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ORIGINAL ARTICLE

Psychosocial and clinical aspects of hypovitaminosis D in a sample of pregnant women: a cross-sectional study from Egypt

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Background Hypovitaminosis D levels have been implicated in a wide array of psychiatric disorders. Yet, the relationship between vitamin D levels and antenatal psychiatric disturbances is ambiguous. This study aimed to identify the psychosocial and clinical factors associated with antenatal hypovitaminosis D.

Patients and Methods A total of 169 pregnant women were recruited from Zagazig University Obstetrics and Gynecology Outpatient clinics, Egypt, where they received antenatal care. The psychometric measures included Hamilton Anxiety Rating Scale, Zagazig Depression Scale, Beck Scale for Suicide Ideation, and Structured Clinical Interview for DSM-IV-TR Axis I Disorders for assessment of associated anxiety and depressive symptoms, current suicide ideation and psychiatric disorders, respectively. Serum 25-hydroxyvitamin D levels were measured using the enzyme-linked fluorescent assay technique.

Results Around 57% of women had antenatal hypovitaminosis D. Those with hypovitaminosis D were likely to be of lower income (P= 0.023), exposed to intimate partner violence (IPV) (P= 0.009), and experienced higher levels of anxiety (P= 0.006). Logistic regression confirmed the association between hypovitaminosis D and history of IPV exposure (odds ratio= 2.0, 95% confidence interval= 1.1, 3.9), and comorbid anxiety symptoms (odds ratio= 2.4, 95% confidence interval= 1.0, 6.2). Predictors of IPV exposure in women with antenatal hypovitaminosis D were lower education (P= 0.045), unplanned pregnancy (P= 0.016), anxiety symptoms (P= 0.036), and current suicide ideation (P< 0.001).

Conclusions Antenatal hypovitaminosis D was prevalent among pregnant women. It would predict IPV exposure and comorbid anxiety symptoms. Women, as part of their antenatal assessment, should be regularly screened for vitamin D insufficiency, IPV exposure, and associated affective symptoms.

Keywords Hypovitaminosis D, Intimate partner violence, Pregnancy, Psychiatric symptoms.
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INTRODUCTION

Emotional disturbances like anxiety and depressive disorders are considered the most common psychiatric disorders during pregnancy and the postpartum periods. These disorders are associated with higher rates of both maternal and neonatal morbidity with sometimes lifelong and catastrophic consequences (Jani *et al.,* 2020). Rates of maternal depression have been on the rise over the last decade (Lamb *et al.,* 2018). It was reported that around 10–20% of women experience depression during pregnancy, while within the first year after giving birth, the risk is approximately one in every seven women (Banti *et al.,* 2011). Moreover, prenatal depression increases the risk for preterm birth, low birth weight, cesarean section, preeclampsia, diabetes, and congenital malformations (Chung *et al.,* 2001). Also, the higher the perinatal depressive symptoms, the higher the incidence of having autism, cognitive disability, and mental illness later in life in the offspring (Sohr-Preston and Scaramella, 2006).

Skin exposure to sunlight and, to a lesser extent, diet are the main sources of vitamin D. Vitamin D is then hydroxylated to 25-hydroxyvitamin D, which then undergoes a second hydroxylation to the active form 1,25-dihydroxyvitamin D. The 25-hydroxyvitamin D is the best indicator of vitamin D status while its active form binds to its receptors in many tissues (Eyles *et al.,* 2005). The presence of vitamin D receptors in the human brain explains the role in maintaining the neurological functioning as it promotes neurogenesis, synaptogenesis, neurotransmission, amyloid clearance, and the prevention of neuronal death (Koduah *et al.,* 2017). It was believed that the active form of vitamin D aids in the neuronal production of serotonin and protects against low levels of dopamine and serotonin (Patrick and Ames, 2014).

Hypovitaminosis D is more prevalent in women of reproductive age. Furthermore, women during pregnancy become more susceptible to vitamin D deficiency. Studies on pregnant women showed high rates of hypovitaminosis D (<25 nmol/l) from various ethnic groups, for example, sub-Saharan Africa (26%), Middle East (40%), and South Asia (45%) (Eggemoen *et al.,* 2016). There is a high demand for Vitamin D as pregnant women must sustain their own vitamin D stores and those of their unborn child (Aghajafari *et al.,* 2018). Besides the physical and psychological burden of pregnancy on women, several mental disorders such as depression, anxiety, and sleep disorders are associated with hypovitaminosis D in pregnant women (Spedding, 2014). However, it was claimed that using medium doses of vitamin D (≥800 IU daily) for correction of low vitamin D levels had some desirable effects on the treatment of depression (McCann and Ames, 2008).

Although, several psychiatric disorders have been linked to low levels of vitamin D in various populations, and its deficiency among patients with psychiatric illnesses is overrepresented (Kjærgaard *et al.,* 2011; Murri *et al.,* 2013), to date, a small number of studies have addressed the association between vitamin D deficiency and psychiatric disturbances in pregnant women. The link between vitamin D deficiency and psychological and clinical comorbidities during pregnancy is an emerging area of research that has not been well established till now. To the awareness of the authors, a few studies have investigated this relationship among pregnant women in Egypt.

PATIENTS AND METHODS

Source of data and sampling

This is a cross-sectional study carried out from October 1st, 2017, till June 30th, 2018. 176 pregnant women between 20 to 40 years were enrolled in this study consecutively, at any trimester of pregnancy. The sample size was calculated at 80% power of the study, 95% confidence level according to the Epi Info 6.0. As of past year, a total of 3053 pregnant women has attended the OPD of antenatal care at Zagazig University hospitals, Sharkia, Egypt. A history of antenatal psychiatric symptoms was reported in 19% of pregnant women (Mongan *et al.,* 2019). The dropout rate of the survey was 4% as 7 women provided incomplete responses or refused to participate in the study. Thus the sample included eventually in total 169 pregnant women. Women who suffered from chronic psychiatric and/or physical illnesses, current substance use disorders, mental retardation, high-risk pregnancy, widowed, divorced, or single pregnant women were excluded from the study.

Data collection and measures

Exposure ascertainment: the main exposure variable was the antenatal hypovitaminosis D assessed by measuring the serum levels of antenatal vitamin D (OH) 25. These levels were measured using the MINI VIDAS immunoanalyzer technique, which is a compact automated immunoassay system based on the enzyme-linked fluorescent assay principles. Blood samples were collected after a 12-h fasting period, then centrifuged at 1500g for 5 min. Plasma and serum samples were separated and stored at -80°C until analysis was performed. Hypovitaminosis D was considered when the vitamin D (OH) 25 level was below 20 ng/dl.

Outcome ascertainment: the primary outcomes were the development of depressive and anxiety symptoms and increased current suicide risk.

The Zagazig Depression Scale: The Zagazig Depression Scale was a standardized self-rating instrument used to screen and assess the severity of depressive symptoms (Fawzi *et al.,* 1982). It covers 17 items about the depression symptoms and entails 52 questions with a total score of 0-30 where scores ranging between 0 and 9 mean no depressive symptoms, scores between 10 and 19 mean mild depressive symptoms, scores between 20 and

29 mean moderate depressive symptoms, and a score of 30 means more severe depressive symptoms.

Hamilton Anxiety Scale: The Hamilton Anxiety Scale was widely used to assess the severity of symptoms of anxiety (Hamilton, 1969). HAM-A included 14 items, and each item score ranged from 0 (not present) to 4 (severe) with a total score between 0 and 56, scores between 0 and 13 mean normal range, scores between 14 and 17 mean mild severity, scores between 18 and 24 mean moderate severity, and scores of 25 or more mean severe anxiety symptoms.' An Arabic version was prepared and standardized (Hallit *et al.,* 2020).

Beck Scale for Suicide Ideation: The Beck Scale for Suicide Ideation was utilized to assess the current suicide risk by evaluating the participant's thoughts, intent, and plans to commit suicide (Beck *et al.,* 1979). It included 21 items. However, only the first 19 items were scored. Responses ranged from 0-2 to each question (Cochrane-Brink *et al.,* 2000).

Covariates: Potential confounders considered in this study were the demographic and clinical variables. Sociodemographic data as personal and family-related information, clinical data as lifetime history of exposure to IPV, past or family history of suicide ideations and/or attempts, and obstetric data as possible pregnancy-related variables were collected using a pre-designed semi-structured questionnaire. Data about lifetime exposure to IPV were collected by asking the participants a "yes or no" questions about experiencing physical, verbal, emotional, economic, and/or sexual violence from their current or previous partners or spouses anytime through their relationships. The Structured Clinical Interview for DSM-IV-TR Axis I Disorders (SCID-I) was used to screen for psychiatric disorders according to the diagnostic guidelines of DSM-IV-TR (First, 1997). An Arabic validated version was used in this study (El Missiry *et al.,* 2003).

Ethical considerations

This study was conducted according to the ethical guidelines outlined in the Declaration of Helsinki. Written informed consent was signed from all participants before starting the study. This study was approved by the Institutional Review Board of Zagazig Faculty of Medicine (IRB: #10237), and the committees of Obstetrics and Gynecology and Psychiatry Departments.

Data processing and statistical analysis

Data analysis was carried out using the software SPSS version 20. Quantitative variables were described using means and standard deviations and the means of two groups were compared using the independent sample t-test. Absolute frequencies were used to describe categorical variables and the chi-square test and Fisher-exact test were used when appropriate to compare the proportion of categorical data. When data were not normally distributed, a nonparametric test (Mann-Whitney) was used to compare the means. To assess the odds ratio of possible variables, multivariate logistic regression was used. 5% was set as the level of statistical significance (S) ($P< 0.05$).

RESULTS

Sociodemographic, clinical, and obstetric characteristics

A total of 169 pregnant women was included in the study. Mean age (in years) was 25.3±4.8. Most of the studied sample were educated (*n*= 115, 68%), 72% were rural residents (*n*= 122), and housewives (*n*= 129, 76%). The mean number of pregnancies was 2.4±1.5 (range= 1-11). Unplanned pregnancy and previous fetal loss were reported in about two-fifths (*n*= 74), and one-fourth (*n*= 45) of respondents, respectively. Lifetime history of IPV exposure was reported in 46% of women (*n*= 78). The prevalence of hypovitaminosis D was 57.4% (*n*= 97). Comorbid suicide ideation, anxiety and depressive symptoms were identified in 48% (*n*= 81), 20% (*n*= 33), and 60% (*n*= 101) of pregnant women, respectively.

Factors associated with hypovitaminosis D in study participants

In terms of sociodemographic and clinical variables, there was significant association between hypovitaminosis D and family income (χ^2= 0.09, *P*= 0.023), and history of exposure to IPV (χ^2= 6.83, *P*= 0.009), as displayed in Tables 1 and 2. In terms of comorbid psychiatric disorders, there was a significant association between hypovitaminosis D and moderate-to-severe anxiety symptoms (χ^2= 7.64, *P*= 0.006). There was no association between hypovitaminosis D and symptoms of depression, as displayed in Table 3.

Further adjusted logistic regression analysis of all statistically significant variables confirmed the association between hypovitaminosis D and history of exposure to IPV, and comorbid anxiety symptoms. It was found that the odds of hypovitaminosis D among pregnant women increased with those who had a history of IPV exposure [odds ratio (odd ratio= 2.0, 95% confidence interval (CI)= 1.1, 3.9] and moderate-to-severe anxiety symptoms (OR= 2.4, 95% CI= 1.0, 6.2), as displayed in Table 4.

Predictors of intimate partner violence exposure in pregnant women with hypovitaminosis D

Among those with hypovitaminosis D (*n*= 97), it was found that women with lower education (OR= 4.1, 95% CI= 1.0, 3.9), unplanned pregnancy (OR= 5.0, 95% CI= 1.4, 18.3), comorbid moderate-to-severe anxiety symptoms (OR= 4.1, 95% CI= 1.1, 15.4), and current suicide ideation (OR= 16.4, 95% CI= 3.4, 79.4) had greater odds of being exposed to IPV, as illustrated in Table 5.

Table 1: Association between sociodemographic variables and hypovitaminosis D in the studied population (*N*=169):

	Hypovitaminosis D [*n* (%)]				
	Yes	**No**	**Total**	χ^2	***P***
Residence					
Rural	71(73.2)	51(70.8)	122(72.2)	0.09	0.759
Urban	26(26.8)	21(29.2)	47(27.8)		
Income					
Low	55(56.7)	28(38.9)	83(49.1)	5.21	0.023*
Middle-to-high	42(43.3)	44(61.1)	86(50.9)		
Education					
Illiterate-to-low education	35(36.1)	19(26.4)	54(32.0)	1.93	0.111
Moderate-to-high education	62(63.9)	53(73.6)	115(68.0)		
Occupation					
Not working	72(74.2)	57(79.2)	129(76.3)	0.65	0.421
Working	25(25.8)	15(20.8)	40(23.7)		
Lifetime history of exposure to IPV					
No	44(45.4)	47(65.3)	91(53.9)	6.83	0.009*
Yes	53(54.6)	25(34.7)	78(46.1)		
	Mean(SD)	Mean(SD)		*t* test	*P*
Age	25.1(4.5)	26.2(5.2)	25.3(4.8)	−1.56	0.122

1.122(SD)history of exposure to *Statistical significance where *P* value less than 0.05.

Table 2: Association between obstetric variables and hypovitaminosis D in the studied population (*N*=169):

	Hypovitaminosis D [*n* (%)]				
	Yes	**No**	**Total**	χ^2	***P***
Gestational age					
1st trimester	15(15.5)	10(13.9)	25(14.8)	2.44	0.295
2nd trimester	33(34.0)	33(45.8)	66(39.1)		
3rd trimester	49(50.5)	29(40.3)	78(46.1)		
Baby sex					
Unidentified	23(23.7)	16(22.2)	39(23.1)	0.82	0.665
Identified as a female baby	26(26.8)	24(33.3)	50(29.6)		
Identified as a male baby	48(49.5)	32(44.5)	80(47.3)		
Parity					
Nulliparous	43(44.3)	22(30.6)	65(38.5)	4.49	0.062
Multipara	54(55.7)	50(69.4)	104(61.5)		
Type of previous labor					
Vaginal	31(32.0)	23(31.9)	54(51.9)	1.35	0.167
Cesarean	23(68.0)	27(68.1)	50(48.1)		
Plan for pregnancy					
Unplanned	45(46.4)	29(40.3)	74(43.8)	0.60	0.269
Planned	52(53.6)	43(59.7)	95(56.2)		
History of previous fetal loss					
No	73(75.3)	51(70.8)	124(73.4)	0.38	0.538
Yes	24(24.7)	21(29.2)	45(26.6)		
	Mean (SD), range	Mean (SD), range		MW	*P*
Number of pregnancies	2.4(1.7)	2.6(1.3)	2.4(1.5)	−1.92	0.054
	1–6	1–11	1–11		
Number of female offspring	1.1(0.8)	1.3(0.6)	1.2(0.7)	−0.93	0.350
	0–2	0–4	0–4		
Number of male offspring	0.8(0.6)	1.1(0.5)	(0.5)	−0.35	0.051
	0–2	0–2	0–2		

*Statistical significance where *P* value less than 0.05.

Table 3: Association between associated psychiatric history and current hypovitaminosis D in the studied population (*N*=169):

	Hypovitaminosis D [*n* (%)]				
	Yes	**No**	**Total**	χ^2	***P***
Depressive symptoms					
No-to-mild	39(40.2)	29(40.3)	68(40.2)	0.01	0.985
Moderate-to-severe	58(59.8)	43(59.7)	101(59.8)		
Anxiety symptoms					
No-to-mild	71(73.2)	65(90.3)	136(80.5)	7.64	0.006*
Moderate-to-severe	26(26.8)	7(9.7)	33(19.5)		
Current suicide ideation					
No	49(50.5)	39(54.2)	88(52.1)	0.25	0.619
Yes	48(49.5)	33(45.8)	81(47.9)		

*Statistical significance where *P* value less than 0.05.

Table 4: Predictors of hypovitaminosis D in the studied population (*N*=169):

Hypovitaminosis D	Model 1[a] OR (95% CI)	Model 2[b] OR (95% CI)
	1.0	1.0
Income (moderate-to-high)		
Low	2.1(1.1–3.8)*	1.6(0.7–3.5)
Lifetime history of IPV (no)		
Yes	2.3(1.2–4.4)*	2.0(1.1–3.9)*
Anxiety symptoms (no-to-mild)		
Moderate-to-severe	3.4(1.4–8.4)*	2.4(1.0–6.2)*

CI, confidence interval; IPV, intimate partner violence; OR, odds ratio. [a]Model 1: unadjusted. [b]Model 2: adjusted for other statistically significant variables. *Statistical significance where the 95% confidence intervals do not include the null value (1.0).

Table 5: Adjusted logistic regression analysis of factors associated with intimate partner violence in pregnant women with hypovitaminosis D:

Variables	B	SE	Wald	P value	OR	95% CI	
Older age	0.1	0.1	2.2	0.143	1.1	0.9	1.3
No-to-low education	1.4	0.7	4.0	0.045*	4.1*	1.0*	15.9*
Unplanned pregnancy	1.6	0.7	5.9	0.016*	5.0*	1.4*	18.3*
Previous fetal loss	0.6	0.6	1.2	0.269	1.9	0.6	5.5
Moderate-to-severe anxiety	1.4	0.7	4.4	0.036*	4.1*	1.1*	15.4*
Current suicide ideation	2.8	0.8	12.1	<0.001*	16.4*	3.4*	79.4*

Logistic regression was adjusted for significant sociodemographic variables. CI, confidence interval; OR, odds ratio. *Statistical significance where 95% confidence intervals do not include the null value (1.00).

DISCUSSION

In the last decade, a large amount of present knowledge concerning vitamin D was published and evidence for vitamin D has dramatically grown (Spedding, 2014). Women of reproductive age, including pregnant women, in many low-income countries suffer from inadequate dietary intake, undernutrition, and micronutrient deficiencies (Lammi-Keefe *et al.,* 2008).

Hypovitaminosis D was found in 57.4% of our studied sample. There is consistent evidence suggesting that Asia, the Middle East, and Africa have the highest prevalence of vitamin D deficiency (Roth *et al.,* 2018). An Egyptian study found the prevalence of vitamin D deficiency [serum 25(OH) D5 below 20 ng/ml] was 40%, vitamin D insufficiency was 28.9%, and only 31.1% had sufficient vitamin D levels among the studied sample (El Rifai *et al.,* 2014). The authors explained that their results were based on differences in clothing, inadequate sun exposure, poor dietary habits, occupation, and cultural practices that predispose women to lower vitamin D status (Robinson *et al.,* 2006).

This study also revealed a significant association between hypovitaminosis D and low family income and exposure to IPV. Unsurprisingly, evidence in literature suggested that populations living in tropical or relatively

low-latitude countries, which included most low-middle-income countries have significant risk of vitamin D deficiency, which is not relevant to the biological differences between males and females regarding vitamin D metabolism (Roth *et al.,* 2018). This was consistent with the Egyptian study that revealed significantly higher proportion of vitamin D deficiency among rural residents compared with urban residents which could be attributed to the educational level differences (El Rifai *et al.,* 2014).

Also, in our study, about 46% of women reported a lifetime history of IPV exposure at least once throughout the relationship with their spouses. Worldwide, about one in every three women has experienced a lifetime incidence of either physical or sexual, IPV or nonpartner violence. Globally, 1–28% of women have been physically abused during pregnancy and 13–61% of women between 15 and 49 years of age experienced IPV and is mostly committed by their partners and in-laws (World Health Organization, 2013). A WHO multinational study on women's health and domestic violence against women had presented a comprehensive picture of the patterns of IPV and sexual violence in low-middle-income countries and found that at some point in their lifespan 15–71% of women were subjected to physical and/or sexual violence by their intimate partners, which has profound adverse effects on the maternal, physical, psychological, reproductive, and sexual health as well as on the child health (World Health Organization, 2005; Parvin *et al.,* 2016). IPV during pregnancy would be associated with low birth weight and stillbirth and predispose the pregnant woman to depression and substance abuse (Jasinski, 2004).

Our study found a significant association between hypovitaminosis D and presence of anxiety symptoms among pregnant women. In line with this finding, Huang *et al.,* (2014) conducted a cross-sectional study on pregnant women to assess the relationship between mental health symptoms and serum level of vitamin D and found an inverse association between serum vitamin D concentration and anxiety symptoms. Other studies on anxiety and depression confirmed the negative correlation with vitamin D levels during pregnancy (Bicikova *et al.,* 2015; Karonova *et al.,* 2015). It has been reported that hypovitaminosis D is linked to irregularities in the HPA axis supporting the relationship between vitamin D and anxiety and involving substrates such as dopamine, serotonin, norepinephrine, GABA, and glutamate (Kaviani *et al.,* 2020). In addition, it is thought that vitamin D may also be a factor in the pathophysiology of anxiety due to oxidative stress and inflammation (Casseb *et al.,* 2019).

This study had a few limitations. The small number of the studied sample and the cross-sectional nature would be of potential concern. Furthermore, others may claim that the pregnant women with more severe depressive or anxiety symptoms are less likely to be adherent to their antenatal visits or voluntarily engage in research studies. However, authors advocate that this study would shed light on the importance of hypovitaminosis D during pregnancy, and the need for routine assessment and proper control for the welfare of the mothers and their babies.

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CONFLICTS OF INTEREST

There are no conflicts of interest.

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