Cihan University-Erbil Scientific Journal (CUESJ)

Research Article

Relationship between Sera Vitamin D, Calcium, and Magnesium Levels in Pregnant Women with and without Postpartum Depression

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ABSTRACT

Postpartum depression (PPD) is a significant mental health case after childbirth, distinguished by behavioral changes and emotional disturbance. PPD is a significant public issue estimated to affect 10–15% of women worldwide. The study's objective was to investigate whether low sera concentrations of Vitamin D, calcium, and magnesium during the third trimester of pregnancy were associated with PPD. The study population included 80 pregnant women between the ages of 25 and 35 years. In this study, we followed up the pregnant women until birth. After childbirth, those women were divided into two groups: Group 1 (40 healthy women as a control group) and group 2 (40 unhealthy women with PPD disorder). When the blood samples were taken, Vitamin D level was determined using an ELISA device. While, calcium and magnesium were measured using the spectrophotometric method. A health questionnaire structure was used for screening depression after birth. After measuring pregnancy serum concentrations of Vitamin D of both two groups, we found that there was no significant relationship between Vitamin D concentrations in pregnant women and PPD ($P = 0.6497$). A significant difference in sera calcium ($P = 0.0003$) and magnesium levels ($P = 0.0005$) between the control group and depressed group was observed. Our study detected that Vitamin D concentrations in the serum of women during their last trimester of pregnancy had no statistical link with their risk of PPD. Whereas direct association in calcium and magnesium deficiency in the third trimester of pregnancy and happening of PPD were reported in this study.

Keywords: Calcium, magnesium, postpartum depression, third trimester of pregnancy, vitamin D

INTRODUCTION

Postpartum depression (PPD) is one of the most common and public health problems of childbirth.[1] Approximately one-fifth of women present depression during pregnancy and after birth,[2] yearly affecting about 10–15% of postnatal women.[3] It sets within a few months to a year after birth. However, some evidence indicated postpartum depression 4 years after birth.[4] It is characterized by low appetite, fatigue, the feeling of guilt, and sleep problems.[5] Untreated maternal illness is potentially associated with adverse consequences for the mother, her infant, and her family.[6] The etiology remains unclear and complex.[7] Most commonly risk factors such as having a history of anxiety and depression during pregnancy, stressful life events, biological factors, and low social support are involved in the progression of postpartum depression.[8]

Furthermore, there are many researches about the contribution of nutritional status of minerals and vitamins, which are associated with several body's metabolic regulations for depression patients.[9] For instance, Vitamin D is one of the nutritional factors linked with cognitive decline in mental health. It has been hypothesized that a low concentration of Vitamin D may take part in depression.[10] Research supports the connect between depression and Vitamin D in three ways. First Menon *et al.*[11], Vitamin D plays as a neuroactive hormone. Sundry sources have demonstrated that receptors of Vitamin D are largely distributed throughout the brain of the human and play a key role in mood regulation.[12] Second, Vitamin D has a role in regulating the immune system and reducing the release of inflammatory substances.[13] Finally, Vitamin D as well has a defensive influence versus a low concentration of specific hormones such as serotonin and dopamine.[14]

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Received: June 16, 2022
Accepted: October 23, 2022
Published: December 20, 2022

DOI: 10.24086/cuesj.v6n2y2022.pp147-152

Concerning macromolecules, calcium (Ca) and magnesium (Mg) are the most predominant intracellular cation. Certain studies have found elevation of Ca and Mg among depressed pregnant women. In contrast, others show a decrease in levels of Ca and Mg.[15] Calcium has several vital functions in the human's body.[16] More than 99% of total Ca is present in the skeleton, supporting their framework. While, the residual 1% is set in the blood, muscle, and the fluid between cells which is necessary for contraction of muscle, expansion and contraction of blood vessel, hormones and enzymes excretion, and posting messages through the nervous system.[17] In human's body, magnesium is one of the fundamental minerals and a cofactor of over 300 enzymatic reactions.[18] Deficiency of Mg has been reported in depression. It is a natural calcium channel blocker, and it is needed for nerve function and appropriate relaxation. Ca enhances the nerves and Mg calms them down. All these systems have been associated with the depression's pathophysiology. Mg as well dampens the calcium ion-protein kinase C-linked neurotransmission and catalyzes the Na-K-ATPase.[19] When Mg is declining, it is possible to notice an increase in the activity of the N-methyl-D-aspartate receptor (NMDA receptor), as well as substance P, which may cause increased pain and elevated hormones related to stress.[20]

According to our investigation, this study was the first trial held to measure Vitamin D, Ca, and Mg levels together in the serum of pregnant women in their last trimester of pregnancy and studying their relation with postpartum depression. The primary goal of this study was to illustrate if low levels of Vitamin D, Ca, and Mg in the sera of pregnant women in their third (last trimester) of pregnancy were linked with their affecting by postpartum depression or not in the Iraqi population/Garmian/Kalar.

METHODS AND CLINICAL MEASUREMENTS

Clinical Measurements

The population of this study was conducted on the sera of 80 healthy pregnant women aged 25–35 years. We measured sera Vitamin D, calcium, and magnesium for those pregnant women in their third trimester of their pregnancy. Afterbirth, we followed their cases. If they did not suffer from postpartum depression, we considered them as group 1; healthy women or control group (40 women). On the other hand, the women who suffered from postpartum depression, we regarded them as group 2; unhealthy women or depressed women (40 women). The pregnant donors did not have any severe diseases in the third trimester of pregnancy. For example, they didn't suffer from hypertension, liver disorders, congenital heart diseases, renal dysfunction, cancers, kidney disorder, rheumatoid arthritis, blood diseases, lung disease, and diabetes or any other diseases. We excluded those pregnancies that took vitamins, minerals, and any other drugs. In addition, group 2 (depressed women) and group 1 (healthy women) provided their written, informed approval to take part in our study.

The blood samples of pregnant women were collected from Shahed Sheray Naqeb Hospital in Kalar which is the center of Garmian region from September (2020) to February (2021).

Approximately 5 ml of blood samples were gained from pregnant donors, then centrifuged at 1500 rpm for about 10 min to obtain the serum, after that divided into tiny fractions, and kept frozen at −30°C for analysis.

Estimation of Vitamin D

Enzyme immunoassay was applied for the fixing of 25(OH)-vitamin concentration in sera of the third trimester of pregnant women using of Monobind kit,[21] using an ELISA device.

Estimation of Calcium

Serum calcium level was estimated using a colorimetric method using Bilbao diagnostic kit.[22]

Estimation of Magnesium

Serum magnesium ion was determined spectrophotometrically using Bilbao diagnostic kit.[23]

Statistical Analysis

Statistical analysis was achieved by GraphPad Prism. The outcomes were expressed as mean ± standard deviation. The *P*-value was considered significant if it was < 0.05.

RESULTS

The comparison of the quantitative variables between group 1 and group 2 is described in Table 1. The ages of both groups were between 25 and 35 years. BMI for group 1 was 28.55 ± 4.419 kg/m^2, while for group 2 was between 27.96 ± 4.014 kg/m^2.

The Table 1 illustrates that there was a significant statistical association between age and group 2 (26.97 ± 5.623), as well as with healthy group 1 (30.09 ± 5.933) and $P = 0.0274$. Box plots of age between two subjects are shown in Figure 1a. For BMI, there was non-significant interaction with both two groups ($P = 0.5987$), that shown in Figure 1b.

The normal ranges of sera kits which used in this study were Ca; 8–10 mg/dL and Mg; 1.7–2.2 mg/dL, whereas Vitamin D was found in the normal sera ranges (v. D; 30–50 ng/ml). As described in the table, there was also a slight decrease in sera Vitamin D concentrations in group 2 compared with group 1 (34.10 ± 4.254 and 34.88 ± 6.495), respectively. However, there was no significant connection between them ($P = 0.6497$). Box plot of Vitamin D is shown in Figure 1c. Besides, group 2 or unhealthy women with PPD had lower sera levels of Ca and Mg than group 1 or healthy women (8.673 ± 0.5503, 1.568 ± 0.3292) and (9.136 ± 0.4401, 1.876 ± 0.2454), sequentially, with a significant statically link between them ($P = 0.0003$ and 0.0005), respectively, as shown in Figure 1d and e, sequentially.

DISCUSSION

Postpartum depression is known as an episode of major depression that is temporally linked with childbirth.[24] PPD is a severe threat to the child, mother, and other members of the family.[19] The findings of our study provide that there was a statistically different in ages between both groups were $P = 0.0274$, as shown in Table 1. Furthermore, there was no

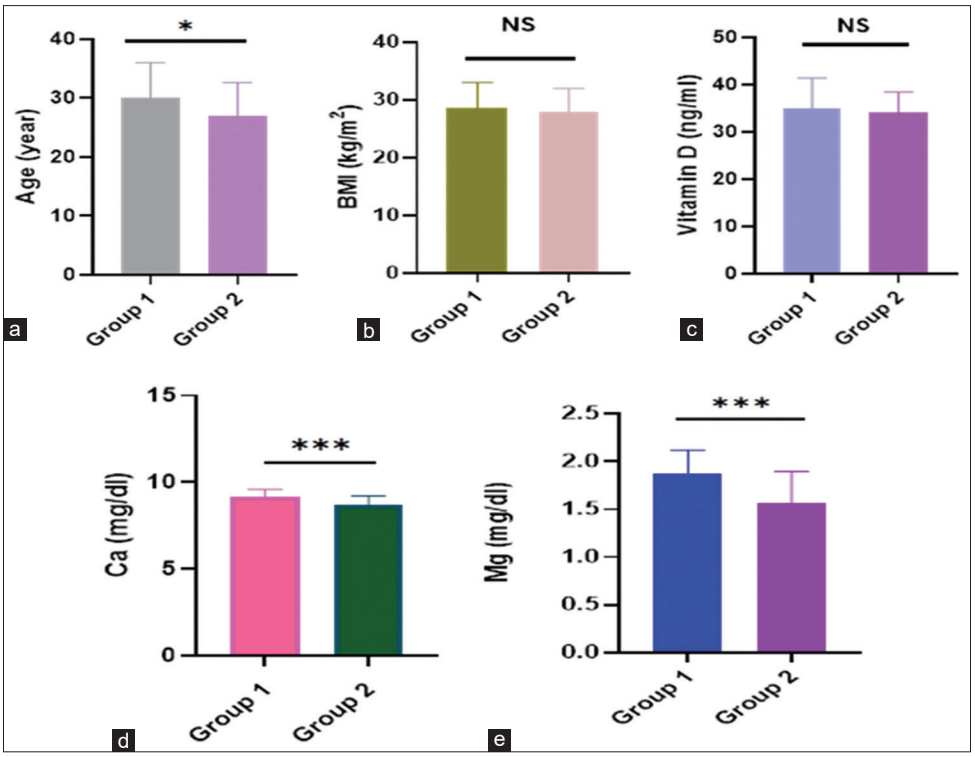

Figure 1: Box plot of the results, (a) age was significantly lower in group 2 in compared with the group 1, (b) body mass index was not significant in both group 1 and group 2, (c) Vitamin D was not significant among both groups, (d) Ca was significantly lower in group 2 in compared to group 1 (e). Mg was significantly lower in the second group in compared to the first group. Group 1: 40 healthy women without postpartum depression (PPD) as a control group. Group 2: 40 unhealthy women with PPD disorder as depressed women

Table 1: Comparisons of numerical variables for group 1 and group 2

Parameters	Group 1 (healthy) Means±SD	Group 2 (depression) Means±SD	*P*
Number	40	40	
Age (years)	30.09±5.933	26.97±5.623	0.0274 S
BMI (kg/m^2)	28.55±4.419	27.96±4.014	0.5987 NS
Vitamin D (ng/ml)	34.88±6.495	34.10±4.254	0.6497 NS
Ca (mg/dL)	9.136±0.4401	8.673±0.5503	0.0003 S
Mg (mg/dL)	1.876±0.2454	1.568±0.3292	0.0005 S

Data are shown as the mean ± standard deviation (means±SD).
SD: Standard deviation, BMI: Body mass index, kg/m^2: Kilogram per meter square, ng/ml: Nanogram per milliliter, mg/dL: Milligram per deciliter, *P* value is the probability, significant $P < 0.05$, S: Significant, NS: Not significant, Student's t-test

statistical link among the BMI (the patients set and the healthy subjects) in which $P = 0.5987$ was considered, as shown in Table 1.

Many factors are placed a woman at danger of developing PPD, such as age, type of insurance, marital status, whether or not the pregnancy was planned, race/ethnicity, type of feeding, and level of educational.[25-29]

In addition, studies have shown the beneficial impact of dietary factors during pregnancy on depressive symptoms. One of those dietary factors is Vitamin D which has been proposed to usefully influence gloom in adults. It has been supposed that Vitamin D may work as a neuroactive hormone.[12] A lot of studies confirm the role of Vitamin D in conception, placentation, improvement of pregnancy, and pregnancy outcomes inclusive the offspring's health. Altogether, Vitamin D supports placental outgrowth and task by regulating placental calcium transport, and by exerting immunomodulatory effects, critical for pregnancy maintenance.[30] Many researchers have found that receptors of Vitamin D are primarily doled out throughout the brain of human, and its lack mutates neurotransmitters which are familiar to be included in of depression's symptoms.[12] Although the results of our study indicated a slight decrease in Vitamin D concentrations among the pregnant women who afterbirth affected by PPD; we found that the sera Vitamin D levels had no significant link between women with PPD and those with non-PPD ($P = 0.6497$), as shown in Table 1. This decrease in Vitamin D levels agrees with those gotten by Abedi *et al.*, Aghajafari *et al.*, Murphy *et al.*, Accortt *et al.*, Ribamar *et al.*, and Lin *et al.*,[5,12,31-34] they also found sera Vitamin D concentrations were significantly lower in depressed women than in the healthy subject. Similarly, the study Wang *et al.*[35] did not record a considerable connect between depressive symptoms and low concentrations of Vitamin D through pregnancy. In addition, Robinson *et al.*[36] showed that at 18 weeks gestation, a significantly low level of Vitamin D in sera was linked with a major danger of the symptoms of PPD. Furthermore, in the study of Fu *et al.*,[37] the researchers reported that sera Vitamin D concentrations after delivery were significantly lower in women with PPD than those without PPD. Moreover, research of Fallah *et al.*[14] at 18 weeks gestation measured concentration of Vitamin D sera,

where they detected a significant association between quality of the sleep through pregnancy and PPD with deficiency of Vitamin D.

On the other hand, our finding did not agree with the study of Nielsen *et al.*[1]; where their outcomes did not find a connection between danger of PPD and low Vitamin D levels through pregnancy. In contrast, an increased danger of postpartum depression was detected among women with the highest levels of Vitamin D. Similarly, Tan *et al.*[38] found contrast data to our results. They reported that high blood sera of Vitamin D concentrations have a preventive impact on maternal depression. Notably, when blood concentration of Vitamin D was raised, the maternal depression risk was the lowest. In addition, in a study Gould *et al.*,[39] concentrations of Vitamin D were measured at delivery, and they did not reveal a consistent link between Vitamin D concentrations and PPD. Finally, a study of Williams *et al.*[40] found that levels of Vitamin D were not linked with diagnoses of generalized anxiety trouble or major depressive turmoil.

Further, Vitamin D has been increasingly attached to mental health cognitive decline, and it has been hypothesized that hypovitaminosis D may give a share to depression.[10]

Electrolyte dysfunction has been reported with depressive disorders for the past six decades. The most predominant intracellular cation is calcium.[15] Dysregulation of Ca is profound in disorders of the nervous system such as depression and dementia.[9] In the biosynthetic pathway, Ca activates tryptophan hydroxylase, leading to the synthesis of serotonin. Furthermore, the calcium/calmodulin-dependent system may promote the synthesis of dopamine in the brain. In the immune system cells, Ca acts as a signal as well. In the extracellular, changes in Ca level may impact the neuromuscular tissues excitability contributed in regulation of emotional.[41]

Despite that, findings from this study suggested that sera Ca levels were considerably lower in group 2 (women with PPD) in comparing to group 1 (healthy women without PPD) ($P = 0.0003$). This finding was in agreement with the study done by Paoletti *et al.*[42]; when their donors' group was randomized to calcium/Vitamin D treatment, they reported a decrease in the degree of depression among healthy puerperal women.

However, our study did not agree with a study that was done by Sharma *et al.*[15] which reported that there was no correlation in the depressive symptoms severity with sera levels of Ca. Further, a previous study done by Li *et al.*[41]; detected no important link between dietary Ca consumption and depression risk.

Mg also plays a role in the entry of Ca into the neuron. Magnesium is probable to keep the neuron versus the cell's death by regularizing this entrance and may be linked with the depression danger through preserving the nervous system. Consumption of magnesium dietary may be connected with depression by safeguarding the nervous system.[41] Mg extends antidepressive action over a set of mechanisms that in the end, encourages a drooping of the glutamatergic pathway, and a raise of brain-derived neurotrophic factor (BDNF) and serotonin.[42]

Regarding the trace element Mg, similarly to Ca results, our data showed that levels sera of Mg were statically lower in group 2 (depressed subject) than group 1 (undepressed donors) ($P = 0.0005$). This finding was in agreement with studies done by Nechifor and Nechifor;[43,44] where they record a reduction of erythrocyte Mg in adult patients with medium, major, and severe depression.

Furthermore, concerning Mg supplementation[41,45] recorded an opposite connection among community-dwelling adults between Mg consumption and symptoms of depressive.

On the other hand, these grades do not agree with those gotten by Wojcik *et al.*[46]. Their results did not elucidate a relevance between decreased sera Mg concentration and severity of depressive symptoms in a specific affective disorder, postpartum depression. Furthermore, this study Fard *et al.*[47] concluded that Mg did not minimize depressive symptoms and postpartum anxiety. In addition, the study of Ram *et al.*[15] indicated no correlation in sera concentrations of Mg and severity of depressive symptoms in patients with a major disorder of depressive. Similarly Widmer *et al.*[48] have reported raised Mg in erythrocytes and plasma of moderate and severely depressed patients.

Deficiency of Mg could lead to numerous psychiatric symptoms involving tremors, headaches, behavior disturbances, irritability and psychotic behavior, generalized tonic–clonic, focal seizures, vertigo, and depression.[19] It has also been suggested that the transmit of huge quantities of this mineral from the blood of mother to the fetus with another nutrient may give a share in the appearance of PPD.[18] Finally, it can be said that vitamin favorably modifies functions of the brain, antagonizing the evolution of PPD.[42]

CONCLUSION

So far, low Vitamin D, Ca, and Mg concentrations may be a neglected danger factor for PPD. However, to our knowledge, this is the first trial that has been carried out to clarify the impact of Vitamin D, Ca, and Mg insufficiencies together on the occurrence of PPD. We have recorded that lower concentrations of Vitamin D, Ca, and Mg in the third trimester of pregnancy are connected to a danger for announcing symptoms of postnatal depressive in the 1st days following delivery. Therefore, ensuring appropriate consumption of Vitamin D, Ca, and Mg through pregnancy may be one way of conserving versus postpartum mood disturbance in mothers. Finally, health policymakers must pay awareness to the reality that measuring Vitamin D, Ca, and Mg concentrations must be considered one of the elementary tests for pregnant women to be treated accordingly.

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