

## Clinical Research

# Investigation of Attention Deficit and Hyperactivity Disorder in Women with Vitamin D Deficiency

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### ABSTRACT

**Objective:** Attention deficit hyperactivity disorder (ADHD) is a psychiatric diagnosis that usually begins in childhood but can also be seen in adulthood and can significantly affect the functioning of the individual. We investigated the diagnosis and symptoms of ADHD in women with vitamin D deficiency and its possible association with clinical variables.

**Material and Method:** One hundred and fifty healthy women and 150 women diagnosed with vitamin D deficiency were included in our study. Blood samples were collected from all participants to evaluate their 25 hydroxyvitamin D (25(OH)D) levels. Additionally, the Sociodemographic and Clinical Data Form, the Wender Utah Rating Scale-Short Form (WURS-25) and the Turkish version of the Adult ADHD Self-Report Scale (ASRS-v1.1) were administered.

**Results:** Participants with vitamin D deficiency scored higher on the Turkish version of the ASRS-v1.1 and WURS-25. Turkish version of the ASRS-v1.1 was positively correlated with WURS-25 and negatively correlated with vitamin D levels. Patients with WURS-25 scores of 36 and above were younger, more likely to be single, lived in urban areas, and had lower vitamin D levels and scored higher on the ASRS-v1.1. We analyzed the optimal cutoff point of vitamin D level, predicting a higher WURS-25 score. Vitamin D level was found to be significant for the WURS-25 score of 36 and above with a cutoff point of  $\leq 24$  (Area under curve: 0.702,  $p = < 0.001$ ).

**Conclusion:** Attention-Deficit and Hyperactivity Disorder symptoms are common among women with vitamin D deficiency during both childhood and adulthood. Early diagnosis and treatment of ADHD may be beneficial for patients with vitamin D deficiency.

**Keywords:** Vitamin D, Attention-Deficit and Hyperactivity Disorder, Adult Women.

### ÖZ

#### D Vitamini Eksikliği olan Kadınlarda Dikkat Eksikliği ve Hiperaktivite Bozukluğunun Araştırılması

**Amaç:** Dikkat eksikliği hiperaktivite bozukluğu (DEHB) genellikle çocukluk çağında başlayan ancak yetişkinlik döneminde de görülebilen ve bireyin işlevselliğini önemli ölçüde etkileyebilen psikiyatrik bir tanıdır. Bu çalışmada, D vitamini eksikliği olan kadınlarda DEHB tanısı ve semptomları ile bunun klinik değişkenlerle olası ilişkisi araştırılmıştır.

**Gereç ve Yöntem:** Bu çalışmaya 150 sağlıklı kadın kontrol grubu ile 150 D vitamini eksikliği tanısı olan kadın dahil edildi. Tüm katılımcılardan 25-hidroksivitamin D (25(OH)D) seviyelerini değerlendirmek için kan örnekleri alınmıştır. Ek olarak Dikkat Eksikliği ve Hiperaktivite Bozukluğu Kendi Bildirim Ölçeği (ASRS-v1.1), Sosyodemografik ve Klinik Veri Formu, Wender Utah Derecelendirme Ölçeği-Kısa Form (WUDÖ-25) uygulandı.

**Bulgular:** D vitamini eksikliği olan katılımcıların ASRS-v1.1 ve WUDÖ puanları daha yüksektir. Erişkin DEHB Öz Bildirim Ölçeği'nin Türkçe versiyonu WUDÖ-25 ile pozitif, D vitamini düzeyi ile negatif korelasyon göstermektedir. WUDÖ-25 puanı 36 ve üzerinde olan hastalar daha genç, bekar ve kentsel bölgelerde yaşamaya eğilimli, D vitamini düzeyleri daha düşük ve ASRS-v1.1 puanı daha yüksektir. Daha yüksek WUDÖ-25 puanını öngören D vitamini düzeyinin optimal kesim noktasını analiz ettik. D vitamini düzeyi,  $\leq 24$  kesme noktası ile 36 ve üzeri WUDÖ-25 puanı için anlamlı bulundu (Eğri altında kalan alan: 0.702,  $p = < 0.001$ ).

**Sonuç:** D vitamini eksikliği olan kadınların hem çocukluk hem erişkin dönemindeki dikkat Eksikliği Hiperaktivite Bozukluğu belirtileri sıktır. ADHD 'nin erken tanınması ve tedavi edilmesi D vitamini eksikliği hastalarında faydalı olabilir.

**Anahtar Sözcükler:** D Vitamini, Dikkat Eksikliği ve Hiperaktivite Bozukluğu, Erişkin Kadın.

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Vitamin D is a fat-soluble vitamin and a prohormone that can be synthesized endogenously. It is estimated to be deficient or inadequate in approximately one billion individuals worldwide (1, 2). Beyond its classical functions in bone mineralization and calcium metabolism, vitamin D is one of the most significant metabolic factors in the body, with activities impacting the im-

mune and cardiovascular systems, skin biology, and calcium and bone homeostasis (3). Vitamin D also plays an active role in neurodevelopmental processes (4).

Vitamin D receptors are present in many tissues, and 1- $\alpha$ -hydroxylase-the enzyme responsible for activating vitamin D-is found in the brain, particularly in the

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prefrontal cortex, hippocampus, and hypothalamus. Moreover, the active form of vitamin D can cross the blood-brain barrier, suggesting its potential involvement in cerebral and cognitive functions (5, 6). In addition to its effects on memory function and cognitive decline, vitamin D deficiency has been linked to neuropsychiatric diseases (7, 8). Almukbil et al. reported that academic performance is poorer in individuals with vitamin D deficiency and suggested that treating this deficiency may support mental health and psychological well-being (9).

Adult attention-deficit and hyperactivity disorder (ADHD) is a neurodevelopmental disorder that begins in childhood and persists into adolescence and adulthood, characterized by symptoms of inattention, emotional dysregulation, impulsivity, and disinhibition (10, 11). The prevalence of ADHD in the general population is estimated to range between 1% and 6% (12). Dopamine has been reported to play a crucial role in the pathogenesis of ADHD due to its regulatory effects on executive functions and psychomotor activity (13). Vitamin D enhances dopamine synthesis and release, thereby regulating the differentiation and functions of dopaminergic neurons (14). It may directly affect dopaminergic signaling by regulating the gene expression of tyrosine hydroxylase, an enzyme involved in dopamine biosynthesis (15). Furthermore, vitamin D may influence synaptic plasticity and neuronal survival by modulating brain-derived neurotrophic factor (BDNF) levels (16). BDNF is an essential neurotrophin that regulates synaptic function in brain regions associated with cognitive control. Studies have suggested that low vitamin D levels suppress BDNF expression, which may contribute to the cognitive dysfunctions observed in ADHD (16, 17). Additionally, vitamin D affects other neurotransmitter pathways, such as the glutamatergic and GABAergic systems, and may have broad effects on multiple biological substrates implicated in neurodevelopmental disorders (18). A potential association between vitamin D deficiency and ADHD symptoms has been suggested (19). Meta-analyses have shown that serum 25(OH)D concentrations are lower in pediatric patients with ADHD compared to healthy controls (20). Vitamin D supplementation has also been shown to reduce ADHD symptoms (21).

Studies have indicated that vitamin D deficiency is more prevalent in women than in men, particularly among individuals whose clothing limits sunlight exposure (22, 23). To the best of our knowledge, no studies have examined the relationship between vitamin D deficiency and ADHD symptoms in adults or the clinical variables influencing this relationship. In this study, we aimed to investigate adult ADHD symptoms in women with vitamin D deficiency and compare them with healthy controls without vitamin D deficiency. Our study differs from previous research in that we focused specifically on adult women and utilized the WURS-25 to assess childhood ADHD symptoms. By doing so, we aimed to evaluate whether psychiatric

scales combined with vitamin D levels can aid in identifying adult patients with ADHD who might otherwise be overlooked, in contrast to previous studies with smaller sample sizes.

## MATERIALS AND METHOD

Approval from the local ethics committee was obtained on September 14, 2023 (Reference number: E-50716828-100-375654). G\*Power software was used for statistical power analysis to estimate the sample size. The calculation, based on a significance level (alpha) of 0.05, indicated that 289 participants would be sufficient to achieve 95% statistical power. To ensure robust power, a total of 300 individuals were initially recruited. The patient group consisted of 154 women diagnosed with vitamin D deficiency who visited the internal medicine clinic of Elazığ Fethi Sekin City Hospital between September 2023 and January 2024, met the study criteria, and had not received any treatment. The healthy control group included 158 women who presented to the same hospital for annual check-ups and had no significant medical issues. This group was frequency-matched to the patient group based on age, gender, educational status, and socioeconomic background to minimize potential confounding effects. All participants were initially evaluated by an internal medicine specialist. This was followed by structured clinical interviews conducted by a psychiatrist according to DSM-5 criteria, each lasting approximately 30 minutes. The inclusion criteria for the patient group were: being a woman aged 18–65 years, having no organic, neurological, or psychiatric diseases, and having no intellectual disability that could impair cognitive function. A diagnosis of vitamin D deficiency was required, with no other comorbid diagnoses. To avoid confounding effects related to comorbidity and to maintain diagnostic specificity, participants with any additional psychiatric diagnoses based on DSM-5 criteria—as assessed through the structured clinical interviews—were excluded. Patients who had used medications such as vitamin D, calcium, or parathyroid hormone in the past year were also excluded. Four participants in the patient group who did not complete the study questionnaires and eight individuals in the control group who declined to participate were excluded from the final analysis. Consequently, the final study sample comprised 150 women with vitamin D deficiency and 150 healthy women in the control group. After obtaining written informed consent from all participants, the Clinical Data Form, the Turkish version of the ASRS-v1.1, and the WURS-25 were administered. Serum 25(OH) vitamin D levels were measured for all participants.

### The Scales Used in the Study:

**Sociodemographic and Clinical Data Form:** Sociodemographic and Clinical Data Form: This semi-structured form, created by the researchers, gathers important sociodemographic information from respon-

dents, including age, economic status, and marital status. It also collects clinical data, such as psychiatric disease history and smoking history.

**Turkish Version of the Adult ADHD Self-Report Scale (ASRS-v1.1):** This scale (24), developed by the World Health Organization to screen for mental disorders, measures the severity of ADHD symptoms in adulthood. The questions in this scale aim to identify a person's mental symptoms over the past six months. The scale was adapted to Turkish, and its validity and reliability were demonstrated (25).

**Wender Utah Rating Scale - Short Form (WURS-25):**

This scale was designed to assess the presence and severity of childhood ADHD signs and symptoms in adults (26). It's important to note that the scale evaluates adults' experiences during childhood and cannot be used for diagnosing adults based solely on the score. The scale has been adapted into Turkish, and its validity and reliability have been confirmed (27). When a score of 36 or above is used as the cutoff point, the scale can accurately classify 82.5% of adults with ADHD, 90.8% of the control group (specificity), 66% of individuals with depression, and 64.3% of those with bipolar disorder.

#### Statistical analysis:

Statistical analyses were conducted using version 14.0 of the Statistical Package for Social Sciences (SPSS). Continuous variables were assessed for normality using the Kolmogorov-Smirnov test and histograms. Nor-

mally distributed parameters were compared using Student's t-test, while parameters that did not follow a normal distribution were analyzed using the Mann-Whitney U test. Categorical variables were compared using either the Chi-square test or Fisher's exact test, depending on the situation.

The strength of the relationship between two variables was evaluated with Spearman's or Pearson's correlation coefficient. A statistical difference was considered significant when the p-value was less than 0.05. To assess the ability of vitamin D levels to predict a higher score on the Wender Utah Rating Scale, receiver operating characteristic (ROC) analysis was performed. The accuracy of the tests was measured by the area under the ROC curve (AUC). An AUC close to 1 indicates a perfect diagnostic test, whereas an AUC of 0.5 suggests the test is not useful.

## RESULTS

The study included 300 participants- 150 with vitamin D deficiency and 150 controls. The clinical characteristics of the participants, including the scores of the Turkish version of the WURS-25 and Turkish version of the ASRS-v1.1 scores, are presented in Table 1.

**Table 1.** Baseline characteristics of participants.

	Without Vitamin D deficiency (n =150)	With Vitamin D deficiency (n =150)	p
Age, median (min-max)	30 (18-64)	32 (16-60)	0.517
Marital Status			
Single, n(%)	56 (37.3)	64 (42.7)	0.346
Married, n(%)	94 (62.7)	86 (57.3)	
Education			
High school or lower, n(%)	64 (42.7)	36 (24)	<b>0.001</b>
University, n(%)	86 (57.3)	114 (76)	
Place of residence			
Rural area, n(%)	2 (1.3)	9 (6)	<b>0.032</b>
Urban area, n(%)	148 (98.7)	141 (94)	
Economical status			
Low, n(%)	37 (24.7)	7 (4.7)	<b>&lt;0.001</b>
Medium or High, n(%)	113 (75.3)	143 (95.3)	
Alcohol consumption			
No, n(%)	149 (99.3)	145 (96.7)	0.214
Yes, n(%)	1 (0.7)	5 (3.3)	
Smoking			
No, n(%)	134 (89.3)	122 (81.3)	0.050
Yes, n(%)	16 (10.7)	28 (18.7)	
History of psychological disorder			
No, n(%)	148 (98.7)	143 (95.3)	0.173
Yes, n(%)	2 (1.3)	7 (4.7)	
Family history of psychological disorder			
No, n(%)	146 (97.3)	144 (96)	0.520
Yes, n(%)	4 (2.7)	6 (4)	
Suicide attempt			
No, n(%)	150 (100)	149 (99.3)	0.317
Yes, n(%)	0 (0)	1 (0.7)	
Vitamin D level, median (min-max)	30 (10-50)	15 (5-28)	<b>&lt;0.001</b>
ASRS-v1.1, mean±SD	24.99 ± 8.63	28.90 ± 9.75	<b>&lt;0.001</b>
WURS-25, median (min-max)	11 (0-63)	19 (0-86)	<b>&lt;0.001</b>

As shown in the table, both age and age range were similar between the two groups. No significant differences were found between the study group and the control group in terms of marital status, alcohol consumption, smoking, history of psychological disorder, family history of psychological disorder, and suicide attempt. However, participants with vitamin D deficiency had higher scores on the Turkish version of the Adult ADHD Self-Report Scale and the WURS-25 scores, as well as higher educational and economic status, compared to those without vitamin D deficiency.

The relationship between age, vitamin D level, the WURS-25 score, and the Turkish version of the ASRS-v1.1 score is presented in Table 2.

**Table 2.** Relationship between Turkish version of the adult adhd self-report scale (ASRS-V1.1) and other numerical parameters.

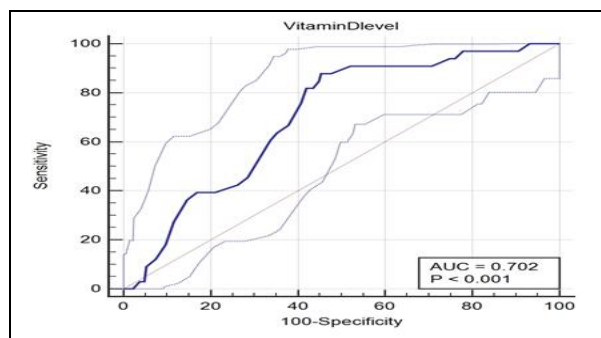
Turkish version of the Adult ADHD Self-Report Scale		
Age	r	-0.097
	p-value	0.094
Vitamin D level	r	-0.157
	p-value	<b>0.006</b>
WURS-25	r	0.492
	p-value	<b>&lt;0.001</b>

The Turkish version of the ASRS-v1.1 showed a positive correlation with the WURS-25 and a negative correlation with vitamin D levels. The participants were categorized into two groups: those with a score of 36 and above on the WURS-25 and those with a score below 36. Participants with Wender Utah Rating Scale scores of 36 and above were younger, more likely to be single, lived in urban areas, had lower vitamin D levels, and scored higher on the Turkish version of the ASRS-v1.1, as summarized in Table 3.

**Table 3.** Relationship between wender utah rating scale score and other numerical parameters.

	Wender Utah Rating Scale score below 36 (n =267)	Wender Utah Rating Scale score 36 and above (n =33)	p
Age, median (min-max)	31 (18-64)	27 (16-58)	<b>0.002</b>
Gender			
Female, n(%)	267 (100)	33 (100)	
Male, n(%)	0 (0)	0 (0)	
Marital Status			<b>0.010</b>
Single, n(%)	100 (37.5)	20 (60.6)	
Married, n(%)	167 (62.5)	13 (39.4)	
Education			0.434
High school or lower, n(%)	91 (34.1)	9 (27.3)	
University, n(%)	176 (65.9)	24 (72.7)	
Place of residence			<b>0.023</b>
Rural area, n(%)	7 (2.6)	4 (12.1)	
Urban area, n(%)	260 (97.4)	29 (87.9)	
Economical status			0.063
Low, n(%)	43 (16.1)	1 (3)	
Medium or High, n(%)	224 (83.9)	32 (97)	
Alcohol consumption			0.133
No, n(%)	263 (98.5)	31 (93.9)	
Yes, n(%)	4 (1.5)	2 (6.1)	
Smoking			0.601
No, n(%)	229 (85.8)	27 (81.8)	
Yes, n(%)	38 (14.2)	6 (18.2)	
History of psychological disorder			0.259
No, n(%)	260 (97.4)	31 (93.9)	
Yes, n(%)	7 (2.6)	2 (6.1)	
Family history of psychological disorder			0.609
No, n(%)	257 (96.3)	33 (100)	
Yes, n(%)	10 (3.7)	0 (0)	
Suicide attempt			0.725
No, n(%)	266 (99.6)	33 (100)	
Yes, n(%)	1 (0.4)	0 (0)	
Vitamin D level, median (min-max)	26 (5-50)	17 (6-37)	<b>&lt;0.001</b>
ASRS-v1.1, mean±SD	25.76 ± 8.82	36.49 ± 8.53	<b>&lt;0.001</b>

We analyzed the optimal cutoff point of vitamin D level for predicting a higher Wender Utah Rating Scale score. Vitamin D levels were found to be significant for the WURS-25 score of 36 and above, with a cutoff point of  $\leq 24$  (Area under the curve: 0.702,  $p \leq 0.001$ ) (Figure 1).



**Figure 1.** Receiver operating characteristic curve for vitamin D level.

## DISCUSSION

This study investigated the diagnosis of ADHD in women with vitamin D deficiency, based on the hypothesis that symptoms and diagnoses of adult ADHD may be more prevalent in this population. The results indicated that women with vitamin D deficiency exhibited significantly more ADHD symptoms compared to healthy controls. Additionally, there was a notable relationship between laboratory markers of vitamin D deficiency and ADHD scale scores. Women who reported higher ADHD symptoms during childhood had lower vitamin D levels and were more likely to be diagnosed with ADHD in adulthood. Furthermore, as vitamin D deficiency worsened, childhood ADHD symptoms became more pronounced.

Symptoms of adult attention-deficit/hyperactivity disorder (ADHD) begin in childhood and often continue into adulthood. However, the factors involved in the etiopathogenesis of ADHD remain unclear. Villagomez et al. reported that children diagnosed with ADHD had lower levels of vitamin D, magnesium, iron, and zinc. Vitamin D deficiency has detrimental effects on cognitive and behavioral functions, and insufficient vitamin D levels can increase the risk of cognitive dysfunction and structural defects in the brain. Naeini et al. demonstrated that children diagnosed with ADHD between the ages of 6 and 13 years exhibited vitamin D deficiency. Additionally, those diagnosed with ADHD often have deficiencies in vitamin D and magnesium; supplementation of these nutrients has been shown to reduce ADHD symptoms.

In a study conducted on 133 patients with ADHD, Landaas et al. associated low levels of vitamins B2, B6, and B9 with ADHD diagnosis, noting that deficiencies in B2 and B6 correlated with symptom severity. Another study found that the prevalence of adult ADHD in female patients with iron deficiency anemia was higher than in the general population. A recent randomized controlled trial indicated that ADHD symptoms significantly decreased in adult patients who took vitamin-mineral supplements.

In this study, the scores from the ASRS-v1.1 and WURS-25, tools used to measure and evaluate adult ADHD symptoms, were statistically significantly higher

in women with vitamin D deficiency compared to healthy individuals in the control group. It was also found that lower levels of vitamin D were associated with higher ADHD scale scores. This finding suggests that vitamin D deficiency may contribute to increased severity of adult ADHD symptoms, consistent with other research examining the relationship between vitamin D deficiency and ADHD.

Furthermore, patients with a WURS-25 score of 36 and above had lower vitamin D levels and higher adult ADHD scores. The study has some limitations, such as its cross-sectional design, small sample size, and being conducted at a single center, which may introduce selection bias. Potential confounding factors, including lifestyle elements (e.g., diet, exercise, sun exposure), other nutrient deficiencies, and comorbidities, may have also influenced the results.

Despite these limitations, this study contributes to the literature by exploring both childhood and adult ADHD in individuals with vitamin D deficiency. Strengths include the inclusion of newly diagnosed patients with vitamin D deficiency and the lack of gender differences affecting the findings, due to the sample consisting solely of females.

## Conclusion

To the best of our knowledge, this study is the first to investigate childhood and adulthood ADHD symptoms in females with vitamin D deficiency. The results indicate that the diagnosis and symptoms of ADHD in adult patients with vitamin D deficiency are not uncommon. These findings suggest that evaluating vitamin D levels in female ADHD patients may enhance the diagnostic process by incorporating biological markers.

Vitamin D deficiency may exacerbate symptom severity by negatively impacting dopamine synthesis and neurotrophic factors. From a clinical standpoint, routinely screening vitamin D levels in women who exhibit symptoms such as attention deficits and executive dysfunction could help identify underlying biological factors.

Early diagnosis and treatment of ADHD are crucial, as it significantly influences individuals in their personal, social, and professional lives. The relationship between vitamin D deficiency and ADHD supports the development of diagnostic algorithms tailored for females, especially considering the gender-specific neurobiological responses and hormonal differences observed in women. However, these findings should be validated through prospective, controlled studies before being integrated into clinical practice.

We believe our study will pave the way for further research examining the relationship between vitamin D deficiency and ADHD. In the future, we recommend conducting longitudinal studies to explore the causal relationship between vitamin D deficiency and ADHD, as well as intervention studies to evaluate the effectiveness of vitamin D supplementation in improving ADHD symptoms.

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