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Investigating the correlation between sleep disorders with inflammatory and anemia indicators in patients with rheumatoid arthritis; a cross-sectional study

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Abstract

Introduction: Rheumatoid arthritis (RA) is a chronic autoimmune disorder characterized by systemic inflammation, leading to joint damage and various comorbidities, including sleep disorders. Sleep disturbances are prevalent among RA patients and can exacerbate disease symptoms, potentially influencing inflammatory markers and anemia indicators.

Objectives: This study investigates the correlation between sleep disorders, inflammatory markers, and anemia indicators in RA patients.

Patients and Methods: This cross-sectional study was conducted on patients diagnosed with RA referred to Imam Hossein Hospital, Tehran in 2023. The research involved collecting clinical and laboratory data, including sleep quality assessments using the Pittsburgh Sleep Quality Index (PSQI) and measurements of inflammatory markers such as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) and anemia indicators, including hemoglobin (Hb) and mean corpuscular volume (MCV). Data collection was conducted in two stages: first, demographic information and sleep quality were assessed through self-reported questionnaires, followed by blood tests to measure inflammatory and anemia indicators. The correlation between sleep quality and inflammatory and anemia indicators was assessed using logistic regression.

Results: The findings revealed that among 59 RA Patients, with a mean age of 53.98 ± 10.37 years, only 28.8% exhibited good sleep quality, while a substantial 71.2% experienced poor sleep quality. Furthermore, the analysis indicated that there was no statistically significant relationship between sleep quality and various inflammatory and anemia markers, including ESR, CRP, Hb, and MCV ($P > 0.05$).

Conclusion: In conclusion, the findings reveal a high prevalence of poor sleep quality among RA patients. Importantly, this poor sleep quality appears to be independent of inflammatory and anemia markers, suggesting that other factors may contribute to sleep disturbances in this population. Further investigation is warranted to better understand the underlying causes of these sleep issues.

Introduction

Rheumatoid arthritis (RA) is a chronic autoimmune illness considered by persistent inflammation of the synovial joints, leading to pain, swelling, and potential joint destruction. The disease is associated with the presence of specific autoantibodies, such as anti-citrullinated protein antibodies, which play a crucial role in its pathogenesis. Recent studies have indicated that these antibodies can be detected not only in serum but also in saliva, suggesting a site-specific mucosal immune response in RA patients (1). The disease has significant systemic implications, including an increased risk of various comorbidities, such as cardiovascular diseases and certain cancers, as evidenced by recent Mendelian randomization studies (2). Current therapeutic strategies focus on controlling inflammation and preventing joint damage, with novel approaches like antibody-drug conjugates showing promise in mitigating the

Key point

This study found that the majority of rheumatoid arthritis (RA) patients experienced poor sleep quality, which was independent of inflammatory and anemia markers. The high prevalence of poor sleep quality among RA patients, as revealed by the findings, underscores the need for health policy and practice to prioritize the assessment and management of sleep disturbances in this population. Given that poor sleep quality appears to be independent of established inflammatory and anemia markers, healthcare providers should consider a broader range of factors that may contribute to sleep issues, including psychological, environmental, and lifestyle influences. Furthermore, integrating sleep quality assessments into routine clinical evaluations for RA patients could enhance overall patient care and inform targeted interventions. Research efforts should also focus on exploring the underlying causes of sleep disturbances in this demographic, as well as developing effective treatment strategies that address both sleep quality and the multifaceted nature of RA.

disease's progression and improving patient outcomes (3). Patients with RA frequently experience sleep disorders, which significantly impact their overall quality of life. A recent multicenter cross-sectional study revealed that approximately 75% of these patients reported poor sleep quality, with insomnia affecting nearly 39% of participants and sleep apnea present in 18% (4,5). The study identified strong correlations between sleep disturbances and factors such as disease activity, fatigue, and depression levels, indicating that higher disease severity is associated with worse sleep outcomes (4). Furthermore, sleep disorders were found to negatively influence daily activities and overall health-related quality of life, emphasizing the need for comprehensive management strategies that address both physical symptoms and sleep issues in RA patients (6).

Rheumatoid arthritis significantly impacts sleep quality, with a high prevalence of sleep disturbances reported among patients. A systematic review indicated that RA patients have poorer sleep quality across various domains compared to healthy controls, with a relative risk of 2.37 for sleep disturbances in RA individuals (7). Inflammation and anemia are common indicators in RA, often exacerbating sleep issues; studies have shown that higher disease activity correlates with increased insomnia and poorer sleep quality (8). Furthermore, poor sleep quality has been linked to heightened anxiety and depression, which are prevalent in RA patients and can further deteriorate their overall health status (8,9). Addressing these interconnected factors is crucial for improving the management of RA and enhancing the quality of life for affected individuals (10).

Objectives

The objective of this study is to investigate the correlation between sleep disorders and inflammatory and anemia indicators in patients diagnosed with RA. By utilizing validated assessment tools to evaluate sleep quality and conducting laboratory tests to measure key inflammatory biomarkers like C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR), as well as anemia indicators including hemoglobin (Hb) and mean corpuscular volume (MCV), this research aims to elucidate the potential relationships between these variables. The findings are expected to enhance the understanding of how sleep disturbances may influence inflammatory processes and anemia in RA patients, ultimately contributing to improved management strategies for this population.

Patients and Methods
Study design and participants
This cross-sectional study was conducted on patients diagnosed with RA referred to Imam Hossein hospital in Tehran, in 2023 to detect the association between sleep disorders and inflammatory biomarkers. The study involved the collection of clinical and laboratory data, including assessments of sleep quality using validated questionnaires such as the Pittsburgh Sleep Quality Index (PSQI), alongside measurements of inflammatory markers like CRP and ESR. By analyzing these variables, the study aimed to identify potential correlations between sleep disturbances and systemic inflammation in RA patients, providing insights into how inflammatory processes may contribute to sleep-related issues in this population.

Inclusion and exclusion criteria
Inclusion criteria for this study contained a definitive diagnosis of RA, the provision of written informed consent, and the ability to read and write to complete the questionnaires. Additionally, participants were required to have a confirmed presence of sleep disorders, as determined through an initial interview and validated by a physician. Exclusion criteria included individuals with a history of psychiatric disorders or chronic infectious diseases, those taking medications known to interfere with sleep, and individuals who were unwilling to continue their participation in the study.

Data collection
Data collection consisted of two main stages. First, demographic characteristics, including age and sex, were gathered, and the sleep quality of patients was assessed using the PSQI through self-reporting by the patients. This validated and standardized tool evaluates seven sleep-related components and provides an overall sleep quality score. In the next stage, inflammatory factors and anemia indicators, including ESR, CRP, Hb, and MCV, were measured through blood tests for each patient.

The PSQI validation
The PSQI is a widely used self-report questionnaire designed to measure sleep quality over one month. It consists of 19 items grouped into seven components: subjective sleep quality, sleep latency (time to fall asleep), use of sleep medication, sleep duration, habitual

sleep efficiency (time asleep versus time in bed), sleep disturbances (e.g., waking during the night), and daytime dysfunction (e.g., fatigue or trouble staying awake). Each component is scored from 0 to 3, with higher scores indicating greater sleep difficulties. These scores are summed to produce a global PSQI score ranging from 0 to 21, where scores above 5 typically indicate poor sleep quality and potential sleep disturbances. The PSQI is widely validated and used in clinical and research settings to assess sleep problems and treatment outcomes (11,12).

Statistical analysis

Data analysis was performed using the Statistical Package for the Social Sciences (SPSS, IBM Corp; version 27). The normality of the data was assessed using the Kolmogorov-Smirnov test. To compare quantitative and qualitative data between the two groups categorized as poor and good sleep quality, independent t-tests and chi-square tests were employed, respectively. Furthermore, univariate and multivariate logistic regression analyses were utilized to explore the correlation between sleep quality disorders and inflammatory and anemia indicators. A *P* value of less than 0.05 was considered statistically significant.

Table 1. Demographic data, inflammatory biomarkers, and anemia indicators in the studied participants

Variable	Frequency		Percent
Gender			
Female	50		84.7
Male	9		15.3
Sleep quality			
Good	17		28.8
Poor	42		71.2
Variable	Mean	SD	Minimum	Maximum
Age (year)	53.98	10.37	30	82
ESR (mm/h)	19.02	13.94	2	59
CRP (mg/L)	5.41	5.77	0.2	24.8
Hb (g/dL)	12.94	1.12	9.7	15.3
MCV (fL)	86.56	5.16	72.70	103.2

ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein; Hb: Hemoglobin; MCV: Mean corpuscular volume; SD: Standard deviation.

Results

The results indicated that among the 59 participants, who had a mean age of 53.98 ± 10.37 years, a significant majority were female (84.7%), while males constituted 15.3% of the sample. Sleep quality, as assessed by the PSQI questionnaires, indicated that 17 participants experienced good sleep quality, whereas 47 participants reported poor sleep quality (Table 1).

The results demonstrated that there was no statistically significant association between sleep quality levels and the frequency distribution of demographic variables, including age and sex, as well as key clinical biomarkers. Specifically, inflammatory markers such as ESR and CRP, along with anemia indicators such as Hb and MCV, did not show significant differences when analyzed about sleep quality. These findings suggest that variations in sleep quality may not be directly linked to these demographic or clinical parameters in the studied population (Table 2).

The analysis of the correlation between sleep quality levels and inflammatory and anemia indices reveals notable findings regarding odds ratios (ORs). In the unadjusted model, the OR for the ESR indicated a slight positive non-significant association with poor sleep quality, and the CRP showed a marginally decreased likelihood of elevated levels of poor sleep quality with non-significant value. For Hb, the OR suggests a non-significant reduced probability of lower levels associated with poor sleep, whereas mean MCV presents an OR indicating a slight increase in risk with a non-significant value. When adjusted for confounding factors, such as age, gender, ESR, CRP, HB, and MCV, all correlations also were non-significant. The ESR's OR reflects a significant positive correlation with poor sleep quality, while the CRP's OR suggests a trend toward lower levels. The adjusted analysis for Hb indicates a continued decreased likelihood of low Hb levels, and MCV shows an increased risk associated with poor sleep quality (Table 3).

Discussion

The results of our study revealed a high prevalence of poor sleep quality among RA patients, affecting 71.2% of

Table 2. The frequency distribution of demographic data, inflammatory biomarkers, and anemia indicators in included participants based on sleep quality levels

Variable		Sleep quality levels						*P* value
		Good quality (n = 17)		Poor quality (n = 42)		Mean differences		
		No.	%	No.	%	Mean	SE	
Gender	Female (n= 50)	15	30	35	70			0.635*
	Male (n = 9)	2	22.2	7	77.8			
Variable		Mean	SD	Mean	SD			
Age (year)		51.94	10.53	54.81	10.32	2.86	2.98	0.340**
ESR (mm/h)		15.65	10.32	20.38	13.96	4.73	3.99	0.241**
CRP (mg/L)		6.30	5.96	5.05	5.72	1.25	1.69	0.456**
Hb (g/dL)		13.10	0.80	12.88	1.23	0.22	0.27	0.501**
MCV (fL)		85.40	3.72	87.03	5.61	1.63	1.48	0.274**

ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein; Hb: Hemoglobin; MCV: Mean corpuscular volume; SD: Standard deviation; SE: Standard error.
*Chi-square, **Independent T-test.

Table 3. The association between sleep quality levels with inflammatory and anemia indices using univariate and multivariate logistic regression

Inflammatory and anemia indices		Sleep quality levels (good/poor)			
				95% CI	
		P value	OR	Lower	Upper
Unadjusted	ESR (mm/h)	0.242	1.02	0.98	1.07
	CRP (mg/L)	0.452	0.96	0.87	1.06
	Hb (g/dL)	0.495	0.83	0.49	1.41
	MCV (FL)	0.272	1.06	0.94	1.20
Adjusted	ESR (mm/h)	0.053	1.08	1.00	1.15
	CRP (mg/L)	0.060	0.86	0.74	1.01
	Hb (g/dL)	0.489	0.79	0.40	1.55
	MCV (fL)	0.47	1.11	0.96	1.29

ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein; Hb: Hemoglobin; MCV: Mean corpuscular volume; OR: Odds ratio; CI: Confidence interval.

the study population. This result is consistent with earlier studies that highlight significant sleep disturbances in this population; the study by Yaseen et al reported that the prevalence of poor sleep quality among patients with RA is notably high, with an indicated rate of around 75.32% (5). A systematic review by Zhang et al indicated that RA patients exhibit higher scores across all domains of the PSQI, with a relative risk of 2.37 for sleep disturbances compared to healthy individuals, reinforcing the notion that sleep issues are prevalent in RA patients (7). Another study reported that up to 92% of RA patients experienced poor sleep quality, emphasizing the severity of this issue (8). However, a lower prevalence of 41.75% was noted in a cross-sectional study by Juárez-Rojop et al, suggesting variability that may be influenced by demographic factors or differences in assessment methodologies (13). Overall, these findings underscore the critical need for targeted interventions to address sleep quality in RA patients, as poor sleep is associated with increased disease activity, anxiety, and depression, ultimately affecting their overall quality of life. Addressing these interconnected issues is vital for improving patient outcomes and enhancing their daily functioning.

Our analysis demonstrated that poor sleep quality was not associated with inflammatory markers, including ESR and CRP. The finding that poor sleep quality in RA patients is not associated with inflammatory markers aligns with some prior studies but contrasts with others. A meta-analysis investigating the effects of n-3 unsaturated fatty acids on RA revealed no significant correlation between changes in CRP and ESR levels and anti-inflammatory effects, suggesting that these markers may not always reflect systemic or subjective health outcomes like sleep quality (14). Similarly, a systematic review of the acute effects of exercise in RA patients found no significant changes in CRP and ESR post-exercise, despite improvements in other health parameters, further questioning the direct link between inflammatory markers and non-inflammatory symptoms like sleep disturbances (15). However, other studies have reported associations between inflammation and poor sleep outcomes, such as pro-inflammatory diets correlating with worse sleep quality, though these results remain inconsistent (16). Overall, these findings suggest that while inflammatory markers like ESR and CRP are critical for assessing disease activity, they may not adequately capture the multifactorial contributors to poor sleep quality in RA. This highlights the need for a broader approach to understanding and managing sleep disturbances in RA patients, considering psychological, behavioral, and lifestyle factors alongside inflammation.

The finding from our study that poor sleep quality did not correlate significantly with anemia markers such as Hb and MCV is consistent with some previous research but diverges from others. For instance, in contrast to our study, a study by Fitria et al focusing on adolescent girls found a significant relationship between sleep quality and anemia symptoms (17). Another study has indicated potential links between sleep quality and nutritional factors that contribute to anemia, highlighting the complexity of these interrelationships (18). Overall, the lack of a significant correlation in our findings suggests that while anemia may impact overall health, its direct influence on sleep quality in RA patients may be limited. This emphasizes the need for further research to explore the multifaceted nature of sleep disturbances in relation to anemia and other health indicators, considering psychological and lifestyle factors that could also play a role.

Conclusion
The results indicated that 71.2% of RA patients experienced poor sleep quality, and notably, this poor sleep quality did not show any correlation with inflammatory and anemia markers. In conclusion, the study highlights a concerning prevalence of poor sleep quality among RA patients. Despite the significant impact of sleep disturbances on overall health and quality of life, the absence of a statistically significant association between sleep quality and inflammatory and anemia markers suggests that other factors may contribute to sleep issues in this population.

These findings underscore the need for further research to explore the multifaceted nature of sleep disturbances in RA and to identify potential interventions that could improve sleep quality and, consequently, patient well-being.

Limitations of the study

First, the cross-sectional design limits the ability to determine causal associations between sleep quality and inflammatory or anemia markers, as data were collected at a single point in time. Additionally, the reliance on self-reported questionnaires for sleep quality assessments may introduce bias, as participants' perceptions of their sleep may not accurately reflect objective sleep patterns. Furthermore, the sample size of 59 patients may limit the generalizability of the findings to the broader RA cases. Lastly, potential confounding factors such as psychological conditions, medication use, and lifestyle habits were not extensively controlled for, which could influence both sleep quality and inflammatory/anemia indicators. Future studies should consider longitudinal designs with larger sample sizes and comprehensive assessments of potential confounders to provide a more nuanced understanding of the association between sleep disorders and inflammatory markers in RA patients.

Authors' contribution
Conceptualization: Parisa Delkash and Amirhossein Shahbazi.
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Project management: Amir Behnam Kharazmi.
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Supervision: Parisa Delkash.
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Writing–original draft: All authors.
Writing–review and editing: All authors.

Conflicts of interest
The authors declare no conflict of interest.

Ethical issues
The research was conducted in accordance with the principles of the Declaration of Helsinki. This study is a component of the MD thesis by Amirhossein Shahbazi (Thesis#43004713), with ethical approval (IR.SBMU.MSP.REC.1401.574; https://ethics.research.ac.ir/EthicsProposalView.php?id=312378) approved by Iran University of Medical Sciences, Tehran, Iran. Prior to any intervention, all participants provided written informed consent. Additionally, the authors have carefully observed ethical guidelines, including avoiding plagiarism, data fabrication, and double publication.

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