Case Series

Chronic liver disease is a risk factor for malnutrition and growth retardation in children

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Background: Despite distinct advancements in nutritional therapy, malnutrition and growth retardation remain inevitable consequences of chronic liver disease. The global prevalence of chronic liver disease in children is about 3%, with a quarter undernourished. Malnutrition itself is a negative prognostic indicator of survival. Further research is necessary for delivering adequate nutritional support to reduce morbidity and mortality. **Objective:** To evaluate the nutritional status and growth of children with chronic liver disease and its contributing factors. **Methods and Study Design:** Data were gathered about 21 children aged 7 months to 13.3 years diagnosed with chronic liver disease at Harapan Kita Women and Children Hospital between November 2014 and February 2016. Physical growth and nutritional status were evaluated using anthropometric percentiles and z-scores. Laboratory measurements were made on their first visit. **Results:** The mean age of participants was 43.9±47.4 months. Mean weight was 13.4±9.31 kg, and mean length/height was 88.8±27.7 cm. Ten (47.6%) and 3 (14.3%) patients had moderate or severe undernutrition, respectively, and 38% (8 patients) had growth retardation. Of those with good nutritional status, 62.5% were older than 5 years. Malnutrition was correlated with growth failure, a low serum albumin, and elevated aspartate transaminase ($p<0.05$ in all cases). **Conclusion:** Early diagnosis of malnutrition should encourage nutritional support, delay illness progression and increase survival in children with chronic liver disease.

Key Words: malnutrition, growth failure, chronic liver disease, risk factors

INTRODUCTION

Chronic liver disease (CLD) constitutes progressive destruction and regeneration of the liver parenchyma leading to fibrosis and cirrhosis, present for at least 6 months. Diagnosis is based on a combination of liver enzyme chemistry and imaging with ultrasound. The liver plays an important role in metabolism, nutrition storage, food absorption, and the immune system.[1] Thus, derangement of its function results in metabolic, nutritional and immunological abnormalities. Many studies have shown that liver disease results in nutritional deficits, especially in children.[2,3]

According to WHO, malnutrition is a cellular imbalance between the intake of nutrients and energy and the body's need to ensure its growth, maintenance, and specific functions.[4] Guidelines and policies have been developed to facilitate the provision and maintenance of adequate nutrition.. Despite efforts to combat malnutrition, approximately a quarter of children diagnosed with chronic liver disease worldwide are undernourished.[5] This is especially frequent in developing countries such as Indonesia.[6] Undernutrition is commonly found in infants who have CLD because of fat malabsorption, abnormal nutrient metabolism, and increased use of energy.[2] Malnutrition during the early months of life has deleterious effects on growth.[3] Children who are diagnosed with CLD at an early age are more prone than others to develop malnutrition, especially those with cholestatic liver disease.[2,7] The incidence of liver disease in neonates is estimated at approximately 1 in every 2500 live births.[2]

Metabolic, structural, obstructive, infectious, and toxic causes of CLD are found.[8,9] The combination of age and pathology further contributes in the development of protein–energy deficiency, which eventually leads to failure to thrive.[3] The metabolic changes associated with CLD also adversely affect growth in children. Children who are becoming nutritionally depleted must therefore be identified quickly so that further damage can be prevented.

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Many studies have demonstrated that managing CLD in children is challenging, and multiple complications often result, including deranged nutritional status and growth failure.[2,10] Both complications are serious consequences of CLD that further increase morbidity and mortality.[11] As many as 20%–30% of severely malnourished children may die during treatment.[12] The prevalence of malnutrition associated with CLD varies according to the severity of hepatic damage and disease progression.[2] There are few reports of malnutrition in children with chronic liver disease, especially in developing countries. The present considers the association of malnutrition and growth retardation in children with CLD, as well as the timeliness of diagnosis.

MATERIALS AND METHODS

This study of children with CLD was conducted in the Department of Gastrohepatology, Harapan Kita Women and Children's Hospital between November 2014 and February 2016. The selection protocol is shown in Figure 1.

Medical history, physical examination, biochemical findings, and imaging methods were performed in all children who presented with the clinical stigmata of chronic liver disease such as icteric sclera, jaundice, spider angiomas, ascites, or encephalopathy. A full blood count, serum aspartate transaminase, alanine aminotransferase (ALT), total protein, albumin, total bilirubin, and direct and indirect bilirubin were routinely assessed; gamma glutamyl transferase, phosphate, and electrolytes were measured if indicated. Inclusion criteria were children age 0 – 18 years with failure of liver synthetic function, with or without fibrosis present for more than 6 months. CLD diagnosis was based on the presence of an increased serum bilirubin, coagulation abnormalities, or hypoalbuminemia, with or without increased serum transaminase. Diagnosis of fibrosis was based on ultrasonography or FibroScan. The diagnosis of coexisting disease that could potentially cause malnutrition such as, but not limited to, cystic fibrosis, renal disease not related to hepatic failure, heart disease, and endocrine disease resulted in exclusion from this study. Anthropometric measurements were conducted by trained fieldworkers. All children were weighed and measured during their first visit to the hospital while wearing lightweight clothing. Weight measurement of children younger than 24 months was

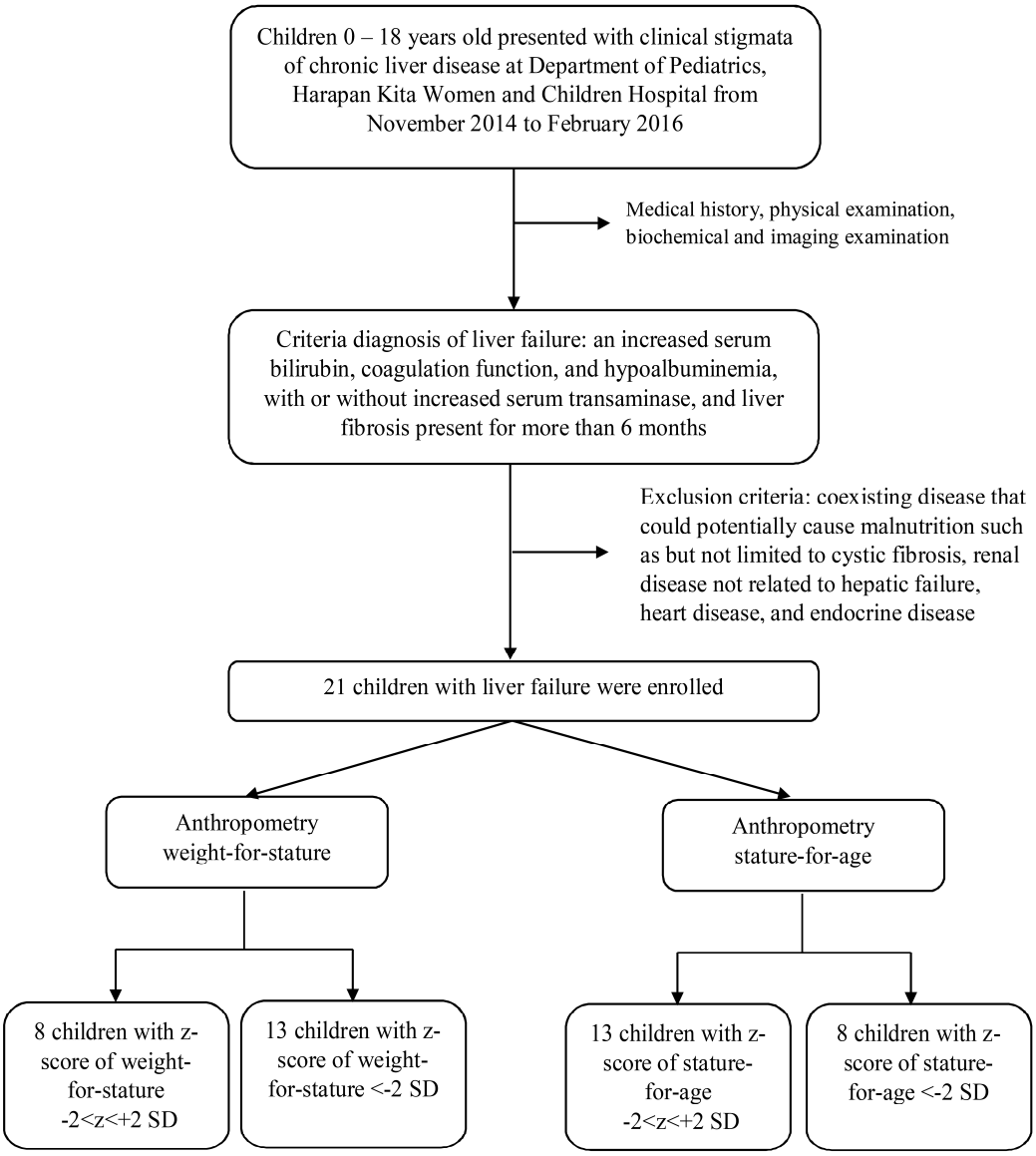

Figure 1. Patient recruitment flow chart.

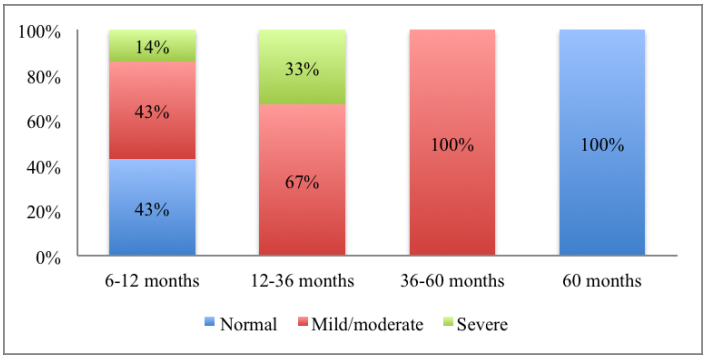

Figure 2. Distribution of status nutrition in children with chronic liver disease based on age group (n=21). Normal: -2<z<+2SD; mild/moderate: -3<z<-2SD; severe: z <-3SD

conducted using a children's scale that had a precision of 0.05 kg and by positioning the child horizontally during the reading. Length was measured using an infant stadiometer that had a precision of 1 cm. Children older than 24 months who could be instructed to stand still were weighed while barefoot by using a scale with a precision of 0.5 kg. Their heights were also measured with a precision of 1 cm while they stood straight on a horizontal surface, facing forward with their heels together. The curve published by the National Center for Health Statistics (NCHS) and the World Health Organization (WHO) standards were used to determine the nutritional status of the participants. Anthropometric measurements were than plotted against these curves and the standard deviations of scores (z-scores) were used to find weight-for-stature and stature-for-age to define wasting and stunting, respectively. For each of the anthropometric indicators of malnutrition, cut-off points below −2 standard deviations (−2 SD) z-score of the WHO reference or below 90% of the NCHS references were used to diagnose undernutrition and growth retardation. Z-score below -3 SD is considered as severe undernutrition and stunting. Accordingly, overweight children defined as having a z-score weight-for-stature higher than +2 SD of the WHO reference or higher than 110% of NCHS reference are also diagnosed as being malnourished. However, none of the participants in this study were so identified. Hence, any reference to "malnutrition" in this study means a z-score of weight-for-stature below -2 SD.

Research design

This study is cross-sectional and descriptive. Participants were enrolled using convenience sampling. The minimum sample for this study estimated the proportion of the absolute source population with an assumption that drop out would be 10% and that the study children hospital would, as a Ministry of Health hospital, constitute one of the 2 major referral centres for children in Jakarta. Thus, a total of 21 children were enrolled in this study. Eleven of the participants were boys

RESULTS

Twenty-one children aged 7 to 160 months were recruited. Their mean age was 43.9±47.4 months. They were divided into groups aged 6–12 months, 12–36 months, 36–60 months, and older than 60 months, comprising 33.3%, 28.6%, 14.3%, and 23.8% of the study population, respectively. They were divided almost evenly by gender; 52.3% (n=11) were boys. At their first visit, weights and lengths/heights were measured. The minimum weight was 4 kg, and the maximum was 31 kg, with a mean of 13.4±9.31 kg. No overweight children were found in this study. Two children had hepatic fibrosis. The minimum and maximum length/height measurements were 57 cm and 145 cm, respectively, with a mean of 88.8±27.7 cm. A total of 10 (47.6%) or 3 (14.3%) of the 21 patients had moderate or severe undernutrition, respectively, with the prevalence detailed in Figure 2. Approximately 38% (8 children; 4 boys and 4 girls) had failure to thrive. Of those children with good nutritional status, 62.5% were 5 years or older. Multiple logistic regression analysis was used to identify factors related to malnutrition. Those considered to have a significant impact on malnutrition (p<0.05) were stunting, low serum albumin, and elevated AST, as illustrated in Table 1.

DISCUSSION

The diagnosis and management of CLD have seen numerous advancements, but malnutrition and stunted growth remain inexorably linked with CLD. This is demonstrated in our study, where 61.9% of the children recruited were undernourished, with 47.6% having mild or moderate undernutrition and 14.3% being severely undernourished. These findings are evidence that preventing malnutrition remains a major challenge. Malnutrition itself is a negative prognostic indicator of survival, especially considering that the presence of malnutrition can determine whether early-stage liver transplants should be conducted.[13-15] Cameron et al have reported that the inability to improve nutritional status before surgery increas-

Table 1. Anthropometric and liver function status of malnourished and apparently healthy children

	Mean±SD		p value
	Malnutrition (n=13)	Normal (n=8)	
Weight (kg)	10.9±6.23	17.6±12.2	0.38
Height (cm)	83.6±22.9	97.3±34	0.31
AST (U/L)	168±191	127±67	0.04
ALT (U/L)	107±124	71±35.1	0.08
Albumin (g/L)	2.86±0.87	2.7±0.66	0.007

AST: aspartate aminotransferase; ALT: alanine aminotransferase.

es the risk of postoperative complications and mortalityy.[14] We found that 38.1% of patients had growth impairment. All who were stunted were younger than 5 years. This shows that CLD has a more significant impact on linear growth if developed at an earlier age, as reported in other studies.[14] Aside from fat malabsorption, altered metabolism, and the increase in energy expenditure in children with CLD, growth retardation can also cause shifts in the growth hormone/insulin-like growth factor/insulin-like growth factor binding protein axis.[2]

The fact that growth retardation is commonly found in children with CLD indicates that nutritional status assessment is relatively difficult in this group. Assessment of weight alone might result in a misleading diagnosis of underweight in stunted children. Any fluid retention (ascites) or organomegaly, a disproportionate organ size, may also result in weight gain, even though overall nutritional status might actually be poor. Clinical acumen, anthropometric inconsistencies and the imaging studies can clarify nutritional diagnosis. The child's growth chart can be invaluable. Appropriate nutritional intervention can then reduce complication rates.[16] One study found that only 59% of children admitted to a hospital underwent a full and accurate nutritional assessment on admission[12] with delay in the diagnosis of malnutrition. Many factors are involved, including equipment availability and medical personnel proficiency. For example, middle-upper arm circumference and triceps skinfold are effective ways to determine nutritional status in children with CLD. Body fat storage is about 50% subcutaneous fat; therefore, measurements of subcutaneous fat reflect total body fat.[10] These assessments are also more helpful than height measurement, because alterations appear earlier than in stature. However, the use of calipers and training in proper technique may be neglected. Nonetheless, both measurements have the potential for overestimation when peripheral oedema is present, which must be taken into account.

Conventional anthropometry alone such as weight and stature measurements is not sufficiently reliable for patients with liver disease, especially those who have fluid retention and poor hepatic synthetic function. Ramaccioni et al[17] propose that body composition analysis which measures fat, cell mass, extracellular water, and fat-free extracellular solids are to be preferred. The body fat compartment is not influenced by oedema because of its anhydrous state and because fat is the major form of stored energy.[17] Thus, it is more appropriate l for assessing nutritional status in children with CLD. Many tools and methods are currently available for this purpose, such as total-body electrical conductivity, total-body potassium, and neutron activation analysis. However, they are prohibitively expensive and available in only a few research centres. Ramaccioni et al[17] recommended dual energy x-ray absorptiometry as a promising nutritional assessment method, as it is noninvasive and can accurately measure body composition as well as bone density, although availability may still be a constraint

Conclusion

Maintaining optimal nutrition in children with CLD is essential for preventing further liver damage. By doing so, the synthesis and storage of fat and other sources of energy can be preserved and perhaps increased; these aspects are crucial for a child's growth. Nutrition also plays a major role in morbidity and mortality, and its optimisation contributes to the success of liver transplantation. To decrease morbidity and improve outcomes, timely assessment and management of malnutrition in children with CLD is vital.

AUTHOR DISCLOSURES

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