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Nutritional status and metabolic profile in neurologically impaired pediatric surgical patients

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Abstract

Background: Malnutrition is reported in pediatric neuromotor disability and impacts the child's health. We described the nutritional and metabolic status in neurologically impaired (NI) children undergoing surgery.
Methods: Anthropometry, body composition, hormonal and nutritional evaluations were performed in 44 NI subjects (13.7 ± 8.0 years). Energy needs were calculated by Krick's formula. Metabolic syndrome (MS) was defined applying the following criteria (≥ 3 defined MS): fasting blood glucose >100 mg/dL and/or homeostasis model assessment for insulin resistance (HOMA-IR) >97.5th percentile, trygliceride level >95th percentile, high-density lipoprotein (HDL)-cholesterol level <5th percentile, systolic/diastolic pressure >95th percentile; while-body mass index – standard deviation score (BMI-SDS) <2 and biochemical malnutrition markers (≥ 2) defined undernutrition.
Results: Energy intake was not adequate in 73.8% of the patients; no correlation between energy intake and BMI was noted. Undernutrition was noted in 34.1% of patients and MS in 11.36% of subjects. Fifty percent of the patients presented with insulin resistance, which was not related to BMI, body composition or other MS components.
Conclusions: Nutritional and metabolic monitoring of disabled children and young adults is recommended to prevent adverse outcomes associated with malnutrition.

Keywords: children; disabilities; metabolic syndrome; nutrition; pediatric surgery.

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Introduction

Malnutrition is one of the primary contributing factors in poor health status [1–3]. Poor nutrition negatively affects growth in children as well as negatively impacts body composition, muscle strength, the metabolic/endocrine profile, cardiovascular and respiratory systems, immune function, wound healing and surgical outcomes. Malnutrition, in general, is the best-studied contributor to poor growth in children [4, 5] and its high incidence and prevalence in neurologically impaired (NI) children [6, 7] may enhance poorer health and development, leading to a perpetuating cycle of sub-optimal nutrition, disability and worsening conditions [8]. The cause of malnutrition in these patients is multifactorial, including inappropriate dietary energy intake, oral motor dysfunction, increased nutrient losses, abnormal energy expenditure (EE) and physical exertion [9].

Nutritional support is essential for the care of NI children and nutritional rehabilitation improves overall health and quality of life for both patients and their families [9, 10]. Children are especially vulnerable to inadequate nutrition support (NS) because of their smaller body size and lesser lean body and fat mass reserves [11]. Suboptimal nutrient provision contributes to nutritional status deterioration and has been shown to increase the

risk of multi-organ failure, length of hospital stays and mortality [11].

A full nutritional risk/benefit assessment should be carried out before gastrostomy tube (GT) placement. In addition, nutritional monitoring is essential to assess the adequacy of the initial nutritional prescription and to guide adjustments to the nutritional regimen [12] in order to ensure growth, counteract NI pediatric patient morbidity and mortality and minimize negative surgical outcomes in debilitated patients.

The primary aim of this study was to describe the nutritional and metabolic status in NI children followed at our pediatric surgical unit for nutritional gastrostomy/digiunostomy tube positioning and surgical procedures such as anti-reflux-surgery or management of nutritional support devices. Increased knowledge and awareness of nutritional screening among all health care professionals involved in surgical procedures is an essential objective to improve outcomes in children with severe disabilities undergoing surgery.

Subjects and methods

Subjects

Forty-four patients (25 males, 19 females, mean age 13.7 ± 8.0) with severe disabilities, scheduled for surgical gastrostomy/digiunostomy tube positioning, anti-reflux surgical treatment and/or management of nutritional support devices were included in the study. The patients were enrolled between February 01, 2016 and May 01, 2016.

Patient diagnoses included: cerebral palsy (CP) (38.6%), epileptic encephalopathy (34.1%), severe psycomotor developmental delay in dysmorphic syndromes (27.3%). All patients, living either at home or in sheltered community accommodations, presented with neuromotor damage that could alter their ability to self-feed and were bedridden.

The study was performed according to the Declaration of Helsinki and with the approval of the Institutional Review Board. After having received information about the nature of the study, the patient's parents or tutors gave written consent for their child's participation.

Methods

Anamnestic investigation, clinical evaluation, anthropometric measurements, body composition estimation, nutritional assessment, biochemical and endocrinological profile were performed in all patients.

Anamnestic investigation, clinical and anthropometric parameters: A medical history was collected including a recall of the underlying disease, gestational and birth data, chronical use of medications; furthermore, the number of physiotherapy treatment sessions was recorded.

Physical examination of the patients included anthropometric measurement of weight, height, body segments, mid upper arm circumference (MUAC), as well as pubertal stage evaluation according to Marshall and Tanner [13, 14] (prepubertal characteristics corresponding to Tanner stage 1) and blood pressure measurement.

To record the weight measurement, the child was first weighed while being held by his/her parent or legal caregiver, next the parent or legal caregiver was weighed, and subsequently, the difference between both weights was obtained. Weight measurement was made using a platform-type balance (Wunder San 200A, Bergamo, Italy).

To obtain reliable measurements of height and length, anthropometry was performed measuring body segment lengths according to Stevenson's method [15]. Total length of the tibia was obtained by measuring the straight distance from the cranial articular surface to the fibular condyle of the tibia, i.e. lateral condyle to the tip of the medial malleolus. Ulna length was measured from the tip of the olecranon process to the tip of the styloid process. Data corresponding to the average of the ulna measurements and tibia lengths were used to obtain an estimate of stature according to specific equations [15].

Body mass index (BMI) was calculated by dividing the patient's weight in kilograms by the square of the height in meters. MUAC was measured at the mid-point between the tip of the shoulder and the tip of the elbow (olecranon process and the acromium), using a standard measuring tape.

Systolic (SBP) and diastolic (DBP) blood pressure readings were taken twice using a mercury sphygmomanometer, after the participant sat comfortably for 5 min, with an appropriately sized cuff on the right arm, which was slightly flexed at heart level. The second BP measurement was used for the analysis.

Body composition: Body composition was estimated by bioelectrical impedance (BIA-101 model; Akern, Florence, Italy), using an alternating electric current at low intensity (800 μA) and fixed rate frequency at 50 kHz.

As previously described [16, 17], measurements were assessed on the non-dominant side of the body between the ipsilateral wrist and ankle bony prominences. The two electrodes were placed on the skin, previously cleaned with alcohol, 5 cm apart from each other. The two distal current-introducing electrodes were placed on the dorsal surfaces of the hand and foot proximal to the metacarpal phalangeal and metatarsal phalangeal joints, respectively. The two voltage-sensing electrodes were applied at the pisiform prominence of the wrist and between the medial and lateral malleoli of the ankle. The patient was placed in a horizontal position for 10 min, in order to allow a homogeneous distribution of body fluids, avoiding any contact that could short-circuit the electrical current pathway; the arms and the legs were abducted at a 30- to 45-degree angle from the trunk. The measurements were taken with the child as relaxed as possible, taking about 1 min in total.

Resistance, reactance and phase angle were registered. Total body water, fat-free mass and fat mass percentage, were afterward estimated using the manufacturer's BIA estimation equations [18, 19].

Nutritional assessment: Nutritional support mode access (pump versus bolus) and feeding regime were recorded. All children were on enteral nutritional support and were divided into three categories: oral nutrition, continuous enteral feeding and bolus enteral feeding.

Nutrient intake was determined with a 24-h recall questionaire administered to the child's parents by a trained dietician, as

previously described [20]. We also registered the kind and quantity of formula, number of meals (for oral nutrition and bolus enteral feeding), timing and length of each meal.

Energy intake was estimated from the 24-h recall data and then compared with the CP-specific equation by Krick et al. [21] that estimates the total EE calculating basal metabolic rate (BMR) according to Fleisch [22], modified for muscle tone, activity and normal growth.

Biochemical and endocrinological parameters: Blood indicators of malnutrition included the following blood chemistry investigations: hemoglobin, hematocrit, mean corpuscolar volume, platelet count, serum iron, ferritin, prealbumin, calcium, vitamin D, folate, vitamin B12, leptin, IGF1 and IGFBP3 blood levels. The subjects were defined as undernourished if they met BMI-SDS < 2 and at least ≥ 2 pathological values of the biochemical markers of malnutrition according to age and sex [23]. Metabolic and hormonal blood assays included fasting blood glucose (FBG), insulin, total cholesterol, high-density lipoprotein (HDL) cholesterol, triglycerides (TG), Glutamic Oxalacetic Transaminase (GOT), glutamate pyruvate transaminase (GPT), Gamma-glutamyl transpeptidase (GGT), free T4 (FT4) and thyroid stimulating hormone (TSH). Insulin resistance was calculated by homeostasis model assessment for insulin resistance (HOMA-IR) [24].

Abnormalities in lipid-fasting levels were considered for TG values exceeding the 95th percentile and HDL cholesterol values below the 5th percentile for age and sex [25]. Impaired insulin sensitivity (ISI) was defined with HOMA-IR that exceeded the 97.5th percentile for age and sex [26, 27]. Elevated SBP or DBP was defined with values exceeding the 95th percentile for age and sex [28].

Patients were considered as having the MS if they met more than three of the following criteria for age and sex: FBG > 100 mg/dL and/or HOMA-IR > 97.5th percentile, TG level > 95th percentile, HDL cholesterol level < 5th percentile, SBP and/or DBP > 95th percentile.

On the basis of gestational age and birth weight, children were defined appropriate for gestational age with a birth weight ≥ 10th percentile and small for gestational age with a birth weight < 10th percentile [29, 30].

Statistical analysis

All analyses were performed using Stata 14 (StataCorp, College Station, TX, USA). Data were described with the mean, standard deviation (SD), median and 25th–75th percentiles if continuous and as counts and percent if categorical. Non parametric correlations between continuous variables were assessed with the Spearman's R test. The association of categorical variables was assessed with the Fisher's exact test. For the purpose of this analysis, biomarkers were dichotomized at the local laboratory cut-off for normality. All tests were two-sided. A p-value < 0.05 was considered statistically significant.

Results

Clinical characteristics

In Table 1, the clinical features and anthropometric parameters of the patients are reported.

Table 1: Clinical features and anthropometric parameters of the patients.

Variable	All patients (n = 44)		Normal nutrition group (n = 29)		Undernutrition group (n = 15)		p-Value[a]
	Mean (SD)	Median (25–75th)	Mean (SD)	Median (25–75th)	Mean (SD)	Median (25–75th)	
Age at evaluation, years	13.7 (8.0)	14.5 (6.81–17.6)	12.9 (9.2)	12.2 (5.5–16.2)	15.1 (4.8)	16.8 (13.6–18.5)	0.08
Gestational age, weeks	36.4 (4.1)	37.0 (35.0–40.0)	35.4 (4.6)	36.0 (34.5–39.5)	37.8 (2.7)	39.0 (35.0–40.0)	0.15
Weight at birth, g	2606.8 (723.0)	2800.0 (1335.0–2300.0)	2403.9 (742.4)	2650.0 (1820.0–2935.0)	2927.9 (583.3)	2915.0 (2600.0–3115.0)	0.08
Height, cm	134.8 (28.2)	142.5 (113.5–145.5)	122.2 (20.4)	125.0 (13.0–140.0)	142.0 (19.5)	146.0 (125.0–15.0)	0.003
Weight, kg	26.9 (9.5)	27.5 (17.4–34.8)	26.4 (9.9)	27.1 (16.0–35.2)	28.0 (8.8)	32.0 (21.50–35.10)	0.74
BMI, kg/m^2	15.1 (5.2)	14.6 (13.7–18.1)	17.2 (3.5)	16.9 (14.9–19.4)	13.6 (2.6)	14.57 (11.2–15.6)	0.001
Tibia length, cm	28.7 (6.5)	29.5 (23.0–34.0)	27.3 (6.4)	28.5 (23.0–31.0)	31.7 (5.9)	33.5 (28.0–35.0)	0.02
Ulna length, cm	21.9 (5.3)	22.0 (19.0–26.0)	21.4 (5.6)	22.5 (16.0–26.0)	22.7 (4.6)	22.0 (20.0–26.0)	0.58
BMI-SDS, kg/m^2	− 2.2 (2.8)	− 1.8 (− 3.8 to 0.4)	− 1.0 (2.2)	− 0.5 (− 1.7 to 0.5)	− 4.6 (2.3)	− 4.1 (− 5.6 to 2.7)	< 0.001
Body surface, m^2	0.9 (0.2)	1.0 (0.7–1.2)	0.9 (0.2)	0.9 (0.7–1.2)	1.0 (0.2)	1.1 (0.8–1.2)	0.30
MUAC, cm	19.7 (4.8)	20.0 (17.0–22.0)	20.5 (4.9)	20.0 (17.0–22.0)	18.2 (4.5)	18.5 (14.5–22.0)	0.26

[a]p-Value is referred to normal nutrition group vs. undernutrition group.

The patients were divided into groups according to their nutritional status (normal nutrition or undernutrition) and data were assessed descriptively and comparatively.

Nutritional support mode access and feeding regime of the enrolled subjects were:

- continuous enteral feeding in ten subjects (23.3%) and bolus enteral feeding in 27 (62.8%), with nasogastric tube in nine patients (20.45%) and gastrostomy in 30 (68.2%);
- oral nutrition (4–6 meals/day) in five subjects (11.4%).

Anticonvulsive drugs (at least two of the following: phenobarbital, valproic acid, phentoyn, lamotrigine, topiramate, carbamazepine and clonazepam) were reported in 39/44 (88.6%) of the whole sample.

Birth weight was appropriate in 87.1% and small in 12.90% of the cases.

Pubertal stage was Tanner 1 in 15 patients (34.9%), Tanner stage 2–3 in six (13.9%. Two of these, 33%, were aged < 8 years) and Tanner stage 4–5 in 22 (51.2%).

At evaluation, BMI was < – 2 SDS in 47.7% of the subjects; in 29.5% of these, BMI was < – 3 SDS. A high correlation between BMI and MUAC was observed ($p < 0.001$, Spearman's $R = 0.66$).

One overweight child was detected but no children with obesity were detected.

Respiratory physiotherapy was recorded in 95% of the cases; the frequency of the sessions was < 2 h/week/month for all of the patients. No ongoing physical therapy was reported.

Body composition and indicators of nutritional status

Table 2 shows the body composition and indicators of the patients' nutritional status.

According to the values of energy needs estimated using Krick's formula, it emerged that the patient's daily energy intake was not adequate in 73.8% of the patients; it was lower than expected in 23.8% of the subjects and higher in 50%. No correlation between energy intake and BMI was noted as in Table 3.

We observed extremely low phase angles (3.33 ± 0.86); however, the phase angle was not significantly correlated to daily energy intake, or to the blood indicators of malnutrition such as IGF1, IGFBP3, prealbumin, or to the auxological parameters such as BMI, MUAC as can be seen from Table 3.

Table 2: Bioelectrical body composition parameters and energy indicators of the patients' nutritional status.

Variable	All patients (n = 44)		Normal nutrition group (n = 29)		Undernutrition group (n = 15)		p-Value[a]
	Mean (SD)	Median (25–75th)	Mean (SD)	Median (25–75th)	Mean (SD)	Median (25–75th)	
Daily energy intake, kcal	1224.0 (416.0)	1150.0 (950.0–1470.0)	1109.5 (380.7)	1032.0 (900.0–1378.0)	1430.8 (407.4)	1322.0 (1105.0–1900.0)	0.01
Energy requirements by Krich's formula, kcal	1116.0 (307.0)	1198.0 (819.0–1335.0)	1062.4 (312.3)	1138.0 (757.0–1333.0)	1216.1 (280.4)	1277.0 (1049.0–1389.0)	0.17
Basal metabolic rate, kcal by Fleisch equation	865.0 (215.0)	913.0 (645.0–1048.0)	2403.9 (742.4)	2650.0 (1820.0–2935.0)	2927.9 (583.3)	2915.00 (2600.0– 3115.0)	0.08
Phase angle (φ), °	3.3 (0.8)	3.3 (2.6–3.8)	3.2 (0.8)	3.0 (2.5–3.5)	3.6 (0.8)	3.7 (3.0–4.2)	0.08
Reactance (R), Ohm	50.0 (14.0)	48.0 (40.0–58.0)	46.8 (13.1)	46.5 (39.0–56.5)	55.8 (14.2)	55.5 (41.0–65.0)	0.09
Resistance (Xc), Ohm	859.0 (112.0)	877.0 (749.0–962.0)	847.3 (107.9)	834.0 (748.0–957.0)	880.4 (119.8)	919.0 (7600–994.0)	0.28
Fat mass (FM), %	21.7 (14.2)	24.3 (8.7–33.4)	8.6 (4.3)	7.8 (7.0–12.8)	3.6 (4.1)	2.6 (0.5–8.1)	0.009
Fat mass (FM), kg	6.7 (4.9)	7.5 (2.5–10.0)	21.41 (5.65)	22.50 (16.00–26.00)	22.77 (4.65)	22.00 (20.00–26.00)	0.58
Fat free mass (FFM), %	78.9 (15.5)	75.7 (66.6–91.3)	71.3 (10.5)	69.1 (64.7–11.0)	91.08 (14.6)	91.3 (79.3–98.6)	< 0.001
Free fat mass (FM), kg	22.4 (6.7)	23.7 (17.9–26.2)	20.1 (6.0)	20.5 (15.5–24.6)	25.9 (6.3)	25.4 (23.6–32.0)	0.01
Total body water (TBW), %	59.8 (13.5)	56.2 (50.6–66.6)	55.3 (10.4)	53.5 (47.4–59.0)	67.0 (15.1)	61.4 (55.3–82.3)	0.01
Observed body mass cell	7.9 (2.7)	8.4 (6.2–9.6)	6.9 (2.4)	6.5 (5.5–8.8)	9.4 (2.3)	9.4 (8.4–10.7)	0.006
Attended body mass cell	8.7 (6.6)	10.6 (4.0–13.6)	6.6 (6.12)	7.5 (0.9–12.0)	12.6 (5.8)	13.8 (7.5–16.5)	0.002

[a]p-Value is referred to normal nutrition group vs. undernutrition group.

Table 3: Relevance of correlations among body composition, nutritional and metabolic markers.

	Spearman's R	p-Value
Phase angle		
Energy intake, kcal	0.15	0.34
IGF, ng/mL	0.08	0.60
IGFB3, ng/mL	−0.09	0.60
Prealbumin, mg/dL	0.32	0.06
Leptin, pg/mL	0.03	0.84
BMI, kg/m^2	−0.04	0.79
MUAC, cm	0.03	0.80
Prealbumin, mg/dL		
Energy intake	0.37	0.019
IGF, ng/mL	0.39	0.011
IGFB3, ng/mL	0.34	0.028
MUAC, cm	0.30	0.055
Leptin, pg/mL		
IGFB3, ng/mL	0.33	0.037
MUAC, cm	0.70	<0.001
BMI, kg/m^2	0.33	<0.001
FM, %	0.62	<0.001
FFM, %	−0.63	<0.001
HOMA-IR		
BMI, kg/m^2	0.12	0.45
FM, %	0.15	0.40
FFM, %	−0.16	0.35
Total cholesterol, mg/dL	−0.19	0.23
HDL-cholesterol, mg/dL	0.33	−0.15
Tryglicerydes, mg/dL	0.21	0.17
Blood pressure, mmHg	0.11	0.50
Tryglicerides, mg/dL		
Leptin, pg/mL	0.45	0.003
FM, %	0.45	0.009
FFM, %	−0.44	0.010

Blood indicators of malnutrition

Blood level malnutrition biomarkers are reported in Table 4. Overall, undernutrition occurred in 34.1% (95% CI 20–49%) of the whole sample: 40% males (95% CI 21 to −61%) and 26.32% females (95% CI 9 to −51%). In Tables 1, 2, 4 and 6, clinical data, body composition and values of nutritional, metabolic and hormonal parameters in normal nutrition and undernutrition groups are reported.

As reported in Table 5, no association between undernutrition and gender (p = 0.5) or type of nutritional support was observed (p = 0.09).

The prevalence of each nutritional alteration is reported in Figure 1. All the patients with high levels of vitamin B12 and folate were receiving anticonvulsivant drugs; no association between B12/folate abnormalities and liver abnormalities or feeding method was noted (p = 0.8).

Table 4: Nutritional blood parameters.

Variable	All patients (n = 44)		Normal nutrition group (n = 29)		Undernutrition group (n = 15)		p-Value[a]
	Mean (SD)	Median (25–75th)	Mean (SD)	Median (25–75th)	Mean (SD)	Median (25–75th)	
Hemoglobin (range 11.7–15.5 g/dL)	13.7 (2.4)	13.80 (12.1–15.1)	14.0 (2.2)	13.9 (12.4–15.3)	13.0 (2.7)	12.6 (11.5–14)	0.17
Hematocrit (38.8–50%)	42.1 (5.5)	43.1 (37.9–45.8)	42.9 (5.2)	43.4 (39.8–46.6)	40.5 (5.8)	41.2 (37.1–43.8)	0.24
Mean corpuscolar volume (range 80–100 fL)	87.5 (9.5)	90.3 (83.7–93.5)	87.7 (8.4)	89.4 (84.2–94.9)	87.0 (11.9)	91.6 (75.4–93.3)	0.83
Platelet count (range 150–450 × 10^3/L)	257.1 (85.6)	242.0 (198.0–294.0)	259.4 (83.8)	238.0 (198.0–294.0)	252.7 (92.3)	247.0 (199.0–266.0)	0.82
Iron (range 31–144 µg/dL)	62.8 (36.4)	58.0 (38.0–78.0)	69.1 (38.2)	68.5 (44.–85.0)	51.67 (31.1)	51.0 (22.0–72.0)	0.15
Ferritin (range M 18–440; F 8–120 ng/mL)	42.7 (72.9)	24.0 (11.0–47.0)	49.9 (89.27)	28.5 (11.0–50.0)	30.2 (26.2)	21.0 (7.0–47.0)	0.39
Vit B12 (range 243–849 pgr/mL)	789.9 (217.4)	854.0 (585.0–1000.0)	813.3 (211.5)	879.0 (646.0.1000.0)	749.47 (229)	807.0 (582.0–979.0)	0.32
Folate (range 2–19 ng/mL)	17.9 (6.5)	19.3 (13.7–24.0)	19.3 (4.5)	19.6 (17.1–24.0)	16.6 (7.9)	17.9 (10.1–24)	0.55
Vit D (range 30–100 nmol/L)	30.4 (9.9)	30.5 (23.0–35.7)	30.3 (9.3)	29.8 (22.3–35.6)	30.6 (11.8)	32.45 (23.0–38.6)	0.64
Calcium (range 8.6 to −10.3 mg/dL)	9.3 (0.4)	9.3 (9.0–9.6)	9.2 (0.44)	9.2 (9.0–9.5)	9.5 (0.4)	9.4 (9.0–9.9)	0.22
Pre-albumin (range 20–20 mg/dL)	22.15 (5.2)	22.0 (19.0–25)	21.9 (4.5)	22.0 (19.0–25.0)	22.6 (6.5)	22.5 (17.0–27.0)	0.88
IGF-1 (ng/mL, range according to age and sex)	231.7 (143.8)	230.0 (110.5–312.5)	230.9 (155.3)	225.0 (111.0–316.0)	233.2 (125.0)	236 (110.0–267.0)	0.93
IGFBP3 (ng/mL, range according to age and sex)	3.6 (1.1)	3.76 (2.9–4.4)	3.6 (1.2)	3.7 (2.9–4.4)	3.7 (1.1)	3.6 (2.7–4.6)	0.90
IGF1/IGFBP3	0.02 (0.02)	0.02 (0.01–0.02)	0.02 (0.03)	0.02 (0.01–0.02)	0.01 (0.01)	0.01 (0.01–0.02)	0.18
Leptin (pg/mL, range M 2205–11149; F 3877–77273)	29164.45 (30602.8)	24113.0 (4146.5–42443.0)	38568.4 (31678.4)	28513.5 (13551.0–54266.0)	12864 (20854)	2475.8 (453.9–18113.0)	<0.001

[a]p-Value is referred to normal nutrition group vs. undernutrition group.

Table 5: Prevalence of undernutrition according to gender, weight at birth and nutritional support.

Variables	Undernutrition		p-Value
	No	Yes	
Gender			
Males	15 (60%)	10 (40%)	0.5
Females	14 (73.7%)	5 (26.3%)	
Weight at birth			
AGA	16 (59.26%)	11 (40.74%)	1.0
SGA	3 (75%)	1 (25%)	
Nutritional support			
Enteral continuous	7 (70%)	3 (30%)	0.09
Enteral bolus	20 (74.1%)	7 (25.9%)	
Oral	1 (20%)	4 (80%)	

AGA, appropriate for gestational age; SGA, small for gestational age.

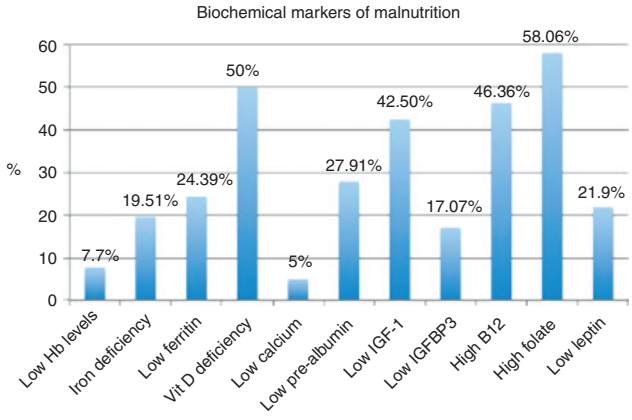

Figure 1: Prevalence of biochemical markers of malnutrition.

A significant correlation between prealbumin levels and energy intake, IGF1, IGFBP3, MUAC was reported (Table 3).

Leptin values were significantly related to IGFBP3, MUAC, BMI, FFM, FM (Table 3).

Vitamin D is far from the optimal level (30–50 nmol/L) in almost all the samples (84%): 50% of the subjects show levels of deficiency, despite the standard supplementation they received with enteral nutrition.

Metabolic and hormonal parameters

Metabolic and hormonal laboratory data are summarized in Table 6. Overall, MS occurred in 11.36% (95% CI 3–24%) of patients, in particular 8% of males (95%CI 0.926%) and 15.8% of females (95% CI 3–39%).

The prevalence of each MS component is described in Figure 2.

Table 6: Metabolic and hormonal values of the patients.

Variable	All patients (n=44)		Normal nutrition group (n=29)		Undernutrition group (n=15)		p-Value[a]
	Mean (SD)	Median (25–75th)	Mean (SD)	Median (25–75th)	Mean (SD)	Median (25–75th)	
Fasting blood glucose, mg/dL	81.2 (49.2)	71.0 (59.0–90.0)	78.4 (59.6)	66.0 (56.0–86.0)	86.3 (21.5)	89.0 (68.0–94.0)	0.03
Fasting insulin, µIU/mL	20.9 (20.1)	14.5 (5.5–28.3)	23.2 (22.7)	14.5 (7.0–31.3)	16.7 (13.9)	16.0 (4.4–19.9)	0.46
HOMA-IR	4.2 (4.7)	2.7 (0.8–5.1)	4.3 (5.0)	1.9 (0.9–6.8)	3.9 (3.9)	3.3 (0.8–4.4)	0.86
Trygliceryde, mg/dL	110.1 (73.4)	83.5 (66.0–121.2)	124.4 (79.0)	95.0 (71.0–145.0)	83.3 (54.3)	66.0 (51.0–85.0)	0.02
Total cholesterol, mg/dL	143.8 (36.8)	137.0 (115.0–168.5)	152.6 (38.5)	144.5 (120.0–174.0)	127.5 (27.6)	122.5 (106.0–138.0)	0.03
HDL-cholesterol, mg/dL	44.1 (13.7)	43.0 (37.0–48.0)	46.3 (15.7)	44.5 (37.0–53.0)	40.0 (7.8)	41.5 (37.0–44.0)	0.23
GOT (range 14–35 U/L)	26.5 (13.5)	21.0 (18.0–30.0)	27.7 (14.0)	22.0 (18.0–30.0)	25.4 (13.1)	20.0 (17.0–29.0)	0.57
GPT (range 10–35 U/L)	21.5 (20.7)	14.0 (9.0–21.0)	19.9 (17.9)	14.0 (8.0–24.0)	24.4 (25.4)	16.0 (11.0–21.0)	0.61
GGT (range 10–35 U/L)	25.8 (21.3)	15.0 (12.0–42.0)	28.5 (17.5)	29.0 (12.0–44.)	23.7 (24.7)	14.0 (12.0–21.5)	0.60
Systolic blood pressure, mmHg	104.5 (17.5)	102.5 (91.0–118.0)	104.3 (15.7)	104.0 (92.0–120.0)	105.1 (21.9)	100.0 (88.0–116.0)	0.87
Diastolic blood pressure, mmHg	66.3 (12.8)	65.0 (56.0–76.5)	66.2 (13.8)	64.0 (56.0–77.0)	66.5 (10.5)	65.0 (65.0–76.0)	0.74
FT4 (range 8–19 µIU/mL)	12.4 (2.9)	11.6 (10.5–13.5)	13.1 (3.5)	12.2 (10.8–13.5)	11.4 (1.6)	10.5 (10.5–12.6)	0.37
FT3 (range 1.8–4.2 µIU/mL)	4.4 (0.7)	4.5 (4.1–4.8)	4.5 (0.5)	4.5 (4.1–4.9)	4.1 (0.8)	4.4 (3.9–4.6)	0.20
TSH (range 0.4–4 µIU/mL)	1.9 (1.2)	1.7 (1.2–2.5)	2.1 (1.4)	1.8 (1.2–2.9)	1.6 (0.9)	1.4 (1.1–2.1)	0.33

[a]p-Value is referred to normal nutrition group vs. undernutrition group.

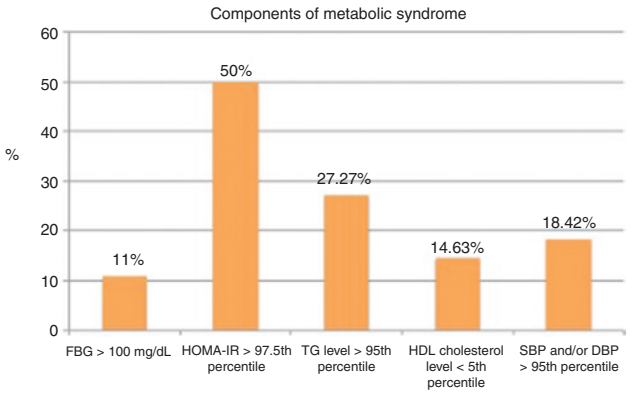

Figure 2: Prevalence of metabolic syndrome criteria.

In summary, insulin resistance was reported in 50% of the patients presented with; this pathological parameter was not related to BMI, body composition or other indicators of MS. The metabolic elements were not correlated to energy intake except for total cholesterol. A significant correlation between trygliceride values and leptin, fat mass as well as free fat mass was revealed as in Table 3.

Elevated transaminase levels were reported in 27.2% and central hypothyroidism was observed in 6.98% of the treated patients.

Discussion

This study confirmed that malnutrition is common in children and young adults with NI and showed that a high prevalence of metabolic disorders is also relevant. The role of nutrition in maintaining health and well-being is crucial and optimal nutrition is a powerful predictor of survival in at-risk disabled populations [9].

Children and young adults with disabilities are particularly vulnerable to malnutrition. Inadequate nutritional status acts synergistically with endocrine dysfunction [31–33], and a variety of other factors, such as mechanical forces and neurological differences [31, 34] affects the growth as well as the nervous system development and function [35–40], the digestive and immune system [41] and cardiovascular endurance [42, 43], all of which influence the prognosis. In addition, malnutrition decreases the energy available for discretionary activity, which in turn decreases social interaction, increases apathy, and negatively affects learning and quality of life [44].

Nutritional support is a part of an integrated treatment approach in NI subjects. Oral intake should be optimized to ensure safe enteral tube feedings in patients with oromotor dysfunction or in children and young adults unable to maintain an adequate nutritional status only by oral intake [9, 45, 46]. Nevertheless, energy needs are difficult to define in this heterogeneous population, and NI children's energy requirements (ER) are disease-specific differing according to disability severity, mobility impairment, feeding difficulties, as well as the degree of altered metabolism [46, 47]. The results of this study confirm that in children with severe intellectual impairment, the nutritional state is not primarily determined by energy intake [48]. Malnutrition also occurs in patients with an energy intake higher than expected. This lack of a direct relationship between intake and nutritional status could reflect the modulating influence of inflammation, eventhough in some cases a "non plausible" parent's reporting of energy intake should not be excluded.

Differences in EE presumably play an important role. The association between intake and physical function could be mediated by an increase of ER in these patients. Individualized nutritional care should be preferably based on EE measured by indirect calorimetry or estimated with specific target equations, in order to meet ER [47].

Repeat nutritional assessment is mandatory to adjust energy intake; and assessment of body composition changes is recommended, as it is a better indicator than weight for health status. In our population, bioelectrical parameters showed higher resistance and lower reactance values compared to normal weight young subjects [49, 50] as well as extremely lower phase angles (3.33 ± 0.86). The parameter of phase angle (PA) in BIA is derived from the measurement of reactance and resistance, and is not conditioned by body weight or fat mass. Lower PA is associated with loss of cell membrane integrity and worse prognosis [51, 52]. Severe malnutrition is common in NI children and young subjects with feeding difficulties and the PA changes as well as its modulation by IL-1β may reflect a reduction in muscle mass influenced by inflammation [53]. However, it is difficult to draw conclusions about the change in body composition over time from a cross-sectional study because of confounding and selection factors and lead-time bias.

As far as nutritional biomarkers are concerned, vitamin D deserves meticulous attention. It is mainly needed for bone growth and bone remodeling [54, 55] but has other roles in the body, including modulation of cell growth, neuromuscular and immune function, and reduction of inflammation [54, 56, 57]. Serum concentration of 25(OH)D is the best indicator of vitamin D status. In this sample, 50% of the subjects had values below 30 nmol/L that constitute a deficiency leading to rickets in children and osteopenia. Since the NI young patients are unlikely

to obtain adequate vitamin D from sunlight, intake of adequate levels of vitamin D from foods and/or supplements is a critical issue. Health care providers should also be aware of potential interaction of vitamin D supplements with several types of medications (phenobarbital, phenitoyn, etc.) and therefore adjust supplement dose to individual needs.

In the present study, low IGF1 and IGFBP3 levels were also detected. IGF-I is the primary mediator of growth hormone effects, and is thought to be the major IGF affecting growth, health and disease following fetal development [58–60]. Nutrition is one of the main regulators of circulating IGF-I [61] and our results confirmed this relationship in NI children and young patients. Leptin may very well be an integral signal which regulates neuroendocrine responses in times of food deprivation. According to the correlation between leptin and IGBP3, the role of leptin as a neuromodulator of the GRF-GH-IGF axis is supported [62–64].

To our knowledge, the metabolic risk in NI children and young adults has not been previously explored. We found a high prevalence of MS and insulin resistance (IR) in these undernourished subjects. MS is usually closely linked to an overweight status and obesity; this condition in normal weight subjects has already been described in the literature [65–71]. The effects of childhood malnutrition on metabolic adult health are poorly understood. This is the first study to report a correlation between undernutrition, IR and metabolic disorders in the NI pediatric population.

Insulin resistance in our patients was not correlated to BMI or energy intake. Negative regulation of insulin signaling could be viewed as a physiologic "adaptive mechanism for human survival" that is activated whenever the organism needs to switch from an anabolic to a catabolic or "insulin resistance" state, such as undernutrition, and to mobilize energy, primarily in the form of glucose released from the liver and free fatty acids released from adipocytes, to support vital metabolic processes [72–74].

Chronic stress also tends to alter the anabolic/catabolic hormonal balance and may be involved in metabolic disorders, hinder the development and function of skeletal muscle mass, increase cortisol levels and insulin resistance in the disabled population [75].

However, the role of restricted physical activity on insulin resistance and metabolic associated disorders should be considered [76–79]. Restricted physical activity causes a rapid loss of lean mass, which is associated with a decline in basal metabolic rate and increased whole body and regional adiposity. The accumulation of ectopic adipose tissue may interfere with insulin signaling and serve as a source of circulating triglycerides and free-fatty acids, which are risk factors for cardiovascular disease. The correlation between trygliceride values and free fat mass may support the adaptative mechanism. Besides restricted physical activity, deterioration in body composition in NI children and young adults may also be attributed to reduced human GH, and IGF-1 levels [80–88].

In NI chidren, IR is a crucial factor in increased cardiovascular risk, in addition to being a determinant factor for stress-induced hyperglycemia, which occurs during stressful situations, such as surgery. This in turn also increases the infection rates and the length of wound healing [89–91]. Pediatric surgeons should also consider anthropometric indexes associated with the clinical profile and nutritional assessment to monitor surgical outcome and avoid complications.

Eventhough children and young patients with NI present a variety of motor disorders, orthopedic problems and other associated conditions that often hinder the performance of much-needed exercise, individual training standardization is recommended, in order to meet the requirements of progressive overload, ameliorating muscle strength and counteracting metabolic issues. Finally, long-term anticonvulsant drugs may be also associated with several metabolic abnormalities [92–99] and their effects on insulin resistance should be considered.

Survival in severerly disabled patients has improved over the past half a century [100–108]. The care and management of this group with special nutritional needs is of particular importance and may improve comorbid metabolic issues. Routine monitoring and follow-up evaluation of the nutritional requirements are strongly recommended in these medically fragile children and young adults; this will improve treatment and care aiming at protecting their chances of growth and survival.

Conclusions

Malnutrition and metabolic disorders are relevant in NI target. A careful evaluation and monitoring of the nutritional and metabolic state in severely disabled children and young adults is recommended to decrease the risk of nutrition-related morbidity and mortality. An early involvement of a multidisciplinary team of pediatric surgeons, pediatricians, clinical nutritionists, nurses, dieticians, physiotherapists, psychologists, speech language specialists and social workers is essential to understanding the child's needs better, to standardize the physiotherapy program, to prevent adverse outcomes associated with feeding difficulties and improve a poor nutritional status.

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