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Trabajo Original

Pediatría

Vitamin D, not iron, is the main nutrient deficiency in pre-school and school-aged children in Mexico City: a cross-sectional study

La vitamina D, y no el hierro, es la principal deficiencia nutricional en niños preescolares y escolares en la ciudad de México: un estudio transversal

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Abstract

Introduction: In 2012, the Mexican National Health Survey (ENSANUT 2012) showed a moderate prevalence rate of vitamin D deficiency, around 16%, in a national representative sample of children. A decreasing prevalence of anemia during the last 15 years has been observed in Mexico. The aim of this study was to determine the levels of vitamin D in children 3-8 years old in four different locations within the metropolitan area of Mexico City and to compare them to levels of iron and zinc as references of nutritional status.

Methods: One hundred and seventeen healthy children aged 3-8 years attending four hospitals in Mexico City were invited to participate. All children received medical and nutritional evaluation, and blood samples were obtained.

Results: Children were selected in four hospitals between April and August 2008. More than half (51.3%) were boys; their average age was 5.5 ± 1.6 years. The prevalence of subjects with deficient levels of 25-OH-vitamin D (< 50 nmol/L) was 24.77%. None of the children had haemoglobin levels below the anaemia threshold, and zinc determination revealed 8.26% of individuals with deficient levels (< 65 µg/dL). These data confirm the findings reported in ENSANUT about the sustained reduction of anaemia prevalence among preschool and schoolchildren and the rising rates of vitamin D deficiency in the same population. Similar to other studies, we found a link between socioeconomic status and micronutrient deficiency, these being markers of better nutrition, and vitamin D is remarkably related to the quality of the diet. This finding has not been considered in our population before.

Conclusions: There is evidence of a sustained decrease of anaemia in Mexican children due to general enrichment of foods and focus on vulnerable populations, while vitamin D deficiency seems to have increased. More studies are needed to obtain more information on vitamin D levels at different ages and definition of susceptible groups in order to investigate the possibility of general population measures such as enrichment, which have proven to be effective.

Key words:

Vitamin D. Iron. Deficiency. Children. Anaemia.

Resumen

Introducción: en 2012 la Encuesta Nacional de Salud y Nutrición (ENSANUT) mostró una prevalencia moderada de deficiencia de vitamina D, alrededor del 16%, en una muestra de niños representativa del país. A su vez, la anemia carencial ha disminuido durante los últimos 15 años en México. El objetivo del presente estudio fue determinar los niveles de vitamina D en niños de 3 a 8 años de edad en cuatro diferentes regiones dentro del área metropolitana de la Ciudad de México y compararlos con los niveles de hierro y zinc como referentes del estado nutricional.

Métodos: ciento diecisiete niños sanos de 3 a 8 años de edad que regularmente asisten a cuatro diferentes hospitales en la Ciudad de México fueron invitados a participar. Todos los niños recibieron una evaluación médica y nutricional, y se obtuvieron muestras de sangre.

Resultados: se reclutaron niños en los cuatro hospitales entre abril y agosto del 2008. Más de la mitad (51,3% fueron niños, su edad promedio fue de 5,5 ± 1,6 años. La prevalencia de sujetos con niveles deficientes de 25-OH-vitamina D (< 50 nmol/l) fue de 24,77%. Ninguno de los niños tuvo niveles de hemoglobina por debajo del umbral de la anemia y la determinación de zinc reveló que 8,26% de los individuos tenían niveles deficientes (< 65 µg/dl). Estos datos confirman los hallazgos reportados en el ENSANUT acerca de la reducción sostenida en la prevalencia de anemia en escolares y preescolares, pero también muestran que se eleva la de deficiencia de vitamina D en esta población. De forma similar a otros estudios, encontramos un vínculo entre el estatus socioeconómico y la deficiencia de micronutrimentos en tanto que estos son marcadores de mejor estado nutricional y la vitamina D se relaciona notablemente con la calidad de la dieta. Estos hallazgos no se han considerado previamente en nuestra población.

Conclusiones: existen datos que sugieren una disminución progresiva de la anemia en niños mexicanos debido a una fortificación general de los alimentos y el enfoque en población vulnerable, mientras que la deficiencia de vitamina D parece haber incrementado. Se requieren más estudios para obtener más información acerca de los niveles de vitamina D en distintos grupos de edad y definir a los grupos susceptibles para investigar la posibilidad de llevar a cabo medidas de impacto en la población general como enriquecimiento de alimentos, que ha probado ser efectiva en otros nutrimentos.

Palabras clave:

Vitamina D. Hierro. Deficiencia. Niños. Anemia.

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INTRODUCTION

Although vitamin D has been known for almost a century as a rickets-preventing factor, and its role in calcium absorption in the intestine is well known (1), it has received a surge of attention during the last decade: In 2015 alone, there were 4350 indexed papers containing the words vitamin D in its title, a number that has increased steadily since the early 2000s (2). There are two main causes for this phenomenon: Numerous reports of a widespread vitamin D deficiency around the world, including a resurgence in developed countries as well as findings in basic research, suggest so-called extraskeletal effects (i.e., putative positive effects in the cardiovascular system, immune regulation, cancer prevention and global health, among others) (3).

Although these latter findings are a subject of intense debate and research, vitamin D deficiency is a matter of great concern because of the implications for bone health and calcium metabolism, besides possible effects on other systems. Children and pregnant women are among the most susceptible groups for developing vitamin D deficiency; a number of reports on the reemergence of once-forgotten rickets, cases of neonatal seizures due to hypocalcemia caused by vitamin D deficiency, and cases of the metabolic syndrome in newborns are the hallmark of the vulnerability of this group (4). On the opposite end of the life cycle, osteoporosis is a matter of concern in societies with an ever-growing group of older people because of its impact on life quality, morbidity, and mortality. Vitamin D deficiency in early life may have long-term consequences in the maximal bone peak mass that could predispose an individual to premature onset of osteoporosis (5).

Vitamin D deficiency in Latin America is being addressed regionally (6). Brazil and Mexico, being the most populous countries, generate most of the information available (7). In a national representative sample of preschool children, the 2006 Mexican National Health Survey found that schoolchildren and adolescents had relatively low prevalence rates of vitamin D deficiency, around 16%. However, the metropolitan area of Mexico City presents the lowest levels of vitamin D in children. Its altitude (2140 m above sea level), high pollution levels (241 days with unacceptable air quality during 2011), and reduced time of outdoor activities for most of the population lead to the assumption that vitamin D levels may be lower than previously described. Additionally, the current obesity epidemic among the pediatric population in our country is related to a high prevalence of vitamin D deficiency, and an inverse association between serum 25-OH vitamin D concentration and obesity has been described (8).

Such deficiency contrasts with the decreasing prevalence of anaemia during the last 15 years in Mexico, achieved mainly due to the widespread availability of enriched milk for low-income families (*Liconsa*) (9), social assistance programs (such as *Oportunidades* focused on minorities and indigenous groups), and a greater awareness of iron deficiency among the general population (10). Worldwide, however, iron deficiency is known to be the most widespread micronutrient deficiency; 25% of preschool children suffer from anaemia, and 33% are zinc deficient (11). Some consequences of iron deficiency during childhood include growth retardation, reduced school achievement, impaired motor, and lowered cognitive development (12). With this background in mind, the present study´s aim was to determine the levels of vitamin D in children 3-8 years old in four different locations within the metropolitan area of Mexico City and to compare it to levels of iron and zinc as references of nutritional status.

SUBJECTS AND METHODS

STUDY SETTINGS AND LOCATION

The study was conducted between April 12, 2008 and August 5, 2008. The sample studied were healthy siblings of patients at four hospitals in the metropolitan area of Mexico City: (1) Hospital Infantil de México Federico Gómez in the center; (2) CIFBIOTEC Médica Sur in the southwest; (3) Hospital General Valle de Chalco in the southeast; and (4) Hospital General de Ecatepec "Las Américas" in the northeast. The population covered by each of these centers correspond roughly to the different socioeconomic levels (SEL) defined by the National Institute of Statistics and Geography (13) as follows in decreasing order: Médica Sur (high, a private practice center), Las Américas (medium-low), and Chalco (low). Hospital Infantil de México Federico Gómez (National Children's Hospital) is a reference hospital and represents a pooled population from a wide area, corresponding to a medium-low to low level.

SELECTION OF STUDY POPULATION

Healthy children from both genders attending the 4 health care facilities, aged 3-8 years with the following criteria were invited and included to participate: Children with a *Z*-score (WHO) between -1.9 and 1.9 (bounds included), written consent from parents for their child to participate in the study, PCR within normal range and with full clinical history and examination.

VARIABLES AND DATA MEASUREMENTS

Once the children were selected, a clinical history and anthropometric data were taken. A sample of 10 ml blood was drawn (one tube for immediate processing and complete blood count, the rest for centrifugation, freezing at -70ºC) to determine iron and zinc; related biomarkers (haemoglobin, transferring, and C-reactive protein) and 25-OH-vitamin D ferritin were measured by quantitative electrochemiluminescence method (ECLIA) (14), hemoglobin concentration by spectrophotometry (15), transferrin by immunoturbidimetry (16), zinc by inductively coupled plasma atomic emission spectrometry technique (ICP-AES) (17), C-reactive protein by highly sensitive assay (CRP) (18), and 25-OH-vitamin D by RIA with a Liaison kit from DiaSorin.

Anthropometric measurements were taken on calibrated scales. Children were classified with *Z*-score BMI (OMS) between

-1.9 and 1.9 (bounds included), excluding malnourished or obese individuals. C-reactive protein results were used to rule out inflammation as a cause of anaemia related to chronic or acute disease when it was below 5 mg/L.

Distribution of study parameters was summarized depending on the type of variable in question. The number of subjects and the number of missing data were presented where relevant.

STATISTICAL METHODS

Descriptive statistics for each parameter are presented and included for:

– *Continuous data:* mean (arithmetic or geometric), standard deviation (SD), standard error of the mean (SEM), range (minimum-maximum), median and quartiles, and confidence intervals.
– *Qualitative data:* number and frequency.

Summary tables of the study parameters were prepared for each analysis in the population.

ETHICS

The protocol was submitted for approval to the Research and Ethics Committee at each of the four hospitals. Written consent was obtained from one or both of the parents for their child to take part in the study.

RESULTS

DEMOGRAPHIC AND OTHER BASELINE CHARACTERISTICS

A total of 117 children who fulfilled the inclusion criteria were selected in the four hospitals (33, 30, 29, and 25 subjects from centers 1 through 4 respectively. The subjects were recruited between April and August, all of them sunny months of the year at longitude 19 degrees north, Mexico city's location.

There were 60 (51.3%) boys and 57 (48.7%) girls in the study, and the average age was 5.5 ± 1.6 years. This report includes 109 samples; 8 samples were excluded due to differences in processing the samples (Fig. 1).

FLOW DIAGRAM OF THE INDIVIDUALS SELECTED FOR THE STUDY

The population's anthropometric data were: for boys, height 111.6 ± 10.8 cm, weight 20.0 ± 4.7, and ages 5.3 ± 1.6 years. Girls had a height of 112.7 ± 11.5 cm, weight of 20.3 ± 5.1 kg, and were aged 5.7 ± 1.7 years. The gender and center averages were very similar, and a homogeneous sample was assumed. Figure 2 shows the distribution of the 117 subjects according to the center and their gender, the only relevant observation being a preponderance of boys in center 3 and girls in center 4; however, the total sample was balanced.

SUBJECTS' DISTRIBUTION ACCORDING TO THE CENTER AND THEIR GENDER

In table I, the demographic characteristics of the children are shown. The mean height and weight of children were 112.1 ± 11.2 cm and 20.2 ± 4.9 kg respectively, with a BMI of 15.8 ± 1.7 kg/m². The mean *Z*-score (BMI) was 0.007 ± 0.999: -0.13 ± 0.86 in center 1, 0.04 ± 0.79 in center 2, 0.23 ± 1.06 in center 3, and -0.10 ± 1.29 in center 4. As can be observed,

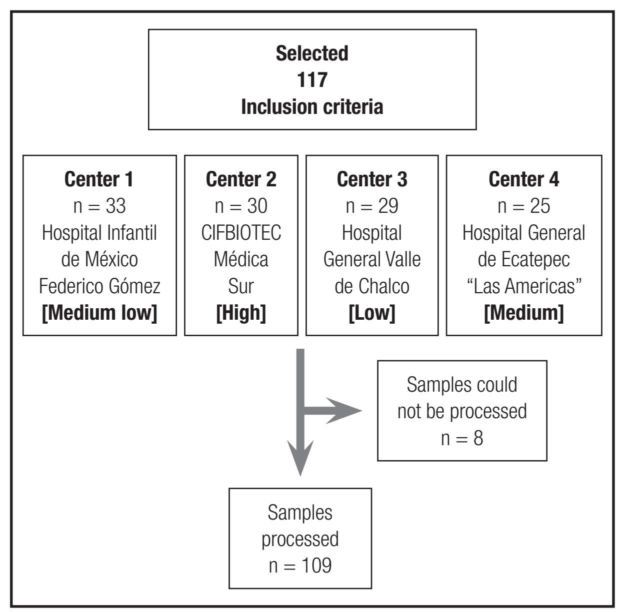

Figure 1.

Flow diagram of the individuals selected for the study.

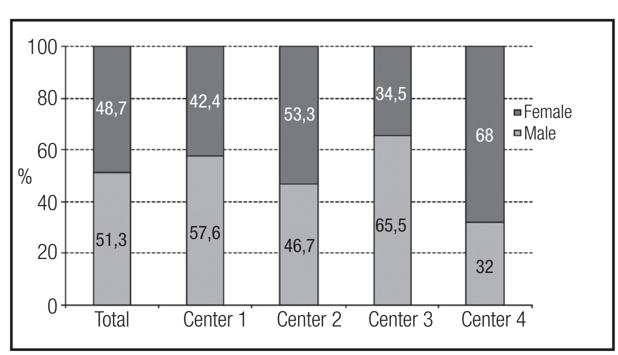

Figure 2.

Subjects' distribution according to the center and their gender.

Table I. Demographic data

		Center 1 *n* = 33	Center 2 *n* = 30	Center 3 *n* = 29	Center 4 *n* = 25	Total *n* = 117
Age (years)	*n*	33	30	29	25	117
	Mean ± SD	5.8 ± 1.5	5.2 ± 1.5	5.3 ± 1.8	5.7 ± 1.8	5.5 ± 1.6
	Median	6	5	5	6	5
Weight (kg)	*n*	33	30	28	25	116
	Mean ± SD	20.11 ± 3.97	19.59 ± 4.33	20.40 ± 5.60	20.58 ± 5.82	20.15 ± 4.87
	Median	20.3	19.5	20.1	18.9	19.8
Height (cm)	*n*	33	30	28	25	116
	Mean ± SD	113.3 ± 9.7	111.2 ± 10.1	110.9 ± 11.9	113.1 ± 13.6	112.1 ± 11.2
	Median	116	113	112	114	113
Body mass index (kg/m²)	*n*	33	30	28	25	116
	Mean ± SD	15.50 ± 1.18	15.70 ± 1.37	16.33 ± 2.12	15.82 ± 2.01	15.82 ± 1.69
	Median	15.6	15.6	15.6	15.3	15.5

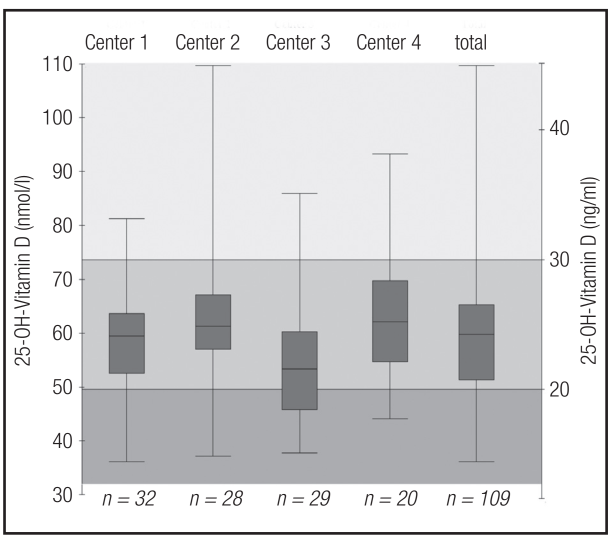

Figure 3.

Vitamin D levels by center and total.

there were no significant differences between the four samples in these parameters.

Table II shows the results of serum ferritin, haemoglobin, serum transferrin, C reactive protein, plasma zinc, and levels of 25 OH-vitamin D. As can be observed, the sample presented adequate levels of iron, indicating that there was no anaemia. Zinc determination revealed 8.26% of individuals with deficient levels (below 65 µg/dL).

The determination of vitamin D levels as shown in figure 3 were found to be below 20 ng/mL in 24.7% of the children.

DISCUSSION

Our results showed that from the 109 patients whose samples were processed, nutrients related to iron sufficiency levels such as ferritin, haemogobin, and transferrin were normal. It is noteworthy that the concentration levels of vitamin D showed that 24.7% of the children had vitamin D deficiency with levels below 20 ng/ml as defined by the Institute of Medicine. Deficient levels of zinc, another relevant nutrient, was detected in 8.2 % of the sample.

Our data confirm the findings reported in the latest National Nutrition Survey in Mexico (ENSANUT 2012), in which a sustained reduction of anaemia prevalence among preschool and school-children has been observed since 1999, while increasing rates of vitamin D deficiency are occurring in the same population.

Vitamin D deficiency –defined as levels below 20 ng/ml by the Institute of Medicine (19)– turns out in our study to be higher than previously described by the 2012 National Nutrition Survey in Mexican children (20) and confirms the findings of a recent survey that found lower levels of vitamin D, particularly in preschoolers 2–5 years old, obese children, and those living in urban areas (8). Although the prevalences in the different studies that looked at the pediatric population in Mexico are different, all of them are consistent in the finding that an important proportion of these children have deficient levels of vitamin D. Some of the known reasons for finding a wide range in the prevalence figures are the different laboratory techniques used for determination of vitamin D as well as seasonal changes (21). Elizondo-Montemayor (8) reported a prevalence figure of 20.2% in their sample of Mexican children, and in the present study, a prevalence of 24.4% is reported; both studies used RIA with a Liaison kit from DiaSorin and yielded similar figures. The 2006 Mexican National Health Survey Study used the 25-(OH) vitamin D direct ELISA kit immunodiagnostics AG and reported a lower prevalence (16%), which agrees with the

Table II. Biological data in total and by center

		Center 1 *n* = 33	Center 2 *n* = 30	Center 3 *n* = 29	Center 4 *n* = 25	Total *n* = 117
Serum Ferritin (ug/L)	*n*	32	28	29	20	109
	Mean ± SD	48.2 ± 30.6	40.9 ± 17.3	45.0 ± 26.8	47.0 ± 20.6	45.2 ± 24.7
	SEM	5.4	3.3	5.0	4.6	2.4
	95% CI	37.6 ; 58.8	34.5 ; 47.2	35.2 ; 54.8	37.9 ; 56.0	40.6 ; 49.9
	Median	42	36	43	42	41
	Q1 ; Q3	28 ; 55	29 ; 50	28 ; 53	34 ; 51	29 ; 53
	Min. ; Max.	3 ; 150	14 ; 82	15 ; 150	22 ; 109	3 ; 150
	Missing	1	2	0	5	8
Hemoglobin Conc (g/L)	*n*	32	28	29	20	109
	Mean ± SD	139.4 ± 9.5	137.6 ± 6.7	142.2 ± 15.0	138.1 ± 7.1	139.4 ± 10.4
	SEM	1.7	1.3	2.8	1.6	1.0
	95% CI	136.2 ; 142.7	135.1 ; 140.1	136.7 ; 147.7	134.9 ; 141.2	137.5 ; 141.4
	Median	140	138	142	136	139
	Q1 ; Q3	132 ; 146	133 ; 142	133 ; 151	134 ; 144	133 ; 146
	Min. ; Max.	121 ; 159	123 ; 149	115 ; 196	127 ; 151	115 ; 196
	Missing	1	2	0	5	8
Serum Transferrin (ug/mL)	*n*	32	28	29	20	109
	Mean ± SD	2886.9 ± 456.2	2772.5 ± 467.7	2729.0 ± 295.0	2518.5 ± 280.5	2747.9 ± 408.1
	SEM	80.6	88.4	54.8	62.7	39.1
	95% CI	2728.8 ; 3044.9	2599.2 ; 2945.8	2621.6 ; 2836.3	2395.5 ; 2641.5	2671.3 ; 2824.5
	Median	2905	2740	2780	2510	2770
	Q1 ; Q3	2670 ; 3085	2395 ; 3195	2590 ; 2880	2390 ; 2660	2460 ; 3050
	Min. ; Max.	2040 ; 3780	1910 ; 3520	2130 ; 3280	1930 ; 3110	1910 ; 3780
	Missing	1	2	0	5	8
C-Reactive Protein (mg/L)	*n*	32	28	29	20	109
	Mean ± SD	2.28 ± 3.17	3.98 ± 6.04	4.22 ± 8.91	2.68 ± 2.95	3.31 ± 5.90
	SEM	0.56	1.14	1.65	0.66	0.57
	95% CI	1.18 ; 3.38	1.74 ; 6.22	0.98 ; 7.47	1.38 ; 3.97	2.20 ; 4.42
	Median	1.5	1.5	1.5	1.5	1.5
	Q1 ; Q3	1.5 ; 1.5	1.5 ; 2.8	1.5 ; 1.5	1.5 ; 1.5	1.5 ; 1.5
	Min. ; Max.	1.5 ; 19.0	1.5 ; 30.0	1.5 ; 46.0	1.5 ; 11.0	1.5 ; 46.0
	Missing	1	2	0	5	8
Plasma Zinc Concentration (umol/L)	*n*	32	28	29	20	109
	Mean ± SD	12.38 ± 1.49	12.64 ± 2.62	13.25 ± 1.63	11.28 ± 1.31	12.48 ± 1.95
	SEM	0.26	0.50	0.30	0.29	0.19
	95% CI	11.86 ; 12.90	11.67 ; 13.61	12.65 ; 13.84	10.70 ; 11.85	12.11 ; 12.84
	Median	12.5	12.2	13.5	11.3	12.2
	Q1 ; Q3	11.3 ; 13.6	11.0 ; 14.4	11.9 ; 14.4	10.7 ; 12.3	11.2 ; 13.8
	Min. ; Max.	9.2 ; 15.1	7.0 ; 17.0	10.7 ; 17.3	8.7 ; 13.9	7.0 ; 17.3
	Missing	1	2	0	5	8
25-OH-Vitamin D (nmol/L)	*n*	32	28	29	20	109
	Mean ± SD	57.51 ± 10.84	62.25 ± 13.62	55.24 ± 13.16	63.12 ± 12.87	59.15 ± 12.82
	SEM	1.92	2.57	2.44	2.88	1.23
	95% CI	53.75 ; 61.26	57.21 ; 67.29	50.45 ; 60.03	57.48 ; 68.76	56.74 ; 61.56
	Median	59.1	60.9	52.9	61.7	59.4
	Q1 ; Q3	52.1 ; 63.2	56.6 ; 66.7	45.4 ; 59.9	54.3 ; 69.4	50.9 ; 64.9
	Min. ; Max.	35.7 ; 80.9	36.7 ; 109.3	37.4 ; 85.6	43.7 ; 92.9	35.7 ; 109.3
	Missing	1	2	0	5	8

finding that ELISA has a large variability in its results and lower sensitivity than other methods.

Although there were no statistically significant differences due to the small sample, it was observed that there were different vitamin D levels in group 3, which had the greatest number of children below the deficiency line and below the rest of the groups. Geographically, group 3 corresponds to Chalco County, which represents the lowest-income population within the sample. A number of studies have noted the link between socioeconomic status and the deficiency of micronutrients (22) as markers of better nutrition, and vitamin D is closely related to the quality of the diet (23). In certain populations such as migrants and dark-skinned people living in northern countries, this used to be attributed to the higher needs of solar radiation for the skin to synthesize vitamin D, but socioeconomic status and quality of nutrition seem to have equally important roles (24). Therefore, our findings might be included in this theory. This finding has not been considered in our population before, and further studies are needed to ascertain whether socioeconomic level need be included in this type of study in order to consider what role socioeconomic disparities play in vitamin D deficiency.

There are many reasons for the recent global resurgence of vitamin D deficiency and they have been summarized extensively (25). There is a concern, not only about new cases of rickets and metabolic disease of the bone in the newborn or the possible alterations on other systems, but also about the degree of skeletal mineralization that may predispose one to fractures in childhood and to later development of early osteoporosis with its associated costs and risks (26). Vitamin D deficiency and its impact on bone health have already been described in pregnant mothers, newborns, and preschool children in all five continents (27). Controversy exists about the optimal levels of vitamin D in the literature that is beyond the scope of this study, but if we were to use the criteria proposed by the Endocrine Society (28) (vitamin sufficiency defined as levels above 30 ng/ml), the figures of insufficiency in our sample would be 63% (i.e., between 20 and 30 ng/ml), and only 12% would have sufficient levels.

Factors such as air pollution, use of sunblock, and little time spent outdoors partly explain the prevalence of vitamin D deficiency in sunny cities (29). Supplementation was eliminated in many countries after several cases of intoxication during the 1950s in the United Kingdom (30) and is being reinstated in a modest and slow fashion worldwide. However, as data regarding Vitamin D deficiency have appeared, the WHO in 2006 issued recommendations on food enrichment including it (11), and many countries have recently changed their supplementation policies successfully, including the United States (31), France (32), Ireland (33), Australia and New Zealand (34), among others.

The dietary allowance for optimal bone health in infants and children up to 1 year of age, according to the Endocrine Society (28) is at least 400 IU/day vitamin D; children 1 year and older need at least 600 IU/day. The detected prevalence of vitamin D deficiency could be related to a failure to meet such allowance and supplementation or enrichment may be needed.

In a systematic review, De-Regil LM (35) showed that intermittent iron supplementation is efficacious to improve haemoglobin concentrations and reduce the risk of anaemia or iron deficiency in children younger than 12 years of age when compared with a placebo or no intervention. Given the prior success on controlling iron and zinc deficiencies, vitamin D enrichment seems a logical next step in food supplementation to improve the nutritional status of Mexican children. Although still controversial, supplementing deficient children may improve bone mineral density during childhood and the teens (36). As with any preventive measure done on a large scale, safety and cost effectiveness are always a concern and need to be carefully monitored.

Besides the inherent limitations of the cross-sectional design, our study might not represent the whole population of Mexico since the sample was only from Mexico City. However, according to INEGI, Mexico City is included in the central megalopolis of Mexico, representing about one-fourth of the Mexican general population (37). Nonetheless, further studies are needed in northern or southern populations of our country.

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