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Original Article

Effect of Zinc Supplementation on Serum Brain-Derived Neurotrophic Factor Level and Geriatric Depression Scale among Elderly Persons with Mild to Moderate Depression

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ABSTRACT

Background and Aim: Depression is a common mental health issue among the elderly. Brain Derived Neurotropic Factor (BDNF) is involved in neuronal survival and modulation of neurotransmitter profiles. Zinc deficiency increases neuronal degeneration. This study aims to investigate the effect of zinc supplementation on serum BDNF level and GDS (Geriatric Depression Scale) among elderly persons with mild to moderate depression. **Methodology:** Total 76 elderly persons with mild to moderate depression according to GDS score were selected and randomly assigned to supplement (zinc or placebo) groups using block randomization. Before and after supplementation of 20 mg zinc tablets/placebo tablets for 3 months, serum zinc levels and serum BDNF levels were measured, using the flame Atomic Absorption Spectrophotometry and the Enzyme-Linked Immunosorbent Assay and GDS score also reassessed in both groups. **Results:** Baseline serum zinc, serum BDNF and GDS score were not significantly different between two groups. After zinc supplementation, serum zinc level and serum BDNF level were significantly increased. GDS score was also significantly reduced in the zinc group. Comparing to the placebo group, zinc group had lower GDS score and higher BDNF level. There was a significant negative correlation between serum zinc level and GDS score after supplementation in the study population. **Conclusion:** Zinc supplementation for three months had a beneficial effect on elderly persons with mild to moderate depression.

Keywords: Zinc, Brain derived neurotropic factor, Depression, Geriatric depression scale.

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INTRODUCTION

According to the World Health Organization, the population aged over 60 years is increasing faster than any other population because the life expectancy rate of elderly is rising and the fertility rate is decreasing. In Myanmar, it is estimated to increase from 8.9% in 2015 to 9.4% in 2017 and it is expected to reach 18.5% in 2050.[1] Ageing results from the impact of the addition of a wide variety of molecular and cellular damages, leading to a gradual decrease in physical and mental capacity.[2]

It is estimated to affect 1.7 billion people (80% of total elderly population) in developing countries by the year 2050.[3] In Myanmar, about 16% to 56% of elderly people had depressive symptoms.[4] Geriatric depression is a multifactorial disorder as it is caused by a combination of factors (genetic, biological and psychosocial).[5] Depression in the elderly can reduce quality of life and increase risk of suicide.[6] Geriatric Depression Scale (GDS) is commonly used in elderly persons. There are many hypotheses regarding the pathophysiology of depression, such as monoamine neurotransmitter hypothesis, hypothalamus-pituitary-adrenal axis dysfunction, neurotrophic hypothesis and cytokine hypothesis.[7,8] Most studies have focused on the relationship between mood disorders and neurotrophin regulation.[9] BDNF, one of the neurotrophins, has been shown to play an important role in the pathophysiology of depression.[10] BDNF is involved in synaptic plasticity, neuronal survival, dendritic branching and modulation of excitatory and inhibitory neurotransmitter profiles.[11] BDNF influences many regions of central nervous system, particularly the cerebral cortex, hippocampus and amygdala. BDNF is important in neurotrophin regulation and neural circuit in ageing.[12] Reduced serum BDNF levels have been reported in patients with major depression when compared to those who are normal.[13]

Previous studies have reported that depression was associated with neuronal plasticity. The association of neuronal plasticity

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involves neurotrophic factors, such as BDNF, which are abundant in the brain, serum and plasma. Zinc homeostasis is important for brain function. One of the antidepressant-like activities of zinc is increasing BDNF gene expression. This effect can induce neurogenesis by increasing BDNF.[14] A systematic review and meta-analysis also concluded that oral zinc supplementation improved mood disorders and neurodegenerative diseases,[15] but other clinically significant outcomes were not reported.

It is interesting that zinc may also have a therapeutic effect on geriatric depression, potentially helping to improve GDS score and reduce the severity of depression. Zinc supplementation may induce serum BDNF levels, which is a prognostic biomarker for depression. Since the previous studies was unable to confirm the benefits of zinc supplementation in treating depression by increasing serum BDNF level, further research is needed to explore the potential antidepressant effect of zinc on mental health among elderly persons. Hence, the present study aims to investigate the effect of zinc supplementation on serum BDNF level and the Geriatric Depression Scale among elderly persons with mild to moderate depression.

METHODOLOGY

Study Design and Population

A community-based double-blind randomized controlled study was conducted in 300 elderly people who live in Magway Township. After obtaining permission from village administrators, the elderly person aged ≥60 years in selected villages (Magikan, Than Taw Kone, Puhto San, Phuto and Zee Khyun) were assessed for their eligibility to the study. The detailed procedure was explained to the participants and written informed consent was obtained from each subject. A second informed consent was obtained from senior household members. After obtaining informed consent, the researcher asked the questions of GDS form to the subjects at their home. The researcher scored the GDS form according to the provided instructions to ensure uniformity. No subjects in this study exhibited signs or symptoms of psychiatric problems.

Elderly persons with a GDS score of 5 to 11 were selected for this study. History taking and physical examination were conducted according to proforma.

Participants Allocation to Groups

There were two groups: the zinc supplement group and the placebo supplement group the selected subjects were given supplement tablets, either zinc or placebo, according to a random allocation sequence. If the selected subjects had missed more than 20% of the pills or no longer wanted to take the drug, they were allowed to withdraw from the study. No subjects withdrew from this study.

The coding of zinc tablets and placebo tablets was done first and separated into identical plastic containers. These plastic containers were labeled with code numbers. These procedures were overseen by the supervisor. Subjects were randomly assigned supplements (zinc or placebo) using block randomization. One group received a daily supplement of 20 mg zinc tablets, while the other group received a placebo for three months.

Procedure

The subjects were requested to fast overnight from 10 pm to 6 am. On the following day, a blood sample was collected at their home at 6 am. Four milliliter of venous blood was collected from a peripheral vein under aseptic condition using a disposable syringe and needle for each subject. The blood was collected in plain tubes and transported to the Department of Pathology, Magway Regional Hospital in a cold-box. The blood was then centrifuged for 15 min at 3000 rpm and the serum was separated and stored in separate screw-tight bottles at -20°C until analysis at the Department of Pathology, Magway Regional Hospital. Serum zinc levels were measured using the flame Atomic Absorption Spectrophotometric method at the Common Research Laboratory, University of Medicine, Magway, while serum BDNF levels were measured using the Enzyme-Linked Immunosorbent Assay method at the Department of Physiology, University of Medicine, Magway. After 3 months of interventions, a second GDS score assessment, measurement of serum zinc levels and measurement of serum BDNF levels were conducted. All procedures were performed in accordance with COVID-19 preventive guidelines.

Statistical Analysis of Data

Data entry and analysis were done by SPSS software (Statistical package for Social Sciences) version 16.0. Data was described by mean±SD. Student's independent `*t*' test was used to compare serum zinc levels, BDNF levels and GDS score between placebo supplement group and zinc supplement group. Paired '*t*' test was used to compare the serum zinc level, BDNF level and GDS score in each group before and after intervention. Pearson's correlation was used to correlate between measuring parameters (serum zinc level, serum BDNF level and GDS score). The p value <0.05 was accepted as significant level.

RESULTS

Table 1 shows general characteristics of the subjects participated in this study. Table 2 shows the comparison of serum zinc level, serum BDNF level and GDS score before and after 3 months of zinc supplement in zinc supplement group. Serum Zinc ($p<0.001$) and BDNF levels ($p<0.05$) were significantly increased after Zinc supplementation with significant decrease in GDS scoring ($p<0.001$).

Table 3 shows the comparison of serum zinc level, serum BDNF level and GDS score before and after 3 months of placebo supplement in placebo supplement group. There was no

significant difference found in serum Zinc, BDNF levels and GDS scoring in the group which received placebo supplement.

Figure 1 shows comparison of serum zinc level between zinc supplement group and placebo supplement group after supplement. Serum zinc levels were significantly increased ($p<0.05$) in the group that received zinc supplementation compared to the placebo supplementation group. Comparison of serum BDNF level between zinc supplement group and placebo supplement group after supplement are shown in Figure 2. BDNF levels were not significant between zinc supplementation group and placebo supplementation group. Figure 3 shows non-significant GDS score between zinc supplement group and placebo supplement group after supplement. Figure 4 shows that the GDS scores were negatively correlated with serum zinc levels.

DISCUSSION

Baseline mean serum zinc level of the zinc supplement group (n=38) was 43.70±7.53 µg/dL and for the placebo supplement group (n=38), it was 44.58±8.14 µg/dL. There was no significant difference between two groups before the study ($p>0.05$). After three months of zinc supplementation, there was a significant increase in the mean serum zinc level from 43.70±7.53 µg/dL to 54.67±9.4 µg/dL in the group receiving zinc supplements ($p<0.001$). Conversely, the group receiving placebo supplements did not change significantly, with levels from 44.58±8.14 µg/dL to 44.25±7.66 µg/dL ($p>0.05$). This study supported the findings of Kilaru et al. in which aging is a risk factor for zinc deficiency and prophylactic supplementation of zinc could be an option to prevent zinc deficiency.[16] By comparing the zinc supplement

Table 1: General characteristics of elderly persons with mild to moderate depression in the placebo supplement group and zinc supplement group.

Variables		Elderly persons with mild to moderate depression				Total
		Placebo supplement group (n=38)		Zinc supplement group (n=38)		N=76
		N	(%)	N	(%)	
Age	60-69yrs	22	45.83	26	54.17	48
	≥70yrs	16	57.14	12	42.86	28
Sex	Male	20	58.82	14	41.18	34
	Female	18	42.86	24	57.14	42
Education	Illiterate	3	37.50	5	62.50	8
	Primary	30	51.72	28	48.28	58
	Secondary	5	50.00	5	50.00	10
Occupation	Non-working	24	50.00	24	50.00	48
	Working	14	50.00	14	50.00	28

Table 2: Comparison of serum zinc level, serum BDNF level and GDS score before and after 3 months of zinc supplement in zinc supplement group.

Parameters	Before zinc supplement (n=38) Mean±SD	After zinc supplement (n=38) Mean±SD	p value
Serum Zinc (µg/dL)	43.71±7.53	54.67±9.41	0.000**
Serum BDNF (ng/mL)	5.11±2.48	5.94±2.41	0.029*
GDS score	7.45±1.03	5±1.63	0.000**

**indicates significant difference at $p<0.001$.*indicates significant difference at $p<0.05$.

Table 3: Comparison of serum zinc Level, serum BDNF level and GDS score before and after 3 months of placebo supplement in the placebo supplement group.

Parameters	Before placebo supplement (n=38) Mean±SD	After placebo supplement (n=38) Mean±SD	*p* value
Serum Zinc (µg/dL)	44.58±8.14	44.25±7.66	0.57
Serum BDNF (ng/mL)	4.55±2.06	4.94±2.32	0.14
GDS score	7.37±1.19	7.32±1.11	0.762

NB: Comparison was done by student paired "*t*" test.All values were expressed as mean±SD.

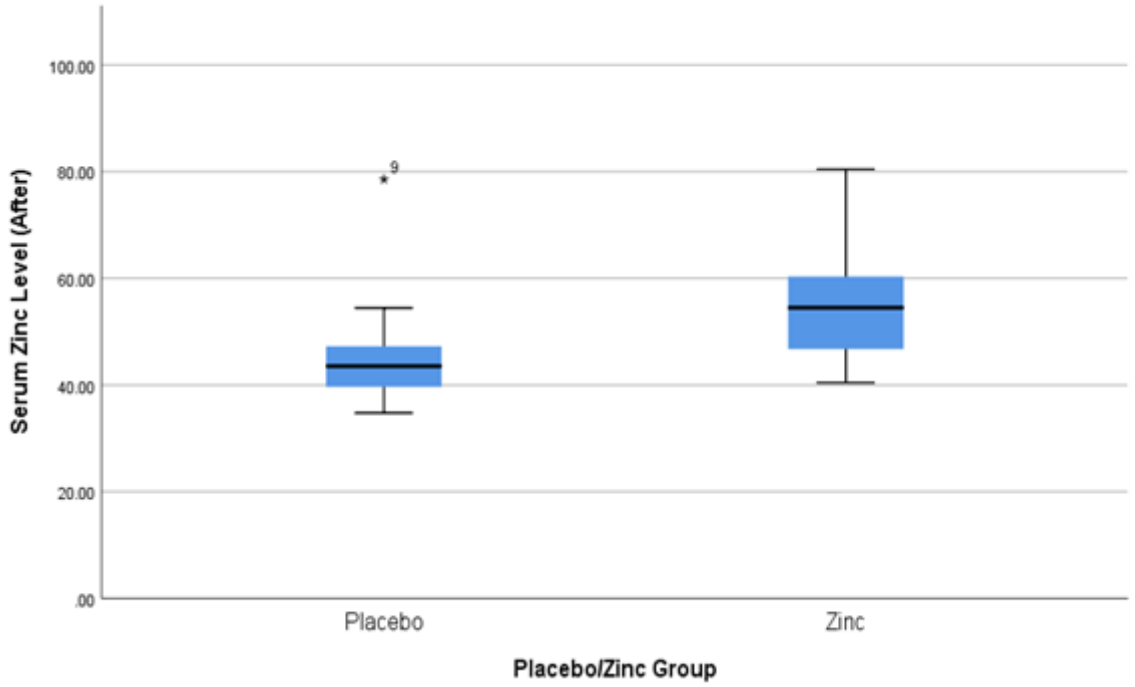

Figure 1: Comparison of serum zinc level between placebo supplement group (n=38) and zinc supplement group (n=38) after supplement.

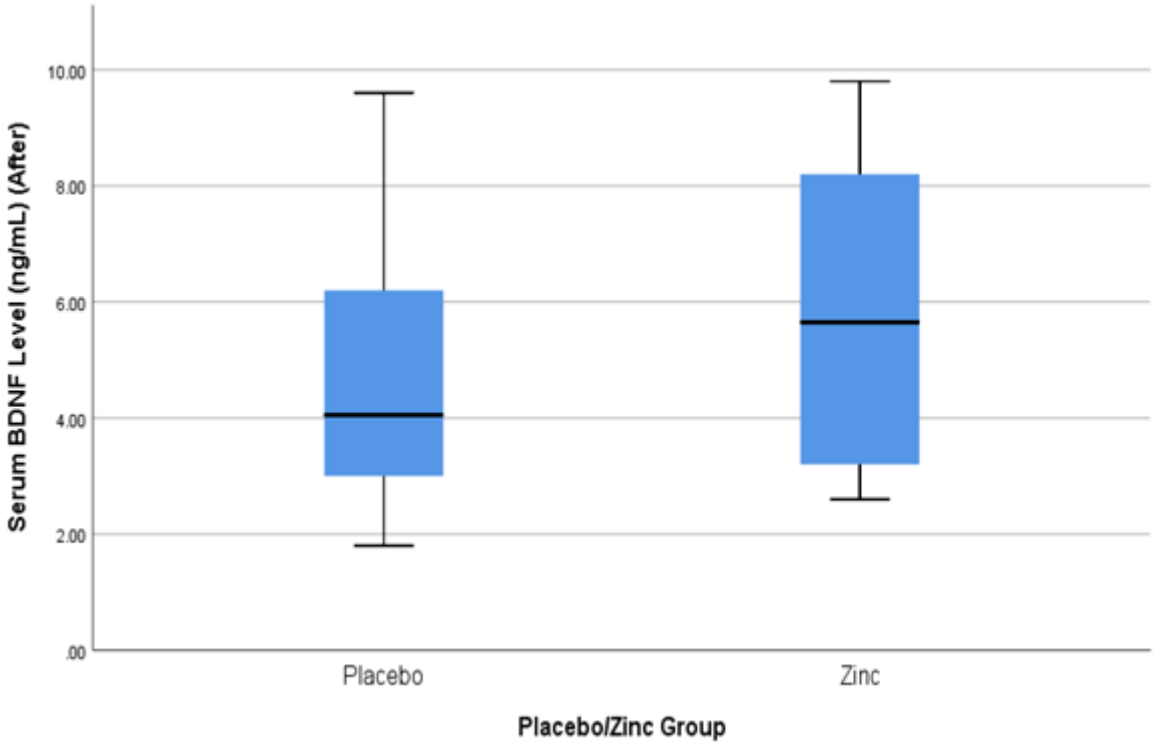

Figure 2: Comparison of serum BDNF level between placebo supplement group (n=38) and zinc supplement group (n=38) after supplement.

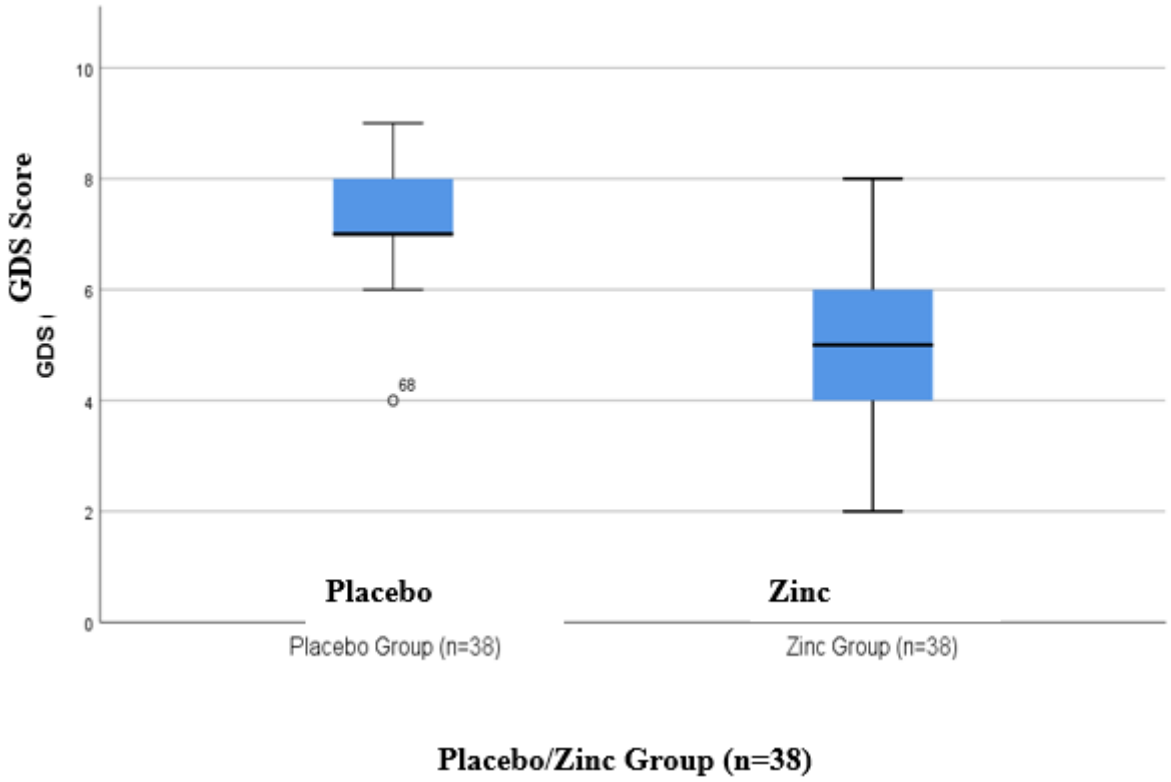

Figure 3: Comparison of GDS score between placebo supplement group (n=38) and zinc supplement group (n=38) after supplement.

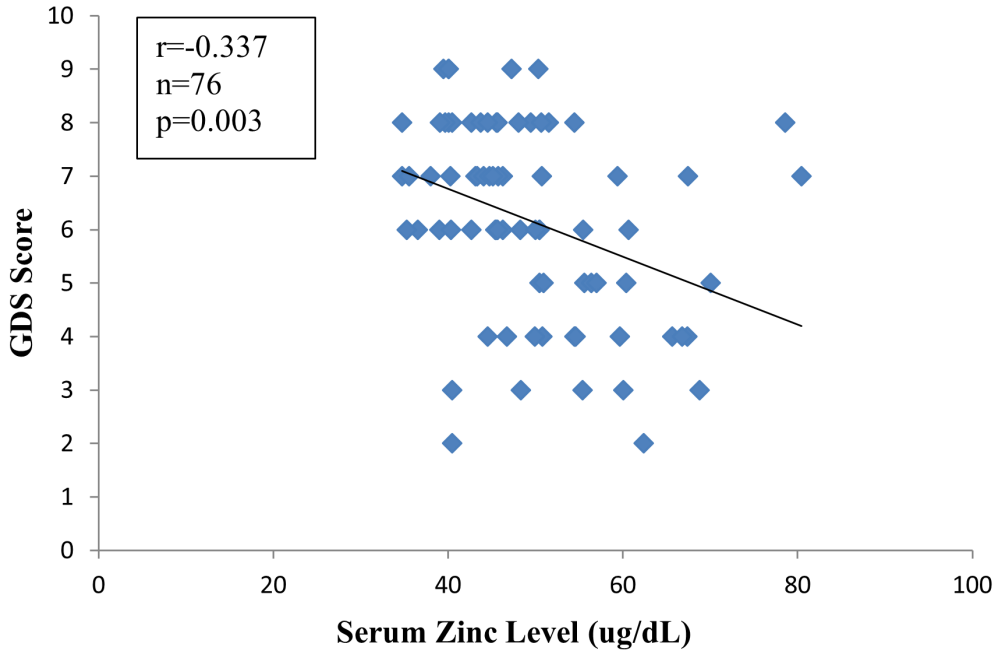

Figure 4: Correlation between serum zinc level and GDS score in study population.

group and placebo supplement group, there was significant difference in serum zinc level between two groups after the study (p<0.001). Baseline serum BDNF level was 5.11±2.48 ng/mL in the zinc supplement group and 4.55±2.06ng/mL in the placebo supplement group. After supplementation, serum BDNF level was 5.94±2.41 ng/mL in the zinc supplement group and 4.94±2.32 ng/mL in the placebo supplement group respectively. In zinc supplement group, there was significant increase in

serum BDNF level after intervention ($p<0.05$). However, there was no significant difference in the placebo supplement group before and after intervention ($p>0.05$). Comparing two groups, serum BDNF level was higher in zinc supplement group than that of placebo supplement group, but it was not statistically significant ($p>0.05$). This study found that mean serum BDNF level was increased not only in the zinc supplement group (from 5.11±2.48 ng/mL to 5.94±2.41 ng/mL), but also in the placebo supplement group (from 4.55±2.06 ng/mL to 4.94±2.32 ng/mL) after intervention. In the present study, baseline mean GDS score was 7.45±1.03 in the zinc supplement group and 7.37±1.19 in the placebo supplement group. Baseline mean GDS score of the zinc supplement group improved to 5.0±1.63 after three months of zinc supplementation. In the placebo supplement group, GDS score was 7.32±1.11 after supplementation and there was no significant difference before and after placebo supplement ($p>0.05$). After conducting a comparative analysis of two groups, it was observed that there was a statistically significant difference after the intervention ($p<0.001$). This study proved that zinc supplementation improved GDS score in elderly persons.

CONCLUSION

The present study was concluded that elderly might be high risk of zinc deficiency and reduced serum BDNF level. It could be assumed that zinc deficiency might be related with depression.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

BDNF: Brain Derived Neurotropic Factor; **GDS:** Geriatric Depression Scale.

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