Rickets and Vitamin D Deficiency in Alaska Native Children

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Abstract

Background—Rickets and vitamin D deficiency appeared to increase in Alaskan children, starting in the 1990s. We evaluated the epidemiology of rickets and vitamin D deficiency in Alaska Native (AN) children in 2001-2010.

Methods—We analyzed 2001-2010 visits with rickets or vitamin D deficiency diagnosis for AN and American Indian children and the general U.S. population aged <10 years. We conducted a case-control study of AN rickets/vitamin D deficient cases and age- and region-matched controls.

Results—AN children annual rickets-associated hospitalization rate (2.23/100,000 children/year) was higher than general U.S. rate (1.23; 95% CI 1.08-1.39). Rickets incidence increased with latitude. Rickets/vitamin D deficiency cases were more likely to have malnutrition (OR 38.1; 95% CI 4.9-294), had similar breastfeeding prevalence, and were less likely to have received vitamin D supplementation (OR 0.23; 95% CI 0.1-0.87), than controls.

Conclusions—Our findings highlight the importance of latitude, malnutrition and lack of vitamin D supplementation as risk factors for rickets.

Keywords

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INTRODUCTION

Nutritional rickets from vitamin D deficiency was once thought to be nearly eliminated from the developed world, but reports of rickets have increased.[1-5] Vitamin D deficiency is caused by lack of exposure to sunlight and insufficient dietary intake, and children at risk for developing vitamin D deficiency and nutritional rickets include exclusively breast-fed infants, those living in northern latitudes and more pigmented racial groups.[1, 6] Given these risk factors, Alaska Native (AN) children may be at higher risk to develop vitamin D deficiency and rickets.

Clinicians in Alaska identified rickets in Alaskan children in the 1990s[7] and one Alaskan study described high prevalence of vitamin D deficiency in a sample of low-income Alaskan children;[8] however, the incidence of rickets in AN children living in the far north with limited sun exposure is unknown. We evaluated the epidemiology of both rickets and vitamin D deficiency in AN children to estimate the incidence of acute rickets in AN children and compare with that of other American Indian (AI)/AN children and the general U.S. child population; we conducted a case-control study to determine risk factors for development of rickets in AN children.

MATERIALS AND METHODS

This study was reviewed and approved by the Alaska Area tribal Institutional Review Board (IRB) and the Centers for Disease Control and Prevention (CDC) IRB, and by tribal organizations: the Alaska Native Tribal Health Consortium, Southcentral Foundation, Arctic Slope Native Association, Norton Sound Corporation, Yukon Kuskokwim Health Corporation, Bristol Bay Area Native Health Corporation, Tanana Chiefs Conference, and Southeast Alaska Regional Health Consortium. Requirement for informed consent was waived under OHRP guidelines [45 CFR 46.116(c)(2)]. Cases from Alaska regions from which approval was obtained were included in the case-control analysis.

For this retrospective analysis of both rickets and vitamin D deficiency morbidity among children <10 years of age, rickets-associated records were defined using the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes for rickets 268.1 (rickets, late effect) and 268.0 (rickets, active), and vitamin D deficiency was defined as ICD-9-CM 268.9 (unspecified vitamin D deficiency).[9] A rickets- or vitamin D deficiency-associated hospitalization and outpatient visit was defined as any of up to 15 diagnoses on individual records listing these ICD-9-CM codes. Statistical significance for analyses was considered as P<0.05, and analyses were completed using SAS/STAT® software Version 9.3.

We analyzed rickets- and vitamin D deficiency-associated hospitalizations and outpatient visits for 2001-2010 for AI/AN children <10 years of age, who received care in Indian Health Service (IHS) or tribal facilities using the IHS direct and contract inpatient and outpatient visit data from the IHS National Patient Information Reporting System (NIPRS).[10] These data consist of all hospital discharge and outpatient visit records from IHS-operated, tribally-operated and IHS-contracted hospitals and facilities for eligible

AI/AN persons.[10, 11,12] The 12 IHS administrative areas were classified into six regions: Alaska, Southwest, Northern Plains, Southern Plains, East, and West.[12] The IHS West region did not have any IHS- or tribally-operated hospitals and was therefore excluded from only the hospitalization analysis, including the denominator. The corresponding IHS user population for fiscal years 2001-2010 were used as the annual denominator; the user population includes all registered AI/AN individuals who received any IHS-funded health care service at least once during the preceding 3 years.[13] Average annual rickets- and vitamin D deficiency-associated hospitalization visits, outpatient visits and outpatient incidence rates were calculated per 100,000 AI/AN children using the number of occurrences with the corresponding denominator for the time period. For the incidence rate, outpatient visits within years were linked and analyzed by patient.

For the U.S. general population of children <10 years of age, we analyzed inpatient rickets- and vitamin D deficiency-associated visits for 2001-2010 using the Nationwide Inpatient Sample (NIS).[14] The NIS is a nationally representative database of hospitalizations conducted by the Healthcare Cost and Utilization Project (HCUP) in collaboration with participating states which includes a 20% sample of participating U.S. community hospitals.[14, 15] The NIS data do not include data from IHS or tribal facilities. Estimates of the number of hospitalizations with standard errors (SEs) were calculated using the HCUP weighting methodology for the NIS. The annual denominators were the National Center for Health Statistics annual bridged race population estimates.[16] Annual and average annual hospitalization rates were calculated per 100,000 persons of the corresponding population. SUDAAN software (RTI International, Raleigh, North Carolina) was used to account for the HCUP NIS sampling design.[17] The rates with 95% confidence intervals (CIs) were calculated as the weighted number of hospitalizations per 100,000 children for the corresponding groups. If the relative standard error (SE) of estimates exceeded 0.30 or if the unweighted number of visits in the strata was <30, the estimates were considered unreliable and not considered.[14]

Case Control Study

We identified potential AN children with a ICD-9-CM diagnosis code for rickets or vitamin D deficiency during 1999-2013 through: 1) the above retrospective database search for AN children using NIPRS IHS/Tribal data, 2) electronic medical records query at approving tribal facilities for AN children < 10 years. We also reviewed electronic medical records for children with a visit at Alaska Native Medical Center during 2001-2012 with 25-hydroxyvitamin D (25(OH)D) level <15 ng/mL (37 IU/mL).[6]

Medical records for potential cases were reviewed for demographic and medical data including date of birth, community of residence, gender, maternal age, birthweight, gestational age, vitamin supplements, date of diagnosis, presentation (e.g. seizures, tibial bowing), and underlying medical conditions (including malnutrition, failure to thrive, hepatic disease, etc.) in provider note or ICD-9-coded diagnosis, weight and height for age (Z scores from norm), vitamin D laboratory tests (25(OH)D, calcium, phosphorous, alkaline phosphatase, intact parathyroid hormone) radiographs, and feeding methods (breast, bottle, solids). Latitude was calculated from community of residence closest to diagnosis date. Two

pediatric endocrinologists (RL, MB) evaluated all available clinical and lab findings, including response to treatment, and categorized children as 1.) nutritional rickets, 2.) nutritional vitamin D deficiency, 3.) rickets/vitamin D deficiency associated with underlying malabsorption or hepatic disease, or 4.) non-cases. Rickets cases had clinical/radiographic evidence of rickets; nutritional vitamin D deficiency cases were defined as a 25(OH)D level <15 ng/mL without recorded clinical or radiographic signs consistent with rickets. Children with non-nutritional rickets and non-rickets children with 25(OH)D level >15 ng/mL were excluded.

Rickets and vitamin D deficiency cases were matched to controls from the same region with closest birthdate. For each confirmed case and matched control we conducted chart reviews from birth to date of diagnosis for medical conditions, measurements, visit diagnoses and laboratory tests. Rickets and vitamin D deficiency cases were compared by chi-square, Fisher's exact, t-test or Wilcoxon rank sum test as appropriate. Cases and matched controls were compared using a conditional logistic regression model to account for the matching. Analysis of healthcare visits is restricted to children with information on one or more visits during the first year of life.

RESULTS

Hospitalization, Outpatient Visit, and Incidence Rates

During 2001-2010, 6 AN children <10 years of age were hospitalized with rickets, for an average annual AN rickets-associated hospitalization rate of 2.23 per 100,000, which is higher than the rate for the general U.S. population <10 years of age of 1.23 (95% CI 1.08-1.39) and the rate for AI children from all other IHS regions combined (0.13). The average annual AN vitamin D deficiency-associated average annual hospitalization rate for children < 10 years was 1.86, compared with 0.73 (95% CI 0.60-0.85) for the general US child population <10 years of age, and 0.04 for AI children < 10 years of age from all other IHS regions combined.

The average annual rickets-associated outpatient incidence rate of 11.15 is higher than that for AI children from all other IHS regions, which ranged from 2.08-4.31 (p<0.05; Table 1). In contrast, the average annual vitamin D deficiency-associated outpatient incidence rate of 8.17 was similar to rates for AI children in the Southwest (7.62) and West (9.94), higher than the Northern Plains (4.86; p=0.008) and Southern Plains (2.93; p<0.001), and lower than the East (16.29; p=0.003) (Table 1).

Alaska Native Case Control Study: Confirmed rickets and vitamin D deficiency cases

We reviewed 56 potential cases and confirmed 30 cases of nutritional rickets (n=16) or vitamin D deficiency (n=14) among AN children during 1999-2013. (Five additional cases diagnosed with nutritional rickets/vitamin D deficiency associated with malabsorption or liver disease are not included.) During 1999-2005, 8 rickets cases and no additional vitamin D deficiency cases were identified; while during 2006-2013, 14 vitamin D deficiency cases and 8 rickets cases were identified (Figure 1). Among the 16 confirmed rickets cases: the mean age of diagnosis was 0.98 years, 63% (n=10) were aged <1 year, and 75% (n=12)

were male. Eleven of the rickets cases were diagnosed during November –April, compared with five diagnosed during May – October (p=0.210); however, only one rickets case was diagnosed during summer months (June-September; p=0.029). Among the 14 children with confirmed vitamin D deficiency, the mean age was 4.04 years and 43% were male (Table 2). Mean age of diagnosis in children with rickets was significantly younger than children with vitamin D deficiency (p=0.002; Table 3, Figure 2). Because these cases constituted the entire known cohort of AN rickets cases, we calculated the rickets average annual incidence as 4.2 per 100,000; the rickets annual incidence increased by latitude of residence from 0.0 in latitude 50-57 degrees (southeast Alaska), to 21.4 per 100,000 in latitude 70-73 degrees (northern Alaska; p<0.001) (Table 3).

The 16 children with nutritional rickets are presented in Table 2. Seven of 10 children with rickets diagnosed in the first 12 months of life presented with hypocalcemic seizures (3) or failure to thrive (FTT) (4), while all 6 children diagnosed after 12 months of age presented with leg bowing (Table 2). We compared cases with vitamin D deficiency resulting in rickets to those with vitamin D deficiency alone (Table 3). Radiographic evidence of rickets was documented in half (8/16) of the rickets cases. As expected, children with rickets were more likely to have radiographic changes (p=0.017) and exam findings (leg bowing, rachitic rosary, frontal bossing, wrist flaring) (p=0.039), than children with vitamin D deficiency alone, who were more likely to have a 25(OH)D level drawn because of an underlying medical condition (p=0.031). Mean 25(OH)D concentrations were similar in rickets cases (6.5 ng/mL) and vitamin D deficiency cases (9.5 ng/mL) (95% CI -0.25, 6.2; p=0.069). Intact parathyroid hormone concentration was only available for 3 rickets cases.

Rickets and vitamin D deficiency cases had similar rates of breast-feeding documented in the medical record (80% and 89%, respectively). Vitamin D supplementation was documented in a low proportion of rickets and vitamin D deficiency cases (22% and 17%, respectively) (Table 3).

Case Control Study: Comparison of rickets and vitamin D deficiency cases with controls

The 26 cases were matched to 90 controls. All cases had between 2-5 controls. Sixty six (71%) of the controls were born within 1 day of the case, 79 (85%) within 5 days, and all within 21 days. Rickets and vitamin D deficiency cases were more likely to have a physician diagnosis of malnutrition/FTT than control children (Odds ratio [OR] 38.1; p=0.001; Table 4). This association remained when restricted to rickets cases (OR 20.5; 95% CI 2.5, 171; p=0.005). The rate of chronic lung disease among rickets cases (33%) was similar to controls (10%) (OR 4.9; p=0.076). Cases and controls also had similar rates of ever breast-feeding (75% vs. 76%) and of ever exclusively breastfeeding (OR 2.1; p=0.292). Similar proportions of cases and controls were exclusively formula-fed at birth. However, cases were less likely than controls to have any documentation of vitamin D supplementation in the first 6 months of life (OR 0.23; p=0.030). This difference remained significant when accounting for children not exclusively breast-fed in the first 6 months of life (OR 0.11; p=0.047).

We compared rickets/vitamin D deficiency cases to controls for inpatient and outpatient visit rates during the first year of life for several conditions that might be associated with low

vitamin D levels. For acute respiratory infections [ARI], asthma and otitis media there was no difference in the percent with any visit, mean or median number of visits or mean age at first visit. Rickets cases alone had a higher proportion with an ARI visit (OR 6.9; 95% CI: 1.1, 73) and lower mean age at ARI visit (diff=0.28 months, (95% CI: 0.07, 0.48) than control children. Seven of 10 rickets (86%) cases diagnosed before 1 year of age had an acute lower respiratory infection (ALRI) before diagnosis compared with 3/17 (18%) matched controls (OR10.9; 95% CI: 1.3, 100). Three of these 7 cases had a presenting diagnosis of FTT.

DISCUSSION

Several authors have described nutritional rickets in North America, primarily in breastfed, more pigmented children who received no supplemental vitamin D.[1, 18] We found higher rickets- and vitamin D deficiency-associated hospitalization rates among AN children <10 years of age than in other similarly aged AI children living in other IHS regions and in the general U.S. child population. In addition, our calculated incidence of confirmed rickets in AN children <10 years of age from the case control study (4.2/100,000) is higher than incidence estimates in Canadian children except among aboriginal children in the far north.[18] In our case control study the number of rickets cases were similar in the early (1999-2005) and late (2006-2013) periods, while vitamin D deficient cases increased in the late period. This may be due to increased provider awareness and recent focus on vitamin D deficiency in the scientific literature. Similar to Canadian children, AN children with rickets were young and presented with physical signs and symptoms of rickets (FTT, hypocalcemic seizures, leg bowing).[18]

Humans manufacture vitamin D from cholesterol following exposure to sunlight, and through diet and dietary supplements.[5, 19] Among these sources, most humans depend on sun exposure to satisfy their requirements for vitamin D. These requirements may be modified by season, latitude, time of day, skin pigmentation, aging, sunscreen use, and glass barriers, which all influence the cutaneous production of vitamin D3. Above 37 degrees latitude during November – February, there is an 80-100% decrease in the number of ultraviolet B photons reaching the earth's surface, making Alaskans and northern latitude populations at higher risk for vitamin D deficiency.[18, 20, 21] Furthermore, the rickets incidence among AN children in our study increased with increased latitude, and fewer rickets cases were diagnosed during summer months. Risk factors for developing vitamin D deficiency and nutritional rickets in children besides low sun exposure, include exclusive breast-feeding (since breast milk is low in vitamin D), low maternal vitamin D stores, preterm birth, immigration to the U.S., darker skin pigmentation, and poor weight gain.[1, 20]

People throughout the United States, including AN people living in Alaska, can achieve adequate vitamin D stores through some combination of vitamin D supplementation, sunlight, and routine consumption of vitamin D rich foods. The latter mechanism may be particularly appropriate for residents of northern Alaskan villages where exposure to sunlight is limited, particularly in the winter. While store bought vitamin D rich foods may be expensive, or not available, many traditional subsistence foods provide an excellent and economical source of vitamin D.[22] For example, salmon typically contains 500-1000 IU/3.5-

ounce serving[23] and consumption of high quantities of oily fish as part of a traditional indigenous diet is associated with higher vitamin D intake.[21, 22, 24] Consumption of high quantities of oily fish with a traditional indigenous diet is associated with higher vitamin D concentration;[21,22] however, Alaska Native people have had increasing dependency on store-bought foods since the 1950s. [21, 22, 25] Given the low traditional food consumption in many arctic populations, vitamin D supplementation is important. Consistent with this, the American Academy of Pediatrics (AAP) recommends that regardless of sunlight and food intake, all breastfed infants/children and those receiving < 1 Liter per day of infant formula receive 400 IU/day of vitamin D supplementation.[26]

Breastfeeding has been associated with increased risk of vitamin D deficiency and rickets since human milk typically contains a vitamin D concentration of 25 IU/L (10 ng/mL) or less;[27] however, vitamin D deficiency has also been recognized in completely formula-fed Canadian infants.[18, 28] The first reports of rickets in Alaska were in breast-fed infants,[7] and breast-feeding without vitamin D supplementation was a risk factor for 25(OH)D concentration <15 ng/mL.[8] In our study, a history of documented breastfeeding was not associated with an increased risk of rickets/vitamin D deficiency; however, lack of vitamin D supplementation was associated with development of rickets and vitamin D deficiency. This finding underscores the importance of supplementation, as recommended by the AAP.[26] In Canada it is recommended that breast-fed infants residing above the 55th latitude receive 800 IU/d during the winter months;[29] however, Ward found no reported cases of rickets among breast-fed children who received regular vitamin D (400 IU/d).[18] This suggests that current AAP guidelines can be effective if consistently implemented.[18] In addition to vitamin D supplementation, overall nutritional intake is likely important. In our study, AN children with confirmed rickets/vitamin D deficiency also had a dramatically higher rate of malnutrition than controls, and Ward identifies FTT in 5% of children with vitamin D deficient rickets in Canada.[18]

Although the IHS/Tribal and NIS data are useful for evaluating rates, these data have some previously described limitations.[30] In addition, the analysis of visit rates and clinical information was dependent on documentation of ICD-9-CM codes, laboratory, clinical data, feeding and vitamin D supplementation in electronic medical records and charts. Lack of documentation of vitamin D supplementation does not necessarily correlate with it not occurring. We were unable to calculate reliable outpatient visit rates for the general U.S. population due to the low disease occurrence. Based on our finding of nearly identical hospital visit rate and incidence in the AI/AN population, we expect that the U.S. annual hospitalization rate is similar to the incidence. For the case/control study, some potential cases could not be confirmed because of missing data. Lastly, our case numbers are small, limiting the generalizability of results.

These findings highlight the importance of northern latitude and malnutrition as potential contributors to vitamin D deficiency and rickets and the importance of vitamin D supplementation in both breast-fed and formula-fed infants. Further studies should evaluate optimal vitamin D supplementation, the contribution of traditional AN diet to healthy vitamin D levels.

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Abbreviations

25(OH)D	25-hydroxyvitamin D
ARI	acute respiratory infection
ALRI	acute lower respiratory infection
AN	Alaska Native
AI/AN	American Indian/Alaska Native
FTT	Failure to thrive
HCUP	Healthcare Cost and Utilization Project
IHS	Indian Health Service
ICD-9-CM	International Classification of Diseases, Ninth Revision, Clinical Modification
NIPRS	National Patient Information Reporting System
NIS	Nationwide Inpatient Sample

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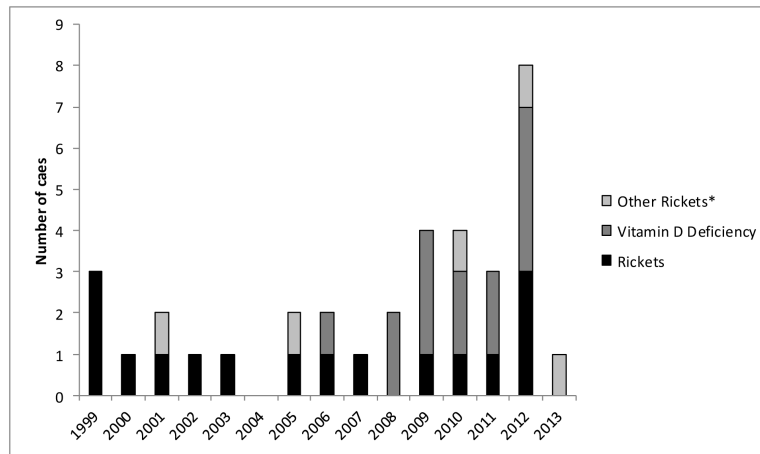
Figure 1.
Alaska Native confirmed rickets and vitamin D deficiency cases < 10 years of age, by year of diagnosis, 1999-2013.

* Other rickets: Children with rickets/vitamin D deficiency associated with hepatic disease or malabsorption.
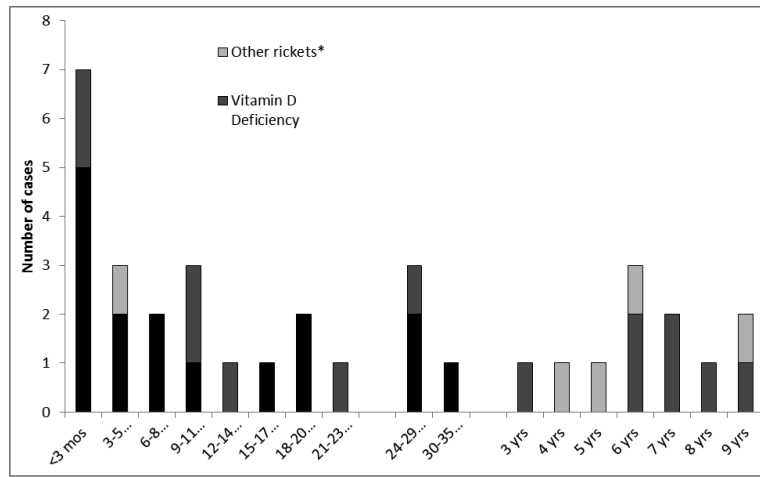
Figure 2.
Age at diagnosis of Alaska Native children < 10 years of age with confirmed rickets or vitamin D deficiency 1999-2013.
* Other rickets: Children with rickets/vitamin D deficiency associated with hepatic disease or malabsorption

Table 1

Average annual Rickets-associated and vitamin D deficiency-associated outpatient visit rates/100,000 and incidence rates/100,000/year in AI/AN children population <10 years, by Indian Health Service (IHS) region, 2001-2010.

IHS region [*]	Rickets				Vitamin D deficiency			
	No. Visits	Visit rate/ 100,000	Incidence	Incidence rate/100,000	No. Visits	Visit rate/ 100,000	Incidence	Incidence rate/100,000
Alaska	89	33.06	30	11.15	50	18.58	22	8.17
East [**]	-	-	-	-	15	18.79	13	16.29
N. Plains	25	4.34	12	2.08	38	6.59	28	4.86
S. Plains	32	5.86	15	2.75	43	7.88	16	2.93
Southwest	101	10.40	30	3.09	114	11.74	74	7.62
West	30	9.95	13	4.31	65	21.55	30	9.95

[*] Rates are from the Indian Health Service direct and contract outpatient visit health care data.

[**] Rates with 5 visits are not reported.

Table 2

Clinical characteristics of Alaska Native children at diagnosis, with confirmed rickets diagnosed 1999–2012.

No.	Age (months)	Sex	Laboratory results at Diagnosis				Presenting Reason	Radiographic findings	Physical exam	Weight for age percent
			25 OHD (ng/mL)	Calcium (mg/dl)	Phos. (mg/dl)	Alk. Phos. (IU/L)				
1	<3	M	5	6.2	2.6	927	Pneumonia, FTT	Fracture, osteopenia	Short Stature	6.1
2	<3	M	0	6.2	4.3	626	FTT, hypocalcemic seizure	--	--	0.5
3	<3	M	4	5.8		1057	Hypocalcemic seizure	--	--	--
4	<3	F	6	9.3		1240	Rickets on x-ray	Rachitic rosary	--	--
5	3-5	F	7	8.5	3.3	953	VSD	Negative		22.0
6	3-5	M	16	9.8	3.2	469	FTT, rachitic rosary	--	Short Stature	<0.1
7	3-5	M	7	8.4		1192	Other	--	--	11.9
8	6-11	M	7	7.7	3.9	124	FTT	Fracture, cup/fray	--	5.7
9	6-11	M	5	6.9	3.5	504	Seizure meds	Negative	Frontal bossing	75.9
10	6-11	F	10	5.8	5.6	628	Hypocalcemic seizure	--	--	91.4
11	12-23	M		8.1	2.6	977	FTT, leg bowing	Metaphyseal changes, tibial bowing	Short stature, tibial bowing	0.5
12	12-23	M	7	8.6	2.7	756	Leg Bowing, hyponatremic seizure	Negative	Tibial bowing	8.9
13	12-23	F	4	9.2	2.8	531	Leg bowing	Metaphyseal changes, rachitic rosary, tibial bowing	Short stature, tibial bowing	34.3

| No. | Age (months) | Sex | Laboratory results at Diagnosis | | | Presenting Reason | Radiographic findings | Physical exam | Weight for age percent |
			25 OHD (ng/mL)	Calcium (mg/dl)	Phos. (mg/dl)	Alk. Phos. (IU/L)				
14	24-35	M		9.2	2	1273	Leg bowing	Metaphyseal changes, radial/tibial bowing	--	17.4
15	24-35	M		10.3	5.2	288	Leg bowing	Metaphyseal changes, tibial bowing	Tibial bowing, fracture	--
16	24-35	M		9.9		597	Leg bowing	Metaphyseal changes, femoral bowing	Tibial bowing	85.3

Table 3

Characteristics of Alaska Native children < 10 years old with rickets or vitamin D deficiency diagnosed during 1999 through 2013.

	Rickets (A)	Vitamin D Deficiency (B)	A+B	p-value A vs. B
	16	14	30	
Latitude of residence:				
70-73.9 degrees	3 (21.4)[*]			
66-69.9 degrees	5 (17.9)			
62-65.9 degrees	2 (2.8)			
58-61.9 degrees	6 (2.7)			
54-57.9 degrees	0			
50-53.9 degrees	0			
Age at Diagnosis				
Mean	0.98 yrs	4.04 yrs	2.41 yrs	**0.002**
Median	0.67 yrs	2.99 yrs	1.14 yrs	**0.014**
<1 year	10 (63%)	4 (25%)	14 (47%)	0.081
Sex Male	12 (75%)	6 (43%)	18 (60%)	0.135
Presenting Reason				
Medical conditions[**]	1 (6%)	6 (43%)	7 (23%)	**0.031**
Physical signs[a], FTT, or Seizure	13(81%)	3 (21%)	16 (53%)	**0.003**
Underlying conditions				
Malnutrition	8 (50%)	6 (43%)	14 (47%)	0.730
Prematurity	1 (6%)	1 (7%)	2 (7%)	1.0
Seizures	1 (6%)	1 (7%)	2 (7%)	1.0
Chronic lung disease	5 (31%)	1 (7%)	6 (20%)	0.175
Gestational age <37 weeks	3/15 (20%)	1/10 (10%)	4/25 (16%)	0.626
Radiologic findings				
No x-ray	5	10	15	
Normal/negative	3 (19%)	3 (21%)	6 (20%)	1.0
Any evidence[β]	8 (50%)	1 (7%)	9 (30%)	**0.017**
Exam Findings[a]	7 (44%)	1 (7%)	8 (27%)	**0.039**
25 (OH)D	(n=12)	(n=12)	(n=24)	
Mean	6.5	9.5	7.98	0.069
(Min, Max)	(0, 16)	(4, 15)	(0, 16)	
Ever Breast-fed within 9 months	8/13 (62%)	8/9 (89%)	16/22 (73%)	0.333
Ever Breast-fed (more restrictive)[€]	8/10 (80%)	8/9 (89%)	16/19 (84%)	1.0
Ever Exclusively breast-fed	5/8 (63%)	6/8 (75%)	11/16 (69%)	1.0
Vitamin supplement before diagnosis	8 (50%)	2 (14%)	10 (33%)	0.058

[*] Incidence of confirmed rickets by degrees latitude among children <10 years of age 2000-2012.

**
Group A (ventricular septal defect), group B (hypothyroid, congenital adrenal hypertrophy, intestinal disaccharidase def, brain malformation, renal disease, apnea).

a
Bowing, rachitic rosary, frontal bossing, wrist flaring.

β
Metaphyseal changes, bowing, fracture, osteopenia, rachitic rosary.

€
Information at birth to 6 months, or known ever breastfed <9 months.

Table 4

Rickets/vitamin D deficiency cases in Alaska Native children <10 years of age, 1999-2013, compared with matched controls

		Case N=26	Control N=93	Matched OR* (95% Confidence Interval)	P value
Sex	Male	14 (54%)	39 (42%)	1.69 (0.69, 4.1)	0.249
Medical conditions					
	Malnutrition	12 (47%)	2 (2%)	**38.1 (4.9, 294)**	**0.001**
	Prematurity	2 (8%)	5 (5%)	1.62 (0.25, 10.5)	0.614
	Chronic Lung Disease	5 (19%)	11 (12%)	1.70 (0.51, 5.7)	0.387
Gestational age <37 weeks		4/22 (18%)	7/71 (10%)	2.06 (0.37, 11.4)	0.408
Ever breast-fed		15/20 (75%)	60/79 (76%)	1.35 (0.36, 5.1)	0.655
Ever breast-fed (restrictive)**		15/18 (83%)	60/76 (79%)	2.56 (0.48, 13.9)	0.277
Ever exclusively breast-fed		10/15 (67%)	39/75 (52%)	2.13 (0.52, 8.6)	0.292
Exclusively formula-fed at birth		2/20 (10%)	13/79 (16%)	0.31 (0.04, 2.6)	0.277
Vitamin D in the first 6 months[β]		3/18 (17%)	32/67 (48%)	**0.23** (0.1, 0.87)	**0.030**

[*] OR = Odds Ratio

[**] Restrictive = Feeding information by 2 months of age or known breast-fed by 9 months of age.

[β] Among cases diagnosed   6 months of age.