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Association Between Trace Element Status and Depression in HTLV-1-Infected Patients: a Retrospective Cohort Study

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Abstract

Depression and Anxiety are two important public health problems that are known to be associated with viral infections. The association between the intake of nutrients such as zinc and copper with symptoms of depression has been studied previously. The aim of the current study was to investigate the association between depression with *human T cell lymphotropic virus type 1* (HTLV-1) infection and serum content of zinc and copper in a large Iranian population cohort. The study population consisted of 279 HTLV-1-positive patients who were identified after recruitment as part of a large cohort study: the Mashhad Stroke and Heart Association Disorder (MASHAD) study. They were divided into two groups of diagnosed with or without depression based on their symptoms. Serum zinc and copper levels of all subjects were measured using the flame atomic absorption spectrometry. The population sample comprised of 279 individuals infected with HTLV-1 of whom 192 (68.8%) were women. The mean serum zinc in the group with and without depression was 78.69 ± 13.79 μg/dl and 86.87 ± 19.44 μg/dl, respectively ($p < 0.001$). Also, the serum copper level was higher in the depressive group (116.75 ± 39.56) than in the non-depressive group (104.76 ± 30.77) (p 0.004). The association between serum zinc and copper with depression in HTLV-1-infected patients which was shown in this study could be considered in the treatment strategies in these patients.

Keywords HTLV-1 · Depression · Zinc · Copper · MASHAD study

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Introduction

Human T cell lymphotropic virus type 1 (HTLV-1) is associated with adult T cell leukemia/lymphoma (ATLL) and may cause other clinical manifestations, such as uveitis, arthritis, infective dermatitis, polymyositis [1], lymphocytic interstitial pneumonia [2, 3], and tropical spastic paraparesis/HTLV-1-associated myelopathy [4, 5]. HTLV-1 is also associated with some psychiatric disorders such as depression [6]. Since depression has important social impact and is associated with economic costs, it is known to be a serious public health problem [7]. Currently, depression is the fourth most common cause of disability around the world and its prevalence is expected to increase [8]. Depression is a frequent comorbidity of other medical conditions [9, 10]. Its high prevalence and economic and social impact have led to depression being considered an important public health problem [7, 11]. Depression is often associated with medical morbidity in the world and is a common cause of disability [10, 12]. The associations between depression and viral infections such as human immunodeficiency virus (HIV) and hepatitis C virus (HCV) have been reported by some researchers [13–15]. Although the association between HTLV-1 infection and the presence of psychiatric disorders has received little attention, existing data suggest that individuals infected with this virus have a high frequency of depressive and anxiety symptoms, resulting in an impaired quality of life [6, 16]. Moreover, the association between the intake of nutrients such as zinc and copper with the symptoms of depression has been investigated [17].

Zinc is an essential micronutrient and is responsible for different biological functions. Some of these functions include being a cofactor for several important enzymes, gene expression, the synthesis and release of insulin, and total body homeostasis [18]. The total amount of zinc in a human adult body is approximately 2–3 g, most of which is in skeletal muscles and bones. Although plasma levels of zinc are used to evaluate its nutritional status, but only 0.1% of the total zinc is found in plasma [19]. Copper is an important part of many metalloenzymes that perform important processes, including the inactivation of histamine, degradation of serotonin, oxidation of iron, production of norepinephrine, and protection against oxidative damage [20]. The enzyme monoamine oxidase (MAO) is important for serotonin degradation and the metabolism of dopamine, two neurotransmitters which play important roles in mental activity [21]. However, the relationship between depression and HTLV-1 infection has not received as much attention. The aim of this study is the evaluation of serum zinc and copper levels and their association with depression in HTLV-1-infected patients.

Methods and Material

Study Population

A total of 9274 subjects (3719 (40%) males and 5555 (60%) females) were recruited as part of the Mashhad Stroke and Heart Atherosclerotic Disorders (MASHAD) cohort study as described previously [18]. The protocols were approved by the MUMS Committee on Ethics. General inclusion and exclusion criteria of MASHAD study and data collected from the sample population which included marital status, occupational status, educational level, drug use, and biochemical and anthropometry measurements were explained previously [22].

HTLV-1 Infection Assessment

The serum samples of all participants of MASHAD study were screened for HTLV-1-specific antibodies using an enzyme-linked immunosorbent assay (ELISA) (Dia.Pro Diagnostic, Italy) method. Positive cases were assessed for the HTLV-1 genome using the polymerase chain reaction (PCR) for TAX- and LTR-specific primers to confirm the infection as describe previously [23]. Patients were confirmed to be infected by HTLV-1 if either of the genes were present. A total of 279 HTLV-1-infected patients (192 women and 87 men) were identified who were enrolled into the current study. HTLV-1-infected patients were divided into two groups: those diagnosed with depression (128 (45.9%)) and those without a diagnosis of depression (151 (54.1%)).

Assessment of Depression

We used the Beck Depression Inventory (BDI) questionnaire which contains 21 items and each question comprises a 4-point scale that provides a score between 0 and 63 [24]. Each item represents a single symptom associated with depression, including crying, feelings of hopelessness, fear and loss of appetite, sadness, feelings of guilt, and sleep disturbance over the past 2 weeks. Scores are classified as the following: 0–13 minimal or no depression, 14–19 mild depression, 20–28 moderate depression, and 29–63 severe depression [25]. According to Beck questionnaire, we merged three groups of depression to one group and made two groups, depression and no depression groups.

Measurement of Serum Zinc and Copper Concentrations

Serum samples were diluted with nitric acid at the ratio of 1:10. Using the flame atomic absorption (Varian AA240FS), the concentrations of Zn and Cu were measured [26, 27]. To avoid trace element contamination, all glass tubes were acid-washed with hydrochloric acid 10%

(HCl) for 24 h before measurement. Also using Zn and Cu standard (Merc and Co. Pharmaceutical Company), Zn and Cu standard curves were created. The accuracy of the methods for Zn was 93 ± 4.8% and 95 ± 3.75 for Cu which were assessed through measuring the confirmed reference material (MercK KGaA 64271 Darmstadt, Germany) comprising known values (1000 ± 2 mg/l) of Zn and Cu. The intra-assay and inter-assay coefficients of variation (CV) for Zn and Cu were 1.5 ± 0.2%, 2.6 ± 0.4%, 1.3 ± 0.12%, and 2.11 ± 0.32%, respectively. The limit of detection was less than 0.1 mg/l for both copper and zinc.

Statistical Analysis

All statistical analyses were undertaken using SPSS version 18(SPSS Inc. Chicago, IL, USA). The normality of zinc and copper and depression score were assessed using the Kolmogorov-Smirnov test. Descriptive statistics including mean, frequency, and standard deviation (SD) were defined for all variables and expressed as mean ± standard deviation (SD). Student's *t* test was determined for comparison between two groups. Chi-square was used to evaluate the categorical parameters. Logistic regression analysis was used to evaluate the relation between depression and 95% reference interval of zinc and copper in HTLV-1-positive subjects. A two-sided p value of < 0.05 was considered statistically significant. SPSS version 18 was used for designing figures.

Result

General Characteristics of the Subjects

The sample was composed of 279 individuals infected with HTLV-1 of whom 128 (45.9%) had depression and 151 (54.1%) did not have depression. The age in the groups without depression and depression was 50.11 ± 7.14 and 50.72 ± 9.79 respectively and there was not a significant difference between the two groups (p 0.51) (Table 1), although we found significant differences between the two groups according to sex (p 0.027) (Table 1).

Table 1 Demographic characteristics of 279 HTLV-1-positive subjects according to depression

		No depression (n 151)	Depression (n 128)	p value
Sex	Male = 87 Female = 192	55 (63.2%) 96 (50.0%)	32 (36.8%) 96 (50.0%)	0.027
Age (year)		50.11 ± 7.14	50.72 ± 9.79	0.51

Serum Zinc and Copper Levels

Table 2 shows that the mean serum zinc in the group without depression was 86.87 ± 19.44 μg/dl while in the group with depression, it was 78.69 ± 13.79 μg/dl ($p < 0.001$). Moreover, serum copper in the non-depressed group was higher than that in the group with depression ($p = 0.004$). In this study, we found that the prevalence of depression in women with HTLV-1 infection was higher than that in men ($p < 0.05$) (Table 1). The mean serum zinc levels were 88.45 ± 19.48 μg/dl and 86.01 ± 15.48 μg/dl and the mean serum copper levels were116.38 ± 36.7 μg/dl and 108.81 ± 34.61 μg/dl in men without and with depression, respectively. Moreover, the mean serum zinc was 85.93 ± 19.46 μg/dl and 82.31 ± 16.08 μg/dl, and the mean serum copper were 104.26 ± 38.52 μg/dl and 110.14 ± 36.83 μg/dl in women without and with depression, respectively. There were no significant differences between mean serum zinc and copper and depression in male and female subjects ($p > 0.05$). In the non-depressed subjects, the mean serum Zn/Cu ratio was 0.93 ± 0.56, 0.86 ± 0.49 and 0.97 ± 0.52 in the total group, men and women, respectively. In the depressed subjects the mean serum Zn/Cu ratio was 0.92 ± 0.75, 0.86 ± 0.32 and 0.94 ± 0.83, respectively. The data showed that there were no significant differences between the mean serum Zn/Cu ratio in depressed and non-depressed subjects ($p > 0.05$).

Zinc and Copper Indices as Risk Factors for Depression in HTLV-1 Patients

As Fig. 1 shows, there was negative correlation between serum zinc (r − 0.196, p 0.001) and copper (r − 0.162, p 0.007) levels and the depression score. Interestingly, HTLV-1 patients with a serum zinc ≤ 118 μg/dl had a 2.37-fold risk of depression (reference 95% percentile, CI 95%). Furthermore, a serum copper ≥ 174 μg/dl was associated with a 1.94-fold higher risk for depression (reference 95% percentile, CI 95%). Our results strongly suggest an association of serum zinc and copper with depression in HTLV-1 patients as independent predictive risk factors for depression in HTLV-1 patients (Table 3).

Table 2 Serum trace element status of HTLV-1-positive subjects according to depression

	No depression	Depression	p value
Zinc (μg/dl)	86.87 ± 19.44	78.69 ± 13.79	< 0.001
Copper (μg/dl)	116.75 ± 39.56	104.76 ± 30.77	0.004

Table 3 Odds ratios and 95% confidence intervals of serum zinc and copper levels according to depression in HTLV-1-positive subjects

	Unadjusted OR (95%, CI) Reference 95% percentile	*p* value	Adjusted by sex and each other OR (95%, CI) Reference 95% percentile	*p* value
Zinc ≤ 118	2.37 (1.955–3.986)	0.005	2.56 (1.73–3.98)	0.008
Copper ≥ 174	1.94 (1.075–2.65)	0.04	1.77 (1.014–2.751)	0.048

Zinc and copper defined to reference interval 95%, zinc > 118 and copper < 174 used as reference

Discussion

In our study, 45.9% of the individuals infected with HTLV-1 were diagnosed with major depression. This finding is higher than what has been reported in three separate studies in Brazil in which the prevalence of depression was 28–39% [28, 29]. This difference could be attributed to the lower prevalence of depression in the Brazilian than in the Iranian population [30, 31].

Depression is a mood disorder that results from complex interactions among multiple factors. A hypothesis says that chronic viral infections like HIV and HCV may produce extensive dysregulation of the immune system which may lead to depressive symptoms [13, 32]. Since HTLV-1 possesses viral characteristics like HIV and HCV, the hypothesis could be applied to HTLV-1 as well. It has been reported that there is a high prevalence of depression among patients infected with the HTLV-I virus as compared to the general population of hospitalized patients [33].

Associations between symptoms of depression and the intake of nutrients such as magnesium have been investigated [34]; however, the relationship between zinc intake and depression has not received as much attention. Almost half of the world's population is at risk for zinc deficiency [35]. As far as we know, this is the first study which investigated the association between serum zinc and copper with depression in HTLV-1-infected subjects. We showed that subjects with HTLV-1 and serum zinc < 118 μg/dl are associated with a 2.37-fold increased risk of depression (reference 95% percentile, CI 95%). Zinc is involved in several structural components of proteins and is a required cofactor for proper function of many enzymes with vital roles in brain function [36]. In a previous study, an inverse relationship between dietary intake of zinc and depression has been reported in 402 individuals. The results of this study show that long-term intake of zinc may decrease the severity of depressive symptoms [37]. In a double-blind randomized clinical trial, it has been indicating that zinc supplementation together with SSRI antidepressant drugs improves major depressive disorders more effectively than in patients with placebo plus antidepressants [38]. Based on research data, it has been known that Zn is associated with regulation of gamma-aminobutyric acid (GABA) and glutamate [39]. Zinc deficiency also leads to alteration of neurotransmitters like gamma-aminobutyric acid and norepinephrine [40].

Abnormal Cu levels have also been associated with depression. It has been found that Cu is an effective inhibitor of responses evoked by GABA, mainly in Purkinje cells. Cu toxicity could result to some degree of chronic $GABA_A$ receptor blockade [41]. In our study, subjects with copper ≥ 174 μg/dl had an increased risk of 1.94-fold for depression. Serum Cu has been suggested as a "trait marker" of unipolar depression [42]. Some studies have suggested that copper status is inversely associated with depression in humans. As an example, plasma copper levels have been observed to be elevated in those diagnosed with major depression [43], and also positively associated with depression in night nurses [44]. Furthermore, a positive association between elevated copper

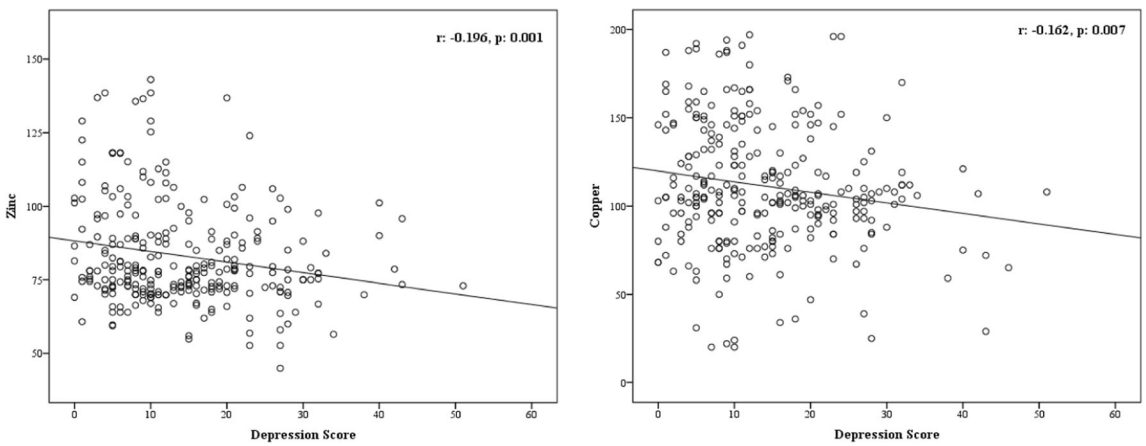

Fig. 1 Correlation between serum zinc and copper with depression score

levels in the blood and the severity of both depressive and anxiety symptoms has also been observed [17]. Furthermore, we have shown that zinc status and copper status of HTLV-1-positive subjects based on depression in both sexes were significantly different ($p < 0.001$ and 0.004 respectively). It has also been observed that gender affects associations, as low zinc intake has been associated with depression in women, but not in men [45, 46].

Study on 14,834 subjects aged 18 years or older showed that total zinc, iron, copper, and selenium intakes were inversely associated with depression in unadjusted model and age- and gender-adjusted model [47].

Moreover, assessment of copper in 247 patients with major depressive disorder and 248 healthy individuals demonstrated that the concentration of copper was significantly increased in the patients than in control subjects, which strongly suggests that there is a disturbance in the element homeostasis [48].

The conflicting results of the studies which have investigated the association between serum levels of copper and the incidence of depression necessitate the implementation of larger studies.

Conclusion

The high prevalence of depression among HTLV-1-infected patients which affects their quality of life requires routine assessment of depressive symptoms in them. The association between serum zinc and copper and their role in neurotransmitter pathway with the incidence of depression in these patients which was shown in this study could be considered in their treatment strategies.

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Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

References

1. Galvão-Castro B, Loures L, Rodriques L, Sereno A, Ferreira O Jr, Franco L et al (1997) Distribution of human T-lymphotropic virus type I among blood donors: a nationwide Brazilian study. Transfusion 37(2):242–243
2. Carneiro-Proietti ABF, Catalan-Soares B, Proietti FA (2002) Human T cell lymphotropic viruses (HTLV-I/II) in South America: should it be a public health concern? J Biomed Sci 9(6): 587–595
3. Hlela C, Shepperd S, Khumalo NP, Taylor GP (2009) The prevalence of human T-cell lymphotropic virus type 1 in the general population is unknown. AIDS Rev 11(4):205–214
4. Bhigjee A, Harvey M, Windsor I, Bill P (1989) Blood transfusion and HTLV-I-associated myelopathy. South African medical journal= Suid-Afrikaanse tydskrif vir geneeskunde 76(12):700
5. Gessain A, Vernant J, Maurs L, Barin F, Gout O, Calender A (1985) Antibodies to human T-lymphotropic virus type-I in patients with tropical spastic paraparesis. Lancet 326(8452):407–410
6. Carvalho AGJ, Galvão-Phileto AV, Lima NS, RSd J, Galvão-Castro B, Lima MG (2009) Frequency of mental disturbances in HTLV-1 patients in the state of Bahia, Brazil. Braz J Infect Dis 13(1):5–8
7. Kessler RC, Barber C, Birnbaum HG, Frank RG, Greenberg PE, Rose RM, Simon GE, Wang P (1999) Depression in the workplace: effects on short-term disability. Health Aff 18(5):163–171
8. Murray CJ, Lopez AD, Organization WH. The global burden of disease: a comprehensive assessment of mortality and disability from diseases, injuries, and risk factors in 1990 and projected to 2020: summary. 1996
9. Harden CL (2002) The co-morbidity of depression and epilepsy epidemiology, etiology, and treatment. Neurology 59(6 suppl 4): S48–S55
10. Kamerow DB (1988) Anxiety and depression in the medical setting: an overview. Med Clin North Am 72(4):745–751
11. Druss BG, Schlesinger M, Allen HM Jr (2001) Depressive symptoms, satisfaction with health care, and 2-year work outcomes in an employed population. Am J Psychiatr 158(5):731–734
12. Pohjasvaara T, Vataja R, Leppävuori A, Kaste M, Erkinjuntti T (2001) Depression is an independent predictor of poor long-term functional outcome post-stroke. Eur J Neurol 8(4):315–319
13. Dwight MM, Kowdley KV, Russo JE, Ciechanowski PS, Larson AM, Katon WJ (2000) Depression, fatigue, and functional disability in patients with chronic hepatitis C. J Psychosom Res 49(5): 311–317
14. Ickovics JR, Hamburger ME, Vlahov D, Schoenbaum EE, Schuman P, Boland RJ, Moore J, HIV Epidemiology Research Study Group (2001) Mortality, CD4 cell count decline, and depressive symptoms among HIV-seropositive women: longitudinal analysis from the HIV Epidemiology Research Study. JAMA 285(11): 1466–1474
15. McDaniel JS, Fowlie E, Summerville MB, Farber EW, Cohen-Cole SA (1995) An assessment of rates of psychiatric morbidity and functioning in HIV disease. Gen Hosp Psychiatry 17(5):346–352
16. Gascón MRP, Capitão CG, Casseb J, Nogueira-Martins MCF, Smid J, Oliveira ACP (2011) Prevalence of anxiety, depression and quality of life in HTLV-1 infected patients. Braz J Infect Dis 15(6):578–582
17. Russo A (2011) Analysis of plasma zinc and copper concentration, and perceived symptoms, in individuals with depression, post zinc and anti-oxidant therapy. Nutr Metab Insights 4:NMI. S6760
18. Maret W (2013) Zinc biochemistry: from a single zinc enzyme to a key element of life. Adv Nutr 4(1):82–91
19. Ghasemi A, Zahediasl S, Hosseini-Esfahani F, Azizi F (2012) Reference values for serum zinc concentration and prevalence of zinc deficiency in adult Iranian subjects. Biol Trace Elem Res 149(3):307–314
20. Skalnaya MG, Skalny AV (2018) Essential trace elements in human health: a physician's view
21. Otten JJ, Hellwig JP, Meyers LD (2006) Dietary reference intakes: the essential guide to nutrient requirements. National Academies Press

22. Ghayour-Mobarhan M, Moohebati M, Esmaily H, Ebrahimi M, Parizadeh SMR, Heidari-Bakavoli AR, Safarian M, Mokhber N, Nematy M, Saber H, Mohammadi M, Andalibi MSS, Ferns GA, Azarpazhooh MR (2015) Mashhad Stroke and Heart Atherosclerotic Disorder (MASHAD) study: design, baseline characteristics and 10-year cardiovascular risk estimation. Int J Public Health 60(5):561–572
23. Hamedi A, Akhlaghi F, Meshkat Z, Sezavar M, Nomani H, Meshkat M (2012) The prevalence of human T-cell lymphotropic virus type 1 in pregnant women and their newborns. ISRN Obstet Gynecol 2012:1–5
24. Dozois DJ, Dobson KS, Ahnberg JL (1998) A psychometric evaluation of the Beck Depression Inventory–II. Psychol Assess 10(2): 83–89
25. Scogin F, Beutler L, Corbishley A, Hamblin D (1988) Reliability and validity of the short form Beck Depression Inventory with older adults. J Clin Psychol 44(6):853–857
26. Ghayour-Mobarhan M, Shapouri-Moghaddam A, Azimi-Nezhad M, Esmaeili H, Parizadeh S, Safarian M et al (2009) The relationship between established coronary risk factors and serum copper and zinc concentrations in a large Persian cohort. J Trace Elem Med Biol 23(3):167–175
27. Taylor A (1996) Detection and monitoring of disorders of essential trace elements. Ann Clin Biochem 33(6):486–510
28. Galvão-Castro AV, Boa-Sorte N, Kruschewsky RA, Grassi MFR, Galvão-Castro B (2012) Impact of depression on quality of life in people living with human T cell lymphotropic virus type 1 (HTLV-1) in Salvador, Brazil. Qual Life Res 21(9):1545–1550
29. Stumpf BP, Carneiro-Proietti AB, Proietti FA, Rocha FL, GROUP IHR (2008) Higher rate of major depression among blood donor candidates infected with human t-cell lymphotropic virus type 1. Int J Psychiatry Med 38(3):345–355
30. Silva MT, Galvao TF, Martins SS, Pereira MG (2014) Prevalence of depression morbidity among Brazilian adults: a systematic review and meta-analysis. Rev Bras Psiquiatr 36(3):262–270
31. Tayefi M, Shafiee M, Kazemi-Bajestani SMR, Esmaeili H, Darroudi S, Khakpouri S, Mohammadi M, Ghaneifar Z, Azarpajouh MR, Moohebati M, Heidari-Bakavoli A, Parizadeh MR, Nematy M, Safarian M, Ebrahimi M, Ferns GA, Mokhber N, Ghayour-Mobarhan M (2017) Depression and anxiety both associate with serum level of hs-CRP: a gender-stratified analysis in a population-based study. Psychoneuroendocrinology 81:63–69
32. Singh N, Gayowski T, Wagener MM, Marino IR (1997) Vulnerability to psychologic distress and depression in patients with end-stage liver disease due to hepatitis C virus. Clin Transpl 11(5 Pt 1):406–411
33. Souza ARM (2009) Frequency of major depressive disorder in HTLV-I infected patients. Arq Neuropsiquiatr 67(2A):365–366
34. Jacka FN, Overland S, Stewart R, Tell GS, Bjelland I, Mykletun A (2009) Association between magnesium intake and depression and anxiety in community-dwelling adults: the Hordaland Health Study. Aust N Z J Psychiatry 43(1):45–52
35. Takeda A, Tamano H (2009) Insight into zinc signaling from dietary zinc deficiency. Brain Res Rev 62(1):33–44
36. Frederickson CJ, Koh J-Y, Bush AI (2005) The neurobiology of zinc in health and disease. Nat Rev Neurosci 6(6):449–462
37. Yary T, Aazami S (2012) Dietary intake of zinc was inversely associated with depression. Biol Trace Elem Res 145(3):286–290
38. Ranjbar E, Kasaei MS, Mohammad-Shirazi M, Nasrollahzadeh J, Rashidkhani B, Shams J et al (2013) Effects of zinc supplementation in patients with major depression: a randomized clinical trial. Iranian J Psychiatry 8(2):73
39. Takeda A, Hirate M, Tamano H, Oku N (2003) Release of glutamate and GABA in the hippocampus under zinc deficiency. J Neurosci Res 72(4):537–542
40. Rahelić D, Kujundžić M, Romić Ž, Brkić K, Petrovečki M (2006) Serum concentration of zinc, copper, manganese and magnesium in patients with liver cirrhosis. Coll Antropol 30(3):523–528
41. Sharonova IN, Vorobjev VS, Haas HL (1998) High-affinity copper block of GABAA receptor-mediated currents in acutely isolated cerebellar Purkinje cells of the rat. Eur J Neurosci 10(2):522–528
42. Schlegel-Zawadzka M, Zieba A, Dudek D, Zak-Knapik J, Nowak G (1999) Is serum copper a "trait marker" of unipolar depression? A preliminary clinical study. Pol J Pharmacol 51(6):535–538
43. Nechifor M (2008) Interactions between magnesium and psychotropic drugs. Magnes Res 21(2):97–100
44. Chang M-Y, Tseng C-H, Chiou Y-L (2014) The plasma concentration of copper and prevalence of depression were positively correlated in shift nurses. Biol Res Nurs 16(2):175–181
45. Jacka FN, Maes M, Pasco JA, Williams LJ, Berk M (2012) Nutrient intakes and the common mental disorders in women. J Affect Disord 141(1):79–85
46. Harris E, Kirk J, Rowsell R, Vitetta L, Sali A, Scholey AB, Pipingas A (2011) The effect of multivitamin supplementation on mood and stress in healthy older men. Hum Psychopharmacol Clin Exp 26(8): 560–567
47. Li Z, Wang W, Xin X, Song X, Zhang D (2018) Association of total zinc, iron, copper and selenium intakes with depression in the US adults. J Affect Disord 228:68–74
48. Islam MR, Islam MR, Qusar MS, Islam MS, Kabir MH, Rahman GM et al (2018) Alterations of serum macro-minerals and trace elements are associated with major depressive disorder: a case-control study. BMC Psychiatry 18(1):94