

Nutritional status of iron, vitamin B12, folate, retinol and anemia in children 1 to 11 years old. Results of the Ensanut 2012

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Abstract

Objective. To describe the frequency of anemia, iron, vitamin B12, folate, retinol and predictors of anemia among Mexican children from Ensanut 2012. **Materials and methods.** Hemoglobin, ferritin, CRP, vitamin B12, retinol and folate concentrations were measured in 2 678 children aged 1-4 y and 4 275 children aged 5-11 y. Adjusted logistic regression models were constructed to assess the risk for anemia and micronutrient deficiencies. **Results.** In preschoolers and scholars, the overall prevalence of anemia was 20.4 and 9.7%, iron deficiency 14 and 9.3%, low vitamin B12 (LB12S) 1.9 and 2.6%; Folate 0.30 and 0%, and retinol depletion (VADp) 15.7 and 2.3%, respectively. ID and VADp were negatively associated with Hb (coefficient: -0.38 and -0.45, $p < 0.05$); a higher log-CRP was associated with higher risk for anemia and VADp (OR=1.13 and OR=2.1, $p < 0.05$, respectively). **Conclusions.** Iron deficiency, anemia and VADp are some of the main nutritional problems among Mexican infants.

Key words: ferritin; vitamin B12; folate; retinol; Mexican children

Resumen

Objetivo. Describir la frecuencia de anemia, deficiencia de hierro, vitamina B12, folato, retinol y predictores de la anemia en niños mexicanos de la Ensanut 2012. **Material y métodos.** Se midieron las concentraciones de hemoglobina, ferritina, PCR, vitamina B12, retinol y folato en 2 678 niños de 1-4 años y 4 275 niños de 5-11 años. Se construyeron modelos de regresión logística para evaluar el riesgo de anemia y deficiencias de micronutrientes. **Resultados.** La prevalencia de anemia en preescolares y escolares fue 20.4 y 9.7%; deficiencia de hierro (DH) 14 y 9.3%; baja concentración de vitamina B12 (BCB12) 1.9 y 2.6%; folato 0.30 y 0%, y depleción de vitamina A (DpVA), 15.7 y 2.3%, respectivamente. La DH y DpVA se asociaron negativamente con la Hb (coeficiente: -0.38 y -0.45, $p < 0.05$); a mayor log-PCR, mayor riesgo de anemia y DpVA (OR=1.13 y OR=2.1, $p < 0.05$, respectivamente). **Conclusiones.** DH, anemia y DpVA son algunos de los principales problemas de nutrición en niños mexicanos.

Key words: ferritina; vitamina B12; folato; retinol; niños mexicanos

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Micronutrient deficiencies in early infancy have negative consequences on growth, development, neuronal and cognitive function in later life. Iron and vitamin A deficiency affects the immune system, making children susceptible to recurrent infections, and insufficient erythropoiesis that negatively affects the transport of oxygen in the blood.¹ Folate and vitamin B12 deficiencies have detrimental effects on neural development and cause megaloblastic anemia.² It is a priority, thus, in public health to identify the magnitude of those deficiencies in order to reformulate strategies aiming to reduce the burden of micronutrient deficiencies.

In recent years, Mexico has experienced challenges in the nutritional status of their population, where although acute malnutrition has reduced, the overload of overweight and obesity is the new challenge.³ One of the main aims in the Ministry of Health is to reduce the burden of nutritional deficiencies in children through nutritional intervention from social programs.⁴ Anemia, iron, zinc, vitamin A and D, as well as other micronutrient deficiencies, have been the main nutritional problems in Mexican infants and scholar children.⁵ These children are facing the double burden of disease (overweight/obesity and micronutrient deficiencies) as part of the nutritional transition of a developing country.

Data from ENN-99⁶ and ENSANUT 2006^{7,8} have shown an important decrease in the prevalence of most vitamin and mineral deficiencies. Nutritional interventions included in social programs have contributed for such reduction.⁹ *Liconsa* distributes fortified milk for children 1-12 years of age and *Oportunidades* is a cash transfer program that distributes fortified baby food for children 2 y or less and a drink for pregnant and lactating mothers containing bioavailable iron, and one recommended dietary allowance of several deficient micronutrients. Nevertheless, anemia and iron deficiency are still highly prevalent in infants.

This paper describes the frequency and distribution of anemia, iron, vitamin B12, folate and retinol deficiencies among Mexican children, and their associated risk factors, aiming to identify opportunities for future nutritional interventions.

Materials and methods

Study population. Information for the present analysis was extracted from the dataset of the Mexican National Health and Nutrition Survey of 2012 (Ensanut 2012). The latter is a probabilistic survey, representative at the national, regional, urban and rural levels. Data corresponding to 30% of the overall sample, from children aged 1-11 y were extracted from the Ensanut 2012. For

the present analysis 2 712 children aged 1-4.9 years and 4 395 children aged 5-11.9 years old with complete set of hemoglobin, serum ferritin, folate, vitamin B12 and retinol determinations were included.

A detailed description of the design and sampling procedures was published elsewhere.¹⁰ Demographic and socioeconomic information was collected using *ad hoc* questionnaires based on the characteristics and possessions of households.

Laboratory methods

Hemoglobin

Capillary hemoglobin was measured using a portable photometer HemoCue (HemoCue, Angelholm, Sweden).

Methods for vitamin concentrations and C reactive protein (CRP).

Fasting venous blood samples were drawn and centrifuged at 3000 g, *in situ*. Serum was separated and stored in coded cryovials, preserved at -70°C in liquid nitrogen until delivery to the central laboratory (Nutrition Biochemistry Laboratory) in Cuernavaca, Mexico.

Serum samples for ferritin, CRP, vitamin B12 and folates were measured in an automatic immunoanalyzer Architect CI8200 (Abbott diagnostics, Wiesbaden, Germany). All four were measured by commercial kits with the following interassay variability: ferritin 3.18%, CRP 5.06% vitamin B12 6.84% and folate 4.95%. Serum Retinol was measured in an HPLC HP1110 LCDAD (Agilent Technology Waldbronn, Germany), using the column Waters, NovaPack C18 4um 3.9 x 150 mm with a flux of 1.5 mL/min and mobile phase of methanol, after extraction with 99% ethanol.

Definition of variables

Anemia was defined if hemoglobin concentration (Hb) adjusted by altitude above sea level¹¹ was <110 g/L for children 1-4 y or <115g/L for children 5-11 y old.¹² Severity of anemia was classified according to WHO criteria as: mild, moderate and severe.¹² Iron deficiency anemia and folate and vitamin B12 deficiency anemia was defined if abnormal Hb value coexisted with low s-ferritin, low folate or LB12S. Iron deficiency (ID) was defined if serum concentrations of ferritin were <12 ug/L in children 1-4 y and <15 ug/L in children 5-11 y of age;¹³ low Vitamin B12 status (LB12S) if <200 pg/mL^{7,14} and folate deficiency (FD) if <4 ng/mL.² Serum ferritin values were considered as outliers if >200 ug/L and vitamin B12 if >1500 pg/mL and excluded from

statistical analysis. Serum ferritin values were adjusted using CRP concentrations, as proposed by Thurnham *et al.* as indicative of inflammation.¹⁵

Vitamin A deficiency was considered if serum retinol was <10 ug/dL, and depletion (VADp) if <20 ug/dL.¹⁶

Sociodemographic characteristics

Ethnicity. A person was classified as indigenous if an indigenous language was spoken by a member of the household. Localities with less than 2 500 inhabitants were considered as rural, otherwise urban. A household wealth index (HWI), as a proxy of socioeconomic status, was constructed based on the household characteristics and family assets by a principal component analysis; the index was divided into tertiles to indicate low, medium and high HWI.¹⁷ The country was divided in four geographic regions: Northern, Center, Mexico City and Southern. Anthropometric variables weight and height were measured using validated and standardized methods.^{18,19} BMI was computed based on height and weight according the WHO standards.²⁰

Children participating in social programs were classified as beneficiaries of *Prospera* or *Liconsa*. The *Prospera* program attends families suffering extreme poverty by increasing the capacities of their members, education, health care and food options. Children <2 y and pregnant women, receive a food supplement containing one RDA of critical micronutrients to improve their nutritional status.^{4,21} The *Liconsa* program distributes low-cost milk to low-income children aged 1-11 years fortified with iron, zinc, and other critical vitamins.²²

Statistical analysis

Characteristics of the sample, distribution and prevalence of micronutrients deficiencies are described as frequencies and 95% confidence intervals, stratified by age. To explore the characteristics of children explaining the variability of Hb concentrations, we performed a multiple linear regression analysis. Logistic regression models were constructed to test the risks for anemia, low tissue iron, vitamin B12 and vitamin A depletion. Data were adjusted by age, HWI, BMI, CRP, dwelling, geographical regions, ethnicity, and being beneficiaries of *Prospera* and *Liconsa*.

Data of continuous variables with biased distributions are presented as medians and 95% CI.

Statistical significance was set at $\alpha=0.05$. All analyses were adjusted for the sampling design of the survey, using STATA SE V13 SVY module for complex samples (College Station, USA).

Ethical aspects

The survey was approved by the Research, Ethics, and Biosecurity Committees of *Instituto Nacional de Salud Pública* (Mexico's National Institute of Public Health). Individual assents and informed consent letters were obtained from the parents of all participants after carefully describing the nature, goals and methods of the Survey.

Results

Descriptive characteristics

Descriptive characteristics of the preschool and scholar children are present in table I.

Nutritional causes and severity of anemia

Preschoolers

The overall prevalence of anemia was 20.4% (95%CI 17.5-23.6) which represents 1 656 153 children, aged 1-4 y; 14.8% had mild anemia, 5.5% had moderate and 0.1% had severe anemia. The main cause of anemia in this population was associated with ID in 16% of cases and in a small proportion (3%) it was associated with LB12 or FD combined to ID (table II). The overall prevalence of iron deficiency anemia (IDA) in preschoolers was 3.4% (95%CI 2.4-4.9); the 1 year old group had the highest prevalence of IDA (10.8%; 95%CI 6.5-17.5), compared with children $\geq 2-4$ years old (table II). We found no differences in the prevalence of anemia by sex, ethnicity, dwelling, geographic region, BMI and being beneficiaries of *Liconsa* or *Prospera*. The 1 year old group children had the highest prevalence (36.3 vs 16.6%, $p=0.004$) compared with children $\geq 2-4$ years old, as have been previously documented in these children.²³

Mean serum concentration of Hb was 121g/L (95%CI 119.8-122) with no differences by sex. In a linear regression model, children with ID and vitamin A depletion were negatively associated to Hb concentration (coefficient: -0.38 and -0.45, $p<0.05$). As age increased, an increment of 0.26 g/dL ($p<0.001$) in Hb was observed (table III, model 1). In a logistic regression model, age was a protection factor for anemia (OR=0.7) while a higher log-CRP concentration was associated with higher risk (OR=1.13, 95%CI 1.01-1.3) for anemia (table III, model 2, preschoolers).

Scholars

The overall prevalence of anemia in scholars was 9.7% (95%CI 8.1-11.7), which represents 1 419 682 children

Table I
DESCRIPTIVE CHARACTERISTICS OF CHILDREN 1-11 YEARS
OF AGE IN THE SAMPLE. MEXICO, ENSANUT 2012*

	Preschoolers (1-4 years)				Scholars (5-11 years)			
	n sample	Expansion			n sample	Expansion		
		N thousands	%	95%CI		N thousands	%	95%CI
Sex								
Males	1 346	4 509.8	50.8	(47.7-53.9)	2 205	8 201.8	50.6	(48.2-53.1)
Females	1 334	4 366.2	49.2	(46.1-52.3)	2 115	7 994.8	49.4	(46.9-51.8)
Dwelling								
Urban	1 502	6 420.4	72.3	(69.2-75.3)	2 492	11 823.7	73	(71.1-74.8)
Rural	1 178	2 455.6	27.7	(24.7-30.8)	1 828	4 372.9	27	(25.2-28.9)
Indigenous								
No	1 398	4 346.1	95.7	(94.3-96.8)	3 964	15 356.6	94.8	(93.6-95.8)
Yes	111	193.3	4.3	(3.2-5.7)	356	840.0	5.2	(4.2-6.4)
Geographic region								
Northern	471	1 742.2	19.6	(17.3-22.2)	855.0	3 134.1	19.4	(17.7-21.1)
Centre and Mexico city	1 010	4 205.9	47.4	(43.5-51.3)	1 662.0	7 648.8	47.2	(44.8-49.6)
Southern	1 199	2 927.9	33	(30.0-36.1)	1 803.0	5 413.7	33.4	(31.4-35.5)
Tertile of socioeconomic status								
1	1 215	3 321.8	37.4	(33.9-41.1)	1 835	5 327.8	32.9	(30.6-35.3)
2	933	3 138.0	35.4	(32.2-38.6)	1 489	5 613.4	34.7	(32.3-37.1)
3	532	2 416.2	27.2	(23.8-31.0)	996	5 255.3	32.4	(29.7-35.3)
Body Mass Index (WHO)								
Thinness	61	18.0	0.7	(0.4-1.3)	231	58.0	1.4	(1.0-2.1)
Normal	7 908.5	2 367.0	91.2	(89.3-92.3)	10 011	2 792.0	62.8	(60.3-65.2)
Overweight	701.9	230.01	8.1	(6.6-9.9)	3 522	851.0	22.1	(20.0-24.3)
Obesity	-	-	-	-	2 183	570.0	13.7	(12.0-15.5)
Inflammation (CRP\geq5 mg/L)								
No	2 325	7 582.60	88.5	(85.9-90.6)	3 890	14 662.50	91.3	(89.8-92.6)
Yes	268	987.2	11.5	(9.4-14.1)	385	1 398.4	8.7	(7.4-10.2)
Beneficiaries of:								
<i>Liconsa</i>								
No	2 197	7 086.5	85.6	(82.3-88.4)	3 635	12 886.3	86	(83.8-88.0)
Yes	299	1 188.9	14.4	(11.6-17.7)	409	2 089.6	14	(12.0-16.2)
<i>Prospera</i>								
No	1 665	6 428.4	77.8	(74.5-80.8)	2 514	11 179.1	74.7	(72.6-76.7)
Yes	822	1 830.8	22.2	(19.2-25.5)	1 525	3 789.1	25.3	(23.3-27.4)

* Data are adjusted by the survey design

WHO= World Health Organization
 CRP= C reactive protein

Table II
PREVALENCE OF ANEMIA, SEVERITY OF ANEMIA AND NUTRITIONAL CAUSES OF ANEMIA
IN MEXICAN CHILDREN. MEXICO, ENSANUT 2012*

	Preschoolers				Scholars			
	n sample	Expansion			n sample	Expansion		
		N thousands	%	CI95%		N thousands	%	CI95%
Anemia	2 352	8 118.4	20.4	(17.5-23.6)	3-774	14 635.9	9.7	(8.1-11.7)
Severity of anemia								
Mild	–	–	14.8	(12.1-17.9)	–	–	8.6	(7.0-10.4)
Moderate	–	–	5.5	(4.0-7.3)	–	–	1.2	(0.6-2.3)
Severe	–	–	0.1	(0.0-0.6)	–	–	–	–
Causes of anemia	400	1 525.8	100		368	1 410.1	100	
Iron deficiency	72	243.7	16	(10.7-23.2)	44	203.9	14.5	(8.8-22.9)
ID + FD ó LBI2S	10	31.7	2.1	(0.8-5.6)	3	5.2	0.4	(0.1-1.4)
FD or LBI2S no ID	7	15.1	1	(0.4-2.4)	5	10.5	0.7	(0.3-2.2)
Others	311	1 235.3	81	(73.7-86.6)	316	1 190.5	84.4	(76.1-90.2)
Iron deficiency anemia								
Preschoolers (age, years)								
1	439	1 598.3	10.8	(6.5-17.5)	–	–	–	–
2	556	2 300.9	3	(1.6-5.7)	–	–	–	–
3	656	1 852.7	0.7	(0.3-1.5)	–	–	–	–
4	668	2 238.4	0.9	(0.2-3.4)	–	–	–	–
1-4 years old	2 319	7 990.3	3.4	(2.4-4.9)	–	–	–	–
Scholars (age, years)								
5	–	–	–	–	440	1 826.5	1.3	(0.5-3.2)
6	–	–	–	–	500	1 960.9	1.6	(0.8-3.4)
7	–	–	–	–	592	2 251.4	2.3	(0.5-9.4)
8	–	–	–	–	565	2 248.5	0.3	(0.1-1.4)
9	–	–	–	–	590	2 636.2	1.5	(0.6-3.3)
10	–	–	–	–	525	1 746.1	0.9	(0.3-2.6)
11	–	–	–	–	558	1 949.9	2.1	(0.6-7.5)
5-11 years old	–	–	–	–	3 770	14 619.5	1.4	(0.9-2.3)

* Prevalences are adjusted by the survey design

ID= Iron deficiency
 FD= Folate deficiency
 LBI2S= Low vitamin B12 status

aged 5-11 y. Children were classified as mild 8.5% and moderate anemia 1.2%. Anemia coexisted in 14.5% (95%CI 8.8-22.9) with ID (table II). The prevalence of IDA in this population was 1.4% (95%CI 0.8-2.3), with no significant differences by age.

There were no differences in the prevalence of anemia by sex, ethnicity, dwelling, geographic region, BMI

or been beneficiary of *Liconsa* or *Prospera*. The youngest children had the highest prevalence of anemia in comparison with the eldest (19.1 vs 7%, $p=0.003$).

Mean concentration of Hb was 137 g/L (95%CI 13.6-13.8), with no differences by sex. In a linear multiple regression model, ID children (coefficient: -0.33 g/dL, $p=0.012$), those living in the Southern region (coefficient:

Table III
LINEAR AND LOGISTIC MULTIPLE REGRESSION MODELS FOR PREDICTORS OF ANEMIA AND MICRONUTRIENT DEFICIENCIES IN MEXICAN CHILDREN, BY GROUP OF AGE. MEXICO, ENSANUT 2012*

	Model 1 Adjusted [‡] hemoglobin Coef (95%CI)	Model 2 Anemia OR (95%CI)	Model 3 Iron deficiency OR (95%CI)	Model 4 Vitamin B12 OR (95%CI)	Model 5 Vitamin A depletion OR (95%CI)
Preschoolers					
n (sample)	1 116	1 116	1 246	830	1 258
n (thousands)	3 375.8	3 375.8	3 656.7	1 862.7	3 708.0
Iron deficiency (yes)	-0.32 (-0.58--0.06)	1.44 (0.87-2.37)	-	1.75 (0.44-7.0)	3.12 (1.06-9.17)
Vitamin B12 deficiency (yes)	-0.13 (-0.78-0.52)	0.81 (0.32-2.03)	1.38 (0.3-6.34)	-	-
Vitamina A depletion (yes)	-0.45 (-0.76--0.14)	1.42 (0.76-2.67)	2.57 (0.81-8.15)	-	-
Age (years)	0.26 (0.15-0.37)	0.7 (0.54-0.9)	1.33 (0.67-2.64)	1 (0.28-3.52)	1.67 (0.96-2.91)
Sex (females)	0.15 (-0.1-0.4)	0.74 (0.47-1.18)	1.15 (0.52-2.56)	0.24 (0.04-1.34)	0.71 (0.4-1.27)
Dwelling (rural)	-0.19 (-0.4-0.01)	0.8 (0.55-1.17)	1.67 (0.94-2.95)	0.62 (0.12-3.13)	1.35 (0.81-2.24)
Geographic region (centre is the reference)					
Northern	-0.21 (-0.45-0.03)	1 (0.61-1.67)	1.04 (0.39-2.75)	-	1.1 (0.51-2.34)
Southern	-0.05 (-0.28-0.17)	0.94 (0.6-1.48)	0.55 (0.27-1.13)	0.22 (0.05-0.95)	1.4 (0.79-2.49)
Tertil of socioeconomic status (first is the reference)					
2	0.07 (-0.18-0.31)	0.84 (0.53-1.32)	1.38 (0.72-2.65)	0.07 (0.01-0.58)	1.39 (0.74-2.63)
3	-0.02 (-0.34-0.3)	1.24 (0.72-2.12)	1.01 (0.42-2.43)	-	0.45 (0.22-0.93)
Indigenous (yes)			1.13 (0.38-3.34)	8.7 (3.2-23.62)	1.24 (0.5-3.11)
Body Mass Index WHO (normal is the reference)					
Overweight	0.26 (-0.32-0.84)	1.02 (0.48-2.18)	0.54 (0.16-1.8)	0.46 (0.06-3.8)	1.02 (0.41-2.58)
C-Reactive protein (mg/dL)	-0.05 (-0.12-0.03)	1.13 (1.01-1.27)	0.87 (0.74-1.03)	0.76 (0.55-1.04)	2.06 (1.72-2.47)
Beneficiary of <i>Prospera</i>	-0.15 (-0.4-0.09)	1.24 (0.81-1.9)	1.36 (0.68-2.7)	0.61 (0.24-1.57)	0.6 (0.33-1.09)
Beneficiary of <i>Liconsa</i>	0.09 (-0.27-0.45)	0.93 (0.5-1.72)	2.56 (1.03-6.33)	1.1 (0.13-9.33)	1.06 (0.48-2.33)
Intercept	11.38 (10.9-11.85)	0.91 (0.39-2.1)	0.01 (0-0.34)	0.46 (0.01-20.62)	0.04 (0-0.37)
Scholars					
n (sample)	2 536	2 536	2 868	3 948	2 881
n (thousands)	9 971.2	9 971.2	10 866.2	14 685.8	10 892.2
Iron deficiency (yes)	-0.22 (-0.53-0.09)	1.36 (0.7-2.65)	-	3.03 (1.35-6.79)	3.9 (1.49-10.19)
Low vitamin B12 (yes)	0.29 (-0.25-0.83)	0.32 (0.11-0.95)	2.86 (1.1-7.43)	-	-
Vitamina A depletion (yes)	-0.23 (-1.04-0.58)	3.48 (1.66-7.29)	3.3 (1.27-8.57)	-	-
Age (years)	0.15 (0.1-0.2)	0.85 (0.75-0.98)	1.01 (0.9-1.13)	1.33 (1.11-1.61)	0.89 (0.78-1.03)
Sex (females)	0.01 (-0.18-0.2)	0.88 (0.56-1.37)	1.29 (0.81-2.07)	0.75 (0.41-1.39)	0.99 (0.52-1.87)
Dwelling (rural)	-0.14 (-0.41-0.12)	0.89 (0.48-1.63)	0.86 (0.54-1.39)	1.36 (0.57-3.21)	1.62 (0.83-3.19)
Geographic region (centre is the reference)					
Northern	-0.33 (-0.56--0.1)	1.61 (0.92-2.8)	0.59 (0.33-1.06)	0.46 (0.12-1.73)	1.95 (0.72-5.27)
Southern	-0.44 (-0.69--0.2)	1.3 (0.73-2.32)	0.54 (0.34-0.88)	0.79 (0.37-1.66)	0.83 (0.37-1.88)
Tertil of socioeconomic status (first is the reference)					
2	-0.2 (-0.5-0.09)	1.5 (0.77-2.92)	0.92 (0.59-1.44)	0.27 (0.1-0.72)	0.78 (0.37-1.64)
3	-0.14 (-0.4-0.13)	1.24 (0.62-2.49)	0.58 (0.31-1.07)	0.21 (0.06-0.69)	0.23 (0.09-0.57)
Indigenous (yes)	-	-	1.16 (0.51-2.65)	2.7 (1.3-5.59)	0.48 (0.13-1.82)
Body Mass Index WHO (normal is the reference)					
Overweight	-0.03 (-0.28-0.21)	1.05 (0.57-1.94)	1.68 (0.98-2.87)	1.17 (0.52-2.66)	0.39 (0.11-1.38)
Obesity	0.3 (0.05-0.55)	0.48 (0.26-0.89)	1.11 (0.4-3.04)	1.89 (0.54-6.68)	0.09 (0.01-0.67)
Log C-Reactive protein (mg/dL)	0.01 (-0.06-0.07)	0.98 (0.85-1.14)	0.63 (0.53-0.75)	0.7 (0.52-0.96)	2.13 (1.74-2.62)
Beneficiary of <i>Prospera</i>	-0.37 (-0.64--0.11)	1.87 (1.08-3.25)	0.76 (0.48-1.2)	1.23 (0.49-3.06)	0.72 (0.34-1.53)
Beneficiary of <i>Liconsa</i>	0.16 (-0.12-0.44)	1.19 (0.59-2.39)	1.8 (0.89-3.63)	0.1 (0.03-0.38)	0.22 (0.04-1.12)
Intercept	12.45 (11.9-13)	0.24 (0.06-0.98)	0.06 (0.02-0.19)	0 (0-0.03)	0.09 (0.02-0.49)

* Data are adjusted by the survey design

‡ Hemoglobin adjusted by altitude above sea level using Cohen & Hass equation¹¹

WHO= World Health Organization

(-0.44 g/dL, $p=0.015$), in the northern region (coefficient = -0.33 g/dL, $p<0.001$) and the beneficiaries of *Prospera* (coefficient: -0.36 g/dL, $p=0.001$) were negatively associated to Hb concentration. As age increased, there was an increment of 0.15 g/dL of Hb concentration ($p<0.001$). Children classified as obese (coefficient: 0.3 g/dL, $p=0.002$) had higher Hb concentration in comparison with normal BMI (table III, model 1). In a logistic regression model, children with VAD (OR=3.5, 95%CI 1.7-7.3), or been beneficiary of *Prospera* (OR=1.69, 95%CI 1.1-2.61) were associated to higher risk of anemia; while older age (OR=0.86, 95%CI 0.77-0.95), and obese children (OR=0.4, 95%CI 0.23-0.67) had the lowest risk of anemia compared with normal BMI, and LB12S (table III, model 2, scholars).

Nutritional status of iron, vitamin B12, folate and vitamin A

Iron deficiency

Preschoolers

Overall prevalence of iron deficiency was present in 13.9% (95%CI 11.7-16.5) of children aged 1-4 y. Median ferritin concentration was 22.5 ng/dL (95%CI 22.2-22.7). Children 12-23 months of age had the highest prevalence of ID (24.9%; 95%CI 19.0-32.0) compared with children of 48-59 mo (9.1%; 95%CI 5.6-14.3). No statistical differences were observed in the prevalence of ID by sex, dwelling, tertile of HWI, geographic region and being beneficiary of *Prospera* or *Liconsa* (table IV).

In a regression model, preschoolers beneficiaries of *Liconsa* (OR=2.56, 95%CI 1.03-6.3) had the highest risk of ID. No significant associations were found with the rest of covariables (table III, model 3, preschoolers).

Scholars

In scholars, overall prevalence of ID was 9.3% (95%CI 7.7-11.2); with no statistical differences by age, sex, ethnicity, dwelling or being beneficiary of *Prospera*. Median ferritin concentration was 29.6 ng/mL (95%CI 29.4-29.9) (table IV). In a logistic regression model, children from the Southern (OR=0.54; 95%CI 0.4-0.9), or from the third tertile of HWI (OR= 0.56; 95%CI 0.33-0.94) had the lowest risk of ID compared with the first tertile and children with higher CRP concentration (OR= 0.6; 95%CI 0.5-0.8) (table III, model 3, scholars); while children with LB12 and VADp had a higher risk (OR=3.08 and OR=3.3, $p<0.05$, respectively).

Low vitamin B12 status

Preschoolers

Overall prevalence of LB12S was 1.9% (1.3, 2.7), with a median of 526 pg/mL (95%CI 520.1-531). Children 12-23 months old had a higher prevalence compared with children 48-59 months (4 vs 1.3%), as well as indigenous (11.2%), rural (3%), individuals from the first tertile of HWI (3.7%) and living in the Southern region (3.5%) compared with their counterparts. No statistical differences were observed in the prevalence of LB12S by sex, BMI, and being beneficiary of *Liconsa* or *Prospera* (table IV). In a logistic regression model, indigenous children (OR=8.7, 95%CI 3.2-23) had the highest risk for B12 deficiency. Living in the southern region (OR=0.22; 95%CI 0.05-0.95) or belonging to the second tertile of HWI (OR= 0.07; 95%CI 0.01-0.58) were protector for LB12S (table III, model 4, preschoolers).

Scholars

In scholars, the overall prevalence of LB12S was 2.6% (95%CI 1.9-3.4), with a geometric mean of 454 pg/dL (95%CI 450.4-457.6). Indigenous children (12.4%), children from rural areas (5.4%), belonging to the first tertile of HWI (5.8%) or beneficiaries of *Prospera* (5.6%) showed higher prevalence of LB12S compare to their counterparts (table IV). In a logistic regression model, the risk factors for LB12S were age (OR=1.13; 95%CI 1.1-1.6), ID (OR=3; 95%CI 1.35-6.8), and indigenous children (OR=2.7, 95%CI 1.3-5.6). On the contrary, the second and third tertiles of HWI, beneficiaries of *Liconsa* and a higher CRP concentration were protection factors to LB12S (table III, model 4, scholars).

Folate deficiency

In preschoolers, overall prevalence of FD was 0.3% (95%CI 0.1-0.9). In scholars, the prevalence of FD was zero. In both cases, the median of serum folates was 15.8 ng/mL. Due to low proportion of children with FD, a regression model was not performed.

Vitamin A depletion

Preschoolers

The 0.6% (95%CI 0.3-1.1) of preschoolers had values of s-retinol below 10 μ g/dL (data not shown). The 15.7% of children had values of s-retinol below 20 μ g/dL. The

Table IV
PREVALENCE OF NUTRIENT DEFICIENCIES AND SERUM CONCENTRATIONS OF MICRONUTRIENTS
IN MEXICAN CHILDREN, 1-11 YEARS OF AGE. MEXICO, ENSANUT 2012¹

	Iron deficiency		s-ferritin		Vitamin B12 deficiency		Vitamin B12		Vitamin A depletion		Vitamin A	
	n sample	Expansion % (95%CI)	n sample	p50 (95%CI)	N thousands	Expansion % (95%CI)	n sample	p50 (95%CI)	N thousands	Expansion % (95%CI)	n sample	p50 (95%CI)
Preschoolers												
Group of age (months)												
12 to 23	501	1 753.3	24.9 (19.0-32.0)	20.5 (19.7-21.2)	522	1 808.1	4 (2.6-6.3)	494 (483.7-504.3)	522	1 771.7	16.5 (11.5-23.3)	27.1 (26.8-27.4)
24 to 35	622	2 451.3	15.8 (11.4-21.4)	22.1 (21.5-22.7)	634	2 474.9	0.9 (0.4-1.7)	545 (529.5-560.5)	637	2 491.2	14.5 (10.8-19.1)	27.1 (26.7-27.5)
36 to 47	730	2 002.5	7.9 (5.5-11.2)	22.5 (21.9-23.1)	744	2 031.9	1.7 (1.0-3.0)	516 (500.6-531.4)	739	2 022.1	14.8 (11.4-18.8)	26.7 (26.3-27.1)
48 to 59	738	2 360.6	9.1 (5.6-14.3)	23.6 (23.3-23.9)	748	2 438.1	1.3 (0.4-4.9)	542 (528.5-555.5)	695	2 255.4	17.1 (11.9-24.1)	26.8 (26.3-27.3)
12 to 59	2 591	8 567.8	13.9 (11.7-16.5)	22.5 (22.2- 22.7)	2 648	8 753.0	1.9 (1.3-2.7)	526 (520.1- 531.9)	2 593	8 540.4	15.7 (13.4-18.3)	27 (26.8- 27.2)
Sex												
Males												
	1 288	4 298.2	14.3 (11.4-17.8)	21.6 (21.2-21.9)	1 327	4 431.5	2.5 (1.5-4.1)	507 (500.1-513.9)	1 296	4 294.4	17.6 (14.0-22.0)	26.6 (26.3-26.9)
Females												
	1 303	4 269.5	13.6 (10.3-17.6)	23.6 (23.2-23.9)	1 321	4 321.5	1.2 (0.8-1.8)	549 (538.7-559.3)	1 297	4 246.0	13.7 (10.9-17.2)	27.4 (27-27.7)
Indigenous												
No												
	1 360	4 174.5	8.6 (6.2-11.8)	23.3 (23-23.6)	1 381	4 276.7	1.1 (0.4-2.8)	543 (534.1-551.9)	1 328	4 091.4	15.9 (12.6-20.0)	26.8 (26.5-27.1)
Yes												
	108	188.6	6.7 (2.7-15.7)	25.5 (22.5-28.5)	111	193.3	11.2 (6.3-19.0)	307 (285.5-328.5)	106	186.1	18.4 (11.7-27.7)	26.9 (24.8-29)
Dwelling												
Urban												
	1 445	6 173.1	13.2 (10.5-16.5)	22.8 (22.5-23.1)	1 479	6 319.7	1.4 (0.8-2.5)	554 (546.3-561.7)	1 451	6 172.5	15.2 (12.2-18.7)	27.1 (26.9-27.3)
Rural												
	1 146	2 394.7	15.9 (12.6-19.9)	21.6 (21.1-22.2)	1 169	2 433.4	3 (2.1-4.4)	442 (429.6-454.4)	1 142	2 367.9	17 (14.2-20.2)	26.5 (26.1-26.9)
Geographic region												
Northern												
	456	1 686.5	16 (11.5-21.9)	22.3 (21.7-22.9)	467	1 721.9	1.2 (0.5-3.1)	555 (539.5-570.5)	457	1 669.1	12.9 (9.5-17.4)	26.5 (26-27)
Centre and DF												
	899	2 711.0	14.4 (10.8-19.1)	22.2 (21.8-22.6)	993	4 124.4	1 (0.3-2.9)	569 (560.7-577.3)	968	4 026.0	13.6 (10.2-17.9)	27.7 (27.4-28)
Southern												
	1 161	2 859.1	12.5 (10.0-15.4)	23.1 (22.5-23.7)	1 188	2 906.8	3.5 (2.5-4.8)	457 (447.2-466.8)	1 168	2 845.2	20.3 (16.3-25.0)	25.6 (25.2-25.9)
Household Wealth Index (tertil)												
1												
	1 184	3 245.6	15.4 (12.1-19.4)	22 (21.6-22.4)	1 202	3 292.5	3.7 (2.4-5.7)	449 (439-459)	1 172	3 197.0	18.6 (15.3-22.5)	26.2 (25.9-26.6)
2												
	895	3 043.8	15.2 (11.3-20.3)	22.6 (22.2-23.1)	926	3 105.3	0.8 (0.4-1.5)	544 (535-553)	909	3 066.2	14.9 (10.6-20.7)	27.1 (26.8-27.4)
3												
	512	2 278.4	10.2 (6.6-15.4)	23.6 (22.9-24.2)	520	2 355.3	0.7 (0.3-2.0)	601 (591.6-610.4)	512	2 277.2	12.5 (8.2-18.6)	27.8 (27.2-28.4)

(Continúa...)

(Continuación)

Body Mass Index (WHO)													
Thinness	18	60.6	37.7 (14.3-68.8)	16.9 (5.6-28.3)	18	60.6	0	408 (302-514)	18	60.6	17.5 (4.7-47.7)	25.8 (25.5-26.2)	
Normal	2 285	76 146	14 (11.5-16.8)	22.6 (22.3-22.9)	2 336	7 791.8	1.9 (1.2-2.8)	518 (511.7-524.3)	2 291	7 605.1	15.5 (13.0-18.3)	27 (26.8-27.2)	
Overweight	225	694.9	11.7 (6.9-19.2)	20.2 (19.6-20.8)	229	695.6	1.5 (0.6-3.6)	606 (593.1-618.9)	224	680.8	16 (9.7-25.1)	25.5 (24.9-26.2)	
Prospera beneficiary													
No	1 603	6 175.8	13.3 (10.7-16.4)	22.4 (22.1-22.7)	1 642	6 320.2	1.5 (0.8-2.6)	549 (541.2-556.8)	1 612	6 227.3	15.3 (12.5-18.5)	27.3 (27-27.5)	
Yes	804	1 801.0	16 (11.5-21.8)	22.5 (21.6-23.4)	817	1 822.7	2.8 (1.8-4.3)	443 (429.9-456.1)	795	1 772.8	17.6 (13.3-23.1)	25.5 (25-26.1)	
Licónsa beneficiary													
No	2 127	6 844.4	13.5 (11.1-16.4)	22.6 (22.3-22.9)	2 172	6 979.4	1.9 (1.3-2.9)	514 (507.3-520.7)	2 126	6 892.4	16.2 (13.5-19.4)	26.5 (26.3-26.8)	
Yes	290	1 150.0	16.2 (10.4-24.4)	22.1 (21.7-22.5)	295	1 179.3	1.1 (0.5-2.7)	627 (613.4-640.6)	290	1 123.9	13.5 (8.8-20.2)	29.7 (29-30.4)	
Inflammation (CRP≥5 mg/L)													
No	2 323	7 580.5	14.5 (12.1-17.2)	22.1 (21.8-22.4)	2 301	7 486.7	2 (1.3-2.9)	527 (521.2-532.8)	2 249	7 285.7	11.5 (9.5-14.0)	27.6 (27.4-27.8)	
Yes	268	987.2	10 (5.3-17.9)	24.1 (24-24.2)	262	972.7	0.7 (0.2-2.0)	494 (463-525)	260	959.4	51 (39.8-62.2)	19.5 (18.9-20)	
Scholars													
Age (years)	5	504	1 993.3	9.7 (6.4-14.6)	27 (26.2-27.8)	500	1 986.0	0.7 (0.2-2.1)	566 (553.7-578.3)	365	1 474.2	4 (2.2-7.2)	32.5 (30.5-34.4)
	6	565	2 149.4	10.3 (6.6-15.6)	28.6 (28.1-29)	562	2 146.4	1.9 (0.7-4.8)	520 (508.5-531.5)	395	1 616.6	1.2 (0.5-3.0)	31.5 (30.1-33)
	7	681	2 503.2	10.5 (6.2-17.4)	27.9 (27.5-28.2)	680	2 499.9	2.7 (1.1-6.8)	480 (473.6-486.4)	487	1 858.1	4 (2.3-6.9)	32.8 (31.6-34)
	8	649	2 453.2	5.9 (3.8-9.0)	30.9 (30.5-31.3)	648	2 451.0	1.2 (0.6-2.2)	453 (444.8-461.2)	468	1 792	1.6 (0.8-3.1)	32.9 (31.9-34)
	9	668	2 899.3	10.1 (6.8-14.7)	32.2 (31.6-32.8)	667	2 905.9	2.3 (1.1-4.9)	431 (424.6-437.4)	493	2 258.4	2.9 (1.3-6.4)	34.3 (33.1-35.4)
	10	604	1 955.7	5.8 (3.8-8.7)	32.7 (31.7-33.6)	602	1 954.0	3.2 (1.5-6.6)	408 (398.8-417.2)	444	1 382.2	1.4 (0.5-3.6)	33.8 (32.5-35.1)
	11	595	2 076.9	12.5 (8.0-19.2)	28.8 (27.8-29.7)	599	2 087.7	6.2 (3.7-10.2)	380 (370.3-389.7)	448	1 503.9	0.7 (0.2-1.9)	36.7 (35.5-37.9)
	5 to 11	4 266	16 030.9	9.3 (7.7-11.2)	29.6 (29.4-29.9)	4 258	16 031.0	2.6 (1.9-3.4)	454 (450.4-457.6)	3 100	11 885	2.3 (1.7-3.1)	33.4 (33-33.9)
Sex													
Males	2 182	8 118.7	9.1 (7.0-11.8)	29.9 (29.4-30.3)	2 170	8 103.2	3 (2.0-4.6)	445 (440.1-449.9)	1 580	5 941.4	2.3 (1.6-3.3)	33.2 (32.5-34)	
Females	2 084	7 912.2	9.5 (7.6-11.8)	29.4 (29.1-29.7)	2 088	7 927.8	2.1 (1.4-3.1)	461 (456-466)	1 520	5 944	2.4 (1.5-3.7)	33.5 (33-34)	
Indigenous													
No	3 912	15 192.9	9.3 (7.6-11.3)	29.6 (29.4-29.9)	3904	15 193.0	2 (1.4-2.9)	465 (461-469)	2 858	11 312	2.3 (1.7-3.2)	33.5 (33-33.9)	
Yes	354	838.0	9.4 (5.7-15.2)	29.7 (28.6-30.8)	354	838.0	12.4 (7.8-19.0)	320 (307.3-332.7)	242	573.2	2 (0.8-5.0)	31.3 (29.7-32.9)	

(Continúa...)

(Continuación)												
Dwelling	2460	11 701.6	9.8 (7.8-12.3)	29.5 (29.2-29.8)	2 452	11 699.1	1.5 (0.9-2.5)	479 (474.9-483.1)	1 787	8 803.4	1.8 (1.2-2.8)	33.5 (33-34.1)
Urban	1 806	4 329.3	7.8 (6.0-10.1)	29.7 (29.1-30.3)	1 806	4 331.9	5.4 (3.9-7.6)	393 (386.8-399.2)	1 313	3 082.1	3.8 (2.6-5.5)	32.7 (31.9-33.4)
Rural												
Geographic region												
Northern	845	3 099.7	7.5 (5.6-10.0)	29.7 (29.2-30.1)	844	3 113.4	0.9 (0.3-3.0)	499 (491-507)	697	2 583.5	3.5 (2.2-5.4)	31.6 (30.8-32.4)
Centre	1 635	7 570.1	11.1 (8.2-14.9)	29 (28.5-29.5)	1 630	7 559.6	2.1 (1.2-3.7)	466 (459.4-472.6)	1 192	5 774.2	1.7 (1.0-3.0)	34.4 (33.6-35.1)
Southern	1 786	5 361.1	7.8 (6.3-9.6)	31.3 (30.7-31.8)	1 784	5 358.0	4.1 (2.9-5.8)	413 (407.6-418.4)	1 211	3 527.7	2.5 (1.6-3.9)	32.8 (32.1-33.4)
Household Wealth Index (tertil)												
1	1 816	5 278.6	10.6 (8.5-13.2)	29.2 (28.8-29.6)	1 815	5 277.8	5.8 (4.1-8.1)	392 (386.6-397.4)	1 294	3 740.1	3.3 (2.3-4.8)	32.8 (32.2-33.4)
2	1 469	5 554.8	9.8 (7.2-13.3)	29.6 (29.2-30)	1 465	5 552.9	1.2 (0.7-2.2)	455 (449.2-460.8)	1 068	4 111.7	2.9 (1.7-4.9)	32.9 (32-33.8)
3	981	5 197.5	7.4 (5.1-10.5)	30.3 (29.8-30.8)	978	5 200.3	0.7 (0.3-2.1)	526 (520.9-531.1)	738	4 033.6	0.8 (0.4-1.6)	34.2 (33.3-35.1)
Body Mass Index (WHO)												
Thinness	57	229.0	12.7 (5.1-28.5)	28.3 (26.9-29.8)	57	229.0	4.2 (1.0-16.0)	551 (486.6-615.4)	44	178.4	1.6 (0.2-10.6)	32.9 (26.8-38.9)
Normal	2 760	9 916.9	10.2 (8.1-12.7)	28.8 (28.5-29)	2 755	9 910.5	2.8 (1.9-4.0)	448 (443.7-452.3)	2 009	7 335	3.1 (2.3-4.1)	32.6 (32.1-33.2)
Overweight	840	3 490.1	9.8 (6.7-14.0)	30.4 (29.7-31.1)	839	3 494.7	2.4 (1.4-4.2)	470 (462.1-477.9)	605	2 610.3	1.5 (0.5-4.6)	34.4 (33-35.7)
Obese	560	2 145.7	4.8 (2.3-9.9)	33 (32-34)	559	2 149.5	1.8 (0.6-5.5)	452 (444.4-459.6)	406	1 567.6	0.6 (0.1-2.6)	35.5 (33.7-37.3)
Prospera beneficiary												
No	2 483	11 064.9	9.5 (7.6-11.9)	29.5 (29.3-29.8)	2 478	11 062.9	1.6 (1.0-2.6)	479 (474.4-483.6)	1 828	8 339.6	2.3 (1.6-3.3)	33.4 (32.9-34)
Yes	1 506	3 749.7	8.7 (6.9-10.8)	28.9 (28.3-29.4)	1 502	3 747.5	5.6 (3.8-8.3)	377 (369.9-384.1)	1 078	2 637.5	2.6 (1.6-4.3)	32.8 (31.9-33.6)
Liconsa beneficiary												
No	3 590	12 745.0	8.5 (6.9-10.3)	29.6 (29.3-29.9)	3 582	12 738.6	3 (2.2-4.1)	444 (440.3-447.7)	2 612	9 349.4	2.7 (2.0-3.6)	33.2 (32.7-33.7)
Yes	404	2 077.3	14.3 (9.1-21.8)	28.6 (28-29.1)	403	2 079.5	0.3 (0.1-1.0)	504 (485.5-522.5)	298	1 633	0.5 (0.1-2.3)	33.8 (31.8-35.8)
Inflammation (CRP \geq 5 mg/L)												
No	3 882	14 633.1	9.7 (8.0-11.8)	29.5 (29.2-29.8)	3 872	14 622.6	2.6 (1.9-3.6)	449 (445.4-452.6)	2 832	10 951	1.7 (1.1-2.5)	33.7 (33.2-34.2)
Yes	384	1 397.7	4.5 (2.2-9.0)	30.7 (29.7-31.6)	382	1 394.9	1.7 (0.7-4.1)	485 (471.4-498.6)	268	934.8	10 (6.3-15.5)	29.1 (27.5-30.7)

* Data are adjusted by the survey design

WHO= World Health Organization

CRP= C reactive protein

median of s-retinol concentration was 27 $\mu\text{g}/\text{dL}$ (95%CI 26.8-27.2). The higher prevalences of vitamin A depletion were observed in preschoolers from the southern region (20.3%), from the first HWI (18.6%) and with inflammation (CRP>5 mg/dl, 51%) in comparison with their counterparts (table IV). After adjusting a logistic regression model, children with ID (OR=3.1) and higher CRP (OR=2.1) were negatively associated to higher risk of VADp ($p<0.05$). On the contrary, children from the third tertile of HWI, had lower risk to VADp (OR=0.45, $p=0.032$) (table III, model 5, preschoolers).

Scholars

A 2.3% of children had values of s-retinol below 20 $\mu\text{g}/\text{dL}$. The median of s-retinol concentration was 33 $\mu\text{g}/\text{dL}$ (95%CI 33-34). The higher prevalences of vitamin A depletion were observed in scholars with inflammation (CRP>5 mg/dl, 10%), from the Northern region (3.5%), or the first tertile of HWI (3.3%), in comparison with their counterparts (table IV). In a logistic regression model, children with ID (OR=3.9) and higher CRP (OR=2.13) were negatively associated to a higher risk of VADp ($p<0.05$). On the contrary, children from the second tertile of HWI and with obesity, had lower risk for VADp (OR=0.23 and OR=0.09, respectively, $p<0.05$) (table III, model 5, scholars).

Discussion

The results of this study show that anemia and iron deficiency were highly prevalent in infants in comparison with children of older ages. The contribution of ID to anemia was low in both groups of age, and could be underestimated since serum ferritin was the indicator of body iron status and it is susceptible to fluctuate with inflammation, despite the partial adjustment using CRP.¹³ The contribution of LB12S and folate deficiency was not significant as a nutritional cause of anemia since their prevalence was very low. The high rate of unexplained anemia found in this study could be in part explained by a high rate of low grade inflammation. However, we did not have the complete set of biomarkers (acid alpha glycoprotein 1 plus serum iron and hepcidin) to classify these children in this category. In addition, since erythropoiesis rate is expected to change over a 3 month period, correlation between micronutrient deficiencies and hemoglobin are not perfect.²⁴

The prevalence of ID and IDA in Mexican children is higher than results reported from USA and Canada. Data from NHANES 2003-2006 showed a prevalence of ID (measured by ferritin) of 4.5% in preschoolers.²⁵ In 2008, the prevalence of anemia and IDA in American

preschoolers was 9% and 2%, respectively.²⁶ It was estimated that ID and IDA in infants and toddlers in USA has decreased in the latter years.²⁷ In Canadian children aged 3-5 y, the prevalence of ID (by ferritin) was 3.2% and anemia 2.2%.²⁸ In Colombia,²⁹ Ecuador³⁰ and Nicaragua,³¹ ID was 10.6, 9.9 and 18.7% in preschool children, respectively.

In our study, the ID affects 1 out of 7 children <5 y old, with a higher prevalence in the 12 to 23 mo old, affecting 1 out of 4 preschoolers. In scholars, ID affects 1 out of 11 children. ID and IDA are known to have negative long-term effects on motor and socioemotional development, cognition and behavior and immune dysfunction in children; therefore, it is important to focus strategies to prevent early ID by introducing early iron supplements or iron-rich complementary foods³² and continue with the interventions of nutritional programs (*Prospera* or *Liconsa*) in infants younger than 2 y at higher risk due to poverty;^{9,33} aiming at reducing the burden of early ID and its consequences.

ID and IDA in Mexico has diminished gradually;³⁴ however, the magnitude of this change is imprecise, because the ID of the 2006 sample was overestimated due to a biased selection of the poorest population; despite the efforts made to adjust the original expansion factors.⁷

Anemia in Mexican children was mostly mild, and in a lower proportion moderate. Mexican preschool children had a higher prevalence of anemia compared with Nicaraguan (10.9%)³¹ and Colombian (15.9%)²⁹ counterparts, and very similar to Ecuadorian (25.7%) children.³⁰ This prevalence is one of the lowest reported in Latin American population.³⁵

The CRP was negatively associated with Hb, a strong predictor for anemia, consistent with similar populations. In indigenous infants,³⁶ CRP was negatively associated to Hb (coefficient: -0.18, $p<0.001$), after considering the adjustment of s-ferritin. We speculate that acute recurrent infections could affect the rate of erythropoiesis having as a consequence long stage inflammation;³⁷ these seems to be supported by the prevalence of anemia in children with CRP \geq 5mg/L (29%), compared with 18% in children with CRP<5mg/L. This association was not observed in scholars.

Vitamin A plays an important role in immune function, iron metabolism and erythropoiesis.³⁸ In the model of VADp predictors in our study, a higher CRP concentration and ID was a clear risk factor. This association suggest that vitamin A depletion may cause a depressed immunity, as well as iron deficiency does, and a higher risk to develop anemia (anemia of inflammation).³⁸ Nutritional deficiencies are often in combination; main retinol food sources are similar for heme

iron; so, the association of iron deficiency to VAD could be partially explained through the scarce consumption of these food sources.

The results in the literature are contradictory as to whether vitamin A supplementation modulates cytokine production that have a negative effect on erythropoiesis.³⁹ VAD affect the normal erythropoiesis by the down-regulation of renal erythropoietin expression in the kidney¹ and by stimulation of apoptosis and programmed death cell in erythropoietic progenitor cells in bone marrow.⁴⁰ VAD upregulate liver hepcidin and ferritin mRNA levels affecting iron mobilization from reticuloendothelial iron stores and iron homeostasis.⁴¹

Between the NNS-99⁴² to ENSANUT-2006, VADp had showed a reduction of 10 pp in preschool children; this reduction could be due to a national campaign delivering megadoses of vitamin A supplementation to children 0.5-4 years old (doses: 100 000 IU for children aged 6 and 12 months and 200 000 IU for children aged 12 and 36 months old).^{43,44}

Scholars with obesity had higher Hb concentration and a lower risk for anemia than children with normal BMI, but we did not observe significant associations between ID and Hb. The prevalence of anemia was always lower in overweight children,²³ a similar trend was observed in overweight children in Brazil.⁴⁵

Vitamin B12 and folates are metabolically linked and both participate in common pathways through the synthesis of S-adenosyl methionine to generate tetrahydrofolate. Deficiency of any of these vitamins results in a disruption of DNA synthesis and megaloblastic anemia.² However, normal concentrations of the vitamins do not necessarily reflect a normal nutritional status;² In our study the prevalence of LB12S was higher in children <2 years old; and the highest prevalence of LB12S was found in indigenous children; this association could be explained by the poor access to foods from animal sources that are expensive to buy. Scholar beneficiaries of *Liconsa* had a protective effect for the risk of LB12S, but no effects were observed in preschoolers. The prevalence of LB12S in 2012 diminished 3 pp over the last 6 years.⁸ The higher risk of LB12S observed in indigenous children, from low HWI and the protection for beneficiaries of *Liconsa* were consistent with the Ensanut 2006;⁸ supporting the contribution of this social program to control the micronutrient deficiencies in children.

Plasma folate is a reliable indicator of recent folate intake and provides a suitable assessment of general folate status of a population and does not necessarily reflect the chronic deficiency. It is evident that FD is no longer a priority in public health in Mexican children; it dropped 5pp in the last 6 years⁸ reaching 0% of FD in 2012. This was similar in Ecuadorian preschool children.³⁰

In Mexico, a wide variety of micronutrient supplementations have been implemented (Fortified milk from *Liconsa*, fortified baby food and drinks from *Prospera*, fortified corn and wheat flour). It seems that these massive micronutrient fortification may have had an impact in the results herein presented.

Conclusion

Iron deficiency, anemia and vitamin A depletion continue to be some of the main nutritional public health problems among Mexican infants. The low frequency of children with low vitamin B12 status and folate deficiency suggest that these vitamins are no longer a priority issue in Mexican children since their prevalence has diminished seriously during the last years.

Declaration of conflict of interests. The authors declare that they have no conflict of interests.

References

1. Da Cunha MS, Siqueira EM, Trindade LS, Arruda SF. Vitamin A deficiency modulates iron metabolism via ineffective erythropoiesis. *J Nutr Biochem* 2014;25(10):1035-1044.
2. Green R. Indicators for assessing folate and vitamin B-12 status and for monitoring the efficacy of intervention strategies. *Am J Clin Nutr* 2011;94(2):666S-672S.
3. Gutiérrez J, Rivera-Dommarco J, Shamah-Levy T, Villalpando-Hernández S, Franco A, Cuevas-Nasu L, et al. Encuesta Nacional de Salud y Nutrición 2012. Resultados Nacionales. Cuernavaca, México: Instituto Nacional de Salud Pública (MX), 2012.
4. Barquera S, Rivera-Dommarco J, Gasca-García A. Policies and programs of food and nutrition in Mexico. *Salud Publica Mex* 2001;43(5):464-477.
5. Shamah-Levy T, Villalpando S, Jauregui A, Rivera JA. Overview of the nutritional status of selected micronutrients in Mexican children in 2006. *Salud Publica Mex* 2012;54(2):146-151.
6. Villalpando S, Montalvo-Velarde I, Zambrano N, García-Guerra A, Ramírez-Silva CI, Shamah-Levy T, et al. Vitamins A, and C and folate status in Mexican children under 12 years and women 12-49 years: a probabilistic national survey. *Salud Publica Mex* 2003;45 Suppl 4:S508-S519.
7. Morales-Ruan M del C, Villalpando S, García-Guerra A, Shamah-Levy T, Robledo-Perez R, Avila-Arcos MA, et al. Iron, zinc, copper and magnesium nutritional status in Mexican children aged 1 to 11 years. *Salud Publica Mex* 2012;54(2):125-134.
8. Cuevas-Nasu L, Mundo-Rosas V, Shamah-Levy T, Mendez-Gomez Humaran I, Avila-Arcos MA, Rebollar-Campos M del R, et al. Prevalence of folate and vitamin B12 deficiency in Mexican children aged 1 to 6 years in a population-based survey. *Salud Publica Mex* 2012;54(2):116-124.
9. Rivera JA, Shamah T, Villalpando S, Monterrubio E. Effectiveness of a large-scale iron-fortified milk distribution program on anemia and iron deficiency in low-income young children in Mexico. *Am J Clin Nutr* 2010;91(2):431-439.
10. Olaiz-Fernández G, Rivera-Dommarco J, Shamah-Levy T, Rojas R, Villalpando-Hernández S, Hernández-Avila M, eds. Encuesta Nacional de Salud y Nutrición 2006. Cuernavaca, México: Instituto Nacional de Salud Pública, 2006.
11. Cohen JH, Haas JD. Hemoglobin correction factors for estimating the prevalence of iron deficiency anemia in pregnant women residing at high altitudes in Bolivia. *Rev Panam Salud Publica* 1999;6(6):392-399.

12. WHO. Haemoglobin concentrations for the diagnosis of anaemia and assessment of severity. Vitamin and Mineral Nutrition Information System. Geneva: World Health Organization, 2011 (WHO/NMH/NHD/MNM/1.1.) [accessed on June 2015]. Available at: <http://www.who.int/vmnis/indicadores/haemoglobin.pdf>.
13. WHO. Assessing the iron status of populations: including literature reviews: report of a Joint World Health Organization/Centers for Disease Control and Prevention Technical Consultation on the Assessment of Iron Status at the Population Level; 2004 April, 6-8; Geneva, Switzerland.
14. Carmel R. Biomarkers of cobalamin (vitamin B-12) status in the epidemiologic setting: a critical overview of context, applications, and performance characteristics of cobalamin, methylmalonic acid, and holotranscobalamin II. *Am J Clin Nutr* 2011;94(1):348S-358S.
15. Thurnham DI, McCabe LD, Halder S, Wieringa FT, Northrop-Clewes CA, McCabe GP. Adjusting plasma ferritin concentrations to remove the effects of subclinical inflammation in the assessment of iron deficiency: a meta-analysis. *Am J Clin Nutr* 2010;92(3):546-555.
16. Stephensen CB, Gildengorin G. Serum retinol, the acute phase response, and the apparent misclassification of vitamin A status in the third National Health and Nutrition Examination Survey. *Am J Clin Nutr* 2000;72(5):1170-1178.
17. Resano-Perez E, Mendez-Ramirez I, Shamah-Levy T, Rivera JA, Sepulveda-Amor J. Methods of the National Nutrition Survey 1999. *Salud Publica Mex* 2003;45 Suppl 4:S558-S564.
18. Lohman T, Roche A, Martorell R. Anthropometric Standardization Reference Manual. Champaign(IL): Human Kinetics Books, 1991.
19. Habicht JP. Standardization of quantitative epidemiological methods in the field. *Bol Oficina Sanit Panam* 1974;76(5):375-384.
20. WHO, Multicentre Growth Reference Study Group. WHO Child Growth Standards: Length/height-for-age, weight-for-age, weight-for-length, weight-for-height and body mass index-for-age: Methods and development. Geneva: World Health Organization, 2006.
21. Rivera JA, Sotres-Alvarez D, Habicht JP, Shamah T, Villalpando S. Impact of the Mexican program for education, health, and nutrition (ProgresA) on rates of growth and anemia in infants and young children: a randomized effectiveness study. *Jama* 2004;291(21):2563-2570.
22. Villalpando S, Shamah T, Rivera JA, Lara Y, Monterrubio E. Fortifying milk with ferrous gluconate and zinc oxide in a public nutrition program reduced the prevalence of anemia in toddlers. *J Nutr* 2006;136(10):2633-2637.
23. de la Cruz-Gongora V, Villalpando S, Mundo-Rosas V, Shamah-Levy T. Prevalence of anemia in Mexican children and adolescents: Results from three national surveys. *Salud Publica Mex* 2013;55 Suppl 2:S180-S189.
24. Koury MJ. Abnormal erythropoiesis and the pathophysiology of chronic anemia. *Blood Rev* 2014;28(2):49-66.
25. Cogswell ME, Looker AC, Pfeiffer CM, Cook JD, Lacher DA, Beard JL, et al. Assessment of iron deficiency in US preschool children and nonpregnant females of childbearing age: National Health and Nutrition Examination Survey 2003-2006. *Am J Clin Nutr* 2009;89(5):1334-1342.
26. Kemmer TM, Novotny R, Ah Ping I. Iron deficiency and anemia: disparity exists between children in American Samoa and children living within the US. *Eur J Clin Nutr* 2008;62(6):754-760.
27. Eden AN, Sandoval C. Iron deficiency in infants and toddlers in the United States. *Pediatr Hematol Oncol* 2012;29(8):704-709.
28. Cooper M, Greene-Finestone L, Lowell H, Levesque J, Robinson S. Iron sufficiency of Canadians. *Health Rep* 2012;23(4):41-48.
29. Encuesta Nacional de la Situación Nutricional en Colombia 2010, ENSIN [accessed on July 23, 2014]. Available at: <http://www.minsalud.gov.co/sites/rid/Lists/BibliotecaDigital/RIDE/VS/ED/GCFI/Base%20de%20datos%20ENSIN%20-%20Protocolo%20Ensin%202010.pdf>
30. Freire WB, Ramirez MJ, Belmont P, Mendieta MJ, Silva MK, Romero N, et al. Resumen Ejecutivo. Encuesta Nacional de Salud y Nutrición del Ecuador. ENSANUT-ECU 2011-2013 Tomo I. Quito, Ecuador: Ministerio de Salud Pública (MSP), 2013.
31. Ministerio de Salud Nicaragua. Sistema Integrado de Vigilancia de Intervenciones Nutricionales (SIVIN): Deficiencias nutricionales y sus tendencias en los niños y niñas de 6 a 59 meses y mujeres de 15 a 49 años. Informe de Progreso, Nicaragua, 2003-2005. Managua: Ministerio de Salud, 2008.
32. Arroyo P, Pardo J, Loria A. Special issue: Iron deficiency and iron deficiency anemia in early infancy; etiology, consequences, prevalence, and prevention. Foreword. *Nutr Rev* 2011;69 suppl 1:S1-S2.
33. Perez-Exposito AB, Villalpando S, Rivera JA, Griffin JJ, Abrams SA. Ferrous sulfate is more bioavailable among preschoolers than other forms of iron in a milk-based weaning food distributed by PROGRESA, a national program in Mexico. *J Nutr* 2005;135(1):64-69.
34. De la Cruz-Gongora V, Villalpando S, Rebollar R, Shamah-Levy T, Mendez-Gomez Humaran I. Nutritional causes of anemia in Mexican children under 5 years. Results from the 2006 National Health and Nutrition Survey. *Salud Publica Mex* 2012;54(2):108-115.
35. Pan American Health Organization. Anemia in Latin America and the Caribbean, 2009: Situation analysis, trends and implications for public health programming. Washington, DC: PAHO, 2010.
36. Pasricha SR, Black J, Muthayya S, Shet A, Bhat V, Nagaraj S, et al. Determinants of anemia among young children in rural India. *Pediatrics* 2010;126(1):e140-e149.
37. Abshire TC. The anemia of inflammation. A common cause of childhood anemia. *Pediatr Clin North Am* 1996;43(3):623-637.
38. Semba RD, Bloem MW. The anemia of vitamin A deficiency: epidemiology and pathogenesis. *Eur J Clin Nutr* 2002;56(4):271-281.
39. Villamor E, Fawzi WW. Effects of vitamin A supplementation on immune responses and correlation with clinical outcomes. *Clin Microbiol Rev* 2005;18(3):446-464.
40. Josefson D, Blomhoff HK, Lomo J, Blystad AK, Smeland EB. Retinoic acid induces apoptosis of human CD34+ hematopoietic progenitor cells: involvement of retinoic acid receptors and retinoid X receptors depends on lineage commitment of the hematopoietic progenitor cells. *Exp Hematol* 1999;27(4):642-653.
41. Citelli M, Bittencourt LL, da Silva SV, Pierucci AP, Pedrosa C. Vitamin A modulates the expression of genes involved in iron bioavailability. *Biol Trace Elem Res* 2012;149(1):64-70.
42. Villalpando S, Montalvo-Velarde I, Zambrano N, Garcia-Guerra A, Ramirez-Silva CI, Shamah-Levy T, et al. Vitamins A, and C and folate status in Mexican children under 12 years and women 12-49 years: a probabilistic national survey. *Salud Publica Mex* 2003;45 Suppl 4:S508-S519.
43. Sepulveda J, Bustreo F, Tapia R, Rivera J, Lozano R, Olaiz G, et al. Improvement of child survival in Mexico: the diagonal approach. *Salud Publica Mex* 2007;49 suppl 1:S110-S125.
44. Ramakrishnan U, Martorell R. The role of vitamin A in reducing child mortality and morbidity and improving growth. *Salud Publica Mex* 1998;40(2):189-198.
45. Batista-Filho M, Souza AI, Miglioli TC, Santos MC. Anemia and obesity: a paradox of the nutritional transition in Brazil. *Cad Saude Publica* 2008;24 Suppl 2:S247-S257.