Clinical Medicine and Medical Research
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CMMR05(02),273−278 (2025)
Received 05 Feb 2025 | Revised 28 Feb 2025 | Accepted 03 March 2025 | Published Online 21 March 2025
https://doi.org/10.52845/CMMR/2025-6-1-1

Zinc Deficiency and Depressive Disorders: A Hospital-Based Study in Kut Governorate, Iraq, 2022

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Abstract:

Background: Studies report that 19–34% of individuals with depression exhibit treatment resistance to antidepressants, with up to 50% experiencing symptom relapse. This underscores the need for alternative therapeutic strategies, such as micronutrient supplementation, in clinical management. Zinc, a trace element integral to cognitive function, learning, and behavioral regulation, has been implicated in mood disorders. Pioneering work by Hansen et al. first highlighted correlations between serum zinc levels and depressive symptoms. **Aim:** This study aimed to evaluate differences in mean serum zinc concentrations between depressed and non-depressed individuals and assess the association between zinc deficiency and depression. **Methods:** A hospital-based cross-sectional study was conducted from May to August 2022, involving 134 participants (aged 18–70 years) recruited from the Psychiatric Unit of a Teaching Hospital in Kut Governorate, Iraq. Depression was diagnosed using DSM-5 criteria. Exclusion criteria included age <18 or >70 years, pregnancy, lactation, postpartum status, diabetes, renal/hepatic failure, gastrointestinal disorders (e.g., Crohn's disease, ulcerative colitis), recent surgery, burns, hematologic conditions (e.g., leukemia), recent zinc supplementation (<1 week), and concurrent use of diuretics, valproate, or psychotropic medications. **Results:** Depressed patients exhibited significantly lower mean serum zinc levels (66.90 ± 30.51 µg/dL) compared to non-depressed subjects (108.45 ± 22.44 µg/dL; $p < 0.001$). Zinc deficiency was prevalent in 53.4% of depressed patients, with 23.3% showing marginal deficiency and 23.3% within normal range. In contrast, 77.9% of non-depressed participants had normal zinc levels, while 22.1% showed marginal deficiency ($p < 0.05$). **Conclusion:** Serum zinc levels are markedly reduced in depressed individuals, suggesting zinc deficiency may serve as a modifiable risk factor for depression. Zinc supplementation could offer therapeutic benefits in alleviating depressive symptoms.

Keywords: Zinc, deficiency, depression, Iraq

Introduction:

Zinc, an essential micronutrient, is obtained from dietary sources such as dairy, poultry, seafood, and red meat (1, 2). Due to significant variability in dietary zinc intake (up to 15-fold differences), maintaining optimal zinc homeostasis is critical. Intestinal absorption of zinc is efficient, yet deficiency may arise from factors including chronic inflammation, Helicobacter pylori infection, alcoholism, prolonged use of antacids or steroids, and certain medical conditions (3, 4). Although skeletal muscle and bone contain the highest zinc concentrations, the micronutrient is ubiquitously distributed across tissues. Circulating zinc exists primarily in protein-bound form, with only 9–17 µg/dL present in free serum fractions (5).

Emerging evidence highlights zinc's role in neurophysiological processes, with deficiencies linked to neurodegenerative and psychiatric disorders (6–12). Depression, a leading contributor to global disability and suicide, significantly impairs quality of life. Despite advances in pharmacotherapy, 19–34% of patients remain treatment-resistant, and nearly half experience relapse (13). This necessitates exploration of adjunct therapies, such as micronutrient supplementation. Zinc, in particular, modulates neurotransmission and neuroplasticity,

with seminal studies by Hansen et al. (14) and Sandstead et al. (15) establishing its relevance to depressive pathophysiology. Subsequent research corroborates associations between low serum zinc and depression severity (16, 17). In Iraq, major depressive episodes affect 7.4% of the population lifetime, with 46% of active cases classified as severe (18). Prior Iraqi studies have identified zinc deficiency as a potential biomarker for depression (19). This cross-sectional study investigates serum zinc disparities between depressed and non-depressed cohorts to elucidate zinc's role in depression etiology.

2. Methodology

Study Design and Participants

This hospital-based cross-sectional study enrolled 134 participants (aged 18–70 years) between May and August 2022. Participants were recruited from the outpatient psychiatric clinic of a teaching hospital in Kut Governorate, Iraq. Depression diagnosis was confirmed by a psychiatrist using DSM-5 criteria (20).

Exclusion Criteria

Exclusion criteria encompassed:

1. Demographic factors: Age <18 or >70 years, pregnancy, lactation, or postpartum status.

2. Medical conditions: Diabetes mellitus (DM), renal/hepatic insufficiency, pancreatic disorders, inflammatory bowel diseases (Crohn's disease, ulcerative colitis), hematologic disorders (leukemia, thalassemia, sickle cell anemia), burns, or recent surgical history (e.g., bariatric surgery within the past month).

3. Pharmacologic factors: Use of zinc supplements, diuretics, or antiepileptics (e.g., valproate/Depakin) within seven days prior to enrollment.

4. Psychiatric comorbidities: Concurrent psychological disorders.

Variables and Measurements

Data collection included demographic profiles, anthropometric measurements (weight, height), medication history, and serum zinc levels. Zinc status was classified as deficient (<60 μg/dL), marginally deficient (60–80 μg/dL), or normal (≥80 μg/dL) based on established thresholds (21).

Ethical Considerations

The study protocol received approval from the Institutional Review Board (IRB) of the participating hospital. Verbal informed consent was obtained from all participants prior to enrollment.

Statistical Analysis

Continuous variables (e.g., serum zinc levels) were compared between depressed and non-depressed groups using independent Student's t-tests. Categorical associations (zinc deficiency vs. depression status) were evaluated via Chi-square tests. A p-value ≤0.05 defined statistical significance. Analyses were conducted using SPSS version 16 (IBM, Chicago, USA).

3. Results

Demographic and Clinical Characteristics

Demographic profiles of the study cohorts were statistically comparable across key variables (Table 1). The depression group (mean age: 37.70 ± 11.53 years) and control group (mean age: 34.88 ± 11.80 years) showed no significant age difference ($p = 0.248$). Gender distribution was similar between groups, with 36.7% males in the depression cohort versus 31.7% in controls ($p = 0.612$). Body mass index (BMI) did not differ significantly between groups (26.41 ± 5.05 kg/m² vs. 28.38 ± 7.00 kg/m², $p = 0.153$).

Serum Zinc Levels

Depressed patients exhibited substantially lower mean serum zinc levels compared to non-depressed participants (66.90 ± 30.51 µg/dL vs. 108.45 ± 22.44 µg/dL, $p < 0.001$) (Table 2). Zinc deficiency (serum zinc <60 µg/dL) was identified in 53.4% of the depression group, with no deficient cases observed in controls. Marginal deficiency (60–80 µg/dL) was present in 23.3% of depressed individuals and 22.1% of controls, while normal levels (≥80 µg/dL) were observed in 23.3% and 77.9%, respectively ($p < 0.001$).

Table 1: Demographic and Clinical Profiles of Study Participants

Characteristic	Depression Group (n=30)	Control Group (n=104)	p-value
Age (years),	**Mean ± SD 37.70 ± 11.53**	**34.88 ± 11.80**	**0.248**
Sex	**N (%)**	**N (%)**	
Male	**11 (36.7%)**	**33 (31.7%)**	**0.612†**
Female	**19 (63.3%)**	**71 (68.3%)**	
BMI (kg/m²),	**Mean ± SD 26.41 ± 5.05**	**28.38 ± 7.00**	**0.153**

Independent t-test; †Chi-square test.
SD: Standard deviation; BMI: Body mass index.

Table 2: Serum Zinc Status Across Study Groups

Parameter	Depression Group (n=30)	Control Group (n=104)	p-value
Serum Zinc (µg/dL)			**<0.001**
Mean ± SD	**66.90 ± 30.51**	**108.45 ± 22.44**	
Range	**39–200**	**61–132**	
Zinc Status, n (%)			**<0.001†**
Deficiency (<60 µg/dL)	**16 (53.4%)**	**0 (0.0%)**	
Marginal (60–80 µg/dL)	**7 (23.3%)**	**23 (22.1%)**	
Normal (≥80 µg/dL)	**7 (23.3%)**	**81 (77.9%)**	

Independent t-test; †Chi-square test.

3. Discussion

This study demonstrates a significant association between serum zinc deficiency and depression, with depressed patients exhibiting markedly lower zinc levels compared to non-depressed controls (66.90 ± 30.51 µg/dL vs. 108.45 ± 22.44 µg/dL; $p < 0.001$). Over half (53.4%) of depressed participants met criteria for zinc deficiency, whereas none of the controls showed deficient levels. These findings align with existing evidence implicating zinc deficiency in the pathophysiology of depressive disorders [22, 28].

The inverse relationship between serum zinc and depression severity is well-documented. Meta-analyses consistently report lower zinc levels in depressed populations, particularly in hospitalized patients, suggesting a dose-dependent effect [22, 29]. Randomized controlled trials further support zinc's adjunctive role in mood enhancement, both in clinical depression and subclinical populations [23–25]. Notably, zinc supplementation has shown promise in alleviating symptoms in treatment-resistant depression, highlighting its therapeutic potential [26, 27].

Mechanistic Insights

Zinc's antidepressant properties may stem from its interaction with brain-derived neurotrophic factor (BDNF), a key mediator of neurogenesis and synaptic plasticity. Depressive states are characterized by reduced BDNF

expression and impaired hippocampal neurogenesis, processes modulated by zinc homeostasis [26, 31]. Preclinical studies reveal that zinc-deficient diets reduce hippocampal zinc concentrations, suppressing progenitor cell proliferation and neurogenesis, whereas zinc repletion restores these effects [31]. Furthermore, zinc directly activates Tropomyosin receptor kinase B (TrkB), a BDNF receptor critical for synaptic plasticity, independent of BDNF binding [32]. This dual regulatory role—presynaptic TrkB activation and postsynaptic modulation—underscores zinc's importance in maintaining synaptic homeostasis [33].

Clinical Implications

The high prevalence of zinc deficiency in our cohort (53.4%) suggests routine serum zinc screening could identify at-risk individuals, particularly in regions with dietary zinc inadequacy. Given zinc's safety profile and low cost, supplementation may serve as a viable adjunct to conventional antidepressants, especially in refractory cases [26, 27]. However, longitudinal studies are needed to establish causality and optimal dosing regimens.

Limitations and Future Directions

This cross-sectional design precludes causal inferences. Confounding factors, such as dietary habits or inflammatory comorbidities, were not assessed. Future research should explore zinc's interaction with inflammatory markers (e.g., interleukin-6) and gut microbiota, both implicated in depression [34, 35].

4. Conclusion

This study demonstrates a significant association between serum zinc deficiency and depression in Kut Governorate, Iraq. Depressed individuals exhibited markedly lower zinc levels compared to non-depressed controls, with over half of the depression cohort meeting criteria for zinc deficiency. These findings align with global evidence implicating zinc in neuroplasticity and mood regulation, particularly through its interaction with BDNF and TrkB signaling. The high prevalence of zinc deficiency in this population underscores its potential role as a modifiable risk factor for depression, suggesting that zinc supplementation could serve as a cost-effective adjunct to conventional therapies.

Recommendations

1. Clinical Practice:

- Screen for serum zinc levels in patients diagnosed with depression, particularly in regions with known dietary zinc inadequacy.
- Consider zinc supplementation (e.g., 15–30 mg/day) as an adjunct therapy for treatment-resistant depression, pending further clinical trials.

2. Public Health:

- Implement nutritional education programs in Kut Governorate to promote zinc-rich diets (e.g., legumes, meat, nuts).
- Explore food fortification initiatives to address widespread micronutrient deficiencies.

3. Research:

- Conduct longitudinal studies to establish causality between zinc deficiency and depression onset.
- Investigate zinc's interaction with inflammatory biomarkers (e.g., CRP, IL-6) in depressive pathophysiology.
- Replicate this study in diverse Iraqi populations to assess regional variability.

4. Policy:

- Integrate micronutrient assessment into national mental health strategies, emphasizing zinc's role in mood disorders.

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Below is a fitted reference list tailored to your article, based on the context and citations provided. These references are commonly cited in studies on zinc and depression and align with your manuscript's focus. Replace the placeholders with the exact sources you used, if available. If you need help verifying or formatting specific references, let me know!

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