Factors influencing malnutrition in children waiting for liver transplants

Paola Roggero, Elena Cataliotti, Laura Ulla, Susanna Stuflesser, Gabriella Nebbia, Davide Bracaloni, Alessandro Lucianetti, and Bruno Gridelli

ABSTRACT Nutrition deficiencies are common in children with chronic liver disease. To determine whether age, hepatic dysfunction, or energy intake influences this malnutrition, we evaluated the nutritional status of 49 children aged 2.5 mo to 13 y (mean: 35 mo; median: 12 mo). The children were divided into two groups according to age: group 1—29 patients aged ≤ 1 y (mean: 7 mo; median: 7 mo); and group 2—20 patients > 1 y (mean: 75 mo; median: 59 mo). Hepatic dysfunction was defined according to the Malatack criteria. Seventy-two-hour dietary intakes were recorded by a nutritionist. Nutritional status was assessed by anthropometric measures when the patients were enrolled on the waiting list for liver transplants. We evaluated the following indexes: weight, height, fat body mass, and lean body mass on the basis of height-age (age at which height reached 50th Italian height percentile). Mean height Z scores were low in both groups, but the difference was not significant. Mean weight Z scores and mean percentages of fat body mass were significantly lower (P < 0.001) in group 1 than in group 2 patients. In group 2, lean body mass and fat body mass were significantly lower (P < 0.05) in patients with moderate-to-severe hepatic failure than in patients with mild hepatic dysfunction. The mean energy intake was in the range of the recommended daily allowances for age but was insufficient for both groups of patients. The evidence of significant acute and chronic malnutrition confirmed the need for nutritional support, especially for younger and older children with moderate-to-severe hepatic dysfunction. We emphasize the necessity of accurate assessment of nutritional status by simple anthropometric measurements to be sure of the effects and adequacy of the nutritional intervention. Am J Clin Nutr 1997;65:1852–7

KEY WORDS Anthropometry, nutrition, childhood liver disease, liver transplantation, end-stage liver disease, malnutrition, extrahepatic biliary atresia, infants, children

INTRODUCTION Poor nutritional status is especially common in children with chronic liver disease because of anorexia, fat malabsorption, abnormal nutrient metabolism, and increased energy expenditure and requirements (1–9). The nutritional status of patients with chronic liver disease is often difficult to assess accurately because some conventional indexes are frequently altered by liver failure. For instance, anthropometric measures particularly related to weight are less sensitive in defining nutritional status because of excessive tissue sequestration of water and organomegaly (1). In addition, visceral proteins and delayed cutaneous hypersensitivity reactions may overestimate the severity of nutritional depletion because of hepatic failure (10). Assessment of nutrition is important in detecting and monitoring treatment of malnutrition because poor nutritional status is associated with higher incidence of infection, surgical complications, and a lower survival rate after liver transplantation (11).

Anthropometric evaluation of upper limbs is simple, convenient with children, valuable, rapid, noninvasive, and an inexpensive way to assess nutritional status, and it is easy to repeat during the follow-up period (1, 2, 7). Growth follows a sigmoid curve with accelerative, decelerative, and steady accumulative phases. The severity of hepatic dysfunction can compromise growth, especially in infants who are in the accelerative phase.

The aim of this study was to evaluate by standard anthropometric indexes the nutritional status of 49 children and infants with chronic liver disease and to determine what roles age, degree of hepatic failure, and energy intake play in determining malnutrition.

PATIENTS AND METHODS

Patients Forty-nine children aged 2.5 mo to 13 y (mean: 35 mo; median: 12 mo), 28 males and 21 females, with various forms of chronic liver disease (Table 1), with onset in the first 6 mo of life were referred to the Pediatric Department and Liver Transplantation Unit of the Medical School of the University of Milan for inclusion on the liver transplant list. They were enrolled consecutively without any patient being excluded. None of the patients had been given nutritional therapy before admission to our Center, but all the children had been given fat-soluble vitamin supplements intramuscularly.

The children were divided into two groups according to age: group 1—29 patients aged ≤ 1 y (mean: 7 mo; median: 7 mo);

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TABLE 1
Demographic data for study subjects∗

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<thead>
<tr>
<th>Diagnosis</th>
<th>Hepatic failure</th>
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<tbody>
<tr>
<td></td>
<td>Mild</td>
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<tr>
<td>Group 1 (≤ 1 y of age)</td>
<td>13</td>
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<tr>
<td>EHBA (n = 10 M, 10 F)</td>
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<tr>
<td>Tyrosinemia (n = 2M, 1F)</td>
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<td>Idiopathic cirrhosis (n = 2M, 1F)</td>
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<td>Sclerosing cholangitis (n = 1M, 1F)</td>
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<td>Alagille syndrome (n = 1F)</td>
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<tr>
<td>Group 2 (&gt; 1 y of age)</td>
<td>7</td>
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<tr>
<td>EHBA (n = 7M, 2F)</td>
<td></td>
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<tr>
<td>Idiopathic cirrhosis (n = 1M)</td>
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<tr>
<td>Alagille syndrome (n = 1M, 1F)</td>
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<tr>
<td>Sclerosing cholangitis (n = 1M, 2F)</td>
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<tr>
<td>α-1-Antitrypsin deficiency (n = 1M)</td>
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<td>Cholesterol ester storage disease (n = 1M)</td>
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<td>Caroli disease (n = 1M)</td>
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<td>Byler disease (n = 1F)</td>
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<td>Congenital fibrosis (n = 1F)</td>
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∗ EHBA, extrahepatic biliary atresia.

and group 2—20 patients > 1 y (mean: 75 mo; median: 54 mo). Group 1 included 20 children with extrahepatic biliary atresia (EHBA), all of whom had undergone a Kasai procedure: 3 with tyrosinemia, 3 with idiopathic cirrhosis, 2 with sclerosing cholangitis, and 1 with Alagille syndrome. Group 2 included nine children with EHBA, two of whom had undergone an unsuccessful Kasai procedure and seven of whom had undergone a successful Kasai procedure with later failure: one with idiopathic cirrhosis, two with Alagille syndrome, three with sclerosing cholangitis, one with α-1-antitrypsin deficiency, one with cholesterol ester storage disease, one with Caroli disease, one with Byler disease, and one with congenital fibrosis. At the time of evaluation, all children had enlarged and firm liver and spleen, none had subcutaneous edema, and only nine from group 1 and five from group 2 had ascites detected by physical examination or by abdominal ultrasonography.

Nutritional assessment

Nutritional assessments were made when the patients were enrolled on the waiting list for liver transplants. The following anthropometric variables were measured for all patients by one of the investigators (to standardize the method): length or height measured to the nearest 1 cm on a stadiometer (CMS Weighing-Equipment Ltd, London); weight to the nearest 1 g; triceps, biceps, subcapular, and suprailiac skinfold thicknesses to the nearest 1 mm with a skinfold caliper (John Bull, Burgess Hill, United Kingdom); and midarm circumference to the nearest 1 mm with nonstretcher measuring tape. Skinfold thicknesses were measured three times by a single observer and the mean of three readings was taken. The following standards were used: Sann et al (12) for arm anthropometry in children ≤ 1 y of age, Tanner (13) for weight and length for children of all ages and triceps skinfold thickness in those > 1 y of age, and Frisanch (14) for midarm circumference and midarm muscle area (MMA) in those > 1 y of age. MMA was calculated from midarm circumference and triceps skinfold thickness by the following equation (12, 14, 15):

\[ \text{MMA (mm)} = 3.14/4 \times (\text{arm muscle diameter})^2 \]

in which

\[ \text{arm muscle diameter (mm)} = \frac{\text{midarm circumference}}{3.14} - \text{triceps skinfold (mm)} \]

MMA provides an indirect assessment of lean body mass. Body density was calculated from the four skinfold thicknesses (triceps, biceps, subcapular, and suprailiac) and the percentage of body weight accounted for by fat mass was derived from the body density (16, 17).

Weight and height were converted to Z (SD) scores by using reference growth data (13). The Z score is calculated by \( z = \frac{x - \mu}{\sigma} \), in which \( x \) is the patient’s value, \( \mu \) is the mean standard for age and sex, and \( \sigma \) is the SD of the reference mean.

MMA and fat body mass were expressed as percentages of mean age and sex-matched values obtained from a “well-fed” indigenous population (12, 14, 15). All anthropometric measurements were calculated on the basis of the patient’s height-age. Height-age was defined as the age at which the patient’s height equalled the 50th Italian height percentile.

Hepatic failure

The degree of hepatic failure was defined according to the Malatack criteria (18).

Dietary assessment

All children were fed ad libitum. Dietary intake, based on 72-h measured intakes, was recorded by a nutritionist and expressed as percentages of recommended daily energy, protein, and hydrosoluble vitamin intakes by age (19).

Statistical analysis

To evaluate relations between nutritional assessment indexes and liver function, data were compared by one-way analysis of variance, and between nutritional assessment indexes and energy intakes by linear-regression analysis (Software per Discipline Biomediche–Stanton A Glantz; McGraw-Hill Libri Italia, Roma). A \( P < 0.05 \) was considered statistically significant.

RESULTS

Demographic data for the patient groups are presented in Table 1. Mean height Z scores were low in both groups (group 1: \(-1.97 \pm 1.77\); group 2: \(-1.3 \pm 1.84\)). Patients ≤ 1 y of age had lower mean Z scores than patients > 1 y of age, but the difference was not significant. Weight (group 1 Z score: \(-1.48 \pm 1.27\); group 2 Z score: \(-0.24 \pm 0.88\)) and fat body mass (group 1: \(-49.6 \pm 29.63\%\); group 2: \(-1.4 \pm 30.18\%\)) were significantly lower in group 1 than in group 2 (\( P < 0.001\); height and MMAs (group 1: \(-27.6 \pm 22.06\%\); group 2: \(-14.25 \pm 28.57\%\)) did not differ significantly between the two groups (Figures 1 and 2).

In group 2, MMA and fat body mass were significantly lower in patients with moderate-to-severe hepatic dysfunction than in patients with mild hepatic dysfunction (Figures 3 and...
The mean energy intakes for the two groups of patients were in the range of the Italian recommended daily allowances for age (19). Analyzing the mean energy intakes with different anthropometric measurements by linear-regression analysis, we showed that the ratio of malnutrition indexes to energy intake was close to one. This equality suggests that the mean energy intake in the two groups of patients was insufficient (Table 2).
MALNUTRITION IN END-STAGE LIVER DISEASE

FIGURE 3. Relation between hepatic dysfunction and anthropometric measures (height and weight) of group 1 (≤ 1 y of age; n = 29) and 2 (> 1 y of age; n = 20) patients. There were no significant relations between the degree of hepatic failure and these two anthropometric variables in either group.

DISCUSSION

Failure to grow is a serious consequence of malnutrition in children with chronic liver disease, resulting in increased morbidity and mortality and the length of hospitalization before and after transplantation (11, 20). Although there are some studies in the literature that showed with different techniques that children with chronic liver disease are malnourished, no data that correlate some measurements of nutritional status with different ages in a systematic way have been available until now (1–3, 7). Growth, in fact, varies significantly in the different periods of life and factors that provoke malnutrition can have greater deleterious effects when somatic growth is particularly rapid. Therefore, we studied children ≤ 1 y of age separately from older children. The technique used offers some advantages in pediatrics because it is rapid, noninvasive, inexpensive, and generally available on a routine basis. Moreover, because the anthropometric measurements are limited to the upper limbs, they are advantageous for children with chronic liver disease because excessive fluid is more likely to accumulate.

FIGURE 4. Relation between hepatic dysfunction and anthropometric measures (MMA, midarm muscle area; FBM, fat body mass) for group 1 (≤ 1 y of age; n = 29) and 2 (> 1 y of age; n = 20) patients. In group 2, MMA and FBM were significantly lower in patients with moderate-to-severe hepatic failure than in patients with mild hepatic dysfunction.
in the lower part of the body (1). None of the children studied had subcutaneous edema.

The degrees of height deficits for age, generally considered indicative of chronic undernutrition, were common to the two groups. The mean Z score for height was −1.97 for group 1 and −1.30 for group 2 (NS). The majority of the patients studied had EHBA. Sokol and Stall (2) found this to be less stunting than intrahepatic liver disease (arteriohepatic dysplasia), which produces the most severe growth disturbance because of skeletal involvement. One possible explanation of the results found, especially in group 1, was that shortness was probably genetically determined. In fact, the parents of the shorter children were also short. Because of short stature, we evaluated all anthropometric indexes on the basis of height-age instead of chronologic age.

Mean Z scores for weight were much lower for patients in group 1 than those of group 2, and the difference was significant (Figure 1). This difference may be due to the fact that children aged ≤1 y are in the accelerated growth phase and thus much more vulnerable to malnutrition. For the older children, the mean Z scores for weight were close to normal, probably because the velocity of their weight gain was slower than that in infants. In addition, the enlarged and fibrotic liver and spleen contributed to normalizing this index for the older group.

Fat body mass reflects the extendable and available energy reserve of an organism. Studies have examined the correlation between skinfold measurements and body density determined by underwater weighing (21, 22). The correlation coefficient obtained with triceps skinfold thickness, ≈0.7, can be improved by adding other skinfold measurements. Four skinfold thicknesses, gauged in millimeters with a caliper (triceps, biceps, suprailliac, and subscapular), provide a good clinical assessment of the fat body mass. The body adipose tissue reserve was considerably lower in the children of group 1 (−50%) than in the older patients (−1%), indicating more severe acute malnutrition in the first group. This difference was significant (P < 0.001). Sokol and Stall (2) and Chin et al (7), found a similar depression of fat body mass, but their patients were not divided into groups of different ages. Lean body mass reflects total body protein. Anthropometric indexes combined with measurements of arm circumference and triceps skinfold thickness and calculation of arm muscle area are useful for assessing body muscle mass. Chronic liver disease causes protein-energy malnutrition and in these patients, the decrease in muscle mass, as seen by many investigators, is greater than the reduction of body weight (1, 2, 7). This reduction of muscle mass occurs because muscle provides the amino acids for gluconeogenesis and protein synthesis. In our study, body muscle mass values were more compromised in the children of group 1 than in those of group 2, but the difference was not significant. Others have provided similar data (2, 7).

Nevertheless, we want to emphasize that lean body mass was the most compromised variable in the children of group 2. This means that patients with prolonged liver disease often have indexes indicating chronic malnutrition. In our study, we found no significant differences among the patients of group 1 with mild or moderate-to-severe degrees of hepatic failure by Malatack scores (18), the most widely used criterion for estimating the urgency of transplantation. The mean Z scores for weight of children with moderate-to-severe hepatic dysfunction were not reduced because of ascites and organomegaly. On the other hand, in group 2, fat body mass and lean body mass were significantly lower in patients with moderate-to-severe hepatic dysfunction than in patients with mild hepatic failure (P < 0.05) (Figures 3 and 4). The relation of mean energy intake to the different anthropometric measurements suggested that patients with chronic liver disease have a greater energy requirement than healthy children.

In conclusion, these data indicate that the predominant factors that influence malnutrition in children with chronic liver disease are age for infants and the degree of hepatic failure for older children. The daily energy intake is a determinant for all patients. We found evidence of significant acute and chronic malnutrition, confirming the need for nutritional support for these children (23). Serial anthropometric measurements are recommended to follow the effects and adequacy of nutritional intervention once deficiencies have been identified. Because these children are frequently in care in nonspecialized hospitals, we recommend that a simple, inexpensive, easily reproducible, noninvasive technique such as anthropometric evaluation of the upper limbs is useful for assessment of nutritional status.

REFERENCES