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Original Article

Association between Vitamin D Deficiency and Suicide Attempts in Patients with Major Depressive Disorder

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ABSTRACT

Major Depressive Disorder (MDD) is significant public health concern that is often associated with an increased risk of suicide attempts. Emerging research suggests that Vitamin D3, a nutrient primarily obtained through sunlight exposure and certain foods, plays a crucial role in brain health and mood regulation and thus affects various psychiatric disorders, including depression. **Objective:** To determine the association between decreased Vitamin-D levels and a history of attempted suicide among patients suffering from Major Depressive Disorder. **Methods:** A comparative cross-sectional study was carried out from December 2020 to June 2021, on a sample of 104 patients diagnosed with Major Depressive Disorder. Half of the samples were with Vitamin-D3 deficiency while half of the sample were without Vitamin-D3 deficiency. This research was carried out at the Department of Psychiatry and Behavioral Sciences, Liaquat University Hospital, Hyderabad, Pakistan. Data were analyzed with SPSS version 21.0. **Results:** The mean age of the sample stood at 44 years (09 ± SD). A majority of the sample comprised of male (55.77%), hailing from an urban background and a middle socioeconomic set-up (60.58%). The mean Vitamin-D level was 18.63 ng/ml, while the mean Vitamin-D3 level was 14.77 ng/ml and 22.05 ng/ml for groups A and B respectively. History of attempted suicide was more prevalent among patients with Vitamin D3 deficiency. **Conclusion:** The research concluded that Vitamin-D deficiency is found to be one of the factor for suicidal attempts in patients with Major Depressive Disorder.

INTRODUCTION

Suicide is a major leading social and public health issue worldwide, with an estimated global suicide death rate of 11/100,000 people (7/100,000 among female and 15/100,000 among male) [1]. In 2016, there were 817,000 suicide deaths globally, making up 1.5% of all deaths [2]. Suicide mostly affects young and middle-aged adults. It is the 2nd foremost reason of mortality among people with 15–29 years of age [3] and the 3rd foremost factor of mortality among people under 40 years of age [4]. In Pakistan, the rate of suicide in 2012 (according to World Health Organization estimates), stood at 7.5 out of every 100,000 people who died by suicide. In other words, around 13,000 people killed themselves that year. More recent statistics by WHO state that the condition is not getting much better and lives are continually being lost. Experts say the number of people dying is likely somewhere between the two figures i.e. 7/100,000 among female and 15/100,000 among male, but the exact situation remains elusive [5]. Official national rates of suicide in Pakistan are unavailable, are neither known nor included in the annual mortality statistics.

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Individual investigations have reported differing rates from a lower range of 0.43 per 100,000 per year in Peshawar to 2.86/100,000 per year for Rawalpindi. Other regions have same trend in the middle of the spectrum. Karachi has a suicide rate of 2.1/100,000, Lahore 1.08/100,000, Faisalabad 1.12/100,000, and Larkana 2.6/100,000 [6]. This suggests that some of the seasonality in suicide rates could be explained by exposure to certain risk factors for suicide in those seasons, since there is also a higher prevalence of suicide in locations with less sunlight [7] and during the holiday spring, when 25-hydroxy Vitamin-D [25(OH)D] levels are at their lowest. Skin exposure to UV-B is tightly linked with the synthesis of pre-Vitamin-D and subsequent levels of 25(OH)D [8], and high degree of seasonal variation in sunlight exposure leads to dramatic variations in amounts light hitting the skin throughout the year [8]. Many studies are bringing forth the beneficial effect of Vitamin-D on brain function. Mechanisms of Vitamin-D neuroprotection may also involve its neurotrophics activities, as it can regulate the transcription of more than 1,000 genes, including those which are related to a range of suicide-related processes [9]. The effects of hypertension on cognitive function and mood might be mediated, at least in part, by angiotensin II activity in adrenal glands, an action that may be induced by Vitamin-D effects (and prevented by anti VDR antibodies) on nuclear VDR present in many brain regions and which gene variations have been identified as associated with cognitive function and depressive symptoms [10, 11]. The causes of suicide are likely multifactorial, involving genetic, environmental, and psychological factors. Given the serious implications of attempted suicide, factors that are related to increased suicide attempts, even to a minute extent, merit exploration so that the appropriate preventive and therapeutic measures can be ensured to decrease the burden. The matter becomes even more important given that there is a high level of Vitamin-D deficiency among all age groups, genders, income levels, and regions in Pakistan (expected to be 53.5% in general population)[11].

The aim of this study was to determine the association between decreased Vitamin-D levels and history of attempted suicide among patients suffering from depression.

METHODS

A comparative cross-sectional study was carried out from December 2020 to June 2021, on 104 individuals of either gender with age range 18-65 years and diagnosed with Major Depressive Disorder. Patients were chosen via non-probability consecutive sampling. Patients with bipolar depression, schizophrenia, obsessive compulsive disorder, and with or without comorbid substance abuse of any illicit drug (as described by DSM-5) and those suffering from major systematic diseases like diabetes mellitus, hypothyroidism, hyperthyroidism, arthritis, etc. were excluded from the study. This research was done at the Department of Psychiatry and Behavioral Sciences, Liaquat University Hospital, Hyderabad, Pakistan. The study was approved by the Research Ethics Committee of Liaquat University of Medical and Health Sciences (IRB-LUMHS/REC/984, Dated; 06/12/2020). Sample size was calculated by using an Open-Epi sample size calculator, by taking the incidence of Vitamin-D3 deficiency in depressed patients with (58%) and without (29%) history of attempted suicide [12], with confidence interval of 95% and power of study as 80%. An informed written consent was obtained from each participant prior to enrollment in the study. An anonymous self-structured questionnaire containing inquiries about the basic biodata, sociodemographic details and details about the history of suicide attempt was used. The Hamilton Depression Rating Scale, Beck's Suicidal Ideation Scale, and Beck's Suicidal Intent Scale were used for the assessment of the severity of depression, suicidal ideation, and intent. The Hamilton Depression Rating Scale (HDRS) was used to evaluate depression severity in patients, consisting of 17 items assessing symptoms like mood, guilt, insomnia, agitation, anxiety, and weight loss. The Beck's Suicidal Ideation Scale (BSIS), a 19-item self-report inventory, measured the frequency, intensity, and duration of suicidal thoughts, identifying individuals at risk of suicide. The Beck's Suicidal Intent Scale (BSIS) assessed the seriousness of suicidal intent through 15 items evaluating the degree of planning and likelihood of rescue. 10 ml venous blood samples of all enrolled participants were collected and sent to the pathology laboratory, to screen for Vitamin-D3 deficiency. Decreased Vitamin-D3 was defined as total serum Vitamin-D3, of less than 20 ng/ml. The patients were divided into 2 groups (A: MDD with Vitamin-D3 deficiency and B: MDD without Vitamin-D3 deficiency) of 52 each and inquired about a history of attempted suicide. Data were analyzed using SPSS version 21.0. Chi-Square test was applied to compare the incidence of suicidal attempts among low and high Vitamin-D3 level patients.

RESULTS

The mean age of participants in Group A with Vitamin-D deficiency was 43 years, while in Group B those without Vitamin-D deficiency, it was 45 years, showing no significant difference between the groups. In terms of gender distribution, Group A had 37 male (71.2%) and 15 female (28.8%), whereas Group B had 21 male (40.4%) and 31 female (59.6%), with a statistically significant difference observed ($p < 0.05$). Regarding residential status, 38 participants (73.1%) in Group A resided in urban areas, compared to 34 (65.4%) in Group B, with no significant

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difference noted ($p > 0.05$). In socioeconomic status, Group A had 21 participants (40.4%) classified as lower, 30 (57.7%) as middle, and 1 (1.9%) as upper, while Group B had 10 (19.2%) lower, 33 (63.5%) middle, and 9 (17.3%) dupper, indicating a significant difference in the lower and upper categories ($p < 0.05$) (Table 1).

Table 1: Descriptive Statistics (Group-Wise Comparison)

Variable	Group A (With Vitamin D Deficiency)	Group B (Without Vitamin D Deficiency)	p-Value
Mean Age (Years)	43	45	> 0.05
Gender			
Male	37 (71.2%)	21 (40.4%)	< 0.05
Female	15 (28.8%)	31 (59.6%)	
Residential Status			
Urban	38 (73.1%)	34 (65.4%)	< 0.05
Rural	14 (26.9%)	18 (34.6%)	
Socioeconomic Status			
Lower	21 (40.4%)	10 (19.2%)	< 0.05
Middle	30 (57.7%)	33 (63.5%)	
Upper	1 (1.9%)	9 (17.3%)	

There were no significant differences in the history of attempted suicide when comparing Vitamin-D status with depression and suicide in Group A (Vitamin-D deficiency) and Group B (Without Vitamin D deficiency) ($p > 0.05$). The Hamilton Depression Rating Scale assessed depression severity, significant differences were found in the mild to moderate ($p < 0.05$) and moderate to severe ($p < 0.05$) categories (Table 2).

Table 2: Vitamin-D Status versus Depression and Suicide

Variable	Group A (With Vitamin D Deficiency)	Group B (Without Vitamin D Deficiency)	p-Value
History Of Attempted Suicide			
Present	9 (17.3%)	6 (11.5%)	< 0.05
Absent	43 (82.7%)	46 (88.5%)	
Hamilton Depression Rating Scale Score			
Mild	14 (26.9%)	11 (21.2%)	< 0.05
Mild To Moderate	32 (61.5%)	19 (36.5%)	
Moderate To Severe	18 (34.6%)	10 (19.2%)	
Becks Suicidal Ideation Scale Score			
Suicidal Ideation Present	28 (53.9%)	25 (48.1%)	< 0.05
Suicidal Ideation Absent	24 (46.1%)	27 (51.9%)	
Hamilton Depression Rating Scale Score			
Suicidal Intent Present	51 (98.1%)	49 (94.2%)	< 0.05
Suicidal Intent Absent	01 (1.9%)	03 (5.8%)	

Examining the relationship between attempted suicide and demographic features revealed no significant differences in gender, residential status, or socioeconomic status between those who had attempted suicide and those who had not ($p > 0.05$). In both gender and residential status categories, the proportion of participants who attempted suicide was similar across subgroups. However, in the socioeconomic status category, a notable difference was observed, with 50% of participants in the upper category reporting attempted suicide (Table 3).

Table 3: Attempted Suicide versus Demographic Features

Variable	Attempted Suicide		p-Value
	Present	Absent	
Gender			
Male	8 (13.8%)	50 (86.2%)	< 0.05
Female	7 (15.2%)	39 (84.8%)	
Residential Status			
Urban	9 (12.5%)	63 (87.5%)	< 0.05
Rural	6 (18.8%)	26 (81.2%)	
Socioeconomic Status			
Lower	4 (12.9%)	27 (87.1%)	< 0.05
Middle	6 (9.5%)	57 (90.5%)	
Upper	5 (50.0%)	5 (50.0%)	

DISCUSSION

The research suggests that low Vitamin-D levels may be linked to suicide attempts in depressed patients, though our findings weren't statistically significant. Our results are consistent with several previous studies that found lower Vitamin-D levels associated with a higher risk of depression [13-15]. Most of these studies focused on older adults. For example, Desai *et al.* [16] found in the Longitudinal Aging Study Amsterdam that depression symptoms, measured by the CES-D score, were significantly connected to 25(OH)D3 levels. People with major and minor depression had 14% lower 25(OH)D3 levels than those without depression. Milaneschi *et al.* conducted a six-year study attempting to analyze both social support sources and the quantity of emotional support on depression development published in 2014. Survival analyses showed that women with low Vitamin-D levels were much more likely to develop a depressed mood (p value=0.005) [17]. In contrast, Jeenduang and colleague reported furnished basolateral membrane-associated ATL3 localization, showing there is no relationship between Vitamin-D levels and depression [18]. The discrepancies between our study and those by Desai and Milaneschi [16-17] are associated with our small sample size, resulting in inadequate statistical power. Prior research has identified multiple potential biological mechanisms underlying the association between Vitamin-D levels and depression. In the same way, may Vitamin-D deficiency perturb the neuroendocrine and central nervous systems in terms of the regulation of neurotransmission, neuroprotection, neuroimmunomodulation, and release of cortisol and neurotransmitters [19, 20]. The average age of the participants was 44 years (09 ± SD), with the sample predominantly composed of males (55.77%), mainly from urban areas and middle socioeconomic backgrounds

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(60.58%). The average Vitamin-D level among the participants was 18.63 ng/ml, with group-wise mean Vitamin-D3 levels of 14.77 ng/ml for group A and 22.05 ng/ml for group B. Vitamin-D insufficiency and deficiency are global concerns impacting individuals of all ages and races. Optimal skeletal health requires 25(OH) Vitamin-D levels above 30 ng/ml. Typically, serum 25(OH) Vitamin-D levels are lower in Black individuals compared to White individuals, and in those who avoid sun exposure. Among older adults in the US and Europe, Vitamin-D deficiency prevalence ranges from 40% to 100%. Bertone-Johnson et al, found that around 25% of men over 50 and 30-35% of women over 50 had 25(OH) Vitamin-D levels below 0.001 [21]. Various studies indicate that Vitamin D deficiency at its binding sites can lead to mood disorders, both major and minor. These studies demonstrate that treatments such as Vitamin D or sunlight therapy (phototherapy), Gene Therapy, or a Vitamin D-supplemented diet can effectively treat depression and other mood disorders. They also reveal a correlation between 25(OH) Vitamin D levels and mood, as well as mood and cognition, across all age groups, including pregnant women, older adults, and Vitamin D deficient populations worldwide [22]. Additionally, plasma Vitamin D levels appear to influence mood and cognitive performance to some extent [23]. Improvements in depression scales were observed with Vitamin-D supplementation, though less so with phototherapy. It is recommended to take at least 800 IU of Vitamin D daily, as this dosage is crucial in studies on mood disorders [24, 25]. A history of attempted suicide was more common among patients with Vitamin-D3 deficiency, although this difference was not statistically significant. Evidence indicates significantly lower Vitamin-D levels in individuals with suicidal tendencies compared to controls. Literature suggests that Vitamin-D deficiency was found in 58% of reported suicide cases, compared to about 30% in healthy controls and non-suicidal depressed patients [26-28].

CONCLUSIONS

The study concluded that the Vitamin-D deficiency is found to be one of the factor for suicidal attempts in patients with Major Depressive Disorder. Awareness and education regarding this association to mental health professionals is recommended to lessen the burden of attempted suicide.

Authors Contribution

Conceptualization: ZAM
Methodology: SA, ASL, HS
Formal analysis: ZAM, SA, AGA, SB
Writing-review and editing: SA, ASL, AGA, SB, HS

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

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