The Impact of Zinc on Depression in Kut Governorate/Iraq (2022)

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Abstract
Background: Approximately 19-34 % of depressed patients are not responded to antidepressants and up to half of them may suffer symptoms recurrence, so search for other approach to treat the disease such as micronutrients supplementation is needed in clinical practice. Aim of the study: The objective was to compare mean serum zinc across depressed and non-depressed people to investigate how zinc and depression are related. Patients and methods: A cross-sectional study included 134 patients ages 18 to 70. The study lasted from May through August 2022. Participants were selected from people who visited the psychiatric unit in Kut Governorate. The DSM-5 was used to assess depression. Exclusion criteria included age over 70 or under 18, pregnancy, puerperium, lactation, DM, renal failure, liver and pancreatic illness, inflammatory bowel diseases, bariatric surgery, burn, leukemia, diuretics, epileptic drug and other psychiatric disorder. Results: The mean serum zinc of the depressed group was lower than that of the non-depressed group, 66.90 ±30.51 (µg/dl) versus 108.45 ±22.44 (µg/dl), significant difference ($p < 0.001$). For depressed patients, zinc deficiency was at 53.4 % and 23.3 % with marginal deficiency, while those with normal level were at 23.3 % only. Whereas, in non-depressed group, marginal deficiency accounted for 23 (22.1 %) and those with normal serum zinc accounted for 81 (77.9 %). The difference was significant ($p < 0.05$). Conclusion: Zinc deficiency can be a modifiable determinant for depression and zinc administration may greatly improve symptoms in those patients.
Keywords: depression, zinc, deficiency, Iraq

1. Introduction

Zinc is a crucial nutrient, derived from many dietary sources, such as dairy, fish, poultry, and red meat (1)(2). The dietary amount of zinc is highly variable reaching 15 folds; for that reason, tight control of zinc levels is important. The zinc can be absorbed easily in the gut. Deficiency can thus be attributed to some drugs such as anti-inflammatory agents, steroid and antacids, infection with H pylori, alcoholism, and a number of medical conditions (3)(4). Although the highest concentration of zinc is within bone and muscular tissues, it is nearly present in all body tissues. Within blood free fraction of zinc is in the range of 9 to 17 microgram and the majority is found bound to protein (5). Literature reported the role of zinc in several neurological disorders (6)(7)(8)(9)(10)(11)(12).

Depression is a leading cause of suicide worldwide because of reduced quality of life. It has been estimated that approximately 19-34 % of individuals with depression show no response to antidepressants and that up to half of them may suffer symptoms recurrence, thus the search for other approach to treat the disease such as micronutrients supplementation is needed in clinical practice (13). Indeed, zinc trace element is enrolled in mental functions, learning and behavior. The first research examining the connection between depression and serum zinc levels were published by Hansen and colleague (14). Sand stead and colleagues reported the association between zinc status and function of brain for the first time (15).Various articles stated zinc effect in mechanisms of action of antidepressants and depression pathophysiology. Low serum concentration of zinc was linked to depression by previous authors (16)(17). In Iraq, lifetime and one year prevalence of major depressive episode were 7.4% and 4.0%, respectively and close to half (46%) of the one year cases were severe or very severe (18). In addition, previous Iraqi authors linked zinc deficiency to depression (19).

In the current cross sectional study, the objective was to estimate the mean of zinc serum level in depressed and non-depressed patients to investigate whether serum zinc levels are related to depression.

2. Patients and Methods

A total of 134 participants aged from 18 to 70 years were included in the study for the period from May 2022 extended through August 2022.

They were recruited from attendants to psychiatric clinic in the teaching hospital in Kut Governorate in Iraq. Depending on DSM-5 criteria depression was diagnosed by the psychiatrist [(20)]. Exclusion criteria were as following: age more than 70 or less than 18 years, pregnant woman, puerperium, lactating woman, DM, renal failure, liver and pancreatic disease, Crohns disease, Ulcerative colitis, bariatric surgery or any new surgical

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operation, burn, blood disease (leukemia, thalassemia, sickle cell anemia), any types of supplements less than one week like zinc supplements, diuretics, epileptic drug like Depakin in addition to other associated psychological diseases. Serum zinc level was categorized into normal, marginal deficiency and deficiency with a levels of (≥80 µg/dl), (60-80 µg/dl) and (<60 µg/dl) respectively [21]. The study was approved by the institutional approval committee and verbal consent was obtained from all participants.

The requested information was demographic data, weight, height, medication, serum zinc level. Chi-square test was used to test association between zinc deficiency and depression. Student t-test was used to study the difference in mean zinc level between depressed patients and non-depressed individuals. P-value of less than or equal 0.05 was regarded significant. Statistical software for social sciences was used to statistically evaluate the data (SPSS version 16, IBM, Chicago, USA).

3. Results

The demographic variables of enrolled subjects are explained in table 1. Mean age of depressed patients was 37.70±11.53 years and that of non-depressed subjects was 34.88±11.80 years, and there was no significant difference (p = 0.248). Proportions of males and females in both groups were also comparable, 11(36.7%) and 19(63.3%) versus 33(31.7%) and 71(68.3%), respectively (p = 0.612). Mean body mass index (BMI) of depressed group was 26.41±5.05 kg/m2 and that of non-depressed group was 28.38±7.00 kg/m2 and the difference was statistically insignificant (p = 0.153).

Mean serum zinc of depressed patients was lower in comparison with that of non-depressed group, 66.90 ±30.51 (µg/dl) versus 108.45 ±22.44 (µg/dl), and the difference was significant (p < 0.001). With respect to depressed group, the proportion of patients with zinc deficiency accounted for 53.4 % and those with marginal deficiency accounted for 23.3 % while those with normal levels accounted for 23.3 % only. Whereas, in non-depressed group, subjects with marginal deficiency accounted for 23 (22.1 %) and those with normal serum zinc accounted for 81 (77.9 %), with significant difference (p < 0.001).

Table 1: The demographic characteristics of patients with depression and control group

Characteristic	Depressed group n = 30	Non-depressed group n = 104	p
Age (years)			
Mean ±SD	37.70±11.53	34.88±11.80	0.248 I NS
Gender			
Male, *n* (%)	11(36.7%)	33(31.7%)	0.612 C NS
Female, *n* (%)	19(63.3%)	71(68.3%)	
BMI (kg/m^2)			
Mean ±SD	26.41±5.05	28.38±7.00	0.153 I NS

SD: standard deviation; *n*: number of cases; C: chi-square test; I: independent samples *t*-test; NS: not significant

Table 2: Comparison of mean serum zinc and zinc deficiency proportion between patients with depression and control subject

Characteristic	Depressed group *n* = 30	Non-depressed group *n* = 104	*p*
Serum zinc (µg/dl)			
Mean ±SD	66.90±30.51	108.45±22.44	< 0.001 I ***
Range	39 -200	61 -132	
Deficiency, n (%)	16(53.4%)	0(0.0%)	< 0.001 C ***
Marginal deficiency, n (%)	7(23.3%)	23(22.1%)	
Normal, n (%)	7(23.3%)	81(77.9%)	

SD: standard deviation; ***n***: number of cases; **C**: chi-square test; **I**: independent samples *t*-test; ***: significant at $p \leq 0.001$

4. Discussion

In the current study, the objective was to demonstrate zinc role in depression. Our results have shown that mean serum zinc in participants with depression was significantly lower than that of control group and that significant proportion of patients had deficiency of zinc according to serum zinc values. The finding that depressed patients showed low level of zinc is reflecting the importance of zinc in maintenance of stable mode, i.e., prevention of depression. It is consistent with that reported in the literature. High percent (53.4 %) was noticed among those with depressive symptoms, and no one was observed among those without depression (0%). Numerous clinical research have demonstrated how a zinc shortage contributes to the emergence of depressive symptoms.

Recent meta-analyses showed significantly inverse relationships between depression severity and blood zinc levels, compared to controls a lower serum zinc levels in groups of cases with depression, and greater effect sizes in cases that were hospitalized (22). Zinc is helpful as an additional treatment for elevating mood in both healthy and depressed people, according to several randomized controlled trials (23)(24)(25). In several studies, adding zinc to the diet also helped those with depression who were resistant to medication (26)(27).

A meta-analysis shows that depression symptoms occurs at serum zinc levels of 1.8 µmol/L or less , and

other investigations show that depressed people have lower serum zinc levels than healthy controls (22). Lower zinc levels were associated with greater Hamilton Depression Rating Scale scores, which is in line with dosage effects and causation (28)(29). Clinical research indicates that groups of people with serious depression had reduced serum zinc levels (22)(30).

Zinc's impact on brain-derived neurotropic factor (BDNF), a growth factor that encourages generation and differentiation of neurons, may have something to do with the relationship between zinc and depression. The hippocampus is a center of lifelong neurogenesis, and significant depressive episodes are accompanied by decreased BDNF expression and impaired neuro/synaptogenesis. The vesicles of hippocampus , a region in the brain that typically contains highest quantities of zinc, showed reduced zinc levels in mice fed a diet low in zinc, along with reductions in immature neurons and progenitor cells. On the other hand, diets high in zinc were associated with an increase in progenitor cells (26)(31).Because zinc and BDNF interact, a lack of it reduces neurogenesis and brings on depressive symptoms. In one clinical investigation, showed an inverse relationship between serum BDNF levels and depression (24). Although research into the precise link between BDNF and zinc is ongoing, one potential function of zinc in synaptogenesis is its part in transactivating Tropomyosin receptor kinase B (TrkB), a significant neurotrophic factor (32).Hippocampal mossy fiber potentiation results from zinc's stimulation of TrkB, which happens independently of BDNF activation. Additional research using mice indicates that zinc is not only necessary for mossy fiber potentiation but can also suppress it postsynaptically. This shows that the dual regulation of zinc may be necessary to maintain homeostasis (33). Zinc controls synaptic plasticity in this way, promoting neurogenesis and averting pathological conditions.

5. Conclusion

Serum zinc level in depressed patients is profoundly lower than non-depressed individuals indicating that zinc deficiency can be a modifiable determinant for depression and zinc administration may greatly improve symptoms in those patients.

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