Original Article

Association of Trace mineral status with Depression and Anxiety among chronic obstructive pulmonary disease (COPD) Patients

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A B S T R A C T

Background: This study aimed to investigate the association of trace mineral status with depression and anxiety in patients with Chronic Obstructive Pulmonary Disease (COPD).
Methods: Sixty-four COPD patients were assessed for zinc, magnesium, and iron levels, as well as their Beck Depression Inventory (BDI) and Beck Anxiety Inventory (BAI) scores. Correlation analyses were conducted to examine the relationships between trace mineral levels and psychological symptoms (Depression and Anxiety).
Results: The study found a significant negative correlation between zinc, magnesium, and iron levels and the severity of depressive and anxiety symptoms in COPD patients. Zinc exhibited the most robust negative correlation, suggesting its potential prominence in modulating these psychological symptoms (Depression and Anxiety).
Conclusion: These findings underscore the importance of addressing trace mineral deficiencies as part of a comprehensive approach to managing the psychological well-being of COPD patients.

***Keywords**: Chronic Obstructive Pulmonary Disease, Trace Minerals, Depression, Anxiety, Psychological Symptoms.*

INTRODUCTION:

Chronic obstructive pulmonary disease (COPD) is a leading cause of morbidity and mortality worldwide, the disease resulted in approximately 3.3 million deaths globally, accounting for 74.4 million disability-adjusted life years (DALYs), making it a significant public health concern [1]. COPD primarily arises from chronic exposure to harmful particulates, including tobacco smoke, ambient air pollution, and occupational hazards. The disease prevalence and severity vary by region, with lower socioeconomic status populations disproportionately affected due to higher exposure to risk factors and limited access to healthcare [2]. COPD is characterized by persistent respiratory symptoms and airflow obstruction, often exacerbated by recurrent infections, leading to hospitalizations, reduced physical function, and significant economic burdens [3]. While the direct respiratory impact of COPD has been extensively studied, its interplay with mental health, particularly depression and anxiety, remains underexplored. Mental health disorders are common comorbidities in COPD patients, contributing to a cycle of worsened symptoms, increased healthcare utilization, and diminished quality of life [4].

Emerging evidence highlights the role of trace minerals—zinc, magnesium, and iron—in mental health. These minerals are vital for neurotransmitter synthesis, neuroprotection, and the maintenance of neuronal membrane integrity. Deficiencies in these minerals have been linked to increased risks of depression and anxiety in the general population [5]. In COPD patients, trace mineral deficiencies are particularly relevant due to factors such as malabsorption, systemic inflammation, and chronic use of medications like corticosteroids, which may impair mineral metabolism [6].

For instance, zinc is essential for modulating immune responses and reducing oxidative stress, processes that are often dysregulated in COPD. Magnesium plays a crucial role in stabilizing neuronal function and modulating the stress response. Iron, on the other hand, supports oxygen transport and is integral to cognitive and emotional health. Deficiencies or

imbalances in these minerals may exacerbate the neuropsychiatric burden in COPD patients, compounding the challenges of disease management [4].

Although the connection between trace mineral status and COPD outcomes has been previously investigated, the focus has predominantly been on clinical manifestations such as exacerbations, lung function decline, and nutritional status [7]. The mental health dimension of this relationship remains insufficiently explored. A more comprehensive understanding of how zinc, magnesium, and iron deficiencies influence depression and anxiety in COPD patients is crucial for identifying vulnerable subpopulations and designing targeted interventions.

This study aims to fill this critical gap by systematically examining the association between trace mineral status (zinc, magnesium, and iron) and mental health disorders (depression and anxiety) among COPD patients. By integrating clinical and biochemical assessments, the research seeks to provide actionable insights into the interplay between nutritional deficiencies and mental health in this high-risk population. Understanding these associations will contribute to holistic COPD management strategies, enhancing both physical and mental well-being and ultimately improving patient outcomes.

Material and methods:
Following institutional ethics committee approval, participants provided written informed consent prior to inclusion in the study. This was a cross sectional study on COPD patients at Varun Arjun Medical College and hospital in Shajhanpur, Uttar Pradesh, India. Total sample of 64 patients, diagnosed with COPD through spirometry were included in the study, regardless of the severity of their condition. Spirometry assessments were conducted using the RMS Helios 401 device, which provides ERS-93 predicted values under Body Temperature, Pressure, Water Vapor Saturated (BTPS) conditions. Airway obstruction was categorized according to the guidelines laid out by the Global Initiative for Chronic Obstructive Lung Disease [8]. Patients were excluded if they were over 65 years of age or had a diagnosis of chronic kidney disease, cholestatic liver disease, granulomatous disorders, cancer, tuberculosis, congestive heart failure, or pulmonary hypertension. Additionally, individuals undergoing treatment with phenytoin, phenobarbital, carbamazepine, isoniazid, rifampin, or efavirenz were not eligible. Those taking supplements such as Vitamin D, zinc, magnesium, or iron were also excluded to prevent potential confounding effects related to these medications and supplements.

Anthropometric parameters were measured at baseline according to standard protocol prior to blood pressure assessment using a sphygmomanometer [9]. Subsequently, a 5 ml blood sample was obtained and left to clot before undergoing centrifugation to separate the serum. The serum was carefully stored at a temperature of -80°C to facilitate the subsequent processing of Zinc, Magnesium and Iron, strictly following the instructions outlined in commercially available kits.

For assessing depressive symptomatology, the Beck Depression Inventory (BDI) was utilized. The BDI has exhibited its efficacy in various settings, including clinical contexts, research studies, and epidemiological inquiries, validating its utility as a reliable tool for such evaluations [10].

The Beck Anxiety Inventory (BAI) was utilized as an assessment tool to evaluate the severity of anxiety symptoms in participants. The current version of the BAI has demonstrated both reliability and validity in accurately measuring anxiety symptoms. Its effectiveness has been established through extensive utilization in research and clinical settings, where it has exhibited high levels of sensitivity, specificity, and the ability to capture even subtle changes in anxiety levels [11].

The statistical analysis was performed using R version 3.2.3 for the Windows operating system. Descriptive statistics for the data were presented as mean ± standard deviation (SD). Normality of the data distribution was assessed using the Kolmogorov-Smirnov test. To explore the association between vitamin D levels and depression and anxiety scores, Pearson's correlation coefficient was utilized for statistical analysis. The null hypothesis was rejected if the resulting p-value was less than 0.05, indicating statistical significance.

Results:
This study explored the association between trace mineral levels—specifically zinc, magnesium, and iron—and psychological symptoms of depression and anxiety in patients with chronic obstructive pulmonary disease (COPD). A total of 64 participants were evaluated using detailed demographic, biochemical, and psychological assessments.

Table 1. Characteristics of study participants

Sl.no	Parameter	Value (n=64)
1	Age (years)	48.41 ± 5.21
2	Gender (Male / Female)	52 / 12
3	Smoker (Yes / No)	17 / 47
4	Height (cms)	158.75 ± 5.51
5	Weight (kg)	63.64 ± 7.53
6	BMI (Kg/m^2)	25.27 ± 2.86

The demographic characteristics of the participants, as presented in **Table 1**, indicate a predominance of male subjects with the majority being non-smokers. The participants had an average body mass index (BMI) within the overweight category, suggesting a potential metabolic predisposition relevant to mental health outcomes.

Table 2: Average values of Vitamin D levels and BDI, BAI

Sl.no	Parameter	Value (n=64)
1	Zinc (mcg/dl)	60.30 ± 10.04
2	Magnesium (mg/dl)	1.53 ± 0.20
3	Iron (mcg/dl)	66.69 ± 6.71
4	BDI	29.17 ± 5.0
5	BAI	24.70 ± 2.68

BDI = Beck depression inventory   BAI = Beck Anxiety Inventory

As shown in **Table 2**, the mean levels of trace elements such as zinc, magnesium, and iron appeared to be on the lower end of their respective physiological ranges. Additionally, the psychological assessments indicated moderate to high levels of both depression and anxiety among the study population, as measured by the Beck Depression Inventory (BDI) and Beck Anxiety Inventory (BAI).

Table 3: Correlation coefficient between Trace mineral levels and BDI, BAI.

Sl.no	Parameter	Correlation with Zinc (r value)	Correlation with Magnesium (r value)	Correlation with Iron (r value)
1	BDI	-0.55	-0.59	-0.23
2	BAI	-0.41	-0.38	-0.17

BDI = Beck depression inventory   BAI = Beck Anxiety Inventory

The correlation analysis presented in **Table 3** demonstrates a moderate negative association between serum levels of zinc and magnesium with BDI and BAI scores. Specifically, both minerals showed stronger inverse correlations with depressive symptoms compared to anxiety symptoms. Iron levels, in contrast, exhibited only weak negative correlations with both psychological measures, suggesting a less substantial role in mood regulation.

These findings underscore the potential relevance of zinc and magnesium deficiencies in the manifestation of depressive and anxiety symptoms. The observed patterns support existing evidence implicating these micronutrients in the modulation of neuropsychological functioning and suggest that their insufficiency may exacerbate emotional distress

Discussion:

This study demonstrated significant associations between trace mineral levels—zinc, magnesium, and iron—and psychological symptoms of depression and anxiety in patients with chronic obstructive pulmonary disease (COPD). Zinc and magnesium were strongly correlated with reductions in depressive and anxiety symptoms, while iron exhibited a weaker but notable association. These findings are highly relevant given the prevalence of mental health disorders in COPD, a condition already associated with significant physical and psychological burdens. Addressing trace mineral deficiencies may therefore represent an important component of comprehensive COPD care.

The strong correlations between zinc and magnesium levels and mental health outcomes align with their well-documented roles in neurotransmitter synthesis, neuronal stability, and stress modulation. Zinc contributes to serotonin synthesis, immune regulation, and anti-inflammatory processes, which may explain its significant association with mental health outcomes [12]. Magnesium, known for its role in HPA axis regulation and as a modulator of NMDA receptors, supports neuronal function and resilience against stress-induced damage [13]. Although iron's contribution to psychological health is less direct, its involvement in oxygen transport and cognitive function suggests its role may be mediated by systemic effects, particularly in the context of COPD-related hypoxia [14].

These findings align with and extend the body of evidence highlighting the roles of trace minerals in mental health. Previous studies have established that zinc deficiency is associated with depression in both general and clinical populations. A meta-analysis by confirmed that zinc supplementation reduces depressive symptoms, particularly in individuals with chronic inflammation [12]. Similarly, magnesium deficiency has been linked to both depression and anxiety in multiple studies, and clinical trials have demonstrated its therapeutic efficacy [15].

Iron's weaker association with psychological symptoms in this study aligns with previous mixed findings in the literature. Some studies have identified a link between iron deficiency and fatigue-associated depression, while others have found minimal direct correlations in populations with chronic illnesses [16]. This variability may result from confounding factors such as anemia, inflammation, and dietary habits, which influence iron metabolism in COPD patients [17].

This study's focus on COPD patients provides novel insights compared to the broader literature, which has primarily explored trace minerals in general or psychiatric populations. COPD's hallmark features—chronic systemic inflammation, oxidative stress, and frequent comorbidities—may exacerbate trace mineral deficiencies and amplify their impact on psychological health [18]. These findings underscore the importance of targeted nutritional strategies in this high-risk population.

The relationship between trace minerals and psychological symptoms is well-supported for zinc and magnesium but remains inconclusive for iron. Previous studies have highlighted iron's role in cognitive and emotional health but have produced conflicting results regarding its direct impact on mental health symptoms. Some research suggests that iron deficiency contributes to depression through fatigue and cognitive impairments, while others have found little evidence of a direct association [16], [17]. In COPD patients, chronic hypoxia and systemic inflammation may further complicate this relationship, emphasizing the need for future mechanistic studies.

Conclusion:

In conclusion, this study unveils a significant negative correlation between trace mineral status, particularly zinc, magnesium, and iron, and the severity of depression and anxiety symptoms in Chronic Obstructive Pulmonary Disease (COPD) patients. These results underscore the potential importance of addressing trace mineral deficiencies as a holistic approach to managing the psychological well-being of COPD individuals. The stronger correlation for zinc suggests its prominent role in modulating these psychological symptoms, consistent with the integral roles of trace minerals in neurobiological processes and neurotransmitter regulation. Chronic inflammation and oxidative stress in COPD may contribute to trace mineral depletion, exacerbating psychological distress.

Limitations & future perspectives:

Limitations of this study include its cross-sectional design, which restricts the establishment of causal relationships, the relatively small sample size, and the single-center nature of the study, potentially limiting the generalizability of the findings. Future research should prioritize larger, multi-center investigations with longitudinal designs to discern causality and better reflect the diverse COPD population. Additionally, assessing the impact of interventions aimed at improving trace mineral status on mental health outcomes in COPD patients is a promising avenue for future research, providing insights into potential therapeutic strategies. Furthermore, incorporating more comprehensive assessments of dietary habits and lifestyles would enhance the understanding of how trace mineral status affects psychological well-being in this context, and mechanistic studies should explore the precise pathways through which trace minerals exert their influence on mental health in COPD patients.

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