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DOSE CHRONIC LIVER DISEASE IN CHILDREN AFFECT SERUM COPPER, IRON AND, FERRITIN? HOSPITAL BASED STUDY

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ABSTRACT

Background: Chronic liver disease (CLD) significantly alters trace element metabolism due to impaired hepatic function. Trace elements such as copper, iron, and ferritin are integral to physiological processes, and their dysregulation may exacerbate liver pathology. This study aimed to evaluate serum levels of copper, iron, and ferritin in children with CLD. **Methods:** A hospital-based case-control study was conducted at the Children Welfare Teaching Hospital in Baghdad between November 2021 and September 2022. The study included 62 pediatric CLD patients and 60 age- and sex-matched healthy controls. Serum levels of copper, iron, and ferritin were measured and statistically analyzed using SPSS version 23, with significance set at $p<0.05$. **Results:** The mean serum copper and ferritin levels were significantly higher in the CLD group compared to controls (118.8 ± 42.9 µg/dL vs. 82.3 ± 19.9 µg/dL, p=0.0001; and 303.8 ± 550.6 ng/mL vs. 146.6 ± 237.7 ng/mL, p=0.049, respectively). Serum iron levels did not differ significantly between groups (p=0.64). Ferritin levels showed positive correlation with time since diagnosis and PTT, while iron levels correlated with total protein. No significant linear correlations were found with serum copper. **Conclusion:** Elevated serum copper and ferritin levels are common in pediatric CLD and may contribute to disease progression through oxidative stress. Regular monitoring and potential dietary or pharmacological interventions targeting trace element imbalances could aid in the management of pediatric CLD.

KEYWORDS: Chronic, Liver, Disease, Children, Serum Copper, Iron, Ferritin.

INTRODUCTION

Much evidence indicates that trace elements play important roles in a number of biological processes. Trace elements act through activating or inhibiting enzyme reactions, competing with other elements and metalloproteins for binding sites, affecting the permeability of cell membranes and exerting enhancing effects on the progression of some diseases.[1] Copper (Cu) is an essential micronutrient. This mineral functions in diverse processes, such as infant growth, bone strength, host defence mechanisms, iron transport, red and white blood cell maturation, myocardial contractility, brain development, and cholesterol and glucose metabolism.[2,3] Iron (Fe) has several vital functions in the body. It has the ability in oxygen transport by hemoglobin, which is the main function of Fe in the body, but also in DNA synthesis and energy production. The loss of regulation of Fe metabolism and subsequent development of Fe overload is seen in hereditary hemochromatosis (HHC), a common inherited disorder which may lead to progressive organ dysfunction including cirrhosis, arthritis, hypogonadism, diabetes mellitus and cardiomyopathy.[3-6] The data in Iraq related to the above trace elements is very limited in its association with chronic liver disease; hence, this study was conducted to assess the serum copper, iron and ferritin levels in patients with chronic liver disease in the pediatric age group. Aim: To evaluate the profile of the serum copper, iron, and ferritin in children with chronic liver disease.

METHOD

We conducted a case-control study to evaluate the levels of copper, iron, and ferritin in children suffering from chronic liver disease. This study was conducted in Baghdad, at Children Welfare Teaching Hospital, in a period from November 2021 till September 2022. The study population involved all children with CLD with the

exclusion of patients who were critically ill children, had uncertainty of diagnosis, or had parental refusal of study participation. Sixty-two patients with CLD younger than 15 years old with 60 matched age and gender were included as a healthy control group. Data collected by direct questions regarding demographic data: (Age, Gender, Diagnosis, Duration of disease (Time since diagnosis), Medical history, Family history of same condition, Weight and height). Blood drawing for both patients and control groups: all investigations were done in the laboratory unit at Children Welfare Teaching Hospital, except for the investigation for serum copper level done in the toxicology centre in Surgical Specialities Hospital. The samples of blood drawn for measuring: S. Iron, GOT, GPT, ALP, Total protein, Albumin, Total bilirubin, Direct and Indirect bilirubin, PT, PTT, and INR, S. copper, and S. ferritin. **Statistical Analysis**: the statistical package for social sciences (SPSS) software version 23 had been used for data entry and analysis. The correlation coefficients in regression were used to find the association between trace elements and other variables. P<0.05 was used as the threshold for statistical significance.

RESULTS

There were 122 participants in this study, 62 patients included as studied group and 60 healthy individual (matched age and gender) included as control group. The mean age was 5.3 ± 4.2 years. The mean weight among patients' group was 18.4 ± 5.1 Kg. Males were representing 54.9% and females representing 45.1% of all participants, the distribution of gender was equal across control and patient groups (Figure 1).

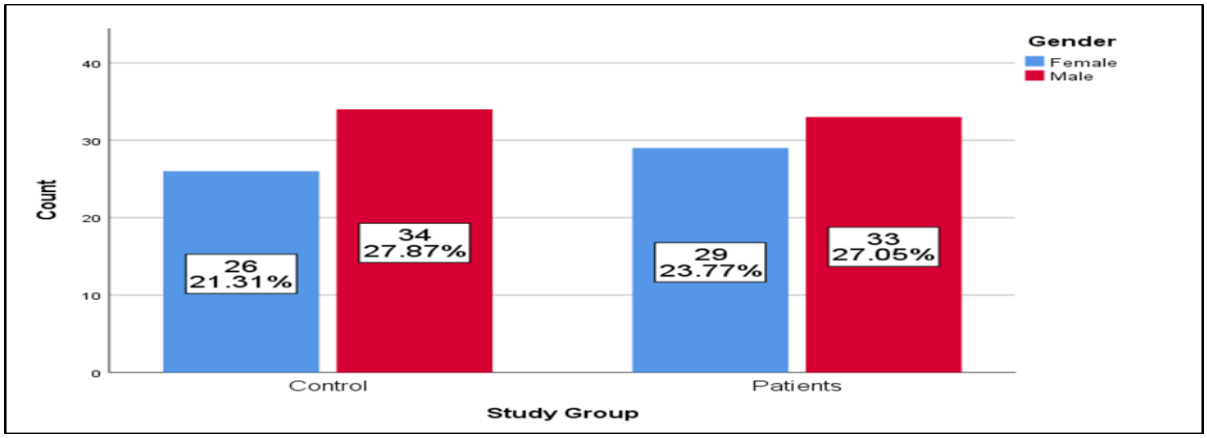

Figure 1: Gender distribution across patients and control groups.

Regarding the diagnosis, the most frequent diagnosis was Wilson disease (9 patients) followed by AIH (8 patients) (Table 1).

Table 1: Diagnosis distribution.

Study sample		Frequency	Percent
Control		60	49.2
Patients	Wilson disease	9	7.4
	AIH	8	6.6
	Biliary atresia	7	5.7
	Undiagnosed CLD	7	5.7
	Hepatitis C virus	6	4.9
	Glycogen storage disease	6	4.9
	Progressive familial intrahepatic cholestasis	5	4.1
	metabolic liver diseases	4	3.3
	Idiopathic neonatal hepatitis	3	2.5
	CMV	2	1.6
	Hepatitis B virus	1	0.8
	Alpha1 antitrypsin deficiency	1	0.8
	Niemann-Pick disease	1	0.8
	Primary sclerosing cholangitis	1	0.8
	Toxoplasmosis	1	0.8
Total		122	100

The mean copper level was 118.8 ± 42.9 among patients' group and 82.3 ± 19.9 among control group. The ferritin level was 303.8 ± 550.6 among patients' group and 146.6 ± 237.7 among control group. Both Copper and ferritin were significantly higher among patients' group in comparison to control group ($p<0.05$). The iron level was 79.5 ± 39.9 among patient group and 86.5 ± 109.6 among control. There was no significant difference in iron level between patients and control groups (p=0.64) (Table 2).

Table 2: Comparison of Copper, Iron, and ferritin between patients and control groups.

	Control		Patients		
	Mean	**SD**	**Mean**	**SD**	**P value**
Copper	82.3	19.9	118.8	42.9	**0.0001**
Iron	86.5	109.6	79.5	39.9	0.64
Ferritin	146.6	237.7	303.8	550.6	**0.049**

The correlation coefficients regression for copper showed that none of the studied variable showed liner correlation with copper (Table 4), while iron showed coefficients regression correlation with TP only (p=0.008) (Table 11), and ferritin showed coefficients regression correlation with time since diagnosis and PTT (p=0.004 and 0.04 respectively) (Table 3).

Table 3: The correlation coefficients regression for copper, iron, and ferritin.

	Copper		Iron		Ferritin	
	Standardized Coefficients	**P value**	**Standardized Coefficients**	**P value**	**Standardized Coefficients**	**P value**
Age	0.482	0.213	0.316	0.351	-0.187	0.563
Weight	0.059	0.710	0.046	0.744	-0.158	0.240
Height	-0.332	0.405	-0.066	0.850	0.099	0.766
Time since diagnosis	-0.091	0.595	0.059	0.695	0.432	**0.004**
TSB	-0.156	0.420	0.053	0.756	-0.017	0.914
Direct	-0.053	0.808	0.106	0.579	0.165	0.366
Indirect	0.127	0.489	0.039	0.806	-0.108	0.485
SGPT	0.169	0.346	0.104	0.509	-0.235	0.124
SGOT	-0.253	0.159	0.040	0.797	0.280	0.066
AIP	0.110	0.469	0.173	0.198	0.025	0.847
T.P	0.090	0.690	0.544	**0.008**	-0.142	0.453
Albumin	-0.205	0.320	-0.200	0.268	-0.164	0.344
Pt	-0.084	0.840	0.343	0.352	-0.426	0.229
PTT	0.160	0.564	-0.098	0.687	0.484	**0.043**
INR	-0.083	0.816	-0.039	0.903	-0.123	0.683

The categorization of lab. results showed that, there were 16 (25.8%) patients had copper level higher than 152.5. There were 16 (25.8%) patients had low Iron level and only 4 (6.5%) patients had high iron level. For ferritin, there were 25 (40.3%) patients had high ferritin level (Table- 4).

Table 4: Laboratory results category.

		Count	**Layer N %**
Copper	≤ 150	46	74.2%
	> 150	16	25.8%
Iron	Low	16	25.8%
	Normal	42	67.7%
	High	4	6.5%
Ferritin	Normal	37	59.7%
	High	25	40.3%

DISCUSSION

This study investigated the levels and correlations of trace elements—specifically copper, iron, and ferritin—among children with chronic liver disease (CLD) compared to healthy controls. Trace elements play dual roles as oxidants and antioxidants, with the liver serving as the central regulator of their metabolism, transport, and excretion, which directly influences their bioavailability and potential toxicity.[7] The mean age of children in the CLD group was five years, consistent with findings by Roy et al.[8] and Tahir et al.[9], where most children with CLD were older than five years, possibly because certain liver diseases take time to present full clinical manifestations. A significantly lower body weight was observed in CLD patients compared to controls, likely due to CLD-related complications such as growth retardation.[10] Slight male predominance was noted in the patient group, consistent with Salih et al.[6] and Tahir et al.[9], though differences in sample size may have influenced the degree of male predominance across studies. Etiologically, Wilson's disease emerged as the most common cause of CLD in the current study, followed by autoimmune hepatitis (AIH). In contrast, Salih et al.[6] found biliary atresia and galactosemia to be

more prevalent in a younger cohort. Pinto et al.[10] and a study from Egypt[11] identified biliary atresia and chronic hepatitis, respectively, as leading causes. Hanif et al.[12] also reported hepatitis B as the most common etiology. These variations are likely due to differences in patient age and regional disease prevalence. Serum copper and ferritin levels were significantly higher in CLD patients compared to controls ($p < 0.05$), while iron levels did not significantly differ. This contrasts with Raouf et al.[13] and Ibrahim[1], who found elevated levels of all three trace elements in CLD patients. Jurczyk et al.[15] observed similarly non-significant differences in iron levels in adults with CLD. These discrepancies may reflect different study populations and methodologies. The observed copper elevation can be attributed to impaired biliary excretion resulting from cholestasis, a common feature of CLD, since bile is the main route for copper elimination. Weak but significant positive correlation was found between serum copper and iron ($r = 0.27$, $p = 0.03$), aligning with Ibrahim's findings[16], while ferritin showed no correlation with copper. Elevated iron levels are known in conditions such as hepatitis and hemochromatosis, while deficiencies may arise from chronic disease or poor intake.[17] Gender analysis revealed no significant differences in trace element levels between males and females, possibly due to similar etiologies across pediatric patients. Regression analysis indicated that none of the clinical or laboratory variables were linearly correlated with serum copper. Given the oxidative and potentially malignant effects of elevated copper, dietary copper restriction may be beneficial in CLD management, as suggested by Goodman et al.[18] High copper levels are known to induce oxidative damage, necrosis, and developmental toxicity through enzyme inhibition.[19] Among the CLD patients, 25.8% had elevated copper, another 25.8% had low iron, and 40.3% had elevated ferritin. These results highlight significant disturbances in trace element homeostasis in over a quarter of the study population.

CONCLUSION

Elevated copper and ferritin levels were characteristic findings in pediatric CLD, with implications for liver function and oxidative stress. Future studies are warranted to determine whether correcting these trace element imbalances could delay or prevent CLD complications.

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