



Applied nutritional investigation

## Vitamin B<sub>12</sub> concentration and its association with sociodemographic factors in Colombian children: Findings from the 2010 National Nutrition Survey



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### ABSTRACT

**Objective:** Rapid changes in dietary patterns, economic development, and urbanization in low- to middle-income countries are fueling complex malnutrition states that need better characterization using population-level data. The aim of this study was to describe the key findings related to vitamin B<sub>12</sub> status to identify the prevalence and associated sociodemographic factors in a representative sample of children in Colombia, based on the 2010 National Nutrition Survey.

**Methods:** We analyzed cross-sectional data from 6910 Colombian children between the ages of 5 and 12. Serum vitamin B<sub>12</sub> concentrations were determined by chemiluminescence. Sociodemographic data was assessed by computer-assisted personal interview technology.

**Results:** Of the children assessed, 2.8% had vitamin B<sub>12</sub> deficiency, defined as levels <200 pg/mL, and 18.1% had marginal vitamin B<sub>12</sub> deficiency, defined as levels between 200 and 300 pg/mL. A multivariate logistic regression analysis revealed increased risks for vitamin B<sub>12</sub> deficiency among children ages ≥9 y and for those living in the eastern, western, and southern regions of the country. No significant associations were found for ethnic groups, socioeconomic status, or urbanity levels. Being 11 y of age (odds ratio [OR], 2.16; 95% confidence interval [CI], 1.56–3.00; *P* = 0.0001), living in the west (Pacific) region of the country (OR, 3.92; 95% CI, 3.14–4.90; *P* = 0.0001), and being male (OR, 1.41; 95% CI, 1.20–1.65; *P* = 0.0001) were the factors most strongly associated with an increased risk for vitamin B<sub>12</sub> deficiency.

**Conclusions:** Compared with data from other Latin American countries, Colombian children have a lower prevalence of vitamin B<sub>12</sub> deficiency; however the prevalence of marginal deficiency is substantial. Continued surveillance and implementation of interventions to improve dietary patterns among the high-risk groups identified should be considered.

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### Introduction

Undernutrition has traditionally been the focus of nutrition agendas in low- and middle-income countries [1]. However, rapid economic development and urbanization have given rise to a nutrition transition, in which energy-dense diets replace traditional ones and sedentary lifestyles prevail [2]. Nutrition-

related non-communicable diseases have their origin very early in life, and they develop during childhood and adolescence [3]. Given the risk for food malnutrition in developing countries, it is necessary to measure its prevalence in vulnerable populations, such as children, pregnant women, and minorities, to prevent subsequent deterioration of their health [4]. To estimate the magnitude of this problem, the use of direct indicators to assess various nutrient levels, such as iron, vitamin A, zinc, and vitamin B<sub>12</sub>, has been proposed [5]. These biochemical estimators reflect the nutritional status that influences important biological processes, including cognitive development, physical growth, and immune response [6].

Vitamin B<sub>12</sub> deficiency, which is common in wealthier countries, principally among the elderly, is even more prevalent in poorer populations worldwide [7]. This deficiency is rare in children and is associated with anemia and strictly vegetarian diets. Humans do not synthesize Vitamin B<sub>12</sub>, and the only sources of this nutrient are foods of animal origin, such as meat, fish, eggs, and dairy [8]. Vitamin B<sub>12</sub> deficiency affects the central nervous system, hematopoiesis, and tissues with high mitotic activity, such as the epithelium of the digestive tract [9]. Therefore, children who are breastfed by vegetarian mothers are at greater risk for serious complications related to vitamin B<sub>12</sub> deficiency. These complications include hematologic (megaloblastic anemia), neurologic (hypotonia, ataxia, developmental delays), and gastrointestinal (inflammatory complications) symptoms [10]. The consequences of anemia are not limited to poor pregnancy outcomes, impaired physical and cognitive development, and increased risk for morbidity in children, but also affect national productivity and economics [6].

Currently, there are few global reports on the prevalence of vitamin B<sub>12</sub> deficiency in children, in particular for low- and middle-income countries experiencing rapid nutrition transitions, such as those in Latin America. According to the Mexican National Nutrition Survey, the prevalence for vitamin B<sub>12</sub> deficiency in school children between the ages of 7 and 10 y is 25% [10]. Similar data were reported in school children in Guatemala [11]. In Colombia, according to estimates from the National Survey of Nutritional Status [12,13], one in five children <5 y of age are at risk for vitamin B<sub>12</sub> deficiency. Vitamin B<sub>12</sub> deficiency is recognized as an important health problem and different studies involving different age groups and both sexes have underscored the magnitude of vitamin B<sub>12</sub> deficiency as a major public health challenge for improving the health status, especially in refugee camps and among vulnerable at-risk groups. However, to the best of our knowledge, the association between vitamin B<sub>12</sub> deficiency and various sociodemographic factors that could help identify risk groups and offer information to better design interventions has not been investigated in a nationally representative sample in the Americas.

Therefore, the aim of this study was to identify factors associated with vitamin B<sub>12</sub> deficiency in a representative sample of Colombian children ages 5 to 12 y.

## Methods

### Study population

The Colombian National Nutrition Survey (ENSIN) was conducted in 2010 by the Colombian Institute of Family Welfare [14]. Details of the survey have been published elsewhere [14]. In brief, participants were selected to represent 99% of the country's population using a multistage stratified sampling scheme. All municipalities from the 32 departments in the country were grouped into strata based on similar geographic and sociodemographic characteristics. One municipality was randomly chosen from each stratum, with probability proportional to the population size. Clusters of about 10 households each were then randomly

chosen from within these strata, and household members were invited to participate.

### Data sources

The survey included 50 670 households, representing 4987 clusters from 258 strata. Of the 7266 children aged to 5 to 12 y, 6910 (95.1%) were enrolled. This study was approved by the ethics committee of the National Survey of Nutritional Status. This study was reviewed and approved by the Institutional Review Board, of the Instituto Nacional de Colombia. Before starting the survey participants were guaranteed the protection of any confidential information obtained (Resolución 8430 de 1993; Ministerio de Salud de Colombia) [15]. The children and their parents signed a written informed consent and study procedures were conducted according to the principles expressed in the Declaration of Helsinki.

### Vitamin B<sub>12</sub> concentrations

In a random subsample of participants, blood was collected by venipuncture and serum was separated into aliquots. Serum vitamin B<sub>12</sub> was quantified in these samples using direct chemiluminescence (ADVIA Centaur equipment, Siemens). This method offers high sensitivity, is less costly, is easier to implement, and is safer than microbiologic, chromatographic, or spectrophotometric assays [14]. The main outcomes of interest were mean serum vitamin B<sub>12</sub> concentrations (pg/mL) and the prevalence of vitamin B<sub>12</sub> deficiency (serum concentration <200 pg/mL) [16] and marginal depletion (serum concentration 200–300 pg/mL) [16].

### Sociodemographic characteristics

The following sociodemographic variables were included as factors potentially associated with vitamin B<sub>12</sub> deficiency: age (5–5.9, 6–6.9, 7–7.9, 8–8.9, 9–9.9, 10–10.9, 11–11.9, and 12–12.9 y); sex (male and female); urbanicity (grouped as urban and rural); ethnicity grouped as indigenous, black or afro-Colombian, and others (mestizo); geographic region: Atlantic (north), eastern, central, and Pacific (west), Bogota, and national territories (south); and social or socioeconomic status determined by the System of Identifying Potential Beneficiaries of Social Programs (SISBEN, for its Spanish initials) (1–3 and ≥4). The SISBEN is a system designed by the Colombian national government to identify families who could benefit from social programs. SISBEN takes into account sociodemographic characteristics (family composition, employment status, family income, and educational level), living conditions (construction type and materials), and access to public utilities (sewer, electricity, potable water, and garbage collection). Households are classified into six levels with 1 being the poorest and 6 being the wealthiest. For this study, we classified SISBEN scores into four categories (1, 2, 3, and ≥4).

### Statistical analyses

We conducted an exploratory analysis of the frequency distribution (measures of central tendency and dispersion for quantitative variables) and relative frequencies (for qualitative variables) using the Pearson  $\chi^2$  test with and without the Yates correction. To estimate the relationship between vitamin B<sub>12</sub> deficiency and sociodemographic variables in children (age, sex, urbanicity, geographic region, ethnicity, and socioeconomic level–SISBEN), binary logistic regression models were used. The first adjusted model was for age and sex, the second was based on ethnic group, geographic area, socioeconomic levels, and urbanicity; the third was adjusted by age, sex, ethnic group, geographic area, socioeconomic levels and urbanicity. Odds ratios were considered a confounder if they shifted the model in a constant direction with a proportional increase in the exposure level of ≥10%. All analyses were conducted with the use of the complex survey design routines of the SPSS Statistical software package version 20 (Armonk, NY, USA).

## Results

The study cohort consisted of 6910 children between the ages of 5 and 12 y (mean age 8.7 y). The range of vitamin B<sub>12</sub> was 45 to 1000 pg/mL (mean 434.9 pg/mL, 95% confidence interval [CI], 429.5–440.4 pg/mL). In all, 2.8% of children had vitamin B<sub>12</sub> levels <200 pg/mL and 18.1% had levels between 200 and 300 pg/mL. Children who live in the Pacific area, were 11 y old, and belonged to SISBEN level 2 had the highest percentage of vitamin B<sub>12</sub> values < 300 pg/mL (36.2%, 27% and 23%, respectively). The distribution of the vitamin B<sub>12</sub> deficiency and depletion in children ages 5 to 12 y is shown in Table 1.

**Table 1**  
Characterization of vitamin B<sub>12</sub> levels among Colombian children (national nutrition survey, 2010)

Characteristics	Adequate B <sub>12</sub> concentration		Marginal vitamin B <sub>12</sub> deficiency		Vitamin B <sub>12</sub> deficiency	
	n	%* (95% CI)	n	%* (95% CI)	n	%* (95% CI)
Total	5371	79.2 (78.7–79.6)	1,304	18.1 (17.2–18.9)	235	2.8 (2.3–3.2)
Characteristics						
Age (y) <sup>†</sup>						
5–5.9	620	85 (83.9–85.8)	125	13.6 (11.4–15.3)	21	1.5 (0.6–2.2)
6–6.9	623	81.1 (80–81.9)	131	16.8 (14.4–18.7)	21	2.2 (0.8–3.3)
7–7.9	685	84.4 (83.5–85.1)	125	13.8 (11.4–15.8)	24	1.8 (1–2.5)
8–8.9	703	81.2 (80.3–81.9)	153	16.1 (13.7–18.1)	30	2.7 (1.5–3.8)
9–9.9	679	79.9 (78.7–80.9)	188	19 (16.8–20.9)	20	1.1 (0.4–1.7)
10–10.9	734	77.2 (76.1–78.2)	188	18 (15.9–19.9)	43	4.7 (3.2–6.1)
11–11.9	694	73.1 (71.8–74.1)	202	23.5 (21–25.6)	39	3.5 (2.1–4.6)
12–12.9	633	74 (72.8–75.1)	192	22 (19.5–24.1)	37	4 (2.4–5.2)
Sex						
Male	2658	76.4 (75.8–77)	749	20.7 (19.5–21.8)	126	2.9 (2.2–3.5)
Female	2713	82.1 (81.6–82.6)	555	15.2 (14.1–16.3)	109	2.7 (2.1–3.2)
Socioeconomic levels by SISBEN						
Level 1	3204	79.5 (78.9–80)	787	17.5 (16.3–18.5)	159	3.1 (2.4–3.6)
Level 2	664	77 (76–77.8)	166	20.8 (18.3–22.9)	20	2.2 (1–3.3)
Level 3	475	79.3 (78.1–80.4)	112	18.4 (15.7–20.5)	13	2.3 (0.7–3.5)
Level 4+	1028	79.6 (78.7–80.3)	239	17.8 (16–19.3)	43	2.7 (1.8–3.4)
Geographic area						
Atlantic (north) <sup>†</sup>	1301	86.5 (86–86.9)	240	12.5 (11.2–13.7)	25	1 (0.6–1.4)
Eastern <sup>†</sup>	732	75.9 (74.9–76.8)	194	20 (18.1–21.7)	41	4.1 (2.9–5.1)
Central <sup>†</sup>	1254	83.9 (83.2–84.5)	230	14.5 (12.9–16)	32	1.6 (0.9–2.1)
Pacific (west)	640	63.8 (62.6–64.8)	285	30.4 (28.4–32.2)	59	5.8 (4.4–7)
Bogotá <sup>†</sup>	252	82.6 (81.6–83.5)	47	15.4 (12.4–17.8)	6	2 (0.4–3.2)
National territories (south) <sup>†</sup>	1192	79.3 (78.6–79.9)	308	17.4 (15.4–19.2)	72	3.3 (2.1–4.4)
Urbanicity						
Urban	3296	79.8 (79.3–80.3)	773	17.5 (16.4–18.4)	134	2.7 (2.2–3.2)
Rural	2075	77.6 (76.9–78.3)	531	19.5 (18–20.8)	101	2.9 (2.2–3.5)
Ethnic group <sup>‡</sup>						
Indigenous <sup>†</sup>	640	78.6 (77–79–8)	204	19.5 (16.5–21.8)	45	1.9 (0.4–3.1)
Black or Afro-Colombian <sup>†</sup>	558	77.4 (76.3–78.3)	155	18.3 (16.1–20.2)	38	4.3 (2.7–5.6)
Others	4145	79.4 (78.9–79.9)	927	18 (17–18.9)	149	2.6 (2.1–3.1)

SISBEN, System of Identifying Potential Beneficiaries of Social Programs

\* It is not correct to calculate the percentages from the “n” presented in this table; these calculations were taken from weighted values given to each participant.

<sup>†</sup> Coefficient of variation is >20% deficiency prevalence, therefore variation should be used with caution.

<sup>‡</sup> We analyzed 6861 children by ethnic group. Another 49 appertained to “Raizal del archipiélago” and “Palenquero de San Basilio,” and were not analyzed because they did not have a representative sample.

Table 2 shows the results for a logistic regression analysis. Being 11 y of age (odds ratio [OR] 2.16; 95% CI, 1.56–3.00), living in the Pacific (west; OR 3.92; 95% CI, 3.14–4.90) or national territories (south; OR, 1.69; 95% CI, 1.32–4.90), and being male (OR, 1.41; 95% CI, 1.20–1.65) were predisposing factors for vitamin B<sub>12</sub> deficiency.

## Discussion

Vitamin B<sub>12</sub> deficiency has serious consequences on neurologic and functional development in children. In Colombia, vitamin B<sub>12</sub> deficiency in children ages 5 to 12 y is relatively low (2.8%). However, 18.1% of children had low values, a factor that should be considered by public health policymakers. Thus, the results of the present study support the conclusion that the prevalence of vitamin B<sub>12</sub> deficiency in Colombian children ages 5 to 12 y is low when compared with rates in Latin American countries, including Mexico [10] and Guatemala [11], which on average exceed 20%.

Similarly, it was observed that the risk for vitamin B<sub>12</sub> deficiency in Colombian children increases with age, with prevalence ranging from 13.6% at age 5 y to 22% for children age 12 y. To our knowledge, only one previous study examined vitamin B<sub>12</sub> concentrations in Colombia. Among low- and middle-income children from Bogotá, the combined prevalence of deficiency and

marginal deficiency was 17% in 2006 [17], similar to the result found for this age group and city in the present survey.

A logistic regression analysis showed an association between being 11 y old and risk for vitamin B<sub>12</sub> deficiency. No variations were observed for ethnic groups, socioeconomic status, or urban and rural area. However, the prevalence was higher in boys (20.7%) when compared with girls (15.2%). The differences observed in the present study are similar to previous reports that analyzed vitamin B<sub>12</sub> deficiency in the Americas [16]. Colombian children living in the Pacific region showed a higher prevalence for vitamin B<sub>12</sub> deficiency (30.4%), whereas those living in the central and Caribbean regions showed a lower prevalence (<15%). Living in the Pacific region was considered a factor associated with vitamin B<sub>12</sub> deficiency in Colombian children, as shown by similar results published by investigators from the Nutrition Department of the World Health Organization [18]. Although not measured in this study, school meals in the Pacific region are likely to have low phytate levels because they consist mainly of fast food, eggs, and milk [15]. Additionally, in Colombia, the Pacific region environments have been associated with aridity, high food prices, limited natural resources, and poor infrastructure development, which often affect the availability of and access to food and health services. Such factors can lead to increased malnutrition among populations residing at this region. Similar challenges can be found in the eastern and south (national territories) areas of the country and may explain the

**Table 2**  
Sociodemographic factors associated with vitamin B<sub>12</sub> deficiency/marginal in Colombian children (national nutrition survey, 2010)

Characteristics	Bivariate	P value	Adjusted model*	P value	Adjusted model <sup>†</sup>	P value	Adjusted model <sup>‡</sup>	P value
Age (y) <sup>§</sup>								
6–6.9	1.32 (0.93–1.86)	0.7945	1.31 (0.93–1.85)	0.7569	1.35 (0.95–1.91)	0.6745	1.34 (0.94–1.90)	0.6909
7–7.9	1.05 (0.74–1.49)	0.5558	1.04 (0.73–1.48)	0.5389	1.08 (0.75–1.55)	0.4669	1.07 (0.74–1.54)	0.4648
8–8.9	1.31 (0.93–1.83)	0.4378	1.30 (0.93–1.83)	0.4067	1.36 (0.96–1.91)	0.1389	1.35 (0.96–1.91)	0.1230
9–9.9	<b>1.42 (1.02–1.98)</b>	<b>0.0410</b>	<b>1.40 (1.01–1.95)</b>	<b>0.0400</b>	<b>1.50 (1.07–2.09)</b>	<b>0.0345</b>	<b>1.48 (1.05–2.07)</b>	<b>0.0378</b>
10–10.9	<b>1.67 (1.21–2.30)</b>	<b>0.0201</b>	<b>1.66 (1.21–2.30)</b>	<b>0.0291</b>	<b>1.73 (1.24–2.40)</b>	<b>0.0280</b>	<b>1.73 (1.24–2.41)</b>	<b>0.0278</b>
11–11.9	<b>2.08 (1.51–2.87)</b>	<b>0.0001</b>	<b>2.06 (1.49–2.83)</b>	<b>0.0001</b>	<b>2.18 (1.57–3.03)</b>	<b>0.0001</b>	<b>2.16 (1.56–3.00)</b>	<b>0.0001</b>
12–12.9	<b>1.98 (1.43–2.74)</b>	<b>0.0001</b>	<b>1.94 (1.40–2.69)</b>	<b>0.0001</b>	<b>2.10 (1.51–2.92)</b>	<b>0.0001</b>	<b>2.06 (1.48–2.87)</b>	<b>0.0001</b>
Sex <sup>  </sup>								
Male	<b>1.42 (1.21–1.66)</b>	<b>0.0001</b>	<b>1.40 (1.20–1.64)</b>	<b>0.0001</b>	<b>1.42 (1.21–1.66)</b>	<b>0.0001</b>	<b>1.41 (1.20–1.65)</b>	<b>0.0001</b>
Socioeconomic levels by SISBEN <sup>¶</sup>								
Level 1	1.00 (0.83–1.22)	0.9756	1.04 (0.85–1.27)	0.7156	1.06 (0.87–1.30)	0.5551	1.09 (0.89–1.34)	0.3981
Level 2	1.17 (0.89–1.52)	0.2734	1.19 (0.91–1.56)	0.2109	1.21 (0.92–1.60)	0.1890	1.23 (0.93–1.63)	0.1426
Level 3	1.01 (0.75–1.37)	0.9321	1.04 (0.77–1.41)	0.8015	1.08 (0.79–1.46)	0.6544	1.10 (0.81–1.50)	0.5350
Geographic area <sup>#</sup>								
Eastern	<b>2.03 (1.61–2.56)</b>	<b>0.0001</b>	<b>1.98 (1.56–2.50)</b>	<b>0.0001</b>	<b>1.96 (1.54–2.49)</b>	<b>0.0001</b>	<b>1.93 (1.51–2.45)</b>	<b>0.0001</b>
Central	1.23 (0.97–1.56)	0.1348	1.21 (0.95–1.54)	0.2380	1.20 (0.94–1.53)	0.2250	1.19 (0.93–1.51)	0.3230
Pacific (west)	<b>3.64 (2.93–4.51)</b>	<b>0.0001</b>	<b>3.69 (2.97–4.57)</b>	<b>0.0001</b>	<b>3.86 (3.10–4.81)</b>	<b>0.0001</b>	<b>3.92 (3.14–4.90)</b>	<b>0.0001</b>
Bogotá	1.35 (0.96–1.89)	0.2245	1.31 (0.93–1.83)	0.2400	1.36 (0.97–1.91)	0.1823	1.33 (0.95–1.88)	0.1978
National territories (south)	<b>1.68 (1.32–2.13)</b>	<b>0.0001</b>	<b>1.69 (1.33–2.16)</b>	<b>0.0001</b>	<b>1.67 (1.31–2.14)</b>	<b>0.0001</b>	<b>1.69 (1.32–2.16)</b>	<b>0.0001</b>
Urbanicity <sup>**</sup>								
Rural	1.14 (0.97–1.34)	0.1269	1.15 (0.97–1.35)	0.1170	1.11 (0.93–1.32)	0.2581	1.11 (0.93–1.32)	0.2609
Ethnic group <sup>††</sup>								
Indigenous	1.05 (0.79–1.40)	0.7450	1.10 (0.82–1.48)	0.5178	0.76 (0.56–1.03)	0.0890	0.79 (0.58–1.07)	0.1311
Black or Afro-Colombian	1.13 (0.90–1.40)	0.3078	1.15 (0.92–1.44)	0.2124	0.79 (0.62–1.01)	0.0689	0.79 (0.62–1.01)	0.0647

SISBEN, System of Identifying Potential Beneficiaries of Social Programs

Odds ratios (95% confidence interval), significant odds ratios are shown in bold

\* Adjusted by age and sex.

<sup>†</sup> Adjusted by ethnic group, geographic area, socioeconomic levels, and urbanicity.

<sup>‡</sup> Adjusted by age, sex, ethnic group, geographic area, socioeconomic levels, and urbanicity.

<sup>§</sup> Reference group: 5–5.9.

<sup>||</sup> Reference group: girls.

<sup>¶</sup> Reference group: level 4+.

<sup>#</sup> Reference group: Atlantic (north).

<sup>\*\*</sup> Reference group: urban.

<sup>††</sup> Reference group: others.

higher prevalence of B<sub>12</sub> deficiency found in those regions compared with more developed areas of the country (Bogotá, central, and Atlantic regions) that include large urban centers. Previous studies have found that children living in urban areas and in geographic regions with greater economic and structural development in general had higher serum concentrations than those from rural and poorer areas [19–23].

In another study in Guatemala City, 24% of 127 infants ages 7 to 12 mo had deficient (<200 pg/mL) and 37% had marginally deficient (200–300 pg/mL) plasma vitamin B<sub>12</sub> concentrations [19]. Plasma vitamin B<sub>12</sub> was lower in those infants who consumed more breast milk ( $r = -0.33$ ;  $P < 0.0001$  with measured breast milk intake, kcal/d) but positively associated with B<sub>12</sub> intake from complementary foods. In a different group of infants ( $N = 304$ ) ages 12 mo in Guatemala City, deficient and marginal plasma vitamin B<sub>12</sub> values were found in 30% and 20% of infants, and 36% and 32% of their mothers, respectively [20].

Vitamin B<sub>12</sub> is a cofactor of methionine synthase in the synthesis of methionine, the precursor of the universal methyl donor S-adenosylmethionine, involved in different epigenomic regulatory mechanisms and especially in fetal growth [21]. Measurement of the total vitamin B<sub>12</sub> concentration in plasma is the usual method for assessing vitamin B<sub>12</sub> status. However, neurologic and hematologic symptoms of depletion can occur in individuals with plasma vitamin B<sub>12</sub> concentrations in the low-normal range [22]. Nevertheless, associations between vitamin B<sub>12</sub> marginal depletion and adverse health outcomes in observational studies are concerning and urgently need further evaluation in clinical trials [23].

Several factors can affect vitamin B<sub>12</sub> concentrations, such as individual genetic variations, disease conditions, and prescriptions. Approximately 20% of Latin American children with low serum vitamin B<sub>12</sub> concentrations have neither clinical nor metabolic signs of vitamin B<sub>12</sub> depletion [21,24]. One of the important causes for lower status of vitamin B<sub>12</sub> could be poor dietary patterns [21]. Based on our dietary survey among indigenous populations in Colombia, the intake of animal protein was very low among children [19]. Thus, enriching the diet and increasing intake of animal-derived foods might be an important way to improve the status of vitamin B<sub>12</sub> of Colombian children.

Measurement procedure errors and other technological problems produce slightly high or low biomarker concentrations. These factors adversely affect the biomarkers' sensitivity and specificity and result in false-positive or false-negative classifications of vitamin B<sub>12</sub> depletion. Systematic bias and spurious results affected some measurement procedures used in the past to derive reference ranges [25–27]. The cutoff used in this study affects ENSIN-2010 prevalence estimates for vitamin B<sub>12</sub> deficiency [25].

In this study, one limitation had to be addressed. The survey addressed the health status of Colombian children, and only vitamin B<sub>12</sub> was measured. Unfortunately, the metabolic precursors of vitamin B<sub>12</sub>—homocysteine (tHcy), methylmalonic acid (MMA), and holotranscobalamin—were not been measured. Studies indicated that these markers increased or decreased when the status of vitamin B<sub>12</sub> were low [28]. However, tHcy and MMA started to increase at vitamin B<sub>12</sub> levels above the typical cutoff value (<200 pg/mL), and they increased quickly when

vitamin B<sub>12</sub> decreased from 400 to 200 pg/mL, which suggests that changes on markers related to nervous system impairment had already begun before the deficiency in vitamin B<sub>12</sub> could be determined [29]. The use of serum vitamin B<sub>12</sub> as a proxy of vitamin B<sub>12</sub> status can benefit from further assessment of its metabolic precursors.

A second limitation of the present study was that dietary intake of vitamin B<sub>12</sub> was not assessed. It has been determined that the bioavailability of vitamin B<sub>12</sub> was greater from dairy products and fish than from meat [26]. One dietary study showed that only 13.4% of the protein in the diets of children was derived from eggs and milk, with 40% of protein coming from meat [17]. Colombia is a country that is geographically, climatically, and ethnically diverse. Clearly, these differences could affect food supply, dietary practices, and consequently vitamin B<sub>12</sub> intakes. The Pacific, eastern, and central parts of Colombia are very diverse, which leads to different dietary patterns and climate. The use of specific cutoff points of serum vitamin B<sub>12</sub> to define deficiency and marginal deficiency also deserves comment. We used the conventionally accepted cutoff points of <200 pg/mL (deficiency) and 200 to 300 pg/mL (marginal deficiency) [21,25]. Although these cutoff points may be considered somewhat arbitrary, there is a pathophysiological rationale to their use. MMA and tHcy concentrations associated with anemia, megaloblastosis, and neuropathy decrease substantially when serum vitamin B<sub>12</sub> concentrations are >200 pg/mL, even in the absence of clinical manifestations [26].

## Conclusion

Vitamin B<sub>12</sub> deficiency remains an area that merits strict monitoring among Colombian children between ages 5 and 12 y. Although its current prevalence is slightly lower than reports from other Latin American countries [10,11,13,17,26,30], the somewhat high prevalence of marginal vitamin B<sub>12</sub> deficiency in this study provides reason to suggest that children could benefit from strategies to supplement vitamin B<sub>12</sub>, in particular in regions of the country where deficiency is more prevalent [31,32]. This can be done through tailored supplementation in clinical settings or through broader public health supplementation strategies as done in other countries such as Guatemala, Puerto Rico, and Mexico [10,20,30]. For example, a sensible strategy may be to include vitamin B<sub>12</sub> along with folic acid in flour fortification programs where a need for additional vitamin B<sub>12</sub> has been established. This could have multiple benefits, including further reduction in neural tube defects, improved vitamin B<sub>12</sub> levels in breast milk and among mothers and young children, and prevention of cognitive decline in the elderly [30]. Additionally, coordination with other dietary interventions and educational strategies can produce viable and sustainable interventions in particular among the high-risk groups identified in this study.

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