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Original

Using of WHO guidelines for the management of severe malnutrition to cases of marasmus and kwashiorkor in a Colombia children's hospital

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Abstract

Background: **In 2007, the Hospital Infantil Los Ángeles (HILA) in Colombia implemented a slightly-modified version of the WHO guidelines for the diagnosis and management of malnutrition during childhood.**

Objective: **To evaluate the efficacy of the WHO-HILA protocol in children hospitalized with severe, chronic marasmus and kwashiorkor malnutrition (MS-KWK) in 2007 and 2008.**

Material and methods: **In this descriptive retrospective study the records of 100 children hospitalized with MS-KWK were initially evaluated. Of these, 30 fulfilled the inclusion criteria: children of both sexes with a primary diagnosis of MS-KWK. Patients with any chronic disease liable to cause malnutrition were excluded. Anthropometric parameters, clinical signs and biochemical indicators of malnutrition were assessed upon admission and again at discharge following application of the WHO guidelines. Univariate analysis was performed for each study variable; serum hemoglobin and albumin levels on admission and at discharge were compared, and data were subjected to bivariate analysis.**

Results: **Marasmus was diagnosed in 23.3% of children, kwashiorkor in 73.3% and marasmic kwashiorkor in 3.3%. The major clinical findings were: edema (70%), emaciation (40%), "flag sign" hair (42.86%), low serum albumin (93%) and anemia (80%). Thirteen children following the WHO-HILA protocol showed a significant nutritional status improvement ($p < 0.05$), whereas no improvement was noted in the 17 children not treated according to the protocol.**

Conclusions: **Application of the WHO-HILA protocol was associated with reduced morbimortality in children with marasmus-kwashiorkor malnutrition. Implementation of this protocol should therefore be considered in all children's hospitals in countries where this disease is prevalent.**

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APLICACIÓN DEL PROTOCOLO DE LA OMS DE MALNUTRICIÓN MARASMO-KWASHIORKOR EN UN HOSPITAL DE COLOMBIA

Resumen

Introducción: **En 2007, el Hospital Infantil de Los Ángeles (HILA) en Colombia implementó una versión del protocolo-OMS para el diagnóstico y tratamiento de la malnutrición en la infancia.**

Objetivo: **Evaluar la aplicación del protocolo de la OMS-HILA en niños hospitalizados con marasmo y/o kwashiorkor (MS-KWK) durante 2007-2008.**

Material y métodos: **En este estudio retrospectivo, se evaluaron 100 niños hospitalizados con MS-KWK; 30 cumplieron los criterios de inclusión: niños de ambos sexos con MS-KWK primario. Los pacientes con enfermedades crónicas que pudieran causar desnutrición fueron excluidos. Se evaluaron determinados parámetros antropométricos, y signos clínicos y bioquímicos de desnutrición según el protocolo de la OMS, al ingreso y al alta. Se realizó un análisis univariante; los niveles de hemoglobina y albúmina séricas fueron comparados al ingreso y al alta, y los datos fueron sometidos a análisis de dos variables.**

Resultados: **Se diagnosticaron de marasmo al 23,3% de los niños, de kwashiorkor al 73,3% y de kwashiorkor marásmico al 3,3%. Los hallazgos clínicos más importantes fueron: edema (70%), emaciación (40%), "signo de bandera" (42,86%), albúmina baja (93%) y anemia (80%). Trece niños mostraron mejoría significativa del estado nutricional tras aplicar el protocolo OMS-HILA ($p < 0,05$), mientras que no ocurrió en 17 niños no tratados según el protocolo.**

Conclusiones: **La aplicación del protocolo de la OMS-HILA se asoció con una reducción de la morbimortalidad en los niños con desnutrición marasmo-kwashiorkor. La aplicación completa y continuada de este protocolo debe ser considerada en los hospitales infantiles de todos los países donde esta enfermedad es prevalente.**

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Palabras clave: *Marasmo. Kwashiorkor. Desnutrición infantil. Patología nutricional.*

Abbreviations

MS-KWK: Marasmic kwashiorkor.
HILA: Hospital Infantil Los Ángeles.

Introduction

Although malnutrition may arise at any stage in life, its occurrence in children is particularly noteworthy for its detrimental effect on growth and development. Severe chronic malnutrition generally occurs during infancy and early childhood.[1] In countries at risk for malnutrition, after weaning —which often starts before the fourth month— children receive little or no dairy food or other products of animal origin. A low-protein, low-energy diet, coupled with frequent digestive and respiratory infections, favours the slow but progressive development of severe malnutrition.[2]

Signs leading to the diagnosis of chronic malnutrition include low height and weight for age, indicating stunted growth, whilst the most common biochemical alterations are low serum hemoglobin and albumin levels; on admission to hospital, patients may also display hypoglycemia and ion deficiencies.[3]

Marasmus is a form of chronic malnutrition characterized clinically by severe wasting of subcutaneous tissue, muscle and fat, which gives rise to a wizened, wrinkled appearance. Affected children tend to be weak and listless, displaying loss of appetite and decreased food tolerance, due to a diet deficient in calories, macronutrients and micronutrients.[3,4]

Kwashiorkor is more frequent in infants with protein deficiency but adequate carbohydrate intake[3]. Serum protein and especially albumin depletion tends to be more severe in this form of malnutrition, which is associated with a higher risk of infection. Weight is often adequate for age, and clinical signs include the characteristic so-called "moon face", depigmented hair (the "flag sign"), edemas mainly in the limbs, bloated abdomen, whimpering and irritability. In the mixed form, known as marasmic kwashiorkor, children display features of both types, the most common combination being wasting of subcutaneous tissue, limb edemas, enlarged liver and severe serum protein depletion.[4,5]

According to the National Survey on Nutritional Status in Colombia (ENSIN), carried out in 2005, the south-western department of Nariño has one of the country's worst records for chronic malnutrition and retarded growth[1]. All children in this area displaying critical marasmic-kwashiorkor (MS-KWK) malnutrition are referred to the third-level "Hospital Infantil Los Ángeles" (HILA), since —due to difficulty of access and economic conditions— cases are not diagnosed and treated by local primary healthcare services.

The management of patients with severe, chronic MS-KWK malnutrition represents something of a challenge, since this condition is often associated with complications such as hypothermia, hypoglycemia and infection, which worsen the prognosis. Once patients with chronic malnutrition are hospitalized, the main aim of treatment is to stabilize hemodynamic function, address pathologies associated primarily with gastrointestinal, genitourinary and respiratory infection, and work towards the recovery of adequate nutritional status. Nutritional recovery may take several years, depending on the severity of malnutrition.[6,7] In 2000, the World Health Organization (WHO) set out guidelines for the inpatient management of protein-energy malnutrition (MS-KWK); these have been periodically updated since then.[4,8] In 2007, aware of the child malnutrition problem at regional level, the Hospital Infantil Los Ángeles (HILA) implemented a slightly-adapted version of the WHO guidelines aimed at improving the diagnosis and management of children with severe malnutrition. The HILA programme comprised a stabilization phase followed by outpatient check-ups intended to achieve full health recovery.

The protocol was established to diagnose and to treat in agreement with the guidelines of the WHO, and hospital personnel became qualified for it's use. Nevertheless, the professionals who covered occasional turns and weekends did not apply it, possibly due to lack of knowledge. In other occasions, when the cause of the admission was another disease, a suitable nutritional diagnosis was obviated. For the children who did not follow the protocol, the modified formulas propose F75 and F100 by the WHO were not provided to them, did not have the suitable isolation or the necessary controls on the admission or at discharge, and seemed that the evolution was not the expected one. For this reason, the aim of this study was if demonstrable difference between both groups existed, already defined a priori by the action of the professionals, and if the application of this protocol was effective to diagnose and to deal suitably with the children with this type of undernourishment.

However, local adoption of the HILA protocol for the management of MS-KWK malnutrition has not yet led to the full achievement of initial objectives, since the protocol has not been used for all children with diagnosed malnutrition.

This study sought to evaluate the application of the WHO-HILA and the results obtained from the treatment of pediatric patients with severe, chronic MS-KWK malnutrition admitted in 2007 and 2008.

Material and methods

This descriptive retrospective study evaluated data drawn from the clinical records of children admitted to the "Hospital Infantil Los Ángeles" in Nariño (Colombia) with severe malnutrition between January 2007 and December 2008. Of a total of 100 such patients, 30 cases fulfilling inclusion criteria were selected for the study. Inclusion criteria were: children of both sexes, hospitalized in the period 2007-2008, with a primary

Table I
Composition of F-75 and F-100 formulas in WHO-HILA protocol

Ingredients	*F75*	*F100*
Infant formula without lactose[a]	25 g	80 g
Sugar	70 g	50 g
Infant cereals[b]	35 g	–
Canola oil	27 g	60 g
Minerals[c]	20 ml	20 ml
Vitamin supplement[d]	140 mg	140 mg
Water	1,000 ml	1,000 ml

The adjustment corresponds to: [a]change WHO proposition with skimmed milk by an infant formula without lactose of low osmolarity; [b]standardized infant cereals and [c,d]standardized supplements of minerals (K, Mg, Zn, Cu, Na) and liposoluble and water soluble vitamins.

diagnosis of MS-KWK malnutrition, changes in anthropometric and biochemical parameters, as well as gastrointestinal and respiratory infections associated. Exclusion criteria were: chronic disease, neurological pathologies involving eating disorders, and any baseline pathology other than malnutrition or an associated condition.

The only adaptation of the original WHO guidelines[9] made in the HILA protocol was with reference to the feeding formulas F-75 and F-100, certain foods being replaced by local ingredients with similar nutritional composition and energy supply, in order to facilitate preparation and administration: banana flour was used instead of cereal flour. Because WHO protocol does not specify the doses and which vitamins or minerals should be used, henceforth a usual multivitamin supplement was added. Volumes and feeding times were as recommended by the WHO (table I). Nevertheless, the nutritional support and all the management was done following the WHO guidelines. It starts with 100 ml/kg to be increasing daily 25 ml/kg until a maximum of 225 ml/kg, in 8 to 12 doses distributed in the 24 h/day according to tolerance. Figure 1 shows an algorithm used for the nutritional management in children with marasmo-KWK.

Data collected during review of clinical records included variables relating to clinical status on admission (hydration, edema, emaciation, hair status, dermatitis), and the anthropometric variables and biochemical parameters recommended in WHO guidelines (weight, height, hemoglobin, hematocrit, total proteins, albumin, total inmunoglobulins and ions). Anthropometric data were evaluated using the percentile growth charts

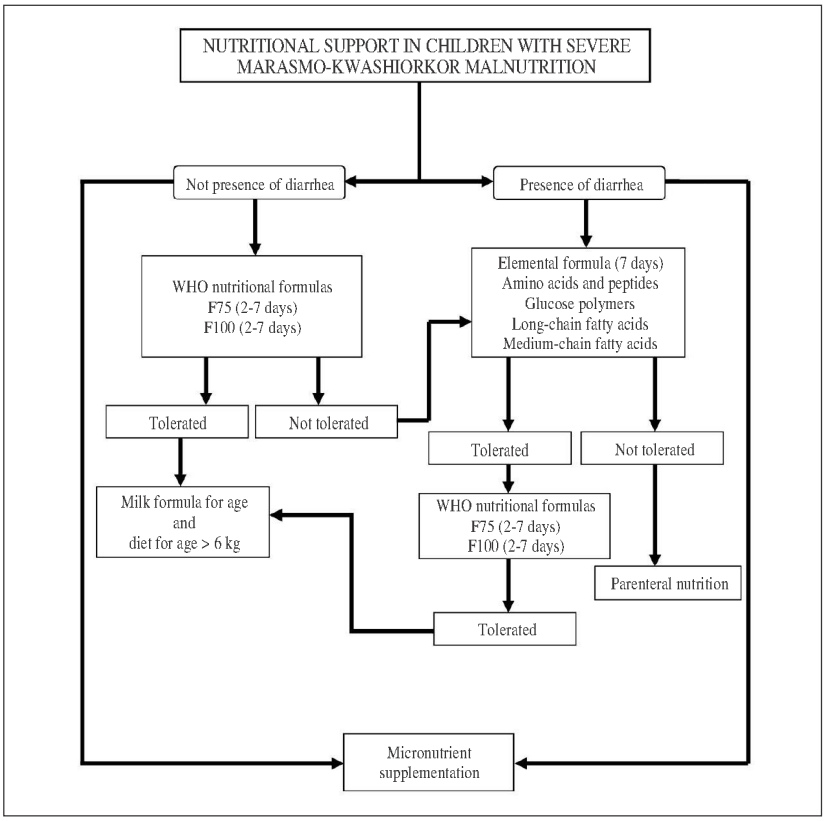

Fig. 1.—Algorithm used in HILA for the nutritional management in children with marasmo-KWK.

published by the Centres for Disease Control and Prevention (CDC).[10] Information was also collected on socioeconomic status,[11] mother's age, duration of breastfeeding, and feed details on admission.

Although the anthropometry is an usual tool to diagnose the undernourishment, in the case of the undernourishment marasmo and kwashiorkor, as well as some biochemical parameters like hipoalbuminemia, the clinical signs also must be kept in consideration. Therefore, children were classified in the kwashiorkor group when they presented edema and hipoalbuminemia, injuries in skin and/or mucous, and alterations in the colour and fragility of the hair. They were included within the group of marasmo when they presented extreme thinness, (weight/age < p5), severe deplection of subcutaneous tissue, facies wrinkled and non appreciation of edema. The children were included in the marasmo-kwashiorkor group when they presented extreme thinness, severe depletion of subcutaneous tissue, edema in extremities, injuries in skin and/or mucous and alterations in the colour and fragility of the hair.[6]

For each patient, anthropometrical and biochemical data on admission and at discharge were compared, and an evaluation was made of protocol application (based on intention to measure all parameters and apply the feeding formulas indicated over the established period, without adding unscheduled treatment), and of patient improvement Serum albumin levels were determined by enzymatic colorimetric assay (Technicon Instrument A-15 Bio System). Hemoglobin was determined by using an automatic hematology method (hematology analyser Mikon Kodhen 64J).[12]

In order to establish the variable "improvement", the following parameters were included: the gain of weight 10 g/kg/day observed in the last week of hospitalization and serum albumin > 2.8 mg/dl and better tolerance to the feeding. These criteria were selected in agreement with the protocol of the WHO, and have been used in other similar studies.[6,9]

For statistical analysis, the software package XLSTAT 7.5.2 was used. A two-sample t-test was used to compare results for serum hemoglobin and albumin levels on admission and at discharge. A bivariate Chi-square analysis was used to test the dependence of the dichotomous variables "Improvement" (YES/NO)" and "Protocol application" (YES/NO).

Results

Of the 30 children whose records were studied, none were diagnosed with chronic diseases associated with nutritional deficiency, was diagnosed. 13 (43.3%) were girls and 17 (56.6%) were boys; 90% of the children were between 3 months and 3 years old. The mean of age was 24 months; 90% of the children were between 3 months and 3 years of age, although two cases of 9 and 14 years old appeared (Group WHO-HILA protocol: 13,7 ± 9,21 months vs non-applied protocol group: 31,8 ± 46,81 months).

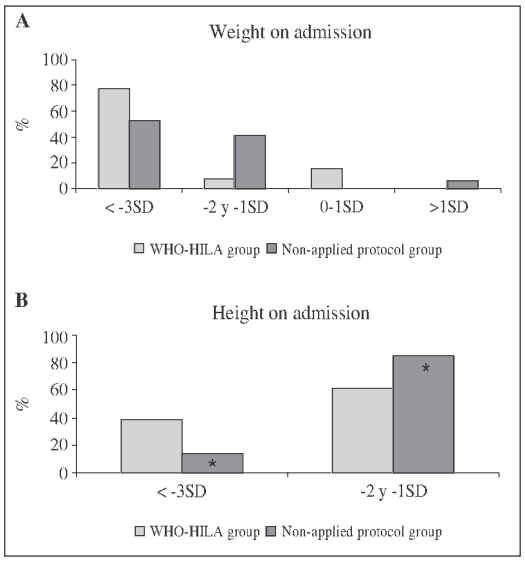

*Fig. 1.—Percentages of children distributed by z-scores for weight and height, in groups of study. Applied protocol WHO-HILA group: N = 13; non-applied protocol WHO-HILA group: N = 17. *: N = 7.*

On admission, 63.3% of the children presented a weight for the age minor than -3DS, 26.6% between -2DS and -1DS, 6.6% between 0DS and 1DS, and 3.3% major to 1DS (associate with edema). For height, only 20 data of children were collected where 43% displayed a smaller height to -3DS and 31% between -2DS and -1DS; 26% had a normal height for age. Figure 2 shows the percentages of z-score for weight and height for the two groups, one of which WHO-HILA protocol was applied, and the other in which there was no application of the protocol.

Socioeconomic status was classed as extremely low in 52.17% of cases, very low in 43.48% and low in the remaining 4.35%.

Diagnosis was marasmic malnutrition in 7 patients (23.3%), kwashiorkor-type in 22 (73.3%) and marasmic kwashiorkor in 1 (3.3%). Ten patients (33.3%) presented associated bronchopneumonia or pneumonia, and 20 (66.6%) had acute diarrhea. The major clinical findings were edema in 70% of cases, emaciation in 40% and the "flag" sign in 42.9% of children.

The average time of hospital stay only could be calculated in the group in which the protocol was applied, because there were no sufficient data in the group that did not receive the protocol. The results were 15 days for the children who did not display alterations of the gastrointestinal function, and 22 days for the children that displayed diarrhoea and bad absorption.

Mean serum albumin levels on admission were below the normal minimum reference value of 3.5

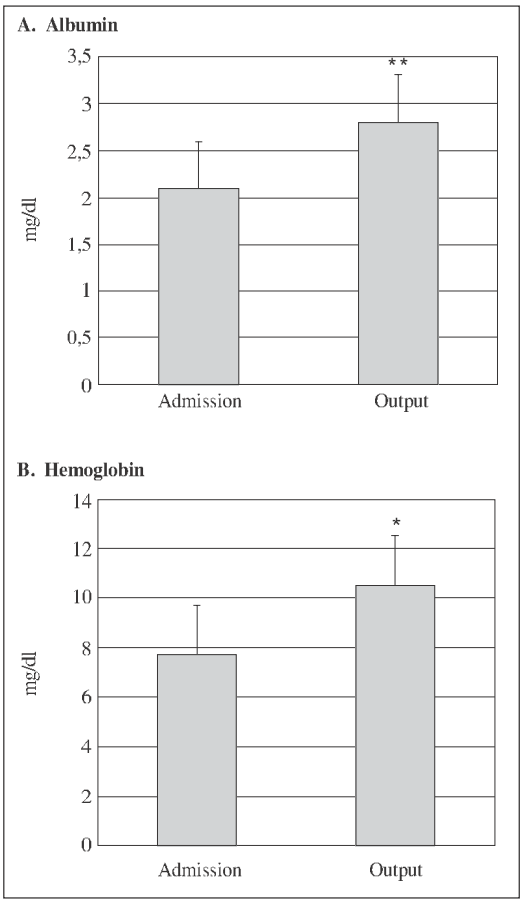

*Fig. 3.—Plasma albumin (n = 11) and hemoglobin (n = 17) values on admission compared to discharge values in children hospitalized for marasmic-kwashiorkor malnutrition, following the protocol. *p < 0.05; **p < 0.005.*

mg/dl (fig. 3A). A total of 93% of patients had moderate or severe hypoalbuminemia. The mean baseline total protein value was 4.9 ± 0.13 mg/dl, compared to a normal minimum reference value of 6.0 mg/dl. Severe anemia was found in 24 (80%) of patients, compared to a normal minimum reference value of 11.0 mg/dl (fig. 3B).

Within the 30 selected patients, 13 (43.3%) were treated in accordance with the WHO-HILA protocol and 17 did not.

Three children died (10%): 1 in the protocol-treated group (7.6%), on day 5 of hospitalization as a direct result of bronchoaspiration, and 2 in the non-protocol group (11.7%) due to sepsis.

Comparison of serum albumin and hemoglobin levels on admission and at discharge revealed significant differences for both parameters (fig. 3).

A statistically-significant correlation was noted between the variables "Improvement" and "Protocol application" (table II).

Table II
Protocol application vs patient improvement

Protocol applied	*Improvement*				*Total*
	No		*Yes*		
	n	*%*	*n*	*%*	
No	17	100	0	0	17
Yes	1	7.6	12	92.3	13
Total	n = 18		n = 12		30

Chi-square test for dependency of variables "Protocol application" vs "improvement": $p < 0.05$.

Discussion

The results obtained in the present study indicate that the use of the WHO-HILA modified protocol for the evaluation and treatment of malnutrition in childhood, was associated with clinical improvement in children with MS–KWK who showed an increase in serum albumin and hemoglobin levels at discharge.

The HILA hospital is located in south-western Colombia, an area in which —according to the ENSIN survey— 20% of children suffer chronic malnutrition and one fifth of them display retarded growth.[1] Most of the children were from "extremely poor" or "very poor" households, a finding also reported in other populations.[13,14]

Although WHO guidelines are widely recommended for the treatment of MS-KWK malnutrition[15,16] those recommendations were not systematically implemented in HILA, due to lack of knowledge or simply non-compliance. Only 43% of children received full protocol treatment. In the limitations of the study, we were not been able to evaluate the time of the stay in the hospital. This factor has not been described as a variable in the study, although it was included in the statistic analysis without presenting significant differences between both groups; this is because this time was influenced by other factors, and not only by the improvement. Among them of these factors, we emphasize that almost all the children presented infection or diarrhoea associated to syndrome of bad absorption, the duration of the administered antibiotherapy was different, and also the prolongation of the hospitalization by social problems as mistreat and/or economic incapacity of the family to continue the treatment at home.

Another major limitation of this study was that detailed evaluation was hindered by lack of patient-reported data on feeding/breastfeeding regimens, and lack of clinical data on malnutrition-related risk factors (e.g. height and head perimeter). Moreover, children were often discharged due to clinical improvement, and were not kept in hospital for the two weeks recommended by the protocol, and full biochemical tests were not always performed.

As in other countries, kwashiorkor was found to be more common than marasmus among children with chronic malnutrition.[15,17] Children were often referred not for malnutrition but for associated conditions, including respiratory infections, hemodynamic instability, persistent diarrhea or even malabsorption syndrome. Sepsis was the main cause of death amongst these patients.[18,19]

The effects of severe malnutrition are usually multisystemic. Initial loss of muscle mass is followed in the most severe cases by marked depletion of subcutaneous fat.[20] Edema is a characteristic sign of declining serum albumin levels, and is associated with greater morbimortality.[21] Skin diseases develop due to chronic vitamin and micronutrient deficiencies.[20,22] Children in this study displayed edema, severe muscular emaciation and depigmented hair ("flag" sign), all of which are clinical signs of severe malnutrition. In the present study, the depletion of subcutaneous fat stores was reversed, and tissue/mucosa lesions improved, in the second week of treatment using nutritional recovery formulas.

Low albumin levels and deficiency anemias were common on admission —as in most reported patients—[23] but a notable recovery was recorded by the end of protocol-based treatment. Most children displayed moderate or severe hypoalbuminemia and severe primary iron-deficiency or vitamin A-deficiency; these constitute a major public health problem in Colombia[1]. Increased albumin and hemoglobin levels by discharge (fig. 1) suggested a satisfactory response among children treated in accordance with the WHO-HILA protocol. In the six non-protocol children displaying increased hemoglobin levels, the increase was attributed to transfusions on admission. There is no consensus in the literature on the advisability of transfusions and serum albumin replacement therapy.[6,8] A study carried out in Ethiopia suggested that these procedures should be limited to cases of severe anemia (hemoglobin 4 mg/dl and hematocrit 12%) and critical albumin deficiency (no specific values adduced).[24] Indeed, Bachou et al. (2008),[25] reporting on the application the WHO guidelines in malnourished children in Africa, recorded greater mortality among those receiving blood transfusions or intravenous fluids on admission (73% of total deaths), concluding that application of the WHO protocol could reduce the need for transfusions, and lower the mortality rate.

In the present study, the overall mortality rate was 10%, a percentage similar to that reported elsewhere in Colombia and Latin America.[14,26] None of the children in the non-protocol group displayed any improvement, whilst 92.3% of children in the protocol-treated group showed some improvement (table II). Among the factors associated with mortality in these patients are the difficulty in ensuring strict isolation, and the exposure of patients to nosocomial infections. Moreover, given the patients' poor clinical condition, symptoms of infection —such as fever— may not always appear, so that appropriate antibiotic therapy may not be implemented.[19] Given the persistently high incidence of disease and death among children with MS-KWK malnutrition, these patients require exhaustive evaluation and constant monitoring. In conclusion, using the WHO-HILA protocol was associated with an improvement in nutritional and overall health status of severely malnourished children. Implementation of the protocol should therefore be considered in all children's hospitals in developing countries where this pathology is prevalent. In general, prospective studies should be carried out in patients with protein-energy malnutrition, in order to monitor the systematic application of the WHO guidelines and ensure their beneficial effects on child health.

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