

# Rickets in the Dairy State

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## ABSTRACT

**Background:** Nutritional vitamin D deficiency rickets occurs when children do not receive adequate vitamin D, which can be obtained from diet or manufactured in the skin when there is adequate sun exposure. A number of reports have described cases of vitamin D deficiency rickets in breastfed infants, but the public health significance of this problem in Wisconsin is unknown.

**Objectives:** Our objectives were to identify cases of vitamin D deficiency rickets in Wisconsin infants and to determine the percentage of these infants participating in the Wisconsin Women, Infant and Children (WIC) program.

**Methods:** All cases of rickets due to nutritional vitamin D deficiency seen at Children's Hospital of Wisconsin or its associated outpatient clinics were identified by retrospective chart review. Data collected included date of birth, age at presentation, race, clinical presentation, diet history, history of vitamin supplementation, x-ray findings, and biochemical studies. The children with nutritional vitamin D deficiency rickets were cross-referenced with the Wisconsin WIC database.

**Results:** Fifty-one definite cases of nutritional vitamin D deficiency rickets were identified. Skeletal deformities, failure to thrive, fractures, seizures, incidental lab finding, tetany, and refusal to walk were the most common reasons for identifying rickets. All of the children were breastfed and did not receive vitamin supplementation. The infants had a mean age of 13.6 months and

46 (90%) were African American. Thirty-seven out of 51 children (73%) were enrolled in the Wisconsin WIC program.

**Conclusion:** Vitamin D deficiency nutritional rickets is an important public health problem in Wisconsin. The Wisconsin WIC program may be an important site for intervention strategies.

## INTRODUCTION

Rickets, a disorder of the growing skeleton, occurs due to inadequate mineralization of bone, especially at the growth plate. Possible etiologies include vitamin D deficiency, calcium deficiency, and phosphate deficiency. Vitamin D deficiency may be primary or secondary to renal, genetic, liver, or gastrointestinal diseases.<sup>1</sup>

Primary vitamin D deficiency, due to inadequate intake, was extremely common in the United States in the early 20th century, but was believed to be essentially eliminated by the introduction of vitamin D supplements and the addition of vitamin D to milk and infant formula.<sup>2</sup> However, a number of reports have shown that rickets has seemingly reappeared in the United States, principally in breastfed African American children.<sup>3,4</sup>

There are multiple factors that have created this "new" public health problem. First, human breast milk is a poor source of vitamin D, with only 12 to 60 units/mL<sup>5,6</sup> (versus 400 IU/mL in formula), and even lower concentrations in the breast milk of African American women.<sup>7</sup> Second, cutaneous synthesis of vitamin D is highly affected by skin pigmentation, with markedly decreased synthesis in dark-skinned individuals.<sup>8</sup> Third, for reasons that are not entirely clear, the routine use of vitamin D supplements in breastfed children has declined.<sup>9</sup> Finally, because of the many benefits of nursing,<sup>10,11</sup> breastfeeding is now actively promoted<sup>12,13</sup> and breastfeeding rates have increased.<sup>14</sup>

We have elected to document the presence of nutritional vitamin D deficiency rickets in Wisconsin. This is especially important because the long winter in

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Wisconsin limits sun exposure, and the winter sun is ineffective at stimulating vitamin D synthesis.<sup>15,16</sup> Along with documenting cases, we also sought to identify a potential site for prevention strategies by determining the percentage of the affected children that were enrolled in the Wisconsin Women, Infant and Children (WIC) program.

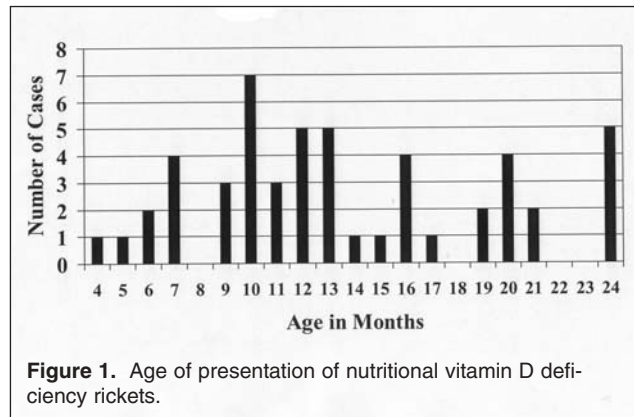
## METHODS

The Children's Hospital of Wisconsin Institutional Review Board approved this study. Medical records were reviewed for patients with an ICD-9 code for rickets (268.0) at Children's Hospital of Wisconsin in Milwaukee from January 1996 through April 2004. Children admitted to the hospital and those seen in the outpatient clinics were included. Data collected included date of birth, age at presentation, race, clinical presentation, diet history, history of vitamin supplementation, x-ray findings, and laboratory studies. The diagnosis of nutritional vitamin D deficiency rickets was based on a combination of radiographic data, laboratory data, and a history of poor intake of vitamin D. We excluded children with vitamin D deficiency due to gastrointestinal or liver disease, or secondary to anti-convulsant use. We also excluded cases if there was no history of poor vitamin D intake or if missing laboratory or radiology data prevented us from making a definitive diagnosis. We identified 3 cases of rickets where there was inadequate data for us to make a diagnosis of vitamin D deficiency and 5 cases where there was evidence of vitamin D deficiency, but the reported diet was either formula (3 cases) or the diet was not documented in the records (2 cases). Only children living in Wisconsin were included. Participation in the WIC program was determined by cross-referencing the names and birth dates of the identified children with the WIC database.

Some patients had undetectable levels of 25-hydroxy vitamin D. For calculating mean levels of 25-hydroxy vitamin D, we therefore assigned these patients a level 1 ng/mL below the level of detection (e.g., 4 when the level was <5 ng/mL). One patient had concomitant benign transient hyperphosphatemia; the extremely elevated alkaline phosphate level was therefore excluded when calculating the mean alkaline phosphate level.

## RESULTS

We identified 51 cases (29 males) of nutritional vitamin D deficiency rickets, all associated with breastfeeding and lack of vitamin supplementation. The children had a mean age of 13.6 months, with a range of 4 to 24



**Figure 1.** Age of presentation of nutritional vitamin D deficiency rickets.

**Table 1.** How Rickets was Identified

| Reason for Evaluation    | Number of Patients |
|--------------------------|--------------------|
| Skeletal Deformity       | 14                 |
| Failure to Thrive        | 8                  |
| Seizure                  | 5                  |
| Fracture                 | 5                  |
| Incidental Lab Finding   | 5                  |
| Tetany                   | 4                  |
| Refusal to Walk          | 4                  |
| Incidental X-Ray Finding | 2                  |
| Cardiorespiratory Arrest | 1                  |
| Limp                     | 1                  |
| Poor Feeding             | 1                  |
| Weight loss              | 1                  |

months (Figure 1). Forty-six (90%) were African American. The remaining patients were Caucasian (2), Hispanic (1), biracial (1), and Asian (1). Thirty-seven (73%) of the infants had been enrolled in WIC.

The patients came to medical attention for a variety of reasons (Table 1). Seven were discovered because of an incidental finding on either laboratory tests (5) or x-rays (2).

The laboratory tests at the time of diagnosis are presented in Table 2. The only test that was abnormal in 100% of the tested patients was the parathyroid hormone (PTH) level, which was elevated. One phosphorus level was elevated because the patient had a cardiopulmonary arrest due to laryngospasm associated with severe hypocalcemia. The children with seizures, tetany, or cardiorespiratory arrest all had hypocalcemia; they had a mean age of 9 months.

## DISCUSSION

We have described 51 cases of rickets due to nutritional vitamin D deficiency in Wisconsin children. We believe this is the largest published case series of American children with this disorder in more than 40 years. As in previous reports, the children in our study were pre-

**Table 2.** Laboratory Findings

| Laboratory Test           | Mean      | SD         | Range            | Normal Values  |
|---------------------------|-----------|------------|------------------|----------------|
| Calcium (51)*             | 7.8 mg/dL | 1.97 mg/dL | 3.2 – 10.4 mg/dL | 8.9-10.7 mg/dL |
| Phosphorus (51)           | 3.4 mg/dL | 1.25 mg/dL | 1.4 – 9.4 mg/dL  | 4.0-7.0 mg/dL† |
| Alkaline Phosphatase (49) | 1137 IU/L | 780 IU/L   | 190 – 3898 IU/L  | 110-320 IU/L‡  |
| 25 Vitamin D (46)         | 8.8 ng/mL | 7.2 ng/mL  | 3 – 35 ng/mL     | 13-67 ng/mL    |
| 1,25 Vitamin D (46)       | 96 pg/mL  | 93 pg/mL   | 6 – 462 pg/mL    | 27-71 pg/mL    |
| PTH (42)                  | 390 pg/mL | 295 pg/mL  | 79 – 1799 pg/mL  | 10-65 pg/mL    |

\*The number of cases with lab tests available for analysis are listed in parentheses.

†Normal values decrease with age. The values shown are for infants.

‡Normal values vary with age. The values shown are for infants.

Abbreviations: PTH = parathyroid hormone

dominantly African American breastfed infants who were not receiving vitamin D supplementation.<sup>3,4</sup> Given the comparatively low rate of breastfeeding in African Americans, the most likely explanation for this observation is the decreased cutaneous synthesis of vitamin D in the skin of these infants due to increased skin pigmentation.<sup>8</sup> It is also possible that other factors may lead to decreased sun exposure in this patient population. In addition, the winter sun at Wisconsin's latitude is known to be ineffective at stimulating cutaneous vitamin D synthesis.<sup>15,16</sup> It is also known that African American women have lower levels of vitamin D in their breast milk than Caucasian women.<sup>17</sup>

Because of the many benefits of nursing,<sup>10,11</sup> there are currently multiple efforts in place to encourage breastfeeding.<sup>12,13</sup> This should be accompanied by a concerted effort to ensure that breastfed infants receive vitamin D supplementation, as recently recommended by the American Academy of Pediatrics (AAP).<sup>18</sup> It is inappropriate to actively promote breastfeeding for a vulnerable patient population, but not encourage use of vitamin D supplementation. This will only lead to mistrust, and ultimately create opposition to breastfeeding.

We have identified the Wisconsin WIC program as 1 site for targeting infants at risk for developing rickets. As a result of this study, the Wisconsin WIC program has created handouts, for both parents and health care professionals, that explain the need for vitamin D supplementation in breastfed infants. Additional efforts outside of the WIC program are needed to educate parents, physicians, and other health care professionals about this issue.

Currently, there is no vitamin D supplement available in the United States that would be appropriate for infants. Instead, vitamin D must be given as part of a multivitamin supplement that contains vitamins A, C, and D. While the AAP recommends 200 IU per day for

breastfed infants,<sup>18</sup> the dropper for the multivitamin preparation delivers 400 IU. But this is not a concern since 400 IU/day per day is clearly safe.<sup>19</sup> Moreover, while not necessary, it is not harmful for infants to receive additional vitamins A and C. At this time, Wisconsin Medicaid covers these vitamin supplements, but the practitioner must document that the child received a comprehensive "HealthCheck" screen within the last 365 days. We believe that this requirement should be eliminated so that 1 barrier to infants receiving vitamin supplements is removed. While the goal is admirable, many physicians find the need for this extra documentation confusing, even if they have done a well-child examination, and therefore do not write an appropriate prescription for vitamins.

While we have described 51 cases of nutritional vitamin D deficiency rickets, this is probably a substantial underestimation of the number of cases statewide. First, additional patients may have been treated at the other tertiary care centers in Wisconsin. Second, we know that primary care providers in our referral base have treated other patients without referring them to our institution (L. Greenbaum, personal observation). Finally, and most intriguingly, 7 of our patients were diagnosed because of an incidental laboratory or radiologic finding. This raises the possibility that many infants develop mild, asymptomatic rickets, but are never diagnosed or treated. This is especially likely given the low index of suspicion for this disease in modern practice. Many children may have resolution of their vitamin D deficiency due to increased sun exposure and the transition from breast milk to formula or cow's milk, both of which contain 400 IU of vitamin D per liter. Nevertheless, this could have long-term public health consequences since childhood is the time when humans acquire the bone mass that will protect them from the morbidity of osteoporosis as adults.<sup>20</sup> For example, use of vitamin D supplementation in Caucasian female in-

fants who were breastfed was associated with increased bone density when the children were 7-9 years old.<sup>21</sup> This issue requires further study, and may have important implications for all Wisconsin infants who receive breast milk.

## CONCLUSION

In summary, we have described 51 cases of vitamin D deficiency rickets in Wisconsin children. This emphasizes the importance of ensuring that breastfed infants receive vitamin D supplementation. We have identified the WIC program as a potential target for intervention, and programs have already been put in place. Future prospective studies are necessary to monitor the effect of these interventions and to identify other approaches for eliminating nutritional vitamin D deficiency rickets in Wisconsin.

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