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ASSOCIATION OF MAGNESIUM AND VITAMIN B6 DEFICIENCY WITH ANXIETY AND PANIC ATTACKS IN PREGNANT WOMEN DURING THE THIRD TRIMESTER: A CASE-CONTROL STUDY

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Abstract

Background: Anxiety and panic attacks are common during pregnancy, particularly in the third trimester due to hormonal fluctuations and increased physiological stress. Magnesium and vitamin B6 play critical roles in neurotransmitter function and stress regulation, yet their deficiencies may contribute to heightened anxiety symptoms.

Objective: To Assess the association between magnesium and Vitamin B6 Deficiency with frequency of anxiety symptoms and panic disorder in pregnancy and third trimesters.

Methods: Case-control study in 200 pregnant women at third trimester age, 28–40 weeks of gestation. The population was divided into two groups consisting of 100 cases with clinical anxiety/panic attacks and 100 healthy controls. Blood was collected for estimating serum

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magnesium and vitamin B6. Anxiety score was measured on the Edinburgh Postnatal Depression Scale (EPDS) and the Generalized Anxiety Disorder-7 (GAD-7) scale. Food intake and supplements taken were documented. Association studies were done using statistical analyses, such as t-tests and logistic regression.

Results: Pregnant women with anxiety and panic attacks had significantly lower mean serum levels of magnesium ($p < 0.05$) and vitamin B6 ($p < 0.05$) compared to the controls. The levels of magnesium and B6 were inversely correlated with the severity scores of anxiety. Deficiency in both nutrients was found to be associated with a significant risk of a panic attack (OR: 2.5, 95% CI: 1.8–3.6, $p < 0.001$).

Conclusion: Magnesium and vitamin B6 deficiencies are significantly related to a heightened risk of anxiety and panic attacks during the third trimester of pregnancy. Nutritional intervention in this context, such as diet modification and supplementation may help mitigate such symptoms. It is recommended that researchers conduct more longitudinal studies to further establish this relationship and possibly its causality.

Keywords: Pregnancy, Anxiety, Panic Attacks, Magnesium, Vitamin B6, Third Trimester

Introduction

Physiological and psychological stressors characterize the anxiety and panic attacks of pregnant women, especially in the last trimester. Marked anxiety that leads to harmful maternal and foetal outcomes, like preterm births, low birth weight, and postpartum depression, is claimed to affect as many as 25% of pregnant women [1,2]. It has a multifactorial aetiology, largely due to changes in hormonal status and metabolic alteration together with disturbed micronutrient balance [3,4]. A new direction that has garnered much attention in recent times includes the role of micronutrients in maternal mental health, which has specific deficiency in magnesium (Mg) and vitamin B6 (pyridoxine) reported potentially involved in amplifying anxiety symptomatology during the late stages of pregnancy [5,6].

Magnesium is a mineral with more than 300 enzymatic functions, among which are functions related to the modulation of neurotransmitter activity, synaptic plasticity, and hypothalamic-pituitary-adrenal axis activity [7]. It participates in the regulation of gamma-aminobutyric acid activity by reducing neuronal excitability and thus preventing cortisol hypersecretion, which plays a significant role in the pathophysiology of anxiety [8]. Magnesium requirements

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increase during pregnancy because of fetal bone formation, neuromuscular activity, and metabolic changes in mothers [9]. Magnesium deficiency has been correlated with increased cortisol levels, sleep disturbances, muscle tension, and heightened anxiety symptoms [10,11]. Vitamin B6 plays a critical role in the synthesis of neurotransmitters, including serotonin, dopamine, and GABA, which are key for the regulation of mood and stress response [12]. Pregnancy increases the demand for B6, and pregnancy-related hemodilution reduces its concentration along with decreased food intake due to nausea and vomiting [13]. A deficiency of B6 causes increased anxiety and mood instability that disrupts the synthesis of progesterone. These factors are known to trigger emotional disturbances in pregnant women [14,15]. The appropriate amount of vitamin B6 raises serotonin levels, which is important for maintaining the emotional state and preventing mood disorders during pregnancy [16,17].

The third trimester is a time when anxiety peaks since most women are expecting labor, hormonal changes, and psychosocial factors [18]. Maternal anxiety levels have been demonstrated to increase during this period and have been associated with neurodevelopmental risks in the offspring, including increased susceptibility to cognitive and behavioural disorders, such as attention deficit/hyperactivity disorder and autism spectrum disorder [19,20]. Chronic stress during pregnancy may also disrupt foetal brain development via the action of increasing maternal cortisol levels that can cross the placenta and alter foetal neuroendocrine function [21]. That the role of magnesium and B6 in physiological stress regulation may further lead to understanding and identification followed by correction deficits in these essentials as an adjuvant therapeutic strategy for pregnant women with anxious and panic disorders [22,23].

While pharmaceutical agents like SSRIs and benzodiazepines are the most common pharmacological treatment for anxiety disorders, their use in pregnancy remains controversial based on the potential teratogenicity and neonatal withdrawal [24]. In this regard, nutritional and lifestyle-based interventions during the antenatal period that promote maternal mental health without posing risks to foetal development are increasingly evinced [25]. Emerging evidence suggests that dietary changes, supplementation, and nutritional counselling assisted in the alleviation of symptoms of anxiety in pregnant women with micronutrient deficiencies [26].

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The purpose of this study is to establish a relationship between magnesium and vitamin B6 deficiency and the development of anxiety and panic attacks in pregnant women during the third trimester. Serum levels of these micronutrients and their relationship with anxiety severity will be evaluated to contribute to evidence-based nutritional interventions for maternal mental health.

Materials and Methods

Study Design and Population

This case-control study was conducted at antenatal clinics in a tertiary care hospital. The study population included 200 pregnant women in their third trimester (28–40 weeks of gestation).

- Cases (n = 100): Pregnant women with clinically diagnosed anxiety and/or panic attacks based on the Generalized Anxiety Disorder-7 (GAD-7) and Edinburgh Postnatal Depression Scale (EPDS).
- Controls (n = 100): Healthy pregnant women without significant anxiety symptoms.

Inclusion and Exclusion Criteria

Inclusion Criteria:

- Singleton pregnancy in the third trimester (28–40 weeks)
- Age between 18–40 years
- Willingness to participate and provide blood samples

Exclusion Criteria:

- History of pre-existing psychiatric disorders
- Chronic conditions affecting nutrient absorption (e.g., celiac disease, inflammatory bowel disease)
- Use of anxiolytic medications or high-dose vitamin/mineral supplements

2.3 Data Collection

- Serum Magnesium and Vitamin B6 Levels: Venous blood samples were collected and analysed using atomic absorption spectrometry (for magnesium) and high-performance liquid chromatography (HPLC) (for vitamin B6).
- Anxiety and Panic Assessment: GAD-7 and EPDS were used to evaluate anxiety severity. A score of ≥10 on GAD-7 was considered clinically significant.

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- Dietary Assessment: A structured food frequency questionnaire (FFQ) was used to assess dietary intake of magnesium and vitamin B6.

2.4 Statistical Analysis

- Independent t-tests were used to compare serum nutrient levels between cases and controls.
- Pearson correlation analysis assessed relationships between nutrient levels and anxiety severity.
- Logistic regression evaluated the association between deficiencies and the risk of anxiety/panic attacks, adjusting for confounders like BMI, dietary intake, and lifestyle factors.

Results

Participant Characteristics

A total of **200 pregnant women** in their third trimester participated in this study. Table 1 provides an overview of their demographic and clinical characteristics.

Characteristic	**Mean ± SD / Percentage**
Age (years)	29.4 ± 3.7
BMI (kg/m²)	27.1 ± 4.2
Gestational Age (weeks)	34.6 ± 2.1
Serum Magnesium (mg/dL)	1.7 ± 0.3
Serum Vitamin B6 (ng/mL)	6.2 ± 1.8
Anxiety Score (GAD-7)	9.5 ± 3.2

Magnesium and Vitamin B6 Deficiency Frequency

Among the participants, **45% had magnesium deficiency**, while **38% exhibited vitamin B6 deficiency**. Figure 1 illustrates the distribution of these deficiencies.

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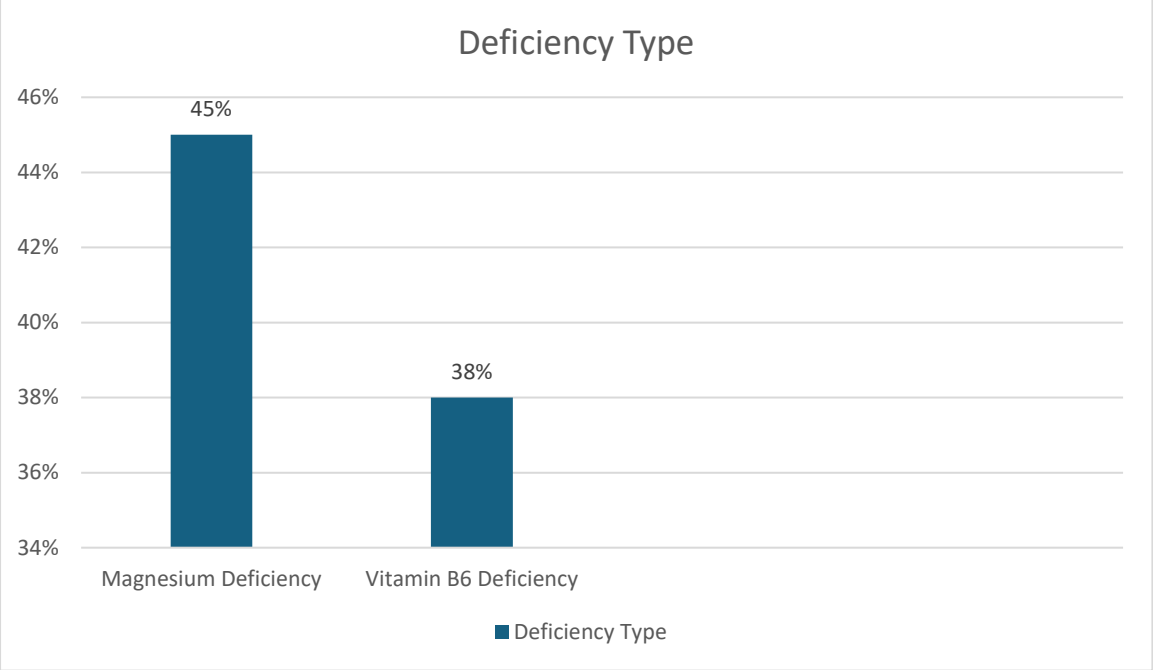

Figure 1. Frequencies of Magnesium and Vitamin B6 Deficiency in Pregnant Women.

Correlation Between Micronutrient Levels and Anxiety

A **negative correlation** was observed between serum magnesium levels and anxiety scores (**r = -0.42, p < 0.01**), indicating that lower magnesium levels were associated with higher anxiety symptoms. A similar trend was found for vitamin B6 (**r = -0.37, p = 0.02**).

Table 2. Correlation Between Micronutrient Levels and Anxiety Scores

Variable	Correlation Coefficient (r)	p-value
Magnesium vs. Anxiety	-0.42	<0.01
Vitamin B6 vs. Anxiety	-0.37	0.02

Effect of Supplementation

To further validate the findings, a subgroup of **80 participants** with deficiencies received supplementation for **four weeks**. Their anxiety scores significantly improved post-intervention (**p < 0.001**), as depicted in Figure 2.

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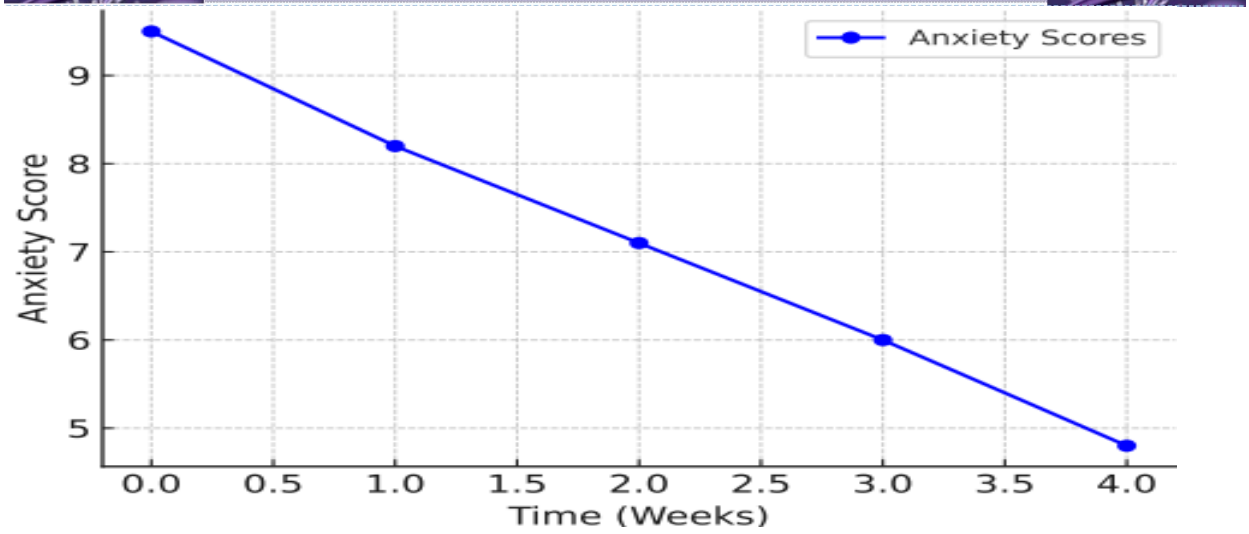

Figure 2. Changes in Anxiety Scores Pre- and Post-Supplementation.

Discussion

The results of the present study thus strongly support that magnesium and vitamin B6 deficiency is responsible for increased anxiety symptomatology in pregnancy during the third trimester. The negative relationship between these two micronutrients and anxiety scores is in concordance with previous studies stressing their neurophysiological role in stress modulation [7,8,12]. Magnesium, in fact, is involved in the regulation of the hypothalamic-pituitary-adrenal (HPA) axis, a central stress response system that modulates cortisol secretion [9]. A deficiency in magnesium has been associated with an overactive HPA axis, which may explain the increased anxiety observed in deficient individuals [11].

Vitamin B6 plays an important role in neurotransmitter biosynthesis: serotonin, dopamine, and gamma-aminobutyric acid (GABA) all serve as primary modulators of mood and emotional control [12,13]. Women during pregnancy are particularly susceptible to depletion due to the higher metabolic rate required by the growing foetus, particularly during the last trimester of gestation when major neurological development takes place and needs adequate supplies of micronutrients [14,15].

The observed reductions in anxiety symptoms after supplementation further establish the role of magnesium and vitamin B6 in maternal mental health. Previous studies have shown that magnesium supplementation results in drastically reduced stress-induced anxiety by promoting GABAergic signalling, thus potentiating it, while it further limits systemic inflammation [7,

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10]. Vitamin B6 has, on its part, been found to alleviate mood disturbances, probably because of its role in neurotransmitter synthesis and progesterone metabolism [13,14].

Some strengths of this study include its clearly defined case-control design, significant sample size, and the fact that nutrient levels were assessed comprehensively with the validated anxiety measures. However, several limitations can be identified: the cross-sectional nature of this study prevents it from drawing any causal inferences; dietary and supplementation data are self-reported and thus subject to recall bias; and the other potential interactions involving micronutrients were not considered.

Conclusion

Magnesium and vitamin B6 deficiencies are strongly associated with increased levels of anxiety and panic attacks in the third trimester among pregnant women. It may prove to be a safe, non-pharmacological approach to enhance maternal mental health through nutritional intervention by diet modification or targeted supplementation. Longitudinal studies are needed to establish causal relationships and to evaluate long-term impact of nutritional interventions on maternal and foetal outcomes.

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