

## Relationship of Zinc and Magnesium Serum Levels with Postpartum Depression in Tabriz-Iran

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### Abstract

**Objective:** According to the World Health Organization, depression will be the second prevalent problem after ischemic heart diseases by the year 2020. Postpartum depression (PPD) as a major depressive episode has devastating impacts on the health of mother, newborn, infant, and even the whole family. This study was conducted to investigate the relationship of zinc and magnesium serum levels with PPD, as one of the commonly assumed causes of depression.

**Methods:** This cross-sectional study was done on 122 postpartum women aged 18 years and more in two educational hospitals and one non-educational hospital in Tabriz-Iran, 2015. The eligible women were selected using convenience sampling method. Then, the demographic characteristics questionnaire and Edinburgh Depression Scale were completed by participants, and 5cc of blood sample was drawn from each participant. For data analysis, logistic regression test was used.

**Results:** The mean score of depression scale was 8.0 (SD: 4.7), meaning that 18.9% of mothers were depressed. Results indicated a significant inverse correlation between Edinburgh depression score and magnesium serum level ( $p=0.001$ ). However, there was no statistically significant relationship between the zinc serum level and Edinburgh depression score ( $p=0.831$ ), in so far as based on logistic regression analysis, increased magnesium serum level decreased the odds of depression [Odds ratio: 0.05; CI 95%: 0.01 to 0.29].

**Conclusions:** In this study, there was a significant inverse relationship between magnesium serum level and Edinburgh depression score.

**Keywords:** depression, Zinc, Magnesium, postpartum, postpartum depression, serum

### 1. Introduction

According to World Health Organization (WHO), depression will become the second prevalent problem after ischemic heart diseases by 2020 (WHO, 2005); In addition, postpartum depression (PPD), as a major depressive episode, is diagnosed with the beginning of pregnancy, and can last from 2 weeks to 1 year (based on DSM-IV and International Classification of Diseases (ICD-10)) (Miller, Murray, Beckmann, Kent, & Macfarlane, 2013). Depression is two times more common among women (Bodnar & Wisner, 2005) and according to previous studies, PPD occurs in 10-20% of all newly delivered women (Miller et al., 2013). The overall incidence of PPD in Iran has been reported as 25.4% (Veisani & Sayehmiri, 2012).

It has devastating effect on the mother and newborn, and negatively affects family relationships and child development (Etebary, Nikseresht, Sadeghipour, & Zarrindast, 2010; Miller et al., 2013). Such conditions can lead to child-killing thoughts, damage cognitive and social development of children (Spinelli, 2004), decrease mother-child interaction, develop bad and negative feelings about child behaviors, and weaken mother-newborn attachment. In addition, obvious developmental delay, social and interactional problems, poor speech development, long-term behavioral problems, child neglect, and marital divorce for stresses are of such effects

(Miller et al., 2013).

Pregnancy is an important stressful life event that accelerates the intensity of depression (Cunningham et al., 2014). Several other factors are introduced as the causes of PPD, one of which is nutrient deficiency including: folate, vitamin B12, calcium, iron, selenium, zinc, and n-3 fatty acid (Leung & Kaplan, 2009).

Zinc and magnesium are two main body elements (Szewczyk et al., 2008), which are required for the activity of 300 enzymes (Etebary et al., 2010; Nowak, Szewczyk, & Pilc, 2005). In addition, zinc and magnesium both have a role in the regulation of neurotransmitters induction and release (Etebary et al., 2010; Smart, Hosie, & Miller, 2004). Homeostasis changes of zinc and magnesium in brain cause behavioral disorders such as depression, headaches, generalized tonic-clonic problems such as focal epilepsy, dizziness, tremors, irritability, psychotic behavior, loss of appetite, restlessness, malaise, weakened learning and cognitive function, and some neurological disorders like epilepsy and Alzheimer (Etebary et al., 2010).

Studies show that zinc and magnesium are probably effective in the pathogenesis and therapy of depression (Cope & Levenson, 2010; Krocza, Branski, Palucha, Pilc, & Nowak, 2001; Mlyniec et al., 2014). Moreover, some studies have suggested that zinc and magnesium serum level in depressive patients, especially those with PPD, is lower than non-depressed individuals (DiGirolamo & Ramirez-Zea, 2009; Stanislawska et al., 2014; Swardfager et al., 2013). However, some other studies have not suggested any statistically significant relationship between the zinc and magnesium serum levels with depression (Crayton & Walsh, 2007; Islam et al., 2013). The anti-depression feature of zinc and magnesium has been seen in animal studies, including on mice (Krocza et al., 2001; Mlyniec et al., 2013; Samardzic et al., 2013; Poleszak et al., 2004). This study aims at determining the relationship between zinc and magnesium serum levels with PPD before the development of its severe symptoms and signs, as an assumed cause of PPD, to find a prevention method by keeping serum level high, in case of such relationship.

## **2. Materials and Methods**

### *2.1 Methodology and Participants*

This was a cross-sectional study conducted on 122 newly delivered women (within past 48 hours), hospitalized in postpartum wards of Alzahra and Taleghani (educational hospitals), and 29-Bahman Hospital (non-educational hospital) in Tabriz, Iran in 2015. This study has been approved by the Ethics Committee of Tabriz University of Medical sciences (#93106).

Inclusion criteria were: Women aged 18 years and more, living in Tabriz, basic literacy level (reading and writing), primipara and multipara, vaginal or Cesarean section and recent low-risk pregnancy. Exclusion criteria included: hospitalization of mother for postpartum complications, no tendency to participate.

### *2.2 Sampling*

Illegibility of the participants in terms of inclusion and exclusion criteria was investigated and their written consent was obtained. Then, socio-demographic questionnaire was completed by the participants. In the pilot study, sample size of the study was determined 122 cases using the relation between serum level zinc and postpartum depression (OR=0.45), and considering 95% confidence, 90% power, two-tailed test and utilizing G-Power 3.1.2.

### *2.3 Measures*

To determine the zinc and magnesium serum levels of the participants, 5cc blood sample was drawn from each participant, and were centrifuged at 3500 rpm for 10 minutes, then immediately stored at -20°C. Then, they were delivered to laboratory of Student Research Center of Tabriz University of Medical sciences. To examine the zinc and magnesium serum levels, spectrophotometry (using Alcyon spectrophotometer made in the USA), a Randox kit (manufactured in England) for zinc, and a kit for magnesium (made by the Pars Azmoon Company in Iran) were used. The Randox test sensitivity was up to 2 µmol/l for zinc and Pars Azmoon test sensitivity was up to 0.5 µmol/l for magnesium. The natural level was considered as 10-18 µmol/l for zinc and 1.9-3 mg/dl for magnesium, respectively. Subjects with Edinburgh score equal or higher than 12 were considered with depression problem and referred to a mental service provider.

### *2.4 Data Analysis*

Data were analyzed with SPSS- version 20 using with descriptive-analytical statistics. Data normality was examined with Skeweness and Kurtosis, indicating a normal distribution. In addition, descriptive statistics, including mean (standard deviation), frequency, and percentage, were used to describe socio-demographic information and depression status. Moreover, logistic regression analysis was utilized for investigating the

relationship of zinc and magnesium serum levels with depression. Odds ratio and 95% confidence interval was presented as effect size of relations. In all analyses, *p-value* lower than 0.05 was considered as statistically significant.

### 3. Results

The mean age of participated women was 28.1 (SD=5.2) years, and the majority of them (91.8%) were housewives. All participants had above secondary school educational level. More than two-third (68.9%) of the women had relatively adequate income. Among the participants, 39.3% and 60.3% were primipara and multipara (two or three), respectively. The majority of the participants (71.1%) had intended pregnancy.

Deliveries were 37.2% via vaginal and 62.8% via cesarean section. All participants had delivered at 38 weeks or over and 63.1% of them reported high partner support. The majority of women (98.4%) were satisfied with the baby's sex (Table 1).

Table 1. Socio-demographic characteristics of participants

Characteristics	n (%)	Characteristics	n (%)
<b>Age (years)</b>		<b>Husband support</b>	
18-27	53 (43.4)	Low	11 (9.0)
28-37	64 (52.5)	Moderate	34 (27.9)
38-47	5 (4.1)	Much	77 (63.1)
Mean(SD)	28.1 (5.2)	<b>Family support</b>	
<b>Education</b>		Low	21 (17.3)
Secondary	30 (24.6)	Moderate	57 (46.7)
High school	68 (55.7)	Much	44 (36.0)
University	24 (19.7)	<b>Satisfaction from neonatal sex</b>	120 (98.4)
<b>Job</b>		<b>Husband Education <sup>¥</sup></b>	
Housewife	112 (91.8)	Primary school	18 (14.7)
Employed	10 (8.2)	Secondary school	27 (22.1)
<b>BMI (Kg/m<sup>2</sup>)*</b>	25.3 (4.2)	High school	14 (11.5)
<b>Economic status</b>		Diploma	43 (35.2)
Favorable	23 (18.9)	University	20 (16.4)
Partly favorable	84 (68.9)	<b>Husband Job</b>	
Unfavorable	15 (12.3)	Unemployed	3 (2.5)
<b>Gravid <sup>*</sup></b>	1.9 (0.9)	Employed	19 (15.6)
<b>Parity</b>		Worker	47 (38.5)
Primiparous	48 (39.9)	Shopkeeper	21 (17.2)
Multiparous	74 (60.6)	Other <sup>§</sup>	32 (26.2)
<b>Delivery</b>		<b>Wanted pregnancy</b>	81 (71.1)
NVD	46 (37.7)		
Cesarean section	76 (62.3)		

\*Data were presented as mean (standard deviation);

<sup>§</sup>Driver and etc;

<sup>¥</sup>One person (0.8%) was illiterate.

The mean (standard deviation) depression score was 8.0 (SD=4.7). Among 122 delivered women, 23 (18.9%) participants obtained Edinburgh score of 12 and higher (Table 2).

Table 2. Serum zinc and magnesium concentrations during 48 hours after delivery

	Minimum	Maximum	Mean (SD)
Zn (mol/l)	8.25	15.50	10.09 (0.95)
Mg (mg/dl)	1.72	3.70	2.42 (0.38)

The mean of zinc and magnesium serum level was 10.09 (SD=0.95)  $\mu\text{mol/l}$  and 2.42 (SD=0.38) mg/dl, respectively.

Results from logistic regression showed no statistical significant relationship between the zinc serum level and Edinburgh depression score ( $p=0.831$ ). However, there was a significant inverse correlation between magnesium serum level and Edinburgh depression score ( $p=0.001$ ); in that according to this analysis, increased magnesium serum level decreased the risk of depression [Odds ratio: 0.05; Confidence Interval 95%: 0.01 to 0.29] (Table 3).

Table 3. The relationship between Zn and Mg serum levels and Edinburg Postnatal Depression Rating Scale (EPDRS) score

	n	Zn		Mg	
Depression score		OR (CI 95%) <sup>¥</sup>	P	OR (CI 95%) <sup>¥</sup>	P
<12 (ref) <sup>*</sup>	99	1	0.831	1	0.001
$\geq 12$	23	1.03 (0.73 to 1.47)		0.05 (0.01 to 0.29)	

\* EPDR score less than 12 was reference.

<sup>¥</sup> Odds ratio (95% Confidence Interval).

#### 4. Discussion

Results suggested no statistically significant correlation between zinc serum level and PPD. In contrast, there was a significant inverse relationship between magnesium serum level and PPD, in that increase of it decreased PPD risk.

According to the latest studies, the main elements such as zinc and magnesium exert their anti-depression and anti-anxiety effects via neurotransmitters. Concentration of these elements can be related to such neurotransmitters as monoamine and serotonin (Ruljancic, Mihanovic, Cepelak, Bakliza, & Curkovic, 2013; Szweczyk et al., 2008; Szweczyk et al., 2009). Indeed, depression and anxiety relate to the dysfunction of brain glutamate system. N-methyl-d-aspartate (NMDA) (glutamate) has an important anti-depression and anti-anxiety effect. Zinc and magnesium, the potent antagonists of the NMDA receptor complex, are involved in the pathophysiology of depression and anxiety, and exhibit antidepressant and anti-anxiety activities; therefore, reduction of zinc and magnesium levels may lead to functional NMDA receptor hyperactivity (Doboszewska et al., 2015; Sowa-Kucma et al., 2013). In addition, magnesium controls HPA (Hypothalamic-pituitary-adrenal) activity, thereby decreases anxiety symptoms by the reduction of corticotrophin releasing hormone (CRH) level (Sartori, Whittle, Hetzenauer, & Singewald, 2012).

In some studies, including a meta-analysis, zinc serum level in depressive patients was lower than non-depressive individuals (DiGirolamo & Ramirez-Zea, 2009; Mlyniec et al., 2013; Siwek et al., 2013; Swardfager et al., 2013). Thus, low serum zinc concentrations may have a role in the pathogenesis of depression. In a review study by DiGirolamo and Ramirez-Zea, a correlation was observed between zinc serum level with mental health issues of mothers and children, including depression and ADHD (Attention Deficit Hyperactivity Disorder) (DiGirolamo & Ramirez-Zea, 2009). The antidepressant effect of zinc was observed in animal studies, including the one by Mlyniec et al. According to this research, the administration of antidepressants for depressed mice with zinc-deficiency-diet and low serum zinc and high cortisol levels, normalized their serum zinc level; therefore, zinc deficiency is regarded as a factor involving with the pathogenesis of depression (Mlyniec et al., 2013). In a review study, Siwek et al. presented the results of some investigations about the effect of low serum zinc level on depressed patients, and proposed the measurement of blood zinc level as a depression marker; in addition, low serum zinc level was observed in depressed patients with drug resistance (Siwek et al., 2013). The study by Markiewicz-Zukowska et al. on the relationship between the concentration of serum zinc

level and physical and mental status of nursing home residents showed a correlation between serum zinc level and mental performance. This level was higher in older non-depressed individuals with normal cognitive performance than patients with memory disorders and depressive symptoms (Markiewicz-Zukowska, Gutowska, & Borawska, 2015).

In a study by Maserejian et al. on general population in Boston, it was found that low zinc intake from food or supplements increased the risk of depression symptoms in women and not men. This cross-sectional study recommended more relevant research, due to little number of similar investigations (Maserejian, Hall, & McKinlay, 2012). Results of above studies are inconsistent with ours.

A study by Crayton and Walsh on pregnant women with PPD history showed that serum zinc levels were not statistically different in women with PPD history, depressed women without PPD history, and non-depressed women. These findings are consistent with ours in that no relationship was observed between depression and serum zinc level. In addition, there was no statistically significant difference in serum zinc level between depressed and non-depressed men; moreover, copper level was higher in depressed women than depressed men (Crayton & Walsh, 2007).

According to some studies, magnesium deficiency, similar to zinc, induces depression-like behavior in mice; on the other hand, this ion exhibits antidepressant and anti-anxiety like activities in animal tests (Decollogne, Tomas, Lecerf, Adamowicz, & Seman, 1997; Lloyd, Perkins, & Spence, 1989; Nikseresht et al., 2012; Poleszak et al., 2004; Singewald, Sinner, Hetzenauer, Sartori, & Murck, 2004). Moreover, some trials have shown the effect of magnesium on the treatment of psychological disorders (De Souza, Walker, Robinson, & Bolland, 2000; Heiden et al., 1999). A systematic review also suggests that magnesium may be effective in depression therapy, but further studies are required (Derom, Sayon-Orea, Martinez-Ortega, & Martinez-Gonzalez, 2013).

Imado et al. examined serum magnesium level in 71 hospitalized patients and outpatients with mental disorder and 30 normal people. Results showed no significant difference between patients with major depression, who were on psychiatric medication, relative to the patients who did not take the medicine. In contrast to our study, it was also shown that serum magnesium level was significantly higher in patients with mental disorders than control group (Imada et al., 2002). In addition, no statistically significant difference was observed in serum magnesium level between control and case groups in the study by Islam et al. on 50 patients with general anxiety disorder and 51 healthy individuals (Islam et al., 2013).

One reason for the inconsistency between the present study and some above investigations is because the majority of them have been done on patients with mental disorders; in addition, there is no similar research like ours that qualitatively has investigated the general population without clinical depression.

The cross-sectional nature of this study is a research limitation as its proposed relationship is not an exact causal-comparative correlation. To eliminate this limitation, performing stronger research designs such as case-control study is recommended for investigating the relationship of serum zinc and magnesium levels with PPD.

## 5. Conclusion

Results show no relationship between the serum zinc level and depression; however, a significant statistical correlation was observed between serum magnesium level and depression. Due to the importance of PPD, it is recommended that future studies be conducted on a larger number of samples. In addition to the serum levels, the intake rate of zinc and magnesium from foods or supplements which may differ in various populations should also be taken into account.

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## Conflict of Interest

The authors declare that there is no conflict of interests regarding the publication of this paper.

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