

# Insomnia is not Associated with Vitamin D Deficiency but is Associated with Abnormal Anxiety and Depression scores in University Students from Jordan

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## ABSTRACT

**Background:** Vitamin D deficiency was recognized to be associated with anxiety, depression and Musculoskeletal Pain (MSP), which themselves may inversely affect individual's sleep. We aimed to investigate the relationships between vitamin D deficiency and low dietary calcium intake, and the comorbidity of insomnia, anxiety, depression, and MSP among university students.

**Methods:** This case-control study involved 95 participants with insomnia and 95 controls. Insomnia was assessed using Insomnia Severity Index (ISI). Anxiety and depression were assessed using Hospital Anxiety and Depression Scale (HADS). Serum 25-hydroxyvitamin D was measured using electrochemiluminescence immunoassay. Calcium intake and MSP were self-reported.

**Results:** Vitamin D deficiency was reported in 84.2% of participants. There was no difference in 25-hydroxyvitamin D between cases and controls ( $p=0.63$ ). Abnormal anxiety (60% vs. 11.6%) and depression (40% vs. 9%) scores were more frequent in cases compared to controls ( $p<0.001$ ). MSP was more frequent in cases compared to controls (69.5% vs. 34.7%,  $p<0.001$ ). Anxiety was correlated with measures of MSP ( $p<0.001$ ). ISI score was positively correlated with anxiety, depression, and measures of MSP ( $p<0.001$ ) and negatively with calcium intake ( $p=0.04$ ). Abnormal anxiety (OR=11.02,  $p<0.001$ ) and depression scores (OR=3.86,  $p=0.01$ ) were significant predictors for insomnia.

**Conclusions:** Insomnia was not associated with vitamin D deficiency itself, but it was associated with abnormal scores of anxiety and depression and correlated with measures of MSP, which are possible symptoms of vitamin D deficiency. Further studies are required to investigate if vitamin D supplement and increasing dietary calcium intake can improve insomnia among university students' population.

## INTRODUCTION

Normal regular sleep is required to maintain human health and achievement [1]. Chronic insufficient or poor sleep contributes in long-term physical and psychological health problems such as obesity, diabetes mellitus, cardiovascular diseases, anxiety, and depression [2]. One of the most common types of sleep disorders is insomnia [3]. It is described as a difficulty in starting sleep or a difficulty in continuing sleep during night [4]. The prevalence of chronic insomnia among adults ranges from 10 to 30% with an increased risk in individuals who are widowed or separated, old, or having chronic psychological or physical illnesses [5]. University students, who are considered

as young adults (18-25 years old), frequently complain of insomnia because of their stressful life styles [6]. Importantly, insomnia in this group of individuals may affect their memory and learning capabilities leading to decreased academic attainments [6].

Additionally, the university students' academic achievements could be affected by the commonly comorbid anxiety and depression disorders. Comorbid depression and anxiety with insomnia have been documented frequently [7]. Studies have provided evidence that the association between insomnia and these psychological disorders is bidirectional; suggesting that anxiety and depression may lead to insomnia and vice versa [7]. Similarly, sleep disorders and chronic pain conditions are usually comorbid [8]. Literatures showed an association between sleep disturbances and chronic Musculoskeletal Pain (MSP) [8]. MSP and insomnia may co-occur and may increase the risk of each other. Pain can interfere with the ability to sleep; conversely, poor sleep can exacerbate pain intensity [8]. MSP and general weakness are symptoms that are usually noticed in individuals with vitamin D deficiency [9]. Deficiency in vitamin D is the most widespread nutrient deficiency among various populations including those live in areas that receive adequate sunlight [10].

Beside its critical function in circulating calcium and phosphate regulation, there is rising evidence suggesting that vitamin D has an important function in the health of brain and nervous system [11]. Decreased vitamin D was found to be related to anxiety and depression [9]. As well, association between decreased vitamin D and risk of sleep problems have been investigated. Decreased vitamin D concentrations were recognized to be linked to sleep disturbances [12]. Some studies suggested that vitamin D has a possible role in sleep, anxiety, and depression that could be due to its action on vitamin D receptors, which are found in hypothalamus and brain regions that organize the sleep and wake states and are involved in the development of psychological symptoms [13]. The role of vitamin D receptors is to keep calcium homeostasis in the central nervous system [14]. Like vitamin D, calcium has an important role in the central nervous system and may have critical role in the development of many psychological disorders [9].

Previously, significant associations between low vitamin D and

decreased calcium intake and risk of anxiety, depression, and MSP have been found [9]. Supplementation of vitamin D resulted in improvement of sleep quality in individuals with sleep disorders [15], MSP, and psychological symptoms [9]. Therefore, we hypothesize that decreased serum vitamin D and decreased calcium intake could be associated with increased risk of MSP, depression, anxiety, and thus insomnia. The aim was to test this hypothesis in university students. If the hypothesis is validated then, insomnia may represent a symptom of vitamin D deficiency and the findings will support recommendation to physician to measure plasma vitamin D level for patients with insomnia.

## METHODS

### Participants

This case-controlled study included 95 young adults with insomnia and 95 controls, who were matched for age and gender. Participants were invited from students of different colleges of a large public university in the North of Jordan between September 2019 and January 2020, by advertising the project on university campus and by word of mouth. Ethical approval of the study was granted by the Institutional Review Board of Jordan University of Science and Technology, Irbid, Jordan (Reference: 3672019). All research was performed in accordance with the relevant guidelines and in accordance with the Declaration of Helsinki. All participants had signed the informed consent forms before they answered the questionnaires by themselves. A well-trained research assistant was available to discuss study aims and procedure and to answer questions.

### Data collection

Data about age, smoking, college, academic level and regular exercise were collected by self-reporting. Participants from medical colleges were recruited from medicine, dentistry, pharmacy, nursing, and applied medical sciences specializations while participants from non-medical colleges were recruited from agriculture, engineering, information technology, sciences, and architecture specializations. Participants who were in their 1<sup>st</sup> or 2<sup>nd</sup> years of study were considered as junior students while participants who were in their 3<sup>rd</sup> to 6<sup>th</sup> years of study were considered as senior students. Regular exercise was defined as doing any type of sports for at least 3 times per week of at least 30 min each.

Body Mass Index (BMI) was reported in kg/m<sup>2</sup>. BMI values <25 kg/m<sup>2</sup> were defined as normal, BMI values of 25-29.9 kg/m<sup>2</sup> were defined as overweight, and BMI values ≥ 30 kg/m<sup>2</sup> were defined as obese [16].

#### **Blood sampling and measurement of serum 25-hydroxyvitamin D concentrations**

Venous blood was collected into anticoagulant-free plain test tubes. Then, fresh blood was centrifuged at 2,100 g for 10 min at room temperature using a high speed Jouan centrifuge (Thermo Fisher Scientific, Inc., Waltham, MA, USA) to collect serum. 25-hydroxyvitamin D was determined in serum by electrochemiluminescence immunoassay using Roche Modular E170 Analyzer (Roche Diagnostics, Basel, Switzerland). Status of vitamin D was determined according to 25-hydroxyvitamin D value as follows: sufficient (≥ 30 ng/mL), insufficient (20-30 ng/mL), or deficient (< 20 ng/mL) [17].

#### **Assessment of participant's insomnia status**

Insomnia status was determined using a self-administered Arabic version of Insomnia Severity Index (ISI) [18]. The ISI determines the status of insomnia using 7 questions. These questions evaluate the difficulty in sleep initiation, ability of remaining asleep, problems in awakening too early, how the individual is satisfied with his/her present sleep pattern, how noticeable to others is the sleep problem disturbing the quality of individual's life, how the individual is concerned about his/her current sleep problem, and how much the present sleep problem is interfering with the individual's daily function. Each question is answered by choosing a number from 0-4 that expresses the severity of the condition with a maximum ISI score of 28. ISI scores from 0 to 7 were classified as no insomnia while ISI scores from 15 to 28 were classified as moderate to severe insomnia. Individuals with ISI scores from 8 to 14 (subthreshold insomnia) were excluded. ISI internal consistency was excellent for our sample (Cronbach's  $\alpha$  of 0.91).

#### **Assessment of anxiety and depression**

Anxiety and depression symptoms were evaluated using a self-administered Arabic translation of Hospital Anxiety and Depression Scale (HADS) [9]. Anxiety was evaluated by answering 7 questions about anxiety-related problems. Each question can be answered by selecting a number from 0 to 3 that reflects the severity of the condition with a maximum score

of 21. Similarly, depression was evaluated by answering 7 questions about depression-related problems. Each question can be answered by selecting a number from 0 to 3 that reflects the severity of the condition with a maximum score of 21. Participants were classified as according to anxiety and depression scores to: normal (scores from 0 to 7), borderline (scores from 8-10) or abnormal (scores from 11-21) [19].

#### **Assessment of MSP**

As previously described [20], participants self-reported their complaint of MSP that was persistent during the last month. The site of MSP was determined from 12 sites including arms, feet, hands, hips, knees, lower back, lower legs, neck, palms, shoulders, upper legs, and wrists. Number of painful body sites was calculated for each participant. Additionally, the mean intensity of MSP in the last month was self-reported using a 0-10 rating scale (0: no MSP, 10: the maximum intensity of MSP) [20].

#### **Determination of dairy calcium consumption**

Calcium, the vital mineral of bone is mostly available in milk. Consequently, milk and its milk are the main sources of calcium. Participants self-reported the amount of milk and other milk products including cheese, yogurt, and labaneh as described previously [21]. These products are the available products in the market and they are considered as the major sources of dietary calcium in Jordan. Frequency of dairy products consumption was determined as zero, one, two, three, or more dairy servings per day. Dairy servings were defined as previously described [21]: one ounce of cream cheese (20 mg calcium), one ounce of cheddar cheese (162 mg calcium), one cup (240 mL) of milk or yogurt (300 mg calcium) and two tablespoons (2 oz) of labaneh (100 mg calcium). The total daily calcium intake was reported in mg/day.

#### **Data analyses**

Data were analyzed using the IBM SPSS version 20. All numerical variables were tested for normality before starting analysis. Nominal variables were presented as frequencies (%) whereas numerical variables were presented as means  $\pm$  standard deviation or medians (25–75<sup>th</sup> percentiles). Differences in nominal variables (i.e., participants with insomnia vs. controls) were detected using Chi-squared test or Fisher exact test. Differences in numerical variables (i.e., participants with insomnia vs. controls) were detected using parametric

Student's t test or non-parametric Mann-Whitney U test. Parametric Pearson's or non-parametric Spearman's correlation analyses were conducted to examine the relationships between numerical variables. Binary logistic regression was used to determine the predictors of insomnia. All statistical tests were 2-tailed and statistical significance was at p values < 0.05.

Table 1: Differences in variables between individuals with insomnia and controls.

	Total (n= 190)	Participants with insomnia (n= 95)	Controls (n= 95)	Cohen's D	P-value <sup>†</sup>
Age	20.94±2.84	21.03±2.87	20.84±2.82	0.06	0.65
Gender					
Male	82 (43.2)	41 (43.2)	41 (43.2)	-	1.00
Female	108 (56.8)	54 (56.8)	54 (56.8)		
College					
Medical	96 (50.5)	42 (44.2)	54 (56.8)	-	0.11
Non-medical	94 (49.5)	53 (55.8)	41 (43.2)		
Academic level					
Junior students (1-2 years)	109 (57.4)	51 (53.7)	58 (61.1)	-	0.38
Senior students (3-6 years)	81 (42.6)	44 (46.3)	37 (38.9)		
BMI (Kg/m <sup>2</sup> )	24.44±4.84	24.19±4.22	24.69±5.39	-0.10	0.48
BMI (Kg/m <sup>2</sup> )					
Normal (< 25 kg/m <sup>2</sup> )	122 (64.2)	63 (66.3)	59 (62.1)	-	0.56
Overweight (25-29.9 kg/m <sup>2</sup> )	43 (22.6)	22 (23.2)	21 (22.1)		
Obese (≥ 30 kg/m <sup>2</sup> )	25 (13.2)	10 (10.5)	15 (15.8)		
Smoking					
Yes	15 (7.9)	12 (12.6)	3 (3.2)	-	<b>0.03</b>
No	175 (92.1)	83 (87.4)	92 (96.8)		
Regular exercise					
Yes	139 (73.2)	68 (71.6)	71 (74.7)	-	0.74
No	51 (26.8)	27 (28.4)	24 (25.3)		
HADS- anxiety score (0-21)	8.42±4.77	11.24±4.10	5.60±3.59	1.46	<b>&lt;0.001</b>
HADS- anxiety score					
Normal (0-7)	87 (45.8)	17 (17.9)	70 (73.7)	-	<b>&lt;0.001</b>
Borderline (8-10)	35 (18.4)	21 (22.1)	14 (14.7)		
Abnormal (11-21)	68 (35.8)	57 (60)	11 (11.6)		
HADS- depression score (0-21)	7.65±4.10	9.57±4.11	5.7±3.07	1.07	<b>&lt;0.001</b>
HADS- depression score					
Normal (0-7)	103 (54.2)	34 (35.8)	69 (72.6)	-	<b>&lt;0.001</b>
Borderline (8-10)	40 (21.1)	23 (24.2)	17 (17.9)		
Abnormal (11-21)	47 (24.7)	38 (40)	9 (9.5)		
Serum 25-hydroxyvitamin D (ng/mL)	11.80 (8.92-17.02)	11.50 (8.95-16.82)	11.86 (8.88-17.74)	0.03	0.63
Vitamin D status					
Sufficient (≥ 30 ng/mL)	4 (2.1)	2 (2.1)	2 (2.1)	-	0.94
Insufficient (20-30 ng/mL)	26 (13.7)	12 (12.6)	14 (14.7)		
Deficient (< 20 ng/mL)	160 (84.2)	81 (85.3)	79 (83.2)		
Dairy calcium intake (mg/day)	307.47 (132.75-501.25)	284.82 (99.05-470.63)	331.75 (165.20-547.70)	0.19	0.07
Complaint of MSP					
Yes	99 (52.1)	66 (69.5)	33 (34.7)	-	<b>&lt;0.001</b>
No	91 (47.9)	29 (30.5)	62 (65.3)		
MSP intensity (0-10)	2 (0-5)	4 (0-6)	0 (0-3)	-0.81	<b>&lt;0.001</b>
Number of painful sites (1-12)	1 (0-2)	2 (0-3)	0 (0-1)	-0.65	<b>&lt;0.001</b>

<sup>†</sup> Student's t- test, Mann Whitney U test, Chi-square test, or Fisher exact test as appropriate (P < 0.05 was considered statistically significant). Data are presented as frequency (%), mean ± standard deviation or median (25<sup>th</sup> – 75<sup>th</sup> percentiles). ISI: Insomnia Severity Index; BMI: Body Mass Index; HADS: Hospital Anxiety and Depression Scale; MSP: Musculoskeletal Pain.

## RESULTS

### Characteristics of the participants

The sample involved 95 university students with insomnia (ISI scores ranged from 15 to 28) and 95 age and gender matched controls with no insomnia (ISI scores  $\leq 7$ ). 108 (56.8%) participants were females and 82 (43.2%) participants were males. 96 (50.5%) participants were from medical colleges and 94 (49.5%) participants were from non-medical colleges. The mean age  $20.94 \pm 2.84$  years and the mean BMI was  $24.44 \pm 4.84$  kg/m<sup>2</sup>.

Participants with insomnia had significantly ( $p < 0.001$ ) higher incidence of MSP, intensity and number of painful sites compared to control. Other characteristics including academic level, smoking, and doing regular exercise are presented in Table 1 with differences in variables between participants with insomnia and controls.

### Vitamin D status among the participants

As presented in Table 1, the median (25<sup>th</sup> – 75<sup>th</sup> percentiles) 25-hydroxyvitamin D concentration among the participants was 11.80 (8.92-17.02) ng/mL. Deficient and insufficient vitamin D levels were reported in 160 (84.2%) and 26 (13.7%) participants, respectively. Serum 25-hydroxyvitamin D was not significantly different between participants with insomnia and controls ( $p = 0.63$ ). As well, Chi-squared testing did not demonstrate any significant association between deficient or insufficient vitamin D levels and insomnia ( $p = 0.94$ ).

### Status of anxiety among the participants

Table 1 also shows that the mean HADS-anxiety score among the participants was  $8.42 \pm 4.77$ . Abnormal and borderline HADS-anxiety scores were reported by 68 (35.8%) and 35 (18.4%) participants, respectively. Participants with insomnia were having significantly larger HADS-anxiety scores compared to the controls ( $p < 0.001$ ). Additionally, Chi-squared testing has shown that 60% and 22.1% of the participants with insomnia were having abnormal and borderline HADS-anxiety scores compared to 11.6% and 14.7% of the controls, respectively ( $p < 0.001$ ).

### Status of depression among the participants

As presented in Table 1, the mean HADS-depression score among the participants was  $7.65 \pm 4.10$ . Abnormal and borderline HADS-depression scores were reported by 47 (24.7%) and 40 (21.1%) participants, respectively. Participants

with insomnia were having significantly higher HADS-depression scores compared to the controls ( $p < 0.001$ ). In addition, Chi-squared testing has shown that 40% and 24.2% of the participants with insomnia were having abnormal and borderline HADS-depression scores compared to 9.5% and 17.9% of the controls, respectively ( $p < 0.001$ ).

### Status of dairy calcium intake among the participants

As presented in Table 1, the median (25<sup>th</sup> – 75<sup>th</sup> percentiles) dairy calcium intake was 307.47 (132.75-501.25) mg/day. Around 98% ( $n = 186$ ) of participants were having daily dairy calcium intake below the Recommended Dietary Allowance ( $< 1000$  mg/day). Level of dairy calcium intake was not significantly different between participants with insomnia and controls ( $p = 0.07$ ).

### Status of MSP among the participants

Table 1 has shown that 99 (52.1%) participants were complaining of MSP. Chi-squared test has shown that 69.5% the participants with insomnia were having MSP compared to 34.7% of the controls ( $p < 0.001$ ). As well, the median (25<sup>th</sup> – 75<sup>th</sup> percentiles) MSP intensity and the number of painful sites among participants with insomnia were 4 (0-6) and 2 (0-3) compared to 0 (0-3) and 0 (0-1), respectively ( $ps < 0.001$ ).

### Correlation between ISI score, measures of MSP, HADS-anxiety and depression scores, dairy calcium intake and serum 25-hydroxyvitamin D

Table 2 has shown that the ISI score was not significantly correlated with serum 25-hydroxyvitamin D ( $r = -0.07$ ,  $p = 0.34$ ). Instead, the ISI score was significantly correlated with both HADS-anxiety ( $r = 0.63$ ,  $p < 0.001$ ) and depression ( $r = 0.41$ ,  $p < 0.001$ ) scores, dairy calcium intake ( $r = -0.15$ ,  $p = 0.04$ ), MSP intensity ( $r = 0.41$ ,  $p < 0.001$ ) and number of painful body sites ( $p = 0.33$ ,  $p < 0.001$ ). Serum 25-hydroxyvitamin D was not significantly correlated with either HADS-anxiety or depression scores ( $ps > 0.05$ ). Serum 25-hydroxyvitamin D was significantly correlated with dairy calcium intake ( $r = 0.15$ ,  $p = 0.04$ ). The HADS-anxiety and depression scores were significantly correlated ( $r = 0.54$ ,  $p < 0.001$ ). The HADS-anxiety score was significantly correlated with MSP intensity ( $r = 0.42$ ,  $p < 0.001$ ) and with number of painful body sites ( $r = 0.35$ ,  $p < 0.001$ ). The HADS-depression score was also significantly correlated with MSP intensity ( $r = 0.23$ ,  $p < 0.01$ ), number of painful sites ( $r = 0.28$ ,  $p < 0.001$ ), and dairy calcium intake ( $r = -0.18$ ,  $p = 0.02$ ). MSP intensity was significantly correlated with number of painful sites ( $r = 0.59$ ,  $p < 0.001$ ).

Table 2: Correlation between ISI score, HADS-anxiety and depression scores, serum 25-hydroxyvitamin D, dietary calcium intake and measures of MSP.

	ISI score	HADS-anxiety score (0-21)	HADS-depression score (0-21)	MSP intensity (0-10)	Number of painful sites (1-12)	Dairy calcium intake (mg/day)
Serum 25-hydroxyvitamin D (ng/mL)	r=-0.07 p= 0.34	r= -0.08 p= 0.27	r= -0.06 p= 0.43	r= 0.05 p= 0.51	r= -0.05 p= 0.50	r= 0.15 p= 0.04
ISI score	-	r= 0.63 p <0.001	r= 0.41 p <0.001	r= 0.41 p <0.001	r= 0.33 p <0.001	r= -0.15 p= 0.04
HADS-anxiety score (0-21)	-	-	r= 0.54 p <0.001	r= 0.42 p <0.001	r= 0.35 p <0.001	r= -0.12 p= 0.11
HADS-depression score (0-21)	-	-	-	r= 0.23 p<0.01	r= 0.28 p<0.001	r= -0.18 p= 0.02
MSP intensity (0-10)	-	-	-	-	r= 0.59 p <0.001	r= -0.03 p= 0.64
Number of painful sites (1-12)	-	-	-	-	-	r= -0.08 p= 0.29

Pearson's or Spearman's correlation tests as appropriate (p values were two-tailed and considered statistically significant at  $p < 0.05$ ). ISI: Insomnia Severity Index; HADS: Hospital Anxiety and Depression Scale; MSP: Musculoskeletal Pain.

Table 3: Predictors of insomnia.

Variable	Value	B (SE)	OR	Confidence interval	P-value†
Constant	-	-1.85 (0.69)	-	-	0.01
Gender	Female Male (reference)	-0.33 (0.42)	0.72	0.32-1.64	0.44
Smoking	Smoker Non-smoker (reference)	0.81 (0.85)	2.24	0.43-11.73	0.34
College	Medical Non-medical (reference)	-0.15 (0.39)	0.87	0.41-1.85	0.71
Academic level	Senior students (3 - 6 year) Junior students (1 - 2 years) (reference)	0.29 (0.40)	1.34	0.62-2.90	0.46
HADS- anxiety score	Abnormal (11-21) Borderline (8-10) Normal (0-7) (reference)	2.40 (0.48) 1.20 (0.49)	11.02 3.33	4.33-28.06 1.26-8.75	<b>&lt;0.001</b> <b>0.02</b>
HADS- depression score	Abnormal (11-21) Borderline (8-10) Normal (0-7) (reference)	1.35 (0.54) 0.51 (0.48)	3.86 1.66	1.35-11.06 0.65-4.22	<b>0.01</b> 0.29
Serum 25-hydroxyvitamin D (ng/ml)	-	0.01 (0.03)	1.01	0.95-1.07	0.81
Dairy calcium intake (mg/day)	-	<0.001 (<0.01)	1.00	1.00-1.00	0.58
MSP intensity (0-10)	-	0.17 (0.10)	1.18	0.98-1.42	0.09
Number of painful sites (1-12)	-	0.11 (0.15)	1.11	0.84-1.48	0.46

†Binary logistic regression (dependent variable: Insomnia versus Controls),  $p < 0.05$  was considered statistically significant.  
B: Coefficient (intercept); SE: standard error; OR: odds ratio; HADS: hospital anxiety and depression score.

### Predictors of insomnia

Binary logistic regression (Table 3) showed that insomnia among the participants can be significantly predicted from abnormal HADS- anxiety scores (OR = 11.02,  $p < 0.001$ ), borderline HADS- anxiety scores (OR = 3.33,  $p = 0.02$ ), and abnormal HADS- depression scores (OR = 3.86,  $p = 0.01$ ). Whereas, insomnia cannot be significantly predicted from serum 25-hydroxyvitamin D, borderline HADS- depression scores, MSP measures, dairy calcium intake, gender, smoking, type of college, or academic level ( $ps > 0.05$ ).

### DISCUSSION

Our study examined the hypothesis that decreased vitamin D levels, decreased dietary calcium consumption, MSP, psychological symptoms could be associated with insomnia among young university adults. The major finding of this study was the high prevalence of vitamin D deficiency, measures of MSP, and abnormal anxiety and depression scores among university students with insomnia compared to controls. Vitamin D exerts several functions beyond keeping bone health. It plays critical roles in muscle function. Deficient vitamin D levels were found to be associated with the chronic pain that is related to defective bone mineralization, myopathy, MSP, increased central sensitivity consequent to mechanical stimulation, and the growth of muscle fibers [22]. Herein, there was no relationship between decreased vitamin D levels and insomnia. Vitamin D level was statistically insignificant between cases and controls (85.3% and 83.2%, respectively), which could be due to the increased prevalence (97.9%) of both deficient and insufficient vitamin D levels among our study participants. This reflects the high incidence (89.7%) of deficient and insufficient vitamin D levels among the Jordanian population [10]. However, we observed an increased prevalence of vitamin D deficiency symptoms (MSP measures, anxiety, and depression) that are co-existed with insomnia among subjects with insomnia compared to controls.

Individuals who experience chronic pain and multisite pain are expected to have higher risk of psychological symptoms [23]. In this study, participants with insomnia experienced significantly higher multisite MSP, which is significantly associated with pain severity and the presence of more pain-related anxiety and depression symptoms compared to controls. Interestingly, pain-related depression was positively

and significantly correlated with anxiety symptoms, suggesting a significant connection and association between pain, anxiety and depression symptoms and thus insomnia. ISI score was significantly and positively correlated with MSP intensity, number of painful sites, anxiety, and depression. This finding is consistent with previous published studies [9,24,25].

Consistent with previous findings [26], the current study revealed that dairy calcium was inversely correlated with depression score, which was positively correlated with anxiety. This suggests a connection between calcium intake and increased risk of psychological symptoms and thus insomnia. This result could be mediated by the role of calcium in the function of the central nervous system [14]. Disruption of  $Ca^{2+}$  regulation can affect the excitability of neurons, which consequently influences network activity and metabolism, and increases risk of developing psychiatric diseases [27]. ISI score was significantly and inversely correlated with daily calcium consumption.

Psychological symptoms (anxiety and depression) were the predictors of insomnia. Abnormal anxiety and depression scores ( $\geq 11$ ) increase the risk of insomnia by 11 and  $\sim 4$  folds, respectively. Our results are consistent with Al-khani et al [28] study, in which poor sleep quality was associated with anxiety and depression in medical university students from Saudi Arabia. Additionally, our results are consistent with other studies that had shown the same relationship between sleep problems and both anxiety and depression [29,30].

Although our study did not investigate the effect of vitamin D supplementation on sleep problems, previous studies had shown that supplementation of vitamin D and increasing intake of dairy products caused significant decrease in MSP severity and decrease in the number of pain sites, which were accompanied by considerable improvements in anxiety and depression scores [9]. The strength of our study comes from its case-control design, its appropriate sample size, and use of validated tools to assess its variables. Even though, the current study has some limitations. University students are young adults who may have other factors that contribute in the development of sleep disorders. These include stress, anxiety, and depression symptoms [28] that may result from their study loads and frequent examinations. In addition, we only recruited participants from one university in Jordan. However, this

university includes students from all areas of the country. Regardless of these limitations, we still consider our results valid and may enhance other researchers to do further investigations about vitamin D deficiency and sleep problems in this study population. Further studies are also required to investigate if vitamin D supplement and increasing dietary calcium intake can improve insomnia among university students.

## CONCLUSIONS

The current study has shown a high prevalence of vitamin D deficiency, MSP, anxiety and depression among university students from Jordan. Insomnia was not significantly associated with serum 25-hydroxyvitamin D levels, but it was associated with abnormal anxiety and depression scores, which themselves were significant predictors for insomnia. In medical practice, our findings suggest that young adults with insomnia should be investigated for anxiety and depression and to consider these problems in the treatment of insomnia.

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## CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

## AUTHORS' CONTRIBUTIONS

MA was responsible for data analysis, manuscript writing, and interpretation of results. HK was responsible for data collection and data entry. KA was responsible for interpretation of results and manuscript writing.

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