ABCResearch

Arch Basic Clin Res 2025;7(3):186-192
DOI: 10.4274/ABCR.2025.25354

Research Article

C-reactive Protein/Albumin Ratio as a Predictor of Comorbidity in Migraine and Restless Legs Syndrome

Gülhan Sarıçam[1], Fahrettin Ege[2], Memet Aslanyavrusu[3]

[1]Clinic of Neurology, Ankara Pursaklar State Hospital, Ankara, Türkiye
[2]Clinic of Neurology, Ankara WM Medical Park Hospital, Ankara, Türkiye
[3]Clinic of Neurology, Kayseri Training and Research Hospital, Kayseri, Türkiye

Cite this article as: Sarıçam G, Ege F, Aslanyavrusu M. C-reactive protein/albumin ratio as a predictor of comorbidity in migraine and restless legs syndrome. *Arch Basic Clin Res*. 2025;7(3):186-192.

ORCID IDs of the authors: G.S. 0000-0002-9032-6877, F.E. 0000-0001-9502-7510, M.A. 0000-0001-8771-3860.

ABSTRACT

Objective: The C-reactive protein/albumin ratio (CAR) is a reliable biomarker in the assessment and monitoring of inflammation. In this study, we aimed to investigate CAR rates in migraine alone and migraine with restless legs syndrome (RLS) and their relationship with migraine frequency, severity, and disease duration.

Methods: A total of 210 patients included in the study were grouped as those with only migraine and those with migraine accompanied by RLS. Variables between the groups were interpreted using a t-test and a Mann-Whitney U analysis. The relationship between CAR and variables was analyzed in migraine patients with RLS using Spearman's rho correlation coefficient.

Results: In patients with migraines with RLS, disease duration (t=-2.496, P = 0.013) was prolonged, and attack frequency (t=-3.971, P < 0.001) significantly increased compared to patients with migraines without RLS. In migraine patients with RLS, the values of CAR (z=-3.396, P = 0.001) and CRP (z=-3.704, P < 0.001) were higher. High CAR values were found to be a risk factor for prolonged disease duration (r = 0.281, P = 0.030) and increased attack frequency (r = 0.260, P = 0.044) in migraine patients with RLS.

Conclusion: CAR levels were significantly higher in migraine patients with comorbid RLS compared to those with migraine alone, showing a positive correlation with disease duration and attack frequency. These findings suggest that CAR could serve as a valuable biomarker for identifying chronicity and RLS comorbidity in migraine patients.

Keywords: Migraine, restless legs syndrome, C-reactive protein/albumin ratio

INTRODUCTION

Migraine is a primary headache that affects 14% of adults worldwide and is the second leading cause of disability. It is characterized by severe, unilateral, and throbbing pain, often accompanied by nausea, phonophobia, photophobia, and vomiting.[1] The pathophysiology of migraine is believed to be associated with the activation of the trigeminovascular pathway, which innervates the dura mater and large cerebral arteries, resulting in neuropeptide release and subsequent neurogenic inflammation.[2] Neurogenic inflammation has been shown to be mediated by pro-inflammatory cytokines, second messengers, and chemokines released from activated central nervous system cells.[3]

Restless legs syndrome (RLS) is a common sensorimotor disorder marked by an uncontrollable urge to move the legs, affecting 4% to 29% of the general population.[4] The increased prevalence of RLS in various inflammatory and autoimmune diseases, such as diabetes, multiple sclerosis, kidney disease, and rheumatoid arthritis, suggests the potential role of inflammatory factors in its pathogenesis.[5] Previous studies have consistently demonstrated that the incidence of RLS is higher in migraine patients compared to the general population.[6] Moreover, both conditions predominantly affect women and

Corresponding author: Gülhan Sarıçam, **E-mail:** gulhansar01@hotmail.com

Received: March 22, 2025 **Last Revision Received:** September 1, 2025
Revision Requested: July 21, 2025 **Accepted:** September 10, 2025 **Publication Date:** November 17, 2025

share abnormalities in iron metabolism, the dopaminergic pathway, and the endogenous opioid system, prompting research into potential shared etiological mechanisms.[7]

C-reactive protein (CRP) is a molecule whose level increases in the blood in inflammatory and infectious conditions, and is frequently used in the prognosis and treatment of some diseases.[8] Albumin is a negative acute phase reactant plasma protein associated with disease severity and mortality, and it decreases in inflammation.[9] The C-reactive protein/albumin ratio (CAR) has recently been used as a reliable biomarker in evaluating and monitoring inflammation, especially in chronic processes.[10] Although the elevation of CRP and inflammatory cytokines in migraine and RLS has been shown separately, to our knowledge, there is no study in the literature investigating CAR rates in the co-occurrence of these diseases.[11,12] Therefore, in our study, we aimed to examine CAR rates in patients with migraine and those with both migraine and RLS, and their relationship with migraine frequency, severity, and disease duration.

MATERIAL AND METHODS

Study Design and Participants

This study retrospectively included 210 patients diagnosed with either migraine or migraine with RLS who applied to our hospital's neurology outpatient clinic between January 2021 and January 2024. Ethics committee approval number 247 was received from Kayseri City Hospital Non-Interventional Clinical Research Ethics Committee for the study on 26.11.2024. While preparing the study, the planning was conducted in accordance with the rules of the Declaration of Helsinki. Since the study was retrospective, only verbal consent was obtained.

Inclusion criteria were a confirmed diagnosis of migraine and/or RLS, and the absence of chronic inflammatory diseases, neoplasms, immunodeficiencies, or chronic conditions such as diabetes mellitus, arterial hypertension, thyroid dysfunction, chronic kidney disease, liver disorders, and hematologic abnormalities. Patients were excluded if their data were unavailable, if they had a history of infection within the last month, if they were pregnant, or if they were under the age of 18.

Migraine diagnoses were made according to the International Classification of Headache Disorders, while RLS was diagnosed using established clinical criteria.[1,13] As a result, 150 patients with migraine alone and 60 patients with comorbid RLS were included in the study. Each patient's visual analog scale (VAS) score and Migraine Disability Assessment (MIDAS) score were recorded.[14] MIDAS is a questionnaire consisting of five items that assess headache-related disability; it categorizes patients into grades I to IV, with higher scores indicating more severe disability. If the total number of days lost by the patient in the last 3-month period is between 0-5, the MIDAS score is considered I; if the number of days lost is between 6-10, the MIDAS score is considered II; if the number of days lost is between 11-20, the MIDAS score is considered III; and if the number is 21 +, the MIDAS score is considered IV. The VAS is a widely used tool to measure pain intensity on a scale from 0 to 10.

Blood parameters, including hemoglobin, white blood cell count, ferritin, total iron-binding capacity (TIBC), CRP, and albumin levels, were retrospectively obtained from medical records. CAR value was obtained by dividing CRP (mg/dL) by albumin (g/dL). CAR = CRP (mg/dL)/albumin (g/dL).[10]

Statistical Analysis

Data from a total of 210 patients, including those with migraines and those with comorbid RLS, were analyzed using IBM SPSS Statistics for Windows, Version 22.0 (IBM Corp., Armonk, NY, USA). The normality of the distribution of continuous variables was assessed using the Kolmogorov-Smirnov test. For variables showing a normal distribution, the Independent Samples t-test was used to compare the migraine and migraine with RLS groups; for those not normally distributed, the Mann-Whitney U test was applied.

Categorical variables were analyzed using the Pearson chi-square test. The Kruskal-Wallis test was used to assess differences in CAR values across different grades of the MIDAS (Migraine Disability Assessment) questionnaire. In the subgroup of migraine patients with RLS, relationships between continuous variables such as CAR values, attack frequency, and disease duration were examined using Spearman's rho correlation coefficient. A P value of < 0.05 was considered statistically significant.

The power of the study was calculated using the G*Power version 3.1.9.7 software. The effect size was determined to be 2.03. Based on this effect size and a total sample size of 210 participants (150 in the migraine group and 60 in the migraine + RLS group), the statistical power of the study was calculated as 100% at the 0.05 significance level.

In addition, a receiver operating characteristic (ROC) curve analysis was performed to evaluate the diagnostic performance of the CAR in predicting the presence of RLS in migraine patients. The optimal cut-off point for CAR was determined using Youden's index. Sensitivity, specificity, and the area under the curve (AUC) were calculated to assess the discriminatory ability of CAR values between the two groups.

MAIN POINTS

- The C-reactive protein/albumin ratio (CAR) emerges as a biomarker of chronic inflammation in patients with migraine and restless legs syndrome (RLS).
- A high CAR value shows a positive correlation with attack frequency and disease duration.
- The comorbidity of migraine and RLS negatively affects the clinical course of migraine.

RESULTS

We analyzed a total of 210 patients, 150 with migraine and 60 with migraine with RLS. The mean age of migraine patients was 42.20 ± 10.59, and 76% (n=114) were female. The mean age

of the migraine with RLS group was 43.17 ± 10.18, and 81.7% (n=49) were female. No difference was found between the groups regarding aura, family history, and migraine severity (*P* = 0.767, *P* = 0.222, *P* = 0.156, respectively). Although MIDAS grade 1 (21.7%) was less common and grade 3 (16.7%) and 4 (25.0%) were more common in the migraine with RLS group, this did not create a statistically significant difference (*P* = 0.156). The duration of the disease (t=-2.496, *P* = 0.013) was significantly prolonged in individuals with migraine and RLS compared to those with only migraine. When evaluated in terms of attack frequency, a statistically significant increase was found in those with migraine with RLS (t=-3.971, *P* < 0.001). (Table 1)

When the groups were compared in terms of blood parameters, hemoglobin (z=-2.100, *P* = 0.036) and albumin (t =2.446, *P* = 0.015) values were found to be statistically significantly lower in the in the migraine with RLS group. CAR (z =-3.396, *P* = 0.001) and CRP (z=-3.704, *P* < 0.001) values were significantly higher in migraineurs with RLS than in those without. (Table 2)

Table 1. Demographic Characteristics of Patients by Groups

	Migraine (n=150)	**Migraine + RLS (n=60)**		
	n (%)	**n (%)**	**Chi-square**	***P***
Gender				
Female	114 (76.0)	49 (81.7)	0.792	0.373
Male	36 (24.0)	11(18.3)		
Aura				
No	125 (83.3)	51(85.0)	0.088	0.767
Yes	25 (16.7)	9 (15.0)		
Family history				
Yes	33 (22.0)	18 (30.0)	1.492	0.222
No	117 (78.0)	42 (70.0)		
MIDAS				
Grade 1	49 (32.7)	13 (21.7)		
Grade 2	60 (40.0)	22 (36.7)	5.222	0.156
Grade 3	13 (8.7)	10 (16.7)		
Grade 4	28 (18.7)	15 (25.0)		
	Mean ± SD	**Mean ± SD**	**t**	***P***
Duration of disease (month)	45.4 ± 30.2	59 ± 34.9	-2.496	**0.013**
Frequency (number/month)	5.23 ± 3.23	7.55 ± 4.14	-3.971	**< 0.001**
Age	42.20 ± 10.59	43.17 ± 10.18	-0.604	0.546
VAS	8.19 ± 1.28	8.50 ± 1.28	-1.565	0.119

Chi-square, Pearson chi-square test; t, Independent Samples t-test; *P* , *P* < 0.05; RLS, restless legs syndrome; MIDAS, Migraine Disability Assessment; VAS, visual analogue scale; SD, standard deviation.

Table 2. Biochemical Test Results and Differences by Groups

	Migraine (n=150)		**Migraine + RLS (n=60)**		**Statistical test**	***P***
	Mean ± SD	**Median (min-max)**	**Mean ± SD**	**Median (min-max)**		
Hb (g/dL)	13.49 ± 2.01	13.5 (4-17.9)	12.87 ± 1.89	13.05 (7-16.7)	-2.100z	**0.036**
WBC (×10³ µL)	7.29 ± 1.41		7.47 ± 1.39		-0.809t	0.419
Ferritin (ng/mL)	39.11 ± 42.03	22.2 (0.04-230)	34.19 ± 44.64	23 (1.2-310.4)	-0.723z	0.470
TIBC (ug/dL)	374.93 ± 59.54		387.48 ± 58.75		-1.386t	0.167
CRP (mg/L)	0.41 ± 0.72	0.2 (0-5.8)	0.56 ± 0.71	0.37 (0.04-4)	-3.396z	**0.001**
Albumin (g/dL)	3.87 ± 0.82		3.55 ± 0.92		2.446t	**0.015**
CAR	0.11 ± 0.21	0.05 (0-1.61)	0.18 ± 0.24	0.12 (0.01-1.38)	-3.704z	**< 0.001**

t, Independent Samples t-test; z, Mann-Whitney U test; *P*, *P* < 0.0; Hb, hemoglobin; WBC, white blood cell; TIBC, total iron binding capacity; CRP, C-reactive protein; CAR, C-reactive protein/albumin ratio; SD, standard deviation.

Table 3. Clinical Features and CAR Relationship in Migraine Patients with RLS

	CAR		Statistical test	*P*
	Mean ± SD	**Median (min-max)**		
Gender				
Female	0.19 ± 0.25	0.12 (0.01-1.38)	z=-0.603	0.547
Male	0.12 ± 0.11	0.11 (0.03-0.37)		
Aura				
No	0.20 ± 0.25	0.12 (0.01-1.38)	z=-1.120	0.263
Yes	0.10 ± 0.08	0.09 (0.01-0.22)		
Family history				
Yes	0.18 ± 0.19	0.08 (0.02-0.63)	z=-0.089	0.929
No	0.18 ± 0.25	0.13 (0.01-1.38)		
MIDAS				
Grade 1	0.05 ± 0.04	0.04 (0.01-0.17)		
Grade 2	0.09 ± 0.08	0.06 (0.01-0.33)	KW = 1.522	0.677
Grade 3	0.23 ± 0.15	0.17 (0.09-0.60)		
Grade 4	0.40 ± 0.35	0.24 (0.13-1.38)		
	r	***P***		
Age	0.106	0.420		
VAS	0.086	0.512		
Frequency (number/month)	0.260	**0.044**		
Duration of disease (month)	0.281	**0.030**		

z, Mann-Whitney U test; KW, Kruskal-Wallis H; r, Spearman's rho correlation coefficient; *P*, *P* < 0.05; MIDAS, Migraine Disability Assessment; VAS, visual analogue scale; CAR, C-reactive protein/albumin ratio; SD, standard deviation.

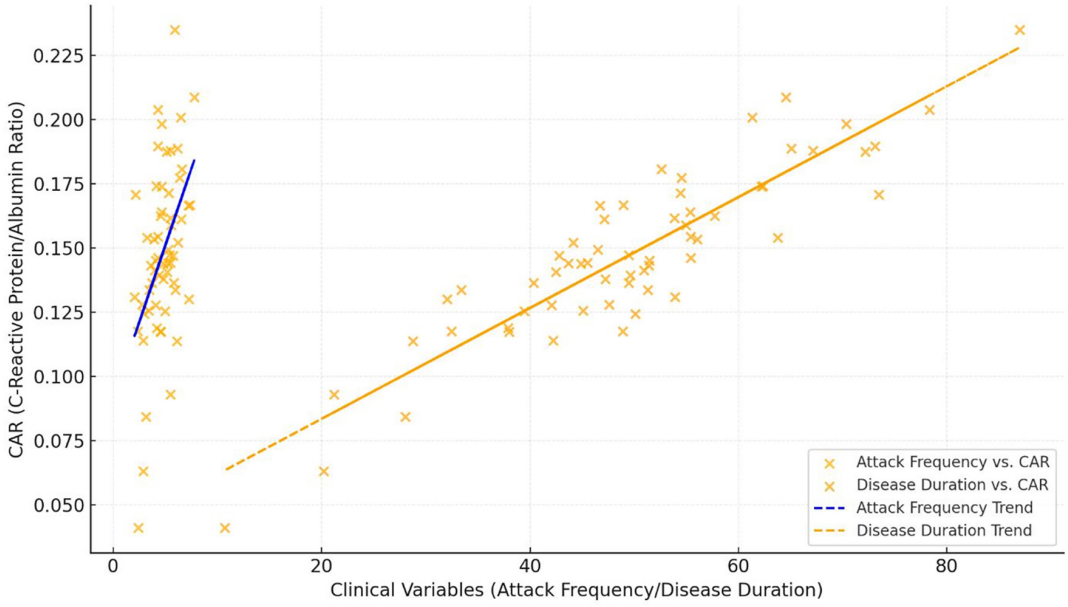

Figure 1. Chart of relationship between CAR values and attack frequency and disease duration in patients migraine with RLS.

CAR, C-reactive protein/albumin ratio; RLS, restless legs syndrome.

When clinical features of patients with RLS migraine were compared against CAR values, no differences were found regarding gender, aura, family history, and migraine severity (*P* and gt; 0.05). In the analyses performed using Spearman's rho correlation coefficient, a statistically significant, low-level positive correlation was found between attack frequency (r = 0.260, P = 0.044) and CAR, as well as between disease duration (r = 0.281, P= 0.030) and CAR. Accordingly, CAR values increased as attack frequency and disease duration increased in patients with RLS migraine (Table 3, Figure 1).

Additionally, a ROC curve analysis was performed to evaluate the diagnostic utility of the CAR value in distinguishing migraine patients with comorbid RLS from those without. The AUC ROC curve was found to be 0.650 (95% CI: 0.572-0.727, P = 0.001), indicating a fair discriminative capacity. To improve both clinical and statistical relevance, a revised cut-off value of 0.035 was selected, ensuring that specificity remained above 50%. At this threshold, the CAR value yielded a sensitivity of 53.3% and a specificity of 76.4%, with a Youden Index of 0.233. These updated findings suggest that CAR provides balanced diagnostic performance in identifying migraine patients with comorbid RLS, with moderate sensitivity and acceptable specificity (Table 4, Figure 2).

Table 4. ROC Cut-off Point for CAR in the Diagnosis of Migraine with Restless Legs Syndrome

Test	Cut-off point	Sensitivity (%)	Specitificity (%)	AUC
CAR	0.035	76.4	53.3	0.650

ROC, receiver operating characteristic; CAR, C-reactive protein/albumin ratio; AUC, area under the curve.

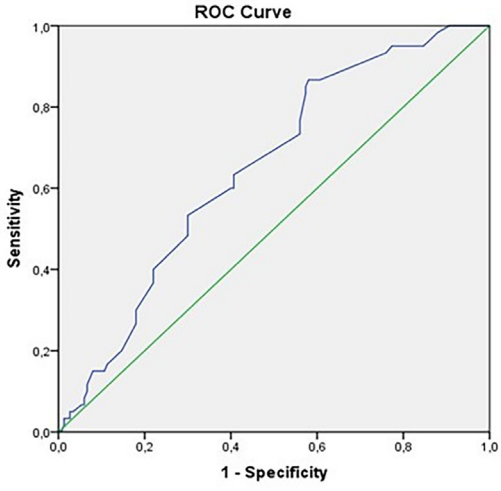

Figure 2. ROC curve for CAR in predicting migraine + RLS.

ROC, receiver operating characteristic; CAR, C-reactive protein/albumin ratio; RLS, restless legs syndrome.

DISCUSSION

We could not find a similar study in the existing literature showing the relationship between disease severity and CAR values, in patients with migraine and RLS. In this study, CAR values were higher in migraine patients with RLS compared to those with migraine alone. Our results showed that in migraine patients with RLS, high CAR values increase the risk of longer disease duration and more frequent attacks. Since high CAR values may reflect increased inflammation and a chronic disease course in migraine patients with comorbid RLS, we suggest that high CAR values could be used as a guiding biomarker for early identification of chronic migraine and for tailoring individualized preventive treatment strategies in this population. Supporting this, the ROC curve analysis demonstrated that CAR has moderate discriminative capacity in distinguishing migraine patients with and without RLS, with an area AUC of 0.650 (95% confidence interval: 0.572-0.727, P = 0.001). The optimal cut-off value for CAR was determined as 0.035, with a sensitivity of 76.4% and a specificity of 53.3%. These results suggest that CAR, while not highly specific, may be used as a sensitive screening biomarker for comorbid RLS in migraine patients.

Migraine and RLS impose a substantial burden on society due to their negative impact on quality of life and increased economic costs. Previous studies have shown both an increase in the prevalence of RLS in migraine patients compared to the healthy population and a greater likelihood that RLS accompanies migraine more often than it does other headaches.[15,16] Suzuki et al.[17] divided patients into two groups as migraine and migraine with RLS, for 7 years in their prospective study. As a result, they found significant sleep disturbances and increased MIDAS values in migraine patients with RLS compared to migraine patients without RLS. In our study, MIDAS grades 3 and 4 were higher in migraine patients with RLS compared to other migraineurs. However, this difference was not statistically significant. However, in another study comparing the relationship between chronic migraine and RLS, it was shown that RLS was associated with increased attack frequency and migraine severity.[18] Similarly, we found that attack frequency increased and disease duration was longer in migraine patients with RLS compared to migraineurs without RLS.

Sleep disturbances are known to exacerbate both the frequency and severity of migraine attacks. Patients with RLS frequently experience difficulty in initiating and maintaining sleep, which may contribute to an increase in pain perception, a reduction in pain thresholds, and impaired recovery following migraine episodes. This bidirectional interaction between RLS and migraine may explain the longer disease duration and more frequent attacks observed in patients with comorbid RLS. Supporting this, previous studies have shown that poor sleep quality is significantly associated with increased migraine severity and disability.[7,17]

Moreover, in another study, when patients were examined in terms of RLS, it was shown that the presence of migraine

significantly increased the severity of RLS.[19] These findings suggest that RLS comorbidity in migraine patients leads to increased disease severity and disability in both conditions. Understanding the shared pathophysiological processes is crucial for developing effective treatment strategies and preventing chronicity at an early stage.

Although the exact pathophysiology of RLS remains unclear, one emerging theory is brain iron deficiency, potentially caused by factors such as low peripheral iron or genetic predisposition.[4] An increase in the prevalence of RLS has been shown in the general population with iron deficiency anemia; furthermore, iron deficiency has also been associated with disease severity.[20] In our study, hemoglobin levels were low in migraine patients with RLS, but no difference was seen in ferritin and TIBC values between those with and without RLS. Similarly, Suzuki et al.[21] reported no association between RLS and serum iron or ferritin levels in migraine patients.

Chronic inflammation is characterized by elevated CRP levels and reduced albumin levels. The CAR value, which represents the ratio of these two parameters, is increasingly recognized as an indicator of inflammation and prognosis in various diseases.[23] Geng et al.[11], in a meta-analysis including 10 studies, showed that serum CRP values were increased in migraine patients compared to controls and associated this result with inflammation in migraine pathophysiology. Additionally, Sun et al.[24] reported that elevated serum CRP levels were not only associated with migraine presence but also correlated with greater migraine-related disability and severity, emphasizing its clinical relevance in the disease course. Furthermore, neurogenic inflammation characterized by neuropeptide release (such as calcitonin gene-related peptide, substance P), mast cell degranulation, vasodilation, and cytokine secretion has been increasingly recognized as a central mechanism in migraine pathogenesis.[24] In another recent study conducted on 235 migraine patients, no difference was found in CAR values between episodic and chronic migraine. In contrast, it was found to be significantly higher in patients with migraine attacks.[25] We found that CAR values were higher in migraineurs with RLS than in those without than in migraineurs. In addition, we showed that high CAR values in migraine patients with RLS are a risk factor for both prolonging the duration of the disease and increasing the frequency of attacks. We thought that increased CAR values in the combination of migraine and RLS, and the increase seen with prolonged disease indicate chronic inflammation in these patients. Our data suggest that increased CAR values in migraine patients may be a useful biomarker in understanding the chronicity of migraine and in developing RLS.

Study Limitations

The first limitation of our study was that it was a retrospective and single-institution study. Second, we excluded those with chronic diseases when determining our patient group, which significantly reduced the number of patients. For these reasons, we believe that larger and prospective studies would be useful to confirm our results. Another limitation of our study is the lack of data regarding body mass index (BMI). As elevated BMI has been associated with increased frequency and severity of both migraine and RLS, the absence of this parameter in our analysis may limit the interpretation of inflammatory mechanisms in this comorbidity.[15]

As a result, we showed that CAR values in migraine patients with RLS are higher than in migraineurs without RLS, and that high CAR values in these patients pose a risk for prolonged migraine duration and increased attack frequency. These data indicate that CAR may be a useful biomarker for determining the chronicity of the process and the development of RLS in migraine patients.

Ethics

Ethics Committee Approval: This study was approved by the Kayseri City Hospital Non-Interventional Clinical Research Ethics Committee (approval no.: 247, date: 26.11.2024).

Informed Consent: Since the study was retrospective, only verbal consent was obtained.

Conflict of Interest: The authors have no conflict of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

Footnotes

Author Contributions

Concept Design – G.S., F.E.; Data Collection or Processing – G.S., M.A.; Analysis or Interpretation – G.S., F.E.; Literature Review – F.E., M.A.; Writing, Reviewing and Editing – G.S., F.E.

REFERENCES

1. Olesen J. The international classification of headache disorders: history and future perspectives. *Cephalalgia*. 2024;44(1):3331024231214731. [CrossRef]
2. Biscetti L, Cresta E, Cupini LM, Calabresi P, Sarchielli P. The putative role of neuroinflammation in the complex pathophysiology of migraine: from bench to bedside. *Neurobiol Dis*. 2023;180:106072. [CrossRef]
3. Edvinsson JCA, Warfvinge K, Krause DN, et al. C-fibers may modulate adjacent Aδ-fibers through axon-axon CGRP signaling at nodes of Ranvier in the trigeminal system. *J Headache Pain*. 2019;20(1):105. [CrossRef]
4. Gossard TR, Trotti LM, Videnovic A, St Louis EK. Restless legs syndrome: contemporary diagnosis and treatment. *Neurotherapeutics*. 2021;18(1):140-155. [CrossRef]
5. Jiménez-Jiménez FJ, Alonso-Navarro H, García-Martín E, Agúndez JAG. Inflammatory factors and restless legs syndrome: a systematic review and meta-analysis. *Sleep Med Rev*. 2023:68:101744. [CrossRef]
6. Ghasemi H, Khaledi-Paveh B, Abdi A, et al. The prevalence of restless legs syndrome in patients with migraine: a systematic review and meta-analysis. *Pain Res Manag*. 2020;2020:2763808. [CrossRef]
7. Yang FC, Lin TY, Chen HJ, et al. Increased risk of restless legs syndrome in patients with migraine: a nationwide population-based cohort study. *Medicine (Baltimore)*. 2016;95(5):e2646. [CrossRef]

8. Ali S, Zehra A, Khalid MU, Hassan M, Shah SIA. Role of C-reactive protein in disease progression, diagnosis and management. *Discoveries (Craiova)*. 2023;11(4):e179. [CrossRef]

9. *Eckart A, Struja T, Kutz A, et al. Relationship of nutritional status, inflammation, and serum albumin levels during acute illness: a prospective study. Am J Med. 2020;133(6):713-722.* [CrossRef]

10. Aktas G. Serum C-reactive protein to albumin ratio as a reliable marker of diabetic neuropathy in type 2 diabetes mellitus. *Biomol Biomed*. 2024;24(5):1380-1386. [CrossRef]

11. Geng C, Yang Z, Xu P, Zhang H. Aberrations in peripheral inflammatory cytokine levels in migraine: a systematic review and meta-analysis. *J Clin Neurosci*. 2022;98:213-218. [CrossRef]

12. Dowsett J, Didriksen M, von Stemann JH, et al. Chronic inflammation markers and cytokine-specific autoantibodies in Danish blood donors with restless legs syndrome. *Sci Rep*. 2022;12(1):1672. [CrossRef]

13. Vlasie A, Trifu SC, Lupuleac C, Kohn B, Cristea MB. Restless legs syndrome: an overview of pathophysiology, comorbidities and therapeutic approaches (Review). *Exp Ther Med*. 2022;23(2):185. [CrossRef]

14. Benz T, Lehmann S, Gantenbein AR, et al. Translation, cross-cultural adaptation and reliability of the German version of the migraine disability assessment (MIDAS) questionnaire. *Health Qual Life Outcomes*. 2018;16(1):42. [CrossRef]

15. Valente M , Janes F, Russo V, et al. Prevalence of restless legs syndrome in migraine patients: a case-control study. Analysis of risk factors for restless legs syndrome in migraine patients. *Headache*. 2017;57(7):1088-1095. [CrossRef]

16. Gupta R, Lahan V, Goel D. Primary headaches in restless legs syndrome patients. *Ann Indian Acad Neurol*. 2012;15(Suppl 1):104-108. [CrossRef]

17. Suzuki K, Suzuki S, Haruyama Y, Kobashi G, Shiina T, Hirata K. Restless legs syndrome is associated with headache-related disabilities in patients with migraine: a prospective 7-year follow-up study. *Eur J Neurol*. 2019;26(2):238-245. [CrossRef]

18. Lucchesi C, Bonanni E, Maestri M, Siciliano G, Murri L, Gori S. Evidence of increased restless legs syndrome occurrence in chronic and highly disabling migraine. *Funct Neurol*. 2012;27(2):91-94. [CrossRef]

19. van Oosterhout WP, van Someren EJ, Louter MA, et al. Restless legs syndrome in migraine patients: prevalence and severity. *Eur J Neurol*. 2016;23(6):1110-1116. [CrossRef]

20. Bae H, Kim KT, Heo MH, Do YR, Cho YW. The prevalence and clinical characteristics of restless legs syndrome in patients with iron deficiency anemia in Korea. *J Clin Sleep Med*. 2021;17(7):1447-1452. [CrossRef]

21. Suzuki S, Suzuki K, Miyamoto M, et al. Evaluation of contributing factors to restless legs syndrome in migraine patients. *J Neurol*. 2011;258:2026-2035. [CrossRef]

22. Du Y, Lin Y, Wang A, et al. Association between the C-reactive protein to albumin ratio and poor clinical outcome in patients with spontaneous intracerebral hemorrhage. *J Stroke Cerebrovasc Dis*. 2024;33(12):108026. [CrossRef]

23. Sun S, Liu C, Jia Y, et al. Association between migraine complicated with restless legs syndrome and vitamin D. *Front Neurol*. 2021;12:777721. [CrossRef]

24. Malhotra R. Understanding migraine: potential role of neurogenic inflammation. Ann *Indian Acad Neurol*. 2016;19(2):175-182. [CrossRef]

25. Yazar HO, Yazar T, Aygün A, Kaygisiz Ş, Kirbaş D. Evaluation of simple inflammatory blood parameters in patients with migraine. *Ir J Med Sci*. 2020;189(2):677-683. [CrossRef]