JOURNAL OF CRITICAL REVIEWS

ISSN- 2394-5125 VOL 09, ISSUE 01, 2022

VITAMIN D DEFICIENCY AND DEPRESSION: WHO CAN BE AFFECTED?

FATHIMATH SHIRANEE[a,b], NURAQMANIZA BINTISHAHRIN[a], ZULHABRIOTHMAN[c]*

[a]School of Graduate Studies, Management and Science University, Shah Alam 40100, Malaysia

[b]Faculty of HealthSciences, The Maldives National University, RahdhebaiHingun, Male' 20371, Maldives

[c] Faculty of Health & Life Sciences, Management and Science University, Shah Alam 40100, Malaysia

Corresponding author:

*** ZULHABRI** OTHMAN

Faculty of Health & Life Sciences, Management and Science University, Shah Alam 40100, Selangor, Malaysia.

Email: zulhabri_othman@msu.edu.my

Abstract:

Vitamin D deficiency and depression are common conditions prevailing throughout the world and of public health concern. This review aims to identify the relationship between the cellular and regulatory mechanisms of vitamin D deficiency and depression, and to identify the prevalence of vitamin D deficiency and depression in selected conditions. Available evidence supports the need for vitamin D for a healthy brain functioning. A number of studies performed have provided useful information as to how the deficiency of vitamin D can interfere with the functioning of the brain and ultimately lead to conditions such as depression. Vitamin D insufficiency is greatly linked to cardiovascular disease, chronic kidney disease and fibromyalgia and also common within elderly adults and those in the perinatal period. Similarly, there is a high prevalence of depression among the above-mentioned groups. Substantial evidences were found between vitamin D deficiency and depression and their effect in various clinical conditions.

Keywords: Vitamin D deficiency, depression, vitamin D receptor, cardiovascular disease, chronic kidney disease, fibromyalgia

1. INTRODUCTION

There are more than 264 million people affected by depression throughout the world and around 800,000 people die every year due to suicide [1]. According to the American Psychiatric Association, depression is a generally known serious medical illness that influence our feelings, thought and actions negatively. The connection between the deficiency of Vitamin D (ergocalciferol or cholecalciferol) and depression has been described in various studies. Deficiency of vitamin D is considered a public health threat throughout the world including among people living in low latitude countries [2]. Even though the two isoforms of vitamin D, cholecalciferol and ergocalciferol has been identified as a cure for rickets many epidemiological studies identifies that vitamin D plays and important role in the functioning of the central nervous system, immunity against bacterial infections, cardiovascular disease and metabolic disorders [3],[4] Likewise an acceptable number of research propose that the deficiency of vitamin D can be connected to various non-skeletal disorders including schizophrenia, cancer, cardiovascular disease, muscle pain, dementia, diabetes, etc. [5].

Vitamin D2 and D3 are found in nature occurring in a few foods and mainly obtained through fortified food or dietary supplements, but most people attain it through exposure to UV-B radiation [6],[7]. When the serum 25-hydroxyvitaminD3 [25(OH)D3] level is less than 10 ng/mL or 31.8nmol/L it is considered as vitamin D deficient or insufficient [8]. Nowadays research propose that the deficiency of vitamin D can be connected to various non-skeletal disorders including schizophrenia, cancer, cardiovascular disease, muscle pain, dementia, diabetes, etc. [5].

ISSN- 2394-5125 VOL 09, ISSUE 01, 2022

1.1. Vitamin D metabolism

Vitamin D2 can be obtained from plant sources and D3 can be obtained through animal sources but the majority is produced in the body through the modification of 7-dehydrocholesterol to pre-vitamin D3 by UV-B radiation (Fig. 1) [9],[10]. Isomerization converts pre-vitamin D3 to D3 or cholecalciferol and gets converted to 25-hydroxycholecalciferol (25(OH)D), the major circulating form, this takes place in the liver by the action of 25-hydroxylase [11],[12]. Apart from the liver, immune cells, gastrointestinal tract cells, brain and skin are capable of the production of 1α,25(OH)2D [13]. The calcifediol produced is transported by vitamin D binding protein (DBP) to the kidney and hydroxylated to calcitriol, the active vitamin D, also known as 1,25 dihydroxycholecalciferol D [14]. The blood level of 1,25(OH)2D is regulated through feedback mechanism involving the *CYP24A1*, calcium, parathyroid hormone and various cytokines and tissue necrosis factors [9]. Previous assumptions that kidney was the only organ competent in converting 25(OH)D to 1,25(OH)2D have been proven otherwise by in-vitro studies showing cells expressing 1α-hydroxylase in keratinocytes, osteoblasts, monocytes, colon cells, macrophages, etc. [9]. It is also known that vitamin D is utilized by various body cells (such as keratinocytes, lymphocytes, pancreatic cells, etc.) for the management of cell proliferation, differentiation and immune modulation [15]. A person having vitamin D level <20 ng/ml is defined as deficient and a value of 21-29 ng/ml is insufficient [15],[16]. Present lifestyle and work environments tend to keep people indoors rather than outdoors decreasing the amount of sunlight exposure leading to one of the factors of vitamin D deficiency [10],[17].

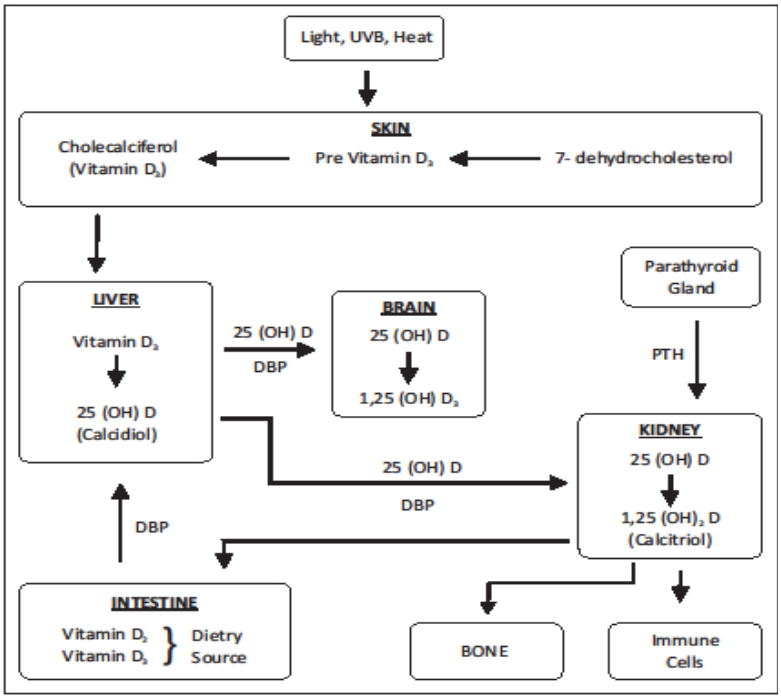

Fig 1: Metabolism of Vitamin D. Vitamin D synthesis occurs primarily through sunlight exposure producing pre-vitamin D3, converted to D3. Vitamin D3 is hydroxylated mainly in the liver and some in kidney and brain as well. 1,25(OH)D3 acts I target sites in bones, intestine, and immune cells.
PTH – parathyroid hormone, UVB- Ultraviolet B.

ISSN- 2394-5125 VOL 09, ISSUE 01, 2022

1.2. Vitamin D receptor and brain function

The effect of vitamin D on brain was first described by Sutherland *et al* in 1992 by showing the presence of VDR messenger RNA expressed in brains of Alzheimer's disease and Huntington disease patients [9],[18]. The hippocampus of the brain is particularly affected by neurogenerative disarray and the presence of VDR and *CYP27B1* in this area was described by Eyles*et al*[9],[19]. Presence of *CYP27B1* in the cerebellar Purkinje cells and neuronal cells present in the cerebral cortex was illustrated by immunohistochemical methods [20]. Apart from the hippocampus, prefrontal cortex, basal forebrain, thalamus, hypothalamus, substantia nigra, etc. also expressed the presence of VDR confirming the utilization of vitamin D in the brain [9]. Both *CYP27B1* and *CYP24A1* are present in the human brain and mediates the synthesis of 1,25-dihydroxy vitamin D and catabolism of 1,25-dihydroxycholecalciferol respectively [21],[22]. The genes *CYP27B1* and *CYP24A1* encodes the enzymes 1α-hydroxylase and 24-hydroxylase respectively and are important for the homeostasis of vitamin D [22]. Neurons and glia contained *CYP27B1* indicating the potential to synthesize the active 1,25OH2D3 [21]. The involvement of vitamin D in processes such as neuroimmunomodulation, neuroprotection and brain development indicate that this vitamin can be linked to depression [23].

1.3. Vitamin D deficiency and depression

1.3.1 Cellular and regulatory mechanisms

Various studies performed indicates that Vitamin D is a neuroactive steroid significant for the development of the brain [24],[25] and a deficiency can be associated with neuropsychiatric disorders such as schizophrenia [24]. Study conducted by Jean & team in 2008 for the first time demonstrated vitamin D_2 as a potent neuro-modulatory compound that increases axogenesis, diameter of axon and physical maturation of the axon [26].

A deficiency in this vital vitamin can result in adverse outcomes including depression, Parkinson's disease and dementia's such as Alzheimer's [24],[27]. As vitamin D is involved in homeostasis of Ca^{2+}Berridge suggests that continuous increase in Ca^{2+} may contribute to the start of depression [28]. A well-coordinated and regulated feedback interaction within the excitatory and inhibitory neurons occur in the brain and alteration in any communication can lead to depression [28]. Glutamate is released from the excitatory neurons which activates local inhibitory neurons and leads to inhibition of the excitatory neurons by the release of γ-aminobutyric acid (GABA) [28]. A decline in GABA level seen in depression can be related to the reduction in size and number of the inhibitory GABAergic neurons in dorsal prefrontal cortex and the occipital cortex [28],[29]. Studies conducted on prefrontal cortex and amygdala postmortem of patient with major depressive disorder (MDD) demonstrated reduction in protein and a reduction in the main enzyme in the synthesis of GABA, known as glutamic acid decarboxylase (GAD)67 [29]. Additionally a research conducted on 20 depressed, unmedicated patients undergoing major depressive disorder (MDD) to measure the glutamate/glutamine (Glx) and γ-aminobutyric acid concentrations of the prefrontal brain areas displayed results of reduced Glx and γ-aminobutyric acid levels obtained from magnetic resonance spectroscopy signals [30].

Studies also suggest that vitamin D plays a role in monoamine regulation by significantly increasing the production of tyrosine hydroxylase (TH), an enzyme which catalyzes the rate-limiting step in the biosynthesis of catecholamines[31]–[33]. One of the oldest hypotheses for the pathogenesis of depression is the deficiency of serotonin (5-HT) and or norepinephrine neurotransmitters in brain [34]. Study conducted by Cui *et al*, provides information that vitamin D aids in the increase in TH expression and promotes survival of dopaminergic neurons while a vitamin D deprivation can cause a decrease in dopamine level with decreased catechol-o-methyl transferase [32],[35]. Study by Józefowicz *et al* demonstrated that 83.5% of depressed patients were deficient in vitamin D levels regardless of the season of the year [36].

1.3.2. Elderly population

Elderly population is considerably increasing over the years and demands an increase in health care services and social security which if neglected can lead to elderly population being more prone to mental disorders [37]. Several studies done to identify the prevalence of depression among elderly population has identified as high as 20% of target population being

ISSN- 2394-5125 VOL 09, ISSUE 01, 2022

affected [38],[39]. To determine the association between altered 25(OH)D and PTH levels with depression in elderly people a study consisting of 1282 participants within the age 65 to 95years were carried out [40]. Blood samples obtained from the participants were tested for serum 25(OH)D and PTH levels and to assess the severity of depression the Center for Epidemiologic Studies-Depression (CES-D) scale was utilized [40] This study for the first time identified the association of depression status to the increased PTH levels and decreased serum 25-hydroxyvitamin D in elderly individuals [40]. A cross-sectional study conducted among old primary care patients to identify the correlation of vitamin D deficiency and depression identified that one fifth of the population involved in the study had reduced levels of vitamin D and those with severe deficiency more likely had depression [41]. Among the 1618 patients 43% with depression had a lower vitamin D level compared to the nondepressed group and the likelihood of depression was twice high in the 3% of severe deficient population [41]. A health survey was conducted in England consisting of 2070 participants above the age of 65years to examine the connection between vitamin D deficiency and depression [42]. The findings of the study conclude that vitamin D deficiency was linked with old age depression [42]. Supplementing psychiatric patients above the age of sixty years with vitamin D was done to identify the relationship between vitamin D insufficiency and depression [43]. Patients with a Geriatric Depression Scale (GDS) score above 5 were selected with no past history of any other psychological ailments and divided into vitamin D group (received 50,000 units of vitamin D) and placebo group [43]. No severe depression was seen in the group supplemented with vitamin D but 25.6% of patients in placebo group had severe depression indicating that vitamin D supplementation improves depression [43] and hence vitamin D deficiency may be related to depression [44].

1.3.3. Cardiovascular disease

Cardiovascular disease (CVD) refers to disorders of the heart including cerebrovascular disease, coronary heart disease and peripheral artery disease [45],[46].Cardiovascular disease happens to be one of the major causes of death in developing countries with the main risk factor being sedentary life style and the lack of exercise among adults [47]Studies suggest that there is a strong link between depression and the increased risk of cardiovascular problems and can contribute to the onset, progress and prognosis of the disease [45],[48]. In 1981 Scragg identified an inverse relationship between UVB radiation and cardiovascular mortality relating to seasonal variation in CVD disease [49]. Additional studies supports the relationship of low levels of vitamin D to higher incidence of cardiovascular events and mortality [50]. Information derived from a prospective cohort study, the Heart and Soul Study, including outpatients with stable heart disease was utilized to understand the association between vitamin D deficiency and cardiovascular disease[51],[52]. Eligible participants selected were 1) patients with a history of myocardial infarction 2) patients with 50% stenosis in either one or more coronary vessels 3) those with an evidence of exercise induced ischaemia and 4) patients with a history of coronary revascularization, but eliminated any who had a myocardial infarction within the previous 6 month of study period [52]. The 25(OH)D levels were assessed and from 946 participants 32% had <20 ng/mL of vitamin D levels and these patients had a 50% greater rate of cardiovascular disease [52]. Vitamin D is believed to have a negative regulation on the renin angiotensin-aldosterone system and may also affect the remodeling of cardiac chambers, coronary vasculature, inflammatory markers and glycemic control [53]. The active form calcifediol is known to lower the pulse pressure indicating a positive effect on cardiovascular disease [54]. Strong relationship between vitamin D deficiency and cardiovascular events have been observed, likewise increased risk of cardiovascular disease can lead to depression [45]. The relationship between vitamin D deficiency in cardiovascular patients and depression was identified in a study conducted by May *et al* including cardiovascular patients above the age of 50 years without history of depression [55].Vitamin D and parathyroid hormone levels were obtained and patients observed for the occurrence of depression or until the end of study or death[55]. A total of 7358 patients with cardiovascular disease participated in the study and 64.2% identified as vitamin D deficient (≤ 30 ng/ml) with an increased level of PTH [55]. A follow-up depression diagnosis revealed that patients with a very low level of vitamin D (≤ 15 ng/ml) had almost a 3-fold increased risk of depression [55].

1.3.4. Chronic kidney disease

A Patient with a reduced glomerular filtration rate alone or together with increased urinary albumin, for a period of three months or more, is defined as a person with CKD[56]–[58]. Individuals over the age of 60 years, a family history of CKD,

ISSN- 2394-5125 VOL 09, ISSUE 01, 2022

diabetes, hypertension or cardiovascular disease are all risk factors for the development of CKD [59]. Apart from the pathological abnormalities occurring in CKD depression remains one of the most frequent psychiatric problems seen in these patientswith an approximate 20% to 30% affected [57],[60]. A prospective follow-up study conducted at Hospital University Sains Malaysia (HUSM) to identify the factors associated with depression and anxiety in hemodialysis patients revealed that a majority of patients suffered from depression and it worsened with the passage of time [61]. 71.3% patients were recognized as suffering from depression at the initial data collection which increased to 78.2% in the post 3 months and 84.9% post 6 months highlighting the importance of regular monitoring and evaluating the factors associated [61].

A common problem identified in CKD patient is the disorder of mineral ion and bone metabolism due to abnormalities of parathyroid hormone-vitamin D axis [62]. To understand the magnitude of vitamin D deficiency in CKD patients a study was conducted with 43 patients having a creatinine level between 1-5mg/dl (calculated glomerular filtration rate of 111-11 ml/min per $1.73m^2$) and 103 patients undergoing hemodialysis [62]. Blood samples were collected from all participants for the estimation of 25(OH)D levels and the results reveled thatamong the 43 patients who did not require hemodialysis, 42% had vitamin D insufficiency (16-30 ng/ml), 42% with deficiency (<15 ng/ml) and 2% had severe deficiency (<5 ng/ml) [62]. Among the patients undergoing hemodialysis 97% was identified as vitamin D insufficient and deficient along with 14% with severe deficiency concluding that a huge majority of patients in the study with CKD had vitamin D deficiency [62]. Low levels of 25(OH)D in hemodialysis patients are associated with cardiovascular event, stroke and mortality [63].

Study by Jhee and team was conducted to identify the relationship between vitamin D deficiency and depression seen in CKD patients. The level of 25-hydroxyvitamin D3 starts decreasing during stage 2 CKD and remains decreased till end stage renal disease (ESRD) [8]. Serum 25-hydroxyvitamin D3 levels and depression score calculated based on a mental health questionnaire filled by the patient under supervision of a trained investigator was collected from 533 patients identified as CKD among the 21,257 participants of Korean National Health and Nutrition Examination Survey (KNHANES) [8]. A high frequency of depression was noted amid the patients with CKD than the general population (24.4%vs 33.8%) and a remarkable increase in prevalence of depression amongpatients with vitamin D deficiency compared to the non-deficient (32.5% vs 50%) was noted [8].

Furthermore study conducted by Selda and team displayed that CKD patients with a low level of 25(OH) D had high prevalence of depression using the beck depression scale [64]. 116 CKD patients who participated were divided into three groups, those who had a vitamin D level $\leq$ 20 ng/mL (deficient), the second group between 21-29 ng/mL (insufficient) and those who were considered to have a sufficient level of vitamin D ($\geq$ 30 ng/mL) [64]. Among the patients 8.6% were CKD stage 1, 10.3% with stage 2, 38.8% in stage 3 and 42.2% in stage 4 CKD [64]. Overall mean vitamin D levels were low and a high PTH level was noted, 43.8% patients had vitamin D deficiency while 17.2% with insufficient vitamin D levels [64]. The mean depression score was higher in vitamin D deficient and normal in 67% of patients with sufficient vitamin D levels [64].

1.3.5. Fibromyalgia

Fibromyalgia, a syndrome of persistent pain and tenderness widespread accompanying sleeping difficulties, fatigue, stiffness and depression [65],[66]. This condition is characterized as a disorder of central pain processing that leads to hyperalgesia (abnormally heightened pain sensation) and allodynia (pain from stimuli that usually do not cause pain)[67],[68]. As the symptoms of vitamin D deficiency and symptoms of fibromyalgia syndrome (FMS) are similar, recent research focuses on understanding the issue further [69]. A group of 70 patients with a diagnosis of fibromyalgia were used to identify the consequences of vitamin D therapy on their quality of life [69]. Blood samples were collected from the participants for vitamin D level and categorized into deficient, inadequate and sufficient, and those with vitamin D < 30 ng/mL were treated with 50,000 IU vitamin D orally for 12 weeks. Assessment tools for assessing the quality of life were filled by patients prior to and post vitamin D therapy [69]. Prior to treatment 60% of patients were vitamin D inadequate or deficient and all returned to normal after treatment, also a significant difference was observed in the fibromyalgia impact questionnaire (FIQ) scoring along with the Beck depression inventory (BDI) score and the visual analog scale (VAS) indicating a link between vitamin D deficiency and fibromyalgia [69]. A very similar study was conducted in 2019 by Ismaiel*et al.* using sixty female

ISSN- 2394-5125 VOL 09, ISSUE 01, 2022

premenopausal individuals, diagnosed with FMS and vitamin D deficiency [70]. This was toto determine the effectiveness of vitamin D supplementation in these individuals and its effect on their quality of life [70]. Serum samples collected for testing

25-OH vitamin D levels at the start of the research indicated that decreased levels of vitamin D levels were detected in patients with FMS (mean 18.34 ± 9.1) in comparison to the control group (mean 31.3 ± 9.99) [70].Quality of life assessed using FIQ, VAS, BDI, short form-36, Arizona sexual life questionnaire (ASEX) exhibited that vitamin D replacement brought about significant positive changes in the patient's life [70].

There is strong evidence that links fibromyalgia with depression as they share similar pharmacological treatment as well as pathophysiology [71]. Patients with fibromyalgia are known to have a 30% likelihood of having major depression at diagnosis also a 74% lifetime risk of depression [72]. Seventy-five Caucasian patients meeting the fibromyalgia criteria of the American College of Rheumatology (ACR) participated in a study to identify the connection between fibromyalgia, vitamin D deficiency and depression [73]. A high impact and depression score were seen in patients with fibromyalgia with 68% of the study defined as "severely affected" in terms of the FIQ score [73]. The association of low levels of vitamin D in fibromyalgia patients can be related to less exposure to sunlight due to less mobility and reduced functional ability compared to controls, also intake of vitamin D maybe suboptimal in FMS [73].

1.3.6. Perinatal period

Perinatal depression, a serious problem that may affect 10% - 13% of pregnant women worldwide and this number can be increased to 15.6% - 19.8% in developing countries says WHO [74]. Perinatal depression or maternal depression refers to episodes of major or minor depression occurring during pregnancy (antenatal) or after delivery within the first twelve months (postnatal)[75].

Study conducted by Cassidy-Bushrow*etal*. investigated the association of antenatal depressive symptoms and low levels of vitamin D in African American expecting women [6]. A total of 178 African American pregnant women participated in the study and their blood collected to measure their serum 25-OHD levels during the first prenatal care visit (mean 9.5 ± 3.6 gestational weeks) and the depressive score was measured using the Centre for Epidemiological Studies Depression Scale (CES-D) [6]. A CES-D is used to measure depression levels in community samples including perinatal and postnatal and consists of a 20-item scale [76]. A mean 25-OHD level of 13.4 ± ng/mL and 15.2±10.7 CES-D scale with 41% individuals showing ≥ 16 on the CES-D scale was identified [6]. A 25-OHD level <20 ng/mL is considered inadequate while a CES-D score ≥ 16 is suggestive of clinical depression [6]. The patients with a CES-D level ≥ 16 had a decreased 25-OHD level and for every 1 unit increase in 25-OHD the elevated depression score decreased by 46% [6]. To determine the efficacy of vitamin D supplementation on antepartum and postpartum depression a randomized clinical trial was carried out [77]. In this study Iranian pregnant women who had a mental score between zero to thirteen by the Edinburgh Postnatal Depression Scale were divided into two groups and one supplemented with 2000IU of vitamin D daily from week 26 to 28 gestation [77]. The group supplemented with vitamin D had the depression score was reduced greatly compared to the control group at gestational weeks 38-40 and 4 and 8 weeks postnatal indicating the effectiveness of decreasing postnatal depression through supplementation of vitamin D at the time of pregnancy [77]. Maternal depression rate has been increasing over the last decade [78] and those struggling with depression during antenatal period poses a higher risk for caesarean birth [79]. Other complications of antenatal depression include premature birth, preeclampsia low birth weight and congenital abnormalities [80]–[82]. Depression may cause complications for mother and might also have negative effects on infant development [77]. Vitamin D is important for reproductive health as it regulates placental development and activity and modulates the immune system[83],[84].

Study conducted by Accortt*et al*. to identify the adverse effects of prenatal vitamin D deficiency and prenatal depression during the antenatal period suggested that there is an increased risk for perinatal adverse outcomes related to vitamin D deficiency [83]. Vitamin D levels were measured during early days of pregnancy and at the time of delivery, depressive symptoms were assessed by applying the Edinburgh Postnatal Depression scale (EPDS) [83]. An EPDS of ≥ 10 being the cutoff for minor depression, nineteen percent of the participants were observed to be within this category and those who had an EPDS score above the minor depression cutoff with a vitamin D level <20 ng/ml were more prone to an adverse perinatal outcome [83]. Lamb *et al* suspected an inverse proportion between depressive symptoms and vitamin D throughout pregnancy

ISSN- 2394-5125 VOL 09, ISSUE 01, 2022

[78]. The main aim of their study was focused in examining the alteration in vitamin D levels and depressive symptoms by identifying the level of 25(OH)D in cord blood and its association with maternal vitamin D status and depression [78]. Data collection for the study was done at three points (T1) early pregnancy, blood sample for 25OHD testing and completed DPDS screening, (T2) third trimester, EPDS screening, cord blood sample for 25OHD and (T3) 10 weeks postpartum, serum sample for 25OHD and EPDS screening [78]. Results indicated that cord blood levels of 25OHD was almost half that of maternal 25OHD levels and decreased cord blood levels are correlated with greater depressive symptoms in the mother during late pregnancy [78]. Low cord blood levels of 25OHD could lead to higher chance of childhood diseases for instance type I diabetes, wheezing and winter-related eczema [85]. And as hypothesized the overall finding of the study demonstrates an inverse relationship with the vitamin D levels and depressive symptoms [78].

CONCLUSION

Evidence from clinical and epidemiological studies support a possible correlation between vitamin D deficiency and depression. Several recent studies demonstrate the strong connection between vitamin D deficiency and depression due to the presence of VDR and enzymes for hydrolyzation of vitamin D in the brain. The result of calcium homeostasis due to vitamin D deficiency and the role it plays in monoamine regulation strongly correlates vitamin D deficiency to depression. Studies conducted in different groups of people with various conditions such as cardiovascular disease, fibromyalgia, chronic kidney disease have shown to have a strong correlation within vitamin D deficiency and the occurrence of depression. A large population of elderly people as well as those in the perinatal period also experiences similar correlations with vitamin D deficiency and depression.

CONFLICT OF INTEREST

None.

ACKNOWLEDGEMENTS

Authors would like to acknowledge Management and Science University for supporting this study.

REFERENCES

1 WHO. WHO | Maternal mental health.

2 Palacios, C.; Gonzalez, L. Is Vitamin D Deficiency a Major Global Public Health Problem? *Journal of Steroid Biochemistry and Molecular Biology*. Elsevier Ltd 2014, pp 138–145. https://doi.org/10.1016/j.jsbmb.2013.11.003.

3 Pilz, S.; Zittermann, A.; Trummer, C.; Theiler-Schwetz, V.; Lerchbaum, E.; Keppel, M. H.; Grübler, M. R.; März, W.; Pandis, M. Vitamin D Testing and Treatment: A Narrative Review of Current Evidence. *Endocr. Connect.***2019**, *8* (2), R27–R43. https://doi.org/10.1530/EC-18-0432.

4 Junaid, K.; Rehman, A. Impact of Vitamin D on Infectious Disease-Tuberculosis-a Review. *Clinical Nutrition Experimental*. Elsevier Ltd June 1, 2019, pp 1–10. https://doi.org/10.1016/j.yclnex.2019.02.003.

5 Bjørklund, G. Vitamin D Deficiency: A Global Health Problem. *Peertechz J. Environ. Sci. Toxicol.***2016**, 023–024. https://doi.org/10.17352/pjest.000004.

6 Cassidy-Bushrow, A. E.; Peters, R. M.; Johnson, D. A.; Li, J.; Rao, D. S. Vitamin D Nutritional Status and Antenatal Depressive Symptoms in African American Women. *J. Women's Heal.***2012**, *21* (11), 1189–1195. https://doi.org/10.1089/jwh.2012.3528.

7 Bhurayanontachai, R.; Maipang, K.; Leelawattana, R. Correlation of Admission Serum 25-Hydroxyvitamin D Levels and Clinical Outcomes in Critically Ill Medical Patients. *Clin. Nutr. Exp.***2018**, *20*, 30–40. https://doi.org/10.1016/j.yclnex.2018.04.004.

8 Jhee, J. H.; Kim, H.; Park, S.; Yun, H. R.; Jung, S. Y.; Kee, Y. K.; Yoon, acsa C. Y.; Park, J. T.; Han, S. H.; Kang, S. W.; Yoo, T. H. Vitamin D Deficiency Is Significantly Associated with Depression in Patients with Chronic Kidney Disease. *PLoS One***2017**, *12* (2). https://doi.org/10.1371/journal.pone.0171009.

9 Holick, M.; Schlogl, M. Vitamin D and Neurocognitive Function. *Clin. Interv. Aging***2014**, *9*, 559. https://doi.org/10.2147/CIA.S51785.

10 Parker, G. B.; Brotchie, H.; Graham, R. K. Vitamin D and Depression. *J. Affect. Disord.***2017**, *208*, 56–61. https://doi.org/10.1016/j.jad.2016.08.082.

11 Bikle, D. *Vitamin D: Production, Metabolism, and Mechanisms of Action*; MDText.com, Inc., 2000.

12 Jeong, S. K.; Choe, S. J.; Lim, C. J.; Park, K.; Park, K. Micronutrients in Skin Immunity and Associated Diseases. In *Immunity and Inflammation in Health and Disease*; Elsevier, 2018; pp 257–270. https://doi.org/10.1016/b978-0-12-805417-8.00021-4.

13 Schuster, I. Cytochromes P450 Are Essential Players in the Vitamin D Signaling System. *Biochim. Biophys. Acta - Proteins Proteomics***2011**, *1814* (1), 186–199. https://doi.org/10.1016/j.bbapap.2010.06.022.

14 Christakos, S.; Dhawan, P.; Verstuyf, A.; Verlinden, L.; Carmeliet, G. Vitamin D: Metabolism, Molecular Mechanism of Action, and Pleiotropic Effects. *Physiol. Rev.***2015**, *96* (1), 365–408. https://doi.org/10.1152/physrev.00014.2015.

15 Umar, M.; Sastry, K.; Chouchane, A. Role of Vitamin D Beyond the Skeletal Function: A Review of the Molecular and Clinical Studies. *Int. J. Mol. Sci.***2018**, *19* (6), 1618. https://doi.org/10.3390/ijms19061618.

16 F. Holick, M. Vitamin D: Evolutionary, Physiological and Health Perspectives. *ingenta Connect***2011**, *12* (1), 4–18.

17 Öberg, J.; Jorde, R.; Grimnes, G.; Almås, B.; Emaus, N. Vitamin D Deficiency and Lifestyle Risk Factors in a Norwegian Adolescent Population. *Scand. J. Public Health***2014**, *42* (7), 593–602. https://doi.org/10.1177/1403494814541593.

18 Kung Sutherland, M.; Somerville, M. J.; Yoong, L. K. K.; Bergeron, C.; Haussler, M. R.; Crapper McLachlan, D. R. Reduction of Vitamin D Hormone Receptor MRNA Levels in Alzheimer as Compared to Huntington Hippocampus: Correlation with Calbindin-28k MRNA Levels. *Mol. Brain Res.***1992**, *13* (3), 239–250. https://doi.org/10.1016/0169-328X(92)90032-7.

19 Eyles, D. W.; Smith, S.; Kinobe, R.; Hewison, M.; McGrath, J. J. Distribution of the Vitamin D Receptor and 1α-Hydroxylase in Human Brain. *J. Chem. Neuroanat.***2005**, *29* (1), 21–30. https://doi.org/10.1016/j.jchemneu.2004.08.006.

20 Zehnder, D.; Bland, R.; Williams, M. C.; McNinch, R. W.; Howie, A. J.; Stewart, P. M.; Hewison, M. Extrarenal Expression of 25-Hydroxyvitamin D $_3$ -1α-Hydroxylase ^{1}. *J. Clin. Endocrinol. Metab.***2001**, *86* (2), 888–894. https://doi.org/10.1210/jcem.86.2.7220.

21 Harms, L. R.; Burne, T. H. J.; Eyles, D. W.; McGrath, J. J. Vitamin D and the Brain. *Best Practice and Research: Clinical Endocrinology and Metabolism*. August 2011, pp 657–669. https://doi.org/10.1016/j.beem.2011.05.009.

22 Lopes, N.; Sousa, B.; Martins, D.; Gomes, M.; Vieira, D.; Veronese, L. A.; Milanezi, F.; Paredes, J.; Costa, J. L.; Schmitt, F. Alterations in Vitamin D Signalling and Metabolic Pathways in Breast Cancer Progression: A Study of VDR, CYP27B1 and CYP24A1 Expression in Benign and Malignant Breast Lesions Vitamin D Pathways Unbalanced in Breast Lesions. *BMC Cancer***2010**, *10*, 1–10. https://doi.org/10.1186/1471-2407-10-483.

23 Anglin, R. E. S.; Samaan, Z.; Walter, S. D.; Mcdonald, S. D. Vitamin D Deficiency and Depression in Adults: Systematic Review Material Supplementary Vitamin D Deficiency and Depression in Adults: Systematic Review and Meta-Analysis. *Br. J. Psychiatry***2013**, *202*, 100–107. https://doi.org/10.1192/bjp.bp.111.106666.

24 Kesby, J. P.; Eyles, D. W.; Burne, T. H. J.; McGrath, J. J. The Effects of Vitamin D on Brain Development and Adult Brain Function. *Molecular and Cellular Endocrinology*. Elsevier December 5, 2011, pp 121–127. https://doi.org/10.1016/j.mce.2011.05.014.

25 Melcangi, R. C.; Panzica, G. Response – Vitamin D: The Neglected Neurosteroid? *Trends Neurosci.***2001**, *24*. https://doi.org/10.1016/s0166-2236(00)01951-2.

26 Chabas, J.-F.; Alluin, O.; Rao, G.; Garcia, S.; Lavaut, M.-N.; Risso, J. J.; Legre, R.; Magalon, G.; Khrestchatisky, M.; Marqueste, T.; Decherchi, P.; Feron, F. Vitamin D $_2$ Potentiates Axon Regeneration. *J. Neurotrauma***2008**, *25* (10), 1247–1256. https://doi.org/10.1089/neu.2008.0593.

27 Evatt, M. L.; DeLong, M. R.; Khazai, N.; Rosen, A.; Triche, S.; Tangpricha, V. Prevalence of Vitamin D Insufficiency in Patients with Parkinson Disease and Alzheimer Disease. *Arch. Neurol.***2008**, *65* (10), 1348–1352. https://doi.org/10.1001/archneur.65.10.1348.

28 Berridge, M. J. Vitamin D and Depression: Cellular and Regulatory Mechanisms. *Pharmacol. Rev.***2017**, *69* (2), 80–92. https://doi.org/10.1124/pr.116.013227.

29 Luscher, B.; Fuchs, T. GABAergic Control of Depression-Related Brain States. In *Advances in Pharmacology*; Academic Press Inc., 2015; Vol. 73, pp 97–144. https://doi.org/10.1016/bs.apha.2014.11.003.

30 Hasler, G.; Van Der Veen, J. W.; Tumonis, T.; Meyers, N.; Shen, J.; Drevets, W. C. Reduced Prefrontal Glutamate/Glutamine and γ-Aminobutyric Acid Levels in Major Depression Determined Using Proton Magnetic Resonance Spectroscopy. *Arch. Gen. Psychiatry***2007**, *64* (2), 193–200. https://doi.org/10.1001/archpsyc.64.2.193.

31 Puchacz, E.; Stumpf, W. E.; Stachowiak, E. K.; Stachowiak, M. K. Vitamin D Increases Expression of the Tyrosine Hydroxylase Gene in Adrenal Medullary Cells. *Mol. Brain Res.***1996**, *36* (1), 193–196. https://doi.org/10.1016/0169-328X(95)00314-I.

32 Cui, X.; Pertile, R.; Liu, P.; Eyles, D. W. Vitamin D Regulates Tyrosine Hydroxylase Expression: N-Cadherin a

Possible Mediator. *Neuroscience***2015**, *304*, 90–100. https://doi.org/10.1016/j.neuroscience.2015.07.048.

33 Kobayashi, K.; Nagatsu, T. Tyrosine Hydroxylase. In *Primer on the Autonomic Nervous System*; 2012. https://doi.org/10.1016/B978-0-12-386525-0.00007-X.

34 Moret, C.; Briley, M. The Importance of Norepinephrine in Depression. *Neuropsychiatr. Dis. Treat.***2011**, *7* (1), 9–13. https://doi.org/10.2147/NDT.S19619.

35 Pertile, R. A. N.; Cui, X.; Eyles, D. W. Vitamin D Signaling and the Differentiation of Developing Dopamine Systems. *Neuroscience***2016**, *333*, 193–203. https://doi.org/10.1016/j.neuroscience.2016.07.020.

36 Józefowicz, O.; Rabe-Jabłońska, J.; Woźniacka, A.; Strzelecki, D. Analysis of Vitamin d Status in Major Depression. *J. Psychiatr. Pract.***2014**, *20* (5), 329–337. https://doi.org/10.1097/01.pra.0000454777.21810.15.

37 R, P.; SS, M.; JV, C. Geriatric Depression Scale: A Tool to Assess Depression in Elderly. *Int. J. Med. Sci. Public Heal.***2013**, *2* (1), 31–35. https://doi.org/10.5455/ijmsph.2013.2.31-35.

38 Steffens, D. C.; Skoog, I.; Norton, M. C.; Hart, A. D.; Tschanz, J. A. T.; Plassman, B. L.; Wyse, B. W.; Welsh-Bohmer, K. A.; Breitner, J. C. S. Prevalence of Depression and Its Treatment in an Elderly Population: The Cache County Study. *Arch. Gen. Psychiatry***2000**, *57* (6), 601–607. https://doi.org/10.1001/archpsyc.57.6.601.

39 Sherina, M. S.; Rampal, L.; Mustaqim, A. The Prevalence of Depression Among the Elderly in Sepang, Selangor. *Med J Malaysia***2004**, *59* (1), 45–49.

40 Hoogendijk, W. J. G.; Lips, P.; Dik, M. G.; Deeg, D. J. H.; Beekman, A. T. F.; Penninx, B. W. J. H. Depression Is Associated with Decreased 25-Hydroxyvitamin D and Increased Parathyroid Hormone Levels in Older Adults. *Arch. Gen. Psychiatry***2008**, *65* (5), 508–512. https://doi.org/10.1001/archpsyc.65.5.508.

41 Lapid, M. I.; Cha, S. S.; Takahashi, P. Y. Vitamin D and Depression in Geriatric Primary Care Patients. *Clin. Interv. Aging***2013**, *8*, 509–514. https://doi.org/10.2147/CIA.S42838.

42 Stewart, R.; Hirani, V. Relationship Between Vitamin D Levels and Depressive Symptoms in Older Residents From a National Survey Population. *Psychosom. Med.***2010**, *72* (7), 608–612. https://doi.org/10.1097/PSY.0b013e3181e9bf15.

43 Alavi, N. M.; Khademalhoseini, S.; Vakili, Z.; Assarian, F. Effect of Vitamin D Supplementation on Depression in Elderly Patients: A Randomized Clinical Trial. *Clin. Nutr.***2019**, *38* (5), 2065–2070. https://doi.org/10.1016/j.clnu.2018.09.011.

44 Milaneschi, Y.; Hoogendijk, W.; Lips, P.; Heijboer, A. C.; Schoevers, R.; Van Hemert, A. M.; Beekman, A. T. F.; Smit, J. H.; Penninx, B. W. J. H. The Association between Low Vitamin D and Depressive Disorders. *Mol. Psychiatry***2014**, *19*, 444–451. https://doi.org/10.1038/mp.2013.36.

45 Penninx, B. W. J. H. Depression and Cardiovascular Disease: Epidemiological Evidence on Their Linking Mechanisms. *Neuroscience and Biobehavioral Reviews*. Elsevier Ltd March 1, 2017, pp 277–286. https://doi.org/10.1016/j.neubiorev.2016.07.003.

46 Othman, Z.; Asmidar, N.; Aleem, A.; Danial, M.; Ramli, C.; Sariman, S.; Harun, H.; Rahman, M. A.; Mastura, S.; Daud, S. M.; Baharudin, H.; Alam, S. *Knowledge, Awareness and Practices on the Risk Factors of Cardiovascular Diseases Among Community in Gombak, Kuala Lumpur*; 2020; Vol. 16.

47 Mohammadi, M. A Review of Cardiac Rehabilitation and Exercise in Cardiovascular Disease Azadeh Naderi Master of Sport Physiology, Iran Comparing the Influence of Two Wrestling Training Methods (Circuit and Continuous) Based on Wrestling Techniques on Anzymes of Indicat. *J. Crit. Rev.***2019**, *7* (1). https://doi.org/10.31838/jcr.07.01.32.

48 Joynt, K. E.; Whellan, D. J.; O'Connor, C. M. Depression and Cardiovascular Disease: Mechanisms of Interaction. *Biol. Psychiatry***2003**, *54* (3), 248–261. https://doi.org/10.1016/S0006-3223(03)00568-7.

49 Scragg, R. Seasonality of Cardiovascular Disease Mortality and the Possible Protective Effect of Ultra-Violet Radiation. *Int. J. Epidemiol.***1981**, *10* (4), 337–341. https://doi.org/10.1093/ije/10.4.337.

50 Kienreich, K.; Tomaschitz, A.; Verheyen, N.; Pieber, T.; Gaksch, M.; Grübler, M. R.; Pilz, S. Vitamin D and Cardiovascular Disease. *Nutrients***2013**, *5* (8), 3005–3021. https://doi.org/10.3390/nu5083005.

51 Whooley, M. A.; De Jonge, P.; Vittinghoff, E.; Otte, C.; Moos, R.; Carney, R. M.; Ali, S.; Dowray, S.; Na, B.; Feldman, M. D.; Schiller, N. B.; Browner, W. S. Depressive Symptoms, Health Behaviors, and Risk of Cardiovascular Events in Patients with Coronary Heart Disease. *JAMA - J. Am. Med. Assoc.***2008**, *300* (20), 2379–2388. https://doi.org/10.1001/jama.2008.711.

52 Welles, C. C.; Whooley, M. A.; Karumanchi, S. A.; Hod, T.; Thadhani, R.; Berg, A. H.; Ix, J. H.; Mukamal, K. J. Original Contribution Vitamin D Deficiency and Cardiovascular Events in Patients With Coronary Heart Disease: Data From the Heart and Soul Study. *Am. J. Epidemiol.***2014**, *179* (11), 1279–1287. https://doi.org/10.1093/aje/kwu059.

53 Wang, T. J.; Pencina, M. J.; Booth, S. L.; Jacques, P. F.; Ingelsson, E.; Lanier, K.; Benjamin, E. J.; D'Agostino, R. B.; Wolf, M.; Vasan, R. S. Vitamin D Deficiency and Risk of Cardiovascular Disease. *Circulation***2008**, *117* (4), 503–511. https://doi.org/10.1161/CIRCULATIONAHA.107.706127.

54 Grootswagers, P.; Vaes, A. M. M.; Tieland, M.; de Groot, L. C. P. G. M. Calcifediol Supplementation to Reduce Pulse

Pressure in a Limited Sample of Vitamin D Deficient Older Adults with Elevated Parathyroid Hormone Levels. *Clin. Nutr. Exp.***2019**, *24*, 77–82. https://doi.org/10.1016/j.yclnex.2019.01.003.

55 May, H. T.; Bair, T. L.; Lappé, D. L.; Anderson, J. L.; Horne, B. D.; Carlquist, J. F.; Muhlestein, J. B. Association of Vitamin D Levels with Incident Depression among a General Cardiovascular Population. *Am. Heart J.***2010**, *159* (6), 1037–1043. https://doi.org/10.1016/j.ahj.2010.03.017.

56 Levey, A. S.; Coresh, J. Chronic Kidney Disease. *Lancet***2012**, *379* (9811), 165–180. https://doi.org/10.1016/S0140-6736(11)60178-5.

57 Jha, V.; Garcia-Garcia, G.; Iseki, K.; Li, Z.; Naicker, S.; Plattner, B.; Saran, R.; Wang, A. Y. M.; Yang, C. W. Chronic Kidney Disease: Global Dimension and Perspectives. *Lancet***2013**, *382* (9888), 260–272. https://doi.org/10.1016/S0140-6736(13)60687-X.

58 Ibrahim, H. A.; Kassim, N. K.; Jamsari, F. Z.; Zainuddin, S. L. A.; Hanafi, M. H.; Adnan, A. S. Periodontal Health of Pre-Dialysis Chronic Kidney Disease Patients in a Northeast Peninsular Malaysia Tertiary Hospital. *Malaysian J. Med. Sci.***2020**, *27* (1), 106–114. https://doi.org/10.21315/mjms2020.27.1.11.

59 Vassalotti, J. A.; Stevens, L. A.; Levey, A. S. Testing for Chronic Kidney Disease: A Position Statement From the National Kidney Foundation. *Am. J. Kidney Dis.***2007**, *50* (2), 169–180. https://doi.org/10.1053/j.ajkd.2007.06.013.

60 Fabrazzo, M.; De Santo, R. M. Depression in Chronic Kidney Disease. *Semin. Nephrol.***2006**, *26* (1), 56–60. https://doi.org/10.1016/j.semnephrol.2005.06.012.

61 Khan, A.; Khan, A. H.; Adnan, A. S.; Sulaiman, S. A. S.; Mushtaq, S. Prevalence and Predictors of Depression among Hemodialysis Patients: A Prospective Follow-up Study. *BMC Public Health***2019**, *19* (1), 1–13. https://doi.org/10.1186/s12889-019-6796-z.

62 González, E. A.; Sachdeva, A.; Oliver, D. A.; Martin, K. J. Vitamin D Insufficiency and Deficiency in Chronic Kidney Disease: A Single Center Observational Study. *Am. J. Nephrol.***2004**, *24* (5), 503–510. https://doi.org/10.1159/000081023.

63 Drechsler, C.; Pilz, S.; Obermayer-Pietsch, B.; Verduijn, M.; Tomaschitz, A.; Krane, V.; Espe, K.; Dekker, F.; Brandenburg, V.; März, W.; Ritz, E.; Wanner, C. Vitamin D Deficiency Is Associated with Sudden Cardiac Death, Combined Cardiovascular Events, and Mortality in Haemodialysis Patients. *Eur. Heart J.***2010**, *31* (18), 2253–2261. https://doi.org/10.1093/eurheartj/ehq246.

64 Selda, T.; Nadiye, S.; Murvet, Y. COULD VITAMIN D DEFICIENCY BE THE CAUSE OF DEPRESSION IN CHRONIC RENAL DISEASE PATIENTS. *Nephrol. Dial. Transplant.***2019**, *34* (Supplement_1).

65 Busch, A. J.; Barber, K. A. R.; Overend, T. J.; Peloso, P. M. J.; Schachter, C. L. Exercise for Treating Fibromyalgia Syndrome. *Cochrane Database Syst. Rev.***2007**, No. 4, 1–64. https://doi.org/10.1002/14651858.CD003786.pub2.

66 Raphael, K. G.; Janal, M. N.; Nayak, S.; Schwartz, J. E.; Gallagher, R. M. Familial Aggregation of Depression in Fibromyalgia: A Community-Based Test of Alternate Hypotheses. *Pain***2004**, *110* (1–2), 449–460. https://doi.org/10.1016/j.pain.2004.04.039.

67 Bradley, L. A. Pathophysiology of Fibromyalgia. *Am. J. Med.***2009**, *122* (12 SUPPL.), S22–S30. https://doi.org/10.1016/j.amjmed.2009.09.008.

68 Clauw, D. J. Fibromyalgia: An Overview. *Am. J. Med.***2009**, *122* (12 SUPPL.), S3–S13. https://doi.org/10.1016/j.amjmed.2009.09.006.

69 Dogru, A.; Balkarli, A.; Cobankara, V.; Tunc, S. E.; Sahin, M. Effects of Vitamin D Therapy on Quality of Life in Patients with Fibromyalgia. *Eurasian J. Med.***2017**, *49* (2), 113–117. https://doi.org/10.5152/eurasianjmed.2017.16283.

70 Ismaiel; El-Hady, A.; Mohsen, A. A.; Safy, M. A. The Role of Vitamin D Therapy in Patients with Fibromyalgia and Its Effect on Quality of Life. *J. Med. Sci. Res.***2019**, *2* (3), 198. https://doi.org/10.4103/JMISR.JMISR_47_19.

71 Gracely, R. H.; Ceko, M.; Bushnell, M. C. Fibromyalgia and Depression. *Pain Research and Treatment*. 2012. https://doi.org/10.1155/2012/486590.

72 Thiagarajah, A. S.; Guymer, E. K.; Leech, M.; Littlejohn, G. O. The Relationship between Fibromyalgia, Stress and Depression. *International Journal of Clinical Rheumatology*. 2014. https://doi.org/10.2217/ijr.14.30.

73 Armstrong, D. J.; Meenagh, G. K.; Bickle, I.; Lee, A. S. H.; Curran, E. S.; Finch, M. B. Vitamin D Deficiency Is Associated with Anxiety and Depression in Fibromyalgia. *Clin. Rheumatol.***2007**, *26*, 551–554. https://doi.org/10.1007/s10067-006-0348-5.

74 WHO. WHO | Maternal mental health https://www.who.int/mental_health/maternal-child/maternal_mental_health/en/ (accessed Mar 27, 2020).

75 Leung, B. M. Y.; Kaplan, B. J. Perinatal Depression: Prevalence, Risks, and the Nutrition Link-A Review of the Literature. *J. Am. Diet. Assoc.***2009**, *109* (9), 1566–1575. https://doi.org/10.1016/j.jada.2009.06.368.

76 Tandon, S. D.; Cluxton-Keller, F.; Leis, J.; Le, H. N.; Perry, D. F. A Comparison of Three Screening Tools to Identify Perinatal Depression among Low-Income African American Women. *J. Affect. Disord.***2012**, *136* (1–2), 155–162.

https://doi.org/10.1016/j.jad.2011.07.014.

77 Vaziri, F.; Nasiri, S.; Tavana, Z.; Dabbaghmanesh, M. H.; Sharif, F.; Jafari, P. A Randomized Controlled Trial of Vitamin D Supplementation on Perinatal Depression: In Iranian Pregnant Mothers. *BMC Pregnancy Childbirth***2016**, *16* (239), 1–12. https://doi.org/10.1186/s12884-016-1024-7.

78 Lamb, A. R.; Lutenbacher, M.; Wallston, K. A.; Pepkowitz, S. H.; Holmquist, B.; Hobel, C. J. Vitamin D Deficiency and Depressive Symptoms in the Perinatal Period. *Arch. Womens. Ment. Health***2018**, *21*, 745–755. https://doi.org/10.1007/s00737-018-0852-z.

79 Chung, T. K. H.; Lau, T. K.; Yip, A. S. K.; Chiu, H. F. K.; Lee, D. T. S. Antepartum Depressive Symptomatology Is Associated with Adverse Obstetric and Neonatal Outcomes. *Psychosom. Med.***2001**, *63* (5), 830–834. https://doi.org/10.1097/00006842-200109000-00017.

80 Accortt, E. E.; Schetter, C. D.; Peters, R. M.; Cassidy-Bushrow, A. E. Lower Prenatal Vitamin D Status and Postpartum Depressive Symptomatology in African American Women: Preliminary Evidence for Moderation by Inflammatory Cytokines. *Arch. Womens. Ment. Health***2016**, *19*, 373–383. https://doi.org/10.1007/s00737-015-0585-1.

81 Grote, N. K.; Bledsoe, S. E. Predicting Postpartum Depressive Symptoms in New Mothers: The Role of Optimism and Stress Frequency during Pregnancy. *Heal. Soc. Work***2007**, *32* (2), 107–118. https://doi.org/10.1093/hsw/32.2.107.

82 Bansil, P.; Kuklina, E. V.; Meikle, S. F.; Posner, S. F.; Kourtis, A. P.; Ellington, S. R.; Jamieson, D. J. Maternal and Fetal Outcomes among Women with Depression. *J. Womens. Health (Larchmt).***2010**, *19* (2), 329–334. https://doi.org/10.1089/jwh.2009.1387.

83 Accortt, E. E.; Lamb, A.; Mirocha, J.; Hobel, C. J. Vitamin D Deficiency and Depressive Symptoms in Pregnancy Are Associated with Adverse Perinatal Outcomes. *J. Behav. Med.***2018**, *41*, 680–689. https://doi.org/10.1007/s10865-018-9924-9.

84 Hollis, B. W.; Wagner, C. L. Vitamin D in Pregnancy and Lactation: A New Paradigm. In *Handbook of Nutrition and Pregnancy*; Springer International Publishing, 2018; pp 71–88. https://doi.org/10.1007/978-3-319-90988-2_4.

85 Camargo, C. A.; Ingham, T.; Wickens, K.; Thadhani, R. I.; Silvers, K. M.; Epton, M. J.; Town, G. I.; Espinola, J. A.; Crane, J. Vitamin D Status of Newborns in New Zealand. *Br. J. Nutr.***2010**, *104* (7), 1051–1057. https://doi.org/10.1017/S0007114510001674.