

# Adherence to multiple micronutrient powders and associated factors in children aged 6 to 35 months treated in sentinel health facilities, Ministry of Health of Peru

*Adherencia a multimicronutrientes y factores asociados en niños de 6 a 35 meses de sitios centinela, Ministerio de Salud, Perú*

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**ABSTRACT:** *Introduction:* Anemia in children is a public health issue, and the current strategies include treatment and iron supplementation, but their level of adherence or compliance is unknown. *Objective:* To consider the adherence to multiple micronutrient powders and the associated factors. *Methods:* Epidemiological study of active surveillance through sentinel facilities in 2,024 children aged 6 to 35 months treated in health facilities of the Ministry of Health of Peru, from October to December 2014. Household visits were conducted in which counting of multiple micronutrient powders was applied and determined an adherence of consumption  $\geq 90\%$  envelopes, besides a form on the associated factors (anemia knowledge, iron-rich food, side effects, dosage regimen, drugs used, and motivation) was applied. Descriptive statistics,  $\chi^2$  test, Odds Ratio with a 95% confidence interval (CI), and binary logistic regression or adjusted Odds Ratio (aOR) were used. *Results:* Of all, 79.1% participants were aged 6 to 23 months; 75.9% received multiple micronutrient powders; and the adherence was equivalent to 24.4% (95%CI 22.3 – 26.6). The factors: continue supplementation (OR = 3.5; 95%CI 1.7 – 7.5); no nausea (OR = 3.0; 95%CI 2.0 – 4.3); no use of antibiotics (OR = 2.5; 95%CI 1.7 – 3.6); and intention to continue treatment (OR = 2.3; 95%CI 1.3 – 4.1) were associated with adherence. The variables: thought of continuing treatment (aOR = 2.6; 95%CI 1.1 – 6.1); presence of side effects, but no discontinuation of the treatment (aOR = 2.5; 95%CI 1.4 – 4.3); no use of antibiotics (aOR = 2.0; 95%CI 1.1 – 3.4); and belief that not only drugs cure anemia (aOR = 1.6; 95%CI 1.0 – 2.6) were associated in the multivariate analysis. *Conclusion:* There was a low prevalence of adherence to a demanding cut-off point ( $\geq 90\%$  of envelopes of multiple micronutrient powders), and the associated factors are associated with absence of infections, side effects, and mother's beliefs.

**Keywords:** Medication adherence. Micronutrient. Child. Anemia. Peru.

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**RESUMEN: Introducción:** La anemia en el niño es un problema de salud pública, las estrategias actuales incluyen el tratamiento y suplementación con hierro, pero se desconoce su nivel de adherencia o cumplimiento. **Objetivo:** Considerar la adherencia a los multimicronutrientes y los factores asociados. **Métodos:** Estudio epidemiológico de vigilancia activa por sitios centinela en 2.024 niños entre los 6 hasta los 35 meses atendidos en establecimientos de salud del Ministerio de Salud del Perú, entre octubre a diciembre de 2014. Se realizaron visitas domiciliarias, en las cuales se aplicaron el conteo de multimicronutrientes, que determinó la adherencia al consumo  $\geq 90\%$  de sobres, y un formulario sobre los factores asociados (conocimiento sobre anemia, alimentos ricos en hierro, efectos secundarios, esquema de dosis, medicamentos consumidos y motivación). Se emplearon estadísticas descriptivas, el test del  $\chi^2$ , *Odds Ratio* con IC95% y la regresión logística binaria u OR ajustado (ORa). **Resultados:** 79,1% tenían entre 6 a 23 meses, 75,9% recibieron multimicronutrientes y la adherencia fue del 24,4% (IC95% 22,3 – 26,6). Los factores: seguir con la suplementación (OR = 3,5; IC95% 1,7 – 7,5); no tener náuseas (OR = 3,0; IC95% 2,0 – 4,3); no tomar antibióticos (OR = 2,5; IC95% 1,7 – 3,6) e intenciones de seguir con el tratamiento (OR = 2,3; IC95% 1,3 – 4,1) se asociaron a la adherencia. El análisis multivariado asoció pensar que debe continuar con el tratamiento (ORa = 2,6; IC95% 1,1 – 6,1); si presentó algún efecto secundario, no suprimió el tratamiento (ORa = 2,5; IC95% 1,4 – 4,3), el niño no tomó antibióticos (ORa = 2,0; IC95% 1,1 – 3,4) y creencia que anemia no solo se cura con medicamentos (ORa = 1,6; IC95% 1,0 – 2,6). **Conclusión:** Hubo una baja prevalencia de adherencia para un punto de corte exigente ( $\geq 90\%$  sobres de multimicronutrientes consumidos) y los factores asociados están relacionados con ausencia de infecciones, efectos secundarios y creencias de la madre.

**Palabras clave:** Cumplimiento de la medicación. Micronutriente. Niño. Anemia. Perú.

## INTRODUCTION

According to the Demographic and Health Survey of Peru<sup>1</sup>, anemia in children aged 6 to 35 months had a small decrease in the last 7 years, from 56.8 (2007) to 46.4% (2013). In the last 10 years, the equity themes that became essential for the regional and supported development were developed in Latin America<sup>2</sup>. Since 2010, we have been living under a health universal assurance in Peru (under the Law 29344), and the health system has implemented strategies to decrease public health issues, among them children's anemia.

The prevention of child's iron deficiency begins in the prenatal care and during breastfeeding. It has been discussed in literature the maternal deficiency on the neonate's iron condition, and the most relevant data seem to indicate that children of mothers with iron-deficiency anemia are born with decreased storages of such substance<sup>3</sup>. After 6 months of breastfeeding, iron intake is not appropriate<sup>4</sup>, therefore food should be reinforced, because if these children do not receive proper treatment, they will have their skills reduced<sup>5</sup>, present growth delay, low body weight, and wasting<sup>6</sup>. Treatments based on the administration of ferrous sulfate against anemia have been cost-effective. A review has found that the consumption of daily supplements is more effective than weekly intakes to improve the hemoglobin levels<sup>7</sup>. However, this treatment as a public health intervention would mainly cause low adherence and side effects<sup>8,9</sup>, although studies have showed high

adherence (32 to 90%)<sup>10</sup> when using multiple micronutrient powders (MMN), including flexible and daily regimens (Bangladesh) (88 to 98%)<sup>11</sup>.

The World Health Organization states that therapeutic adherence is the level in which the behavior of a person, medication use, food diet compliance, and performance of life-style alterations correspond to the recommendations agreed with the sanitation care provider<sup>12</sup>, which is also applied in children. A Cochrane review has demonstrated that the MMN, also called Chispitas<sup>®</sup> or Sprinkles, reduce the rate of anemia in 31% and iron-deficiency in 51% when compared with placebo<sup>10</sup>. MMN are an important strategy and an option to solve and prevent anemia in Asia, Africa, and in prioritized communities in developed countries<sup>13</sup>. The locations that have widely implemented the MMN, such as Mongolia, were seen with a high rate of compliance (76.6% of the parents or guardians want to continue their use)<sup>14</sup>. In Bolivia, 69% of the guardians are still supplying the MMN<sup>15</sup>.

Due to the high prevalence of anemia in children, the Peruvian government with international support implemented, between the years of 2009 to 2011, a pilot program in three regions of the country to supplement children's diets with MMN<sup>16</sup>. Then, the program was extended to other regions through a progressive implementation, and, in 2014, the globalization of the supplementation began with an estimated population of 1,400,000 children aged 6 to 35 months<sup>17</sup>. To do this, the respective directive was officially published together with other activities such as counseling and monitoring<sup>18</sup>, and this regimen was initially applied as a supplement, which will also be used for anemia treatment<sup>19</sup>.

A study conducted in Apurímac (Peru, in 2010) including 664 children aged 6 to 35 months evaluated the proper consumption of MMN, which reached 4.1% in children who consumed less than 30 envelopes and 14.5% in those that consumed between 30 or less than 60 envelopes. Therefore, the authors found out that not only we need to deliver or consume the necessary amount, but also ensure the proper consumption process<sup>20</sup>. Another study conducted in Ayacucho, Andahuaylas, and Huancavelica found that 20.5% of the patients discontinued the supplementation<sup>21</sup>. In Kenya (2013), the factors associated with adherence to MMN included: early age (higher prevalence of children aged 6 – 23 months than 24 – 35 months, adjusted Odds ratio (aOR) = 1.5;  $p = 0.02$ ), more than two quintiles of socioeconomic level (aOR = 1.7;  $p = 0.04$ ), home care (aOR = 2.8;  $p < 0.001$ ), and promotion of free consumption, calendars, cups, and T-shirts (aOR = 1.7;  $p = 0.04$ )<sup>9</sup>. The objective of this study was to consider the adherence to MMN and its factors associated in children aged 6 to 35 months cared in the Ministry of Health institutions from 12 regions in Peru, from October to December 2014.

## METHODS

### TYPE OF STUDY AND OUTLINE

This is an epidemiological study of active surveillance sentinel facilities<sup>22,23</sup>. A specialized surveillance<sup>24</sup> of children cared in institutions from the Ministry of Health was carried

out to choose the facilities, considering their distribution and space-population representativeness<sup>22</sup>. According to the plan to decrease anemia, 65.0% of the children aged 6 – 35 months should have received MMN in 2014.

## SELECTION OF SENTINEL FACILITIES

The main information from 2013 of the institutions that reported data of children's anemia to the National Center of Food and Nutrition (CENAN) of the National Institute of Health (NHI) was collected. A total of 4944 institutions were included: 108 hospitals, 1083 health centers, and 3753 health clinics. Micro-field areas of information with enough sensitivity to monitor the supplementation with MMN were considered. Such facilities presented a rate of anemia similar to the region and had a similar territorial relation, that is, if the area was from the countryside and had a 45% prevalence of children's anemia, institutions in the same place that had a similar proportion of anemia and that historically sent information to CENAN were searched. Therefore, the facility with the largest population was chosen and, by following the same criterion, we achieved 34 institutions: 3 hospitals, 22 health centers, and 9 health clinics that had a space-population representation based on the urban–rural and regional scope from 12 regions in Peru.

## SAMPLE

Data were collected from October to December 2014. The 34 institutions registered a total amount of 4896 children in the growth and development offices (CRED). The inclusion criteria were children aged 6 – 35 months, cared in the last 30 days, with a located home, whose mother or guardian accepted to participate in the study; whereas children diagnosed with non-iron deficiency anemia of any other etiology were excluded, thus corresponding to a total of 2024 children chosen by convenience.

## VARIABLES

Age (in months), educational level of the mother or guardian, altitude of sea level, kind of health institution (health clinics, health center, or hospital), and the scope (urban or rural) were measured. The factors associated with adherence include:

- Dosage regimen – continuing supplementation is healthier to the child, and the treatment is easy to comply with;
- Side effects – the child has had nausea; if the child presented any side effects, the treatment would be interrupted;
- Consumed medications – the child has taken antibiotics; it has been hard to provide the child with the iron supplement;

- Motivation – intends to continue the treatment with the child, he/she is getting better with the treatment, he/she plans to finish treatment, he/she has received a good care in the health institution;
- Beliefs – his/her family believes he/she should continue treatment, he/she believes anemia can only be cured with medications;
- Anemia knowledge – he/she has anemia due to lack of supplements or vitamins and knows the importance of iron; and
- Consumption of iron-rich foods – his/her child consumes chicken blood, and has difficulties in providing iron-rich foods to the child.

The Ministry of Health of Peru approved the MMN structure: 12.5 mg of elemental iron, 5 mg of zinc, 160 µg of folic acid, 300 µg of retinol (RE) equivalents of vitamin A, and 30 mg of vitamin C<sup>18</sup>. To establish the adherence to MMN, an evaluation of what was received and consumed in the last 30 days was carried out, using the following formula:

$$\text{Adherence to MMN} = \frac{\text{Amount of consumed MMN envelopes}}{\text{Total amount of delivered MMN envelopes}} \times 100$$

The child was considered an adherent when such proportion was equal to or higher than 90%<sup>21</sup>.

## PROCEDURES

The documentation and guidance were sent to the Health Departments of the regions chosen by CENAN. The field team was trained, and a pilot study was conducted to use the techniques and procedures with such team. The investigators visited each nominated health center and coordinated it with the institution staff. The information was obtained from the CRED area, which is usually ruled by nurses, to determine the total amount of children through the care notebook, nominal standard, Health Information System (HIS), Nutritional Condition Information System (SIEN), CRED card, or other equivalents. After collecting all information, the visitations were planned with three possibilities: all the institutions with less than 30 children were visited; in the institutions with more than 30 children, 30 of them were randomly chosen and nine others were included; in the facilities with more than 30 children that were found in dispersed regions, we proceeded to zoning and division into populated centers or urbanizations, taking by chance regions with more than 30 children. Then, a route of visitations was done and, in some cases, the institution staff provided support; in other cases, the investigators did it independently. The mothers or guardians were identified and the objectives of the study were reported to them before the study. After their acceptance, we applied the informed consent and the forms of data record and observation of documents and counting of MMN envelopes. Structured interviews were carried out to obtain information about the general variables

and the associated factors. Data forms and the record sheet of adherence to MMN were used as instruments. The supervision of investigators was implemented in the field; the CENAN staff verified the quality of registrations; each investigator received a supervision visit with the exception of three areas that received a second supervision. A specific app was developed so that investigators could type all information. The forms in physical medium were sent to CENAN for information processing.

## ETHICAL ASPECTS

In 2014, due to the increase of anemia in children younger than 5 years old in Peru, as a response, the Ministry of Health implemented a plan to decrease child chronic malnutrition and prevent anemia, which was published by the ministerial resolution 258-2014/MINSA (March 31, 2014), considering anemia a public health issue. CENAN is in charge of the sentinel surveillance of the adherence to MMN in such plan.

This study is part of the implementation of such strategy, because it did not have a surveillance system for this event. The General Administration of CENAN approved this activity. Due to this need and because we are dealing with surveys, the evaluation had minimal risk. The ethical principles were applied in the investigation to the participating mother, who were also offered educational reports on anemia and were asked to inform the health institution after their participation ended. The principle of autonomy was followed in the entire process. The study comprised of volunteers, and all participants signed the informed consent. The information was obtained confidentially, that is, the identification data were not used for the study, no blood samples were taken, and data were collected from CRED cards and from interviews with the mothers or guardians.

## DATA ANALYSIS

The information was processed in the IBM database, SPSS, version 20. To estimate the adherence to MMN, the adherence formula with its respective 95% confidence intervals and  $\chi^2$  statistical or Fisher's exact tests were applied based on a statistical significance level of  $p < 0.05$ . The Odds Ratio (OR) with its 95% confidence intervals (crude OR) was applied in the bivariate analysis. The variables with significant results in the bivariate analysis ( $p < 0.05$ ) were included for the binary logistic regression analysis, following the introduction method. The model was validated through Hosmer-Lemeshow test, with  $p > 0.05$  as the significant value. Cox and Snell  $R^2$  and Nagelkerke  $R^2$  were applied to determine the variance explained with the factors. The global percentage of the model and the  $\chi^2$ -test of the omnibus were used for the significance of the factors, as well as the adjusted OR with its corresponding 95% confidence intervals. Finally, the ROC curve indicated the model's predictive value with its lower and upper limits and its level of significance of  $p < 0.05$ .

## RESULTS

A total of 79.1% children were aged 6 – 23 months, 34.4% between 6 to 11 months, and 44.7% between 12 to 23 months. Of all, 57.7% mothers or guardians had a secondary educational level; 56% children came from an altitude of less than 1000 meters above sea level (masl), and 23% at one between 3001 and 4000 masl. A total of 70.8% were from health centers and 60.3% were from the rural area (Table 1).

Among the 2204 children aged 6 – 35 months evaluated, 75.9% had received the MMN (n = 1536); the adherence proportion was of 24.4% in those receiving MMN (95%CI 22.3 – 26.6%), which was a significant value (p < 0.001). The adherence was higher in mothers who did not have an educational level (46.2%). There were no differences regarding

Table 1. Rates of adherence to multiple micronutrient powders in children aged 6 – 35 months from sentinel facilities, Ministry of Health, 2014.

Variables	n (%)	Adherence to multiple micronutrient powders		p-Value
		%	95CI%	
Age (months)				
6 to 11	529 (34.4)	23.3	19.7 – 26.9	0.299
12 to 23	686 (44.7)	24.3	21.1 – 27.6	
24 to 35	321 (20.9)	26.5	21.7 – 31.3	
Guardian's educational level				
No educational level	13 (0.8)	46.2	19.1 – 73.3	0.038
Primary	271 (17.7)	28.8	23.4 – 34.2	
Secondary	884 (57.7)	23.3	20.5 – 26.1	
Higher	364 (23.8)	22.8	18.5 – 27.1	
Altitude (masl)				
11 to 1,000	841 (56.3)	25.8	22.8 – 28.8	0.191
1,001 to 2,000	103 (6.9)	9.7	4.0 – 15.4	
2,001 to 3,000	205 (13.7)	27.3	21.2 – 33.4	
3,001 to 4,000	344 (23.1)	21.2	16.9 – 25.5	
Institution				
Health clinics	308 (20.1)	24.4	19.6 – 29.1	0.152
Health center	1.087 (70.8)	23.3	20.8 – 25.8	
Hospital	141 (9.2)	33.3	25.6 – 41.1	
Area				
Urban	610 (39.7)	22.6	19.3 – 25.9	0.185
Rural	926 (60.3)	25.6	22.8 – 28.4	
Total	1.536 (100.0)	24.4	22.3 – 26.6	< 0.001



children's age ( $p = 0.299$ ), sea level altitude ( $p = 0.191$ ), health institution ( $p = 0.152$ ), and urban and rural regions ( $p = 0.185$ ) (Table 1).

The factors associated with adherence were:

- Dosage regimen – continuing supplementation, it is healthier to the child (OR = 3.5; 95%CI 1.7 – 7.5);
- Side effects – the child has not had nausea (OR = 3.0; 95%CI 2.0 – 4.3), if the child presented a side effect, the treatment was not discontinued (OR = 2.1; 95%CI 1.6 – 2.8);
- Consumed medications – the child has not taken antibiotics (OR = 2.5; 95%CI 1.7 – 3.6), it is not hard to give him/her the iron supplement (OR = 2.3; 95%CI 1.8 – 2.9);
- Motivation: he/she intends to continue the treatment of his/her child (OR = 2.3; 95%CI 1.3 – 4.1), the child gets better with the treatment (OR = 2.3; 95%CI 1.6 – 3.2), he/she plans to finish treatment (OR = 2.2; 95%CI 1.2 – 4.1), he/she received good care in the health institution (OR = 1.8; 95%CI 1.2 – 2.6);
- Beliefs – the family believes he/she should continue treatment (OR = 1.9; 95%CI 1.4 – 2.7) and does not believe anemia cured only with drugs (OR = 1.6; 95%CI 1.3 – 2.1);
- Consumption of iron-rich foods – he/she does not have difficulties in giving the child iron-rich foods (OR = 1.4; 95%CI 1.0 – 1.8), his/her child consumes chicken blood (OR = 1.3; 95%CI 1.0 – 1.6), and it is not hard to give iron-rich foods to the child (OR = 1.4; 95%CI 1.0 – 1.8);
- Other factors such as anemia knowledge were also associated but without significant values (Table 2).

The logistics regression model indicated four factors associated with adherence to MMN: no use of antibiotics (aOR = 2.0; 95%CI 1.1 – 3.4); if the child had any side effects, the mother did not discontinue treatment (aOR = 2.5; 95%CI 1.4 – 4.3); if the family believed the child should continue with the supplementation (aOR = 2.6; 95%CI 1.1 – 6.1), and lack of believe that anemia is only cured with drugs (aOR = 1.6; 95%CI 1.0 – 2.6). This model was considered appropriate (Hosmer–Lemeshow test = 2.063;  $p = 0.914$ ), and explained 6 – 9% of the problem variance (Table 2), even though it had a good predictive power (area under the ROC curve = 0.659), thus indicating that these factors differentiate the adherent child from the non-adherent child well (Figure 1).

## DISCUSSION

Treatment with iron salts is ideal to decrease the rate of anemia rate. The consumption of MMN significantly reduces the rate of anemia in children. A technical report published by the INS indicated that the MMN reduced the rate of anemia in 31% and the iron deficiency in 51%<sup>12</sup>. However, a study conducted in Colombia (2014)



Table 2. Factors associated with adherence to multiple micronutrient powders in children aged 6 – 35 months, Ministry of Health, 2014.

Factors	Adherence		Crude OR (95%CI)	Adjusted OR* (95%CI)
	Yes	No		
	n (%)	n (%)		
<b>Dosage regimen</b>				
Continue supplementation, it is healthier to the child			p < 0.001	
No	8 (1.6)	57 (5.4)	1.0	
Yes	494 (98.4)	992 (94.6)	3.5 (1.7 – 7.5)	
It is easy to comply with the treatment			p = 0.001	
No	450 (89.5)	870 (82.9)	1.0	
Yes	53 (10.5)	179 (17.1)	0.6 (0.4 – 0.8)	
<b>Side effects</b>				
The child has nausea			p < 0.001	
Yes	37 (7.4)	200 (19.1)	1.0	
No	465 (92.6)	849 (80.9)	3.0 (2.0 – 4.3)	
Presence of side effect, therefore the treatment was discontinued			p < 0.001	p = 0.002
Yes	75 (16.5)	269 (29.0)	1.0	1.0
No	380 (83.5)	657 (71.0)	2.1 (1.6 – 2.8)	2.5 (1.4 – 4.3)
<b>Used medications</b>				
Antibiotics			p < 0.001	p = 0.016
Yes	108 (58.7)	283 (77.7)	1.0	1.0
No	76 (41.3)	81 (22.3)	2.5 (1.7 – 3.6)	2.0 (1.1 – 3.4)
It has been hard to give the iron supplement to the child			p < 0.001	
Yes	114 (22.7)	422 (40.2)	1.0	
No	388 (77.3)	628 (59.8)	2.3 (1.8 – 2.9)	
<b>Motivation</b>				
Intends to continue the child's treatment			p = 0.004	
No	14 (2.8)	65 (6.2)	1.0	
Yes	488 (97.2)	983 (93.8)	2.3 (1.3 – 4.1)	
The child gets better with the treatment			p < 0.001	
No	39 (7.8)	167 (15.9)	1.0	
Si	463 (92.2)	881 (84.1)	2.3 (1.6 – 3.2)	

Continue...

Table 2. Continuation.

Factors	Adherence		Crude OR (95%CI)	Adjusted OR* (95%CI)
	Yes	No		
	n (%)	n (%)		
Plans to finish treatment			p = 0.008	
No	13 (2.6)	59 (5.6)	1.0	
Yes	489 (97.4)	990 (94.4)	2.2 (1.2 – 4.1)	
Good care received in the health institution			p = 0.004	
No	35 (7.0)	123 (11.7)	1.0	
Yes	467 (93.0)	926 (88.3)	1.8 (1.2 – 2.6)	
Beliefs				
Family believes treatment should be continued			p < 0.001	p = 0.023
No	51 (10.2)	188 (17.9)	1.0	1.0
Yes	451 (89.8)	861 (82.1)	1.9 (1.4 – 2.7)	2.6 (1.1 – 6.1)
Anemia can only be cured with medications			p < 0.001	p = 0.049
Yes	172 (34.3)	485 (46.2)	1.0	1.0
No	330 (65.7)	564 (53.8)	1.6 (1.3 – 2.1)	1.6 (1.0 – 2.6)
Knowledge about anemia				
Knows the importance of iron			p < 0.001	
No	243 (48.5)	653 (61.6)	1.0	
Yes	258 (51.5)	407 (38.4)	1.7 (1.4 – 2.1)	
Has anemia due to lack of supplements or vitamins			p < 0.001	
Yes	84 (16.7)	260 (24.5)	1.0	
No	419 (83.3)	800 (75.5)	1.6 (1.2 – 2.1)	
Consumption of iron-rich foods				
The child consumes chicken blood			p = 0.046	
No	361 (71.9)	805 (76.6)	1.0	
Yes	141 (28.1)	246 (23.4)	1.3 (1.0 – 1.6)	
It is hard to give iron-rich food to the child			p = 0.032	
Yes	80 (15.9)	215 (20.5)	1.0	
No	423 (84.1)	835 (79.5)	1.4 (1.0 – 1.8)	

\*R<sup>2</sup> Cox and Snell = 0.06; R<sup>2</sup> Nagelkerke = 0.09; Hosmer–Lemeshow test = 2.063; gl = 6; p = 0.914; global percentage = 76.3.

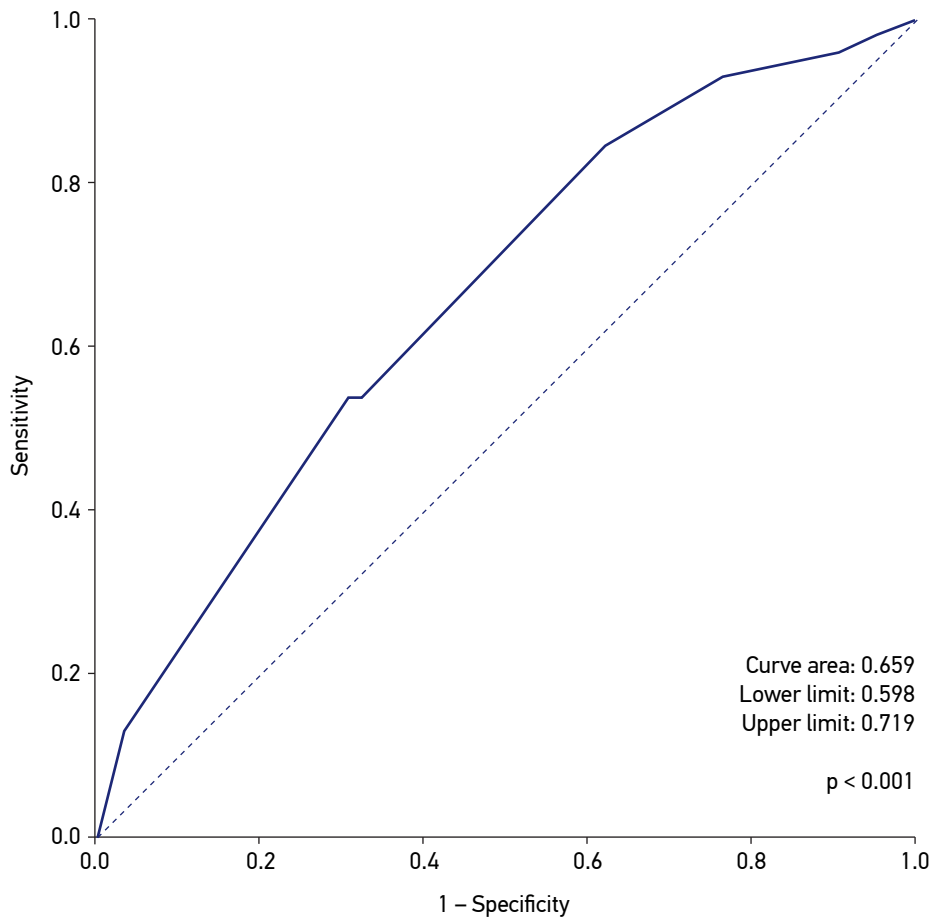


Figure 1. ROC curve to predict the factors associated with adherence to multiple micronutrient powders in children aged 6 – 35 months.

in children aged 6 – 24 months showed that MMN administration in non-controlled situations did not present an improvement in the hemoglobin levels<sup>25</sup>. The supplementation with MMN improved children's anemia in Kenya, but its use is more difficult due to incorrect dosage, equipment, low insurance coverages, and worries on the side effects associated with the dosage and safety<sup>26</sup>. In Argentina (2013), a study on the adherence to ferrous sulfate in children younger than 42 months found that the causes of non-adherence were digestive intolerance (38%) and forgetting the treatment (36%). Adherence of mothers was studied in the group of children who were taking iron for at least 1 month or had stopped taking it during the 6 months before the day of the interview<sup>27</sup>.

Among the 2024 studied children, 75.9% received MMN, and this rate was higher than the expected for the same year (65%); but it was estimated this would get to 95%<sup>17</sup> in 2016. Thus, it indicates that for the study months, the coverage was higher than the expected.

The rate of adherence was 24.4% (95%CI 22.3 – 26.6). According to a report from the World Health Organization, there is not a “gold standard” to measure the behavior of adherence. Therefore, to determine the adherence to MMN, the use of a new counting of the consumed envelopes can be a strategy, which is recommended both in the household visit and in the clinics. However, new counting errors are common and open space characteristically to the overestimation of the behavior<sup>28</sup>, which can be complemented with other instruments, such as standardized tests. The patient should consume a 100% rate of the recommended amount, which is not very practical, but it is the main point for the ideal determination of the therapeutic adherence. This was tried to MMN cases in which the cut-off point varied from 75 to 100% of the consumption.

An evaluation carried out by the CENAN found that 25% of the children from the urban region and 32.1% from the rural region older than 1 year consumed the MMN completely (90 or more envelopes). It also indicated that in children that finished more than 75% of the dosage, there was a decrease of anemia<sup>12</sup>. A review with studies from Bangladesh, Kenya, and Nepal about programs with MMN concluded that the prevalence of anemia was smaller in children aged 6 – 24 months that consumed more than 75% of the MMN compared to those that had an adherence < 75% (50.0 versus 61.0%)<sup>29</sup>. Another study showed a cut-off point of 80%<sup>30</sup>. Adherence is more difficult to be complied with when treatments are longer and happen on a daily basis, thus an investigation compared three regimens for MMN: a group consumed them for 4 months on a flexible basis, another during 3 months in the same basis, and the last one during 2 months on a daily basis. The rate of children who consumed all prescribed envelopes (100% adherence) was higher in the flexible group of 4 months (86.4%) compared to the flexible group of 3 months (58.4%) and the group of 2 months on a daily basis (13.5%)<sup>11</sup>. The results show that the process of adherence is complex and requires the effort of the mother or guardian and of the family, with supervision of the health team<sup>28</sup>.

The strategies to improve adherence include simplification of the regimens, counseling sessions, reminding systems, health team supervision and motivation, family therapy, psychological therapy, and phone monitoring. There is a tendency of combining more than one strategy to reinforce the message and increase the impact. For the specific case with the MMN, some options are the communicational educative intervention, family and community's participation, reinforcement of the monitoring, supervision<sup>20</sup>, and strengthening of the surveillance systems<sup>31</sup>.

We have found some factors that can improve effectiveness in medical clinics, in home visits, or in educational sessions in this study. In the medical clinics, we recommend verifying if the child had nausea, took antibiotics and had difficulties in receiving MMN, as well as on how to achieve that he/she does not discontinue treatment due to side effects. These can be decreased if the MMN is consumed together with the meals, although some studies have showed that the absorption is decreased in 40% in such cases<sup>32</sup>.

In home visits, which is a high-impact activity, we suggest the inclusion of five questions that could facilitate the adherence: intends to continue treatment with the child; his/her plans include finishing treatment; his/her family believes treatment should be continued; he/she has received good care in the health institution; and if the child consumes chicken blood. This should be applied together with a reinforcement regimen of the main points: continuing the supplementation and the treatment are healthier to the child, among others.

The importance of iron, iron-rich foods, iron supplementation, the correct form of MMN intake and signals of children's improvement must be incorporated into the educational sessions. A person's nutritional iron condition depends on the balance determined through the interaction between the content on the diet, bioavailability, losses and requirements by growth<sup>3</sup>, which should be part of the mothers' educational process.

A proposal of indicators of the clinic process could be the rate of children whose families believe they should continue the treatment and the rate of children with MMN without prescription of antibiotics. The rate of children who presented side effects and discontinued treatment should be verified in home visits. In the educational sessions, the rate of mothers or guardians who believe anemia is not cured only with medications should be reviewed.

We consider this as the first approximation to the factors that are associated with adherence to MMN, because it was a sentinel surveillance sample, and thus a sample by convenience. The rates found have differences regarding their level of significance, so we recommend the conduction of analytical studies with representative samples by regions that would allow us to find the factors based on each context. However, due to the size of the sample, we were able to find the most characteristic factors, considering we live in a multicultural and multilingual country, which allows corresponding to the historical and cultural reality of each area.

## CONCLUSIONS

There was a low prevalence of adherence to a demanding cut-off point ( $\geq 90\%$  of envelopes of multiple micronutrient powders), and the associated factors are associated with absence of infections, side effects, and mother's beliefs.

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