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ORIGINAL ARTICLE

Study pattern of nutritional recovery in edematous and non-edematous malnourished children after a short hospital stay of nutrition rehabilitation

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ABSTRACT

Background: Severe acute malnutrition (SAM) is a state of deficiency that manifests itself in two forms: edematous and non-edematous. There have been significant advances in the clinical management of this disease state, but to date, data on nutritional recovery outcomes are scarce. **Aims:** We aimed to compare nutritional recovery in edematous and non-edematous malnourished children. **Subjects and Methods:** This is a prospective observational study of 98 children (3 – 60 months) with SAM (25 edematous and 73 non-edematous) receiving nutritional rehabilitation, according to the WHO guidelines, during a short hospitalization (SH) of 21 days. **Results:** Complete biochemical and nutritional recovery was completed in both edematous and non-edematous groups as indicated by normalized serum levels of retinol-binding protein, transthyretin, albumin, transferrin, fibronectin and hemoglobin, as well as C-reactive protein and acid alpha glycoprotein. Biochemical and nutritional recovery was faster in edematous children compared to non-edematous, as indicated by the significant difference ($p < 0.001$) in the rate of recovery of albumin, transthyretin, and retinol-binding protein. At discharge, despite full biochemical nutritional recovery there remains a severe stunting in both groups with the persistence of moderate wasting in the non-edematous group. **Conclusions**: Complete biochemical and nutritional recovery can be achieved after short hospitalization for nutritional rehabilitation and an early discharge of children cured is possible for edematous children but not convincing in non-edematous ones, as they remained moderately malnourished.

Key words: nutritional rehabilitation, short hospitalization, recovery, edematous, non-edematous.

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1 Introduction

Severe acute malnutrition [SAM] remains a major health concern [1]. SAM classically presents as one of two phenotypically distinct forms: edematous SAM (ESAM) and non-edematous SAM (NESAM) or marasmus [2]. In Morocco, malnutrition is qualified as a public health problem at the community level [3,4] as well as at the hospital level [5]. Considerable progress has been made in the prevention and treatment of SAM over the past 50 years. But the reviews demonstrate that the mortality rate in hospitals is approximately 20 to 30 percent in non-edematous cases and up to 60 percent in edematous ones during the past 40 years[6-8]. These unacceptably high mortality rates have prompted the World Health Organization [WHO] to recommend the use of guidelines for the treatment of SAM[9,10]. The goal of the WHO guideline [9,10] is to achieve better nutritional recovery by promoting the best possible treatment and shortening hospitalization in both edematous and non-edematous forms of SAM. The literature review showed that there is heterogeneity in the time of recovery from SAM, it varied from 11 days [11] to 59 days [12]. The average length of stay in therapeutic centers recommended by the WHO [2] to treat SAM is 30 days, but in developing countries, most malnourished patients come from poor family backgrounds and are highly sought after. Besides, SAM is widespread in underdeveloped countries, [1] which have limited resources to deal with this public health problem. Therefore, the use of a short inpatient nutrition rehabilitation stay is advantageous because more children can be treated in a given time period at less cost [13]. As well, to have an impact at the population level, management protocols must take into consideration the realities of socioeconomic conditions, balancing the potentially conflicting demands and ethics of clinical medicine with those of public health. It is therefore essential to proactively treat complicated SAM with very intensive medical and nutritional treatments aimed at rehabilitating the child during a short hospitalization [14]. In this context, we aimed to study the pattern of nutritional recovery in children with edematous and non-edematous malnutrition after a short 21-day hospitalization for nutritional rehabilitation.

2 Subjects and Methods

2.1 Patients

According to the recommendations of the Ministry of Health, children diagnosed with moderate or severe malnutrition should be hospitalized to treat their nutritional disorders. However, in our study, every child diagnosed as severely malnourished was agreed to be hospitalized as part of standard health care. Children were enrolled in the study if they were aged 3 to 60 months and admitted as inpatients because of SAM. Children were not included in the study if their birth weight was less than 2500 g, if they had received a blood transfusion (hemoglobin concentration less than 40 g/L), if they had been referred to other departments, or if their parents had refused to participate. In addition, in our study, the children's mothers were asked to stay with their children by providing breastfeeding and frequent feeding, especially at night. All the mothers participated in the preparation of meals for their children with the help of the dietician as part of improving their nutritional knowledge. The children's mothers received nutritional education to prepare for the integration of their family environment with the aim of preventing relapses and ensuring the continuation of the child's development after discharge.

2.2 Sample size and data analysis

In order to determine the number of participants needed, we calculated the required sample size in advance using the statistical program G*Power software 3.1.9.7. In the present study, we planned to examine the difference in mean (independent means) between two groups using Student's *t*-test. However, we entered the required variables into the G*Power software to estimate the sample size. These variables were defined as follows: the effect size (d) was set to 0.8, alpha error probability to 0.05, power (1- β error probability) to 0.95, and the allocation ratio of N1/N2=0.45. After computation, the first group consisted of 57 children, which we increased to 73 children (non-edematous group) and the second group was composed of 25 children (edematous group). Thus, a total of 98 participants was obtained.

2.3 Study design and nutritional rehabilitation

This is an observational prospective study conducted in the pediatric unit, Ibn Khatib Hospital, Fes, Morocco. The study was designed to compare the pattern of nutritional recovery in edematous and non-edematous children after a short hospital stay (SHS) of 21 days for nutritional rehabilitation. The children hospitalized with SAM were followed-up by the head physicians of the pediatric department, the pediatricians, the dietician, as well as the nurses involved in child health care at the pediatric ward, Ibn Khatib, Fes, following the treatment recommended by the World Health Organization [9,10]. Data on children, mothers, and families were collected in a questionnaire during admission interviews. The ninety-eight children enrolled in the study were divided into two groups based on Wellcome's (1970) classification [15]: non-edematous (73 children) and edematous (25 children). During the follow-up period of nutritional rehabilitation, the healthcare team examined the children and monitored their nutritional and health status, with a progressive approach according to the standard WHO protocol [9,10], which divides their treatment into seven stages through two phases: stabilization and rehabilitation.

Upon admission, the diagnosis was performed by pediatricians with the purpose to detect conditions that might put in danger the vital prognosis of the child. Nutrition rehabilitation started within the first 24 hours after admission. During the initial phase (3 to 9 days) the children were placed under medical and nutritional treatment. Pediatricians treated and prevented hypoglycemia, hypothermia, and electrolyte imbalance. Children with acute diarrhea (more than three liquid stools/day) were maintained on saline oral hydration solution for severely malnourished children (ReSoMal). Broad-spectrum antibiotic treatment (Gentamicin 7.5 mg/kg, Ampicillin 50 mg/kg oral, and Amoxycillin 15 mg/kg) was directly initiated on admission. From baseline to discharge, all children received oral micronutrient supplements (vitamins and minerals) that meet WHO specifications for the treatment of children with SAM. Dietary treatment was based on the use of a commercial infant formula-fed (Guigoz 2), containing 498 kcal/100g of energy, 9.9 g/100g of protein, and 23.5 g/100g of fat. The initial feeding phase started with an energy of 75 Kcal per kg per day and 1.2 g protein per kg per day without stopping breastfeeding. Nasogastric tube feeding was used when children did not want to eat or did not have enough appetite or if the child was seriously ill.

The nutritional rehabilitation phase was initiated in malnourished non-edematous children when weight gain was perceived, the infection attenuated and appetite regained. For edematous malnutrition, this nutritional phase was defined clinically by a return of appetite with a substantial loss of edema. The weight loss was accepted as a sign of a positive response to treatment for edematous malnutrition. The frequency and quantity of milk were calculated based on the weight of the child as recommended by the WHO guidelines[9]. Iron supplementation was started when the infection was subsided. In addition, to achieve a consistent intake and rapid weight gain, a highly-sustained diet was maintained during the nutritional rehabilitation phase. During this period, the children were fed a high energy density formula that provided 100-135 kcal per kg per day.

2.4 Blood sample

Blood samples were considered part of standard health care. Two blood samples (5 mL) were collected from the radial artery. The first was collected on admission to hospital, within the first 24 hours of hospitalization and before the start of nutritional rehabilitation. While, the second was collected at discharge, after 21 days. The collected blood was centrifuged at 1500 rpm for 15 minutes to separate the sera. The 360 µL quantity of sera was placed in an Eppendorf tube and stored at -20 °C until subsequent nutritional protein analysis. ~~The~~ Hemoglobin concentration was measured by the cyan-methemoglobin method [16] at the biology laboratory of Ibn Khatib Hospital. The determination of the concentrations of acute-phase protein (Acid alpha glycoprotein (AAG) and C-reactivate protein (CRP)) was carried out by immunoturbidimetry methods (Hitachi 911, France). The concentration of retinol-binding protein (RBP), transthyretin (TTR), albumin (ALB), transferrin (TRF)) and fibronectin (FN)) were determined by immunoprecipitation in liquid medium using enzyme immunoassay kit on a Dade Behring Bn-100 System Nephelometer. Inflammatory and nutritional proteins were analyzed at the biochemical laboratory, biology department, Faculty of Sciences Dhar Elmahraz Fez.

2.5 Anthropometric measurements and Nutritional status assessment

Anthropometric measurements were performed according to the standard technique of the World Health Organization (1976) [17]. At follow-up, children were weighed with minimal clothing in the morning on a scale (RGZ-20), which is accurate to 10 grams. The scale was calibrated every morning before being utilized. Height was measured at admission and discharge by an interchangeable stadiometer (Holtain, Crymych, UK) for standing and recumbent length measurements with the assistance of the dietician. For children < 2 years of age, recumbent length was measured. Mid-upper-arm circumference (MUAC) was measured with a plastic flexible tape at hospital admission and discharge (21 days), and the readings were recorded at 0.1 cm near. Age was obtained from interviews with mothers. The collected anthropometric measures were converted into weight-for-height z-score (WFH-Z), weight-for-age z-score (WFA-Z), height-for-age z-score (HFA-Z), mid-upper-arm circumference-for-age Z-score (MUAC-Z), and head circumference-for-age Z-score (HC-Z) indices by age and sex using WHO Anthro V3.2.2 for PC [18]. We assessed the nutritional status of the children referring to the WHO criteria for SAM [10] as follows: MUAC less than 11.5cm and/or a WFH-Z less than -3SD or the presence of bipedal pitting edema [10]. Additionally, children were classified as severely stunted if (HFA-Z<-3SD) and severely underweight if (WFA-Z< -3SD) according to the 2017 WHO classification [19].

2.6 Nutritional recovery assessment and statistical analysis

The biochemical assessment concerned serum levels of RBP, TTR, ALB, and TRF which have been clinically recognized as the most sensitive proteins used in the assessment of overall nutritional status [20, 21]. However, the nutritional and biochemical recovery scheme was assessed in both the edematous and non-edematous groups by calculating the rates of change in serum levels of main nutritional biomarkers (RBP, TTR, ALB, and TRF) between admission and discharge (21-day). Rates of change of major serum nutritional proteins from admission to discharge were calculated as follows:

$$Rate\ (\%) = \frac{(\text{discharge concentration} - \text{admission concentration})}{\text{discharge concentration}} x100$$

The normality of the data distribution was analyzed by the Kolmogorov-Smirnov test. Rate change data of RBP, TTR, ALB, and TRF, which were not normally distributed, were expressed as the median with a 95% confidence interval (Table 3). However, differences in the rate change of nutritional protein were analyzed by the non-parametric Mann-Whitney U-test, due to their skewed distribution (Rate of nutritional recovery data on table 3). Differences were analyzed with Student's *t*-test for the normally distributed variables (mean of anthropometric measurements and Z-score indices shown in Tables 1 and 4 and mean of biochemical markers in Table 2). The Chi-Square test was used to compare the categorical variable between the two groups (Difference between age groups and between sex groups in Table 1). The difference was significant when the p-value was < 0.05. All data was analyzed by MedCal (version 9.3.0.0).

2.7 Regulatory and ethical aspects

Following the national recommendations of the Ministry of Health, any child who visits a health facility or a hospital is assigned to the assessment of his nutritional status. And any child considered undernourished must be hospitalized to treat their nutritional issue.

This study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics and Research Committee of the Regional Directorate of the Ministry of Health. The administration of the Ibn Khatib hospital gave its approval to carry out this study. Parents of children who agreed to have their children participate in the study were informed of the purpose and nature of the study. After giving their oral consent for their child's participation, parents were asked to sign a written consent. Mothers were asked to stay with their children during the short hospital stay for nutritional rehabilitation in order to take care of their children and to continue breastfeeding especially at night. If the mothers refused their children's participation in the study, their children had to be hospitalized and receive medical treatment with nutritional rehabilitation as part of the standard treatment.

3 Results

A total of 25 (25.51 %) edematous children and 73 (74.75 %) non-edematous children participated in the survey. The median age in the edematous [15.00 (10.17 to 22.45)] was significantly higher (p = 0.004) than in the non-edematous group [7.00 (6.00 to 10.21) at 95 %] with a male predominance in both groups (Table 1). The age distribution shows the predominant proportion of children aged [12 to 60] months in the edematous group and [6 to 12] months in the non-edematous group. A comparison of all anthropometric measurements between the edematous and non-edematous groups revealed a significant difference, except for weight.

Table 1. Characteristics and anthropometric parameters upon hospital admission in edematous and non-edematous malnourished children

Characteristics	Non-edematous	Edematous	p-value
- Female n (%)	25 (34.24)	10 (40.00)	0.781
- Male n (%)	48 (65.75)	15 (60.00)	0.782
- Median age (Months) *	7.00 (6.00 - 10.21)	15.00 (10.17 - 22.45)	0.004
Age group n (%)			
- [3-6[	18 (24.65)	2 (8.00)	0.134
- [6-12]	34 (46.57)	6 (24.00)	0.080
-]12-60]	21 (28.76)	17 (68.00)	0.001
Anthropometric parameters (Mean ± SD)			
- BW (Kg)	5.11 ± 2.19	6.02 ± 2.75	0.096
- Height (cm)	63.47 ± 11.61	69.68 ± 10.07	0.019
- MUAC (cm)	9.22 ± 1.62	10.54 ± 1.84	0.001
- HC (cm)	41.54 ± 4.64	44.63 ± 4.19	0.004

* CI: Confidence Interval at 95%; Age is expressed in months; BW: body weight; HC: Head circumference; MUAC: Mid-upper-arm circumference. Chi-Square test was used to compare the difference between age groups

Table 2 shows the results of nutritional recovery at hospital admission and discharge in edematous and non-edematous children. In both groups, all nutritional proteins and hemoglobin were under the normal range and showed a significant increase to reach their baseline range in the non-edematous and edematous groups except for FN. In contrast, at admission, serum CRP and AAG levels were above normal in both groups and decreased significantly to normal levels at discharge. At discharge, the edematous group showed significantly higher levels of RBP, ALB, TRF and Hg levels than the non-edematous children.

As we observed, the rate of recovery of RBP, TTR, and ALB was positive and significantly higher in the edematous than the non-edematous group (p < 0.001), except for TRF which showed an insignificant improvement (p = 0.324).

Table 2. Comparison of nutritional recovery outcome between children with edematous and non-edematous malnutrition after a 21-day of short hospital stay for nutrition rehabilitation

Serum concentration (Reference range)	Studied group	Admission	At discharge	P1 (T-test value)	P2 (T-test value)	P3 (T-test value)	P 4 (T-test value)
Retinol binding protein (0.033 – 0.07 g/L)	None Edem	0.027 ± 0.007 0.019 ± 0.005	0.036 ± 0.007 0.042 ± 0.004	<0.0001 (7.76)	<0.0001 (30.69)	<0.0001 (-7.94)	0.0005 (6.35)
Transthyretin (0.15 – 0.30 g/ L)	None Edem	0.13 ± 0.034 0.09 ± 0.018	0.25 ± 0.10 0.281 ± 0.067	<0.0001 (-9.82)	<0.0001 (23.52)	< 0.0001 (6.27)	0.963 (1.44)
Albumin (> 35g/ L)	None Edem	34.22 ± 9.18 19.10 ± 5.33	36.03 ± 5.11 40.12 ± 4.32	0.14 (1.472)	<0.0001 (26.17)	< 0.0001 (-7.78)	0.0005 (3.58)
Transferrin (2 - 4g/ L)	None Edem	1.73 ± 0.45 1.19 ± 0.62	2.28 ± 0.44 2.89 ± 0.51	<0.0001 (7.46)	<0.0001 (18.09)	0.0003 (-4.68)	<0.0001 (5.74)
Fibronectin (0.030 - 0.195g/ L)	None Edem	0.184 ± 0.09 0.159 ± 0.061	0.201 ± 0.194 0.189 ± 0.102	0.498 (0.67)	0.213 (1.157)	0.20 (-1.28)	0.768 (-0.29)
Hemoglobin (>120 g/d L)	None Edem	8,79 ± 2,54 9,78 ± 1,66	11,22 ± 1.42 12.15 ± 1.94	<0.0001 (7.15)	<0.0001 (7.93)	0.072 (1.81)	0.012 (2.56)
C-reactive protein (<10 mg/ L)	None Edem	55.23 ± 34.04 40.13 ± 38.67	3.28 ± 1.6 4.13 ± 1.34	<0.0001 (-13.02)	<0.0001 (-7.94)	0.067 (-1.84)	0.019 (2.34)
Acid alpha-1 glycoprotein (0.55 – 1.40 g/ L)	None Edem	2.78 ± 1.03 2.99 ± 0.22	1.03 ± 0.89 1.55 ± 0.26	<0.0001 (-10.98)	<0.0001 (-36.12)	0.19 (1.01)	0.045 (2.87)

None: Non-edematous group; Edem: Edematous group; P1: comparison between admission and at discharge in the non-edematous group; P2: comparison between admission and at discharge in the edematous group; P3: comparison between the edematous and non-edematous group upon hospital admission; P4: comparison between the edematous and non-edematous group at discharge; Serum concentration of protein expressed as mean ± standard deviation; The Student T-test considered significant at P-value <0.05.

Table 3. Comparison of the rate of nutritional recovery between the edematous and non-edematous children after a short hospital stay for nutrition rehabilitation

Markers	Recovery rate in non-edematous group Median (%) at 95% C.I	Recovery rate in the edematous group Median (%) at 95% C.I	p-value	Mann-Whitney U-Test
Retinol binding protein	44.00 (22.12 - 65.23)	115.65 (60.44 to 162.23)	<0.0001	18.50
Transthyretin	89 (93.00 - 155.64)	154.00 (77.20 to 288.22)	0.005	99.00
Albumin	10.00 (0.74 - 20.83)	98.00 (29.23 to 145.84)	<0.0001	38.00
Transferrin	30.00 (5.79 - 47.33)	40.00 (-4.09 to 144.65)	0.324	84.50

C.I: Confidence interval at 95%; Tests of Mann-Whitney U-Test are significant at p < 0.05.

4 Discussion

After a short hospital stay for nutritional rehabilitation, we found differences in the pattern of nutritional recovery between children with edematous and non-edematous malnutrition. As shown in Table 3, the magnitude of the response to renutrition was greater in the edematous children than in the non-edematous group, as indicated by the significant increase in recovery rate of nutritional protein (RBP: 115.65 % vs. 44.00; TTR: 154.00 % vs. 89.00; ALB: 98.00 % vs. 10.30; $p < 0.001$). However, the response to the renutrition was assigned to a different degree between the two groups; the edematous children recovered faster than the non-edematous. These findings are in accordance with previous studies [22-24]. Furthermore, previous studies have reported a significant difference in recovery kinetics between edematous and non-edematous malnutrition [25, 26].

More importantly, in the present study, we revealed that at the time of admission, edematous children had significantly lower concentration levels of RBP, TTR, ALB, TRF, and Hg, than the non-edematous group, which has also been demonstrated in previous studies [27, 28]. Furthermore, a recent study has revealed serious metabolic disturbance in the edematous child than those without edema [29]. In our study, at discharge, all nutrition-related proteins increased significantly to normal in both groups (Table 4) reflecting satisfactory nutritional recovery except for Hg which remained below normal in the non-edematous group. Additionally, the present study found that after SHS for nutritional rehabilitation, both edematous and non-edematous groups had similar concentrations of RBP, TTR, and FN as reported previously [26]. The repletion of the serum pool of RBP, TTR, ALB, and TRF within the normal range was due to a rapid increase in the rate of synthesis of these proteins in response to adequate protein intake [30, 31].

Moreover, acute-phase protein (APP) study demonstrated that both edematous and non-edematous children had significantly higher serum concentrations of CRP and AAG. These results are in agreement with the study by Reid et al. [32] who showed that both edematous and non-edematous malnourished children had higher plasma concentrations of APP. On the other hand, at the time of admission, there was no significant difference in the CRP and AAG concentrations (40.13 ± 38.67 v.s 55.23 ± 34.04 mg/L for CRP and 8.79 ± 2.54 v.s 29.78 ± 1.66 g/L for AAG) between the edematous and non-edematous, respectively. This result followed that of previous research [33, 34]. However, the high CRP and AAG values at admission, in both groups, provide evidence of a response to the infectious process and indicate complicated SAM in these children. After a short hospital stay for nutritional rehabilitation, acute phase proteins decrease significantly to normal in both edematous and non-edematous patients (4.13 ± 1.34 vs. 3.28 ± 1.6 mg/L for CRP and 1.55 ± 0.26 vs. 1.03 ± 0.89 g/L for AAG, respectively). This reduction revealed an attenuation of the inflammatory state and thus testified to the successful clinical recovery. In addition, the return of the serum nutritional protein to normal in both groups provides evidence of a positive response to SHS for nutrition rehabilitation. However, overall, the nutritional recovery profile showed the expected improvement in edematous and non-edematous malnutrition children after SHS. This result is in agreement with recent studies that reported a complete nutritional recovery after a short period of renutrition ranging from 14 to 26 days [35-37].

Furthermore, based on serum protein concentration (Table 2), we conclude that these children were fully recovered and must return to their home environment after SHS. Yet, the nutritional rehabilitation of malnourished children must allow them to recover a normal nutritional state and to prevent relapses post-discharge in the medium and long term. It should be noted that the anthropometric indicators (Table 4) were still under the WHO recommended discharge criteria [10] for the non-edematous children compared to the edematous group that reached this threshold. The WHO discharge criteria recommends that after nutritional rehabilitation - performed for at least two weeks - malnourished children should reach the threshold of (WFH-Z > - 2SD) of the WHO reference population or (MUAC ≥ 12.5 cm) with the absence of nutritional edema[10]. In the present study, after the SHS, the non-edematous children still had wasting (WFH-Z = -2.02 ± 2.43) than the edematous group (WFH-Z = -1.30 ± 1.05) who met the threshold (WFH-Z > -2SD) (Table 4). This result is in agreement with the finding of Saaka et al. [24] who showed that non-edematous children stay longer before recovery than their edema counterparts. Furthermore, despite this improvement in WFH-Z, both groups showed persistence of severe stunting (-3.96 ± 2.76 and -3.45 ± 1.78 in the non-edematous and edematous group, successively) (Table 4). This reflects the insufficient anthropometric recovery after a 21-day of SHS. It is recognized that full catch-up growth is not achieved after a short-term nutritional rehabilitation at the hospital [38]. A study from Jamaica reported that full muscle recovery is slow or impossible after clinical nutritional recovery from SAM [39]. However, in the present study, the biochemical nutritional recovery precedes anthropometric recovery in non-edematous malnutrition children. This result is in agreement with the previous study[37] which emphasizes that the weight/height relationship as a recovery indicator does not coincide with the recovery of other physiological or anthropometric parameters. In light of this, we suggest that early discharge based on biochemical nutritional recovery is possible for both the edematous and non-edematous groups because the children were clinically cured, but not convincing for the non-edematous children because the WHO anthropometric discharge criteria (WFH-

Z > -2SD or MUAC ≥ 12.5 cm with no nutritional edema)[10] were not reached in this group.

Given our results, the difference in nutritional recovery between the edematous and non-edematous groups is indicative of intrinsic pathophysiological differences between the two groups (Table 3). We have shown that the response to renutrition differs according to the pathophysiology of SAM as well as within the same group (Table 3). This indicates variability in metabolic and adaptive capacity for each group of children depending on the clinical form of SAM.

It therefore seems to us that the therapeutic approach to the treatment of SAM, proposed by the WHO, should take into consideration the physiological differences between the edematous and non-edematous forms. However, further research is needed to understand the nutritional recovery pattern and physiological abnormalities in edematous and non-edematous malnutrition and their response to renutrition. These detailed clinical studies performed in these two forms of malnutrition with precisions on metabolic status, clinical status and response to different nutritional therapies, during the first period of nutritional rehabilitation in the hospital, will be an essential basis for offering specific management and clinical practices for each type of SAM.

Like any research study, some limitations were unavoidable. In the literature review, we encountered the heterogeneity of the protocols used to treat malnourished children. All previous studies were carried out using different types of dietary treatment (protein, energy, and micronutrients), duration of treatment, admission and discharge criteria, definitions used for SAM, and age of children studied. This heterogeneity made it difficult to compare the results of our study. In addition, the study's small sample size is an important limitation. The small sample size limits the generalization of our results and is due to the reduced prevalence of SAM in our country. However, further studies with a large sample size in other different populations are needed. Furthermore, in our study, we did not investigate relapse after discharge. Proposed WHO guidelines for the treatment of children with severe acute malnutrition recommend follow-up of children after discharge from hospital to prevent relapses.

5 Conclusions

Our study found that the pattern of nutritional recovery appeared to differ between edematous and non-edematous malnutrition. The edematous child seems to recover faster than their non-edematous counterparts. Furthermore, normalization of the serum pool of RBP, TTR, ALB, TRF, and attenuation of inflammatory status indicated by decreases in CRP and AAG, after a short-term inpatient nutritional rehabilitation program of 21 days, provides evidence of complete biochemical nutritional recovery in edematous and non-edematous malnutrition. In addition, at discharge, despite complete biochemical nutritional recovery, severe stunting persisted in both groups, with the presence of moderate wasting in the non-edematous group compared with the edematous group, which met WHO anthropometric criteria for discharge from nutritional programs.

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Conflicts of Interest: we have no conflict of conflict of interest.

References

[1] Black, R. E., Victora, C. G., Walker, S. P., Bhutta, Z. A., Christian, P., De Onis, M., Ezzati, M., Grantham-McGregor, S., Katz, J., Martorell, R., & Uauy, R. (2013). Maternal and child undernutrition and overweight in low-income and middle-income countries. *The Lancet*, *382*(9890), 427-451. https://doi.org/10.1016/s0140-6736(13)60937-x

[2] WHO Child Growth Standards and the Identification of Severe Acute Malnutrition in Infants and Children: A Joint Statement by the World Health Organization and the United Nations Children's Fund. (2009). World Health Organization. From: https://apps.who.int/iris/bitstream/handle/10665/44129/9789241598163_eng.pdf;jsessionid=A7C8E8CDD450F86ED47F4A80D42BE05F?sequence=1

[3] Barouaca, H. (2012). Malnutrition in Moroccan children. What results after 40 years of struggle? *Nutrcion Clínica Dietética Hospitalaria*, *32*: 76-81.

[4] Hassan, B., & Mohamed, R. (2012). Nutritional paradox of the Moroccan population: Coexistence of

undernutrition and obesity. *Nutrcion Clínica Dietética Hospitalaria*, *32*: 70-75.

[5] Hassan, B., Dalal Ben, L., Bachir, E. B., Nabil, T., & Adil, E. M. (2020). The role of body mass index-for-age in the assessment of acute malnutrition and obesity in moroccan hospitalized children. *Journal of Applied Pharmaceutical Science*. https://doi.org/10.7324/japs.2021.110710

[6] UNICEF., UNICEF. Nutrition Section, United Nations Children's Fund, The (UNICEF), United Nations System Standing Committee on Nutrition, World Food Programme, & World Health Organization. (2007). *Community-based management of severe acute malnutrition*. World Health Organization.

[7] Schofield, C., & Ashworth, A. (1996). Why have mortality rates for severe malnutrition remained so high?. *Bulletin of the World Health Organization*, *74*(2), 223–229.

[8] Tickell, K. D., & Denno, D. M. (2016). Inpatient management of children with severe acute malnutrition: a review of WHO guidelines. *Bulletin of the World Health Organization*, *94*(9), 642–651. https://doi.org/10.2471/BLT.15.162867

[9] Food Safety. (1999, April 18). *Management of severe malnutrition: a manual for physicians and other senior health workers*. Who.int; World Health Organization. https://www.who.int/publications/i/item/9241545119

[10] *Guideline: Updates on the management of severe acute malnutrition in infants and children*. (2013, August 9). Who.int; World Health Organization. https://www.who.int/publications/i/item/9789241506328

[11] Fikrie, A., Alemayehu, A., & Gebremedhin, S. (2019). Treatment outcomes and factors affecting time-to-recovery from severe acute malnutrition in 6-59 months old children admitted to a stabilization center in Southern Ethiopia: A retrospective cohort study. *Italian Journal of Pediatrics, 45*(1), 46. https://doi.org/10.1186/s13052-019-0642-x

[12] Moramarco, S., Amerio, G., Ciarlantini, C., Chipoma, J., Simpungwe, M., Nielsen-Saines, K., Palombi, L., & Buonomo, E. (2016). Community-based management of child malnutrition in Zambia: HIV/AIDS infection and other risk factors on child survival. *International Journal of Environmental Research and Public Health*, *13*(7), 666. https://doi.org/10.3390/ijerph13070666

[13] Ashworth, A., & Khanum, S. (1997). Cost-effective treatment for severely malnourished children: What is the best approach? *Health Policy and Planning*, *12*(2), 115–121. https://doi.org/10.1093/heapol/12.2.115

[14] Kliegman, R. M., Behrman, R. E., Jenson, H. B., & Stanton, B. (2007). *Nelson textbook of pediatrics E-book* (18th ed.). Saunders.

[15] Classification of infantile malnutrition. (1970). *Lancet*, *2*(7667), 302–303.

[16] Wintrobe, M. M. (1990). The size and hemoglobin content of the erythrocyte. Methods of determination and clinical application. 1932. *The Journal of Laboratory and Clinical Medicine*, *115*(3), 374–387.

[17] World Health Organization, Food and Agriculture Organization of the United Nations & United Nations Children's Fund (UNICEF). (1976). Methodology of nutritional surveillance: report of a Joint FAO/UNICEF/WHO Expert Committee [meeting held in Geneva from 1 to 10 October 1975]. World Health Organization. https://apps.who.int/iris/handle/10665/41207

[18] World Health Organization. (2006). WHO child growth standards: length/height-for-age, weight-for-age, weight-for-length, weight -for-height and body mass index-for-age: methods and development. World Health Organization. https://apps.who.int/iris/handle/10665/43413

[19] Guideline: Assessing and Managing Children at Primary Health-Care Facilities to Prevent Overweight and Obesity in the Context of the Double Burden of Malnutrition: Updates for the Integrated Management of Childhood Illness (IMCI). (2017). World Health Organization.

[20] Gallagher-Allred, C. R., Voss, A. C., Finn, S. C., & McCamish, M. A. (1996). Malnutrition and clinical outcomes: the case for medical nutrition therapy. *Journal of the American Dietetic Association*, *96*(4), 361–366, 369; quiz 367–368. https://doi.org/10.1016/s0002-8223(96)00099-5

[21] Qureshi, R., Rasool, M., Puvanesarajah, V., & Hassanzadeh, H. (2018). Perioperative nutritional

optimization in spine surgery. *Clinical Spine Surgery*, *31*(3), 103–107. https://doi.org/10.1097/bsd.0000000000000579

[22] Lapidus, N., Minetti, A., Djibo, A., Guerin, P. J., Hustache, S., Gaboulaud, V., & Grais, R. F. (2009). Mortality risk among children admitted in a large-scale nutritional program in Niger, 2006. *PloS One*, *4*(1), e4313. https://doi.org/10.1371/journal.pone.0004313

[23] Ahmed, A. U., Ahmed, T. U., Uddin, M. S., Chowdhury, M. H. A., Rahman, M. H., & Hossain, M. I. (2013). Outcome of standardized case management of under-5 children with severe acute malnutrition in three hospitals of Dhaka city in Bangladesh. *Bangladesh Journal of Child Health*, *37*(1), 5–13. https://doi.org/10.3329/bjch.v37i1.15345

[24] Saaka, M., Osman, S. M., Amponsem, A., Ziem, J. B., Abdul-Mumin, A., Akanbong, P., Yirkyio, E., Yakubu, E., & Ervin, S. (2015). Treatment outcome of severe acute malnutrition cases at the tamale teaching hospital. *Journal of Nutrition and Metabolism*, *2015*, 1–8. https://doi.org/10.1155/2015/641784

[25] Trehan, I., Goldbach, H. S., LaGrone, L. N., Meuli, G. J., Wang, R. J., Maleta, K. M., & Manary, M. J. (2013). Antibiotics as part of the management of severe acute malnutrition. *The New England Journal of Medicine*, *368*(5), 425–435. https://doi.org/10.1056/nejmoa1202851

[26] John, F. M., Terrence, F., Melanie, D. R., Margaret, F., & Farook, J. (1998). Repletion of the Plasma Pool of Nutrient Transport Proteins Occurs at Different Rates during the Nutritional Rehabilitation of Severely Malnourished Children. *The Journal of Nutrition, 128*(2), 214-219. https://doi.org/10.1093/jn/128.2.214

[27] Reeds, P. J., & Laditan, A. A. (1976). Serum albumin and transferrin protein-energy malnutrition. Their use in the assessment of marginal undernutrition and the prognosis of severe undernutrition. *The British Journal of Nutrition*, *36*(2), 255–263. https://doi.org/10.1079/bjn19760077

[28] Ingenbleek, Y., Van Den Schrieck, H.-G., De Nayer, P., & De Visscher, M. (1975). Albumin, transferrin and the thyroxine-binding prealbumin/retinol-binding protein (TBPA-RBP) complex in assessment of malnutrition. *Clinica Chimica Acta; International Journal of Clinical Chemistry*, *63*(1), 61–67. https://doi.org/10.1016/0009-8981(75)90379-4

[29] Kumar, D., Rao, S. K., & Singh, T. B. (2020). Clinico-biochemical profile of sick children with severe acute malnutrition. *Journal of Family Medicine and Primary Care*, *9*(5), 2269–2272. https://doi.org/10.4103/jfmpc.jfmpc_1236_19

[30] Hsu, J. W., Badaloo, A., Wilson, L., Taylor-Bryan, C., Chambers, B., Reid, M., Forrester, T., & Jahoor, F. (2014). Dietary supplementation with aromatic amino acids increases protein synthesis in children with severe acute malnutrition. *The Journal of Nutrition*, *144*(5), 660–666. https://doi.org/10.3945/jn.113.184523

[31] Le Moullac, B., Gouache, P., & Bleiberg-Daniel, F. (1992). Regulation of hepatic transthyretin messenger RNA levels during moderate protein and food restriction in rats. *The Journal of Nutrition*, *122*(4), 864–870. https://doi.org/10.1093/jn/122.4.864

[32] Reid, M., Badaloo, A., Forrester, T., Morlese, J. F., Heird, W. C., & Jahoor, F. (2002). The acute-phase protein response to infection in edematous and nonedematous protein-energy malnutrition. *The American Journal of Clinical Nutrition*, *76*(6), 1409–1415. https://doi.org/10.1093/ajcn/76.6.1409

[33] Manary, M. J., Broadhead, R. L., & Yarasheski, K. E. (1998). Whole-body protein kinetics in marasmus and kwashiorkor during acute infection. *The American Journal of Clinical Nutrition*, *67*(6), 1205–1209. https://doi.org/10.1093/ajcn/67.6.1205

[34] Velásquez, C., Navarro, C., Muñoz, C., & González, Á. (n.d.). *Inflammatory response in Colombian children with severe protein-energy malnutrition before and after nutritional intervention*. Redalyc.org. Retrieved from https://www.redalyc.org/pdf/283/28316817003.pdf

[35] Desyibelew, H. D., Fekadu, A., & Woldie, H. (2017). Recovery rate and associated factors of children age 6 to 59 months admitted with severe acute

malnutrition at inpatient unit of Bahir Dar Felege Hiwot Referral hospital therapeutic feeding unite, northwest Ethiopia. *PloS One*, *12*(2), e0171020. https://doi.org/10.1371/journal.pone.0171020

[36] Tirore, M. G., Atey, T. M., & Mezgebe, H. B. (2017). Survival status and factors associated with treatment outcome of severely malnourished children admitted to Ayder referral hospital: a cross-sectional study. *BMC Nutrition*, *3*(1), 66. https://doi.org/10.1186/s40795-017-0186-7

[37] Baraki, A. G., Akalu, T. Y., Wolde, H. F., Takele, W. W., Mamo, W. N., Derseh, B., Desyibelew, H. D., & Dadi, A. F. (2020). Time to recovery from severe acute malnutrition and its predictors: A multicentre retrospective follow-up study in Amhara region, north-west Ethiopia. *BMJ Open, 10*(2), e034583. https://doi.org/10.1136/bmjopen-2019-034583

[38] Gat-Yablonski, G., Pando, R., & Phillip, M. (2013). Nutritional catch-up growth. *World Review of Nutrition and Dietetics*, *106*, 83–89. https://doi.org/10.1159/000342607

[39] Hansen-Smith, F. M., Picou, D., & Golden, M. H. (1979). Growth of muscle fibres during recovery from severe malnutrition in Jamaican infants. British Journal of Nutrition, 41(2), 275-282. https://doi.org/10.1079/bjn19790036