Clinics and Research in Hepatology and Gastroenterology (2018) xxx, xxx–xxx

Available online at ScienceDirect www.sciencedirect.com

Elsevier Masson France EM|consulte www.em-consulte.com/en

ORIGINAL ARTICLE

Evaluation of vitamin D status bone mineral density and dental health in children with cholestasis

Nashwa M. Samra[a], **Shaimaa Emad El Abrak**[b], **Hanaa H. El Dash**[a,*], **Mona El Said El Raziky**[c], **Manal A. El Sheikh**[d]

[a] *Department of Pediatrics, Fayoum University, Fayoum city, Egypt*
[b] *Department of Pediatrics, National Hepatology and Tropical Medicine Research Institute, Cairo University, Cairo, Egypt*
[c] *Department of pediatric, Cairo University, Cairo, Egypt*
[d] *Faculty of Oral and Dental Medicine, Cairo University, Cairo, Egypt*

KEYWORDS
CLD;
DXA scan;
BMD;
BMC;
25(OH)D;
PFIC

Summary
Background: Hepatic osteodystrophy caused by vitamin D and calcium malabsorption is thought to develop in children with cholestatic liver disease leading to secondary hyperparathyroidism and rickets or osteomalacia. The aim of this study was to evaluate the dental and bone mineral densities and the serum level of vitamin D in cholestatic infants and children and to correlate this process with clinical and laboratory parameters.
Methods: This is a cross-sectional study that include 50 patients presenting with cholestasis. Thirty age and sex matched controls recruited not complaining of liver disease. All cases were subjected to full history taking, clinical and dental examination, 25(OH)D level, ALT, AST, bilirubin, albumin, GGT, alkaline phosphatase, PT, INR, calcium, corrected calcium, phosphorus and DXA scan to those above 5 years old. Controls were subjected to measuring the serum levels of 25(OH)D, total bilirubin, direct bilirubin, ALT, GGT, AST, PT, INR, alkaline phosphatase, albumin, calcium and phosphorus.
Results: Out of the 50 cases; 23 were females (46%), with a mean age of 6.17 ± 3.9 years ranging from 1.1 to 17 years. Twenty-eight of the cases had signs of rickets (56%), 6 of them had bone fracture (12%) and 42.8% had milky teeth caries. The level of 25(OH) vitamin D was below normal range in around half of the patients. There was significant difference between cases and controls in calcium and phosphorus levels, ALT and alkaline phosphatase. Low bone mineral

* Corresponding author.
E-mail address: hanaaeldash@yahoo.com (H.H. El Dash).

https://doi.org/10.1016/j.clinre.2017.11.010

Please cite this article in press as: Samra NM, et al. Evaluation of vitamin D status bone mineral density and dental health in children with cholestasis. Clin Res Hepatol Gastroenterol (2018), https://doi.org/10.1016/j.clinre.2017.11.010

density (BMD) was present in 50% and 5 cases (17.9%) were diagnosed as having osteoporosis. There was a negative correlation between the Z-score, BMD of total body, BMD and bone mineral content (BMC) of spine and total and direct bilirubin. There was a positive correlation between (BMD of total body, spine and BMC of spine) and serum phosphorus, alkaline phosphatase and albumin. There was a positive correlation between the Z-score of total body and serum calcium.
Conclusion: Decreased level of 25-OH vitamin D is present in more than half of cholestatic patients, and is correlated positively to serum calcium. Decreased BMD was present in more than half of studied cholestatic patients correlated to the low serum calcium rather than the vitamin D level. The decreased BMD and the dental affection in cholestatic children is related to the level of hyperbilirubinemia.

Introduction

Cholestasis could be defined as a pathological condition of decreased bile formation or flow, in which normally excreted substances into bile are retained including conjugated bilirubin and bile salts which are the commonly measured substances [1].

Irrespective of causes, cholestasis, which is accompanied with hepatic insufficiency additionally, increases malnutrition (increased metabolism, anorexia, vomiting, diarrhea, impaired gastrointestinal absorption of lipids and vitamins A, D, E and K) [2].

Vitamin D which is necessary for bone metabolism is converted in the liver into 25-hydroxyvitamin D (25[OH] D) and then converted into 1, 25-dihydroxy vitamin D in the kidney in order to be metabolically active. So, liver and kidney play vital roles in vitamin D activation [3].

One of the most significant extrahepatic expression of chronic cholestatic liver disease is hepatic osteodystrophy and denotes the ending result of several mechanisms leading to bone fragility [4]. Hepatic osteodystrophy is caused by calcium and vitamin D malabsorption, producing secondary hyperparathyroidism and osteomalacia or rickets [5]. The etiopathogeny of hepatic osteodystrophy is not completely understood [6].

It has been indicated over years that the main bone disorder in chronic hepatic dysfunction is loss of bone mass. Some studies denoted the association of 25-hydroxyvitamin D deficiency and bone disorders in chronic cholestatic liver disease (CCLD) patients due to the significant role of the liver in vitamin D metabolism [7]. The development bone mass is impaired in cholestatic children even in the early stage of chronic cholestatic disease (CCD) [8].

Low bone mineral density, osteopenia and high incidence of fractures in children with cholestatic liver diseases have been denoted by previous finding [3]. The overall objectives of bone densitometry are to detect patients at highest risk of skeletal fragility fractures, to guide decisions concerning management, and to monitor responses to therapy. It is recommended to do skeletal assessments for children with frequent fractures, bony pain or deformities, or osteopenia on regular radiographs or to monitor treatment [9].

Dual-energy X-ray absorptiometry (DXA) has been recognized as a significant device for comprehensive skeletal assessment of children and teenagers but not yet of infants [10].

Studies revealed that a few months after liver transplantation for children with osteopaenia due to CCLD they showed an increase of bone loss; nevertheless, in the long-standing follow-up, these children present a significant increase in bone mineral density (BMD). These data denote the effect of cholestatic disorders on bone mass loss and the significance of normal hepatic function for bone mass gain in CCLD patients [11].

Opacity and hypoplasia of enamel and greenish brown hyperpigmentation of teeth caused by accumulation of biliverdin in dental tissues are odontogenic manifestations of cholestasis [2].

The development of the masticatory system, including odontogenesis is affected by systemic disorders caused by CLD leading to dental hypomineralization of the enamel [12].

In developing countries there is insufficient data regarding serum level of vitamin D and bone affection in cholestatic children and their correlation with laboratory parameters.

Aim of work

The aim of this study was to evaluate the dental and BMD and the serum level of vitamin D in cholestatic infants and children and to correlate this process with clinical laboratory parameters.

Patients and methods

This is a cross-sectional study that include 50 patients presenting with cholestasis. Patients were recruited from the hepatology outpatient clinic at Cairo University Pediatric Hospital and the National Hepatology and Tropical Medicine Research Institute (NHTMRI). The study also included 30 age- and sex-matched controls. The protocol was approved by the Faculty of Medicine Research Ethics Committee. Assent of the children and consent was obtained after proper orientation of the care givers regarding the study objectives.

Please cite this article in press as: Samra NM, et al. Evaluation of vitamin D status bone mineral density and dental health in children with cholestasis. Clin Res Hepatol Gastroenterol (2018), https://doi.org/10.1016/j.clinre.2017.11.010