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Highlights:

- **Question:** Is vitamin D deficiency associated with depression in Nepalese population?
- **Findings:** vitamin D deficient individuals had 3.5 times higher odds of developing clinically significant depression in comparison to those with sufficient vitamin D after adjusting for confounding variables.
- **Meaning:** Vitamin D deficient people are associated with increased likelihood of having clinically significant depression in Nepalese population.

Title: Association between vitamin D deficiency and depression in Nepalese population

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Abstract

Recent studies link vitamin D deficiency with depression; however evidences from the Nepalese population are scarce. The current study explored the association between vitamin D deficiency and depression among 300 adults of 18 years and above age residing in eastern Nepal. Validated Nepali version of the Beck Depression Inventory scale (BDI-Ia) was used to determine depressive symptoms and a BDI cutoff score of ≥ 20 was considered as clinically significant depression. Sociodemographic data were collected using semi-structured questionnaire. Blood samples were collected to measure serum 25-hydroxy vitamin D (25(OH)D) and classify vitamin D status (deficient, insufficient and sufficient). We used Chi-square test to identify the association of sociodemographic variables and vitamin D status with clinically significant depression. We found a significant association of gender, geographical location of residence, marital status, religion and vitamin D status with clinically significant depression. Binary logistic regression model was used to examine the likelihood of clinically significant depression among vitamin D deficient individuals. Vitamin D deficiency was significantly associated with increased odds of clinically significant depression even after adjusting for confounding variables. This finding suggests Vitamin D deficient people have increased odds of having clinically significant depression.

Keywords: Beck Depression Inventory scale, Nepal, Depression, Vitamin D deficiency.

1. Introduction

Depression is a mental disorder which diminishes the functioning and quality of life. World Health Organization (WHO) had identified depression as a leading cause of disability worldwide affecting 300 million people (World health organization, 2017). Major depressive episodes (MDE) starts typically during early to mid-adulthood, which is the most productive part of one's life (Kessler et al., 2013). Even, when diagnosed and treated with medication the chronic recurrent nature of the disease and non-compliance to medication pose as a major challenge. Non-compliance to medication occurs mainly due to the fear of dependence, emergence of side effects to medication and the high cost of treatment (Penckofer et al., 2010). This leads to high relapse rate adding further to the global burden of the disease. Hence, one needs to examine other modifiable risk factors that can be targeted to prevent and treat depression besides medication.

Over the past decade, a substantial amount of observational and animal experimental studies have confirmed a broader role of vitamin D in health and disease, including mental health (Ganji et al., 2010; Atoum et al., 2017; Kočovská et al., 2017; Williams et al., 2014). The demonstration of Vitamin D receptor (VDR) in the pre-frontal cortex and the limbic system have elucidated the role of vitamin D in maintenance of mood, affect and cognitive functions (Eyles et al., 2005; Schlögl et al., 2014; Di Somma et al., 2017). Similarly, empirical evidences have also identified a link between vitamin D deficiency and depression (Penckofer et al., 2010; Ganji et al., 2010). A meta-analysis examining the relationship between vitamin D and depression reported inverse relation between depression and vitamin D level (Ju et al., 2013).

However, majority of these studies have been conducted in other parts of the world which are not representative of Nepalese population. The sociocultural complexities of Nepalese population due to its diverse caste and ethnic groups, religious practices, latitude, gender differences are important factors that cannot be undermined as they could have potential confounding effect. This urges us to take a deeper insight into the matter in our part of the world. To address these variations we examined the association between serum 25-hydroxyvitamin D [25(OH)D] concentrations and depressive symptoms in a Nepalese population after considering for probable confounding factors.

2. Method

2.1 Study design and setting

This cross section study was conducted in the department of Biochemistry at B.P Koirala Institute of Health Sciences, Dharan from February to June 2017. The study population comprised of patients between the ages of 18 years and above who were sent from various clinical departments for serum vitamin D measurement. Individuals with pre-existing conditions affecting vitamin D and/or calcium metabolism including liver or kidney disease, eating disorders, skin diseases and use of oral corticosteroids, anticonvulsants, insulin or bisphosphonates were not enrolled in the study. Pregnant and lactating women were also excluded. Apart from them, patients who provided informed consent verified by a signature or a thumb print were enrolled in the study. Ethical approval was obtained from the Institutional Review Committee, B.P Koirala Institute of Health Sciences.

2.2 Data collection

2.2.1 Depression assessment

Depression was assessed using Nepali version of Beck Depression Inventory (BDI Ia) scale. This 21-item Beck Depression Inventory (BDI) Scale was validated for use in Nepal with the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) for diagnosis of major depressive disorder (Kohrt et al., 2002; Kohrt et al., 2012). Based on this validation, a cut off score of 20 suggests moderate depression requiring mental health intervention [sensitivity=0.73, specificity=0.91] (Niraula et al., 2013). Participants with BDI cutoff scores of ≥ 20 were considered as having clinically significant depression.

2.2.2 Sociodemographic Characteristics

A semi-structured questionnaire was administered to the patients to collect information on socio-demographic characteristics (age, gender, ethnicity, religion, geographical region of residence, marital status, family type, duration of outdoor activity/day, socioeconomic status, education, and employment). Ethnicity was classified as brahman and chhetri, newar, janjati and occupational caste (dalit). (Gurung., 2005) Religion was divided after attaining the data into hindu, buddhist, kirat and others (muslims, christians, prem dharma.) Geographical region of residence was divided into terai region and hill and mountain region, while family type was classified as either living alone (alone), single married couple with unmarried children (nuclear family), married couple living with married children or three different generations living together (joint family). Marital status was classified as married, unmarried (never married) and marital discord (divorced / separated, in conflict with spouse or with in-laws). Socioeconomic status of people was categorized using Kuppuswamy scale (Ghosh and Ghosh., 2009) and then dichotomized into upper class (upper and upper middle class), lower class (lower middle and lower class). Duration of outdoor physical activity per day (included leisure time physical activity, walking to and from work, working outdoors) was classified into duration greater than 30 minutes and duration ≤ 30 minutes. Educational status was divided depending on level of education they had acquired (above high school, high school and middle school, primary school and no formal education). Type of employment of the study population was categorized depending upon the sector of work as agriculture, service, business, housewife, others and unemployed.

Questionnaire was followed by standardized measurements of body weight and body height of the participants. Body Mass Index (BMI) was calculated as body weight in kg divided by squared body height in metres. BMI was classified as per World Health Organization recommendations for Asian populations: underweight (<18.5 kg/m^2), normal weight (18.5–22.9 kg/m^2), and overweight (≥23.0-24.99 kg/m^2) and (BMI≥25kg/m^2) as obese. (Lim et al., 2017)

2.3 Vitamin D estimation:

Venous blood samples were obtained in plain vial. Sample was centrifuged and serum was separated. Vitamin D 25(OH)D was measured in serum in department of Biochemistry using chemiluminescence immunoassay (CLIA) technique in fully automated Maglumi 1000 analyzer (SNIBE Co, Ltd, China). Internal quality control provided by the manufacturer was used to assure quality. Vitamin D level was stratified as: 30-100 ng/ml 25(OH)D as sufficient vitamin D level, 29 and 20 ng/ml as insufficient vitamin D, < 20 ng/ml as deficient vitamin D (Ringe et al., 2012).

2.4 Statistical analyses

Data was analyzed using Statistical Package of Social science (SPSS) version 11.5. Descriptive statistics was used to express the demographics and anthropometric characteristics of the study sample. Statistical comparison of sociodemographic characteristics among three cut-off levels of serum 25(OH)D (deficient, insufficient and sufficient vitamin D status) was done using χ^2 test for categorical and Kruskal Wallis for continuous variables. Prevalence of clinically significant depression among various categories of vitamin D status and sociodemographic characteristics was conducted using χ^2 test and Mann Whitney test for categorical and continuous variables respectively. Binary logistic regression was used to calculate unadjusted and adjusted odds ratio (OR) and 95% confidence interval (CI) for vitamin D status and Depression category (Clinically significant depression Vs non-significant). A probability P<0.05 was considered statistically significant.

3. Result

3.1 Baseline Characteristics of the study population

The study included 300 participants (36.3% male and 63.7% female). The mean age was 38.3 ± 10.2 years. Majority of study population lived in nuclear family (55.3%), practiced hinduism (75.7%), were residents of terai region (90.7%), 42% had studied upto high school. The most common ethnic group was brahman and chhetri (45%) followed by janajati (37%). More than half of the participants were married (84.3%) and belonged to lower class families (lower middle class and lower class) (81%). (Table 1)

3.2 Vitamin D status

Majority (51.3%) had vitamin D deficiency (<20 ng/ml), 27.3% had insufficient vitamin D (20 to 29 ng/ml) and 21.3% had sufficient vitamin D (≥30 ng/ml) and the median (25^{th} -75^{th} centile) of serum vitamin D level was 19(14-28). The median Serum 25(OH)D level in females was 18 (13-23) which was significantly lower than males having median 22 (15-33) (p<0.001).Vitamin D status had significant association with gender (Chi-sq=30.3, d.f.=2, $p<0.001$), education level (Chi-sq=13.6, d.f.=6, $p=0.03$), socioeconomic status (Chi-sq=9.0, d.f.=2, $p=0.01$) and geographical region of residence (Chi-sq=7.2, d.f.=2, $p=0.02$) and employment (Chi-sq=24.1, d.f.=10, $p=0.007$).(Table 1)

3.3 **Depression**

We found 16.3% of participants had clinically significant depression (BDI cutoff scores of ≥ 20) with higher prevalence among vitamin D deficient compared to sufficient ($p=0.006$), female compared to male ($p=0.02$) and people residing in hills and mountains region than terai residents ($p=0.01$), in marital discord than married people ($p=0.04$) and people practicing kirat religion than hindu ($p=0.01$) (Table 2) (Table 3). The median (25^{th}-75^{th} centile) of depression score was 12 (8-16.7) with significantly higher scores among females 13(10-17.5) compared to males 9(6-13), $p<0.001$.

3.4 **Association between serum 25(OH)D and clinically significant depression.**

In binary logistic regression, the OR (95% CI) for clinically significant depression was significant for vitamin D deficient category 4.4(1.4-12.9, $p=0.007$) when compared to vitamin D sufficient. However, the association with vitamin D insufficient was not significant 2(0.6-6.9, $p=0.2$). After adjusting for ethnicity, gender, family, religion, geographical location of residence, marital status, outdoor physical activities, socioeconomic status, education, employment and body mass index the association was significant ($p<0.05$) for vitamin D deficient category compared to vitamin D sufficient, (Table 4) people practicing kirat religion compared to hindu and among marital discord group compared to married people.

Table 1: The Baseline characteristics of study population according to Serum 25(OH)D level.

		Total *n(%)*	Serum 25(OH)D level (ng/ml)			*p*-value
			<20	**20–29**	**≥30**	
n(%)[1]			154(51.3)	82(27.3)	64(21.3)	
Age(Years)[a]		38.3±10.2	37.5±9.8	38.8±10.7	39.5±10.5	0.2
Gender	Male	109(36.3)	45(15)	22(7.3)	42(14)	0.001
	Female	191(63.7)	109(36.3)	60(20)	22(7.3)	
Ethnicity	Brahman, Chhetri	135 (45)	61(20.3)	44(14.7)	30(10)	0.4
	Newar	31(10.3)	19(6.3)	5(1.7)	7(2.3)	
	Janjati	111(37)	63 (21)	26(8.7)	22(7.3)	
	Occupational caste (Dalit)	23(7.7)	11(3.7)	7(2.3)	5(1.7)	
Religion	Hindu	227(75.7)	109(36.3)	65(21.7)	53(17.7)	0.07
	Buddhist	25(8.3)	13(4.3)	5(1.7)	7(2.3)	
	Kirat	40(13.3)	27(9)	11(3.7)	2(0.7)	
	Others	8(2.7)	5(1.7)	1(0.3)	2(0.7)	
Geographical location	Terai	272(90.7)	133(44.3)	77(25.7)	62(20.7)	0.02
	Hill and Mountain	28(9.3)	21(7)	5(1.7)	2(0.7)	
Family type	Alone	16 (5.3)	12(4)	1(0.3)	3(1)	0.1
	Nuclear Family	166 (55.3)	88(29.3)	41(13.7)	37(12.3)	
	Joint Family	118 (39.3)	54(18.0)	40(13.3)	24(8)	
Marital status	Married	253 (84.3)	125(41.7)	70(23.3)	58(19.3)	0.4
	Unmarried	30(10)	17(5.7)	9(3)	4(1.3)	
	Marital discord	17(5.7)	12(4)	3(1)	2(0.7)	
Outdoor physical activity	30 minutes or less	113 (37.7)	54(18)	35(11.7)	24(8)	0.5
	> 30 minutes	187 (62.3)	100(33.3)	47(15.7)	40(13.3)	
Body Mass Index	Normal	66 (22)	27(9)	23(7.7)	16(5.3)	0.3
	Underweight	10 (3.3)	3(1)	4(1.3)	3(1)	
	Overweight	44 (14.7)	23(7.7)	11(3.7)	10(3.3)	
	Obese	180 (60)	101(33.7)	44(14.7)	35(11.7)	
Socioeconomic status	High class	57 (19)	38(12.7)	7(2.3)	12(4)	0.01
	Low class	243 (81)	116(38.7)	75(25)	52(17.3)	
Education	Above high School	103 (34.3)	61(20.3)	23(7.7)	19(6.3)	0.03
	High, Middle school	126 (42.0)	60(20)	31(10.3)	35(11.7)	
	Primary school	29 (9.7)	16(5.3)	9(3.0)	4(1.3)	
	No formal education	42 (14.0)	17(5.7)	19(6.3)	6(2.0)	
Employment	Unemployed	26 (8.7)	8(2.7)	9(3)	9(3)	0.007
	Housewife	101 (33.7)	54(18)	34(11.3)	13(4.3)	
	Agriculture	47 (15.7)	20(6.7)	14(4.7)	13(4.3)	
	Service	46 (15.3)	30(10)	8(2.7)	8(2.7)	
	Business	60 (20)	32(10.7)	16(5.3)	12(4)	
	Others	20 (6.7)	10 (3.3)	1 (0.3)	9(3)	
Serum 25(OH)D[b]		19(14,28)	14(11,17)	23(21,26)	34(32,40)	-

Baseline characteristics are expressed as number (percentage) [*n*(%)] of row or mean±SD (age[a]) or median (25th and 75th centile) for Serum 25(OH)D[b], *n*(%)[1] represents values of column. *p* value from χ^2 test, kruskal wallis for age[a]

Table 2: Prevalence of Clinically significant depression according to vitamin D status

	n(%)	Vitamin D status[a]			*p*-value
		Deficient	**Insufficient**	**Sufficient**	
Depression BDI Ia scores					0.006
BDI cutoff scores < 20	251(83.7)	119(39.7)	72(24)	60(20)	
BDI cutoff scores ≥ 20[b]	49(16.3)	35(11.7)	10(3.3)	4(1.3)	

Values are expressed as number (percentage) [*n*(%)] of row

p-value obtained from χ^2 test

[a]Vitamin D status as per serum 25(OH)D level (ng/ml): Deficient(<20), Insufficient(20-29), Sufficient(≥30-100).

[b]BDI cutoff scores ≥ 20 : Clinically significant depression.

Table 3: Prevalence of Clinically Significant Depression according to Sociodemographic characteristics

Characteristic		Total *n(%)*	Depression (BDI Ia) scores		*p*-value
			scores <20	**scores ≥ 20**	
n(%)[1]			251(83.7)	49(16.3)	-
Age(Years)[a]		38.3±10.2	38.3±10.5	37.9±8.9	0.9
Gender	Male	109(36.3)	98(32.7)	11(3.7)	0.02
	Female	191(63.7)	153(51)	38(12.7)	
Ethnicity	Brahman, Chhetri	135 (45)	116(38.7)	19(6.3)	0.6
	Newar	31(10.3)	26(8.7)	5(1.7)	
	Janjati	111(37)	89(29.7)	22(7.3)	
	Occupational caste (Dalit)	23(7.7)	20(6.7)	3(1)	
Religion	Hindu	227(75.7)	198(66)	29(9.7)	0.01
	Buddhist	25(8.3)	20(6.7)	5(1.7)	
	Kirat	40(13.3)	27(9.0)	13(4.3)	
	Others	8(2.7)	6(2)	2(0.7)	
Geographical location	Terai	272(90.7)	233(77.7)	39(13)	0.01
	Hill and Mountain	28(9.3)	18(6)	10(3.3)	
Family type	Alone	16 (5.3)	15(5)	1(0.3)	0.5
	Nuclear Family	166 (55.3)	139(46.3)	27(9)	
	Joint Family	118 (39.3)	97(32.3)	21(7)	
Marital status	Married	253 (84.3)	212(70.7)	41(13.7)	0.04
	Unmarried	30(10)	28(9.3)	2(0.7)	
	Marital discord	17(5.7)	11(3.7)	6(2)	
Outdoor physical activity	30 minutes or less	113 (37.7)	91(30.3)	22(7.3)	0.2
	> 30 minutes	187 (62.3)	160(53.3)	27(9)	
Body Mass Index	Normal	66 (22)	57(19)	9(3)	0.9
	Underweight	10 (3.3)	8(2.7)	2(0.7)	
	Overweight	44 (14.7)	37(12.3)	7(2.3)	
	Obese	180(60)	149(49.7)	31(10.3)	
Socioeconomic status[c]	High class	57 (19)	51(17)	6(2)	0.1
	Low class	243 (81)	200(66.7)	43(14.3)	
Education	Above high School	103 (34.3)	93(31)	10(3.3)	0.09
	High, Middle school	126 (42.0)	104(34.7)	22(7.7)	
	Primary school	29 (9.7)	22(7.3)	7(2.3)	
	No formal education	42 (14)	32(10.7)	10(3.3)	
Employment	Unemployed	26 (8.7)	24(8)	2(0.7)	0.07
	Housewife	101 (33.7)	82(27.3)	19(6.3)	

	Agriculture	47 (15.7)	34(11.3)	13(4.3)	
	Service	46 (15.3)	43(14.3)	3(1)	
	Business	60 (20)	52(17.3)	8(2.7)	
	Others	20 (6.7)	16(5.3)	4(1.3)	
Median Depression score[b]		12(8-16.75)			-

Baseline characteristics are expressed as number (percentage) [*n*(%)] of row or mean±SD (age[a]) or median (25th and 75th centile) for Median Depression score[b], *n*(%)[1] represents values of column. *p* value from χ^2 test, Mann Whitney for age[a]

Table 4: Odds of having clinically significant depression according to Vitamin D status

	Vitamin D status		
	Sufficient	**Insufficient**	**Deficient**
Unadjusted odds (95% CI)[a]	Reference	2.0(0.6-6.9)	4.4(1.4-12.9)
p-value		0.2	0.007
Model 1: Adjusted odds (95% CI)[b]	Reference	1.4(0.4- 5.1)	3.2(1.1- 9.9)
p-value		0.5	0.03
Model 2: Adjusted odds (95% CI)[c]	Reference	1.5(0.3-5.9)	3.5(1.1-11.9)
p-value		0.5	0.04

[a]Odds ratio and 95% Confidence Interval calculated from Logistic regression analysis.
[b]Adjusted for ethnicity (brahman, chhetri, newar, janjati, occupational caste [dalit]), gender, family type (alone, nuclear family, joint family), religion (hindu, buddhist, kirat, others)
[c]Adjusted for variables in Model 1, geographical region of residence (terai, hill and mountain), marital status (married, unmarried, marital discord), outdoor physical activities (30 minutes or less, > 30 minutes), socioeconomic status (lower class, higher class), education (above high school, high, middle school, primary school, no formal education), employment (unemployed, housewife, agriculture, service, business, others), body mass index (normal, underweight, overweight, obese).

4. Discussion:

We conducted a cross sectional study among adult population residing in eastern part of Nepal and examined the association between vitamin D status and depression. Vitamin D status was determined using serum 25(OH)D level and depression was measured using BDI Ia scoring tool validated for Nepalese population.

We found 16.3% had clinically significant depression (BDI cutoff scores of ≥ 20) and the prevalence of clinically significant depression (CSD) was higher among vitamin D deficient individuals in comparison to individuals with sufficient vitamin D. These findings were similar to the conclusions drawn from meta-analysis (Okereke and Singh., 2016) and cross sectional studies conducted across the globe (Ganji et al., 2010; Chu et al., 2017; Jhee et al., 2017; McCann and Ames, 2008). However, most of these studies were conducted in various parts of the world which differ from ours in terms of sociocultural factors, latitude, measurement and cut-off scores of 25(OH)D and seasons of sample collection. Hence, establishing a link between vitamin D and depression was relatively new in our setup. Over the past decade a growing number molecular studies have attempted to explain the molecular mechanism behind the onset of depression due to vitamin D deficiency. It has been postulated that vitamin D prevents depression by maintaining normal serotonin levels in the brain by regulating the expression of serotonergic gene coding for tryptophan hydroxylase (Patrick and Ames, 2015; Kaneko et al., 2015). Vitamin D also maintains reduced level of calcium required for proper neuronal function by down regulating L-Type calcium channel in hippocampus (Brewer et al., 2001) while promoting calcium buffering proteins as calbindin and parvalbumin (De Viragh et al., 1989).

We also found higher prevalence of CSD among marital discord group, people following kirat religion and residents of hills and mountains. Gender analysis in our study revealed three times higher prevalence of CSD among women in comparison to men. This finding was higher than the previous population studies reporting about two-fold higher prevalence in females (Albert, 2015). Such high occurrence cannot be solely attributed to higher number of female participants (female to male ratio 1.7:1) in our study. Studies have implicated the role of estrogen on cognitive function and mood due to its differential distribution in male and female brain (McEwen and Milner, 2007; Gillies and McArthur, 2010). However, these studies cannot explain why women in our country have higher occurrence of depression than women of developed countries. Hence, we postulate sociocultural constraints faced by women may be an important factor associated with depression in a developing country like Nepal.

Our study also found a significantly higher prevalence of CSD in residents of hilly and mountainous region compared to terai. This finding was in agreement with a study conducted by Risal et al, reporting a higher occurrence of depression among high altitude dwellers (Risal et al., 2016). Similarly, another study conducted in Pakistan reported higher incidence of depression and anxiety in people working in high altitudes (Ahmad and Hussain, 2017). The reason for high altitude depression may be linked to continuous hypoxia experienced at such height that affects the functioning and synthesis of neurotransmitters required for critical neuronal functions (Kumar, 2011). An animal experimental study done in rats kept in simulated high altitudes with hypobaric hypoxic environment reported higher depression like behavior in female rats (Kanekar et al., 2015). This emphasizes the need of further studies to analyze the factors responsible for altitude related depression.

We found a greater prevalence of depression amongst people practicing kirat religion. Studies have highlighted that religion acts as a buffering factor against depression. (Salsman et al.,2015). Nevertheless, the variations of effect on mental health between different religious practices have yet to be examined. Our finding was in contrast to another study conducted in Nepal where religion was not found to have any significant association with depression. (Niraula et al., 2013) Our study highlights the need for a detailed insight into the religious practices of kirat to understand this association.

People who had marital discord had higher prevalence of CSD than married and single people. We had included people who were divorced / separated, in conflict with spouse or with in-laws in marital discord category. This was similar to previous studies depicting marital conflicts as a predictor for depression (Du Rocher et al., 2011). We found significantly greater number of marital discord among the working population. This may be especially true in case a woman is employed which changes the power dynamics in the household, where husband may perceive her economic independence as a threat fostering hostility and marital conflicts (Sayer et al., 2011; Krishnan et al., 2010).

In our logistic regression analysis, we established significantly higher odds of developing CSD among vitamin D deficient individuals compared to those with sufficient vitamin D. This finding remained parallel even after adjusting for various confounding factors. We exercised caution not to over adjust, and only adjusted for factors significant in bivariate analysis. After adjustment we found vitamin D deficient individuals had 3.5 higher odds of developing depression in comparison to those with sufficient vitamin D.

Conclusion

Vitamin D deficiency is associated with increased odds of having depression. In a country like Nepal where cultural beliefs are deeply rooted and have profound influence in lifestyle choices, one has to go beyond merely correcting serum vitamin D level to impede depression. This study warrants a need for clinical trial to assess if supplementing vitamin D improves depression symptoms.

Conflict of Interest

None declared

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References

1. World health organization. Depression factsheet.(2017) Retrived on December 12, 2017, from http://www.who.int/mediacentre/factsheets/fs369/en/
2. Kessler RC, Bromet EJ. The epidemiology of depression across cultures. Annual review of public health. 2013;34:119-138. doi:10.1146/annurev-publhealth-031912-114409.[PubMed] [PMC free Article]
3. Penckofer S, Kouba J, Byrn M, EstwingFerrans C. Vitamin D and depression: Where is all the sunshine? Issues in Mental Health Nursing. 2010 May;31(6):385-393.[PubMed] [PMC free Article]
4. Ganji V, Milone C, Cody MM, McCarty F, Wang YT. Serum vitamin D concentrations are related to depression in young adult US population: the Third National Health and Nutrition

Examination Survey. International Archives of Medicine. 2010;3:29. [Pub Med][PMC free Article]

5. Atoum M, Alzoughool F. Vitamin D and Breast Cancer: Latest Evidence and Future Steps. Breast Cancer: Basic and Clinical Research. 2017 Dec 19;11:1178223417749816. [PubMed]
6. Kočovská E, Gaughran F, Krivoy A, Meier UC. Vitamin-D deficiency as a potential environmental risk factor in multiple sclerosis, schizophrenia, and autism. Frontiers in psychiatry. 2017 Mar 27;8:47. [PubMed]
7. Williams JA, Sink KM, Tooze JA, Atkinson HH, Cauley JA, Yaffe K, Tylavsky FA, Rubin SM, Simonsick EM, Kritchevsky SB, Houston DK. Low 25-hydroxyvitamin D concentrations predict incident depression in well-functioning older adults: the health, aging, and body composition study. Journals of Gerontology Series A: Biomedical Sciences and Medical Sciences. 2014 Oct 18;70(6):757-63. http://doi.org/10.1093/gerona/glu184
8. Eyles DW, Smith S, Kinobe R, Hewison M, McGrath JJ. Distribution of the vitamin D receptor and 1α-hydroxylase in human brain. Journal of chemical neuroanatomy. 2005 Jan 1;29(1):21-30.
9. Schlögl M, Holick MF. Vitamin D and neurocognitive function. Clinical Interventions in Aging. 2014;9:559-568. doi:10.2147/CIA.S51785.[Pub Med] [PMC free article]
10. Di Somma C, Scarano E, Barrea L, et al. Vitamin D and Neurological Diseases: An Endocrine View. International Journal of Molecular Sciences. 2017;18(11):2482. doi:10.3390/ijms18112482.[PubMed] [PMC free Article]
11. Ju SY, Lee YJ, Jeong SN. Serum 25-hydroxyvitamin D levels and the risk of depression: A systematic review and meta-analysis. J. Nutr. Health Aging. 2013;17:447–455. https://doi.org/10.1007/s12603-012-0418-0
12. Kohrt BA, Kunz RD, Koirala NR, Sharma VD, Nepal MK. Validation of a Nepali version of the Beck Depression Inventory. Nepalese Journal of Psychiatry. 2002;2(4):123-30. www.researchgate.net/publication/285869290
13. Kohrt BA, Hruschka DJ, Worthman CM, Kunz RD, Baldwin JL, Upadhaya N, Acharya NR, Koirala S, Thapa SB, Tol WA, Jordans MJ. Political violence and mental health in Nepal: prospective study. The British Journal of Psychiatry. 2012 Oct 1;201(4):268-75. [PubMed] [PMC free Article]
14. Niraula K, Kohrt BA, Flora MS, Thapa N, Mumu SJ, Pathak R, Stray-Pedersen B, Ghimire P, Regmi B, MacFarlane EK, Shrestha R. Prevalence of depression and associated risk factors among persons with type-2 diabetes mellitus without a prior psychiatric history: a cross-sectional study in clinical settings in urban Nepal. BMC psychiatry. 2013 Dec;13(1):309.[PubMed]

15. Gurung H. Social exclusion and Maoist insurgency. Paper presented at National Dialogue Conference on ILO Convention 169 on Indigenous and Tribal Peoples, Kathmandu, 19–20 January 2005
16. Ghosh A, Ghosh T. Modification of Kuppuswamy's Socioeconomic Status Scale in context to Nepal. Indian Pediatr. 2009 Dec;46(1):1104–1105. [PubMed]
17. Lim JU, Lee JH, Kim JS, et al. Comparison of World Health Organization and Asia-Pacific body mass index classifications in COPD patients. International Journal of Chronic Obstructive Pulmonary Disease. 2017;12:2465-2475. doi:10.2147/COPD.S141295. [PubMed]
18. Ringe JD, Kipshoven C. Vitamin D-insufficiency: An estimate of the situation in Germany. Dermato-endocrinology. 2012;4(1):72-80. doi:10.4161/derm.19829. [PubMed] [PMC free Article]
19. Okereke OI, Singh A. The Role of Vitamin D in the Prevention of Late-life Depression. *Journal of affective disorders*. 2016;198:1-14. doi:10.1016/j.jad.2016.03.022. [PubMed]
20. Chu F, Ohinmaa A, Klarenbach S, Wong Z-W, Veugelers P. Serum 25-Hydroxyvitamin D Concentrations and Indicators of Mental Health: An Analysis of the Canadian Health Measures Survey. Nutrients. 2017;9(10):1116. [PubMed]
21. Jhee JH, Kim H, Park S, et al. Vitamin D deficiency is significantly associated with depression in patients with chronic kidney disease. Aguilera AI, ed. PLoS ONE. 2017;12(2):e0171009. doi:10.1371/journal.pone.0171009. [PubMed]
22. McCann JC, Ames BN. Is there convincing biological or behavioral evidence linking vitamin D deficiency to brain dysfunction? FASEB J. 2008;22:982–1001.[PubMed]
23. Patrick RP, Ames BN. Vitamin D and the omega-3 fatty acids control serotonin synthesis and action, part 2: relevance for ADHD, bipolar disorder, schizophrenia, and impulsive behavior. The FASEB Journal. 2015 Jun 1;29(6):2207-22.[PubMed][Cross Ref]
24. Kaneko I, Sabir MS, Dussik CM, Whitfield GK, Karrys A, Hsieh JC, Haussler MR, Meyer MB, Pike JW, Jurutka PW. 1, 25-Dihydroxyvitamin D regulates expression of the tryptophan hydroxylase 2 and leptin genes: implication for behavioral influences of vitamin D. The FASEB Journal. 2015 Sep 1;29(9):4023-35.[PubMed][Cross Ref]
25. Brewer LD, Thibault V, Chen KC, Langub MC, Landfield PW, Porter NM. Vitamin D hormone confers neuroprotection in parallel with downregulation of L-type calcium channel expression in hippocampal neurons. Journal of Neuroscience. 2001 Jan 1;21(1):98-108.[PubMed]
26. De Viragh PA, Haglid KG, Celio MR. Parvalbumin increases in the caudate putamen of rats with vitamin D hypervitaminosis. Proceedings of the National Academy of Sciences of the United States of America. 1989;86(10):3887-3890.[PubMed]

27. Albert PR. Why is depression more prevalent in women? Journal of Psychiatry & Neuroscience : JPN. 2015;40(4):219-221. doi:10.1503/jpn.150205. [PubMed] [PMC free Article]
28. McEwen BS, Milner TA. Hippocampal formation: shedding light on the influence of sex and stress on the brain. Brain research reviews. 2007;55(2):343-355. doi:10.1016/j.brainresrev.2007.02.006.[PubMed]
29. Gillies GE, McArthur S. Estrogen Actions in the Brain and the Basis for Differential Action in Men and Women: A Case for Sex-Specific Medicines. Pharmacological Reviews. 2010;62(2):155-198. [PubMed]
30. Risal A, Manandhar K, Linde M, Steiner TJ, Holen A. Anxiety and depression in Nepal: prevalence, comorbidity and associations. BMC Psychiatry. 2016;16:102. doi:10.1186/s12888-016-0810-0. [PubMed]
31. Ahmad S, Hussain S. Mood changes at very high altitudes in Pakistan. Pakistan Journal of Medical Sciences. 2017;33(1):231-235. doi:10.12669/pjms.331.11393. [PubMed]
32. Kumar GK. Hypoxia. 3. Hypoxia and neurotransmitter synthesis. American Journal of Physiology - Cell Physiology. 2011;300(4):C743-C751.[PubMed]
33. Kanekar S, Bogdanova OV, Olson PR, Sung Y-H, D'Anci KE, Renshaw PF. Hypobaric Hypoxia Induces Depression-like Behavior in Female Sprague-Dawley Rats, but not in Males. High Altitude Medicine & Biology. 2015;16(1):52-60. doi:10.1089/ham.2014.1070. [PubMed]
34. Salsman JM, Pustejovsky JE, Jim HSL, et al. A Meta-Analytic Approach to Examining the Correlation Between Religion/Spirituality and Mental Health in Cancer. Cancer. 2015;121(21):3769-3778. doi:10.1002/cncr.29350.
35. Du RocherSchudlich TD, Papp LM, Cummings EM. Relations between Spouses' Depressive Symptoms and Marital Conflict: A Longitudinal Investigation of the Role of Conflict Resolution Styles. Journal of family psychology : JFP : journal of the Division of Family Psychology of the American Psychological Association (Division 43). 2011;25(4):531-540.[PubMed] [PMCfree Article]
36. Sayer LC, England P, Allison P, Kangas N. She Left, He Left: How Employment and Satisfaction Affect Men's and Women's Decisions to Leave Marriages. Ajs; American Journal of Sociology. 2011;116(6):1982-2018. [PubMed]
37. Krishnan S, Rocca CH, Hubbard AE, Subbiah K, Edmeades J, Padian NS. "Do Changes in Spousal Employment Status Lead to Domestic Violence? Insights from a Prospective Study in Bangalore, India." Social science & medicine (1982). 2010;70(1):136-143. doi:10.1016/j.socscimed.2009.09.026. [PubMed]