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Anemia frequency in children living at Andean high altitude in Ecuador, Peru, and Bolivia

Prevalencia de anemia en niños que viven en la altitud andina de Ecuador, Perú y Bolivia

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Abstract

OBJECTIVE: To establish the frequency of anemia among children living in the Andean region of Ecuador, Perú, and Bolivia.

MATERIALS AND METHODS: A transversal descriptive study based on the risk association of anemia in children between 6 and 59 months living in the Andean region, through a secondary source published by institutions of health from Ecuador, Peru and Bolivia.

RESULTS: A total of 155,007 children were included; 65,161 living in the Andean region. Anemia was observed in 46.69 to 60.59% in the Andes of Ecuador, Peru, and Bolivia. Opposing, in low-lying regions varied from 33.96 to 43.37%. Anemia was more prevalent in the high altitude, regarding to severe anemia, the risk association was significant in Andean Region of Ecuador during 2013 (OR:4.98; p<0.01) and 2014 (OR:5.32; p<0.01), Bolivia (OR:4.65; p<0.01), and Peru (OR:1.78; p<0.01).

CONCLUSIONS: A higher frequency of anemia was evident in children residing in the Andean region of Ecuador, Peru, and Bolivia. However, although a significant risk association was demonstrated, this could be a multifactorial phenomenon that requires more detailed investigation.

KEYWORDS: Andean region; Anemia; Risk; Children; Peru; Ecuador; Bolivia.

Resumen

OBJETIVO: Estimar la prevalencia de anemia en niños residentes de los Andes de Ecuador, Perú y Bolivia.

MATERIALES Y MÉTODOS: Estudio descriptivo, transversal, basado en la asociación de riesgo de anemia en niños de 6 a 59 meses de edad, residentes en los Andes de Ecuador, Perú y Bolivia. Los datos se obtuvieron del análisis de una fuente secundaria publicada por instituciones de salud pública de Ecuador, Perú y Bolivia.

RESULTADOS: Se incluyeron 155,007 niños; 65,161 vivían en la región andina. Se encontró anemia en 46.69 y 60.59% de quienes habitaban en los Andes de Ecuador, Perú y Bolivia. En contraposición, en las regiones de baja altitud varió entre 33.96 y 43.37%. La anemia fue más prevalente en la altitud geográfica. En el caso de anemia grave, la asociación de riesgo fue significativa en la región andina de Ecuador durante 2013 (RM: 4.98; p < 0.01) y 2014 (RM: 5.32; p < 0.01), Bolivia (RM: 4.65; p < 0.01) y Perú (RM: 1.78; p < 0.01).

CONCLUSIONES: Existe mayor prevalencia de anemia en los niños residentes de la región andina de Ecuador, Perú y Bolivia. Si bien se demostró una asociación de riesgo significativa, podría represenar un fenómeno multifactorial que requiere investigarse con más detalle.

PALABRAS CLAVE: Región andina; anemia; riesgo; niños; Perú; Ecuador; Bolivia.

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BACKGROUND

Anemia a widespread and highly prevalent disease mainly affects children under 5 years of age as well as pregnant women, mostly in the developing or low-income countries. Anemia, according to the World Health Organization (WHO), has emerged as a significant public health problem that has impacted an estimated 2000 million people.[1] In Latin America, the prevalence of anemia varies from 5.1% in Chile, up to 45.5% in Haiti. While it is considered a moderate public health problem (PHP) in Ecuador (25.7% in children below 5 years of age) and Peru (32.9% in children from 1 to 4 years of age), it is regarded as a severe PHP in Bolivia (61.3%).[2] However, in these three countries different rates of anemia prevalence have been reported in children, more common in the regions located in the Andes, characterized by a geographical altitude greater than 2400 meters above sea level (masl), and the prevailing hypoxic and hypobaric conditions.[3-6] Living at high altitude (HA) has been linked to the biological phenomenon of adaptation in which the erythrocyte number increases in response to the hypoxic environment.[7] Further, the Andean population has been recognized to have both high and normal erythropoietin (EPO) levels, which suggested other possibilities that could explain the pathways leading to the increased hemoglobin values in this population.[8] While erythrocytosis is significant among the Andean highlanders, the Tibetan highlanders experience slight or no erythrocytosis at all.[9] Moreover, to obtain an adequate EPO response, proper iron storage in the body is necessary;[10] this is particularly significant in a population characterized by inadequate iron intake because the close association between high EPO levels with low iron intake could result in anemia. In this context, it is crucial to recall studies which highlighted the inadequate iron intake among the Andean population.[11] The cumulative sum of these factors could be the basic reasons for the high frequency of the incidence of anemia in the Highlands of Ecuador, Perú, and Bolivia. In this context, the advice given by WHO in terms of hemoglobin correction to people living in high altitudes remains current.[12]

It therefore becomes essential to establish the prevalence, and significance of the comparison between the anemia rates of those living in HA and the low-lying regions (LR). This study thus aims at establishing the frequency of anemia among children living in the Andean region, and compare it versus children residing in the Coastal and Amazon regions of Ecuador, Perú, and Bolivia.

MATERIALS AND METHODS

A transversal descriptive study was conducted in May 2018, in Quito, Ecuador, based on the association of prevalence rates of anemia in HA (Andes) compared with those of the low lying regions (Coastal, Amazon and Galapagos) in children between the ages of 6 and 59 months, through a secondary source published by the national authorities of health and statistics from Ecuador (Ministry of Public Health), Peru (National Institute of Statistics and Informatics), and Bolivia (National Institute of Statistics along with the Ministry of Health). Living in the Andean region was considered the main exposure factor. The variable that we studied was the state of anemia, and the exposure factor was living at high altitude. Confounders such as the nutritional intake of each patient and any infectious condition were not included because the database that we used didn't provide this information. Sampling methods wasn't used as we worked with data provided by a secondary source.

Study location

Ecuador, Perú, and Bolivia are South American countries that the Andean mountain range extends across. This geographic feature divides each of these nations into the Andean highland regions (AHR) and low-lying regions (LR). The altitude in the AHR ranges from 600 to 5000 masl. However, the most significant percentage of the population lives above 2000 masl. On the other hand, the altitudes of the LR range between 0 and 1000 masl.

Data from Ecuador

The frequency of anemia in Ecuadorian children between 6 and 59 months was calculated using the data published by the Nutrition Unit, Ministry of Public Health of Ecuador. This information was compiled through the Integrated System of Food and Nutritional Surveillance (Sistema Integrado de Vigilancia Alimentaria y Nutricional, SIVAN) (https://www.salud.gob.ec/unidad-de-nutricion/),[13] which is actualized every day by physicians working throughout the country. During the time of this study, published information for 2013 and the first trimester of 2014 was available. However, the report of the non-delimited Areas (NDA) which was also published was not included. To obtain this data, firstly, we enter into the website provided.

Data from Peru

Data from the Peruvian population was gathered from the Demographic and Family Health Survey (Encuesta Demográfica y de Salud Familiar, ENDES 2016) conducted by the National Institute of Statistics and Informatics and supported by the National Centre for Food and Nutrition (Centro Nacional de Alimentación y Nutrición, CENAN) and the National Police of Peru (Policía Nacional del Perú, PNP). (https://www.inei.gob.pe/media/MenuRecursivo/publicaciones_digitales/Est/Lib1433/index.html).[14]

Data from Bolivia

The information for the Bolivian population was obtained via the Demography and Health Survey 2016 (Encuesta de Demografía y Salud, EDSA 2016), conducted by the National Institute of Statistics (NIS) together with the Ministry of Health (MH) (https://www.minsalud.gob.bo/images/Documentacion/EDSA-2016.pdf).[15]

Hemoglobin determination

HemoCue® was used to determine the hemoglobin (Hb) levels. The HemoCue® B-hemoglobin system is based on the azide-methemoglobin reaction. Aditionally, it became clear that though automatized methods provide a higher level of precision, HemoCue® is a reliable, accurate, rapid, cheap, and easy method of use.[16]

Hemoglobin adjustment in HA

Both, the EDSA 2016 and ENDES 2016 corrected the hemoglobin level using the formula of the CDC/PNSS and Dirren which is adjustment = -0.032*(alt) + 0.022*(alt*alt), Being; alt = [(geographical altitude in m)/1 000]*3.3. The SIVAN utilizes the hemoglobin correction factor established by WHO.

Degree of Anemia

The WHO recommends that anemia must be diagnosed in children between 6 and 59 months of age when hemoglobin below 11 g/dL is detected. Moreover, anaemia can be classified as mild (10-10.9 g/dL), moderate (7-9.9 g/dL), and severe (under 7 g/dL).[17] This parameter was used in all three countries.

Data analysis and statistics

The number of patients tested during the statistical analysis was inferred from the percentages of anemic children, as well as the total number of patients included in each survey in this study. Data was organized using the software Excel for Microsoft Windows. The statistical significance was determined using the latest version of the SPSS software package. Furthermore, the risk association was calculated using the Odds Ratio (OR) and chi square. To compare the percentage of anemic children between AHR and LR, we used the absolute number of children affected in each country as well as the pooled data of all the countries included.

The categorical variables were represented through Tables of frequencies, proportions, and percentages, while the continuous variables were depicted via the averages.

RESULTS

From the data collected from SIVAN 2013, SIVAN 2014 (first trimester), EDSA 2016 and ENDES 2016, a total number of 155 007 children from 6 to 59 months of age were included. In Ecuador, a total of 106 303 children were evaluated in 2013, as well as 37 118 children during the first trimester of 2014. In Perú, ENDES 2016 was done on a sample that included 10060 children between 6 and 59 months of age. Also, in Bolivia, EDSA 2016 consists of the data from 15 160 homes, from where a total of 1 526 children between 6 and 59 months of age were evaluated. From the whole group of 155 007 patients included, 61 006 were anemic, with 30 399 located in the HAR and 30607 in the LR. **Tables 1 and 2** show the total number of patients in each region, as well as the percentage of anemic patients.

Anemia in Ecuadorian children

In 2013 and the first trimester of 2014, we observed that anemia was more frequent in the HAR, 46.69%, and 47.34% respectively, compared with the LR which had anemia in the 34.38% and 33.96% of children during the same years. However, in both regions, mild anemia had higher percentages over moderate or severe anemia, varying from 21.31% to 24.52%. The five provinces more affected by anemia in 2013 were Imbabura (63.00%), Carchi (59.25%), Napo (58.40%), Pichincha (54.53%), and Cañar (53.98%). These provinces remained to be the five more affected in the first trimester of 2014. The two areas in the LR with higher percentages of anemic children were Napo and Morona Santiago, both situated in the Amazon region (AR). Apart from this, Santa Elena and Esmeraldas recorded the highest number of anemic children, corresponding to the Coastal region. *Anemia in Peruvian children*.

In the Peruvian children from AHR, the percentage of anemic patients was 38.69%, being higher than the 30.68% observed in the LR. Also, seven out of the ten departments which registered the highest percentage of anemic children were located in the AHR; Puno (62.30%), Pasco (49.90%), Cusco (46.80%), Huancavelica (45.40%), Junín (41.90%), Ayacucho (41.10%), and Apurímac (39.70%). Similarly to the observations made in Ecuador, the three departments more affected by anemia in the low LR were part of the AR; Loreto (49.90%), Ucayali (47.20%), and Madre de Dios (42.90%).

Anemia in Bolivian children

In the Bolivian children, we found anemia being more frequent in the AHR (60.59%) compared to LR (43.37%). The five departments more affected by this condition were La Paz (74.40%), Potosí (69.00%), Oruro (67.20%), Pando (61.80%) and Chuquisaca (54.90%). And as was observed in Ecuador and Perú, among the departments located in the LR, the highest percentage of anemia was found in Pando which is located in the AR.

AHR associated as a risk factor for acquiring anemia

When compared the number of patients affected by anemia between the HAR and LR through OR, we found a higher risk for anemia affecting

Table 1. Prevalence of anemia in children between 6 and 59 months of age, in the different provinces of Ecuador

Zone / Province	Ecuador, SIVAN 2013; A total of 106303 children included					Ecuador, SIVAN 2014; A total of 37118 children included				
	Mi.A (%)	Mo.A (%)	SA (%)	AA (%)	T(n)	Mi.A (%)	Mo.A (%)	SA (%)	AA (%)	T(n)
AHR (Total)	24.04	21.85	0.80	46.69	44312	24.52	22.07	0.75	47.34	16702
Chimborazo	18.77	16.37	0.96	36.11	7591	17.21	15.26	0.82	33.29	1592
Cotopaxi	25.67	19.57	0.38	45.62	1313	19.04	16.32	0.78	36.14	772
Pichincha	21.45	14.98	0.44	36.87	2056	18.56	22.68	0.26	41.49	388
Carchi	30.23	28.02	0.99	59.25	4925	32.44	26.04	0.42	58.90	1421
Tungurahua	25.10	19.55	1.49	46.14	1478	21.27	19.05	1.41	41.73	992
Imbabura	26.31	35.59	1.11	63.00	3330	28.34	36.48	0.94	65.76	2237
Bolívar	17.78	19.42	2.23	39.43	1344	21.88	21.45	1.70	45.03	704
Pichincha*	27.87	26.07	0.59	54.53	7487	28.39	22.07	0.46	50.92	1740
Azuay	21.17	15.33	0.42	36.92	3789	20.27	17.21	0.70	38.18	1993
Cañar	23.04	29.64	1.30	53.98	2912	26.61	25.15	0.12	51.88	823
Loja	23.68	16.85	0.37	40.91	8087	25.37	19.03	0.72	45.12	4040
LR (Total)	**21.58**	**12.60**	**0.20**	**34.38**	**61991**	**21.31**	**12.48**	**0.18**	**33.96**	**20416**
Sucumbíos	22.46	13.64	0.53	36.63	374	32.10	12.76	0.00	44.86	243
Napo	34.63	23.51	0.26	58.40	387	26.63	21.99	0.00	48.63	582
Orellana	21.05	16.07	0.09	37.21	1145	20.69	16.75	0.10	37.54	1039
Esmeraldas	24.57	20.85	0.59	46.00	2715	23.61	14.99	0.62	39.22	487
Pastaza	22.59	15.28	0.33	38.21	602	23.86	9.09	0.00	32.95	88
Galápagos	8.65	7.69	0.00	16.35	104	17.24	0.00	0.00	17.24	29
Manabí	21.95	2.44	0.00	24.39	41	20.38	11.22	0.34	31.94	1747
SDT	26.83	19.58	0.54	46.95	1476	12.15	14.04	0.00	26.18	634
Guayas	18.53	5.21	0.11	23.85	4587	20.00	4.61	0.12	24.74	1605
Los Rios	20.53	16.03	0.23	36.79	9920	21.74	14.44	0.14	36.33	3463
Santa Elena	25.33	22.52	0.77	48.62	1816	19.05	21.08	0.35	40.48	1134
MS	27.01	25.36	0.33	52.70	2429	28.51	23.55	0.43	52.48	705
El Oro	15.02	5.69	0.13	20.85	3794	12.70	6.25	0.39	19.34	512
ZC	19.99	12.62	0.15	32.76	2717	20.09	8.71	0.05	28.85	2135
Guayas**	22.04	10.43	0.11	32.58	29884	22.33	10.84	0.15	33.33	6013

SIVAN, Sistema Integrado de Vigilancia Alimentaria y Nutricional (Integrated System of Food and Nutritional Surveillance); Mi.A, Mild anemia; Mo.A, Moderate anemia; SA, Severe anemia; AA, All cases of anemia; T, Total number of patients included; *Metropolitan District of Quito;**Metropolitan District of Guayaquil ; AHR, Andean highland region; LR, Low-lying region; SDT, Santo Domingo de los Tsachilas; MS, Morona Santiago; ZC, Zamora Chinchipe.

Table 2. Prevalence of anemia in children between 6 and 59 months of age, in the different departments of Peru, and Bolivia

Zone / Department	Peru, ENDES 2016; A total of 10,060 children included					Bolivia, EDSA 2016; A total of 1526 children included					
	Mi.A (%)	Mo.A (%)	SA (%)	AA (%)	T(n)	Zone / Department	Mi. A (%)	Mo.A (%)	SA (%)	AA (%)	T(n)
AHR (Total)	24.65	13.63	0.38	38.69	3230	AHR (Total)	28.04	29.45	3.07	60.59	917
Áncash	19.60	9.00	0.10	28.80	354	Chuquisaca	29.70	23.30	2.00	54.90	102
Apurímac	26.60	12.80	0.20	39.70	165	La Paz	32.60	38.00	3.70	74.40	261
Arequipa	22.10	10.10	0.00	32.20	359	Cochabamba	26.60	19.20	0.60	46.40	278
Ayacucho	27.40	13.40	0.30	41.10	192	Oruro	19.60	40.80	6.80	67.20	92
Cajamarca	15.90	6.80	0.20	22.90	544	Potosí	27.20	35.50	6.20	69.00	138
Cusco	29.30	17.20	0.30	46.80	378	Tarija	26.60	15.60	0.00	42.20	46
Huancavelica	27.30	17.40	0.70	45.40	142						
Huánuco	22.80	12.70	0.10	35.70	253						
Junín	27.70	13.80	0.40	41.90	392						
Pasco	30.00	17.90	1.50	49.40	106						
Puno	33.90	27.10	1.30	62.30	345						
LR (Total)	**21.88**	**8.67**	**0.14**	**30.68**	**6830**	**LR (Total)**	**22.92**	**19.87**	**0.58**	**43.37**	**610**
Piura	21.50	8.80	0.00	30.40	773	Santa Cruz	23.90	18.50	0.30	42.70	494
Ica	23.40	7.70	0.00	31.10	333	Beni	19.40	22.40	0.60	42.40	94
PCC	25.70	8.80	0.10	34.60	337	Pando	16.40	39.00	6.40	61.80	23
La Libertad	16.30	7.40	0.20	23.80	618						
Lambayeque	17.90	8.80	0.20	26.90	417						
Lima (1)	19.00	5.80	0.10	24.90	2377						
Lima (2)	22.40	8.00	0.00	30.40	324						
Loreto	33.10	16.50	0.40	49.90	578						
Madre de Dios	26.30	15.50	1.10	42.90	63						
Moquegua	21.70	7.40	0.20	29.20	50						
San Martín	24.90	10.90	0.00	35.80	336						
Tacna	18.40	6.60	0.60	25.50	100						
Tumbes	25.60	12.00	0.20	37.80	101						
Ucayali	31.50	15.40	0.30	47.20	254						
Amazonas	22.10	11.60	0.10	33.80	169						

ENDES: Encuesta Demográfica y de Salud Familiar (Demographic and Family Health Survey); EDSA: Encuesta de Demografía y Salud (Demography and Health Survey); Mi.A: mild anemia; Mo.A: moderate anemia; SA: severe anemia; AA: all cases of anemia; T: total number of patients included; AHR: Andean highland region; LR: low-lying region; PCC: Provincia Constitucional del Callao; (1) It includes the 43 districts that make up the Province of Lima; (2) It includes the provinces: Barranca, Cajatambo, Canta, Cañete, Huaral, Huarochirí, Huaura, Oyón and Yauyos.

children inhabiting the AHR. All the comparisons revealed a significant statistical result excluding the case of mild anemia in the Bolivian population (OR:1.21; p=0.05). The most significant risk association was identified for severe anemia in the Ecuadorian children; SIVAN 2013 (OR:4.98; p<0.01) and SIVAN 2014 (OR:5.32; p<0.01). Likewise, in the EDSA 2016, the risk association reported for severe anemia was (OR:4.65; p<0.01). In ENDES 2016 the most relevant risk association occurred in the total value of anemia (OR:2.25; p<0.01). **Table 3** summarizes all the ORs calculated for each comparison made in this study.

Table 3. Risk association of anemia and living in AHR in children between 6 and 59 months of age, in Ecuador, Peru, and Bolivia (continúa en la siguiente columna)

Comparison	Odds Ratio	95% CI	p value
Ecuador, SIVAN 2013			
Total of anemic cases	1.67	1.63-1.71	<0.05
Mild anemia	2.09	2.03-2.15	<0.05
Moderate anemia	2.13	2.06-2.21	<0.05
Severe anemia	4.98	4.05-6.13	<0.05
Ecuador, SIVAN 2014			
Total of anemic cases	1.75	1.68-1.82	<0.05
Mild anemia	1.44	1.37-1.52	<0.05
Moderate anemia	2.22	2.09-2.35	<0.05
Severe anemia	5.32	3.67-7.72	<0.05
Peru, ENDES 2016			
Total of anemic cases	2.26	1.99-2.56	<0.05
Mild anemia	1.43	1.31-1.56	<0.05
Moderate anemia	1.27	1.15-1.41	<0.05
Severe anemia	1.78	1.55-2.03	<0.05
Bolivia, EDSA 2016			
Total of anemic cases	2.87	1.24-6.65	<0.05
Mild anemia	1.22	0.97-1.53	0.05
Moderate anemia	1.48	1.17-1.88	<0.05
Severe anemia	4.65	1.62-13.32	<0.05
All the countries included			
Total of anemic cases	1.37	1.34-1.40	<0.05
Mild anemia	1.13	1.10-1.15	<0.05
Moderate anemia	1.75	1.71-1.80	<0.05
Severe anemia	4.19	3.52-4.98	<0.05

Table 3. Risk association of anemia and living in AHR in children between 6 and 59 months of age, in Ecuador, Peru, and Bolivia (continúa en la siguiente columna)

AHR: Andean highland region; CI: confidence interval; SIVAN: Sistema Integrado de Vigilancia Alimentaria y Nutricional (Integrated System of Food and Nutritional Surveillance); ENDES: Encuesta Demográfica y de Salud Familiar (Demographic and Family Health Survey); EDSA: Encuesta de Demografía y Salud (Demography and Health Survey)

Anemia as a public health problem

Anemia can be classified as a PHP based on the degree of its prevalence as mild (between 5 and 19.9%), moderate (between 20 and 39.9%) and severe (higher or equal to 40%). The findings of this study showed that while anemia was frequently a moderate or severe problem in a majority of the provinces or departments of Ecuador and Peru, in all the Bolivian regions it was a severe problem (**Table 4**).

DISCUSSION

As observed in this study, anemia is not only a common disease, it is also a moderate or severe PHP in many provinces of Ecuador, Peru, and Bolivia. The average prevalence of anemia in Ecuador and Peru had registered a rise when compared with the data published by Mujica et al., in 2015. They had reported a prevalence of 25.7% in Ecuador and 32.9% in Peru. On the contrary, Bolivia recorded a decrease in its average prevalence of anemia, but, relmained as a severe PHP across the country.[2] Concurring with this result, a recent study revealed an upward

Table 4. The severity of the prevalence of anemia as PHP in children between 6 and 59 months of age, in the different provinces or departments of Ecuador, Peru, and Bolivia

Ecuador, SIVAN 2013		Ecuador, SIVAN 2014		Peru, ENDES 2016		Bolivia, EDSA 2016	
Province	Prev (%)	Province	Prev (%)	Department	Prev (%)	Department	Prev (%)
Azuay	36.92	Azuay	38.18	Amazonas	33.80	Beni	42.40
Bolivar	39.43	Bolivar	45.03	Áncash	28.80	Chuquisaca	54.90
Cañar	53.98	Cañar	51.88	Apurímac	39.70	Cochabamba	46.40
Carchi	59.25	Carchi	58.90	Arequipa	32.20	La Paz	74.40
Chimborazo	36.11	Chimborazo	33.29	Ayacucho	41.10	Oruro	67.20
Cotopaxi	45.62	Cotopaxi	36.14	Cajamarca	22.90	Pando	61.80
El Oro	20.85	El Oro	19.34	Cusco	46.80	Potosí	69.00
Esmeraldas	46.00	Esmeraldas	39.22	Huancavelica	45.40	Santa Cruz	42.70
Galapagos	16.35	Galapagos	17.24	Huánuco	35.70	Tarija	42.20
Guayas	23.85	Guayas	24.74	Ica	31.10		
Guayas*	32.58	Guayas*	33.33	Junín	41.90	Average	55.67
Imbabura	63.00	Imbabura	65.76	La Libertad	23.80		
Loja	40.91	Loja	45.12	Lambayeque	26.90		
Los Rios	36.79	Los Rios	36.33	Loreto	49.90		
Manabí	24.39	Manabí	31.94	Madre de Dios	42.90		
MS	52.70	MS	52.48	Moquegua	29.20		
NAPO	58.40	NAPO	48.63	Pasco	49.40		
Orellana	37.21	Orellana	37.54	PCC	34.60		
Pastaza	38.21	Pastaza	32.95	Piura	30.40		
Pichincha**	54.53	Pichincha**	50.92	Lima (1)	24.90		
Pichincha	36.87	Pichincha	41.49	Puno	62.30		
Santa Elena	48.62	Santa Elena	40.48	Lima (2)	30.40		
SDT	46.95	SDT	26.18	San Martin	35.80		
Sucumbios	36.63	Sucumbios	44.86	Tacna	25.50		
Tungurahua	46.14	Tungurahua	41.73	Tumbes	37.80		
ZC	32.76	ZC	28.85	Ucayali	47.20		
Average	40.96	Average	39.33	Average	36.55		

PHP: Public health problem; Anemia as a PHP is classified based on its prevalence as mild (between 5 and 19.9%,), moderate (between 20 and 39.9%) and severe (higher or equal to 40); Prev, prevalence; *Metropolitan District of Guayaquil; **Metropolitan District of Quito; (1) It includes the 43 districts that constitute the Province of Lima; (2) It includes the provinces of Barranca, Cajatambo, Canta, Cañete, Huaral, Huarochirí, Huaura, Oyón and Yauyos. SDT, Santo Domingo de los Tsachilas; MS, Morona Santiago; ZC, Zamora Chinchipe.

swing in the prevalence of anemia in Ecuador. However, differing from our report, an upward trend was noted in Bolivia but a downward one in Peru, in children under 5 years of age.[18] Besides, this study demonstrated the prevalence of iron deficiency in children between 6 and 59 months of age, as 9.9% for Ecuador in 2012, and 32.9% for Bolivia in 2002. The ENDES 2016 survey reported diverse percentages in the frequency of oral intake of iron supplements in children, with variations in each age group as follows; 39.70% (6 to 8 months), 50.00% (9 to 11 months), 42.30% (12 to 17 months), 26.20% (18 to 23 months), 15.80% (24 to 35 months), 9.20% (36 to 47 months), and 6.20% (48 to 59 months). The EDSA 2016 reported similar findings for the consumption of iron-rich food, in which the children group that benefitted the least was between 6 and 8 months (45.20%); however, the other age groups revealed a reported prevalence of anemia of over 80%.

The results for Bolivia are in sharp contrast, showing a higher prevalence of anemia. On the other hand, Peru revealed a gradual decrease in iron supplementation as the children increased in age. This is of great importance because the proper iron day-by-day intake must be maintained in children. Iron deficiency, however, is not the only cause for anemia. It is essential to emphasize hemoglobin correction in all the data used in our findings.

Hemoglobin correction in AHR

Sufficient evidence indicates the prevalence of erythrocytosis in AHR. Among the Andeans, the association of the phenotype of chronic mountain sickness with a single-nucleotide polymorphism (SNP) in the sentrin-specific protease 1 (SENP1), which is linked to the control of erythropoiesis, has suggested that an increase in the SENP1 expression could explain the incidence of erythrocytosis in the (mal-adapted) Andean population. This is a genetic characteristic and different from that of the Tibetans. The Tibetan highlanders are genetically "protected" against erythrocytosis and show low Hb concentration values, according to the observations made by the SNPs in the Endothelial PAS domain-containing protein 1 (*EPAS1*) and Egl-9 Family Hypoxia Inducible Factor 1 (*EGLN1*).[19] The higher hemoglobin level in the Andean population compared with that of the Tibetans may suggest that hemoglobin correction based on the geographical altitude could be maintained in the AHR.[20] Our recommendation is to maintain this correction, as has been indicated by WHO.

Risk of anemia in the AHR. A physiological view

In this research study, we investigated for the first time, the risk of children suffering from anemia, associated with living at AHR in Ecuador, Peru, and Bolivia. The significant risk that we observed can be explained first, by considering erythrocytosis in the Andean population via SENP1. During normoxia, the prolyl hydroxylase domain proteins (PHDs) hydroxylate the hypoxia-inducible factor α (HIFα) which is to be ubiquitinated by the Von Hippel-Lindau proteins and then lysed by the proteasome. However, during hypoxia, the HIFα can circumvent the lysis and enter into the nucleus. The HIF, however, could undergo SUMOylation and then be ubiquitinated.[21] The SENP1 activity is crucial to the deSUMOylation of HIF1α and GATA. The HIF1α is an EPO up-regulator, and the GATA acts as an erythropoietin receptor (EpoR) up-regulator.[22] The significance of this pro-erythropoietic pathway in the Andean population is dependent on the fact that for such patients their iron requirements could be increased unlike the people living in the LR, similar to specific patient groups which utilize erythropoiesis-stimulating agents.[23] However, some studies have reported normal EPO levels in people residing in AHR. In this context, there was a possible mechanism to explain this phenomenon based on the presence of daily rhythm in serum EPO levels, this circadian rhythm in EPO levels could influence the results depending on the moment when the sample was taken.[24]

Erythropoiesis is the biological phenomenon whit the highest requirement of iron; this is evidenced as the higher the erythropoietic activity, the lower the activity of hepcidin. The decreased presence of hepcidin produces an increased capacity of iron absorption. Thus, when EPO increases the erythropoietic activity, it is required adequate iron intake to support the production of new erythrocytes. In this context, as erythrocytosis is a recognized phenomenon in AHR, adequate iron intake should be necessary to sustain the production of healthy red blood cells in this population.[25]

Nutritional deficiency in the AHR, Iron deficiency anemia (IDA), and other types of anemia

A systematic review published in 2014 on the nutritional adequacy of the diet in the Central Andes suggested that this region is characterized by a low intake of micronutrients like iron, zinc, vitamin A, riboflavin, vitamin B12, folate, and zinc. This poor nutritional pattern, as well as the theoretical higher iron requirements necessary to sustain the increased erythropoiesis in the AHR, can be the reason for the increased risk of anemia in the Andean population.[26] However, as the surveys employed in this study did not differentiate among all the possible types of anemia, it is crucial to emphasize the zinc, vitamin B12 (Vit B12) and folate deficiencies. As zinc participates as a cofactor in iron metabolism, an association is suggested between the zinc concentrations and IDA.[27] Besides, in light of the frequency of zinc deficiency (ZD) among the Ecuadorian children,[28] we consider it vital to further explore the association between ZD and IDA in our population. Another perspective is that folate and Vit B12 deficiency anemia could occur frequently in our population, particularly in the context of a parasitic infection, which continues to pose a problem in Latin America.[29,30]

The frequency of sickle cell anemia in the African-American population varies, with Brazil 6.2%, Colombia 11.9%, Costa Rica 8.1%, Cuba 6.1%, Mexico 11.2%, Panama 16.0%, the Honduras 10.0%, Belize 27.7%, Ecuador 17.8%, Guatemala 18.3%, Haiti 13.2%, Honduras 10.0%, and Panama 16.0%, but the epidemiology could be diverse even within the same country.[31] Also, it is significant to emphasize the fact that Esmeraldas is one of the provinces most affected by anemia in the LR, and is the Ecuadorian region supporting the highest population density of people of African descent. However, as there is extensive miscegenation in Latin America, a detailed evaluation of the incidence of anemia is essential during the national surveys to avoid undervaluation of the other causes of anemia. Thalassemia is another relatively frequent form of hemoglobinopathy. In fact, an approximate 200 million carriers of the altered β-thalassemia gene have been estimated worldwide, with the highest prevalence, considering one coincidence of the α and β variants, in the South-east Asian (45.50%), African (44.40% Any variant) and Eastern Mediterranean (21.70%).[32] Therefore, it could be useful to add indexes in order to differentiate IDA from thalassemia, such as the Mentzer index or RDWI, which are reliable tools in the first approach to a hemogram.[33] However, no actualized data of the prevalence of thalassemia are available for the populations of Ecuador, Peru, or Bolivia.

Anemia not only a problem of AHR

From our observations it was evident that the provinces or departments in the LR more affected by anemia are located in the AR. The poverty rate in the AR varies among the different countries, from 45% in the Brazilian Amazon up to almost 80% in some regions of Guyana. However, these differences were clearly observed between the rural and urban areas. For instance, in 2014, in Peru, 42% of the total population in the rural regions of the Amazon lived in poverty, with 12% living under conditions of extreme poverty.[34] Poverty could also be an important risk factor in children causing them to suffer from anemia, not only for those living in the AR but even those in the AHR, because some indigenous people groups in the AHR continue to suffer from poverty. However, no investigations are available at present which have investigated these two variables in our population. Other causes of anemia in this population, in addition to micronutrients deficiency, could be chronic infectious diseases, or even benign erythroid defects. In this context, we suggest using additional parameters such as ferritin levels, peripheral blood smear, Mentzer index or RDWI, inflammatory markers to classify the anemia properly in children from the AR.

Are there another conditions associated with living in AHR in the general population?

In the AHR it has been reported that the prevalence of chronic obstructive pulmonary disease is lower in HA, although the mortality levels are higher in this region.[35] Besides, the incidence of pneumonia in children living at HA is presented as a more severe disease and anemia in such patients increases the risk of poor outcomes for those being treated for severe pneumonia.[36] In the Ecuadorian population, we discovered from an earlier study, higher prevalence and mortality levels for cancer in HA.[37] On the contrary, a reduction in the overall mortality of cardiovascular and cerebrovascular diseases was reported.[35] Therefore, living at HA is a complex biological phenomenon that could exert a high impact on the human physiopathology.

Limitations

As this study was based on the analysis of a secondary data source, some limitations are present, which need to be considered. The lack of other hematological parameters included in the complete blood count, iron metabolism studies, as well as the clinical status of each patient are some limitations which restricted us to relate living at HA to each type of anemia, that could be employed in studies with smaller groups of children. Another important aspect is that the dietary habit, socioeconomic condition, ethnic group, and a coexistent infection of the patients included in this study were not known. We deem it necessary to investigate the way each of these aspects influences the risk for developing anemia in the AHR.

Implications for research and practice

These findings provide evidence of the different percentages of anemia in children between 6 and 59 months of age among geographical regions of Ecuador, Perú, and Bolivia, with the highest rates localized in the HAR. This study provides a background for investigating the precise type of anemia that affects the children from the Andean region, being important because it would be the start point to take public health decisions to overcome this PHP, being important because anemia is associated with poorer cognitive and academic achievements, as well as retarded physical growth compared with the non-anemic children. Also, this study poses the necessity of clarifying if the hemoglobin correction proposed by the WHO works properly for the Andean population, something that would change the nutritional evaluation of paediatric patients radically

CONCLUSION

From the results of this study, anemia was more frequent children residing in the Andean region of Ecuador, Peru, and Bolivia. Additionnaly, we found that living in the AHR could be a risk factor for children to suffer from anemia, a phenomenon that can be explained as the Andean population has an SENP1 pro-erythropoietic phenotype that may be responsible for a high requirement of iron intake. But, some controversy prevails as a few among the Andean population have registered normal erythropoietin values. Although significant risk of anemia in children between 6 and 59 months living in the AHR, were identified in this study, it is difficult to conclude which is the predominant type of anemia. It also became evident that anemia is a problem in certain coastal and Amazonian provinces. Therefore, further research is necessary in this field, both to understand the biology of iron at geographical altitudes, the main types of anemia and their underlying causes, as well as the possible modifications in the micronutrient doses to be administered to the Andean children during the national nutritional campaigns as well as in the anemia treatment.

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