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ORIGINAL RESEARCH

Dialysis Headache in Hemodialysis Patients: Is a History of Recurrent Headaches Prior to Hemodialysis a Risk Factor?

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Background: Headache is a frequent but underrecognized complication in patients undergoing hemodialysis. This study aimed to estimate the frequency and describe the clinical characteristics of dialysis headache, and to identify associated risk factors, particularly a pre-dialysis history of recurrent headaches, in patients with end-stage renal disease.

Methods: A cross-sectional study was conducted at the hemodialysis unit of King Khalid University Hospital. Data were collected from adult end-stage renal disease patients receiving maintenance hemodialysis using a structured questionnaire administered via direct interviews and phone calls.

Results: Seventy-nine patients were included; 40 (50.6%) met criteria for dialysis headache. Females were more common in the dialysis headache group, while males predominated among those without headache. Diabetes mellitus was significantly more prevalent in the non–dialysis headache group. A prior history of headaches was associated with dialysis headache. Most dialysis headaches were of moderate intensity, described as dull or throbbing, or with mixed characteristics, typically located in the temporal or frontotemporal regions and lasting about five hours. Diastolic blood pressure during dialysis was significantly lower in patients with dialysis headache. On multivariate analysis, female sex and prior headache history were independently associated with dialysis headache, whereas diabetes mellitus was associated with a lower likelihood of DH.

Conclusion: Dialysis headache was observed in a substantial proportion of patients with end-stage renal disease undergoing hemodialysis. A history of recurrent headaches, female sex, and lower intradialytic diastolic blood pressure were associated with dialysis headache, while diabetes mellitus showed an inverse association. Given the cross-sectional design, single-center setting, and relatively small sample size, the findings should be considered exploratory. Further multicenter studies with larger sample sizes are needed to confirm these findings and better elucidate the underlying mechanisms.

Plain Language Summary: Patients with end-stage renal disease who undergo hemodialysis often experience headaches during or after dialysis sessions, a condition known as dialysis headache. Despite being common, this condition is often overlooked in clinical practice. In this study, we found that about half of the patients receiving hemodialysis experienced dialysis headaches. These headaches typically occurred during the second half of the dialysis session, were of moderate intensity, and resolved within 24 hours. We also found that patients who had a history of headaches before starting the dialysis program were more likely to develop dialysis headaches. Additionally, female patients were at higher risk, while patients with diabetes appeared less likely to experience these headaches.

These findings highlight the importance of recognizing dialysis headache and identifying patients at higher risk. Improved awareness may help clinicians better manage this condition and improve patients' quality of life.

Keywords: dialysis headache, end-stage renal disease, hemodialysis, headache classification, risk factors

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Introduction

Hemodialysis is an effective therapeutic intervention for reducing morbidity, mortality, and enhancing the quality of life in patients with end-stage renal disease.[1] However, its implementation is frequently complicated by various neurological manifestations that affect the central or peripheral nervous system. Such complications include dialysis dementia, dialysis disequilibrium syndrome, hypertensive encephalopathy, stroke, and headache.[2]

Headache is a common symptom experienced by patients undergoing hemodialysis. It has been suggested that hemodialysis-related headache affects anywhere from 28% to 73% of hemodialysis patients. These headaches can occur during and after the dialysis sessions.[3–5]

Headache during hemodialysis, now called Dialysis Headache (DH), was first described in 1972 by Bana et al[6] According to the third edition of the International Classification of Headache Disorders (ICHD-3), DH is characterized as a headache with no distinct features that occurs during and is caused by hemodialysis, and that worsens during the hemodialysis and/or subsides spontaneously within 72 hours following the completion of haemodialysis.[7]

The characteristics of DH are little studied.[4,8–10] This headache has been frequently described as bilateral, fronto-temporal in location, either throbbing or dull, moderate in severity, and associated with photophobia and phonophobia as the most common reported associated symptoms.[9,10]

The pathophysiology of DH is not fully understood. Previous studies have shown that variations in blood pressure, in body weight, blood urea nitrogen (BUN) levels, sodium and magnesium levels, and serum osmolality could all be possible triggers for the development of DH.[3] Variations in calcitonin gene-related peptide (CGRP), substance P, and changes in cerebral vasculature during dialysis may also contribute to the pathophysiology of DH.[10,11]

In the literature, studies evaluating the association between primary headaches and DH have yielded conflicting results. One prospective study investigating the presence of primary headache disorder before the initiation of hemodialysis treatment found that 68% of the study cohort with DH reported having headaches prior to beginning hemodialysis.[8] The majority of patients in this study with DH had a diagnosis of migraine without aura (30.5%) and episodic tension-type headache (18.6%), suggesting that pre-existing primary headache disorders may be associated with DH.[8] However, another study found no association between migraine or tension-type headache and DH.[10] These discrepancies may be related to differences in study design, patient populations, and whether pre-existing headaches were distinguished from those developing after dialysis initiation. From a pathophysiological perspective, patients with pre-existing primary headache disorders such as migraine or tension-type headache, may exhibit increased susceptibility to DH due to altered pain processing, central sensitization, and shared neurovascular mechanisms.[11–13]

In Saudi Arabia, the number of End Stage Renal Disease (ESRD) patients undergoing dialysis was estimated in 2021 to be more than 20,000 patients.[14] Despite the estimated high number of dialysis patients in Saudi Arabia, research on the occurrence of DH in this population is scarce. To address this gap, we aimed to investigate the frequency, characteristics, and associated factors of DH among Saudi patients with ESRD who are receiving hemodialysis. Additionally, we aimed to determine whether there is an association between a previous history of primary headache disorders and the increased risk of developing DH. We hypothesized that a prior history of recurrent headaches is associated with an increased likelihood of developing DH in patients undergoing hemodialysis.

Methods

In this study, adult patients (≥18 years old) with ESRD who attended hemodialysis sessions in King Khalid University Hospital's hemodialysis unit from June 2021 to April 2022 were included. To meet the inclusion criteria, patients must have been on a regular dialysis program for at least 6 months and be able to provide the required information concerning this study, including the presence or absence of headache during hemodialysis. Patients who have cognitive impairment had been excluded.

All recruited patients in this study provided written informed consent. This study was approved by the Institutional Review Board (IRB) for Health Sciences Colleges Research on Human Subjects, King Saud University, Riyadh, Saudi Arabia.

Hemodialysis patients were enrolled on various weekdays and interviewed onsite by the investigating team during their hemodialysis sessions. All patients who attended these hemodialysis sessions were enrolled during their visit to the

hemodialysis units. However, some patients were interviewed later through phone calls due to scheduling conflicts, early discharge from the dialysis center, or their preference for remote communication. Each patient was interviewed once during the study period.

During the interview, hemodialysis patients were given a structured questionnaire consisting of 22 items distributed across three domains: demographic data (5 items; eg, age and sex), clinical characteristics (7 items; eg, comorbidities, dialysis parameters, and blood pressure measurements), and headache-related features (10 items; eg, onset, duration, location, intensity, self-reported history of prior headache attacks and associated symptoms).

Hemodialysis patients who reported having a history of headache attacks after initiating hemodialysis were asked further detailed questions about their headache characteristics, including the character, location, timing, duration, and any associated features, such as photophobia, phonophobia, nausea, and vomiting, with their headache. The intensity of these headache attacks was quantified using the Visual Analogue Scale (VAS).

Patients were considered to have DH if they met the diagnostic criteria of ICHD-3 by having at least three episodes of headache; each episode developed or got worse during the hemodialysis session and resolved within 72 hours after the end of the session.[7]

All hemodialysis patients were asked about any previous history of headache attacks prior to initiating the hemodialysis program, including the frequency of their headache attacks before starting hemodialysis. Potential triggers for headache during hemodialysis were also considered by asking hemodialysis patients about excessive caffeine intake, smoking, and drugs. Patients were defined as excessively using caffeine when they reported having more than three cups of coffee daily. All patients were prescribed standard online hemodiafiltration, administered four hours per session, three times a week.

Data were analyzed using SPSS (IBM Corp., Version 27.0, New York, USA). Categorical variables are presented as frequencies with percentages. The Shapiro–Wilk test was conducted to assess the distribution pattern of continuous variables. Normally distributed variables are reported as mean ± standard deviation (SD), while non-normally distributed variables are presented as median with interquartile range (IQR). Statistical significance was determined using the chi-square test for categorical variables and the independent samples *t*-test for normally distributed continuous variables. A p-value of less than 0.05 was considered statistically significant.

A multivariate logistic regression analysis model was employed to identify factors associated with DH. Variables included in the model were selected based on prior literature and clinical relevance.[4,15,16] The variables included in the model were age, sex, hypertension, diabetes mellitus (DM), prior headache history, smoking, and caffeine intake. The reference categories were male sex, age ≥65 years, absence of DM, no prior history of headache, absence of hypertension, no caffeine intake, and non-smoking status. Standard assumptions of logistic regression were considered during the analysis.

Results

A total of 83 were interviewed during this study. Four patients were excluded due to incomplete interview data or declining participation, leaving 79 patients who were included in the study. Out of the 79 hemodialysis patients, 40 (50.6%) had DH. Females were significantly more represented in the DH group 20 (50.0%) compared to the non-DH group 9 (23.1%) (p = 0.013), while males were predominant in the non-DH group 30 (76.9%). Most patients in both groups were aged between 45 and 64 years. Hypertension was common in both groups 29 (76.3%) vs. 29 (82.9%) (p = 0.490), with no significant difference. Diabetes Mellitus was significantly more prevalent in the non-DH group 23 (59.0%) than the DH group 13 (32.5%) (p = 0.018). Hypertension was the most common etiology of ESRD in the DH group, while DM was more common in the non-DH group. There were no significant differences between groups in age distribution, caffeine use, smoking, mean hemodialysis duration, or the number of weekly sessions. A history of headaches prior to starting hemodialysis was significantly more frequent in patients with DH 26 (65.0%) compared to those without 13 (33.3%) (p = 0.005). Among those with a prior headache history, the most reported frequency in both groups was 1–2 days per week (Table 1).

In the DH group, moderate headache intensity was most common 21 (52.5%). Patients described the headache characteristics as throbbing 11 (27.5%), dull 12 (30.0%), heaviness 1 (2.5%), or a combination of all these headache characteristics 16 (40.0%) and typically located in the temporal 10 (25.0%) or frontotemporal regions 14 (35%). The average headache duration

Table 1 Demographics and Clinical Characteristics Stratified by Dialysis Headache (DH)

Parameter	With DH (n=40)	Without DH (n=39)	p-value
Sex			0.013*
- Male	20 (50.0%)	30 (76.9%)	
- Female	20 (50.0%)	9 (23.1%)	
Age group			0.593
– 18–44	14 (35.0%)	10 (25.6%)	
– 45–64	16 (40.0%)	16 (41.0%)	
– 65+	10 (25.0%)	13 (33.3%)	
BMI (median [IQR])	25.2 [22.3–31.0]	23.8 [20.9–28.5]	0.3102
Hypertension	29 (76.3%)	29 (82.9%)	0.490
Diabetes Mellitus	13 (32.5%)	23 (59.0%)	0.018*
Caffeine Users	5 (12.5%)	6 (15.4%)	0.711
Smokers	5 (12.5%)	5 (12.8%)	0.966
ESRD etiology:			
Hypertension	16 (40%)	10 (25.6%)	
Diabetes	5 (12.5%)	11 (28.2%)	
Glomerular disease	3 (7.5%)	3 (7.7%)	
Urinary obstruction	2 (5%)	2 (5.1%)	
Cystic kidney disease	2 (5%)	1 (2.6%)	
Unrecovered AKI	1 (2.5%)	2 (5.1%)	
Malignancy	1 (2.5%)	1 (2.6%)	
Unknown	10 (25%)	9 (23%)	
History of prior attacks of headache	26 (65.0%)	13 (33.3%)	0.005*
Frequency of prior attacks of headache†:			0.582
- 1–2/week	15 (57.7%)	8 (61.5%)	
– 3–4/week	3 (11.5%)	3 (23.1%)	
– 5–7/week	4 (15.4%)	1 (7.7%)	
Mean HD duration (hours)	3.9 ± 0.3	3.9 ± 1.9	0.272
HD Sessions per Week	3.00 ± 0.00	3.00 ± 0.00	> 0.999

Notes: *Statistically significant ($p < 0.05$). P-values were calculated using the chi-square test for categorical variables and the independent samples *t*-test for continuous variables. † Analysis includes only patients with a prior history of headache.

was 5.2 ± 5.4 hours. Photophobia 6 (15.0%) and nausea 5 (12.5%) were the most common associated symptoms, while other symptoms such as blurred vision, chest pain, and scalp numbness were reported less frequently. Most headaches began during the latter half of HD sessions, and all resolved within 72 hours post-HD (Table 2).

Blood pressure measurements were numerically lower among patients with DH compared to those without, with a statistically significant difference observed in diastolic pressure during hemodialysis (61.1 ± 14.7 mmHg vs. 68.7 ± 14.7 mmHg, $p = 0.028$) (Table 3).

A multivariable logistic regression model revealed that female sex was associated with a significantly higher risk of DH (OR = 3.25, 95% CI 1.03–10.33; $p = 0.045$). A history of prior headache episodes was the most substantial associated risk factor, quadrupling the odds of developing DH (OR = 4.08, 95% CI 1.42–11.75; $p = 0.009$). On the contrary, the presence of DM was independently protective (OR = 0.28, 95% CI 0.09–0.90; $p = 0.033$). Age, hypertension status, high caffeine intake, and current smoking did not show significant associations with DH (all $p > 0.05$) (Figure 1).

Table 2 Dialysis Headache Features and Characteristics (n=40)

Feature	Value (n, %) or Mean ± SD
Headache Intensity (VAS)*	Mild: 14 (35%) Moderate: 21 (52.5%) Severe: 5 (12.5%)
Headache Character	Throbbing: 11 (27.5%) Dull: 12 (30%) Heaviness: 1 (2.5%) Combination of all above: 16 (40%)
Headache Location	Temporal: 10 (25%) Occipital: 9 (22.5%) Frontotemporal: 14 (35%) Generalized: 7 (17.5%)
Average Headache Duration (hours)	5.2 ± 5.4
Associated Symptoms	Photophobia: 6 (15%) Nausea: 5 (12.5%) Blurred vision: 1 (2.5%) Chest pain: 1 (2.5%) Scalp numbness: 1 (2.5%)
Headache starts during the second half of hemodialysis sessions	23 (57.5)
Headache resolves within 72h of the hemodialysis sessions	40 (100)

Notes: *VAS: Mild (1–3), Moderate (4–6), Severe (7–10).

Table 3 Comparison of Blood Pressure Measurements Between Patients with and Without DH

Blood Pressure Parameter	With DH (n=40)	Without DH (n=39)	p-value
Pre-HD systolic, mean ± SD	139.5 ± 29.7	140.1 ± 29.9	0.932
Pre-HD diastolic, mean ± SD	65.1 ± 17.1	69.8 ± 17.3	0.227
During HD systolic, mean ± SD	126.9 ± 25.3	137.3 ± 31.1	0.107
During HD diastolic, mean ± SD	61.1 ± 14.7	68.7 ± 14.7	0.028*
Post-HD systolic, mean ± SD	129.4 ± 24.9	133.7 ± 24.9	0.448
Post HD diastolic, mean ± SD	62.1 ± 12.5	67.6 ± 13.0	0.058

Notes: *Statistically significant ($p < 0.05$). P-values were calculated using the independent samples *t*-test.

Discussion

In this study, DH was observed in a substantial proportion of patients with ESRD undergoing hemodialysis. The observed associations with female sex and a prior history of headache suggest that individual susceptibility factors may contribute to the development of DH. In contrast, the inverse association observed with DM warrants further investigation. Additionally, the association with lower intradialytic diastolic blood pressure highlights the potential role of hemodynamic changes during dialysis in triggering headache.

Most patients with DH (65%) in our ESRD cohort reported a prior history of headaches before initiating hemodialysis, and multivariate analysis demonstrated approximately fourfold higher odds of DH in these individuals. This finding suggests an underlying neurobiological susceptibility related to altered pain processing, whereby patients with pre-

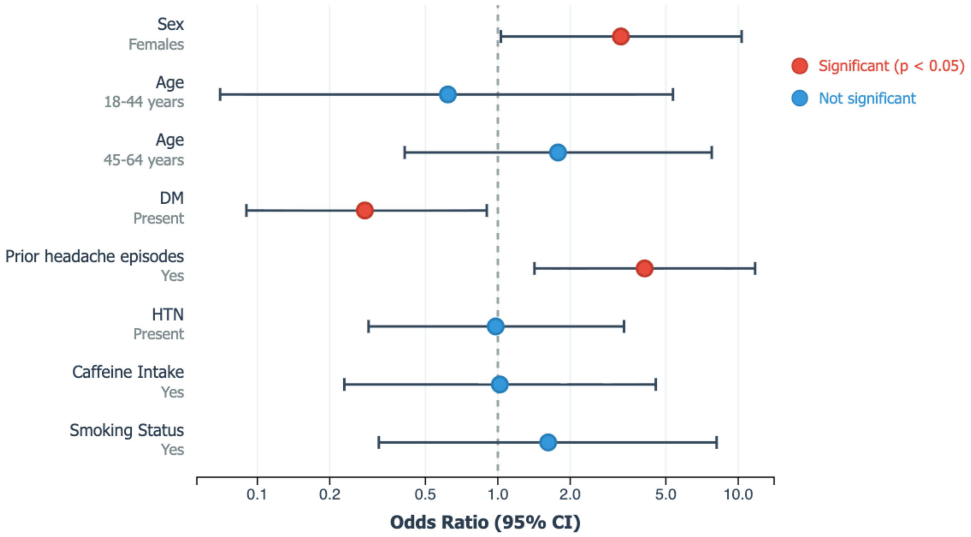

Figure 1 Forest plot showing odds ratios (ORs) and 95% confidence intervals (CIs) from multivariate logistic regression analysis of factors associated with dialysis headache. For categorical variables, the reference categories were male sex, age ≥65 years, absence of DM, no prior history of headache, absence of hypertension, no caffeine intake, and non-smoking status. Red markers indicate statistically significant associations ($p < 0.05$), while blue markers indicate non-significant associations.
Abbreviations: OR, odds ratio; CI, confidence interval; DH, dialysis headache; DM, diabetes mellitus; HTN, hypertension.

existing primary headache disorders may exhibit enhanced central sensitization and increased trigeminovascular responsiveness. These mechanisms are partly mediated by neuropeptides such as CGRP and substance P, which have been shown to be elevated in patients with DH during hemodialysis[11] and are also central to the pathophysiology of migraine and tension-type headache.[12,13] Consequently, physiological stressors during hemodialysis, including hemodynamic and metabolic changes, may more readily trigger headache in this susceptible population. Similar associations between pre-existing headache disorders and secondary headaches have been described in other conditions, such as post-COVID-19 and post-ischemic stroke headaches,[16–18] further supporting the biological plausibility of this relationship.

Regarding the clinical characteristics of DH, our findings indicate a consistent pattern characterized by moderate-intensity, dull or throbbing pain in the frontotemporal region, typically occurring during the latter half of the hemodialysis session and resolving shortly after completion. These features are consistent with previous studies, which have similarly described DH as predominantly throbbing, moderate in intensity, and commonly localized to the frontotemporal area.[4,19] Associated symptoms such as photophobia and nausea were also observed in our cohort and have been reported in prior studies.[20] Despite some variability in frequency and duration across populations, these findings suggest that DH presents with a relatively consistent clinical profile, supporting its recognition as a distinct entity.

In our study, lower intradialytic diastolic blood pressure was associated with DH, suggesting a potential role of hemodynamic changes during dialysis. Previous studies examining the relationship between blood pressure and headache in hemodialysis patients have reported inconsistent findings. For example, some studies have suggested that higher blood pressure may be associated with headache occurrence,[6] while others have demonstrated significant differences in intradialytic blood pressure variability between patients with and without DH.[4,21,22] These discrepancies may reflect differences in study design, patient populations, and blood pressure assessment methods. One possible explanation for our findings is that lower blood pressure during dialysis may contribute to transient cerebral hypoperfusion or impaired autoregulation, which could trigger headache in susceptible individuals. However, these associations should be interpreted with caution, and further studies are needed to clarify the role of hemodynamic factors in the pathophysiology of DH.

Notably, the present study identified an inverse association between DM and the occurrence of DH. This observation is consistent with findings from large-scale epidemiological studies, such as the Head-HUNT study, which reported a lower prevalence of migraine among individuals with DM.[23] However, this finding should be interpreted with caution, as it may be influenced by residual confounding or differences in patient characteristics. Although the underlying

mechanisms remain incompletely understood, it has been suggested that DM-related alterations in vascular reactivity and peripheral nerve function may influence pain perception and headache susceptibility.[23]

Caffeine withdrawal has been proposed as a potential mechanism contributing to DH in patients undergoing hemodialysis.[24] However, a clinical trial evaluating caffeine intake during dialysis sessions found no significant difference in the occurrence of DH between patients receiving caffeinated and decaffeinated beverages.[25] Our findings are consistent with this observation, as no association was identified between caffeine consumption and DH in our cohort. Although caffeine withdrawal is recognized in the ICHD-3 as a potential differential diagnosis of DH,[7] these results suggest that it may not play a major role in the occurrence of DH in this population.

In addition to the factors evaluated in this study, other mechanisms have been proposed in the literature to explain the pathophysiology of DH. Nitric oxide (NO)-mediated vasodilation has been suggested as a contributing factor, with increased NO levels during hemodialysis potentially leading to cerebral vasodilation and headache onset, particularly during the later stages of the dialysis session.[26] This process may reflect impaired cerebral autoregulation and reduced vasoreactivity.[27] Similarly, although CGRP levels were not assessed in the present study, previous research has demonstrated elevated CGRP concentrations in patients with DH prior to dialysis.[11] Given the role of CGRP in vasodilation, nociception, and neurogenic inflammation,[27,28] it may also contribute to the development of DH. These mechanisms highlight the multifactorial nature of DH and suggest that additional biological pathways beyond those assessed in this study may be involved.

Beyond patient-related factors and clinical characteristics, dialysis-related factors may also influence the occurrence of DH. All patients in our cohort underwent online hemodiafiltration, a modality that combines convection and diffusion and is generally regarded as more effective in removing middle- and large-sized molecules. Although this technique has been associated with fewer intradialytic complications compared to conventional hemodialysis,[15] its impact on DH remains unclear. A previous study reported a lower frequency of DH in patients undergoing online hemodiafiltration (12.5%) compared to both our findings and conventional hemodialysis.[19] In contrast, the frequency observed in our study was comparable to that reported in conventional dialysis, suggesting that online hemodiafiltration may not necessarily reduce the occurrence of DH. This discrepancy may be related to differences in patient characteristics, dialysis parameters, or study design, and suggests that factors beyond dialysis modality may play a more important role in the pathophysiology of DH.

This study provides data on DH in a Saudi population and contributes to the limited literature examining the association between prior headache history and DH. However, several limitations should be considered when interpreting our findings. The single-center design and relatively small sample size may limit generalizability and statistical power, contributing to imprecision in the estimated associations, as reflected by wide confidence intervals. Additionally, prior headache history was based on patient self-report and was not formally classified using standardized diagnostic criteria, which may have introduced misclassification and recall bias.

Regarding the multivariate logistic regression analysis, the number of events relative to the number of predictors may be limited, increasing the risk of model overfitting and affecting the stability of the estimates. Furthermore, no formal sample size or power calculation was performed, and no adjustment for multiple comparisons was applied, which may increase the risk of type I error. Model diagnostics, such as goodness-of-fit and multicollinearity, were not formally assessed.

The cross-sectional design precludes causal inference, and the observed associations should be interpreted as exploratory. Finally, residual confounding may have influenced some findings, particularly the inverse association observed with diabetes mellitus. Future studies with larger sample sizes, prospective designs, and multicenter involvement are needed to validate these findings and provide more robust estimates.

Conclusion

In this study, DH was observed in a substantial proportion of patients with end-stage renal disease undergoing hemodialysis. It was typically characterized by moderate intensity, frontotemporal location, and onset during the latter half of dialysis sessions. A prior history of headache attacks, female sex, and lower intradialytic diastolic blood pressure were associated with DH, while DM showed an inverse association.

These findings provide insight into the clinical characteristics and factors associated with DH in this population. Given the cross-sectional design and relatively small sample size, the results should be considered exploratory. Further multicenter studies with larger sample sizes and prospective designs are needed to validate these findings and better elucidate the underlying mechanisms.

Data Sharing Statement

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Ethical Considerations

This study was reviewed and approved by the Institutional Review Board (IRB) for Health Sciences Colleges Research on Human Subjects, King Saud University, Riyadh, Saudi Arabia (approval date: 10 June 2021; IRB reference number: 21/0495/IRB; research project number: E-21-5924). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Consent to Participate

Written informed consent was obtained from all participants prior to their inclusion in the study.

Consent for Publication

Participants provided written consent for publication of anonymized data included in this article.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

Dr Sait Ashina reports personal fees from AbbVie, personal fees from Eli Lillly, personal fees from Pfizer, personal fees from Teva, personal fees from Lundbeck, personal fees from Theranica, personal fees from Linpharma, personal fees from Axsome Therapeutics, during the conduct of the study. Authors declare no other potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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