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High serum zinc levels in HELLP syndrome

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Abstract

Aim: HELLP syndrome is a possibly fatal complication of severe preeclampsia that occurs throughout pregnancy. Biochemical abnormalities are one of the hypotheses proposed to explain the disease's physiopathological symptoms. According to studies, different congenital illnesses are caused by a lack of nutrients such as zinc, copper, iron, manganese, and folic acid, the demand for which increases during pregnancy. The objective of this study was to compare serum zinc and copper levels in healthy women and pregnant women with HELLP, as well as to investigate if there was a relationship between the two.

Materials and Methods: The serum zinc and copper levels of 20 healthy pregnant women and 20 pregnant women with HELLP were measured using an Atomic Absorption Spectrophotometer.

Results: Serum Zn levels in HELLP syndrome patients were significantly higher than in healthy pregnant women ($p<0.05$). Furthermore, a negative connection was found between Zn levels and PLT, and a positive correlation between LDH (r:-0.322, $p<0.05$; r:0.384, $p<0.05$ respectively).

Conclusion: In conclusion, high serum zinc levels in HELLP syndrome can be evaluated in the laboratory.

Introduction

Pregnancy-related hypertension is one of the most serious pregnancy problems that might risk the mother's life. The most severe symptom of this disease, also known as pregnancy-induced hypertension, is Hemolysis, Elevated Liver Enzymes, and Low Platelet (HELLP) syndrome (PIH) [1]. Trace elements are those found in milligrams per kilogram or less in human and animal tissues. In the case of total absence, the organism dies; in the case of restricted intake, the organism survives. Excessive ingestion results in toxicity, whereas ingestion in the proper proportions results in a healthy life and good condition of biological functions [2].

Zinc (Zn), an outstanding biological trace element, is essential for all cell growth, DNA replication, RNA transcription, cell division and activation, and the action of more than 300 enzymes. During pregnancy, the body's need for zinc grows considerably [3]. Many studies have shown that Zn deficiency causes a wide range of congenital abnormalities [4]. Copper (Cu) is a trace element that is present in the structure of numerous enzymes, including lysyl oxidase, cytochrome oxidase, trosinase, ceruloplasmin, and superoxide dismutase. Protein metabolism problems, anemia, growth problems, abnormal keratinization, hypothermia, skeletal deformities, and neonatal low birth weight have all been associated to Cu deficiency [5].

While the metabolism of abundant elements such as Ca and Mg has been studied in patients with HELLP syndrome in recent years, no studies on its association with trace elements have been reported. The goal of this study was to assess blood Zn and Cu levels in HELLP syndrome patients and healthy pregnant women, as well as to investigate trace element levels in HELLP syndrome patients.

Materials and Methods

Study design

The study was approved by the Non-Drug Academic Research Ethics Committee (Ataturk University Health Sciences Ethics Committee date: 29.11.2021, no: 2012.5.1/7). It was carried out in accordance with the Declaration of Helsinki Principles and informed consent was obtained from all participants. 20 Tweenty patients with HELLP syndrome (HELLP) and 20 healthy controls (CG) were

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hospitalized to the Gynecology and Obstetrics Clinic at Ataturk University Research Hospital. The study involved 40 pregnant women, Pregnant women who presented to the hospital for routine pregnancy follow-up, with gestational hypertension, serum total protein<1.7 mg/dL, AST>70 IU/mL PLT<100,000 cells/L, and were diagnosed with HELLP were chosen for the HELLP group. The CG consisted of pregnant women who presented to the hospital for routine pregnancy follow-up and were the same age as the HELLP group but did not have any health issues. The estimated power (1-beta) test value was calculated as 0.85 with the G-Power program. Initially, 30 individuals with HELLP syndrome were to be included in the research. Because it is a rare disease, however, this amount could not be attained. Due to additional comorbidities, five pregnant women were eliminated from the study, out of a total of 25 patients with HELLP syndrome. Blood samples were unavailable because three pregnant women gave birth in different hospitals. Pregnant women with chronic diseases, fetal abnormalities, impaired obstetric anamnesis, or gestational diabetes, on the other hand, were excluded from the study. Approximately 5 mL of venous blood was drawn from both groups immediately after birth and put into gel biochemistry tubes. Alanine transferase (ALT), aspartate transferase (AST), platelet (PLT), total protein (TP), and lactate dehydrogenase (LDH) levels were determined in all participants using a conventional biochemistry autoanalyzer (Beckman Coulter 5008). The blood samples were drawn for 30 minutes to analyze Zn and Cu levels. After waiting at room temperature, it was centrifuged for 10 minutes at 3500 rpm. Aliquoted serum samples were maintained in a deep freezer at -80 °C until the day of trace element analysis.

Biochemical analysis

To plot standard Zn and Cu graphs, 999±2 mg/L Zn and 1000±2 mg/L Cu stock standards (Merck, Germany) were used. 100 µL of the stock standard was obtained for Zn analysis, and the volume was diluted to 10 mL (10 mg/L) with 0.2% HNO_3 (Merck, Germany). Similarly, 100 µL of the Cu stock standard was collected and the volume was diluted to 10 mL (10 mg/L) with 0.2% HNO_3. After diluting the intermediate stock standard solutions with 0.2% HNO_3, Zn and Cu standard solutions with concentrations of 100, 50, 25, and 12.5 µg/dL were created. A Zn hollow cathode lamp (213.9 nm wavelength) was utilized for Zn analysis, and a Cu hollow cathode lamp (324.8 nm wavelength) was used for Cu analysis. Standard graphics were developed after measurements were taken in the flame unit of the atomic absorption spectrophotometer (AAS, Perkin Elmer AAnalyst 800). All serum samples were withdrawn from the freezer and brought to room temperature before being vortexed on the working day. Serum samples were diluted 10-fold with 0.2% HNO_3 for measurements. The blank was 0.2% HNO_3, and all samples were read against the Zn and Cu standard curves and measurements were obtained.

Statistical analysis

SPSS for Windows (IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp. IBM Corp. Released 2012) was used to do data analysis. The Kolmogorov-Smirnov test revealed that the data had a normal distribution, hence the independent sample t-test, one of the parametric tests, was used. The Pearson correlation test was utilized for normally distributed variables in the correlation analysis. All data is presented as means and standard deviations. Statistically, p<0.05 was judged significant.

Table 1. Age distribution of HELLP and CG and results of measured parameters.

	HELLP n=20 X ± SD	CG n=20 X ± SD	P value
Age (year)	32.4±6.8	29.1±5.3	0.84
ALT (U/L)	147.9±106.5	12.0±5.8	<0.001[a]
AST (U/L)	315.3±355.6	24.0±7.8	<0.001[a]
PLT (10^3/µl)	100.7±35.3	216.1±48.6	<0.001[a]
TP (g/dL)	5.2±0.7	6.1±1.8	0.051
LDH (U/L)	938.8±593.2	265.5±99.2	<0.001[a]
Zn (µg/dL)	123.7±65.3	92.6±23.5	0.038[a]
Cu (µg/dL)	200.5± 44.1	204.4±34.6	0.751

HELLP:Hemolysis, Elevated Liver Enzymes ve Low Platelet, CG:Control Group, PLT: Platelet ALT: Alanine Aminotransferase, AST: Aspartate Aminotransferase, LDH: Lactate Dehydrogenase, TP:Total protein, Zn:Zinc, Cu:Copper, a:Statistically significant.

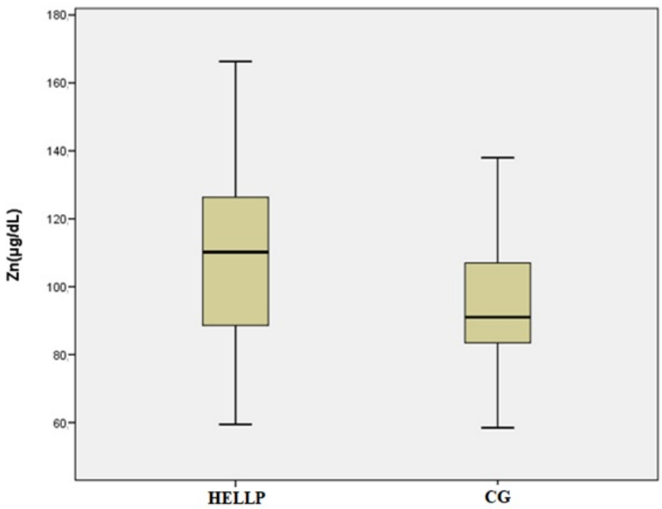

Figure 1. The comparison of serum Zn levels in the HELLP and CG groups (p<0.05).

Results

There was no age difference between the HELLP and control groups in the current study (p>0.05). When ALT, AST, PLT, and LDH levels from routine analyses were examined, it was discovered that the HELLP group had a significantly higher level than the CG (p<0.001). The HELLP group had a significant increase in TP levels (p:0.05).

A significant rise in serum Zn levels was reported in HELLP compared to CG as a consequence of AAS trace element assays (p<0.05). Although serum Cu levels in HELLP were found to be lower than in CG, there was no statistical significance (p>0.05). Table 1 shows the age,

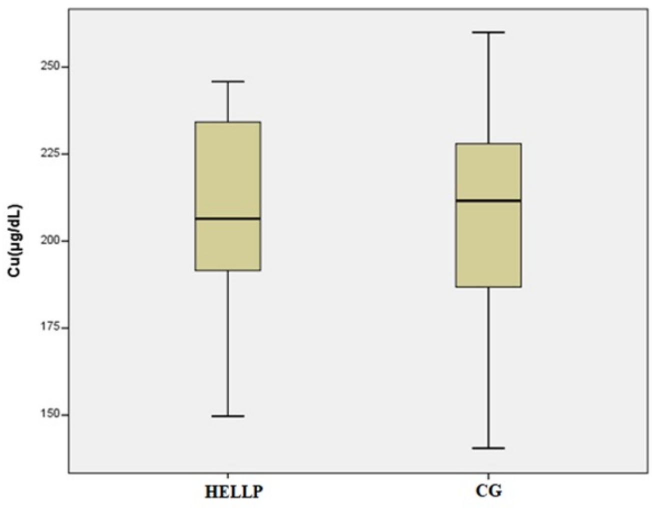

Figure 2. The comparison of serum Cu levels in the HELLP and CG groups p>0.05).

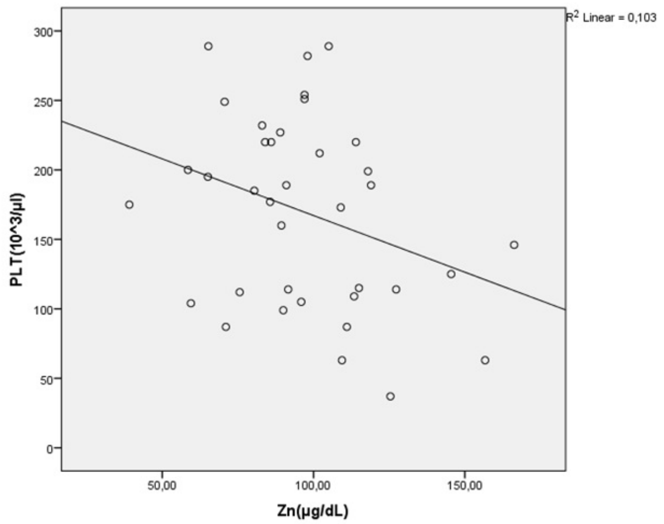

Figure 3. The correlation graph between serum Zn and PLT (r:-0.322, p<0.05).

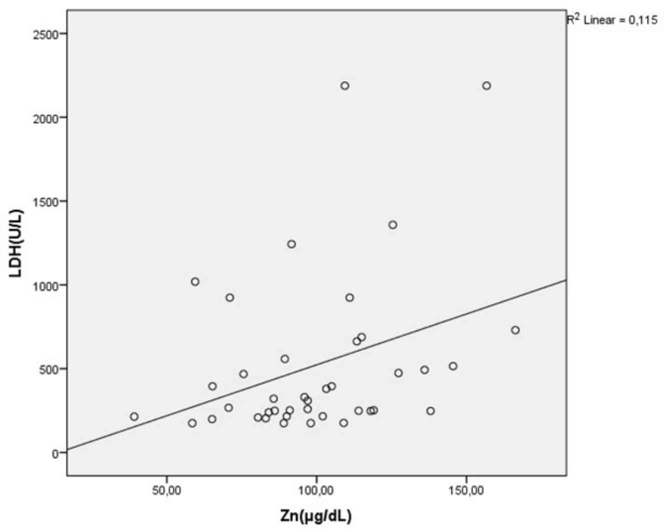

Figure 4. The correlation graph between serum Zn and LDH (r:0.384, p<0.05).

ALT, AST, LDH, PLT, TP, Zn, Cu levels of HELLP and CG in our study. Figures 1 and 2 show a comparison of serum Zn and Cu levels in HELLP and CG.

In the correlation analysis performed to determine whether there is a relationship between the measurements, a negative (r:-0.322, p<0.05) correlation was found between serum Zn levels and PLT, and a positive (r:0.384, p<0.05) correlation was found between LDH. There was no correlation identified between serum Cu levels and any other measures Figures 3 and 4 show the relationship between serum Zn levels and PLT and LDH.

Discussion

This is the first study to investigate zinc levels in HELLP syndrome. In the current investigation, we used an AAS device to detect serum Zn and Cu levels to determine whether there is a change in zinc and copper levels, which are critical trace elements, in pregnant women with HELLP syndrome. While there was no difference in copper levels, serum Zn levels were substantially greater than in healthy individuals. We also observed a negative relationship between zinc and PLT levels, as well as a strong positive relationship between zinc and LDH.

Combined macronutrient and micronutrient deficits are significant health issues in undeveloped countries, particularly among pregnant women. The need for numerous minerals, such as Zn, Cu, B12, and vitamin C for the development of the fetus increases even more during pregnancy [6-8]. Elements such as Zn, Cu, selenium (Se), and magnesium (Mg) are necessary for the body's function and growth. Through various enzymes and transcription factors, Zn and Cu play a significant role in the regulation of developmental processes in both humans and animals. Changes in their levels during pregnancy can have an impact on the fetus [9].

Trace elements are well known to play an important role in living organisms. In this regard, the concentrations of these elements in various regions of the human body have been determined, and their associations with various disorders have been thoroughly examined [10]. As a result, it has been found that several diseases are caused by trace element deficiencies or excesses [11-12]. Similarly, it has been shown that some pathological circumstances alter the normal metabolism of many elements [13].

There was little research on trace elements in patients with HELLP syndrome in the literature. However, in a research of preeclamptic pregnant women, the relationship between high blood pressure and changes in serum Ca, Mg, and Zn levels was investigated. In this study, individuals with preeclampsia had a considerable reduction in serum Ca, Mg, and Zn levels, which was assumed to be due to hemodilution. Recent research has concentrated on the role of zinc in preeclampsia. In these investigations, serum levels of Zn and Mg were measured in both pregnant women with preeclampsia and normal pregnant women. However, diverse conclusions were reached in this research, indicating that there was no decrease, increase, or change [14-21]. Another study revealed that low Zn, Ca, and Mg levels may be predisposing factors in the pathophysiology of preeclampsia [22].

Serum Ca, Mg, and Zn levels in preeclamptic women were evaluated in a study conducted by Jain et al., and these two elements were shown to be lower in the patient group. They hypothesized that this outcome was related to blood pressure and stressed that a deficiency of these elements may cause an increase in blood pressure in preeclamptic women [23]. In a cohort analysis, Liu et al. reported that low blood Mn and high Cd values were more likely to develop preeclampsia in women [24].

Koçak et al. analyzed the plasma Zn values collected from preeclampsia patients and healthy control groups in their study and showed that the plasma Zn values of the patient group were significantly lower. They noted that future investigations in pregnant women with problems should investigate plasma Zn levels [25]. The only study on trace element levels in HELLP syndrome, Sak et al. In their study, Cu and ceruloplasmin values were examined in this patient group, and they found that Cu levels were higher in the HELLP group than in the mild and severe preeclampsia groups. In our study, Cu values were found to be lower than healthy controls, but this decrease was not statistically significant [26].

Conclucion

Serum Zn levels in pregnant women with HELLP syndrome were found to be considerably higher than in healthy pregnant women. This elevation reminds us of hemolysis, a clinical symptom of HELLP syndrome. Because the zinc level in the erythrocyte is higher than that in the plasma, and the content of the damaged erythrocytes is spilled into the plasma, the zinc levels may be elevated. Again, the positive link between Zn and LDH gives support to this. As a result, we reported an increase in zinc levels as well as an increase in liver enzymes in HELLP syndrome as a laboratory finding.

Limitations

Since the incidence of HELLP syndrome is 8.5% in our country, the small number of patients is one of the limitations of our study.

Author contributions

All authors have accepted responsibility for the entire content of this manuscript and approved its submission.

Competing interests

The authors state no conflict of interest.

Informed consent

Informed consent was obtained from all individuals included in this study.

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Ethics approval

The study was approved by the Non-Drug Academic Research Ethics Committee (Ataturk University Health Sciences Ethics Committee date: 29.11.2021, no: 2012.5.1/7).

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