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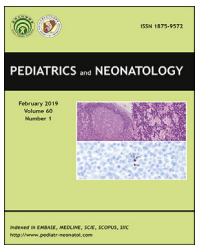

Editorial

Fat-soluble vitamin deficiency in pediatric patients with chronic liver disease

Nutritional deficiencies have become a common problem among patients with chronic liver disease (CLD) and may easily be underestimated by clinical appearance alone; they negatively impact the neurocognitive development and growth. CLD is defined as the process of long-term progressive destruction and regeneration of liver parenchyma leading to fibrosis and cirrhosis. Children with CLD are more at risk than adults for severe malnutrition and feature lower reserves. In the United States, the overall incidence of liver disease in neonates is approximately 1 in every 2500 live births[1] with extrahepatic biliary atresia (BA), metabolic disorders, and neonatal hepatitis being the most common causes of CLD in neonates, whereas metabolic disorders, chronic intrahepatic cholestasis, obesity-related steatohepatitis, drug- and toxin-induced disorders, and viral hepatitis are common causes in older children.[2]

Approximately 25% of children diagnosed with CLD worldwide are undernourished, with a higher incidence observed in developing countries.[3] Malnourishment is considered a predictor of poorer outcomes in liver transplantation and is often associated with increased risks for morbidity and mortality. The development of malnutrition in children with CLD is complex and multifactorial, involving a decreased dietary intake, malabsorption, increased energy expenditure, and disordered substrate synthesis and metabolism. CLD affects absorption, metabolism, and storage of fat-soluble vitamins (FSVs). The decreased delivery of bile salts to the small bowel results in malabsorption of fat and FSVs A, D, E, and K. Young et al.[4] reported that the incidence of vitamin deficiency could reach 20%–30% in patients with cholestatic liver disease; this phenomenon also common affects children with BA. Dong et al.[5] observed that FSV deficiency was more notable in patients with BA than in patients with other cholestatic liver diseases, especially vitamin D deficiency (VDD).

The global prevalence of VDD in the general population affects all age groups and ranges from 20% to 100% when referring to serum 25 (OH)D concentrations $<$20 ng/ml.[6] The prevalence of vitamin D levels $<$20 ng/ml in CLD has been reported to range from 64% to 92% and is commonly inversely related to disease progression.[7] VDD is the major cause of hepatic osteodystrophy. In Taiwan, Shen et al.[8] reported that the proportion of patients with FSVs A, D, E, and K deficiencies under conventional supplementation amounted to 73.9%, 81.8%, 91.3%, and 20.0%, respectively.

However, limited knowledge can explain about the prevalence of VDD and metabolic bone disease in children with CLD from tropical setting with abundant sunlight. In this issue of *Pediatrics and Neonatology*, Lee et al.[9] investigated the vitamin D status in children with CLD in a tropical country. They demonstrated that VDD was prevalent in children with CLD despite vitamin D supplementation. Overall, 28% of the subjects were either vitamin D deficient or insufficient. In addition, more than 1 in 5 children (22%) with CLD presents at least one physical symptom of VDD. In patients with total bilirubin levels of 3.0 mg/dL, the proportion of at least 1 FSV deficiency equals 100%; the deficiency rates of vitamins A, D, E, and K are 78.6%, 100.0%, 100.0%, and 21.4%, respectively. This study confirmed the prevalent nature of VDD in children with CLD in a tropical setting with plenty of sunlight throughout the year, irrespective of gender, age group, or whether the disease was progressive or stable in nature. However, the study failed to assess the duration of exposure to sun. Thus, the correlation between the duration of sunlight exposure and serum vitamin D status was unclear. Furthermore, dietary intake of vitamin D, duration, dosage, and compliance to vitamin D supplementation, and severity of diseases were not addressed, limiting further assessment of actual efficacy of oral vitamin D supplementation. We recommend further exploration of these factors that influence the serum vitamin D status in children with CLD in tropical countries.

General guidelines have been developed for nutritional management in adult patients with CLD. However, the ideal dose of vitamin D and minerals in children with CLD to prevent and treat hepatic osteodystrophy is not well defined. For children who are vitamin D deficient, the Pediatric Endocrine Society recommends an initial daily dose

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of 1000—10,000 IU for 8—12 weeks, followed by a daily maintenance dose of 400—1000 IU.[10] Routine vitamin supplementation within recommended daily allowances has been considered to be a reasonable approach. In a Taiwan study,[8] no adverse events nor overdose effects were detected among the 10 patients receiving standard daily dose of FSVs for 3 months. The rates of vitamins A, D, and E deficiency in the patients receiving FSVs decreased from 80.0%, 100%, and 100%—70.0%, 60.0%, and 60.0%, respectively, after 3 months of oral supplementation.

In conclusion, malnutrition commonly occurs in children with CLD, may easily be underestimated, and requires aggressive and appropriate management. The clinicians should maintain alertness and evaluate the children with CLD to determine the possibilities of nutritional deficiencies. Clinical and laboratory assessment of FSV levels should be undertaken periodically to detect deficiency and to monitor response to any supplementation. A better nutritional status is associated with better survival before and after liver transplantation for advanced liver diseases. Thus, aggressive nutritional management is an important part of the care of these children, and close monitoring of various serum nutrient levels and routine oral vitamin supplementation in all pediatric patients with CLD are mandatory.

Conflicts of interest

The author declares that he has no financial conflicts of interest related to the subject matter or materials discussed in the manuscript.

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