

Calcium absorption in Nigerian children with rickets¹⁻⁴

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ABSTRACT

Background: Nutritional rickets is common in Nigerian children and responds to calcium supplementation. Low dietary calcium intakes are also common in Nigerian children with and without rickets.

Objective: The objective was to assess intestinal calcium absorption in Nigerian children with rickets.

Design: Calcium absorption was assessed in 15 children with active rickets (2–8 y of age) and in 15 age- and sex-matched children without rickets by using a dual-tracer stable-isotope method. The children with rickets were supplemented with calcium for 6 mo; calcium absorption was reevaluated 12 mo after the baseline study. Fractional calcium absorption could be determined in 10 children with rickets and in 10 children without rickets.

Results: The children with and without rickets had dietary calcium intakes of ≈ 200 mg/d. Compared with the control children, the children with rickets had lower serum 25-hydroxyvitamin D and calcium concentrations and greater 1,25-dihydroxyvitamin D and parathyroid hormone concentrations. In fact, there were 15 rachitic and 15 control children in the study. Mean (\pm SD) fractional calcium absorption did not differ between those with ($61 \pm 20\%$) and without ($63 \pm 13\%$) rickets ($P = 0.47$). Calcium absorption was not associated with serum concentrations of calcium, alkaline phosphatase, 25-hydroxyvitamin D, 1,25-dihydroxyvitamin D, or parathyroid hormone. Mean fractional calcium absorption was significantly greater after ($81 \pm 10\%$) than before ($61 \pm 20\%$) calcium supplementation for the treatment of rickets ($P = 0.035$).

Conclusions: In Nigerian children with rickets, the capacity to absorb calcium is not impaired; however, fractional calcium absorption increases after the resolution of active disease. Calcium absorption may be inadequate to meet the skeletal demands of children with rickets during the active phase of the disease, despite being similar to that of control children. *Am J Clin Nutr* 2004;80:1415–21.

KEY WORDS Stable isotopes, diet, vitamin D, calcium excretion, Nigeria, nutritional rickets, dietary calcium deficiency, intestinal calcium absorption

INTRODUCTION

Rickets causes bone deformities through the impaired mineralization of actively growing bone. Rickets is ranked among the 5 most prevalent diseases of young children in developing countries (1) and is frequently found in African (2–4), Asian (5, 6), and Middle Eastern (7, 8) settings. Up to 9% of children in central Nigeria have physical findings consistent with rickets (9),

including bowing of the legs, impaired mobility, pain, and pathologic fractures. Besides the long-term sequelae associated with the bone deformities, rickets is also associated with an increase in acute morbidity. In Ethiopia, a case-control study described a 13-fold greater prevalence of rickets among children with pneumonia than in control children (10).

Although nutritional rickets is often attributable to vitamin D deficiency (11), recent reports suggest that an insufficient calcium intake is also an important cause of rickets (12–15). Children with calcium-deficiency rickets have higher serum concentrations of 1,25-dihydroxyvitamin D [$1,25(\text{OH})_2\text{D}$] and parathyroid hormone and lower serum concentrations of calcium and 25-hydroxyvitamin D [$25(\text{OH})\text{D}$] than do children without rickets. Calcium supplementation, with or without vitamin D, heals rickets more rapidly in children than does vitamin D alone (12). However, despite uniformly low calcium intakes, calcium intakes are not lower in Nigerian children with rickets than in those without rickets (16). Reduced calcium absorption or relative resistance to $1,25(\text{OH})_2\text{D}$ could account for rickets in these children. No studies of calcium absorption in children with calcium-deficiency rickets have been reported. This study was designed to measure fractional calcium absorption in Nigerian children with and without rickets and to test the hypothesis that children with rickets have lower intestinal calcium absorption than do children without rickets.

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SUBJECTS AND METHODS

General design

We conducted a case-control study of children with and without rickets living in or around Jos, Nigeria, to compare calcium intake and fractional calcium absorption. This study was approved by the Jos University Teaching Hospital (JUTH) Ethics Review Committee and the University of Utah Health Science Center Institutional Review Board. Participation in the study was voluntary and written informed consent was obtained from the parent or guardian of each child before enrollment.

Recruitment and enrollment

Children with rickets ($n = 15$) aged 2 to 8 y of age, from the General Outpatient clinic of JUTH, participated in the study. Active rickets was defined radiographically as widening of the epiphyseal plate and metaphyseal cupping or fraying in the wrists and knees, corresponding to a score of ≥ 1.5 with the use of a validated 10-point scoring method (17). Fifteen unrelated, age- (within 8 mo) and sex-matched control children with no clinical signs of rickets were recruited by parents of rachitic children or hospital staff. Exclusion criteria for both groups of children included a history of renal or liver disease, tuberculosis, chronic diarrhea and the use of phenytoin and calcium or vitamin D supplements within 4 wk before enrollment.

Study design

We admitted enrolled children to a JUTH hospital ward at 0700 after the subjects had fasted overnight. Subjects voided to empty their bladders, and 10 mL blood was collected. After the blood collection, ^{44}Ca (0.03 mg in 2 mL normal saline) was administered intravenously over 20–30 s. Immediately afterward, ^{46}Ca (0.6 μg in 100 mL maize porridge) was given orally followed by a typical, standardized Nigerian breakfast of maize porridge and fried cakes of ground cowpeas. The breakfast was estimated to contain 80 mg Ca. A standard hospital diet that provided ≈ 200 mg Ca was given over the subsequent 24 h. Urine was collected for 24 h, and the volume was recorded.

For each child, we recorded the tribe, sex, religion, parents' education, family size, family history of rickets, current medication use, duration of breastfeeding, and age the child began walking. We measured standing height, weight, midarm circumference, and triceps-skinfold thickness using standard techniques. Midarm muscle area and fat area were also calculated (18, 19). No attempt was made to adjust for differences in height due to leg deformities. Dietary intakes of calcium, phosphorus, and energy were calculated from 2 different 24-h dietary recalls (one weekday and one weekend day) by using Nigerian nutrient data (20–22).

Biochemical analyses

Serum was stored at -20°C and transported frozen to the Mayo Clinic (Rochester, MN). Serum calcium, albumin, and alkaline phosphatase concentrations were measured by using standard methods. We measured serum 25(OH) $_2$ D concentrations by competitive protein binding assay after alcohol extraction (Nichols Institute Diagnostics, San Juan Capistrano). Serum concentration of 1,25(OH) $_2$ D was measured after C-18 column extraction by calf thymus radioreceptor assay using H^3 tracer (Nichols Institute Diagnostics, San Juan Capistrano, CA). Serum

1,25(OH) $_2$ D values reported as >150 pg/mL were assigned values of 150 pg/mL in the analysis if insufficient serum was available to characterize the values more precisely through serial dilution. Parathyroid hormone was measured by a two-site chemiluminescent immunometric assay with the Immulite automated system (Diagnostic Products Corp, Los Angeles).

Calcium isotopes in urine were measured by magnetic-sector thermal ionization mass spectrometry (Finnigan MAT, Bremen, Germany) after ammonium oxalate precipitation (23). We used the relative excretion of oral and IV administered calcium isotopes to calculate fractional absorption of calcium (α), by the following formula:

$$\alpha = \frac{\int_0^t \text{oral } ^{46}\text{Ca concentration in urine}}{\int_0^t \text{iv } ^{44}\text{Ca concentration in urine}} \quad (1)$$

where the numerator and the denominator represent the 24-h urinary excretion of ^{46}Ca and ^{44}Ca , respectively.

Treatment and follow up

After the baseline measurements, all 15 children with rickets were treated daily for 6 mo with chewable calcium carbonate tablets, which provided 1000 mg elemental Ca (400 mg in the morning and 600 mg in the evening). Healing of rickets was confirmed in all children by radiographs of the wrists and knees after 6 mo of treatment. Twelve months after the baseline study, calcium absorption was measured again in the 15 children with rickets after the resolution of active disease with the use of a protocol identical to that used in the baseline study, except that 2.7 mg ^{44}Ca was given intravenously and 8 μg ^{46}Ca orally to each child to increase the yield of isotope in urine.

Statistical analysis

Statistical analyses were performed with EXCEL 2002 (Microsoft Corp, Redmond, WA) and SPSS for Windows (version 8.0; SPSS Inc, Chicago). The sample size of 15 children in each group was chosen to provide 80% power to detect a difference of 20% in fractional calcium absorption between groups with an average SD of 16%. Anthropometric z scores were calculated with the nutritional anthropometric program of EPI INFO 2002 (Centers for Disease Control and Prevention, Atlanta) with the use of the 1978 Centers for Disease Control and Prevention/World Health Organization reference standards. Paired t tests were used to evaluate differences in normally distributed continuous variables between children with and without rickets. The unpaired Mann-Whitney U test was used to compare variables with skewed distributions between groups. P values < 0.05 were considered significant for all comparisons of differences. Pearson's correlation coefficients were determined to examine associations between continuous variables. Multiple linear regression analysis is not reported, because the small sample size precludes reliable interpretation.

RESULTS

Fifteen children with rickets and 15 control children were enrolled. Both groups had 6 boys and 9 girls ranging in age from 2 to 8 y. The group of children with rickets included 7 Muslim and



TABLE 1
Characteristics of children with and without rickets¹

Characteristic	Children with rickets (n = 15)	Children without rickets (n = 15)	P
Age (mo)	46 ± 22 ²	47 ± 22	0.86
No. of children in family	4.5 ± 3.0	4.0 ± 2.0	0.11
Duration of breastfeeding (mo)	14.5 ± 6.5	18.7 ± 3.4	0.08
Age started walking (mo)	17.8 ± 14.0	11.6 ± 2.4	0.11
Father's education (y)	11.5 ± 6.5	11.2 ± 5.0	0.62
Mother's education (y)	7.0 ± 5.6	9.6 ± 3.5	0.19
Height (cm)	83.6 ± 10.1	96.1 ± 10.3	<0.001
Weight (kg)	11.2 ± 2.6	14.1 ± 3.2	0.03
Weight-for-age z score	-2.7 ± 0.9	-1.1 ± 1.2	<0.001
Height-for-age z score	-3.9 ± 1.7	-1.0 ± 1.4	<0.001
Weight-for-height z score	-0.6 ± 1.3	-0.6 ± 0.8	0.96
BMI (kg/m ²)	16.0 ± 2.3	15.1 ± 1.2	0.11
TSF (mm)	7.3 ± 1.8	8.1 ± 2.4	0.42
MAC (mm)	146 ± 14	160 ± 13	0.02
MAC-for-age z score	-1.3 ± 1.1	-1.2 ± 1.8	0.84
AMA (mm ²)	1210 ± 20	1340 ± 42	0.26
AFA (mm ²)	500 ± 19	710 ± 36	0.11

¹ TSF, triceps-skinfold thickness; MAC, midupper arm circumference; AMA, arm muscle area = [MAC - (TSF × 3.14)]²/12.57; AFA, arm fat area = [(MAC)²/12.57] - AMA (24).

² $\bar{x} \pm SD$ (all such values).

8 Christian children compared with 4 Muslim and 11 Christian children in the control group ($P = 0.10$). There were no significant differences in family history of rickets, parental education level, age at which the child started to walk, or duration of breastfeeding between groups (**Table 1**). The children with rickets were significantly shorter and lighter but did not have greater wasting than did children without rickets (ie, no difference in weight-for-height between groups). However, the children with rickets had a lower midupper arm circumference than did the children without rickets.

Calcium, phosphorus, and energy intakes of the study participants are presented in **Table 2**. The mean dietary calcium intake of children in both groups was well below the dietary reference intakes of 500–800 mg/d for children in this age range (25) but

did not differ significantly between groups. When indexed to body weight (mg Ca · kg⁻¹ · d⁻¹) or to energy intake (mg Ca · 1000 kcal⁻¹ · d⁻¹), the calcium intake did not differ significantly between groups. Calcium intake derived from milk was very low in all children and did not differ significantly between groups.

Serum concentrations of alkaline phosphatase, parathyroid hormone, and 1,25-dihydroxyvitamin D values were significantly greater in children with rickets than in control children (**Table 3**). Serum 25(OH)D and calcium concentrations were significantly lower in children with rickets than in those without rickets. Two children with rickets (13%) had 25(OH)D values <12 ng/mL, consistent with vitamin D depletion. Serum concentrations of calcium correlated negatively with dietary calcium intake (**Figure 1**), serum alkaline phosphatase (**Figure 2**), and parathyroid hormone and positively with serum 25(OH)D (**Figure 3**) in children with rickets. These relations were not present in children without rickets.

Ten urine samples (5 children with rickets and 5 control subjects) were not included in the analysis of absorption results, because calcium isotope concentrations were below the limit of detection or because of fecal contamination. The characteristics of children who were excluded from the absorption analysis did not differ significantly from those who were included (data not shown). Urinary calcium excretion was lower in the children with rickets (0.72 ± 0.88 mg/d) than in the control children (1.06 ± 0.42 mg/d), but this difference was not significant ($P = 0.09$). We found no difference in fractional calcium absorption between the children with and without rickets (61 ± 20% and 63 ± 13%, respectively; $P = 0.47$). When the children with and without rickets were considered together, there were no significant relations of fractional calcium absorption with age ($r = 0.33$, $P = 0.16$), sex ($P = 0.28$), weight-for-age z score ($r = -0.42$, $P = 0.06$), weight-for-height z score ($r = -0.37$, $P = 0.11$), height for age z score ($r = -0.26$, $P = 0.27$), serum calcium ($r = -0.22$, $P = 0.34$), alkaline phosphatase ($r = 0.06$, $P = 0.79$), 25(OH)D ($r = -0.22$, $P = 0.36$), 1,25-dihydroxyvitamin D ($r = -0.08$,

TABLE 2
Dietary intakes of calcium, phosphorus, and energy

Characteristic	Children with rickets (n = 15)	Children without rickets (n = 15)	P
Calcium intake			
(mg/d)	198 ± 112 ¹	221 ± 85	0.32
(mg · kg ⁻¹ · d ⁻¹)	18 ± 12	16 ± 6	0.94
(mg · 1000 kcal ⁻¹ · d ⁻¹)	166 ± 87	172 ± 58	0.83
Calcium intake from milk			
(mg/d)	43 ± 62	34 ± 58	0.71
(% of total calcium intake)	22	15	0.43
Phosphorus intake			
(mg/d)	621 ± 242	754 ± 228	0.09
(mg · kg ⁻¹ · d ⁻¹)	57 ± 22	55 ± 17	0.92
(mg · 1000 kcal ⁻¹ · d ⁻¹)	526 ± 70	593 ± 134	0.10
Calcium:phosphorus intake	1:3	1:3	
Energy intake			
(kcal/d)	1167 ± 361	1288 ± 352	0.50
(kcal · kg ⁻¹ · d ⁻¹)	107 ± 36	94 ± 26	0.21

¹ $\bar{x} \pm SD$ (all such values).

TABLE 3

Serum concentrations of biochemical markers

Biochemical marker	Children with rickets, baseline (n = 15)	Children without rickets (n = 15)	P^1	Reference range	Children with rickets, after treatment (n = 15)	P^2
Calcium (mg/dL)	8.5 ± 0.8 ³	9.6 ± 0.4	<0.001	9.6–10.6	10.1 ± 0.7	<0.001
Albumin (g/dL)	4.7 ± 0.4	4.5 ± 0.5	0.23	3.5–5.0	4.2 ± 0.3	0.001
Alkaline phosphatase (IU/L)	2946 ± 1738	564 ± 138	<0.001	<400	701 ± 1358 ⁴	<0.001
25-Hydroxyvitamin D (ng/mL)	15 ± 5.4	29 ± 4.6	<0.001	8–38	22 ± 8.5	0.007
1,25-Dihydroxyvitamin D (pg/mL)	164 ± 37	130 ± 49	0.007	16–74	95 ± 42	0.005
Parathyroid hormone (pmol/L)	32 ± 33	4.0 ± 3.1	0.003	1.0–5.2	4.9 ± 2.1	0.007

¹ For the baseline comparison of children with and without rickets.² For the comparison of values after treatment with those at baseline.³ $\bar{x} \pm SD$ (all such values).⁴ After exclusion of an outlier of 5412 IU/L, the value was 339 ± 75 IU/L.

$P = 0.75$), and parathyroid hormone ($r = 0.20$, $P = 0.40$). Remarkably, even the 2 children with 25(OH)D values <5 ng/mL had high fractional calcium absorption (ie, 76% and 88%). Fractional calcium absorption was inversely related to estimated dietary calcium intake in the control children ($r = -0.83$, $P = 0.005$), but no such relation was found in the children with rickets ($r = 0.51$, $P = 0.13$; **Figure 4**). Among the children with rickets, fractional calcium absorption was moderately, but not significantly, related to the radiographic severity of rickets ($r = 0.40$, $P = 0.25$).

Serum 1,25(OH)₂D concentrations were not significantly related to fractional calcium absorption or to 25(OH)D concentrations in the children with [$r = -0.29$, $P = 0.41$ for fractional calcium absorption and $r = 0.40$, $P = 0.16$ for 25(OH)D] or without [$r = 0.10$, $P = 0.78$ for fractional calcium absorption and $r = -0.39$, $P = 0.16$ for 25(OH)D] rickets. Serum 1,25(OH)₂D concentrations were related to parathyroid hormone concentrations in the children with rickets ($r = 0.60$, $P = 0.02$) but not in the children without rickets ($r = 0.28$, $P = 0.32$).

All 15 children with rickets had radiographic resolution or improvement of rickets after 6 mo of treatment with supplemental calcium. The radiographic score declined from a mean (±SD) value of 6.3 ± 2.5 at baseline to 0.9 ± 0.9 after treatment ($P < 0.001$). The mean (±SD) estimated calcium intake 12 mo after baseline (195 ± 109 mg/d) was not significantly different from

baseline values ($P = 0.94$). At the 12-mo follow-up visit, the children with rickets had a height increase of 9.6 ± 2.1 cm and a weight increase of 2.8 ± 0.8 kg. Compared with baseline values, mean z scores of weight-for-height (-0.0 ± 1.1 ; $P = 0.008$), weight-for-age (-1.8 ± 0.9 ; $P < 0.001$), height-for-age (-2.9 ± 1.6 ; $P < 0.001$), and midupper arm circumference for age (-0.9 ± 0.9 ; $P = 0.004$) had improved significantly by the 12-mo follow-up visit. Biochemical improvement occurred in all children with rickets by the 12-mo follow-up study (Table 3).

We were able to determine the fractional absorption of calcium in 14 of the 15 children with rickets at the 12-mo follow-up visit. The fractional absorption of calcium 12 mo after baseline was significantly greater than the baseline values (81 ± 10% compared with 61 ± 20%; $P = 0.035$). The mean fractional calcium absorption in the 10 children with baseline data available was also 81 ± 10%. One child with ichthyosis, reported elsewhere (26), had a persistently elevated alkaline phosphatase concentration (5412 IU/L) and a persistently low 25-hydroxyvitamin D concentration (7 ng/mL). However, this subject's fractional absorption of calcium was 88%. At the 12-mo follow-up, the fractional calcium absorption of the entire group of children with rickets was not significantly related to 25(OH)D ($r = -0.30$, $P = 0.29$) or 1,25(OH)₂D ($r = -0.40$, $P = 0.18$) concentrations. However, 1,25(OH)₂D concentrations were directly related to 25(OH)D concentrations ($r = 0.60$, $P = 0.025$).

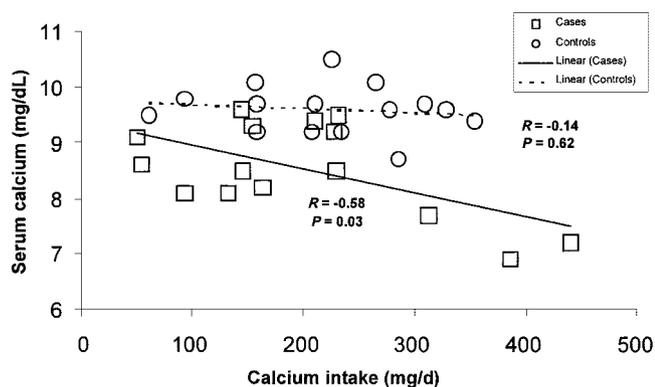


FIGURE 1. Relation of serum calcium with calcium intake in children with rickets (cases) and in matched control subjects. The regression lines of cases and control subjects are significantly different ($P \leq 0.01$). P values on the graph indicate whether the slope of the regression line is significantly different from zero.

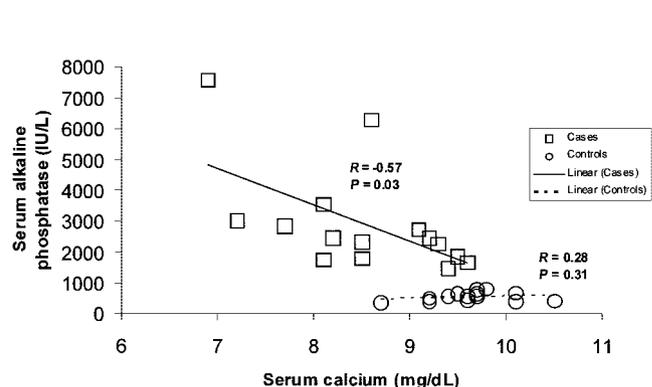


FIGURE 2. Relation of serum calcium with alkaline phosphatase concentrations in children with rickets (cases) and in matched control subjects. The regression lines of cases and controls are significantly different ($P \leq 0.01$). P values on the graph indicate whether the slope of the regression line is significantly different from zero.

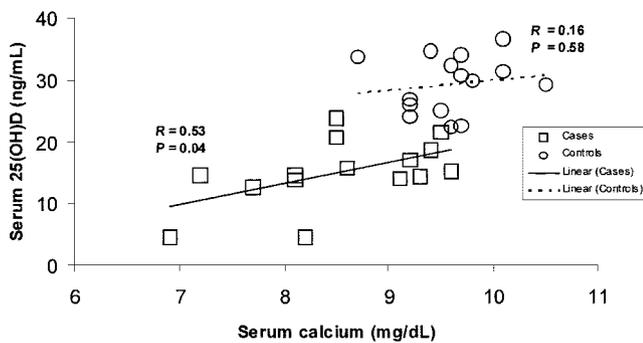


FIGURE 3. Relation of serum calcium with 25-hydroxyvitamin D [25(OH)D] concentrations in children with rickets (cases) and in matched control subjects. The regression lines of cases and controls are significantly different ($P \leq 0.01$). P values on the graph indicate whether the slope of the regression line is significantly different from zero.

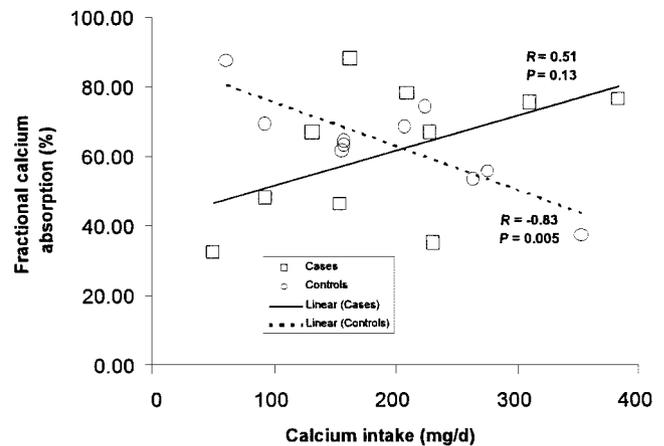


FIGURE 4. Relation of fractional calcium absorption with dietary calcium intake in children with rickets (cases) and in matched control subjects.

DISCUSSION

On the basis of the results of stable-isotope methods, we found no significant difference in fractional calcium absorption between the children with and without active rickets, despite lower 25(OH)D concentrations in the children with rickets. Calcium absorption was not related to estimated dietary calcium intake or to serum 1,25-dihydroxyvitamin D concentrations. After treatment, the children with rickets had significantly greater fractional calcium absorption and higher 25(OH)D concentrations but lower 1,25(OH)₂D and parathyroid hormone concentrations than they did before treatment.

Dietary calcium, phosphorus, and energy intakes in the children with and without rickets were not significantly different. The Nigerian diet includes a high amount of grains and seeds that contain phytic acid, a known inhibitor of calcium absorption. The estimated daily calcium intake in both groups of children was ≈ 200 mg, which is well below the dietary reference intake of 500–800 mg for children in this age range (25). The low ratio of calcium to phosphorus that we observed (1:3) has been shown in rats to lead to progressive bone loss (27). However, similar results were not observed in humans, and our data do not suggest a difference in phosphorus intakes between children with and without rickets. Dietary-recall methods and food-composition tables are not sufficiently sensitive to detect small differences in calcium and phosphorus intakes (28), and wide variation in the calcium and phosphorus contents of plant foods has been observed. In addition, possible differences in phytate intake between children with and without rickets could affect the bioavailability of absorbable calcium.

Mean calcium absorption was $\approx 60\%$ for the children with rickets and the age- and sex-matched control children. In US children aged 3–5 y of age, who had a relatively low calcium intake of 502 ± 99 mg/d, calcium absorption measured with the same technique as used in the current study was 36% (29). In that study, the load of calcium with the isotope was 150 mg/d, which is substantially higher than the value in the current study. However, on the basis of data in adults (30), calcium absorption in US children at a load of 80 mg/d would have been $\approx 45\%$, which is well below the value observed in the Nigerian children in the current study.

We were unable to show a relation between fractional calcium absorption and calcium intake, possibly because of the small range of calcium intakes and the limitations of the dietary-recall

method for estimating individual intakes. We suspect that Nigerian children have adapted to low calcium intakes via an increase in fractional calcium absorption in the gut. Additionally, the extremely low urinary calcium excretion observed suggests efficient renal reabsorption of calcium in an effort to conserve calcium. A similar average fractional calcium absorption of $63 \pm 10\%$ was reported in 19 healthy Chinese children aged 7-y with an average daily calcium intake of 360 mg (31). The investigators concluded that children accustomed to a habitually low-calcium diet were able to enhance the efficiency of calcium absorption. This conclusion is supported by the findings of a recent study of pubertal girls, whose fractional calcium absorption increased from 45% with a dietary calcium intake of 1259 mg/d to 63% with a dietary calcium intake averaging 389 mg/d (32).

We did not measure the endogenous secretory loss of calcium. This variable is likely to be decreased at high levels of fractional calcium absorption with a slope of 0.63 ± 0.15 for the relation between endogenous fecal calcium excretion and fractional absorption of calcium (33). The inability of some children to optimally conserve calcium via this mechanism may also be related to an increased risk of rickets, although no specific data are available to demonstrate this. It is also feasible that other micronutrient deficiencies, such as zinc, led to the inability to absorb or utilize calcium during acute rickets.

Biochemical differences between children with and without rickets were similar to those of previous studies (2, 13, 16). Despite lower 25(OH)D values in the children with rickets than in the children without rickets, both groups had high fractional calcium absorption. Theoretically, vitamin D–dependent mechanisms of absorption are more critical at lower than at higher intakes of calcium. All of the children with rickets had elevated 1,25(OH)₂D values. Calcium deficiency alone reduces serum 25(OH)D values, because elevated 1,25(OH)₂D concentrations increase the conversion of 25(OH)D to polar inactivation products that are excreted in the bile and feces (34, 35). The inverse relation of 25(OH)D values with alkaline phosphatase and parathyroid hormone and the positive relation with serum calcium support this mechanism for the reduction in 25(OH)D concentrations in the children with rickets. The fact that we did not observe the expected inverse relation of 25(OH)D with 1,25(OH)₂D among children with rickets may have resulted from the limitations of the laboratory methods. In 8 of the 15 children

with rickets, 1,25(OH)₂D values were reported as >150 pg/mL, and the quantity of sera was inadequate to further characterize these values. All children with rickets, even the 2 children with very low 25(OH)D concentrations, absorbed calcium efficiently, thus supporting the hypothesis that a calcium deficiency, rather than a vitamin D deficiency, was the primary mechanism that caused rickets in these children.

We could not exclude the possibility that dietary inhibitors of calcium absorption might be present in the children's usual diets eaten at home that were not present in the test meal. The test meal consisted of maize porridge, and maize is known to have a relatively high quantity of phytates. Preparation of the porridge includes soaking and partial fermentation of the maize. Because much of the phytic acid in cereals is water soluble and can be removed by diffusion, variation in the duration of soaking could result in variable quantities of phytate in maize porridge from different sources.

The greater fractional calcium absorption after the resolution of active rickets than before treatment began suggests that the metabolic state of active rickets could itself impair calcium absorption. It seems counterintuitive that the children with greater calcium absorption than the baseline values of control children would be prone to develop rickets. On the basis of the results of other studies, advancing age is associated with a declining fractional calcium absorption rather than with the increase that we observed. Another possibility is that, compared with the baseline study, the children had adapted to a lower calcium intake relative to their age and weight 12 mo later, which resulted in an increased fractional calcium absorption. Calcium absorptive capacity is related to both intake and height during puberty. As rickets resolves, rapid catch-up bone growth possibly results in a greater calcium absorption to mineralize the growing bone.

In summary, we found no evidence that impaired calcium absorption accounts for the development of rickets in Nigerian children. Future studies of the relations between calcium absorption and vitamin D metabolites will require larger sample sizes. The adaptation of fractional calcium absorption to variations in calcium intake and the effect of inhibitors of calcium absorption require further investigation. 

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MG developed the study design, carried out the absorption study, analyzed and interpreted the data, and wrote the manuscript originally as a thesis in partial fulfillment of the requirements for the degree of Master of Science in Foods and Nutrition. TDT developed the study design, enrolled the children, supervised and carried out the study, analyzed and interpreted the data, and wrote the manuscript. PRF and DS developed the study design, interpreted the results, supervised the writing of the thesis, and edited the manuscript. SDP developed the study design, enrolled the children, carried out the study, interpreted the data, and edited the manuscript. JMP conceived the study, developed the study design, interpreted the data, and edited the manuscript. COI developed the study design, enrolled the children, carried out the study, processed the samples, and edited the manuscript. SAA developed the study design and the absorption methodology, performed the isotope measurements, interpreted the data, and edited the manuscript. No author had any potential conflict of interest to report.

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