Nutritional rickets among children in the United States: review of cases reported between 1986 and 2003

Pamela Weisberg, Kelley S Scanlon, Ruowei Li, and Mary E Cogswell

ABSTRACT

Reports of hypovitaminosis D among adults in the United States have drawn attention to the vitamin D status of children. National data on hypovitaminosis D among children are not yet available. Reports from 2000 and 2001 of rickets among children living in North Carolina, Texas, Georgia, and the mid-Atlantic region, however, confirmed the presence of vitamin D deficiency among some US children and prompted new clinical guidelines to prevent its occurrence. We reviewed reports of nutritional rickets among US children <18 y of age that were published between 1986 and 2003. We identified 166 cases of rickets in 22 published studies. Patients were 4-54 mo of age, although in 17 studies the maximal age was <30 mo. Approximately 83% of children with rickets were described as African American or black, and 96% were breast-fed. Among children who were breast-fed, only 5% of records indicated vitamin D supplementation during breast-feeding. The American Academy of Pediatrics (AAP) recently recommended a minimal intake of 200 IU/d vitamin D for all infants, beginning in the first 2 mo of life. AAP recommends a vitamin D supplement for breast-fed infants who do not consume at least 500 mL of a vitamin D-fortified beverage. Given our finding of a disproportionate number of rickets cases among young, breast-fed, black children, we recommend that education regarding AAP guidelines emphasize the higher risk of rickets among these children. Education should also emphasize the importance of weaning children to a diet adequate in both vitamin D and calcium.

KEYWORDS Vitamin D deficiency, rickets, breast-feeding, case reports, children, African American children

INTRODUCTION

Recent studies reported high rates of hypovitaminosis D among adolescents and adults in the United States, particularly among black subjects (1-3). National data on the prevalence of hypovitaminosis D among children are not yet available; however, published reports from 2000 and 2001 of cases of nutritional rickets among young children living in North Carolina (4), Texas (5), Georgia (6–8), and the mid-Atlantic region (9) confirmed the presence of severe vitamin D deficiency among some US children and stimulated renewed interest in the disease and new American Academy of Pediatrics (AAP) clinical guidelines to prevent its occurrence (10).

Rickets is associated with biochemical abnormalities, bone deformities, impaired growth, developmental delays, and, late in the course of the disease, seizures. Vitamin D₃ functions with parathyroid hormone (PTH) to maintain intracellular and extracellular calcium concentrations within a physiologically acceptable range (11). When vitamin D concentrations are inadequate, intestinal absorption of calcium is decreased. The slight decrease in serum calcium concentrations that results stimulates PTH secretion, which in turn mobilizes calcium and phosphorus from bone to restore serum calcium concentrations to normal levels. Serum alkaline phosphatase (ALP) concentrations increase once clinical signs of rickets are apparent. Low serum 25-hydroxyvitamin D [25(OH)D] concentrations can confirm vitamin D deficiency as the cause of rickets if treatment with vitamin D has not yet been initiated, whereas serum 1,25-dihydroxyvitamin D concentrations can be low, normal, or elevated in vitamin D deficiency (11). The biochemical abnormalities detected vary, depending on the stage of deficiency and the PTH response in mobilizing calcium and phosphorus. The characteristic bone changes of rickets include bowing of the legs, rachitic rosary of the rib cage, frontal bossing, and epiphyseal enlargement of the wrists and ankles.

Vitamin D is available to humans through the photochemical action of sunlight or ultraviolet light on 7-dehydrocholesterol in skin and through dietary sources such as fish liver oils, fatty fish, and foods fortified with vitamin D, particularly liquid cow’s milk, infant formula, and breakfast cereals (11, 12). Infants with darkly pigmented skin are at elevated risk for deficiency because melanin in the skin competes with 7-dehydrocholesterol for ultraviolet-B photons, thus decreasing vitamin D₃ synthesis in the skin (12, 13).

In 1985, Cosgrove and Dietrich (14) reviewed 65 clinical cases of nutritional rickets that were reported between 1975 and 1985, in 11 publications, from medical centers in 9 US states. The children with rickets were 2-45 mo of age and were still breast-feeding or were consuming a milk-free vegetarian diet at the time of diagnosis. Among the 44 children for whom race was reported, 40 were described as black. The purpose of our study was to review all cases of nutritional rickets reported in the literature between 1986 and 2003 and to provide an expanded review of...
characteristics common to its occurrence. Information on common factors associated with rickets in the United States should help health care providers educate families regarding the new AAP clinical guidelines on preventing rickets and vitamin D deficiency, by emphasizing the children who are at greatest risk of deficiency.

METHODS

This review includes published case reports of nutritional rickets among children in the United States. The MEDLINE database was used to identify all case reports of rickets published between 1986 and 2003. Key words used in the MEDLINE search were rickets and vitamin D deficiency. The search was limited to reports of children < 18 y of age, in the United States. Eighteen articles met our selection criteria. Another 6 articles were identified from the references of the articles, for a total of 24 articles published between 1986 and 2003. The 24 publications reported on 22 case studies; 3 articles (6–8) reported on different cases and aspects of one case group. The cases reported were identified from inpatient and outpatient clinical records with various methods. We reviewed all reports to examine the region, month, and year of diagnosis, clinical findings, age, sex, race/ethnicity, infant feeding and supplementation practices, and exposure to sunlight. Abnormal clinical findings were designated by the medical laboratory or clinic making the assessment and were limited to those reported in the article. Reference ranges for the laboratory assays used varied among the studies, but there was insufficient information for individual cases to set standard cutoff values for this review. Furthermore, not all studies provided information on the biochemical assays performed.

RESULTS

Characteristics of the clinical rickets cases reported in the literature between 1986 and 2003 are presented in Table 1. The cases were ascertained through case findings and clinical encounters in at least 17 states and at 1 center representing the mid-Atlantic region (4–9, 15–32). The 17 states that reported cases represented all regions of the United States. A total of 166 cases of rickets were reported in the 22 case reports. Patients presented to the hospital or clinic with clinical signs such as delayed growth or motor development, inability to walk, bone abnormalities, or seizures and were diagnosed on the basis of radiographic, biochemical, or clinical evidence of rickets. Of the 159 cases with radiographs (one study had no radiographs for 7 cases) (18), all except 3 showed radiographic evidence of rickets, including metaphyseal flaring, cupping, or fraying. Of the 3 cases with no radiographic evidence, one involved an 8-mo-old child with normal radiographic findings but biochemical evidence of hypovitaminosis D, hypocalcemia, hyperparathyroidism, and elevated ALP concentrations who responded to vitamin D and calcium supplementation (23), one involved a 4-mo-old child with normal radiographic findings but biochemical evidence of hypocalcemia and elevated ALP concentrations who responded to vitamin D and who was described as a child with “biochemical rickets” by the authors (27), and one involved a 7-mo-old child with normal scout films of the abdomen and chest who presented with a hypocalcemic seizure, elevated ALP and PTH concentrations, and low serum 25(OH)D concentrations and who responded clinically to combined vitamin D and calcium supplementation (26).

Biochemical indicators reported in the studies included low serum 25(OH)D concentrations for 68% of the children tested (67 of 98 children), hypocalcemia for 55% of those tested (77 of 141 children), hypophosphatemia for 64% of those tested (95 of 148 children), elevated ALP concentrations for 99% of those tested (142 of 144 children), and hyperparathyroidism for 94% of those tested (74 of 79 children). Biochemical studies were sometimes performed after treatment with vitamin D had been initiated, as was the case for the 4 children with normal serum 25(OH)D concentrations in the North Carolina study (4). Clinical findings included seizures, failure to thrive, delay or regression in motor development, weight-for-age or length-for-age less than the 5th percentile, and bone abnormalities, such as bowing of the legs, fractures, rachitic rosary, frontal bossing, or widened wrists and ankles.

The children with rickets described in the 22 case studies ranged from 4 to 54 mo in age at the time of diagnosis (Table 1). In 17 studies, however, the maximal age at diagnosis was < 30 mo. Only 3 studies presented cases involving children < 6 mo of age (4, 27, 32). When mean ages were reported (15 studies), they ranged from 10.5 to 25 mo. Among the 12 studies that reported the length of gestation for all cases (5, 6, 9, 17, 19, 21–24, 30–32), all except 2 cases were described as full term (37 wk of gestation completed). The 2 preterm cases were 35-wk gestations (data not shown) (32).

Most studies provided the sex and racial/ethnic distribution of cases, indicating that overall 54% of cases (80 of 148 cases) with reported sex were male and 83% (138 of 166 cases) were African American or black, 4% nonwhite (of African American or Indian decent), 6% white, 2% Hispanic, 2% Alaskan native, and ≤ 1% Middle Eastern, Asian, or unknown. The 5 studies that reported cases among white children were reports from northern states, ie, Washington, Minnesota, New York, Connecticut, and New Hampshire (18, 23, 27, 30, 32).

A common characteristic among cases was that the dietary history indicated that the children were breast-fed without vitamin D supplementation. All except 7 cases (96%, 152 of 159 cases) for which this information was reported involved children who were breast-fed. Among the 151 children who were breast-fed and for whom it was reported whether supplementation was used, only 8 (5%) received a vitamin D supplement during the breast-feeding period, as indicated in the medical records or by the parent (18, 25, 27, 32). Administration of the supplement was reported as sporadic or intermittent for 2 of those children. Among the studies that reported on liquids introduced after weaning (6, 15, 17, 18, 25, 30), consumption of vitamin D-fortified milk was reported by the parents for only 3 children (15, 18, 25) and a vitamin D-enriched soy beverage was reported by the parent of 1 child (30). The authors of 5 studies made qualitative comments about poor overall dairy consumption among the patients (5, 17, 24, 27, 32). Kreiter et al (4) reported poor intake of fortified cow’s milk and other dairy foods among patients ≥ 1 y of age.

Twelve studies provided information on sunlight exposure, but they varied greatly in how they reported exposure (5, 6, 16, 17, 19–22, 24, 27, 29, 31). Parents interviewed by Tomashek et al (6) responded that sun exposure was minimal for 3 of 6 children with rickets. The mother of one child with rickets presented by Bhowmick et al (19) reported that she restricted sunlight exposure for the first 8 mo of her infant’s life, and the mother of
Cases with vitamin D treatment. The vitamin D was administered in all rickets cases to treatment (data not shown). Those studies reported resolution of the radiographic and biochemical features of all rickets cases with vitamin D treatment. The vitamin D was administered with or without the addition of a calcium supplement or dairy foods. DeLucia et al (32) reported on responses to treatment for 3 of the 43 cases presented and found that 1 case responded to supplementation without vitamin D.

**TABLE 1**

Reports of rickets cases in the United States published between 1986 and 2003

<table>
<thead>
<tr>
<th>Author and year (ref)</th>
<th>Data source</th>
<th>Study duration (mo)</th>
<th>No. of cases</th>
<th>Season of diagnosis</th>
<th>Clinical findings (no. of cases/no. assessed)</th>
<th>Age (mo) at diagnosis, range (mean)</th>
<th>Sex</th>
<th>Racial/ethnic distribution</th>
<th>Infant diet, supplement use during breast-feeding, and sunlight exposure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jacobsen et al, 1986 (15)</td>
<td>Case reports from outpatients in Cincinnati, Ohio, 1/1981–5/1983</td>
<td>29</td>
<td>8</td>
<td>All in winter or spring</td>
<td>Radiographic evidence of rickets (8/8); low phos (5/7); high PTH (8/8); low PTH (1/8); seizure (1/8); w/a &lt; 5th %ile (5/8); l/a &lt; 5th %ile (7/8); skeletal abnormalities (2/8); fracture (1/8)</td>
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<tr>
<td>Hayward et al, 1987 (16)</td>
<td>Case reports from outpatient in San Diego, California</td>
<td>Not provided</td>
<td>1</td>
<td>Not provided</td>
<td>Radiographic evidence of rickets; low Ca; low phos; high ALP; high 1,25(OH)2D; high protein; high albumin; l/a &lt; 5th %ile; w/a &lt; 5th %ile; skeletal abnormalities</td>
<td></td>
<td></td>
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<tr>
<td>Kruger et al, 1987 (17)</td>
<td>Case reports from orthopedic clinic in Michigan</td>
<td>Not provided</td>
<td>3</td>
<td>All in winter or spring</td>
<td>Radiographic evidence of rickets (3/3); low Ca (1/2); low phos (2/2); high ALP (2/2); low 25(OH)D (2/2); high 1,25(OH)2D (2/2); w/a ≤ 5th %ile (2/3); (l/a) ≤ 5th %ile (1/3); abnormal gait (1/3); frontal bossing (1/3); rachitic rosary (2/3)</td>
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<tr>
<td>Feldman and Marcus, 1990 (18)</td>
<td>Case reports from clinic in Seattle, Washington</td>
<td>Not provided</td>
<td>18</td>
<td>6 in winter, 10 in spring/summer, 2 in fall</td>
<td>Radiographic evidence of rickets (11/11); low Ca (5/16); low phos (5/16); high ALP (16/17); hypocalcemic seizure (2/18); tetany (1/18); b/a &lt; 5th %ile (8/18); w/a &lt; 5th %ile (3/18); bowing of legs (14/18); dental abnormalities (2/18)</td>
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<tr>
<td>Bhowmick et al, 1991 (19)</td>
<td>Case reports from pediatric clinic in Mississippi</td>
<td>Not provided</td>
<td>4</td>
<td>Not provided</td>
<td>Radiographic evidence of rickets (4/4); low Ca (0/4); low phos (2/4); high ALP (4/4); high PTH (3/3); low 25(OH)D (3/3); w/a ≤ 5th %ile (4/4); b/a ≤ 5th %ile (4/4); bowing of legs (2/4); muscle weakness (1/4); FTT (3/4)</td>
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(Continued)

the child presented by Hayward et al (16) reported that she remained indoors with her child most of the time. In 7 other studies, the authors provided qualitative reports that some of the children with rickets were not outside very often (20, 21, 27, 29, 31) or had “limited sunlight exposure” (16, 17). Shah et al (5) reported that there was no evidence of reduced sunlight exposure for the 9 “limited sunlight exposure” (16, 17). Shah et al (5) reported that there was no evidence of reduced sunlight exposure for the 9

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**DISCUSSION**

In a 1985 review, Cosgrove and Dietrich (14) described characteristics of 65 cases of nutritional rickets reported in the literature between 1975 and 1985. The cases described involved children 2–45 mo of age who had been breast-fed and either were Group 5

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</tr>
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<tbody>
<tr>
<td>Key, 1991 (20)</td>
<td>Case reports (1 from Massachusetts, 2 from unspecified location)</td>
<td>Not provided</td>
<td>3</td>
<td>1 in winter, 2 unknown</td>
<td>Radiographic evidence of rickets (3/3); low Ca (2/3); low phos (2/3); high ALP (3/3); high PTH (1/3); low 25(OH)D (3/3); low 1,25(OH)2D (1/3); growth delay (1/3); h/a &lt; 5th %ile (3/3); ceased walking and crawling (1/3); bone abnormalities (2/3); bowing of legs (1/3); hypotonic (1/3); developmental delay (1/3)</td>
<td>12–36 (22.7)</td>
<td>All male</td>
<td>All black</td>
<td>2 breast-fed (duration: &gt; 9 mo); feeding not specified for 1 child; 1 family strict vegetarian; 1 child ate vending machine food and occasional raw milk; no vitamin D given during breast-feeding; 1 child not taken outside during winter</td>
</tr>
<tr>
<td>Sills et al, 1994 (21)</td>
<td>Case reports from 1 hospital in New Jersey</td>
<td>36</td>
<td>7</td>
<td>2 in spring, 3 in summer, 2 in fall</td>
<td>Radiographic evidence of rickets (7/7); low Ca (3/7); low phos (2/7); high ALP (7/7); high PTH (5/6); low 25(OH)D (7/7); short stature (1/7); delayed walking (1/7); bone abnormalities (7/7); fracture (1/7)</td>
<td>15–29 (18)</td>
<td>Not given</td>
<td>All black</td>
<td>All breast-fed (duration unknown); all with diet low in calcium and vitamin D; 4 children were vegetarian; no vitamin D given during breast-feeding; children spent most time indoors</td>
</tr>
<tr>
<td>Colson et al, 1996 (22)</td>
<td>Case report from unspecified state</td>
<td>Not provided</td>
<td>1</td>
<td>Spring</td>
<td>Radiographic evidence of rickets; low Ca; low phos; high ALP; low 25(OH)D; h/a ≤ 5th %ile; thickened wrists</td>
<td>9</td>
<td>Male</td>
<td>Black</td>
<td>Breast-fed; consumes small amounts of fruits and vegetables; no vitamin D given during breast-feeding; little exposure to sunlight</td>
</tr>
<tr>
<td>Euggster et al, 1996 (23)</td>
<td>Case reports from outpatient records in Twin City, Minnesota, metropolitan area, 4/1994–2/1995</td>
<td>10</td>
<td>7</td>
<td>3 in winter, 4 in spring</td>
<td>Radiographic evidence of rickets (6/7); low Ca (5/7); low phos (6/7); high ALP (7/7); high PTH (7/7); low 25(OH)D (5/7); low normal 25(OH)D (2/7); high 1,25(OH)2D (2/7); tetany (1/7); seizure (1/7); h/a &lt; 5th %ile (4/7); w/a &lt; 5th %ile (4/7); enlarged wrists (5/7); rachitic rosary (3/7); frontal bossing (1/7); neurologic symptoms (2/7); FTT (2/7); motor regression (1/7); developmental delay (1/7)</td>
<td>6–20</td>
<td>Not given</td>
<td>3 black, 2 white, 1 Iranian, 1 mixed race,</td>
<td>All breast fed; no vitamin D given during breast feeding; no information on sunlight</td>
</tr>
<tr>
<td>Gessner et al, 1997 (24)</td>
<td>Case reports from outpatient records at 3 medical institutions in Alaska, 1993-1996</td>
<td>36</td>
<td>5</td>
<td>2 in winter, 1 in spring, 2 in fall</td>
<td>Radiographic evidence of rickets (5/5); low Ca (4/5); low phos (3/5); high ALP (4/5); seizure/anorexia (1/5); growth delay (1/5); h/a ≤ 5th %ile (3/5)</td>
<td>11–20 (15.5)</td>
<td>2 male, 3 female</td>
<td>3 black; 2 Alaskan native</td>
<td>All breast fed (duration unknown); breast milk only milk source for 2 children; 4 children on table foods; 3 children refused most dairy products; no vitamin D given during breast feeding; limited sunlight assumed because of season</td>
</tr>
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</table>

(Continued)
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<th>Author and year (ref)</th>
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<tr>
<td>Menking, 1997 (25)</td>
<td>Case reports from pediatric endocrinology clinic in Wichita, Kansas</td>
<td>Not provided</td>
<td>2</td>
<td>Spring</td>
<td>Radiographic evidence of rickets (2/2); low Ca (1/2); low phos (2/2); high ALP (2/2); low 25(OH)D (1/1); high 1,25(OH)D (2/2); l/a 5th %ile (1/1); rachitic rosary (1/2); thickened wrist</td>
<td>7–14 (10.5)</td>
<td>Not provided</td>
<td>All black</td>
<td>All breast fed (duration: 7–12 mo); 1 child weaned to 16 ounces milk daily at 12 mo; 1 child given 400 IU vitamin D 3 times per week from age 4 wk; 1 child not given vitamin D during breast feeding; no information on sunlight</td>
</tr>
<tr>
<td>Moss, 1997 (26)</td>
<td>Case report from hospital emergency department in Juneau, Alaska, 1997</td>
<td>Not provided</td>
<td>1</td>
<td>Spring</td>
<td>No radiographic evidence of rickets; low Ca; normal phos; high ALP; low 25(OH)D; hypocalcemic seizure; no rachitic rosary, wrist thickening, or frontal bossing</td>
<td>7</td>
<td>Male</td>
<td>Alaskan native</td>
<td>Breast fed; recent introduction of cereal and fruit; no vitamin D given during breast-feeding; no information on sunlight</td>
</tr>
<tr>
<td>Pugliese et al, 1998 (27)</td>
<td>Case reports from 1 medical center (inpatient and outpatient emergency) in Nassau, New York</td>
<td>Not provided</td>
<td>4</td>
<td>Not provided</td>
<td>Radiographic evidence of rickets (3/4); low Ca (3/4); low phos (3/4); high ALP (4/4); high PTH (3/4); low 25(OH)D (2/4); high 1,25(OH)D (2/4); low 1,25(OH)D (1/4); iron deficiency (2/4); seizures (1/4); l/a 5th %ile (3/4); w/a 5th %ile (3/4); head circumference 10–25 %ile (2/4); skeletal abnormalities (3/4)</td>
<td>4–24 (14)</td>
<td>1 male, 3 female</td>
<td>3 black, 1 white</td>
<td>All breast fed (duration: 3.5–11 mo); introduction of fruits, vegetables, and cereal, but no significant source of dairy products; 1 child given vitamin D intermittently during breast feeding; 1 child stayed indoors (4 mo old)</td>
</tr>
<tr>
<td>Herman and Bulthuis, 1999 (28)</td>
<td>Case reports, location not provided</td>
<td>Not provided</td>
<td>2</td>
<td>Not provided</td>
<td>Radiographic evidence of rickets; low Ca (1/2); high ALP (2/2); l/a 5th %ile (1/2); w/a 5th %ile (1/2); right clavicle fracture (2/2)</td>
<td>14–15 (14.5)</td>
<td>Not provided</td>
<td>1 black, 1 not specified</td>
<td>Both children breast fed (duration: 13–15 mo); no vitamin D given during breast feeding; no information on sunlight exposure</td>
</tr>
<tr>
<td>Fitzpatrick et al, 2000 (29)</td>
<td>Case report, Vermont</td>
<td>Not provided</td>
<td>1</td>
<td>Winter</td>
<td>Radiographic evidence of rickets; low Ca; low phos; high ALP; high PTH; low 25(OH)D; normal 1,25(OH)D; unable to walk; bowing of legs; frontal bossing; flared radii; flared distal tibiae</td>
<td>13</td>
<td>Male</td>
<td>Black</td>
<td>Breast fed for 12 mo with limited table foods introduced at 12 mo (fruit, pasta, rice, and beans); no vitamin D given during breast feeding; child rarely outside during infancy</td>
</tr>
<tr>
<td>Kaper et al, 2000 (30)</td>
<td>Case reports from New Hampshire and Connecticut</td>
<td>36</td>
<td>4</td>
<td>Not provided</td>
<td>Radiographic evidence of rickets (4/4); low Ca (0/3); low ionized Ca (1/1); low phos (3/4); high ALP (4/4); l/a 5th %ile (1/4); w/a 5th %ile (1/4); bowing of legs (4/4); rachitic rosary (2/4); widening of elbows, wrists, knees, or ankles (3/4)</td>
<td>20–38 (25)</td>
<td>2 male, 2 female</td>
<td>3 black, 1 white</td>
<td>3 breast fed (duration: 16–20 mo); for 1 child infant feeding not specified but vegan diet with vitamin D enriched soy milk indicated; 1 child poor eater once weaned; no vitamin D given during breast feeding; no information on sunlight exposure</td>
</tr>
<tr>
<td>Author and year (ref)</td>
<td>Data source</td>
<td>Study duration (mo)</td>
<td>No. of cases</td>
<td>Season of diagnosis</td>
<td>Clinical findings (no. of cases/no assessed)</td>
<td>Age (mo) at diagnosis, (mean)</td>
<td>Sex distribution</td>
<td>Racial/ethnic distribution</td>
<td>Infant diet, supplement use during breast-feeding, and sunlight exposure</td>
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<tr>
<td>Kreiter et al, 2000 (4)</td>
<td>Case finding through review of records at 2 medical centers in North Carolina, 1/1990–6/1999</td>
<td>114</td>
<td>30</td>
<td>14 in spring, 16 in winter/fall</td>
<td>Radiographic evidence of rickets (30/30); low Ca (18/30); low phos (29/30); high ALP (30/30); low 25(OH)D (19/23); hypocalcemic tetany/seizures (2/30); lα &lt; 5th %ile (17/26); skeletal abnormalities (16/30); FTT (13/30); developmental delay (1/30)</td>
<td>5–25 (14.9)</td>
<td>17 male, 13 female</td>
<td>All black</td>
<td>All breast fed (duration: 5–24 mo); poor intake of fortified cow’s milk or other dairy foods among children age ≥ 1 yr; no vitamin D given during breast-feeding; no information on sunlight</td>
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<tr>
<td>Shah et al, 2000 (5)</td>
<td>Case reports from referrals to 2 hospitals in Dallas, Texas, 6/1995–10/1998</td>
<td>40</td>
<td>9</td>
<td>Not provided</td>
<td>Radiographic evidence of rickets (9/9); low Ca (5/9); low phos (5/9); high ALP (8/8); high PTH (9/9); low 25(OH)D (8/9); high 1,25(OH)₂D (6/8); hypocalcemic seizure (1/9); lα &lt; 5th %ile (5/9); inability to walk (1/9); skeletal abnormalities (9/9); FTT (1/9)</td>
<td>8–23 (16.1)</td>
<td>4 male, 5 female</td>
<td>8 black, 1 Mexican American</td>
<td>All breast fed (duration: 8–14 mo); minimal intake of dairy products; no vitamin D given during breast-feeding; no evidence of reduced sun exposure</td>
</tr>
<tr>
<td>Biser-Rohrbough et al, 2001 (9)</td>
<td>Case reports from referrals to Johns Hopkins Hospital for bowleggedness and intoeing, mid-Atlantic region, United States, 1995–1998</td>
<td>36</td>
<td>6</td>
<td>Not provided</td>
<td>Radiographic evidence of rickets (6/6); low phos (1/2); high ALP (2/2); high PTH (2/2); low 25(OH)D (1/2); high 1,25(OH)₂D (1/2); skeletal abnormalities (2/2)</td>
<td>12–37 (25)</td>
<td>All female</td>
<td>All nonwhite (black or Indian descent)</td>
<td>All breast-fed (duration: up to 32 mo); no vitamin D given during breast-feeding; no information on sunlight</td>
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<tr>
<td>Tomashek et al, 2001 (6); CDC, 2001 (7); Carvalho et al, 2001 (8)</td>
<td>Case finding through review of inpatient hospital discharge records in Georgia, 1/1997–6/1999</td>
<td>30</td>
<td>6</td>
<td>3 in spring, 3 in winter/fall</td>
<td>Radiographic evidence of rickets (6/6); low Ca (4/6); low phos (1/6); high ALP (6/6); high PTH (5/6); low 25(OH)D (6/6); hypocalcemic tetany/seizures (2/6); lα &lt; 5th %ile (3/6); developmental delay (2/6)</td>
<td>8–21 (13.8)</td>
<td>All male</td>
<td>All black</td>
<td>All breast-fed (duration: 8–20 mo); 1 child weaned to unfortified soy beverage at 10 mo; no vitamin D given during breast-feeding; 1 child given vitamin D 1 mo before diagnosis; sun exposure was 6–12 h/wk for 1 child, 21 h/wk for 1 child, minimal for 3, and unknown for 1</td>
</tr>
<tr>
<td>Hartman and Benjamin, 2002 (31)</td>
<td>Case report, Georgia</td>
<td>Not provided</td>
<td>1</td>
<td>Winter</td>
<td>Radiographic evidence of rickets; low Ca; low ionized Ca; high ALP; high PTH; low 25(OH)D; low 1,25(OH)₂D; lα &lt; 5th %ile; wα &lt; 5th %ile; prominent forehead; rachitic rosary; not bearing weight on legs; unable to walk</td>
<td>18</td>
<td>Male</td>
<td>Black</td>
<td>Breast-fed (duration: 18 mo, exclusively for 12 mo); poor eater once foods introduced at 12 mo; information on vitamin D during breast-feeding not provided; child rarely outside during infancy</td>
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</table>

(Continued)
still breast-feeding or were consuming a milk-free vegetarian diet at the time of diagnosis. Among the 44 children for whom race was reported, 91% were described as black. We found similar characteristics among the 166 clinical cases of rickets published in the literature between 1986 and 2003, and we expanded our review to include information on vitamin D supplementation and details of clinical presentation and responses to treatment. The clinical cases we reviewed occurred among children 4–54 mo of age; 83% were described as black, and 96% were breast-fed. Among breast-fed infants, only 5% of records indicated that the infant received supplementation with vitamin D during breastfeeding. When additional dietary information was available, we noted that often these children were weaned onto a diet low in vitamin D and calcium. All except 3 cases showed radiographic evidence of rickets. In the 19 studies with information on responses to treatment, all rickets cases treated with vitamin D responded clinically and biochemically to treatment. The vitamin D was administered with or without added calcium or dairy foods. One case responded to calcium without vitamin D (32). The authors of nearly all case reports indicated that the rickets resulted from severe vitamin D deficiency; however, we cannot rule out low calcium intake as a contributor to the development of rickets in some US cases (32, 33).

The vitamin D content of breast milk from a mother with adequate vitamin D status is ~22 IU/L (34) and thus cannot provide, by itself, the adequate intake of 200 IU/d recommended for infants (12). Most breast-fed infants may obtain adequate vitamin D through sunlight exposure. However, the amount of vitamin D synthesized through sunlight exposure is affected by the time spent outside, the amount of skin exposed, air pollution, cloud cover, time of day, latitude, and skin pigmentation (6).

Specker et al (35) estimated that white infants require ~30 min of sunlight per week to obtain adequate vitamin D if they are wearing only a diaper and they require 2 h per week if they are fully clothed with no hat. However, because melanin in skin decreases the amount of vitamin D3 synthesized from sunlight, infants with dark skin need to spend more time exposed to sunlight to synthesize the same amounts of vitamin D3 as infants with light skin. One study suggested that an adult with dark skin would need to spend at least 6 times as long a time exposed to sunlight to synthesize the same amount of vitamin D as an adult with white skin (36). Comparable figures are not available for infants. Furthermore, infants living at northern latitudes in the US synthesize less vitamin D3 from sunlight because more ultraviolet-B photons are absorbed by the atmosphere (5, 11). In our review, we noted that all rickets cases involving white infants occurred among infants living at northern latitudes. Finally, breast-fed infants may not obtain adequate vitamin D3 from sunlight because exposure is limited, because of parental concerns about air quality or subsequent skin cancer risk. In fact, the AAP recommends that infants < 6 mo of age be kept out of direct sunlight to reduce the risk of skin cancer (37).

Recommendations for vitamin D supplementation for infants have varied somewhat since 1963, when the AAP recommended that all infants receive supplementation with vitamin D (38). The recommendation was modified in 1978, when vitamin D was listed as a possible supplement for breast-fed infants (39). In 1997, the AAP Work Group on Breastfeeding (40) recommended that all infants be breast-fed for a minimum of 12 mo and noted that vitamin D might need to be given before 6 mo of age to infants whose mothers have vitamin D deficiencies and those with inadequate exposure to sunlight. Near the same time, the
1998 AAP Pediatric Nutrition Handbook was released, which recommended vitamin D supplementation at 400 IU/d for all breast-fed infants in the chapter on vitamins but limited the recommendation to dark-skinned infants, particularly if they are exposed to minimal sunlight, in the chapter on breast-feeding (41).

In April 2003, as a result of continued reports of rickets in the United States and inconsistent recommendations regarding who should receive supplementation with vitamin D, the AAP published new guidelines on preventing rickets and vitamin D deficiency among children (10). The AAP (10) recommended that, “all infants, including those who are exclusively breastfed, have a minimum intake of 200 IU of vitamin D per day beginning during the first 2 months of life” (p. 908). Because the adequate intake of 200 IU/d cannot be met with human milk alone and the adequacy of sunlight exposure is difficult to determine for all breast-fed infants, the AAP recommended that all breast-fed infants be given supplemental vitamin D by 2 mo of age unless they are consuming at least 500 mL of vitamin D-fortified formula or milk (10). In addition, non–breast-fed infants who consume < 500 mL of vitamin D-fortified formula or milk should be given a vitamin D supplement. The AAP recognizes that variations in this guideline may be appropriate in specific circumstances (10). Evaluation of physician advice regarding vitamin D supplementation for infants since the release of the new guidelines will be important, as will continued surveillance of hypovitaminosis D and rickets cases in the United States.

Currently, there is no national surveillance of diagnosed clinical cases of nutritional rickets in the United States. The National Hospital Discharge Survey (NHDS) data can be used to provide national estimates of hospitalizations for diagnosed conditions, including rickets (42). Scanlon and Grummer-Strawn (unpublished data cited in reference 43) used the NHDS data to estimate that 9 children per 1 million children in the population were hospitalized with rickets between 1990 and 1998. However, they concluded that the rarity of rickets diagnoses in the NHDS (ie, 20 cases in 9 y) results in an unstable estimate of rickets that should be interpreted with caution (43). Furthermore, rickets cases resulting from nutritional deficiency cannot be distinguished from rickets cases resulting from other causes in the NHDS. Only one of the case groups we reviewed provided an estimate of the incidence of nutritional rickets in the population (7). In that study, the rate of 5 cases per 1 million children 6 mo to 5 y of age reflects hospitalized cases of nutritional rickets in one US state during a 2.5-y period (7).

Breast-feeding is the preferred method of infant feeding and provides infants with important nutrients and immunologic factors (44, 45). Breast milk alone, however, does not provide infants with adequate vitamin D (10). Most breast-fed infants do not develop clinical vitamin D deficiency rickets because sufficient vitamin D is synthesized through casual sunlight exposure or obtained from a supplement. As noted above, however, environmental conditions and concerns, as well as skin pigmentation and covering, make it difficult to rely on sunlight as a source of vitamin D for exclusively breast-fed infants. Our review identified breast-feeding without vitamin D supplementation among black children as a key similarity among cases. The biologic mechanisms relating these factors to vitamin D deficiency are well established. The new AAP clinical guideline to provide a minimal intake of 200 IU/d vitamin D for all infants, beginning in the first 2 mo of life, should be emphasized in the education of all families but particularly the families of children at greatest risk of vitamin D deficiency. Furthermore, children should be weaned to a diet adequate in both vitamin D and calcium.

REFERENCES