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Hypovitaminosis D and linkages to sleep and fatigue in Turkish patients with and without rheumatoid arthritis

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Ethics Committee Approval
The study was approved by the inical Research Ethics Committee of Gaziosmanpaşa Training and Research Hospital (Date: February 5, 2020, No: 30).
All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

Conflict of Interest
No conflict of interest was declared by the authors.

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Abstract

Background/Aim: We investigated Vitamin D levels in Turkish patients with and without rheumatoid arthritis (RA) to examine relationships with disease activity, sleep quality, sleepiness, fatigue, and physical capacity. Additionally, we evaluated the broader implications of the recent withdrawal of vitamin D testing from primary care settings.

Methods: A single-center, analytical study was conducted using laboratory records and various questionnaires: the Health Assessment Questionnaire (HAQ), Disease Activity Score (DAS-28), Pittsburgh Sleep Quality Index (PSQI), Epworth Sleepiness Scale (ESS), Fatigue Severity Scale (FSS), Visual Analogue Scale (VAS) for pain, and Physical Activity Questionnaire for Primary Care (PAQ-PC).

Results: A total of 192 patients were evaluated, including106 with RA that had a mean age of 53.5 (14.2) years; we also studied 86 controls that had a mean age of 49.8 (13.4) years with similar Vitamin D levels (21.02 [10.78] ng/mL vs 20.22 [8.81]) ng/mL; P=0.578). The prevalence of hypovitaminosis D was also similar across the groups (52.8% vs 48.8%; P=0.578). The Vitamin D levels of the RA patients were negatively correlated with pain (r=-0.286; P=0.033), tender joint count (r=-0.197 P=0.042), and disease activity (r=-0.286 P=0.003). In addition, RA patients exhibited poorer sleep quality and more daytime sleepiness compared with the controls; the RA patients had significantly poorer sleep quality scores (P<0.001). Similarly, the control group with hypovitaminosis D were found to have higher levels of fatigue and daytime sleepiness compared with individuals with normal Vitamin D levels (P=0.035 and P=0.019, respectively).

Conclusion: Given the high prevalence of hypovitaminosis D and its associations with disease activity, pain, fatigue, and poor sleep in patients with RA, these findings highlight the need to reconsider routine vitamin D screening in primary care, particularly for vulnerable and chronically ill populations.

Keywords: Vitamin D, fatigue, sleep, rheumatoid arthritis

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Introduction

The prevalence of Vitamin D deficiencies is increasing worldwide and has been reported to range from 20–90% in the Middle East, the United States, and Europe [1]. Additionally, roughly three quarters of patients with fatigue exhibit low Vitamin D levels [2]. Vitamin D is recognized for its critical role in calcium and bone homeostasis; however, its impacts are not limited to skeletal manifestations [1, 3]. It also confers immunomodulatory effects [3]. Low Vitamin D status is a prevalent condition that has been linked to a wide range of adverse health outcomes [4]. Consequently, Vitamin D deficiencies have been implicated in the pathogenesis of various autoimmune disorders, cardiovascular diseases, diabetes, hypertension, preeclampsia, cancer, and sleep disorders [3, 4]. Recent studies have suggested that Vitamin D status may potentially contribute to inflammatory disorders such as rheumatoid arthritis (RA) [5].

Patients with RA frequently suffer from poor sleep quality, which detrimentally impacts their overall well-being [6]. The chronic inflammation and pain associated with RA often disrupt sleep, resulting in fatigue and a heightened burden of disease [3, 6]. Research has shown that individuals with RA experience more significant sleep disturbances and lower sleep quality compared with healthy individuals [3]. Although studies have not provided conclusive evidence that Vitamin D levels have a direct impact on fatigue and sleep quality in RA patients [3, 5, 6], Vitamin D deficiencies have been linked to poor sleep quality in the general population [4]. Studies examining effects before and after Vitamin D supplementation have reported significant improvements in sleep quality. Sleep deprivation has been identified as a significant factor contributing to hyperalgesia (i.e., an increased sensitivity to pain). Recent studies have also linked Vitamin D deficiencies to both sleep disturbances and hyperalgesia, suggesting a potential interplay among sleep, pain sensitivity, and Vitamin D levels [7, 8]. Meta-analyses have indicated a significant reduction in Pittsburgh Sleep Quality Index scores for individuals receiving Vitamin D [4]. Additionally, Vitamin D deficiency has been linked to reduced muscle strength and increased disease activity in RA patients [7].

In Turkey, periodic follow-ups for pregnant women, children, and individuals with chronic diseases—groups at high risk for Vitamin D deficiencies—are typically conducted in primary care settings. Unfortunately, these primary care facilities lack the resources to measure Vitamin D levels, hindering the effective monitoring and management of Vitamin D deficiency in these vulnerable populations. A comprehensive meta-analysis, which included 40 research articles that spanned 111,582 individuals from various communities in Turkey, found that the overall prevalence of Vitamin D deficiency was around 63% [9]. This high prevalence suggests that even higher figures are expected for the Turkish population with chronic diseases.

We evaluated the prevalence of hypovitaminosis D and its correlation with RA disease activity, sleep quality, sleepiness, fatigue, and physical activity among RA patients compared with an RA-free population. We conducted this study to address the conflicting findings of previous studies in Turkey and the lack of sufficient studies on Vitamin D levels in RA patients within primary care. Furthermore, we assessed the broader implications of the recent cessation of Vitamin D testing from primary care settings in Turkey, highlighting its potential impact on patient management and clinical outcomes.

Materials and methods

Study design

This analytical case-control study was conducted with 192 subjects (106 RA patients and 86 control patients). The RA patients were selected from the Rheumatology Clinic at University of Health Sciences Gaziosmanpaşa Training and Research Hospital, (Istanbul, Turkey) provided that they had not taken Vitamin D supplements within the last three months; control cases were randomly selected from the Family Medicine Clinic at Gaziosmanpasa Training and Research Hospital (Istanbul, Turkey) from February 25, 2020 through May 15, 2020. Informed consent was obtained from the patients prior to their participation in the study. The ethics committee of the Gaziosmanpaşa Training and Research Hospital approved the study February 5, 2020 (No: 30).

A rheumatologist followed and evaluated patients with RA. Control cases included patients who visited the family medicine clinic for routine health checks or prescriptions for chronic diseases (e.g., hypertension, diabetes, asthma, chronic obstructive pulmonary disease) and who had their Vitamin D levels measured within the last three months. We excluded individuals with connective tissue diseases, endocrine disorders related to bone health (such as thyroid, parathyroid, adrenal disorders, and electrolyte imbalances), malnutrition, renal dysfunction, people receiving medications that could affect bone health (including corticosteroids, chemotherapy, anticonvulsants, diuretics, thyroxin, H2 blockers, or proton pump inhibitors), and individuals diagnosed with psychiatric disorders, dementia, or sleep disorders. Finally, we excluded anyone who was taking Vitamin D supplements.

Data Collection and Measurements

Participant data, including age, gender, Body Mass Index (BMI), education level, occupation information, income level, disease duration, comorbidity, medications currently used, rheumatoid factor (RF), anti-cyclic citrullinated peptide (anti-CCP), 25(OH)D levels, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), complete blood count, parathormone levels, electrolytes, liver, kidney, thyroid function tests, and electrolyte values were recorded for the RA patient group. 25(OH)D levels were assessed as follows: normal Vitamin D (25(OH)D) level (30–100 ng/ml) and hypovitaminosis D (0–29.9 ng/ml) [9]. The Health Assessment Questionnaire in Rheumatic Diseases (HAQ), Disease Activity Score 28 (DAS28), Fatigue Severity Scale, Pittsburgh Sleep Quality Index (PSQI), and the Physical Activity Test Score in Primary Care were administered.

Health assessment questionnaire in rheumatic diseases

The Health Assessment Questionnaire in Rheumatic Diseases (HAQ) scale developed by Fries et al. [10] was adapted into Turkish by Küçükdeveci et al. [11]. The scale has a 4-point Likert structure, and a higher score corresponds to lower levels of health. A minimum of 0 points and a maximum of 3 points can be obtained for each question: 0 points correspond to "I can do it comfortably.", and 3 points correspond to "I can't do it at all." [10, 11].

Disease Activity Score 28

The Disease Activity Score 28 (DAS28) score, developed by Fransen et al. [12], indicates RA disease activity. The score incorporates the count of tender and swollen joints across 28 specific sites, a patient global assessment via a Visual Analogue Scale (VAS), and inflammatory markers such as Erythrocyte Sedimentation Rate (ESR) or C-Reactive Protein (CRP). The minimum score is 0, and the maximum score is 9.4. A DAS28 score less than 2.6 corresponds to remission, a score of 2.6–3.2 corresponds to mild disease, a score of 3.3–5.1 corresponds to moderate disease, and a score of greater than 5.1 corresponds to severe disease [12].

Fatigue Severity Scale

The Fatigue Severity Scale developed by Krupp et al. [13] is a 9-item, 7-point Likert-type scale (1="I completely disagree," 7="I completely agree") adapted to Turkish by Armutlu et al. [14]. The cut-off value for pathological fatigue is 4 points. As the total score decreases, the severity of fatigue decreases [13, 14].

Pittsburgh Sleep Quality Index

The Pittsburgh Sleep Quality Index (PSQI), developed by Buysse et al. [15], was validated in Turkish by Agargun et al. [16]. The total score of the 7-component scale yields the PSQI value. It is a 4-point Likert-type scale with a score ranging from item 0 (no distress) to item 3 (severe distress). A total score of at least 5 points on the PSQI indicates poor sleep quality [15, 16].

Epworth Sleepiness Scale

The Epworth Sleepiness Scale (ESS) developed by Johns et al. [17] was adapted into Turkish by Ağargün et al. [18]. It is an 8-item scale that is simple to apply, easy to understand, and has proven validity and reliability in assessing general sleepiness levels in adults. A score of 6 points and above is considered sleepy. A score of 6–10 points indicates normal but increased daytime sleepiness, a score of 11–12 points indicates considered increased but moderate daytime sleepiness, a score of 13–15 points to increased, moderate daytime sleepiness, and a score of 16–24 points indicates increased and severe daytime sleepiness [17, 18].

Physical Activity Test Score in Primary Care

The Physical Activity Test Score in Primary Care scale, which was developed by Ahmad et al. [19] and consists of three subheadings and seven questions, was adapted to Turkish by Noğay et al. [20]. The first section evaluates the person's mobility at work; the second section assesses activities performed in the past seven days and the number of hours spent on them per week; and the last section includes a question evaluating the person's normal walking speed. The scale categorizes daily physical activity levels into four groups: active, moderately active, less active, and inactive [19, 20].

Statistical Analysis

Statistical analyses were performed using the e-PİCOS calculator (https://e-picos.com.tr/apps/calculation) program. The Kolmogorov-Smirnov test, skewness, and kurtosis values were applied to evaluate the normality of the data. Continuous variables were summarized using means, medians, standard deviations, and interquartile ranges; categorical variables were reported as frequencies and percentages. The chi-square test was used to compare categorical data. For quantitative data, the Independent Samples T-Test and One-Way ANOVA were used for data with a normal distribution; the Mann-Whitney U test and Kruskal-Wallis test were used for non-normally distributed data. Correlations were analyzed between Vitamin D levels and study-related parameters. Additionally, ROC (Receiver Operating Characteristic) analysis was used to determine cut-off levels for scale scores based on the presence of hypovitaminosis D.

Results

The mean age of the RA patients was 53.59 (14.2) years; the mean age of the controls without RA was 49.8 (13.4) years. As shown in Table 1, baseline characteristics, including age, gender, and BMI, were comparable between the RA and control groups; socioeconomic indicators differed significantly between the two groups. The proportions of individuals with low income, those with no education, and those who were unemployed were significantly higher than in the control group (P=0.022, P<0.001, and P<0.001, respectively).

Data pertaining to hypovitaminosis D, fatigue, sleep quality, daytime sleepiness, and physical activity between the study (RA) and control groups are listed in Table 2. Despite a similar prevalence of hypovitaminosis D in the RA and control groups (P=0.582), RA patients exhibited higher levels of fatigue (P<0.001), sleepiness (P<0.001), poorer sleep quality (P<0.001), and lower physical activity levels (P<0.001) compared with patients in the control group.

Table 1: Baseline characteristics of patient and control groups

Variables		Study (RA) group n=106	Control group n=86	*P*-value
Age, mean (SD)		53.49 (14.2)	49.8 (13.44)	[1]0.068
		n (%)	**n (%)**	
Gender	Female	83 (78.3)	61 (70.9)	[2]0.241
	Male	23 (21.7)	25 (29.1)	
Marital status	Single	16 (15.1)	17 (19.8)	[3]0.509
	Married	90 (84.9)	69 (80.2)	
Education	None	28 (26.4)	5 (5.8)	**[2]<0.001***
	Basic education	53 (50)	44 (51.2)	
	High school	15 (14.2)	18 (20.9)	
	University	10 (9.4)	19 (22.1)	
Income level	Low	70 (66)	40 (46.5)	
	Moderate	16 (15.1)	18 (20.9)	**[2]0.022***
	High	20 (18.9)	28 (32.6)	
Occupation	Unemployed	65 (61.3)	22 (25.6)	**[2]<0.001***
	Retired	18 (17)	26 (30.2)	
	Desk job	5 (4.7)	16 (18.6)	
	Physical work	18 (17)	22 (25.6)	
Comorbidity	Yes	76 (71.7)	65 (75.6)	[2]0.545
	No	30 (28.3)	21 (24.4)	
BMI, mean (SD)		28.76 (6.48)	28.48 (4.2)	[1]0.719
Number of medications, median (IQR)		2.11 (2.03) (2)	1.88 (2.02) (1)	[4]0.362

[1] Student t Test, [2] Continuity (Yates), [3] Ki-Square Test, [4] Mann Whitney U Test, * P<0.05

Table 3 lists scale scores according to the presence of hypovitaminosis D in the study (RA) and control groups. Patients with RA and low Vitamin D levels had higher DAS-28 and PSQI scores compared with the control group (P=0.040 and P=0.005, respectively). Individuals in the control group with low Vitamin D levels exhibited higher levels of fatigue and sleepiness scores (P=0.035 and P=0.019, respectively).

Table 4 lists variables related to RA, DAS-28 score, HAQ score, VAS pain score, VAS patient global score, and the number of swollen or tender joints (SJN or TJN) according to Vitamin D levels in study (RA) and control groups. We observed negative correlations between Vitamin D levels and TJN (r=-0.197; P=0.042), VAS pain score (r=-0.208; P=0.033), and DAS-28 score (r=-0.286; P=0.003).

Table 2: Evaluation of hypovitaminosis D, fatigue, sleep quality, daytime sleepiness, and physical activity between the study (RA) and control groups.

Variables		Study (RA) group n=106	Control group n=86	*P*-value
		Mean (SD) or Median (IQR)	Mean (SD) or Median (IQR)	
25(OH)D level		21.02 (10.78)	20.22 (8.81)	[1]0.578
Fatigue severity score		4.30 (3.36)	2.00 (2.00)	[2]**<0.001***
PSQI score		7.00 (5.25)	4.00 (2.00)	[2]**<0.001***
Epworth sleepiness scale score		9.00 (6.00)	6.00 (5.00)	[2]**<0.001***
Physical activity score		0.00 (1.00)	1.00 (2.00)	[2]**<0.001***
		n (%)	**n (%)**	
Vitamin D groups	Hypovitaminosis D	56 (52.8)	42 (48.8)	[3]0.582
	Normal 25(OH)D level	50 (47.2)	44 (51.2)	
Fatigue groups	No fatigue	29 (27.4)	53 (61.6)	[3]**<0.001***
	Fatigue	56 (52.8)	32 (37.2)	
	Chronic fatigue	21 (19.8)	1 (1.2)	
Presence of daytime sleepiness	No	64 (60.4)	75 (87.2)	[4]**<0.001***
	Yes	42 (39.6)	11 (12.8)	
Poor sleep	No	38 (35.8)	74 (86)	[4]**<0.001***
	Yes	68 (64.2)	12 (14)	

[1] Student t Test, [2] Mann Whitney U Test, [3]Ki-Square Test,[4] Continuity (Yates) Correction, * *P*<0.05

Table 3: Evaluation of scale scores according to vitamin D levels in study (RA) and control groups

		Vitamin D groups		*P*-value
	Scores	**Hypovitaminosis D** (n=108)	**Normal 25(OH)D level** (n=84)	
		Mean (SD) or Median (IQR)	**Mean (SD) or Median (IQR)**	
Study (RA) group	DAS-28 score (median)	3.94 (1.42)	3.43 (2.46)	[1]**0.040***
	HAQ score	28.18 (12.24)	23.98 (14.81)	[2]0.113
	Fatigue severity score (median)	4.9 (3.18)	4.00 (3.58)	[1]0.597
	PSQI score (median)	8.00 (7.00)	6.00 (4.00)	[1]**0.005***
	Epworth sleepiness scale score (median)	9.5 (6.75)	9.00 (7.00)	[1]0.473
Control group	Fatigue severity score (median)	2.95 (2.46)	1.95 (1.33)	[1]**0.035***
	PSQI score (median)	4.00 (2.25)	4.00 (1.75)	[1]0.758
	Epworth sleepiness scale score (median)	7.5 (4.00)	5.00 (4.00)	[1]**0.019***

[1] Mann Whitney U Test, [2] Student t Test, **P*<0.05, DAS: disease activity score, HAQ: health assessment questionnaire, VAS: visual analogue scale, PSQI: Pittsburgh Sleep Quality Index

Table 4: Analysis of the relationship between disease-related parameters and vitamin D levels in RA patients.

Study (RA) group (n=106)		25(OH)D level
Age of symptom onset	**r**	**-0.039**
	p	**0.691**
Age of RA diagnosis	**r**	**0.044**
	p	**0.656**
Disease duration	**r**	**0.071**
	p	**0.471**
Swollen joint count (SJC)	**r**	**-0.136**
	p	**0.165**
Tender joint count (TJC)	**r**	**-0.197**
	p	**0.042***
VAS Patient global score	**r**	**-0.185**
	p	**0.058**
VAS pain score	**r**	**-0.208**
	p	**0.033***
DAS-28 score	**r**	**-0.286**
	p	**0.003***
HAQ score	**r**	**-0.185**
	p	**0.058**

*Pearson Correlation Analysis, * P<0.05, r=Correlation co-efficient, DAS: disease activity score, HAQ: health assessment questionnaire, VAS: visual analogue scale

Table 5 lists data pertaining to Vitamin D levels and age, BMI, fatigue severity score, PSQI score, Epworth sleepiness scale score, and physical activity score. In the RA group, higher vitamin D levels were associated with a decrease in PSQI scores, which indicates better sleep quality (r=-0.205; *P*=0.035). In the control group, Vitamin D levels were negatively correlated with age (r=-0.226; *P*=0.037), fatigue severity (r=-0.254; *P*=0.018), and daytime sleepiness (r=-0.285; *P*=0.008).

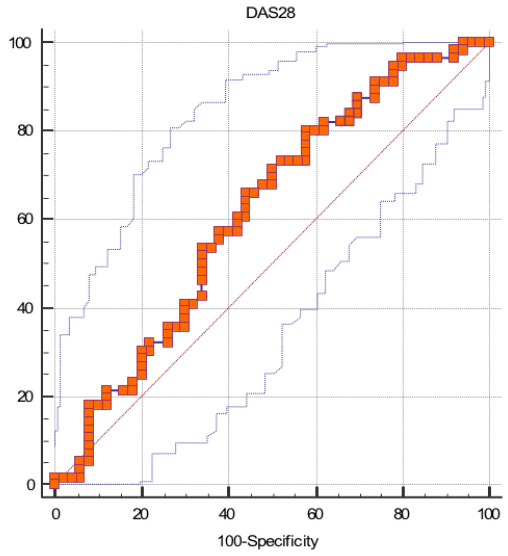
Table 5: Relationship between vitamin D level and age, BMI, fatigue severity score, PSQI score, Epworth sleepiness scale score and physical activity score

		25(OH)D level		
		All (n=192)	**Study (RA) group (n=106)**	**Control group (n=86)**
Age	**r**	-0.046	0.057	***-0.226***
	p	0.527	0.562	***0.037****
BMI	**r**	-0.024	-0.038	**0.007**
	p	0.745	0.696	**0.949**
Fatigue severity score	**r**	-0.111	-0.087	***-0.254***
	p	0.127	0.375	***0.018****
PSQI score	**r**	-0.131	*-0.205*	**-0.117**
	p	0.071	***0.035****	**0.283**
Epworth sleepiness scale score	**r**	*-0.166*	-0.137	***-0.285***
	p	0.022*	0.161	**0.008***
Physical activity score	**r**	-0.010	0.038	**-0.042**
	p	**0.894**	**0.697**	**0.700**

Pearson Correlation Analysis, * *P*<0.05, r: Correlation co-efficient, PSQI: Pittsburgh Sleep Quality Index, BMI: Body Mass Index

Figure 1 shows the ROC (Receiver Operating Characteristic) curve for DAS-28 score in the presence of hypovitaminosis D. The cutoff point determined for DAS-28 was 3.03 in corresponding to low disease activity (2.6–3.2) according to EULAR criteria. The sensitivity of this value was found to be 80.4%, with a specificity of 42.0%. The positive predictive value was 60.8%, and the negative predictive value was 65.6%. Clinically, these results indicate that RA patients with a DAS-28 activity score of 3.03 (i.e., exhibiting moderate to severe disease activity), are likely to have hypovitaminosis D (*P*=0.037).

Figure 1: ROC curve for DAS-28 in the diagnosis of hypovitaminosis D



Discussion

We assessed the relationship between Vitamin D levels and various health parameters in RA patients, including disease activity, sleep quality, fatigue severity, and physical activity levels. We then made comparisons with a control group. Hypovitaminosis D was noted in 52.8% of RA patients and 48.8% of control group patients. Our findings revealed that RA patients with hypovitaminosis D experienced significantly poorer sleep quality and had more fatigue and daytime sleepiness than the control patients. Notably, all RA patients with moderate to severe DAS-28 disease activity require Vitamin D supplementation. Similarly, control group patients with hypovitaminosis D were found to have higher levels of fatigue and daytime sleepiness compared to individuals with normal Vitamin D levels. These findings highlight the association between Vitamin D levels and parameters such as sleep and fatigue.

In Turkey, the Ministry of Health has implemented new regulations to address the significant increase in Vitamin D testing that began in 2019. These regulations are intended to optimize testing and reduce unnecessary demand. The relevant measures include removing Vitamin D testing in primary care facilities and limiting the service in secondary and tertiary care settings to specific specialists, such as pediatricians, internists, obstetricians, physiatrists, orthopedists, and neurologists. A mandatory 90-day interval has been introduced for repeat tests, but exceptions are made for inpatients and intensive care patients. In emergency departments, test requests are similarly restricted to the specialists noted above. These changes are intended to conserve resources and ensure that Vitamin D testing is prioritized for patients with clear clinical indications.

However, in primary care Vitamin D levels are critical for monitoring chronic diseases, the health of women aged 15-49, geriatric patients, pregnant women, and children. Requiring every patient with specific needs to consult a specialist may not be practical for Vitamin D testing. Many studies of RA have reported that more women than men are afflicted by the disease [21]. For instance, Grabovac et al. [22] showed that 32.6% of RA patients were male, while 67.4% were female. Our study is consistent with this trend, with 78.3% of the participants being female and 22.7% being male.

Although no prior studies have linked low income with the prevalence of RA, our findings showed that Vitamin D deficiencies were more prevalent among RA patients with low socioeconomic status. This finding suggests that financial barriers may contribute to Vitamin D deficiencies in this population. But in healthcare systems where primary care services—including laboratory testing and examinations—are provided free of charge, income level may no longer be a limiting factor when it comes to monitoring and replacing Vitamin D. That situation only holds true, however, provided that Vitamin D testing is available at the primary care level.

In addition, low Vitamin D levels have been associated with an increased risk of developing RA and are linked to higher RA disease activity and poorer general health status [23]. A 2016 meta-analysis of 15 studies that encompassed 1,143 RA patients and 963 controls found significantly lower Vitamin D levels in RA patients; Vitamin D levels were inversely correlated with RA disease activity [24]. Another meta-analysis of 3,489 patients reported a similar inverse correlation between low Vitamin D levels and disease activity [25]. A 2020 meta-analysis showed that VAS scores significantly decreased in patients taking at least 50,000 IU of Vitamin D supplements per week for at least 12 weeks; patients in that group also exhibited a reduction in DAS-28 activity scores. No changes were observed in patients who took less than 50,000 IU of Vitamin D per week or followed that regime for less than 12 weeks [26]. In a 2017 randomized, double-blind, placebo-controlled study with 39 RA and 31 control patients, new-onset RA patients who received 300,000 IU of 1.25 dihydroxy cholecalciferol exhibited significantly better general health assessments after three months compared with patients in the placebo group [27]. Another controlled trial of 121 new-onset RA patients compared patients receiving only DMARDs (Disease-Modifying Antirheumatic Drugs) with patients also receiving 500 IU of Vitamin D daily. After three months, patients in the Vitamin D group reported significantly decreased pain, but no relationship was noted between Vitamin D levels and DAS-28 scores [28]. Di Franco et al. [29] showed that in patients with new-onset RA and low Vitamin D levels, disease activity reduction, remission rates, and treatment responses were notably lower after 12 months compared with patients with normal Vitamin D levels. This result highlights the role of Vitamin D in modulating RA and suggests that assessing and supplementing Vitamin D might improve the management of new-onset RA.

In our study, Vitamin D levels were inversely correlated with pain, tender joint count, and disease activity. Patients with RA with low Vitamin D levels exhibited significantly higher disease activity. The cut-off point for DAS-28 in hypovitaminosis D was determined to be 3.03. Clinically, this result indicates that RA patients with a DAS-28 activity score of 3.03 or above are likely Vitamin D deficient. According to the RA disease activity classification of our study cohort, Vitamin D levels in cases of moderate and severe disease activity require supplementation. The VAS pain scores of patients in our RA group were negatively correlated with Vitamin D levels, a finding that is consistent with that reported in the literature [22, 24, 25].

Low levels of Vitamin D are one factor influencing fatigue during inflammatory rheumatisms [30]. In a 2014 study by Oy et al. conducted in the United States, the authors found that fatigue severity in individuals with Vitamin D deficiencies decreased after Vitamin D supplementation [31]. Patients with RA may suffer from poor sleep quality, which is attributed to depression, fatiguability, disability and disease activity [32]. In our control group, patients with sufficient Vitamin D levels had significantly lower fatigue severity compared with patients with insufficient Vitamin D levels; this finding is consistent with the literature [30, 31]. However, the Vitamin D levels of RA patients in our study did not correlate with fatigue severity, unlike in the control group.

A 2018 meta-analysis by Gao et al. [33] linked Vitamin D deficiencies with an increased risk of sleep disorders and decreased sleep quality. Similarly, Sarıyıldız et al. [34] used the PSQI scale and found that RA patients had lower sleep quality than patients in their control group; this team primarily associated low sleep quality with high RA disease activity . A review of non-pharmacological methods for relieving fatigue in RA patients demonstrated that physical activity positively impacted fatigue levels [35]. Exercise is known to improve sleep disorders in patients with RA [36]. Despite studies suggesting that all patients should exercise and take supplements to prevent muscle mass loss, Vitamin D supplementation, with or without exercise, did not significantly affect other aspects of body composition or metabolic health outcomes [37]. On the other hand, a population-based study by Mirzaei-Azandaryani et al. [38] found that sleep quality significantly improved in patients receiving Vitamin D compared with patients in the control group. In summary, higher PSQI scores—indicating poorer sleep quality—were observed in individuals with low vitamin D levels compared to those with normal levels, in both the RA and control groups.

Limitations

One limitation of this study is that a fatigue assessment may lack objectivity when it is solely based on scale scores; fatigue can be influenced by poor sleep quality or can occur

independently of sleep issues. Additionally, seasonal effects may have influenced our findings—this study began in February and concluded in May; that cycle potentially affected Vitamin D synthesis and measurement levels: Vitamin D levels are often lowest in March, as cutaneous synthesis is limited due to the angle of sunlight during the winter months [39]. We recommend conducting additional research with larger sample sizes and including Vitamin D replacement interventions to obtain more generalizable results.

Conclusions

Patients with RA and hypovitaminosis D are more fatigued and sleepy, have poorer sleep quality, and exhibit a larger number of swollen and tender joints compared with those with normal vitamin D levels.

Routine follow-ups for populations at a high risk of Vitamin D deficiencies—including pregnant women, children, the elderly, and individuals with chronic diseases—are typically conducted in primary care settings. However, the lack of resources to measure Vitamin D levels in these facilities hampers effective monitoring and management of Vitamin D deficiencies in these vulnerable groups.

Monitoring Vitamin D status during primary care follow-up for patients with chronic diseases, such as RA, is paramount for optimizing long-term clinical outcomes. We strongly advocate for the reinstatement of routine annual Vitamin D screening in primary care settings, especially for at-risk populations. In light of these findings, the broader contribution of micronutrients to health maintenance and disease prevention necessitates a thorough re-evaluation.

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