals with slight sacral angulation from childhood rickets are unlikely to be included.

Due to the small number of individuals with adolescent rickets, an osteobiographical approach is valuable and will be taken here to better understand the development of sacral angulation using HT15S012. This individual was a female from Hattem who died between the ages of 36 and 49 years. Her left third molar was found to have six separate episodes of IGD spanning from ages 8–25 years. The episodes appeared to occur at yearly intervals, with one episode extending down into the roots. The frequency of the episodes of IGD suggests that this individual may have been deficient in vitamin D on a seasonal basis. HT15S012 was the only individual with IGD present during adolescence accompanied by a statistically significantly angled sacrum. There are several possible causes for this individual's repeated episodes of vitamin D deficiency. The recurrent episodes may have been due to her pattern of indoor work limiting the replenishment of vitamin D each summer. Children in the Netherlands were expected to help their parents work as early as five years of age, although work at this age would have consisted of easy tasks such as cow herding, chores in the home and caring for the younger children in the family (Schenkeveld, 2008). It is possible that the style of dress dictated by a combination of preferences and social norms influenced the levels of skin exposure to sunlight and time spent outdoors. Another possibility is that she may have suffered from a chronic illness that kept her indoors for long periods and genetic factors may have played a role in disease susceptibility and/or absorption of nutrients. Lastly, the mid-19th century was a period of widespread decrease in quality of life and an increase in diseases such as smallpox, typhoid fever, and cholera, and coincides with the Dutch potato famine, which caused a peak in mortality between 1843 and 1853 (Drukker and Tassenaar, 1997). If this individual was chronically ill, she may have spent longer periods of time, in a sitting position, than her peers, which may have contributed to the development of her sacral angulation.

5. Limitations

The small sample size available for sectioning third molars has limited our ability to identify individuals with interglobular dentine. Additionally, several individuals with severe sacral angulation were too damaged to be metrically assessed and did not have molars available for sampling. Further research using larger sample sizes will help to improve our understanding of sacral angulation and adolescent rickets.

The use of sacral angle measurement also has limitations. The sacral angle measurements can only be taken on individuals with well preserved, fused sacra. Osteophytes on the sacral promontory obstruct accurate recording. Additionally, z-scores can only be evaluated on samples of more than 30 individuals. As such, the use of the sacral angle measurement may not be suitable for all populations.

While there is a strong clinical and biomedical association between IGD and disorders of mineral metabolism and rickets (Mellanby, 1929; 1934; McDonnell et al., 1997; Foster et al., 2014), along with a robust and growing body of work showing that it is associated with rickets in the archaeological record (D'Ortenzio et al., 2016; Veselka et al., 2019), there is currently no evidence-based threshold for what counts as pathological IGD and no known levels of serum 25(OH)D_3 triggering the development of IGD. Of equal concern is clinical research indicating that IGD can form in normal dentinal development (see discussion in D'Ortenzio et al., 2018).

6. Conclusion

The current work suggests that significant anterior sacral angulation might be an indicator of adolescent rickets. The statistical use of z-scores was an effective method in identifying shape changes possibly linked to residual adolescent rickets. Z-scores reduce the subjectivity in the identification of shape changes allowing paleopathologists to distinguish between normal variation and pathological shape changes. Further research on the association between sacral angulation and adolescent rickets is needed to improve our understanding of the mechanisms behind this shape change, and what factors contribute to the severity of the angulation.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.ijpp.2022.12.006.

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