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Tesis

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in Peru**

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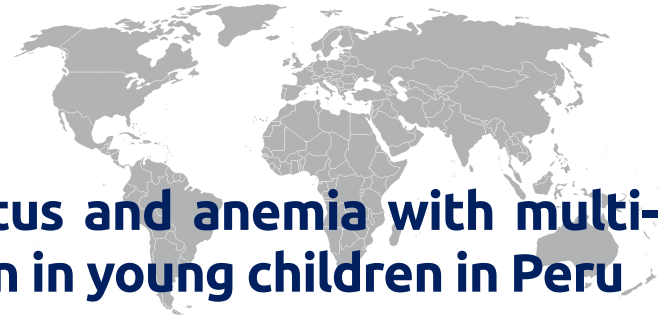
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# Association of nutritional status and anemia with multi-micronutrient supplementation in young children in Peru

## Asociación del estado nutricional y anemia según suplementación con múltiples micronutrientes en niños pequeños en Perú

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### ABSTRACT

**Introduction:** Although several social interventions have been developed by the Peruvian State, anemia is present in one out of every two children in Peru. Thus, it is important to evaluate whether such interventions are achieving their objectives.

**Objective:** This study aimed to determine the association of nutritional status and anemia with multi-micronutrient supplementation in children younger than three years in Huancayo, Peru.

**Materials and Methods:** This retrospective, longitudinal, analytical, and observational study included secondary data of children younger than 3 years from the Sicaya District, in the Huancayo province. Data were collected from health center medical records. Nutritional and anemia status, and socio-demographic characteristics of children receiving multi-micronutrient supplementation were recorded. Statistical analyses were based on generalized linear models.

**Results:** Data of 76 children with available medical records were analyzed, and their pre- and post-intervention median ages were 6 and 11 months (range: 7–35 months), respectively. Significant positive linear correlations were observed between the number of multi-micronutrient doses and weight, height, and hemoglobin concentration. In bivariate and multivariate analyses, no significant associations were observed between anthropometric measurements and anemia (after multi-micronutrient intervention) ( $p > 0.05$ ), nor between the number of received doses of multi-micronutrients, sex, and age.

**Conclusion:** Multi-micronutrient supplementation may be correlated with both physiological and anthropometric variables, but not with indicators of child development. These associations require further evaluations to determine whether social programs promoting multi-micronutrient supplementation improve the development of children with anemia.

**Keywords:** micronutrients, dietary supplements, nutritional status, anemia, children

### RESUMEN

**Introducción:** Aunque muchas intervenciones sociales han sido desarrolladas por el Estado peruano, la anemia está presente en uno de cada dos niños en Perú. Por lo tanto, es importante evaluar si tales intervenciones están logrando sus objetivos.

**Objetivo:** Este estudio tuvo como objetivo determinar la asociación del estado nutricional y la anemia con la suplementación con múltiples micronutrientes en niños menores de tres años en Huancayo, Perú.

**Materiales y Métodos:** Este estudio retrospectivo, longitudinal, analítico y observacional, incluyó datos secundarios de niños menores de 3 años del distrito de Sicaya, en la provincia de Huancayo. Los datos se obtuvieron de los registros médicos del centro de salud. Se registraron el estado nutricional y de anemia, y las características sociodemográficas de los niños que reciben suplementos de micronutrientes múltiples. Los análisis estadísticos se basaron en modelos lineales generalizados.

**Resultados:** Se analizaron los datos de 76 niños con registros médicos disponibles, y sus edades medias antes y después de la intervención fueron 6 y 11 meses (rango: 7–35 meses), respectivamente. Se observaron correlaciones lineales positivas significativas entre el número de dosis de multi-micronutrientes y el peso, la altura y la concentración de hemoglobina. En los análisis bivariados y multivariados, no se observaron asociaciones significativas entre las mediciones antropométricas y la anemia (después de la intervención con multi-micronutrientes) ( $p > 0,05$ ), ni entre el número de dosis de multi-micronutrientes recibidos, sexo y edad.

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**Conclusión:** La suplementación con micronutrientes múltiples puede correlacionarse tanto con variables fisiológicas como antropométricas, pero no con indicadores de desarrollo infantil. Estas asociaciones requieren evaluaciones adicionales para determinar si los programas sociales que promueven la suplementación con micronutrientes múltiples mejoran el desarrollo de los niños con anemia.

**Palabras clave:** micronutrientes, suplementos dietéticos, estado nutricional, anemia, niños

## INTRODUCTION

Multi-micronutrients (MMN) play vital roles in growth and development during childhood (1). Therefore, an adequate intake of these compounds may be essential during this period of life (2). MMN deficiency can lead to important adverse functional consequences, including poor cognitive development, inadequate growth, and reduced physical abilities. Some studies report that such deficiency may also reduce the intelligence quotient of children (3). Therefore, this is a serious problem, as indicated by cases of high prevalence of anemia, which suggest significant nutritional deficits (4). Moreover, this situation is often accompanied by deficiencies in other nutrients, including vitamin B12 and folic acid (5).

On the other hand, an adequate MMN supplementation has been reported to significantly reduce vitamin A deficiency, anemia, and chronic malnutrition (6). In addition, an effective administration of MMN enhances responses to supplementation (7).

According to the Ministry of Health of Peru (MINSa), the prevalence of chronic malnutrition and of anemia among children younger than 3 years decreased by 7.3%, and 19.3%, respectively, during 2000–2001. In this context, poverty and a lack of prenatal monitoring have been correlated with the prevalence of anemia (8).

The findings of a study conducted in three Peruvian regions (Ayacucho, Huancavelica, and Andahuaylas) between 2009 and 2012 demonstrated that lipid based nutritional supplementation represents an effective anti-anemia strategy (9,10). The National Plan for the Reduction and Control of Anemia, implemented by the MINSa in 2017, gives an estimate that shows that 44% of children aged 6–36 months still suffer from anemia (11). The MINSa has invested millions of soles (Peruvian currency) in the fight against anemia, but some specific investigations have found that the results achieved have not been satisfactory (12).

Up till now, few studies have evaluated the outcomes of implementing nutritional supplementation for children in Peru. Thus, our study aimed to determine the association of nutritional status and anemia with MMN supplementation in children younger than three years in Huancayo, Peru.

## MATERIALS AND METHODS

This retrospective, longitudinal, analytical, and observational study was conducted from January to May 2015 at the Sicaya Health Center in Huancayo, Peru.

The study included children younger than three years who had received MMN supplementation since they were 6 months of age and were attended in a Growth and Development (*Crecimiento y Desarrollo* – CRED) office from a health facility in the Sicaya District, in the Huancayo province. Specifically, included children lived in the Sicaya District and had completed CRED control. Four records were excluded because of incomplete data. Census-type convenience sampling was applied.

Collected variables included sex, age, weight, height, last CRED control, hemoglobin levels, and the number of received doses of MMN (including folic acid, iron, zinc, vitamin A, and vitamin C; the latter was administered at a 1-g daily dose from 6 to 18 months of age).

Anthropometric data were collected and checked against the anthropometric nutritional assessment table for children <5 years old, which was developed by the World Health Organization and is generally used by the MINSa (13). Values within a standard deviation of  $\pm 2$  were considered normal. The anthropometric analysis was based on the usual parameters for weight/age, height/age, and weight/height. To evaluate anemia, hemoglobin levels were determined in consideration of the regional altitude. Accordingly, the measured hemoglobin values were adjusted using an appropriate altitude-related factor. Hemoglobin cut-offs were: severe, moderate, and mild anemia that were defined using hemoglobin ranges of <7.0, 7.0–9.99, and 10.0–10.99 g/dl, respectively.

Permission to conduct the study was requested from the relevant health facility, along with a document endorsed by the Dean of the Human Medical School of Continental University, Peru. The data were collected through an assistance/social program implemented by the Peruvian government in similar districts. Therefore, the studied population was very similar to those from other areas of moderate or extreme poverty. Furthermore, the dates and times

**Table 1:** Pre- and post-supplementation with MMN versus physiological, demographic, and anthropometric variables in children from Huancayo, Peru

Variable	Intervention with MMN n (%)		p-value
	Pre	Post	
<b>Weight (kg)*</b>	6.9 (5.6-8.7)	8.9 (6.4-13.6)	<0.001§
<b>Height (m)*</b>	64.8 (58-71)	72.0 (64-90)	<0.001§
<b>Hemoglobin**</b>	10.9 (1.0)	11.1 (0.6)	0.075£
<b>Weight/Age</b>			
Normal	69 (90.8)	72 (94.7)	0.348¥
Low weight-for-age	4 (5.3)	7 (9.2)	
<b>Height/Age</b>			
Normal	66 (86.8)	68 (89.5)	0.616¥
Low height-for-age	10 (13.2)	8 (10.5)	
<b>Weight/Height</b>			
Normal	76 (100.0)	75 (98.7)	1.000‡
Overweight-for-age	0 (0.0)	1 (1.3)	

MMN= multi-micronutrients. \*Median and range. \*\* Mean and standard deviation. P-value obtained with: § Mann-Whitney U test; £ paired Student's t-test; ¥ Chi-square test; ‡ Fisher's exact test

of data collection were arranged with the head of the CRED service. A data collection sheet was developed to gather the relevant information and the double data entry was performed using a database Excel for Windows (Microsoft Corp., Redmond, WA, USA).

Data were statistically analyzed using STATA, version 11.1 (STATA Corp., College Station, TX, USA). Quantitative data were summarized using measures of central tendency and dispersion following a preliminary analysis of the normality of the variables. Qualitative data were summarized using frequencies and percentages. A statistical significance level of  $p < 0.05$  was set for statistical analysis. Categorical variables were analyzed using Chi-square or Fisher's exact test, while numerical variables were assessed using Student's t or the Mann-Whitney U test. Relative risk (RR), 95% confidence intervals (CI), and p-values were obtained using generalized linear models together with a *Poisson* distribution and a log link function.

## Study Definition

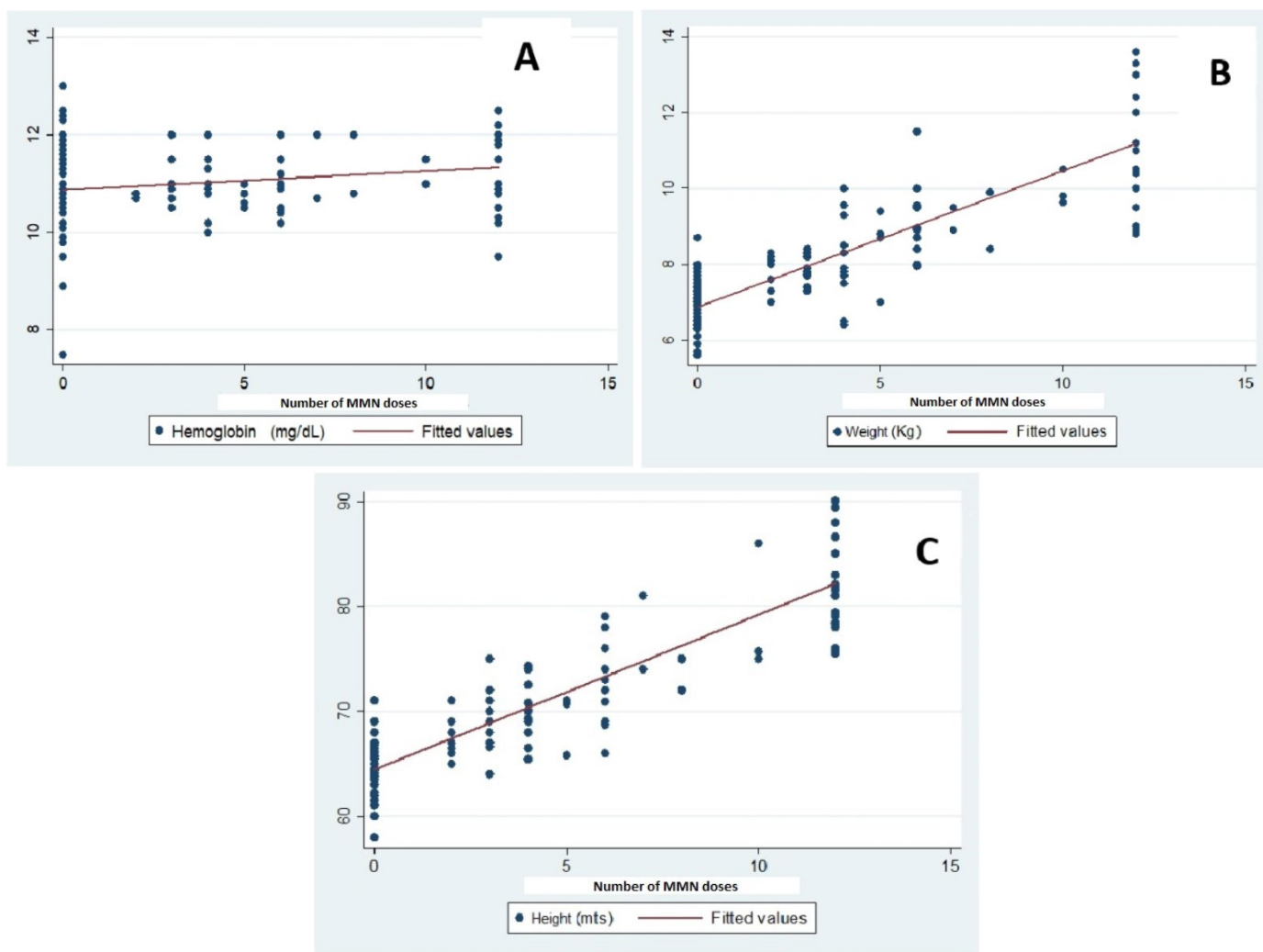
Multimicronutrients are vitamins provided by the Peruvian Government to children from low-income areas. Vitamins should be taken in small amounts in order to provide appropriate supplementation and positive impacts on the health, with an appropriate relation between weight/age, height/age, and weight/height.

## RESULTS

Of the 76 children with records available at the health facility, 51.3% (39) were male. The pre- and post-intervention median ages were 6 (range: 6-6 months) and 11 months (range: 7-35 months), respectively. **Table 1** presents the pre- and post-intervention physiological and anthropometric variables, and highlights the significant differences in weight and height over time, in contrast to other evaluated parameters (**Table 1**).

The number of MMN doses to the evaluated children was found to exhibit statistically significant positive linear correlations with hemoglobin concentration (**Figure 1A**,  $p=0.032$ ), weight (**Figure 1B**,  $p<0.001$ ), and height (**Figure 1C**,  $p<0.001$ ) (**Figure 1**).

Bivariate and multivariate analyses of the association between anthropometric values and anemia (post-MMN intervention) did not yield statistically significant findings. Similarly, no significant associations were observed for the number of MMN doses, sex, and age (**Table 2**).



**Figure 1:** Correlation between the number of MMN doses and hemoglobin (A), weight (B), and height (C) of the studied children

MMN= multi-micronutrients

**Table 2:** Analysis of the influence of MMN doses on temporal changes between demographic and anthropometric variables in children from the Sicaya District, in the Huancayo province

Variable	Post-intervention		Adjusted by RR (95% CI) and p-value		
	With Anemia	Without Anemia	Bivariate	Doses	Doses+age+sex
<b>Weight/Age</b>					
Normal	27 (93.1)	35 (94.6)	0.9 (0.2-3.7)	0.9 (0.2-3.8)	0.9 (0.2-3.7)
Low weight-for-age	2 (6.9)	2 (5.4)	0.850	0.893	0.839
<b>Height/Age</b>					
Normal	25 (86.2)	34 (91.9)	0.7 (0.3-2.1)	0.6 (0.2-1.9)	0.6 (0.2-1.9)
Low height-for-age	4 (13.8)	3 (8.1)	0.579	0.416	0.411
<b>Weight/Height</b>					
Normal	28 (96.6)	37 (100.0)	0.4 (0.1-3.2)	0.5 (0.1-3.4)	0.4 (0.1-3.3)
Overweight-for-height	1 (3.4)	0 (0.0)	0.408	0.448	0.411

RR = relative risk; CI = confidence intervals

## DISCUSSION

In Peru, pediatric anemia is a public health problem (10,13). It is known that such condition is associated with multiple factors, and one of the most important of them is the ingestion of nutrients, which should be obtained through an adequate diet (intake of milk, meat, and other foods in a well-balanced diet). However, there is often inability to meet basic food needs in low-income areas (14,15).

Anemia may affect a child's cognitive level (unless well controlled) when its onsets in early developmental stages. This nutritional disorder can thus lead to physical problems and to a poor quality of life (15). In Huancayo, the prevalence of anemia among children aged 6–35 months was 44.5% in 2012, while the prevalence of chronic pediatric malnutrition was 24.6% (16). Consequently, MMN supplementation emerged as a strategy to reduce the prevalence of these indicators of poor health (17,18). Despite this, no local study has been conducted to determine whether this intervention was beneficial; therefore, the findings of our study should be very important in this regard.

Although in this study some indicators improved in relation to MMN supplementation, the parameters of weight/age, height/age, and weight/height did not associate significantly with MMN intake. This differs from the findings of studies conducted in the Huando and Anchonga communities of Peru (19,20), where MMN supplementation was found to affect the nutritional status of children younger than 3 years. This discrepancy may be attributable to a variety of causes, including lack coverage of actual intakes, a lack of parental knowledge about the importance and benefits of MMN supplementation, or non-compliance with other potentially influential factors.

In contrast, we observed statistically significant differences in weight, height, and hemoglobin values related to the number of MMN doses, which may be due to physiological development during childhood. In addition, the hemoglobin concentration increased by 0.2 g/dl with the use of a daily regimen of supplementation for 12 months (30 sachets per month). Studies on the growth-MMN ratio have showed similar results, reporting an effect non-related to the use of a specific type of supplementation (21,22).

Interestingly, in the present study, the increases in anthropometric values did not exhibit statistically significant associations with the number of received doses of MMN, the evaluated children's sex, or age. Nonetheless, the prevalence of anemia decreased slightly. Studies conducted in other locations within Latin America and elsewhere suggest that these improvements are insufficient because a significant reduction in anemia could not be achieved in the most affected populations, including children living in low-income rural areas (23,24). This suggests, therefore, that supplementation is unsatisfactory, which may be attributable to the process of MMN preparation, inadequate intake, or other intervening factors (25); however, these issues are beyond the scope of our study. Further investigations are needed to determine at which point the social program failures occur, as this will allow corrective actions based on a more ambitious objective of reducing anemia in this population.

It is also worth noting that our findings are limited to the real setting in which children received care and MMN supplementation at the health center in Sicaya; therefore, the findings do not include pediatric populations from other towns or throughout Peru as a whole, and the conditions of those populations remain unknown. Additionally, as the study data were collected only from medical records, we were unable to gather other pertinent information regarding MMN intake. However, this study was conducted based on the use of MMN under similar conditions at several locations throughout Peru. Thus, our findings may serve as a good approximation of reality at provincial, departmental, and even national levels.

Limitations on weight and height values should also be taken into account, as these can be influenced by the normal growth pattern of patients. Data on weight and height were placed in **Table 1** in order to characterize the population, and the most important results were in terms of weight/age, height/age, and weight/height values for each child (as these have been calculated for each age and according to World Health Organization reference values).

Another important limitation was the fact that there was no access to other variables that can directly influence the growth/development process (such as diet, exercise, parasitosis, pre-natal monitoring, etc.). These information could not be obtained as this was a study based on secondary data. On the other hand, our results can be considered as a baseline, in order to allow new studies to measure the influential variables in greater details. Moreover, the selection bias of the study population is implicit, since only a small population group was analyzed; however, as mentioned in the methodology section, the studied group may be similar to others at the national level, since the Peruvian government provides the social/assistance program to low-income areas across the country.

The findings obtained in this study lead us to conclude that in young children, hemoglobin levels, weight, and height are associated with the MMN intake. Nevertheless, we did not find a statistically significant association between the nutritional status and anemia.



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