Original article

Risk factors of malnutrition in children with severe motor and intellectual disabilities

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Abstract

Background: Children with severe motor and intellectual disabilities (SMID) are at a high risk of malnutrition and often require tube feeding to maintain their nutritional status. However, determining their energy requirements is difficult since inadequate dietary intake, severe neurological impairment, respiratory assistance, and cognitive impairment are all factors that affect malnutrition in SMID.

Aim: This study investigated the factors affecting malnutrition and identified problems affecting the nutritional status of children with SMID.

Methods: Forty-two children with SMID with oral motor dysfunction who were receiving home medical care at one of four hospitals were enrolled. Their nutritional status was assessed using a 3-day dietary record, anthropometric measurements, and laboratory tests. The clinical findings associated with malnutrition were compared, and a body mass index (BMI) z-score less than −2SD was defined as malnutrition. The relationship between BMI z-score and other potential predictors was also investigated.

Results: Thirty-three (79%) children received tube feeding, and 20 (48%) experienced malnutrition. The median age of the malnourished children was older than that of non-malnourished children. Respiratory assistance was significantly correlated with higher BMI z-score, independent of other potential confounders such as nutrition method, muscle tonus, and energy intake. Cholesterol levels were significantly higher in children receiving a standard infant formula beyond 3 years of age than in those who switched to enteral formula before 3 years of age.

Conclusions: Malnutrition in children with SMID was mainly associated with age or respiratory condition. Energy requirements should be regularly re-evaluated with considering these factors.

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Keywords: Malnutrition; Cerebral palsy; Body mass index; Associated factors; Respiratory assistance; Enteral formula; Energy requirement; Micronutrients

1. Introduction

Severe motor and intellectual disability (SMID) is a heterogeneous group of disorders that includes severe...
physical disability and profound mental retardation [1].
Most children with SMID related to the central nervous
system or neuromuscular disorders experience feeding
problems because of the progression of oral motor dys-
function, which causes impairment of mastication and
swallowing due to weakness or impairment of oral atre-
sia function, tongue motor function, or chin motor func-
tion [2]. Many of these children require tube feeding to
maintain their nutritional status. However, currently,
there is no gold standard approach for the nutritional
management of children with SMID [3], and the assess-
ment of energy requirements often varies depending on
the treating physician. The energy requirements of these
children are typically less than those of their healthy
counterparts. According to some studies, the estimated
daily energy requirement of children with SMID is
approximately 60%–70% of healthy children [4,5]. Vari-
ous other external factors are also influenced by their
energy requirements. Several studies have suggested that
various risk factors lead to malnutrition in children with
SMID; however, the results varied depending on the
study [6]. For example, inadequate dietary intake, severe
neurological impairment, and cognitive impairment
have already been reported as risk factors of malnutri-
tion. However, limited research regarding the involve-
ment of respiratory assistance as an associated factor
of malnutrition is available.

The precise amount of nutrients required for each
patient varies markedly by energy level and dietary pat-
terns, and therefore, imbalances can occur for multiple
reasons. Imbalances in the macronutrients often corre-
late with a dietary pattern that includes a lower intake
of carbohydrates and a higher intake of lipids [7,8]. Vita-
min and mineral deficiencies [9,10] are associated with
either reduced energy intake in children with SMID
[11] or lower vitamin and mineral content of the enteral
nutrients they receive. Moreover, other imbalances that
cause nutritional problems can also occur. However,
limited information is available regarding the nutritional
assessment of children with SMID receiving home medi-
cal care. The present study investigated the risk factors
of malnutrition and the problems related to nutritional
status in children with SMID receiving home medical
care.

1.1. Subjects

Children with SMID and oral motor dysfunction
receiving home medical care were enrolled between
November 2013 and January 2015 after obtaining writ-
ten informed parental consent according to the ethical
guidelines of each participating institution. All patients
were aged ≤20 years and periodically visited the Nara
Medical University Hospital, Todaiji Ryoiku Hospital
for Children, Nara Prefecture General Medical Center,
and the Kinki University Nara Hospital, all located in
Nara Prefecture, Japan. Patients receiving intravenous
nutrition were excluded from this study. Oral motor
dysfunction was defined as oral motor impairment
owing to weakness or impairment of oral atresia func-
tion, tongue motor function, and chin motor function.
This study was approved by the Medical Research
Ethics Committee at all the participating institutions.

Forty-eight children were initially enrolled. Of these,
three failed to collect food diary records from parents
and three were excluded because they took the ketogenic
diet, which was a special dietetic treatment. Thus, a total
of 42 children were eligible for inclusion in this study.
The basic characteristics of the children are shown in
Table 1. Eleven children had congenital anomalies (mal-
formation syndrome, n = 2; central nervous system
anomaly, n = 5; and chromosomal anomalies, n = 4),
17 had a history of perinatal adverse event (severe
asphyxia, n = 9; premature delivery, n = 7; and
intrauterine growth retardation, n = 1), 10 were affected
by postnatal factors (hypoxic-ischemic encephalopathy,
n = 7; epilepsy, n = 1); and the underlying cause was
unknown in four children.

2. Methods

2.1. Study design

This study was a cross-sectional study, investigated
the risk factors of malnutrition, and sought to identify
problems in the nutritional content of the diets of chil-
dren with SMID receiving home medical care.

2.2. Data collection

The attending doctors performed nutrition-related
blood examinations and detailed anthropometry,
including measurements of body weight, body height,
circumferential length of the upper arm using a measur-
ing tape, and subcutaneous fat of the triceps brachii
muscle using an adipometer. A body height was
expressed by measuring three sections (Division
method) [12]. Nutrition-related blood examinations

Table 1
Basic characteristics of children with severe motor and intellectual
disabilities.

<table>
<thead>
<tr>
<th>Basic characteristics</th>
<th>Male, n (%)</th>
<th>Underlying medical problem</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median (IQR)*</td>
<td>5.7 (3.1, 14.2)</td>
<td>Congenital anomaly, n (%)</td>
</tr>
<tr>
<td></td>
<td>23 (55)</td>
<td>Perinatal adverse event, n (%)</td>
</tr>
<tr>
<td>Unknown, n (%)</td>
<td>4 (10)</td>
<td>Postnatal factor, n (%)</td>
</tr>
</tbody>
</table>

* Interquartile range.
included lymphocyte counts and levels of serum albumin, glucose, lipid metabolism markers, rapid turnover proteins such as transthyretin, retinol-binding protein, and serum micronutrients. The parents were asked to complete a food diary (a daily dietary record) for 3 days. The following clinical information was collected from the parents by the attending doctors: i) underlying medical problems and complications; ii) method of respiratory assistance (respirator, containing noninvasive positive-pressure ventilation, or tracheostomy); iii) 3-grade evaluation of muscle tonus (weak, normal, or strong); iv) nutrition method (oral intake or partial or full tube feeding); and v) devices used for tube feeding, such as nasogastric, gastrostomy, or nasoduodenal tube.

### 2.3. Body mass index (BMI) z-score

The physical status of the children was assessed using the BMI z-score. BMI was calculated as weight (kg)/height² (m²), and the BMI z-score was calculated on the basis of BMI reference data for Japanese children [13]. A BMI z-score of less than −2SD was regarded as malnutrition in this study.

### 2.4. Potential predictors associated with BMI z-score

Total energy intake, muscle tonus, respiratory assistance, nutrition method of enteral feeding, and complications such as gastroesophageal reflux disease (GERD) and epilepsy were extracted as potential predictors that were associated with the BMI z-score. Energy intake per body weight (kcal/kg/day), the ratio of energy intake to the recommended dietary allowance for each age [14], and energy sufficiency rate were used as an index of energy intake. The ratio of total energy intake per body weight to the recommended dietary allowance per standard body weight for each age was defined as the energy sufficiency rate.

### 2.5. Other variables

Based on the collected data, the following parameters were evaluated: i) arm muscle circumference (AMC) z-score and triceps skinfold thickness (TSF); ii) mean daily macronutrient, vitamin, and mineral intake; iii) Protein:Fat:Carbohydrate (PFC) ratio; iv) the relationship between the daily macronutrient intake and their respective serum levels; and v) the relationship between fat ratio and lipid metabolism markers. AMC (cm) was calculated by arm circumference (cm) – 0.314 × TSF (mm), and the AMC z-score was calculated by converting the percentile of AMC, which was the reference data of the United States, to z-score [15]. Vitamin and mineral intake for all children were compared with an age-specific, recommended dietary allowance [14]. The PFC ratio was evaluated in 41 children based on the food diary; one infant was excluded. The relationship between fat ratio and lipid metabolism markers was sub-analyzed in 25 of the 42 children.

### 2.6. Statistical analyses

Data were analyzed using SPSS Statistics, version 26 (IBM, Tokyo, Japan). P < 0.05 was considered significant. A two-tailed Mann–Whitney U test was used for between-group comparisons of the median values for continuous variables, and multiple comparisons among the different patient groups were performed using the Kruskal–Wallis test. The Spearman correlation coefficient was used to assess the correlation between the two groups. Simple linear regression analysis was conducted to investigate the relationship between BMI z-score and the other potential predictors, and adjustments were made for some predictors, except for age and gender, via multiple regression analysis. Independent variables included i) nutrition method (oral intake only or partial and full tube feeding), ii) muscle tonus (weak, normal, or strong), iii) respiratory assistance (yes or no), iv) energy intake (continuous variable), v) GERD (yes or no), and vi) epilepsy (yes or no). Regarding energy intake, the energy sufficiency rate was selected as the independent variable of multiple regression analysis because the P-value was lowest for the three markers of energy intake. Age and gender were excluded from the model because the BMI z-score was already standardized for age and gender.

### 3. Results

#### 3.1. Comparison between malnutrition and non-malnutrition in children with SMID

The distribution of the BMI z-score in the study population is shown in Table 2. First, clinical findings of children with malnutrition and non-malnutrition were compared, and the results are summarized in Table 3. The median age in the malnutrition group was signifi-

<table>
<thead>
<tr>
<th>Table 2</th>
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<tbody>
<tr>
<td>Distribution of BMI z-scores in the study population.</td>
</tr>
<tr>
<td>BMI z-score (SD*)</td>
</tr>
<tr>
<td>&lt; −04</td>
</tr>
<tr>
<td>≤ −04, &lt; −06</td>
</tr>
<tr>
<td>≤ −06, &lt; −08</td>
</tr>
<tr>
<td>≤ −08, &lt; −010</td>
</tr>
<tr>
<td>≤ −010, &lt; −013</td>
</tr>
<tr>
<td>≤ −013, &lt; 0</td>
</tr>
<tr>
<td>≤ 0, &lt; 002</td>
</tr>
<tr>
<td>≤ 002, &lt; 004</td>
</tr>
<tr>
<td>≤ 004, &lt; 006</td>
</tr>
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<td></td>
</tr>
</tbody>
</table>


Significant older than that in the non-malnutrition group. Anthropometry analysis revealed that the BMI z-score, AMC z-score, and TSF were significantly lower in the malnutrition group than in the non-malnutrition group.

<table>
<thead>
<tr>
<th></th>
<th>Malnutrition (n = 20)</th>
<th>Non-malnutrition (n = 22)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age, median (IQR)</strong></td>
<td></td>
<td></td>
<td>0.0008</td>
</tr>
<tr>
<td></td>
<td>13.6 (5.1, 15.6)</td>
<td>3.8 (2.5, 6.4)</td>
<td></td>
</tr>
</tbody>
</table>

**Anthropometry**

- **Weight z-score, mean ± SD**
  - Malnutrition: -3.1 ± 1.1
  - Non-malnutrition: -1.7 ± 1.4
  - P = 0.0006

- **Height z-score, mean ± SD**
  - Malnutrition: -3.2 ± 3.1
  - Non-malnutrition: -3.5 ± 2.7
  - P = 0.76

- **BMI z-score, mean ± SD**
  - Malnutrition: -5.2 ± 2.7
  - Non-malnutrition: 0.5 ± 2.0
  - P < 0.0001

- **AMC z-score, mean ± SD**
  - Malnutrition: -2.7 ± 2.0
  - Non-malnutrition: 1.0 ± 1.9
  - P = 0.005

- **TSF (mm), median (IQR)**
  - Malnutrition: 6.0 (2.3, 9.0)
  - Non-malnutrition: 12.0 (9.5, 15.2)
  - P = 0.001

**Complications**

- **GERD, n (%)**
  - Malnutrition: 7 (35)
  - Non-malnutrition: 5 (23)
  - P = 0.30

- **Epilepsy, n (%)**
  - Malnutrition: 15 (75)
  - Non-malnutrition: 9 (41)
  - P = 0.05

**Nutrition intake**

- **Nutrition method**
  - Oral intake only, n (%)
    - Malnutrition: 8 (40)
    - Non-malnutrition: 1 (5)
  - Full tube feeding, n (%)
    - Malnutrition: 8 (40), GT†; 8/NT; 5
    - Non-malnutrition: 13 (59), GT; 8/NT; 5
  - Partial tube feeding, n (%)
    - Malnutrition: 4 (20), GT; 2/NT; 2
    - Non-malnutrition: 8 (36), GT; 2/NT; 6

**Dietary contents**

- **Pureed foods or chopped foods, n (%)**
  - Malnutrition: 15 (75)
  - Non-malnutrition: 11 (50)

- **Enteral formula, n (%)**
  - Malnutrition: 11 (55)
  - Non-malnutrition: 12 (55)

- **Standard/follow-up infant formula, n (%)**
  - Malnutrition: 6 (30)
  - Non-malnutrition: 11 (50)

- **Dietary intake (kcal/kg/day), mean ± SD**
  - Malnutrition: 69.5 ± 32.2
  - Non-malnutrition: 61.3 ± 27.4
  - P = 0.38

- **Dietary intake (% of RDA‡), mean ± SD**
  - Malnutrition: 55.9 ± 18.9
  - Non-malnutrition: 62.2 ± 24.0
  - P = 0.53

- **Energy sufficiency rate ** (%), mean ± SD**
  - Malnutrition: 120.4 ± 56.9
  - Non-malnutrition: 81.7 ± 33.1
  - P = 0.02

**Clinical findings**

- **Muscle tonus**
  - Strong, n (%)
    - Malnutrition: 14 (70)
    - Non-malnutrition: 7 (32)
  - Normal, n (%)
    - Malnutrition: 0 (0)
    - Non-malnutrition: 8 (36)
  - Weak, n (%)
    - Malnutrition: 6 (30)
    - Non-malnutrition: 7 (32)

- **Respiratory assistance**
  - **Respirator, n (%)**
    - Malnutrition: 2 (10)
    - Non-malnutrition: 8 (NPPV §§ 1) (36)
  - **Tracheostomy without respirator, n (%)**
    - Malnutrition: 5 (25)
    - Non-malnutrition: 7 (32)
  - **No assistance, n (%)**
    - Malnutrition: 13 (66)
    - Non-malnutrition: 7 (32)

**Laboratory findings**

- **Serum albumin (g/dL), mean ± SD**
  - Malnutrition: 4.2 ± 0.3
  - Non-malnutrition: 4.2 ± 0.5
  - P = 0.63

- **Zn (µg/dL), mean ± SD**
  - Malnutrition: 70.1 ± 9.8
  - Non-malnutrition: 78.8 ± 14.3
  - P = 0.03

P < 0.05 was significant difference (bold).

* Interquartile range.
† Body mass index.
‡ Arm muscle circumference.
§ Triceps skinfold thickness.
k Gastroesophageal reflux disease.
* Recommended dietary allowance.
** The ratio of total calorie intake to the recommended dietary allowance for each age based on body weight.
†† Gastrostomy tube.
†‡ Nasogastric tube.
§§ Noninvasive positive pressure ventilation.

Nine (21%) of the 42 children did not use a feeding tube and received only oral intake; however, eight of them were found to be malnourished. Twenty-six (62%) children received normal food as pureed foods and chopped
foods, and there was no significant difference between the two groups in dietary contents. The mean total energy intake of the study population was 59.2 ± 21.7% of the recommended dietary allowance for the corresponding age based on the Dietary Reference Intake for the Japanese Population [14], and there was no significant difference between the two groups. Additionally, 70% of the malnourished children had strong muscle tonus and 66% did not receive respiratory assistance. Moreover, eight of ten children with respiratory assistance, including noninvasive positive-pressure ventilation, were found to be non-malnourished.

The nutrition-related blood examinations were compared between the two groups. Only the serum zinc levels was significantly lower in the malnutrition group than in the non-malnutrition group (p = 0.03). Two children exhibited serum albumin levels less than 3.5 g/dL; however, no significant differences were found in the serum albumin levels between the two groups. The rapid turnover of proteins such as transthyretin and the retinol-binding proteins were analyzed, and levels below the standard values for each respective age were regarded as low [16]. Two (7%) of 27 children had low transthyretin levels, whereas retinol-binding protein levels were within the normal range in all children. It was difficult to compare the rapid turnover of proteins between the two groups because the normal range of these proteins tended to vary depending on age. Other markers such as lipid metabolism or serum micronutrient levels failed to show a significant difference between the two groups.

3.2. Determination of the associated factors involved in the BMI z-score

Based on the above results, differences in BMI z-scores using nutrition method, muscle tonus, and respiratory assistance were analyzed. Children in the oral intake group exhibited significantly lower BMI z-scores than those who were dependent on either partial or full tube feeding (Fig. 1A). There were no significant differences in BMI z-scores for the strength of the muscle tonus (Fig. 1B). The BMI z-scores of the children with respiratory assistance were significantly higher than those of children without respiratory assistance (Fig. 1C). Three of four children whose BMI z-score was more than +2SD received respiratory assistance, whereas 90% of malnourished children received no respiratory assistance. In the adjusted model, respiratory assistance was significantly associated with higher BMI z-score (regression coefficient = 3.099; 95% confidence interval = 0.499–5.699; p = 0.021) independent of other potential confounders such as nutrition method, muscle tonus, energy intake, and complications such as GERD and epilepsy (Table 4).
Table 4
Relationship between BMI z-score and potential predictors based on simple and multiple linear regression analysis.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Regression coefficient (95%CI)</th>
<th>P value</th>
<th>Adjusted β (95%CI)*</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>−0.354 (−0.519, −0.189)</td>
<td>&lt;0.0001</td>
<td>−0.158 (−0.321, 0.008)</td>
<td>0.080</td>
</tr>
<tr>
<td>Male</td>
<td>0.583 (−1.77, 2.936)</td>
<td>0.619</td>
<td>0.631 (−0.041, 0.068)</td>
<td>0.164</td>
</tr>
<tr>
<td>Tube feeding†</td>
<td>3.316 (0.636, 5.976)</td>
<td>0.016</td>
<td>1.468 (−1.276, 4.212)</td>
<td>0.285</td>
</tr>
<tr>
<td>Muscle tonus§</td>
<td>−0.705 (−2.022, 0.612)</td>
<td>0.29</td>
<td>−0.086 (−1.264, 1.092)</td>
<td>0.883</td>
</tr>
<tr>
<td>Respiratory assistance</td>
<td>4.281 (1.885, 6.676)</td>
<td>0.001</td>
<td>3.099 (0.499, 5.699)</td>
<td>0.021</td>
</tr>
<tr>
<td>Energy intake (kcal/kg/day)</td>
<td>−0.026 (−0.065, 0.013)</td>
<td>0.181</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Energy intake/RDA* (%)</td>
<td>0.013 (−0.041, 0.068)</td>
<td>0.624</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Energy sufficiency rate**</td>
<td>−0.033 (−0.054, −0.011)</td>
<td>0.004</td>
<td>−0.017 (−0.041, 0.007)</td>
<td>0.164</td>
</tr>
<tr>
<td>GERD</td>
<td>−1.239 (−3.882, 1.403)</td>
<td>0.349</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Epilepsy</td>
<td>−1.14 (−3.486, 1.206)</td>
<td>0.332</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

† Adjusted for all variables with low P-value (<0.3).
‡ Age and gender were excluded from the model, because BMI z-score was already standardized for age and gender.
§ Including partial and full tube feeding.
§ Muscle tonus was assessed using three-point scale as follows: Scale 1 = weak, 2 = normal, 3 = strong.
* Recommended dietary allowance.
** The ratio of total calorie intake to the estimated energy requirement based on age and body weight.

3.3. Assessment of vitamin and mineral intake in children with SMID

The deficiency status of vitamin and mineral intake in children with SMID was investigated. Although all children had achieved the recommended daily intake of vitamins, the daily calcium, zinc, and iodine intakes of the recommended dietary intake were not optimal, i.e., 78.2%, 78.8%, and 65.7%, respectively. Furthermore, 95.8% of the children exhibited sufficient selenium intake; however, only 64.1% of children with tube feeding exhibited sufficient selenium intake. The percentage of children exhibiting sufficient iodine intake was significantly higher in those with oral intake than in those with tube feeding (p < 0.01). The relationship between daily intake and serum micronutrient levels was also assessed. Serum selenium levels in 6 of 12 children were low and were defined as below age-specific normal levels [17]. There was no significant correlation between the daily intake and the serum levels of zinc and copper. However, the serum selenium levels exhibited a positive correlation with daily selenium intake (r = 0.667, p = 0.03).

3.4. Relationship between fat ratio and lipid metabolism markers

Evaluation of dietary content demonstrated that eight (24%) of the 33 children continued to receive standard infant formula or follow-up formula beyond the age of 3 years. It is known that standard infant formula and follow-up formula contains more lipid than enteral formula. The relationships between the fat ratio and lipid metabolism markers were examined. Proteins, fats, and carbohydrates accounted for 13.2 ± 2.9%, 30.7 ± 8.5%, and 56.1 ± 7.5% of the total dietary intake, respectively. The percentage of fat intake in the study population was greater than that of the Dietary Reference Intake for the Japanese Population. The fat ratio accounted for more than 40% of the total energy intake in 7 (17%) children, and all of them had received the standard infant formula. Furthermore, lipid metabolism markers in six children who received standard infant formula despite being aged >3 years were compared with those of 19 children who had switched entirely from standard infant formula to enteral formula by the age of 3 years. The total and low-density lipoprotein (LDL) cholesterol levels were significantly higher in children who had received standard infant formula than in those who had switched to enteral formula (p = 0.003 and 0.005, respectively; Fig. 2A, B).

4. Discussion

Reportedly, approximately 46%–90% of children with SMID experience malnutrition [18]. In the present study, approximately half of the enrolled children were malnourished, and the nutritional content of some of their diets could become problematic over time. Thus, determining the appropriate nutritional requirements for individual SMID cases can be challenging owing to the diversity of their underlying diseases, complications, and severity of symptoms. Furthermore, the energy requirements of children with SMID are generally lower than that of the neurologically healthy children, and this discrepancy depended on the degree of motor impairment [5,19]. The estimated daily energy requirement (kcal/day) of children with SMID should be calculated as follows: i) basal energy expenditure × 1.1; ii) basal energy expenditure × muscle tone × activity + growth; iii) 14.7 kcal/cm in children without motor dysfunction, 13.9 kcal/cm in children with motor dysfunction who are ambulatory, and 11.1 kcal/cm in children who are non-ambulatory [3,20].
In the present study, the mean daily energy intake of the children with SMID was 59.2% of the recommended dietary allowance for the corresponding age, with no significant differences found between malnourished and non-malnourished children. Therefore, their physical status was also influenced by total energy intake and various external factors and was an indication of the difficulty involved in estimating the energy requirements of these children. In the present study, we considered some causes that potentially influenced the physical status of children with SMID and found that respiratory assistance was the factor with the most impact on nutritional status. We found that the etiology of the malnutrition in children with SMID was multifactorial, including inadequate dietary intake, which was a consequence of oral motor dysfunction; GERD; constipation; severity of the underlying neurological disability; and antiepileptic use [6]. Almuneef et al. [21] reported that the risk factors of malnutrition were younger age (<5 years), cognitive impairment, anemia, and inadequate energy intake. Hung et al. [22] reported that undernutrition was significantly associated with girls, those who experienced more feeding problems, shorter duration per meal, and poor communication ability. Some studies reported that the risk of malnutrition was higher in children with greater severity of neurological impairment [23,24].

Gale et al. [25] studied patients with SMID with ventilation and found that the resting energy expenditure of patients with brain impairment who were dependent on chronic ventilation was 46% lower than the estimated caloric requirements of healthy children. Children with SMID often suffer from respiratory distress such as chronic lung disease, pulmonary atelectasis, and obstructive apnea. The energy requirements of children with SMID are usually lower than that of their healthy counterparts, and it is possible that the energy requirement of those with labored respiration is similar to or greater than that of neurologically healthy children. Children with SMID without respiratory assistance were found to have a higher risk of malnutrition, and physicians should be careful not to underestimate the energy requirements of these children. Moreover, children with a BMI z-score less than −2SD were significantly older than those with a BMI z-score more than −2SD. This finding strongly suggested that the current energy requirement standards should be regularly reevaluated.

Some children in this study developed abnormal lipid metabolism due to an imbalanced PFC ratio because they continued to receive standard infant formula beyond the age of 3 years. This suggested that a delay in switching from standard infant formula to enteral formula adversely affected lipid metabolism. The recommended age for switching from standard infant formula to enteral formula was beyond the age of 1 year [20]. A delay in this switch resulted in an abnormal body composition caused by excess lipid intake and insufficient protein intake; however, an earlier switching time also increased the renal solute load due to excess protein intake. Previous reports have suggested that children with SMID tend to have high lipid intake, and therefore, we should consider a diet with balanced macronutrients as well as energy intake [7,8]. The dietary composition should also be modified depending on the modality of the nutritional intake, such as oral, gastrostomy tube, or nasogastric tube feeding. In children fed using gastrostomy feeding tubes, the use of pureed food might improve nutrient balance. An earlier report also suggested that gastrostomy tube feeding might improve their growth and general health condition [26], and the switch to gastrostomy tube feeding should

![Fig. 2. Comparison of lipid metabolism markers among children aged >3 years receiving standard infant formula feed and enteral formula. Evaluation of serum total cholesterol (panel A) and low-density lipoprotein cholesterol (panel B) levels in children aged >3 years receiving standard infant formula and enteral formula. The Mann–Whitney U test was used to perform comparisons between groups. Long horizontal lines indicate median values, and short horizontal lines indicate interquartile ranges. P < 0.05, significant.](image-url)
be considered if adequate nutritional intake is difficult to achieve using nasogastric tube feeding.

Micronutrient deficiency is an important nutritional issue in children with SMID. Moreover, a few studies have reported micronutrient deficiencies such as zinc, copper, and iron in children with cerebral palsy [9,10]. Thus, for children receiving enteral formula alone, micronutrient intake is often deficient and similar to energy intake [11]. A recent report has highlighted the need to consider selenium deficiency [27]. Some enteral feeding preparations lack certain nutrients, such as iodine, selenium, and carnitine; in addition, some follow-up feeding formulas are deficient in zinc and copper. Therefore, necessary nutritional adjustments should be considered based on the characteristics of the enteral formula. Serum albumin and rapid turnover protein levels are generally used as indices of nutritional status. Serum albumin level less than 3.5 g/dL and the rapid turnover of protein levels below the standard values for each respective age are regarded as low. In the present study population, however, the levels of these proteins were not low, even in the severely thin children. Thus, a nutritional assessment based only on laboratory markers is unlikely to be accurate [28]. An appropriate nutritional assessment should include other markers such as anthropometric measurements and their change rate in addition to the nutritional index.

Some limitations of this study should be considered while interpreting the results. First, our results are based on a small population of children with SMID. Second, malnutrition status was assessed at only one point rather than in the long term because this study was a cross-sectional study. Third, we did not measure energy expenditure using the doubly labeled water method or indirect calorimetry. Fourth, there were no fixed evaluation criteria for the muscle tonus, and it depended on the subjective judgments of the individual doctors. Nevertheless, we successfully demonstrated an association between respiratory assistance and malnutrition of children with SMID receiving home medical care and the relationship between fat intake ratio and lipid metabolism markers. In conclusion, malnutrition in children with SMID was mainly associated with age or respiratory condition and appropriate energy requirements should be determined by considering these factors. In addition, nutritional intake should be periodically re-evaluated based on age, the rate of change in the BMI z-score, and nutritional status.

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Conflict of Interest Disclosures

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Author Contributions

MH: designed the research, performed the experiments, collected the data, analyzed the data, and wrote the paper; KT: designed the research, collected the data, and supervised the manuscript; YH, MK: designed the research, collected the data, analyzed the data, and wrote and edited the manuscript.

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