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Radiographic Scoring Method for the Assessment of the Severity of Nutritional Rickets

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Summary

Radiographic changes of rickets are well characterized, but no method of grading the severity of these changes has been in general use. Consequently, it is difficult to compare objectively or follow radiographic improvement. We prospectively evaluated the utility and reproducibility of a scoring method for measuring the severity of rickets. A 10-point score for radiographs of wrists and knees was devised to assess the degree of metaphyseal fraying and cupping and the proportion of the growth plate affected. The score progresses in half point increments from zero (normal) to 10 points (severe). Four trained physicians independently scored radiographs on two separate occasions from 67 children with active rickets. A broad representation of mean radiographic scores was moderately correlated with alkaline phosphatase ($r = 0.58$). Interobserver correlation of radiographic scores was 0.84 or greater for all observer pairs and intraobserver correlation was 0.89 or greater for each observer. Researchers and clinicians should find the score useful to assess objectively the severity of rickets.

Introduction

Rickets results from impaired mineralization of growing bone. The disease remains prevalent in many developing nations, and contributes to childhood disability and morbidity.[1,2] Deficiency of vitamin D may cause nutritional rickets, but recent evidence suggests dietary calcium deficiency may more frequently cause rickets in tropical countries.[3–5]

Radiographic changes of active rickets are evident at the growth plate (physis) of rapidly growing long bones. These changes reflect expansion of the cartilaginous growth plate and delayed mineralization. The junction of the mineralizing metaphysis with the cartiliginous physis (zone of provisional calcification) increases in longitudinal thickness. Consequently, the lucent gap between metaphysis and epiphysis expands because the shadow of the zone of provisional calcification is partially or totally invisible.[6] The rachitic metaphysis can appear indistinct, frayed, and irregular on radiographs.[7] The visible calcified margin of the metaphysis can be concave and spread transversely, resulting in a cupped, 'champagne-glass' shape. Other radiographic signs of rickets include generalized osteopenia, green-stick fractures, delayed appearance of ossification centres, and curving of long bones.

To our knowledge, no radiographic index for assessing the severity of rickets has been in general use. Consequently, it is difficult to measure objectively radiographic response to treatment over time, or to compare different groups of subjects by disease severity. Scoring methods have been developed for other disorders, such as osteoarthritis[8] and rheumatoid arthritis,[9] to quantify disease severity. Radiographic scoring methods are particularly suited to diseases like rickets, where radiographic findings reflect disease pathophysiology.[9] To facilitate comparison of the radiographic severity by researchers and clinicians, we developed and prospectively evaluated a 10-point scoring method based on radiographs of the wrists and knees.

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Methods

Study subjects

Bilateral posteroanterior radiographs of the wrists and knees were obtained for children with clinical

TABLE 1
Ten-point radiographic scoring method for rickets

WRIST[a]—score both radius and ulna separately		
	Grade	Radiographic features
	1	Widened growth plate, irregularity of metaphyseal margin, but without concave cupping
	2	Metaphyseal concavity with fraying of margins
2 bones × 2 points = 4 points possible		
KNEE[a]—score both femur and tibia separately		
Multiply the grade in A by the multiplier in B for each bone, then add femur and tibia scores together		
A:	Grade	Degree of lucency and widening of zone of provisional calcification
	1	Partial lucency, smooth margin of metaphysis visible
	2	Partial lucency, smooth margin of metaphysis not visible
	3	Complete lucency, epiphysis appears widely separated from distal metaphysis
B:	Multiplier	Portion of growth plate affected
	0.5	≤ 1 condyle or plateau
	1	2 condyles or plateaus
2 bones × 1 point × 3 points = 6 points possible		
Total: 10 points possible		

[a]Score the worst knee and the worst wrist.

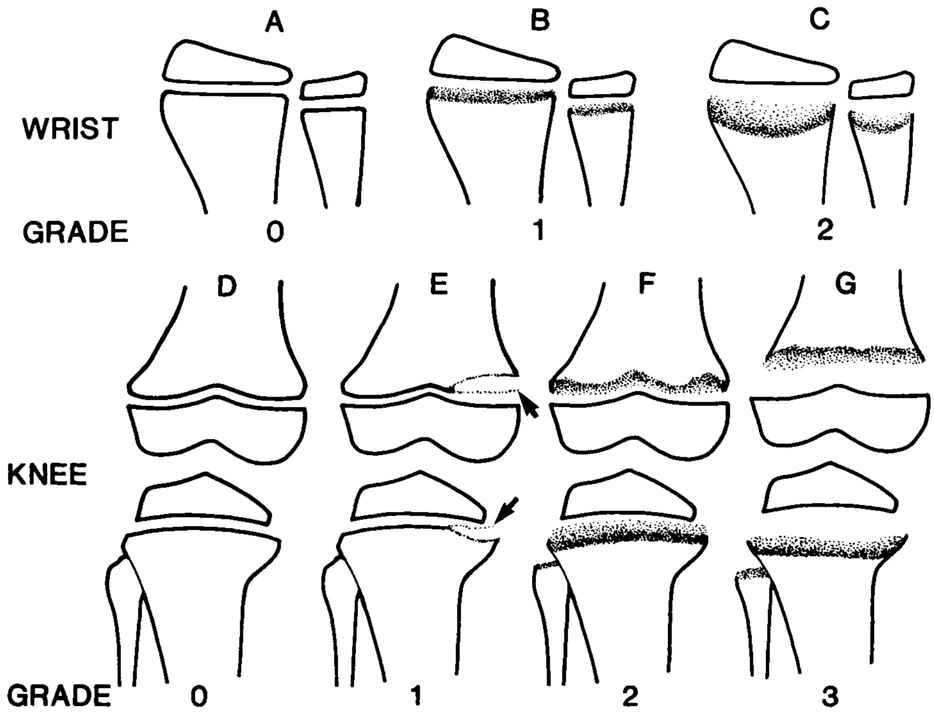

FIG. 1. Diagram of various grades of radiographic changes in rickets. A: a normal wrist; B: irregularity and widening of the growth plate, but without concave cupping; C: concave metaphyseal cupping and frayed margins. D: a normal knee. E: only the medial portions of the femoral and tibial metaphyses are affected. There is partial lucency of the metaphyses, but the margins are clearly visible (arrows). F: partial lucency of the metaphyses, but the margins are not sharply defined. However, the zones of provisional calcification are not completely lucent and display some calcification. G: complete lucency of the zone of provisional calcification. The epiphyses appear widely separated from the distal metaphyses.

deformities of rickets (genu varum, genu valgum, widened wrists) as part of a study of nutritional rickets in Nigeria. All children were between the ages of 1 and 14 years.

Participation was voluntary and written informed consent was obtained from the parent or guardian of each subject. Approval for the study was obtained from the Nigerian Ministry for Health and the Ethical Review Boards of the Jos University Teaching Hospital and the University of Utah.

Scoring method

A 10-point scoring method was devised to measure the severity of radiographic changes in the wrists and knees (Table 1). Changes in the radius and ulna were graded according to the presence of fraying and irregularity of the metaphyseal margin and by the degree of concave cupping. The femur and tibia were scored by the degree of lucency and widening of the zone of provisional calcification and according to the proportion of the growth plate affected (Fig. 1). Examples of radiographs corresponding to various scores are shown in Figs 2–5.

Each radiograph was independently scored by four trained physicians on two separate occasions. For each radiograph the physician was blind to the score given by other physicians and to the score previously given in the first reading.

Serum was obtained from all subjects prior to treatment and within 2 weeks of radiography for measurement of alkaline phosphatase. Serum was stored at -70°C until transported on dry ice to the University of Utah. All samples were assayed together to exclude the effect of interassay variability.

Statistical methods

Pearson's r was used to quantify intraobserver and interobserver (between any two observers) correlation of radiographic scores and to compare radiographic scores with values of alkaline phosphatase. In addition, the intraclass correlation coefficient was used to estimate interobserver agreement among all four observers combined.[10] The mean radiographic score for each radiograph was calculated from the eight individual scores (four observers $\times$ two readings each). The mean difference of scores was determined by calculating the difference in scores awarded by each observer pair (four observers gave six possible pairs) and then calculating the mean of the differences.

Results

The scoring method was tested on 67 radiographs of children with active rickets. Mean radiographic scores broadly represented all degrees of severity and correlated moderately well with serum alkaline phosphatase ($r = 0.58$, $p < 0.0001$; Fig. 6). The mean age of the children in our study was 4.5 years. We noted a weak inverse correlation of mean radiographic scores with age

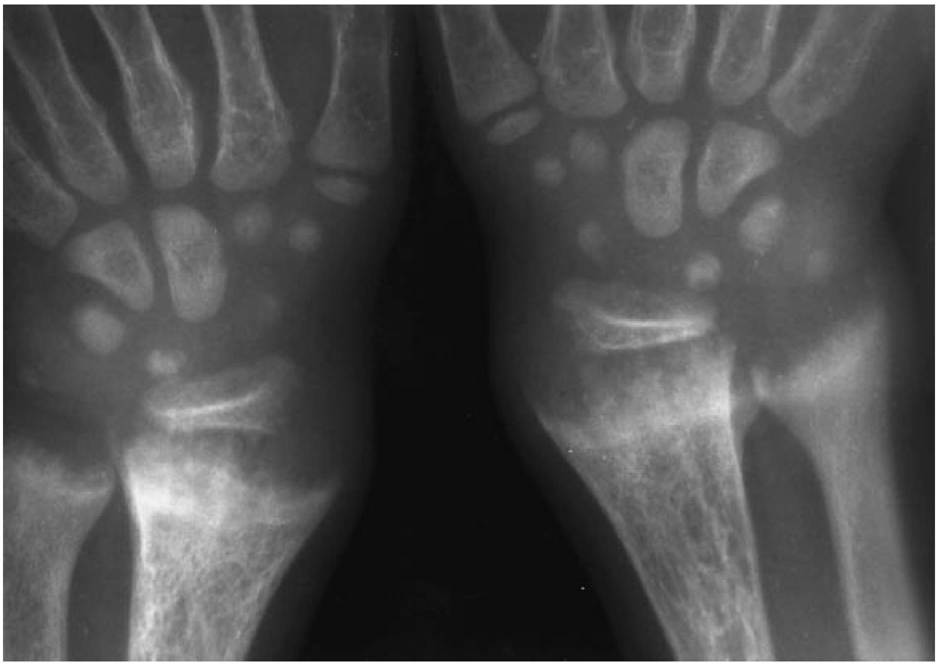

FIG. 2. Radiograph of wrist demonstrates fraying and concavity of the metaphyseal margins of both the radius and ulna. A score of two points each was given for the radius and ulna giving a wrist score of four points.

FIG. 3. Radiograph of knee shows broad, lucent zones of provisional calcification. The growth plates underlying both femoral condyles and both tibial plateaus are affected. A score of three points each was given for both the femur and the tibia giving a knee score of six points.

FIG. 4. Radiograph of knee shows partial lucency of the femoral zone of provisional calcification. The epiphysis does not appear separated from the metaphysis by a lucent zone as in Fig. 3. Note the absence of a distinct smooth margin of the mineralized femoral metaphysis. The femur and the tibia each scored two points for growth plate lucency. Both femoral condyles and both tibial plateaus are affected giving a knee score of four.

($r = -0.26$, $p = 0.03$). Both mean wrist and knee subscores individually correlated with alkaline phosphatase ($r = 0.50$, $p < 0.0001$ for the wrist; $r = 0.60$, $p < 0.0001$ for the knee).

Intraobserver correlation of radiographic scores was 0.84 or greater for all observer pairs (Table 2). The intraclass correlation for the radiographic scores was 0.82. Interobserver correlation of wrist sub-scores alone was 0.80 or greater, and of knee sub-scores alone it was 0.70 or greater for all six observer pairs. The intraclass correlations for wrist and knee sub-scores was 0.77 for each.

Intraobserver correlation of radiographic scores was 0.89 or greater for each of the four observers. Intraobserver correlation of wrist sub-scores alone was 0.83 or greater, and of knee sub-scores alone it was 0.80 or greater for each observer. The mean ($\pm$ SD) difference of scores recorded by separate observers (Fig. 7) was 1.49 ($\pm$ 0.75), and by the same observer at separate readings (Fig. 8) it was 0.74 ($\pm$ 0.50). The mean difference of scores did not vary with radiographic score or with age. Overall, 76 per cent of scores awarded by separate observers and 94 per cent of scores awarded by the same observer were within two points of each other.

We also tested agreement among observers in the assignment of grades to individual bones of the wrists and knees (Table 3). In the majority of cases, for each individual bone, the scores of at least three of four observers' were in perfect agreement. There was no relationship between the mean difference of observers' scores and the severity grade as measured by the mean score of four observers.

Discussion

We found that a 10-point radiographic scoring method for measuring the severity of nutritional rickets was reproducible between and within observers. Furthermore, radiographic scores correlated with alkaline phosphatase, another measure of disease activity. Because our ordinal scale of measurement ranges from zero to 10 in half-point increments, the ability to make

FIG. 5. Radiograph of knee shows partial lucency of the medial femoral growth plate, but the smooth margin of the distal metaphysis is clearly visible. The femur scored one point and the tibia two points for metaphyseal lucency. Only the medial femoral condyle and medial tibial plateau were scored as affected, giving a knee score of 1.5. In this child with genu varum, note that radiographic abnormalities are visible on the medial, weight-bearing side.

statistical comparisons between groups of children with rickets is enhanced. The scoring method can also measure response to treatment quantitatively.

The radiographic score may depend, in part, upon radiographic technique. If, for example, the plane of the metaphyseal–physeal junction is not perpendicular to the radiographic plate, the metaphyseal margins of the radius or ulna may appear concave and may be confused with early rickets. However, the two metaphyseal margins are generally visible in a normal subject and thus should not be confused with active disease.

In the knee, rotation of the femur or tibia could possibly mimic the mildest grade of rickets with partial lucency and a smooth, visible metaphyseal margin (Fig. 5). In rachitic children it can be difficult to obtain a true antero–posterior view of the knee due to marked bowing of the tibia and femur. However, radiographic appearance of this mild grade is unlikely to represent a purely rotational effect. When radiographic abnormalities are detected in the growth plate of only one femoral condyle or tibial plateau, they typically affect the weight-bearing side (medially in genu varum, laterally in genu valgum). Thus, it could be argued that these changes represent pressure effects on the bone rather than active rickets. Whether radiographic changes in the knee which we have designated the lowest grade reflect active rickets or healed rickets cannot be determined from our data. However, the utility of the scoring method in assessing severity is retained in either case. Furthermore, in treated subjects, we have observed a progression to less severe grades as healing occurs.

Age also affects growth plate appearance and could potentially alter the score awarded. When age was included as a covariate, there was minimal change in

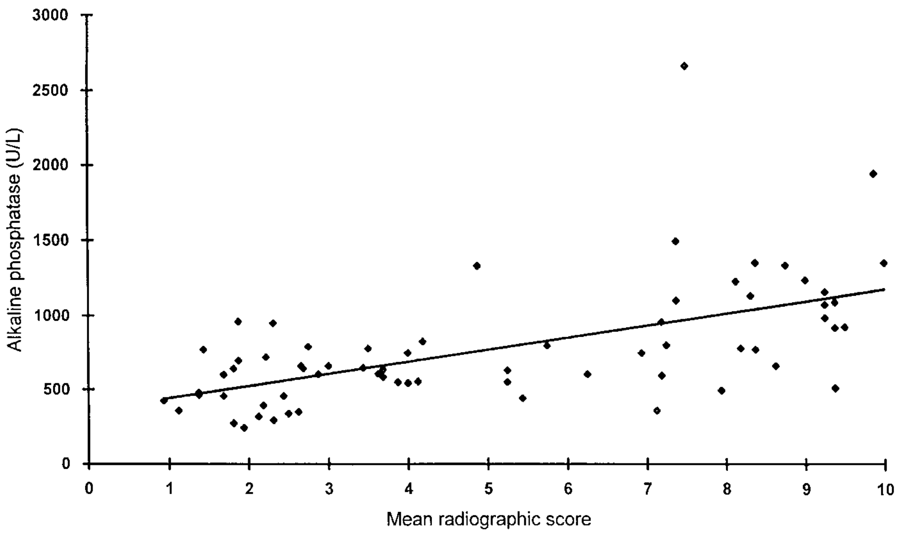

FIG. 6. Alkaline phosphatase values in relation to mean radiographic scores of four readers in 67 children with rickets. A least-squares regression line is drawn through the data points ($r = 0.58$, $p < 0.001$).

TABLE 2
Intraobserver and interobserver correlation (Pearson's r) of radiographic scores recorded for 67 children with rickets

		Observer			
		1	2	3	4
Observer	1	0.97			
	2	0.93	0.96		
	3	0.87	0.88	0.89	
	4	0.87	0.90	0.84	0.93

Ordinal numbers on column and row headings refer to four different observers. The outlined diagonal refers to intraobserver correlation of radiographic scores recorded by the same observer on two separate readings. All other values refer to interobserver correlation between radiographic scores recorded by the observers on the first reading.

the correlation of radiographic scores with alkaline phosphatase. We did not find the scoring method to have a limited use in any age group of children with rickets. The scoring system may become less useful as the growth plates narrow and close during and after puberty. However, few of the children in the study were pubertal and, thus, this possible problem could not be assessed.

Although different observers sometimes assigned different scores to the same radiograph, we were unable to ascribe the variability to a particular bone or severity of disease. Differences in observers' scores occurred with similar frequencies among all grades of severity and among all bone sites. Although we sought to make scoring radiographic changes of rickets objective, a degree of subjectivity remained in categorizing borderline radiographs. However, the proposed scoring method proved adequately reproducible for clinical use in spite of these limitations.

Our scoring method compares favourably with scoring methods in general use for osteoarthritis and rheumatoid arthritis. For example, using Kellgren and Lawrence grading scales for osteoarthritis, interobserver and intraobserver correlation, respectively, were 0.73 and 0.81 for distal interphalangeal joints, 0.83 and 0.83 for the knee, 0.42 and 0.52 for the lumbar spine, and 0.57 and 0.66 for the cervical spine.[8] These values are similar to our reported interobserver and intraobserver correlations of 0.84 and 0.89, respectively, for the 10-point rickets score.

In a study of skeletal changes in premature infants, Koo and colleagues classified abnormal wrist and ankle radiographs into three grades: grade 1 was loss of dense

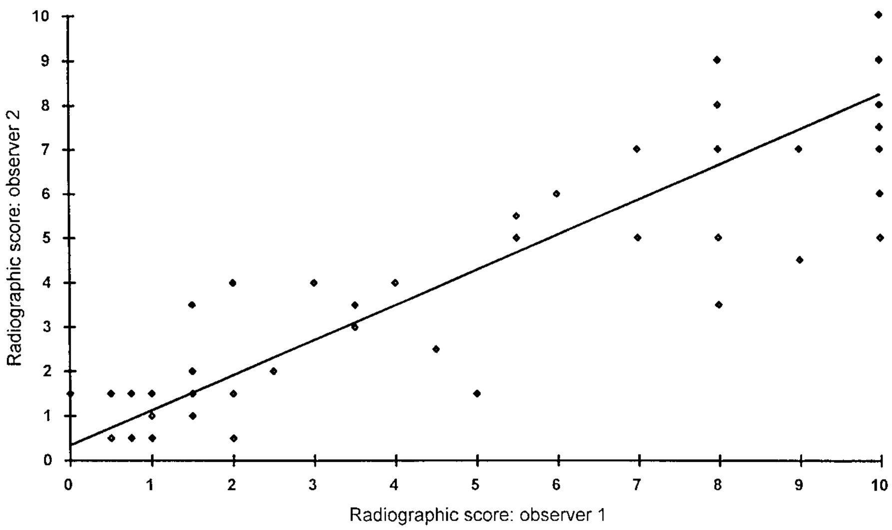

FIG. 7. Example of radiographic scores awarded by two individual observers. The horizontal axis represents the score awarded by one observer, and the vertical axis represents the score awarded by a second observer. Some points represent more than one pair of observations. A least-squares regression line is drawn through the data points ($r = 0.93$).

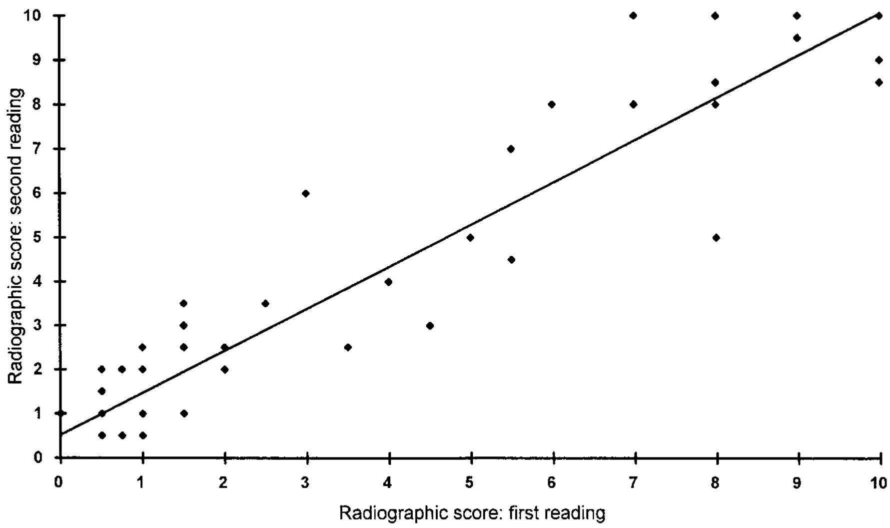

FIG. 8. Example of radiographic scores awarded by an individual observer on two separate occasions. The horizontal axis represents the first score awarded by the observer, and the vertical axis represents the second score. Some points represent more than one pair of observations. A least-squares regression line is drawn through the data points ($r = 0.97$).

TABLE 3
Number of scores in perfect agreement between four observers grading the severity of rickets at various sites in 67 subjects with rickets

Bone site	Three or more observer's scores in agreement	All four observers' scores in agreement	Mean (± SD) difference of scores[a]
Radius	56 (84%)	32 (48%)	0.28 (± 0.28)
Ulna	44 (67%)	18 (27%)	0.44 (± 0.30)
Femur	47 (70%)	21 (31%)	0.43 (± 0.36)
Tibia	34 (51%)	13 (19%)	0.60 (± 0.39)

[a]Mean difference of scores was determined by calculating the difference in scores awarded by each observer pair and then calculating the mean of the differences. When three of four observers' scores are in perfect agreement, and the remaining observer's score differs by one from the other three, the mean difference of scores is 0.5.

white line at metaphyses, increased submetaphyseal lucency, and cortical thinning; grade 2 included changes of grade 1 plus irregularity and fraying of metaphyses, with splaying and cupping; grade 3 included changes of grade 2 with evidence of fractures.[11] Because radiographic changes in premature infants reflect a different spectrum of disease than nutritional rickets,[12] Koo's grading system does not distinguish between various degrees of severity in nutritional rickets. Our scoring system does not include features of osteopenia and fractures used in defining Koo's grades 1 and 3, but instead describes changes of Koo's grade 2 in greater detail.

We considered including other radiographic features of rickets in the scoring method. Interpretation of osteopenia was judged to be too dependent upon radiographic technique. Measuring the actual width of the zone of provisional calcification was rejected because the metaphyseal margin is often indistinct and the width varies across the growth plate. Furthermore, in young children bone epiphyses may not be visible with plain radiographs, so the width of the growth plate cannot be measured. We chose to include features easily identified and interpreted, applicable even to those with limited radiographic facilities.

In summary, the 10-point scoring method for assessing the severity of rickets shows promise as a useful tool for researchers and clinicians. The scoring method is practical and not too cumbersome for day-to-day use by physicians in countries where rickets is prevalent. Scores were adequately reproducible for research and clinical use in our population, but we recommend validation of the scoring method in other populations.

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