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Evaluation of micronutrients among pediatric liver cirrhosis in Shiraz, Iran

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Abstract

Background: Cirrhosis is the final result of most types of liver disease. Zinc, magnesium, and vitamin D have a significantly vital role in the immunologic and physiologic mechanisms in the body. The current study aimed to measure magnesium, zinc, and vitamin D level among children with liver cirrhosis.

Results: One hundred cases were included in the current study. Vitamin D deficiency was found in 53% of the cases. Zinc deficiency was present in 23% of the cases. The magnesium level was more than the normal level among 99% of the cases. There is a significant inverse correlation between zinc level and PELD score (Pearson correlation = −0.314, $P = 0.007$).

Conclusion: Zinc deficiency and vitamin D deficiency were seen in children with liver cirrhosis. Serum magnesium level in children with liver cirrhosis was higher than standard. A significant correlation was seen between zinc level and PELD score.

Keywords: Cirrhosis, Liver, Magnesium, Zinc

Backgrounds

The liver is the primary organ for metabolism. Liver disease has a profound effect on protein and energy metabolism [1, 2]. Cirrhosis of the liver has several etiology including biliary atresia, Wilson's disease, and autoimmune hepatitis [3]. Zinc is an essential trace element with various biological actions [4]. In patients with hepatic encephalopathy, zinc deficiency may have a role. Zinc supplementation for the treatment of hepatic encephalopathy was proposed in the literature [5–7]. Magnesium deficiency was reported among 30% of children with liver disease [8]. Vitamin D deficiency is an independent risk factor for infection among children with cirrhosis [9]. There are limited studies about zinc, magnesium, and vitamin D deficiencies among children with liver cirrhosis. This study aimed to evaluate the level of zinc, magnesium, and vitamin D among children with liver cirrhosis.

Methods

In this cross-sectional study, all children aged less than 18 years with liver cirrhosis who visited at Pediatric Gastroenterology and Hepatology Clinic of Shiraz University of Medical Sciences were included. The duration of the study was 2 years starting from February 2017. Children with a history of zinc, magnesium, and vitamin D supplementation before the diagnosis of cirrhosis were excluded from the study. Cirrhosis was confirmed after liver biopsy in children using the clinical and radiologic criteria for liver biopsy. For zinc, magnesium, and vitamin D measurement; 5 ml of blood sample was obtained. Zinc and magnesium level measurement was done using atomic absorption spectrometry. Normal zinc level was considered to be 50–150 mcg/dl. The normal level of magnesium was considered to be 0.8–1 mmol/dl. The normal level of vitamin D was considered to be 20–100 ng/dl. In the current study, standard levels of zinc, magnesium, and vitamin D were used for comparison as control.

This study was approved by the ethical committee of the Shiraz University of Medical Sciences. An informed consent form was signed by parents. SPSS ver 25.0 was

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Table 1 Etiology of liver cirrhosis

Etiology	Frequency (%)
Cryptogenic cirrhosis	15
Progressive familial intrahepatic cholestasis	26
Biliary atresia	27
Autoimmune hepatitis	6
Neonatal hepatitis	6
Wilson's disease	5
Tyrosinemia	6
Idiopathic neonatal hepatitis	3
Primary sclerosing cholangitis	2
Congenital heart failure	1
Intrahepatic bile duct paucity (non-syndromatic)	2
Allagile syndrome	1

normal range. Among 31% of the cases, the albumin level was lower than the normal range.

INR was normal among 59% of children with liver cirrhosis. The mean of INR was 1.334, and the median was 1.1 (min = 0.94, max = 4.7) (Table 2).

The minimum and maximum of serum Na were 128 and 158, respectively. The mean of serum Na was 137.9 meq/dl.

PELD score was used for 89% of the children. Among 31% of children, the PELD score was 1. The MELD score was used for 11% of children. The minimum and maximum MELD scores were 6 and 17, respectively.

Zinc level distribution was normal using the Kolmogorov-Smirnov test. The mean of zinc level (71.32 ± 25.01) was significantly lower than normal population (P value = 0.0001, CI95% = 65.5–76.5) (Fig. 1) (Table 3).

Table 2 Liver function test among children with liver disease

Descriptive statistics								
	N	Range	Minimum	Maximum	Mean		Std. deviation	Variance
	Statistic	Statistic	Statistic	Statistic	Statistic	Std. Error	Statistic	Statistic
Albumin	100	3.30	1.20	4.50	3.6810	.05479	.54785	.300
INR	99	3.76	.94	4.70	1.3343	.05583	.55552	.309
Total bilirubin	100	32.00	.50	32.50	5.2163	.64702	6.47024	41.864
AST	100	1444.00	11.00	1455.00	195.7800	23.25283	232.52829	54,069.406
ALT	100	1588.20	1.80	1590.00	138.6380	20.37269	203.72693	41,504.664

used for data analysis. The chi-square test was used for comparison.

Results

In the current study, 100 children (m = 52, f = 48) aged less than 18 years were finally included. The mean age of the cases was 7.17 ± 4.84 (min = 5 months, max = 18 years) years with a median age was 6.0 years. Biliary atresia and progressive familial intrahepatic cholestasis were the most frequent etiology of liver cirrhosis among our cases (Table 1).

Hepatic encephalopathy was seen in 2% ($n = 2$) of the cases. Among 2 children with hepatic encephalopathy, one child had zinc deficiency.

Ascites were the most common finding among children with liver cirrhosis and were seen in 21% of children. Among the children, 10% had a history of gastrointestinal bleeding.

The mean of albumin was 3.681 with minimum and maximum levels of 1.2 g/dl and 4.5 g/dl, respectively. Among 69% of cases, the albumin level was in the

The minimum and maximum levels of zinc were 25.2 mcg/dl and 147.1 mcg/dl, respectively. Zinc level was lower than the normal range among 23% of children with liver cirrhosis. The mean level of zinc was 71.32 ± 25.01 mcg/dl. The median level of zinc was 69.7mcg/dl (Table 3).

There is a significant inverse correlation between zinc level and PELD score (Pearson correlation = −0.314, $P = 0.007$)

The distribution of magnesium levels was abnormal (Fig. 2). There was a significant difference between children with liver cirrhosis and the normal population in terms of the level of magnesium using the chi-square test ($\chi^2 = 32.67$, $P = 0.0001$) (Table 3). Magnesium level according to etiology of cirrhosis is shown in Fig. 3.

There was a significant difference between the level of vitamin D among children with liver cirrhosis and normal level (chi-square = 4, $P = 0.0455$) (Table 2). There was no significant correlation between vitamin D level and PELD score (Pearson correlation = −0.205, $P = 0.058$). Vitamin D, zinc, and magnesium levels according to underlying disease are shown in Table 4. As seen

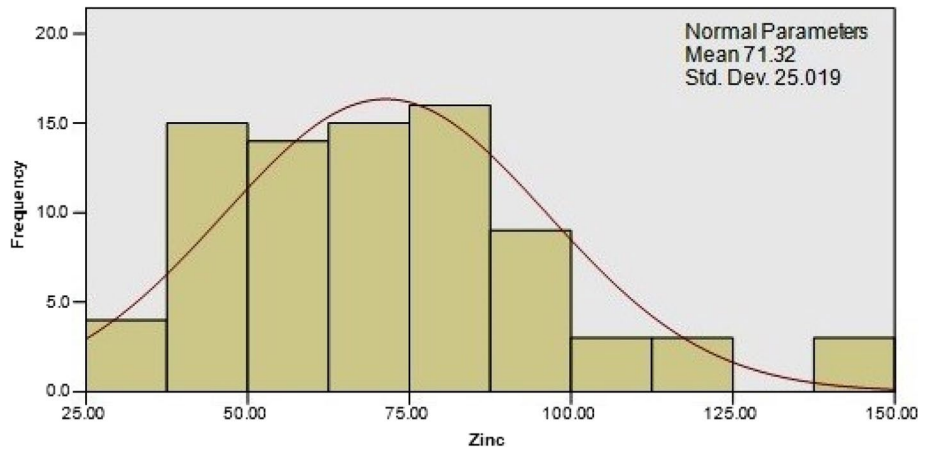

Fig. 1 Zinc level among children with liver cirrhosis

Table 3 Magnesium, zinc, and vitamin D level among children with liver cirrhosis

	Normal range	Median	Mean ± SE	Higher than normal	Lower than normal	Within normal range	Range (min, max)
Magnesium	0.8–1 mmol/L	2.1	2.07 ± 0.275	99%	–	1%	0.93–2.6
Zinc	50–150 mcg/dl	69.7	71.32 ± 25.01	–	23%	77%	25.–147.1 mcg/dl
Vitamin D	20–100 ng/ml	19.3	31.41 ± 52.5	6%	53%	41%	1475 ng/ml

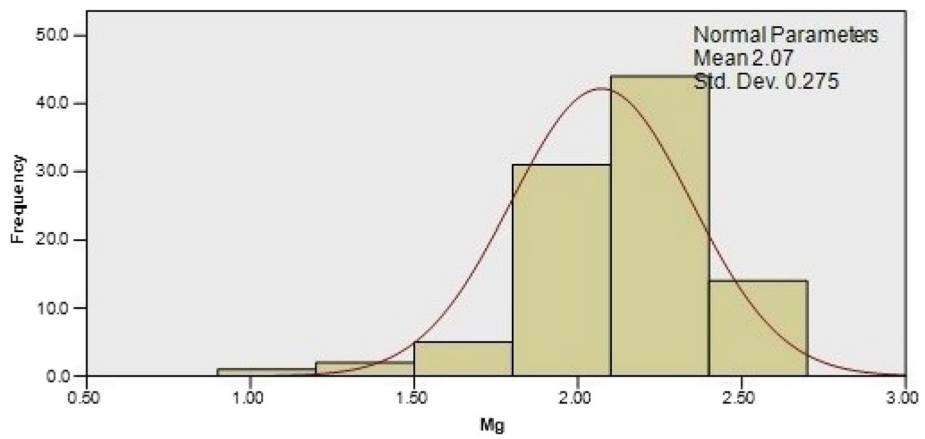

Fig. 2 Magnesium level among children with liver cirrhosis

in Table 4, the highest mean level of vitamin D was seen among PFIC patients. Vitamin D levels according to etiology of liver disease are shown in Fig. 4.

Discussion

The liver is the main organ for the metabolism of nutrients.

Our study showed that 53% of the children with liver cirrhosis had vitamin D deficiency. In the study by Jamil et al., vitamin D deficiency was found in 88% of patients with liver disease [10]. In the study by Paternostro et al., vitamin D deficiency was seen in 40% of the patients with liver cirrhosis [11]. In the study by Konstantakis et al., vitamin D deficiency had a great relationship with liver function [12]. In the study by Buonomo et al., vitamin D

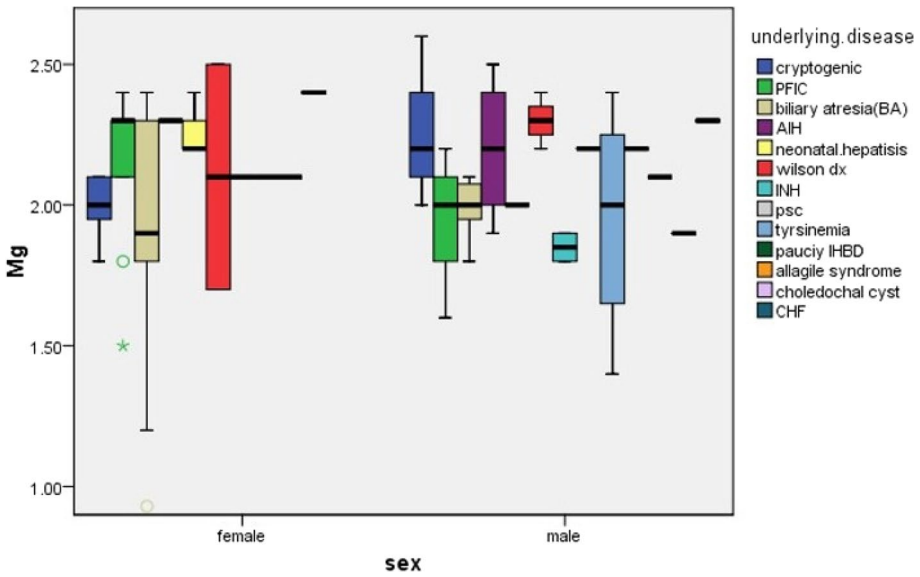

Fig. 3 Magnesium level according to the etiology of liver cirrhosis

deficiency harmed the survival of the patients with liver cirrhosis [13]. We did not find a significant correlation between vitamin D level and PELD score. A significant correlation between vitamin 25-OH vitamin D3 level and poor outcome according to MELD and Child-Pugh score was found by Kim et al. [14].

Kumar et al. found that 80% of patients with liver cirrhosis had some degree of vitamin D deficiency [15]. In another study, 87% of patients with chronic liver disease showed insufficient or deficient vitamin D [16]. Vitamin D deficiency was shown in most studies. In the study by Jazayeri et al., the prevalence of vitamin D deficiency in Iranian boys and girls were 35% and 61%, respectively [17]. The prevalence of vitamin D insufficiency in Iranian children and adolescents was 31% [17]. As a result, the frequency of vitamin D deficiency was higher than healthy apparent Iranian children.

In the current study, magnesium level was higher than the normal level among 99% of children with liver cirrhosis. But in the study by Kohen et al., magnesium deficiency was frequent among patients with liver cirrhosis [18]. In the study by Wang et al., magnesium deficiency was reported in patients with liver cirrhosis [19]. Significant changes in magnesium levels between patients with liver disease and the healthy population were not found in the study by Rahelic et al. [20]. In another study by Göksu and Ozsoylu, magnesium was decreased among children with liver cirrhosis [21]. Other studies had similar findings in terms of magnesium deficiency in liver cirrhosis [22]. Among Iranian healthy children, the prevalence of hypomagnesemia was 5.9% [23]. Magnesium

Table 4 Magnesium, zinc, and vitamin D among children according to the underlying disease

Underlying disease		Vit. D (ng/dl)	Mg (mmol/dl)	Zinc (mcg/dl)
PFIC	*N*	24	24	20
	Mean	50.3267	2.0917	77.1900
Biliary atresia (BA)	*N*	26	26	22
	Mean	25.4619	1.9492	69.9045
AIH	*N*	6	5	5
	Mean	35.7383	2.2200	56.2400
Neonatal hepatitis	*N*	5	6	4
	Mean	33.5080	2.2167	62.8750
Wilson disease	*N*	5	5	3
	Mean	11.4880	2.2200	71.8667
INH	*N*	3	3	2
	Mean	12.9900	1.9333	99.4500
PSC	*N*	2	2	2
	Mean	34.1000	2.1500	47.0000
Tyrosinemia	*N*	5	5	5
	Mean	39.23	1.98	81.06
Paucity IHBD	*N*	2	2	2
	Mean	18.87	2.30	87.00
Alagille syndrome	*N*	1	1	1
	Mean	6.27	2.10	89.00
Choledochal cyst	*N*	1	1	1
	Mean	10.47	1.9000	76.00
CHF	*N*	1	1	1
	Mean	23.7000	2.30	73.90
Total	*N*	81	81	68
	Mean	33.22	2.06	72.66

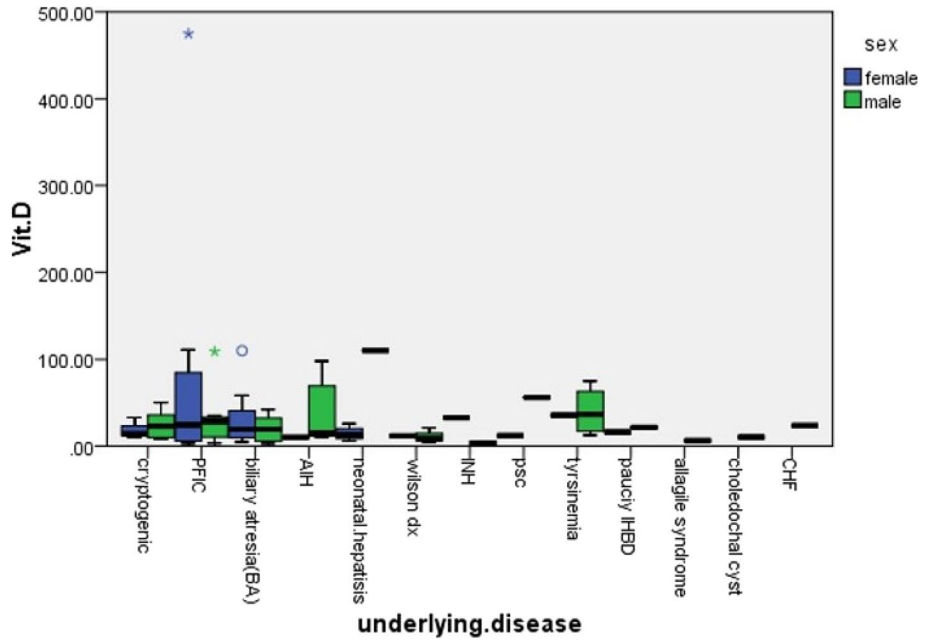

Fig. 4 Vitamin D level among different etiologies of cirrhosis

deficiency was expected in children with liver cirrhosis. But this difference has happened. Diet may have played an important role for example rice which was an important source of Iranian food [24]. Another study is recommended to find the cause of hypermagnesemia among children with liver cirrhosis.

Zinc deficiency was seen in 23% of children in our study. Zinc deficiency is a major health problem especially in developing countries [25]. Zinc deficiency was very frequent among developing countries rated between 46% in the Middle East and 79% in South Asia [26, 27]. Even in Western European countries, the prevalence of zinc deficiency was high [28]. Zinc deficiency may lead to hepatic encephalopathy [29, 30]. Zinc deficiency was reported as a frequent finding among cirrhotic patients [31]. In the study by Katayama et al., zinc deficiency was common among patients with liver cirrhosis. In the study by Sengupta et al., zinc deficiency was highly prevalent among children with liver cirrhosis [32]. Sengupta and colleagues recommended screening for zinc deficiency [32]. In the study by Azemati et al. among 3500 Iranian healthy children aged 7–15 years, the prevalence of zinc deficiency was 5% [33]. In the study by Dehghani et al., the prevalence of zinc deficiency was 7.9% [27]. In the study by Dehghani et al. on 902 children without liver disease [27], zinc level was 122.3 ± 55 mcg/dl. The result of our study was lower than Dehghani et al.'s study and show zinc level was lower in children with cirrhosis than in children without liver disease. Although due to the high frequency of zinc deficiency in the world [26], multiple factors play a role in zinc deficiency in children with liver cirrhosis. As a result, the prevalence of zinc deficiency among children with liver cirrhosis was higher than that among Iranian healthy apparent children [27]. According to the high prevalence of zinc deficiency in the world, cirrhosis may play as one factor in zinc deficiency.

Conclusion

Zinc and vitamin D deficiency was prevalent among children with liver cirrhosis. The serum magnesium level was higher in cirrhotic children compared to the standard level. Further studies are recommended to clarify changes in magnesium and zinc in children with liver cirrhosis with more samples.

Limitation

This study was a single-center study. In this study, we used standard values as the reference instead of healthy control. We used the standard level of zinc and magnesium for comparison. Due to the low sample size of some etiologies, some analysis was not possible. Dietic history was not included in the current research.

Abbreviations

AIH: Autoimmune hepatitis; CHF: Congenital hepatic fibrosis; INH: Idiopathic neonatal hepatitis; PELD Score: Pediatric Endstage Liver Disease Score; PFIC: Progressive familial intrahepatic cholestasis ; PSC: Primary sclerosing cholangitis.

Authors' contributions
SMD had the main idea and wrote the manuscript and also has a role in the revision of the manuscript. AA has arole in writing the manuscript and revision of the manuscript. PB has a role in data collection, writing a researchproposal, and data analysis. HJ performed the literature review and has a role in writing manuscript, revision ofmanuscript, and data analysis. All the authors read and approved the manuscript.

Declarations

Competing interests
The authors declare that they have no competing interests.

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