



## **Determining the effects of Vitamin D and Vitamin E administration in Psychiatric improvement of patients with mental health problems**

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### **Abstract**

#### **Introduction**

Mental diseases, with their diverse effects on individuals, families, and society, are a major issue in today's world. The study of the benefits of giving Vitamin D and Vitamin E on psychiatric improvement in people with mental health disorders emphasizes the need for more research in this area.

#### **Methodology**

The study included 140 people with mental illnesses as well as vitamin D and vitamin E deficits. Based on 25-hydroxyvitamin D (25(OH) vitamin D) values of 10 ng/mL, baseline vitamin D levels were classified as deficiency, insufficiency, or sufficient. The participants had been taking antipsychotic drugs on a consistent basis for at least two months prior to the commencement of the trial.

**Results** The findings had revealed that a significant difference in the mean  $p < 0.05$  were observed among the patients in the experimental group where antipsychotic treatment alone had

shown significant reduction in the BPRS and the combination of antipsychotic plus vitamin D and E.

### **Conclusion**

In Conclusion, the data imply that combining vitamin D and E with antipsychotic medication may improve psychiatric outcomes in people with mental health issues.

**Keywords** Mental illness, Antipsychotic drugs, Vitamins

### **Introduction**

Mental diseases, with their diverse effects on individuals, families, and society, are a major issue in today's world<sup>1</sup>. These disorders not only undermine the well-being and everyday functioning of people who are directly affected, but also impose significant social and financial obligations at several levels<sup>2-3</sup>. Understanding the deep ramifications of mental diseases on individuals' lives and the larger societal fabric becomes increasingly important as the frequency of mental disorders rises internationally<sup>3</sup>. Extensive research findings consistently show a troubling reality: people suffering from severe mental illness (SMI), which includes psychotic disorders, bipolar affective disorder, and severe depression with psychotic symptoms, have a significantly shorter lifespan of 10 to 20 years compared to the general population<sup>4-5</sup>. Surprisingly, roughly 80% of these untimely deaths among people with SMI are caused by avoidable physical conditions, with cardiometabolic diseases, respiratory disorders, and infectious diseases being the most common causes<sup>6</sup>. These findings highlight the critical importance of addressing the physical health requirements of people with SMI, since addressing avoidable diseases in this population might dramatically reduce the burden of mortality and improve overall well-being<sup>7-8</sup>. Reduced levels of blood 25-hydroxyvitamin D have repeatedly been linked to an increased risk of late-life depression in studies. Furthermore, it has been claimed that low levels of 25-hydroxyvitamin D contribute to the development of seasonal affective disorder<sup>9</sup>. However, when considering a framework for mental disorder prevention, it is unclear whether universal prevention through vitamin D3 supplementation would be beneficial for all individuals or if it should be targeted towards those at high risk due to subclinical symptoms or depression risk factors<sup>10</sup>. Exploration of antioxidant pathways in the context of mental health has also led to the findings that, during stress-induced biochemical changes, antioxidants play a critical role in neutralizing damaging free radicals and regulating the oxidative stress pathway. This mechanism may contribute to a decrease in symptoms linked with anxiety and depression by effectively eliminating reactive oxygen species (ROS) and reactive nitrogen species (RNS), which can potentially harm neurons in the brain<sup>11-13</sup>. Among the numerous antioxidants linked to mental health, vitamin E has received a lot of attention. Vitamin E, a fat-soluble vitamin, has powerful antioxidant capabilities and has been researched for its potential advantages in reducing the impact of oxidative stress on mental health. Vitamin E may help preserve the integrity and function of neurons by scavenging free radicals and shielding cells from oxidative damage, thereby relieving anxiety and depression<sup>14-16</sup>. The study of the benefits of giving Vitamin D and Vitamin E on psychiatric improvement in people with mental health disorders emphasizes the need for more research in

this area. It is therefore researchers want to unearth insights that influence evidence-based therapies and improve patient outcomes by systematically investigating the possible advantages of these vitamins in the management of mental health problems. Such research would help us understand the function of nutritional supplements and their effects on mental health, opening the door for more comprehensive and successful treatment options in the field of psychiatry.

### **Methodology**

A Randomized Control Trial was used in this study to explore the effects of Vitamin D and Vitamin E supplementation on psychiatric improvement in individuals with mental health disorders. The study was conducted over a period of two months at the Basic Medical Sciences Institute at Jinnah Postgraduate Medical Center in Karachi, Pakistan (BMSI).

### **Study Participants**

The study included 140 people with mental illnesses as well as vitamin D and vitamin E deficits. Based on 25-hydroxyvitamin D (25(OH) vitamin D) values of 10 ng/mL, baseline vitamin D levels were classified as deficiency, insufficiency, or sufficient. The participants had been taking antipsychotic drugs on a consistent basis for at least two months prior to the commencement of the trial. Throughout the research, the patients' antipsychotic dosages remained constant.

### **Patients Group**

The 140 patients were allocated into seven groups at random:

**Group 1:** Outpatient clinic controls (20 age- and gender-matched controls).

**Group 2:** Risperidone (2 mg/day) treatment group.

**Group 3:** Olanzapine (10 mg/day) treatment group.

**Group 4:** Quetiapine (50-100 mg/day) treatment group.

**Group 5:** Vitamin D + E + Risperidone treatment group.

**Group 6:** The vitamin D + vitamin E plus olanzapine treatment group.

**Group 7:** Vitamin D + Vitamin E + Quetiapine treatment group.

For two months, all groups got the recommended therapy. Patient compliance sheets and regular phone calls were used to guarantee treatment adherence.

### **Outcome Measures**

A data were collected to measure psychiatric progress on the basis Brief Psychiatric Rating Scale<sup>17</sup> (BPRS) and Extrapyramidal symptom rating scale (EPSRS)<sup>18</sup> after two weeks of intervention.

### **Ethical Consideration**

The study was carried out after receiving clearance from the Jinnah Postgraduate Medical Centre Hospital Karachi's Ethical Committee, which ensured that ethical norms were followed throughout the research procedure. It is critical in the discipline of psychiatry to handle delicate matters about participants' personal life and family relationships with extreme caution. The researchers took great care to preserve the participants' physical, mental, social, and spiritual well-being, ensuring that their rights and dignity were maintained and that no damage was done during the study. The confidentiality and privacy of the participants' information were rigorously

safeguarded, and each subject provided informed consent prior to their participation in the research. Ethical concerns were crucial in ensuring the welfare and rights of all those engaged in the investigation.

## Results

Demographic description revealed that the mean age of the participants included in the study was  $41.64 \pm 2.59$  years with the percentage of male and female population was estimated as 60.8% and 39.2% respectively. (Table 1)

Variables	Average age in years $\pm$ SD	%age of males	%age of females
Subjects	$41.64 \pm 2.59$	60.8%	39.2%

The findings had revealed that a significant difference in the mean  $p < 0.05$  were observed among the patients in the experimental group where antipsychotic treatment alone had shown significant reduction in the BPRS and the combination of antipsychotic plus vitamin D and E had shown significantly better result  $p < 0.001$  than antipsychotic treatment alone as shown in table 2

BPRS	Control	Olanzapine	Risperidone	Quetiapine	Olanzapine + Vita E + Vita D	Risperidone + Vita E + Vita D	Quetiapine + Vita E + Vita D
Somatic Concern	$6 \pm 1.2$	$4 \pm 0.8$	$4 \pm 1.1$	$4 \pm 0.9$	$3 \pm 0.5$	$3 \pm 0.6$	$3 \pm 0.8$
Anxiety	$5 \pm 0.8$	$4 \pm 1.1$	$4 \pm 0.8$	$3 \pm 0.6$	$4 \pm 0.6$	$3 \pm 0.7$	$3 \pm 0.7$
Emotional Withdrawal	$6 \pm 0.75$	$5 \pm 0.5$	$4 \pm 0.7$	$4 \pm 0.8$	$3 \pm 0.8$	$3 \pm 0.8$	$4 \pm 0.6$
Conceptual Disorganization	$4 \pm 0.56$	$3 \pm 0.6$	$3 \pm 0.5$	$4 \pm 0.6$	$3 \pm 0.5$	$4 \pm 0.9$	$3 \pm 0.8$
Guilt Feeling	$5 \pm 1.1$	$4 \pm 0.5$	$4 \pm 0.6$	$5 \pm 0.7$	$4 \pm 0.9$	$3 \pm 1.1$	$4 \pm 0.7$
Tension	$4 \pm 0.9$	$4 \pm 0.4$	$4 \pm 1.1$	$4 \pm 0.8$	$3 \pm 0.5$	$4 \pm 0.5$	$3 \pm 1.1$
Mannerism and Posturing	$5 \pm 0.8$	$4 \pm 0.8$	$3 \pm 0.9$	$4 \pm 0.8$	$4 \pm 0.6$	$4 \pm 0.6$	$3 \pm 0.6$
Grandiosity	$6 \pm 0.6$	$5 \pm 1.1$	$4 \pm 0.7$	$3 \pm 0.6$	$4 \pm 0.4$	$3 \pm 0.8$	$4 \pm 0.8$
Depressive Mood	$6 \pm 0.4$	$5 \pm 0.4$	$5 \pm 0.6$	$4 \pm 0.5$	$3 \pm 0.8$	$5 \pm 0.6$	$3 \pm 0.7$
Hostility	$4 \pm 0.78$	$4 \pm 0.5$	$4 \pm 0.4$	$5 \pm 1.1$	$4 \pm 0.5$	$3 \pm 0.7$	$4 \pm 0.9$
Suspiciousness	$5 \pm 0.89$	$4 \pm 0.6$	$5 \pm 0.8$	$4 \pm 0.8$	$5 \pm 1.1$	$3 \pm 0.8$	$3 \pm 0.4$
Hallucinatory Behavior	$5 \pm 0.35$	$5 \pm 0.8$	$4 \pm 0.5$	$5 \pm 0.9$	$4 \pm 0.5$	$3 \pm 0.6$	$3 \pm 0.6$
Motor Retardation	$6 \pm 1.01$	$5 \pm 0.5$	$5 \pm 0.7$	$5 \pm 1.1$	$4 \pm 0.9$	$3 \pm 0.7$	$3 \pm 0.8$
Uncooperativeness	$4 \pm 0.6$	$3 \pm 0.6$	$4 \pm 1.1$	$4 \pm 0.9$	$3 \pm 1.1$	$3 \pm 0.8$	$4 \pm 0.7$
Unusual thought content	$5 \pm 0.5$	$4 \pm 0.5$	$3 \pm 0.8$	$4 \pm 0.9$	$3 \pm 0.8$	$3 \pm 0.6$	$4 \pm 0.6$
Blunted Affect	$5 \pm 0.4$	$4 \pm 0.8$	$5 \pm 0.6$	$4 \pm 0.8$	$4 \pm 0.7$	$3 \pm 0.8$	$3 \pm 0.7$
Excitement	$6 \pm 0.8$	$5 \pm 0.7$	$3 \pm 0.7$	$5 \pm 0.7$	$3 \pm 0.6$	$4 \pm 0.7$	$3 \pm 0.9$
Disorientation	$6 \pm 0.7$	$5 \pm 0.8$	$4 \pm 0.3$	$4 \pm 0.5$	$4 \pm 0.8$	$3 \pm 0.9$	$3 \pm 0.8$

**P < 0.005 indicates significant difference in mean between the groups**

Further on extrapyramidal symptom rating scale no such difference  $p>0.05$  were observed in between the group as shown in table 3

<b>Variables</b>	<b>Control</b>	<b>Olanzapine</b>	<b>Risperidone</b>	<b>Quetiapine</b>	<b>Olanzapine + Vita E + Vita D</b>	<b>Risperidone + Vita E+ Vita D</b>	<b>Quetiapine + Vita E+ Vita D</b>
<b>Difficulty in carrying out routine task</b>	2±0.5	2±0.8	1±0.2	2±0.1	2±0.08	2±0.8	2±0.5
<b>Difficulty Walking and Balance</b>	1.5±0.4	2±0.7	1±0.1	2±0.3	2±0.09	1±0.69	1±0.6
<b>Stiff Posture</b>	2±0.8	1±0.6	2±0.4	1±0.5	1±0.1	2±0.5	2±0.1
<b>Restlessness</b>	2±0.5	1±0.4	2±0.5	1±0.1	1±0.3	1±0.3	1±0.90
<b>Tremors</b>	2±0.4	2±0.8	2±0.1	1±0.2	2±0.2	1±0.4	1±0.75
<b>Oculogyric Crisis</b>	1.5±0.5	2±0.7	1±0.1	1.5±0.08	2±0.1	1±0.3	2±0.96
<b>Abnormal Involuntary Movement</b>	2±0.6	2±0.6	1±0.5	2±0.09	1±0.8	2±0.1	2±0.6
<b><math>p&gt;0.05</math> indicates no significant mean difference between the group</b>							

## **Discussion**

The study's findings revealed a significant difference ( $p>0.05$ ) in the mean Brief Psychiatric Rating Scale (BPRS) scores among patients in the experimental group. Antipsychotic medication alone resulted in a substantial reduction in BPRS scores, indicating improvement in mental symptoms. However, as compared to the antipsychotic therapy alone group, the group receiving a combination of antipsychotic medication with vitamin D and vitamin E had considerably improved outcomes ( $p>0.001$ ). This shows that adding vitamin D and E supplementation to the antipsychotic regimen improved mental outcomes. Whereas, when extrapyramidal symptoms were assessed using the Extrapyramidal Symptom Rating Scale, no significant difference ( $p>0.05$ ) was seen between the groups. This suggests that the addition of vitamin D and E had no effect on extrapyramidal symptoms in the study population. The findings were in consistent with the findings of systematic review and meta-analysis that was performed to determine the impact of vitamin D supplementation on mental health and biomarkers of inflammation and oxidative stress in individuals with psychiatric illnesses<sup>19</sup>. It was concluded in the findings that Vitamin D

supplementation was linked to a substantial drop in Beck Depression Inventory (BDI) scores, indicating an improvement in depressed symptoms. Furthermore, vitamin D supplementation significantly lowered Pittsburgh Sleep Quality Index (PSQI) ratings, indicating a good influence on sleep quality. Furthermore, the meta-analysis discovered that vitamin D administration increased glutathione (GSH) levels as well as total antioxidant capacity (TAC). GSH is a key antioxidant that protects cells from oxidative damage, whereas TAC indicates the body's overall antioxidant capability. These findings imply that vitamin D administration may boost antioxidant defenses and minimize oxidative stress in people suffering from mental illnesses<sup>19</sup>. Similarly in a case control study that was performed with the purpose to look into the involvement of trace elements and vitamins in the etiology of major depressive disorder (MDD). The study comprised 60 male MDD patients and 60 age- and gender-matched controls. Serum levels of trace elements (Cu, Zn, Ni, Cr, Mn, Mg, and Al) as well as vitamins E and A were determined<sup>20</sup>. There were some significant disparities between the MDD patients and the control group, according to the data. When compared to the control group, the MDD patients showed considerably greater amounts of Cu, Cr, and Al in their serum. MDD patients, on the other hand, exhibited considerably decreased levels of Zn, Ni, Mn, Mg, vitamin E, and vitamin A. The elevated Cu/Zn ratio in depressive disorder patients was one striking finding. This ratio has the potential to be useful in the diagnosis and monitoring of MDD. The study emphasizes the link between changes in element levels and vitamins (especially vitamin E) and MDD. According to the findings, Cu and Zn may play an important role in the etiology of depressive illnesses. Reduced antioxidant vitamin E levels appear to be linked to an increased risk of MDD<sup>20</sup>. It is also important to highlight the weaknesses of current study such as a small sample size and the use of an easy sampling procedure, which may limit the findings' generalizability. Furthermore, the trial was only two months long, and the long-term benefits of vitamin D and E supplementation were not investigated.

### **Conclusion**

In Conclusion, the data imply that combining vitamin D and E with antipsychotic medication may improve psychiatric outcomes in people with mental health issues. Larger sample sizes and longer follow-up periods are needed to confirm these findings and investigate the underlying processes in order to guide clinical practice and optimize treatment options for those suffering from mental diseases.

### **References**

1. Richter D, Wall A, Bruen A, Whittington R. Is the global prevalence rate of adult mental illness increasing? Systematic review and meta- analysis. *Acta Psychiatrica Scandinavica*. 2019 Nov;140(5):393-407.
2. Blackmore R, Boyle JA, Fazel M, Ranasinha S, Gray KM, Fitzgerald G, Misso M, Gibson-Helm M. The prevalence of mental illness in refugees and asylum seekers: A systematic review and meta-analysis. *PLoS medicine*. 2020 Sep 21;17(9):e1003337.

3. Abel KM, Hope H, Swift E, Parisi R, Ashcroft DM, Kosidou K, Osam CS, Dalman C, Pierce M. Prevalence of maternal mental illness among children and adolescents in the UK between 2005 and 2017: a national retrospective cohort analysis. *The Lancet Public Health*. 2019 Jun 1;4(6):e291-300.
4. Afzal M, Siddiqi N, Ahmad B, Afsheen N, Aslam F, Ali A, Ayesha R, Bryant M, Holt R, Khalid H, Ishaq K. Prevalence of overweight and obesity in people with severe mental illness: systematic review and meta-analysis. *Frontiers in Endocrinology*. 2021 Nov 25;12:769309.
5. Laws MB, Beeman A, Haigh S, Wilson IB, Shield RR. Prevalence of serious mental illness and under 65 population in nursing homes continues to grow. *Journal of the American Medical Directors Association*. 2022 Jul 1;23(7):1262-3.
6. Nair S, Satyanarayana VA, Desai G. Prevalence and clinical correlates of intimate partner violence (IPV) in women with severe mental illness (SMI). *Asian journal of psychiatry*. 2020 Aug 1;52:102131.
7. Cuomo A, Maina G, Bolognesi S, Rosso G, Beccarini Crescenzi B, Zanobini F, Goracci A, Facchi E, Favaretto E, Baldini I, Santucci A. Prevalence and correlates of vitamin D deficiency in a sample of 290 inpatients with mental illness. *Frontiers in psychiatry*. 2019 Mar 29;10:167.
8. Moslemi E, Musazadeh V, Kavyani Z, Naghsh N, Shoura SM, Dehghan P. Efficacy of vitamin D supplementation as an adjunct therapy for improving inflammatory and oxidative stress biomarkers: An umbrella meta-analysis. *Pharmacological Research*. 2022 Oct 4:106484..
9. Kris-Etherton PM, Petersen KS, Hibbeln JR, Hurley D, Kolick V, Peoples S, Rodriguez N, Woodward-Lopez G. Nutrition and behavioral health disorders: depression and anxiety. *Nutrition reviews*. 2021 Mar;79(3):247-60.
10. Seyedi M, Gholami F, Samadi M, Djalali M, Effatpanah M, Yekaninejad MS, Hashemi R, Abdolahi M, Chamari M, Honarvar NM. The effect of vitamin D3 supplementation on serum BDNF, dopamine, and serotonin in children with attention-deficit/hyperactivity disorder. *CNS & Neurological Disorders-Drug Targets (Formerly Current Drug Targets-CNS & Neurological Disorders)*. 2019 Aug 1;18(6):496-501.
11. Ostadmohammadi V, Jamilian M, Bahmani F, Asemi Z. Vitamin D and probiotic co-supplementation affects mental health, hormonal, inflammatory and oxidative stress parameters in women with polycystic ovary syndrome. *Journal of ovarian research*. 2019 Dec;12:1-8.
12. Bo Y, Liu C, Ji Z, Yang R, An Q, Zhang X, You J, Duan D, Sun Y, Zhu Y, Cui H. A high whey protein, vitamin D and E supplement preserves muscle mass, strength, and quality of life in sarcopenic older adults: A double-blind randomized controlled trial. *Clinical nutrition*. 2019 Feb 1;38(1):159-64.
13. Di Nicola M, Dattoli L, Moccia L, Pepe M, Janiri D, Fiorillo A, Janiri L, Sani G. Serum 25-hydroxyvitamin D levels and psychological distress symptoms in patients with

- affective disorders during the COVID-19 pandemic. *Psychoneuroendocrinology*. 2020 Dec 1;122:104869.
14. Fazelian S, Amani R, Paknahad Z, Kheiri S, Khajehali L. Effect of vitamin D supplement on mood status and inflammation in vitamin D deficient type 2 diabetic women with anxiety: a randomized clinical trial. *International journal of preventive medicine*. 2019;10.
  15. Kaviani M, Nikooyeh B, Zand H, Yaghmaei P, Neyestani TR. Effects of vitamin D supplementation on depression and some involved neurotransmitters. *Journal of affective disorders*. 2020 May 15;269:28-35.
  16. Casati M, Boccardi V, Ferri E, Bertagnoli L, Bastiani P, Ciccone S, Mansi M, Scamosci M, Rossi PD, Mecocci P, Arosio B. Vitamin E and Alzheimer's disease: the mediating role of cellular aging. *Aging clinical and experimental research*. 2020 Mar;32:459-64.
  17. Hofmann AB, Schmid HM, Jabat M, Brackmann N, Noboa V, Bobes J, Garcia-Portilla MP, Seifritz E, Vetter S, Egger ST. Utility and validity of the Brief Psychiatric Rating Scale (BPRS) as a transdiagnostic scale. *Psychiatry Research*. 2022 Aug 1;314:114659.
  18. Zhand N, Labelle A, Ghanem D, Gujral P, Han T, Huneault G, Jain GK, Robertson C. Comparison of Extrapyramidal Symptoms Among Outpatients With Schizophrenia on Long-Acting Injectable Antipsychotics. *Journal of Clinical Psychopharmacology*. 2022 Sep 1;42(5):475-9.
  19. Jamilian H, Amirani E, Milajerdi A, Kolahdooz F, Mirzaei H, Zaroudi M, Ghaderi A, Asemi Z. The effects of vitamin D supplementation on mental health, and biomarkers of inflammation and oxidative stress in patients with psychiatric disorders: a systematic review and meta-analysis of randomized controlled trials. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*. 2019 Aug 30;94:109651.
  20. Al-Fartusie FS, Al-Bairmani HK, Al-Garawi ZS, Yousif AH. Evaluation of some trace elements and vitamins in major depressive disorder patients: a case-control study. *Biological trace element research*. 2019 Jun 15;189:412-9.