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Role of Trace Elements in Chronic Liver Disease

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ABSTRACT

Background: A major side effect of Cyclophosphamide during chemotherapy is haemotoxicity. Use of natural products like Royal jelly reduces the adverse effect of a drug. A Current study was an effort to find out the potential defensive effects of Royal jelly against hemotoxicity induced by cyclophosphamide in male albino mice.

Methods: Male Swiss albino mice of 20±5 gms were unevenly divided into six groups; G1: normal control group 0.9% saline solution I.P. weekly, G2: Royal jelly (100 mg/kg/d) CMC suspended administered by orally, G3: cyclophosphamide (50 mg/kg/week) was injected intra peritoneally, G4: I.P. cyclophosphamide (50 mg/kg/week) along with Royal jelly(100 mg/kg/d), G5: I.P. cyclophosphamide (50 mg/kg/week) with Royal jelly(250 mg/kg/d), G6: I.P. cyclophosphamide (50 mg/kg/week) and Royal jelly (500 mg/kg/d). Experiment lasted for 12 weeks. The measurement of hematological parameters CBC was performed using automated hematology system. Mean±SEM one way ANOVA followed by Tukey's test were performed to find out the significant difference between groups.

Results: Cyclophosphamide treated mice exhibit leucopenia, erythrocytopenia, thrombocytopenia and the significant reduction in hemoglobin (Hb), (PCV), (MCV), (MCH), and (MCHC) as compared to control group. The administration of Royal jelly to CPA treated mice, according to the present experimental plan significantly improves the alterations induced in haemogram.

Conclusion: It was suggested that Royal jelly ameliorate cyclophosphamide-induced hematological alterations, thus it might be used as a dietary protective natural remedy during the chemotherapy.

Key-words: Heliothis armigera, Argemone mexicana, Ethanol, acetone, Epithelial lining, Epithelial cells, vacuoles, Gut lining, Gut wall

INTRODUCTION

Trace elements are mineral elements present in small quantities in the human body and are essential for maintaining several physiological, cellular, metabolic, and immune functions. Among these, zinc, magnesium, and copper have important biological roles and are required for the synthesis and functioning of antioxidant enzymes, including catalase, superoxide dismutase, and glutathione peroxidase. Impairment of antioxidant defence mechanisms has been described in chronic liver disease and may contribute to oxidative stress and disease progression [1,2]. The liver plays an important role in the metabolism, storage, and homeostasis of several micronutrients and trace elements. Alteration of hepatic function may therefore disturb normal trace element metabolism. In addition, several trace elements undergo biliary excretion, and impaired liver function may alter their excretion and systemic availability. Consequently, patients with chronic liver disease may develop abnormalities in trace element concentrations through multiple mechanisms [2].

Nutritional abnormalities are common among patients with chronic liver disease and may have an important influence on clinical status and quality of life. Malnutrition in these patients may result from inadequate dietary intake, altered gastrointestinal absorption, changes in nutrient metabolism, and increased nutritional requirements. It has been

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associated with poorer health-related quality of life and may adversely influence the clinical course of liver disease [3,4].

The nutritional burden is particularly important in alcohol-related liver disease and alcoholic hepatitis. Protein-calorie malnutrition has been reported frequently in patients with alcoholic hepatitis, with the severity of malnutrition showing an association with the severity of the underlying liver disease [4,5]. Reduced nutritional intake and impaired nutritional status may consequently affect not only macronutrient balance but also the availability of essential micronutrients and trace elements.

Zinc is one of the most extensively studied trace elements in liver disease. It participates in numerous enzymatic reactions, antioxidant defence mechanisms, cellular proliferation, immune regulation, and maintenance of normal tissue function. Disturbances in zinc status have been reported in chronic liver disease and may be associated with disease severity and prognosis. Magnesium is also an important mineral involved in numerous enzymatic and cellular processes, and reduced magnesium levels have been reported in patients with chronic liver disease [2].

The causes of trace element deficiency in chronic liver disease are multifactorial. Reduced dietary intake, altered intestinal absorption, impaired metabolism, and changes in hepatic or biliary excretion may all contribute to abnormalities in trace element status. These abnormalities may coexist with protein-calorie malnutrition, making it difficult to determine whether trace element deficiency represents an independent factor or a component of overall nutritional impairment [3-5].

Nutritional intervention has an important role in the management of patients with advanced liver disease. Studies in alcoholic liver disease have demonstrated that improving calorie intake can influence clinical outcomes and survival [6,7]. However, while protein-calorie malnutrition has received considerable attention, micronutrient and trace element deficiencies may remain under-recognized. Assessment of these deficiencies may therefore provide additional information regarding the nutritional and metabolic status of patients with chronic liver disease.

Despite the recognized physiological importance of trace elements, their clinical significance in chronic liver disease requires further evaluation. Understanding alterations in serum zinc and magnesium levels may help to identify nutritional deficiencies that could potentially be addressed as part of comprehensive management. Therefore, the present study was undertaken to assess serum zinc and magnesium levels in patients with chronic liver disease and to compare these levels with those observed in healthy controls.

MATERIALS AND METHODS

Study Design and Setting- This was an observational case-control study conducted in the Department of Medicine, Chitradurga Medical College and Research Institute (CMCRI), Chitradurga, over a period of 10 months from June 2025 to May 2026. A total of 80 subjects were prospectively included in the study, comprising 40 cases of chronic liver disease and 40 healthy controls.

Study Population- The study included patients with chronic liver disease as the case group and healthy individuals as the control group. Serum zinc and magnesium levels were assessed in both groups for comparison and correlation.

Inclusion and Exclusion Criteria- The available manuscript does not specify separate inclusion and exclusion criteria for the cases or controls. Therefore, these criteria should be added based on the original study protocol/records rather than being assumed or retrospectively created.

Sample Collection- A venous blood sample of 3 mL was collected from each participant under all aseptic precautions. The sample was allowed to clot, following which serum was separated by centrifugation for biochemical analysis.

Biochemical Analysis

The following trace elements were assessed:

- **Serum Magnesium:** Estimated by the Xylidyl Blue method using a kit supplied by Raichem Diagnostics [8,9].
- **Serum Zinc:** Estimated by the NITRO-PAPS method using a kit supplied by Tulip Diagnostics [10].

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Statistical Analysis- Data were expressed as mean ± standard deviation (SD). The Chi-square test was applied to assess differences between the two groups. The unpaired *t*-test was used to compare serum magnesium and zinc levels between cases and controls. Pearson correlation analysis was performed to assess the relationship between the study variables. A *p*-value <0.05 was considered statistically significant.

Ethical Considerations- Ethical clearance was obtained from the Institute's Ethical Clearance Committee. Informed consent was obtained from both cases and controls after explaining the study procedure.

RESULTS

Table 1 presents the age-wise distribution and comparison of the study participants between the alcoholic liver disease (ALD) group and healthy controls. The study included 40 participants in each group. The mean age of patients with ALD was 55.40 ± 10.02 years, whereas the mean age of healthy controls was 56.00 ± 9.35 years. The age distribution of participants across the different age categories is also presented, allowing comparison of the demographic profile between the two groups.

Table 1: Mean age of cases and controls

	Cases	Controls	p-value
Mean age (years)	55.40±10.02	56.00±9.35	0.01

Table 2 presents the comparative serum levels of magnesium and zinc among patients with alcoholic liver disease and healthy controls. The mean serum magnesium level was considerably lower in the ALD group (1.57 ± 0.80 mg/dL) than in healthy controls (2.44 ± 0.70 mg/dL). Similarly, the mean serum zinc concentration was lower among patients with ALD (62.5 ± 10.6 µg/dL) compared with controls (94.18 ± 13.2 µg/dL). The differences observed for both magnesium and zinc were highly statistically significant ($p < 0.001$), demonstrating significant alterations in these trace element levels among patients with ALD.

Table 2: Various biochemical parameters in cases and controls

	Cases	controls	p-value
Mean serum magnesium levels(mg/dl)	1.570 ± 0.8	2.44± 0.7	0.001
Mean serum zinc levels(µg/dl)	62.5 ± 10.6	6 94.18 ± 13.2	0.001

Fig. 1 graphically illustrates the comparison of serum magnesium levels between patients with alcoholic liver disease and healthy controls. The figure demonstrates a clear difference between the two groups, with patients with ALD showing a substantially lower mean serum magnesium concentration than healthy controls. The mean magnesium level was 1.57 ± 0.80 mg/dL in the ALD group compared with 2.44 ± 0.70 mg/dL in controls. The observed difference was highly statistically significant ($p < 0.001$), supporting the finding of reduced serum magnesium levels in patients with ALD.

Fig. 2 illustrates the comparison of serum zinc levels between patients with alcoholic liver disease and healthy controls. A marked reduction in serum zinc concentration is evident among patients with ALD compared with healthy controls. The mean serum zinc level was 62.5 ± 10.6 µg/dL in the ALD group, whereas it was 94.18 ± 13.2 µg/dL among controls. This difference was highly statistically significant ($p < 0.001$), indicating a significant reduction in serum zinc levels among patients with alcoholic liver disease.

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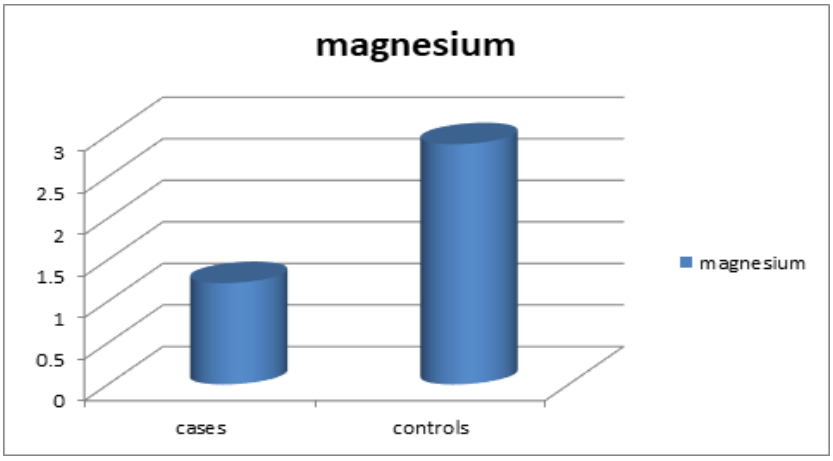

Fig. 1: Comparison of serum magnesium between cases and controls

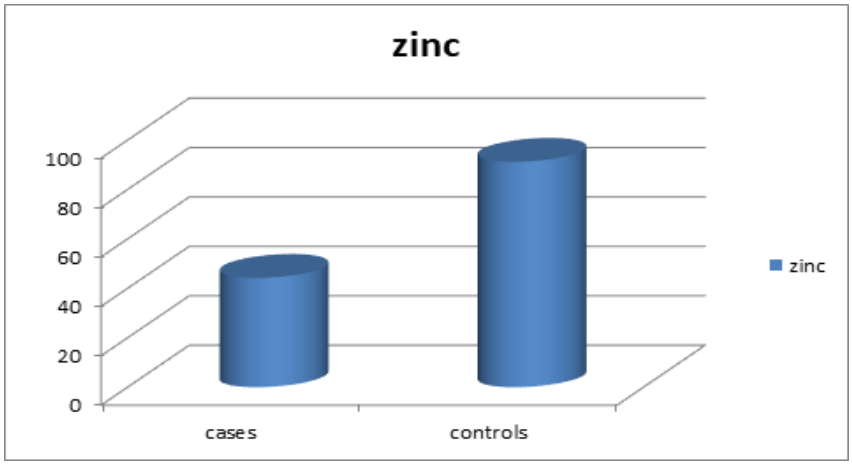

Fig. 2: Comparison of serum zinc in cases and controls

DISCUSSION

Reduced serum levels of trace elements have been reported in patients with a range of chronic liver diseases and have been shown to correlate with disease severity [6,7]. The causes of trace element deficiency are multifactorial and are mainly related to reduce dietary intake and altered gastrointestinal absorption. Zinc and selenium are among the most extensively studied trace elements in the context of liver disease. In particular, zinc deficiency has been associated with disease severity and prognosis in patients with chronic liver disease [8-10].

Magnesium deficiency has also been reported in several studies involving patients with chronic liver disease, although its association with clinical outcomes has not been consistently demonstrated [10-14]. In the present study, serum magnesium levels were markedly reduced among patients with alcoholic liver disease compared with healthy controls. The mean serum magnesium level was 1.570 ± 0.8 mg/dL in cases compared with 2.44 ± 0.7 mg/dL in controls, and this difference was highly statistically significant ($p < 0.001$).

This finding supports the presence of significant magnesium deficiency among patients with alcoholic liver disease.

Similarly, serum zinc levels were substantially lower among patients with alcoholic liver disease. The mean serum zinc concentration was 62.5 ± 10.6 µg/dL in cases compared with 94.18 ± 13.2 µg/dL in healthy controls, with the difference being highly significant ($p < 0.001$). The observed reduction in zinc levels is consistent with previous observations regarding trace element abnormalities in chronic liver disease and further supports the importance of assessing micronutrient status in these patients [8-10].

Protein-calorie malnutrition is almost universal among patients with alcoholic hepatitis and is already recognised as an important contributor to the severity of alcoholic hepatitis. Previous studies have demonstrated that nutritional status is closely related to the clinical condition of patients with alcoholic liver disease, and calorie supplementation has been reported to improve survival [14-17]. Thus, nutritional deficiency in alcoholic

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liver disease should not be considered only in terms of protein and calorie intake.

In addition to protein-calorie malnutrition, the present findings demonstrate the importance of micronutrient deficiencies in alcoholic liver disease. Both zinc and magnesium were significantly reduced in cases compared with healthy controls, suggesting that trace element abnormalities may represent an additional component of the nutritional disturbances associated with alcoholic liver disease. The causes of such deficiencies are likely to be multifactorial and may involve not only reduced dietary intake but also altered absorption, metabolism, and excretion [17,18].

The reduced levels of zinc and magnesium observed in the present study may have clinical relevance because trace elements participate in several important physiological processes. Their altered status may reflect the nutritional and metabolic disturbances accompanying chronic liver disease. However, the present cross-sectional findings cannot determine whether trace element deficiencies are independent of the overall nutritional status of patients. Nevertheless, they are likely to have additional clinical impact beyond protein-calorie malnutrition alone.

The findings of the present study therefore highlight the need for greater attention to micronutrient status in patients with alcoholic liver disease. Assessment of serum zinc and magnesium may provide useful information regarding nutritional abnormalities and may help identify patients who require further nutritional evaluation. However, whether correction of these deficiencies can directly improve clinical outcomes cannot be established from the present study.

Future experimental and longitudinal studies with larger sample sizes are needed to establish the underlying mechanisms responsible for trace element abnormalities and to determine their independent relationship with disease severity, complications, and clinical outcomes in alcoholic liver disease.

The major limitation of the present study was the small sample size**.** The cross-sectional nature of the study also limits the ability to establish a causal relationship between trace element deficiency and alcoholic liver disease. Further large-scale studies are required to confirm these findings and to establish the diagnostic and prognostic role of trace elements in alcoholic liver disease.

CONCLUSIONS

Trace element deficiency appears to be an important nutritional and metabolic abnormality among patients with alcoholic liver disease (ALD). In the present study, patients with ALD demonstrated significantly lower serum magnesium and zinc levels compared with healthy controls, suggesting substantial alterations in trace element status in this population. These deficiencies may reflect the complex nutritional and metabolic disturbances associated with chronic alcohol-related liver disease. The findings highlight the potential importance of assessing trace element status as part of the overall evaluation of patients with ALD, particularly those with advanced disease. Although the present findings demonstrate significant differences in serum zinc and magnesium levels, further studies are required to clarify their biological significance and relationship with disease progression, complications, and clinical outcomes. Future prospective studies with larger sample sizes may help determine whether correction of trace element deficiencies can contribute to improved nutritional status and clinical outcomes in patients with ALD.

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CONTRIBUTION OF AUTHORS

Research concept- Arati Ganiger, K Mallikarjuna Swamy
Research design- Arati Ganiger, K Mallikarjuna Swamy
Supervision- K Mallikarjuna Swamy
Materials- Arati Ganiger, K Mallikarjuna Swamy
Data collection- Arati Ganiger
Data analysis and Interpretation- K Mallikarjuna Swamy
Literature search- Arati Ganiger
Writing article- Arati Ganiger, K Mallikarjuna Swamy
Critical review- K Mallikarjuna Swamy
Article editing- Arati Ganiger, K Mallikarjuna Swamy
Final approval- K Mallikarjuna Swamy

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