Review Article

Chronic Kidney Disease and Migraine: A Systematic Review of Prevalence, Incidence, and Genetic Associations

Maha M. Bilal[1], Amani M. Mahzari[2], Hajar A. Al Mustanyir[3], Raghad K. Alzahrani[4], Omar M. Al Farhan[5], Salem S. Al Sharyah[5], Yasir A. Awaji[5], Mohammed A. Alyami[2], Ismail A. Alkinani[6], Mohammed A. Saleh[5], Omar A. Alshahrani[5]

[1]Consultant Family Medicine, Najran University, Najran, KSA. [2]Medical Student, Najran University, Najran, KSA. [3]General Practitioner, King Khalid Hospital, Najran, KSA. [4]General Practitioner, Albaha University, KSA. [5]Medical Intern, Najran University, Najran, KSA. [6]Medical Student, Umm Al-Qura University, KSA.

ABSTRACT

Chronic kidney disease (CKD) and migraine are prevalent conditions with substantial burden, yet their association remains unclear due to inconsistent observational evidence. Following PRISMA 2020 guidelines, we systematically searched PubMed/MEDLINE, Scopus, and Web of Science (2021-2025) for studies examining CKD–migraine associations with defined diagnostic criteria and reported risk estimates. Quality was assessed using Newcastle-Ottawa, JBI, and MR-BASE tools. Four studies were included. In advanced CKD and hemodialysis patients, headache prevalence was markedly elevated (36.6% in pediatric CKD vs. 15.2% post-transplant, p=0.03) among those with headache, 68% had migraine, with improvement after transplantation. Conversely, a large Korean cohort found an 11% reduced hazard of new-onset migraine in CKD patients (aHR=0.89, 95%CI 0.81-0.97). Genetic analyses showed no causal effect of migraine on CKD (OR=1.03, p=0.28) but revealed significant biological pleiotropy, with four shared genomic regions and 28 shared expression-trait associations. Migraine also emerged as a risk factor for posterior reversible encephalopathy syndrome in CKD patients. The CKD–migraine relationship is stage-dependent—prevalence rises in advanced disease but is not consistently linked to milder CKD. Genetic evidence refutes a causal role for migraine in CKD development, instead pointing to overlapping biological pathways. Clinically, screening for migraine in advanced CKD is likely warranted and migraine should be considered a risk marker for neurological complications.

Keyword: Chronic Kidney Disease; Migraine; Prevalence; Systematic Review; Mendelian Randomization; Pleiotropy; End-Stage Renal Disease.

Introduction

The prevalence of chronic kidney disease (CKD) is dangerously rising globally, making it a serious public health concern. The global age-standardized prevalence of CKD is roughly 14.2%, according to latest data from the Global Burden of Disease Study [1]. This represents a relative rise of 3.5% since 1990. A predicted 788 million persons over the age of 20 had chronic kidney disease (CKD) by 2023, which is almost twice as many as the 378 million cases recorded in 1990 [2].

Access this article online	
Quick Response Code:	Website: www.smh-j.com
	DOI: 10.54293/smhj.v6i3.214

Address for correspondence: Amani Mohammed Ali Mahzari, Medical student Najran University, Najran, KSA.
E-mail: skewa365@gmail.com

Received: 22 Jun 2026 **Accepted:** 8 Oct 2026

This is an open access article by SMHJ is licensed under Creative Commons Attribution 4.0 International License.
(https://creativecommons.org/licenses/by/4.0)

Please cite this article as: Maha Mohammed Bilal, Amani Mohammed Ali Mahzari, Hajar Ahmed Y. Al Mustanyir, Raghad Khalid Alzahrani, Omar Mohammed Saad Al Farhan, Salem Saleh Al Sharyah, Yasir Abdullah Hussain Awaji, Mohammed Aedh Mahdi Alyami, Ismail Abdulmajeed Alkinani, Mohammed Al Murdef H. Saleh, Omar Abdullah H. Alshahrani. Chronic Kidney Disease and the Prevalence of Migraine: A Systematic Review. SMHJ [Internet]. 2026;6(3):340-352.

© Saudi Medical Horizons Journal

With 1.5 million fatalities in 2023, chronic kidney disease (CKD) is presently the tenth most common cause of mortality worldwide [3]. In addition to causing end-stage renal illness that necessitates dialysis or kidney transplantation, the increasing loss of kidney function also significantly raises the risk of cardiovascular events and other neurological problems [4]. Recurrent episodes of moderate to severe headaches, frequently accompanied by nausea, vomiting, photophobia, and phonophobia, are the hallmark of migraine, a prevalent chronic neurological condition. The Global Burden of Disease Study indicates that migraine affects an estimated 14–15% of the global population, making it the second leading cause of years lived with disability (YLDs) worldwide [5]. Migraine accounts for approximately 4.9% of global population ill health when quantified as YLDs, representing a substantial burden on individuals, healthcare systems, and economies [5]. The prevalence is particularly high among females and young adults, with the disorder significantly impairing quality of life and productivity [6]. Several studies have attempted to characterize the association between CKD and migraine, but the findings have been inconsistent. In the pediatric population, headache—particularly migraine-type headache—appears to be highly prevalent with advanced CKD and those undergoing hemodialysis [7]. Despite these epidemiological observations, several critical questions remain unanswered. First, it is unclear whether the association between CKD and migraine differs according to CKD stage, with advanced disease potentially driving different mechanisms compared to early-stage CKD. Second, the direction of causality—whether CKD predisposes to migraine, migraine predisposes to CKD, or both share common underlying pathways—has not been rigorously established. Therefore, the aim of this systematic review is to synthesize available evidence regarding the prevalence of migraine among patients with CKD across all stages, including those receiving dialysis or kidney transplantation.

Methods

The Preferred Reporting Items for Systematic Reviews and Meta Analyses (PRISMA) 2020 statement [8, 9] was followed in the conduct of this systematic review. Search Strategy: Three electronic databases were used for a thorough literature search: PubMed/MEDLINE, Scopus, and Web of Science. The search was limited to the years 2021–2025. For two primary concepts, “chronic kidney disease” (including CKD, chronic renal insufficiency, end-stage renal disease, dialysis, and hemodialysis) and “migraine” (including migraine disorders, migraine with aura, migraine without aura, and headache with migraine features), the search strategy incorporated MeSH terms and free-text keywords. The two concept groups were combined using the Boolean operator “AND.” The following search strings were used: PubMed/MEDLINE: ("chronic kidney disease"[MeSH] OR "renal insufficiency, chronic"[MeSH] OR "CKD" OR "chronic renal failure" OR "end stage renal disease" OR "hemodialysis") AND ("migraine disorders"[MeSH] OR "migraine" OR "migraine with aura" OR "migraine without aura" OR "headache")
Scopus: TITLE-ABS-KEY(("chronic kidney disease" OR "chronic renal insufficiency" OR "CKD" OR "chronic renal failure" OR "end-stage renal disease" OR "end stage renal disease" OR dialysis OR hemodialysis) AND ("migraine" OR "migraine disorders" OR "migraine with aura" OR "migraine without aura" OR headache)) AND PUBYEAR > 2020 AND PUBYEAR < 2025 Web of Science: TS=(("chronic kidney disease" OR "chronic renal insufficiency" OR "CKD" OR "chronic renal failure" OR "end-stage renal disease" OR "end stage renal disease" OR dialysis OR hemodialysis) AND ("migraine" OR "migraine disorders" OR "migraine with aura" OR "migraine without aura" OR headache)) AND PY=(2021-2025). No language restriction was applied. In order to identify any additional relevant research that the computerized search may have missed, the reference lists of the included studies and pertinent review articles were also manually searched. Eligibility Criteria: Studies were included if they met the following criteria: (1) original peer reviewed research (observational studies including cohort, cross sectional, case control, or genetic association studies); (2) clearly defined CKD according to established criteria (e.g., eGFR <60 mL/min/1.73m², proteinuria, or diagnostic codes); (3) clear definition or assessment of migraine, preferably using International Classification of Headache Disorders (ICHD) criteria or validated questionnaires; (4) reported any outcome related to the association between CKD and migraine (prevalence, incidence, risk, genetic correlation, or migraine as a risk factor for a complication in CKD); and (5) published within the 5 year search window2021–2025. Exclusion criteria were: (1) editorials, letters, case reports, conference abstracts, or review articles without original data; (2) studies focusing on acute kidney injury rather than CKD; (3) studies where headache was reported only as a

nonspecific symptom without differentiation of migraine; (4) animal or in vitro studies; and (5) studies with insufficient data to extract relevant outcome measures. Study Selection: The web-based systematic review management application Rayyan received all retrieved records [10]. Rayyan's automated duplicate detection and manual verification were used to eliminate duplicate records. Titles and abstracts were vetted by two independent reviewers based on the eligibility requirements. A comprehensive text review was conducted for any record that at least one reviewer thought might be significant. The same two reviewers then evaluated full text articles on their own. Any disagreements were settled by discussion or, if required, by consulting a third reviewer. Data Extraction: Microsoft Excel was used to create a uniform data extraction form. Each included study's data was independently extracted by two reviewers. Two primary tables were created from the retrieved data. A third reviewer double-checked the accuracy of all retrieved data. The original publication was consulted in order to settle any differences. Risk of Bias Assessment: Tools suitable for each study design were used to evaluate quality. The Newcastle Ottawa Scale (NOS), which assigns a maximum score of nine stars to the selection, comparability, and outcome areas, was utilized for cohort studies. The Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Prevalence Studies was used for the cross-sectional prevalence study. The MR BASE quality framework and the GRADE MR standards were applied for the Mendelian randomization genetic observational study. Risk of bias ratings (low, moderate, or high) were separately assigned by two reviewers, and differences were settled by consensus. Data Synthesis: Given the substantial heterogeneity in study designs, populations, outcome definitions, and effect measures across the included studies, a meta-analysis was not feasible. Instead, a narrative synthesis was conducted. The findings were organized thematically according to three main patterns: (1) prevalence of migraine in advanced CKD and ESRD; (2) incidence or risk of migraine in community dwelling adults with milder CKD; and (3) genetic and causal evidence (pleiotropy vs. causality).

Results

The research selection procedure for this systematic review is depicted in the PRISMA flow diagram. Database searches yielded 148 records in total. 53 distinct records were left for title and abstract screening after 95 duplicate records were eliminated; 31 of them were eliminated. Five of the 22 reports that remained could not be retrieved. Thirteen papers were excluded after the entire texts of seventeen publications were evaluated for eligibility: two because they were conference abstracts only, nine because the population was not focused on both CKD and migraine, and two because the outcome was incorrect. As a result, four studies were included in the final systematic review after meeting the inclusion criteria. (Table 1) summarizes the demographic and study characteristics of the four included studies that reported migraine related findings in patients with chronic kidney disease (CKD) [11- 14]. The first column lists each study by first author, year, and its reference number in square brackets, starting from [11] for He et al. (2025) [11], followed by Elron et al. (2022) [12], Zhang et al. (2023) [13], and Kwon et al. (2024) [14]. The table then presents the geographical location, study design, sample size, sample type, population, age range, percentage of females, CKD definition, key inclusion/exclusion criteria, and data source or time period. He et al. [11] used a large retrospective cohort from the US Nationwide Inpatient Sample (2016–2019) including 12,605 adult patients with posterior reversible encephalopathy syndrome (PRES), but age and sex distribution were not mentioned (NM). In contrast, Elron et al. [12] conducted a comparative cross-sectional study in Israel on 87 pediatric CKD and kidney transplant patients, with a female proportion of 52.9% (46/87). Zhang et al. [13] performed a multi-center observational and genetic analysis using UK Biobank and GWAS data; their sample comprised European ancestry individuals with sample sizes exceeding 500,000 for kidney function traits, though specific age and sex breakdowns were not provided in the abstract. Kwon et al. [14] analyzed a Korean population based longitudinal cohort of 15,443 CKD patients and 61,772 matched controls, with a mean age of 45.9±14.4 years in the CKD group and 42.3% females. All studies defined CKD using either estimated glomerular filtration rate (eGFR) <60 mL/min/1.73m² or ICD 10 codes, except for He et al. [11] who used different CKD stages based on administrative codes.

(Table 2) focuses on migraine related outcomes and findings. He et al. [11] aimed to evaluate PRES incidence and risk factors in CKD; they identified migraines as a risk factor for PRES, but no quantitative effect measure was reported for migraine alone, and the study concluded that CKD strongly associates with PRES while migraine is one among several risk factors. Elron et al. [12] directly compared headache prevalence between pediatric CKD and transplant

recipients; they found that 25.3% of the total cohort reported headaches, and among them 68% had migraine, giving a migraine prevalence of approximately 17% in the entire CKD group. Importantly, migraine was significantly more common in CKD patients (36.6%) than in transplant patients (15.2%, p=0.03), and lower glomerular filtration rate and higher phosphate level were associated with headaches. Zhang et al. [13] performed extensive genetic and Mendelian randomization analyses, demonstrating no causal effect of migraine on CKD (OR=1.03, 95% CI 0.98–1.09, p=0.28) but identified significant biological pleiotropy, including four shared genomic regions and 28 shared expression trait associations. They also reported a weak putative effect of migraine on urinary albumin to creatinine ratio that disappeared after accounting for pleiotropy. Kwon et al. [14] assessed the incidence of new onset migraine in Korean CKD adults and observed an 11% reduced risk of migraine occurrence (aHR=0.89, 95% CI 0.81–0.97) over a 16 year follow up, with subgroup analyses showing this protective association mainly in individuals aged ≥70 years, females, overweight, non smokers, and those without hypertension or diabetes.

(Table 3) systematically evaluates the risk of bias for all four included studies using tools appropriate to each design. Overall, no study was excluded based on bias, but readers should interpret findings from Elron et al. [12] and He et al. [11] with more caution, while Kwon et al. [14] and Zhang et al. [13] provide more robust estimates of migraine CKD associations. This risk of bias assessment should be integrated into the systematic review's discussion of evidence quality and heterogeneity.

Discussion

One of the most consistent observations across the literature is the elevated prevalence of migraine in patients with advanced CKD, particularly in those receiving hemodialysis. Elron and colleagues found that among 87 pediatric patients with CKD or kidney transplants, 25.3% reported headaches, of whom 68% had migraine, and headache prevalence was significantly higher in the CKD group (36.6%) than in the transplant group (15.2%, p = 0.03) [12]. Lower estimated glomerular filtration rate (eGFR) and higher serum phosphate levels were associated with headache presence. These findings align closely with earlier pediatric work by Davidovits and Markus, who studied 60 children and adolescents with CKD with or without hemodialysis and reported that 43.3% experienced headaches, with the hemodialysis group having a markedly higher headache rate than non-dialysis CKD patients (76.2% vs. 25.5%, p < 0.001); among those on hemodialysis, 14 out of 16 (87.5%) had migraine characteristics [15]. The same study identified hemodialysis, CKD grade, lower eGFR, anemia, and higher parathyroid hormone levels as independent associates of headache [15]. In the adult ESRD population, the high migraine prevalence is even more striking. Antoniazzi and colleagues reported that 48% of hemodialysis patients had migraine prior to initiating dialysis, and 57.5% experienced headache during dialysis sessions [16]. A Brazilian study of 151 ESRD patients documented that 76.1% of patients experienced headache, and before dialysis initiation, 47.9% had migraine without aura and 6.7% migraine with aura [17]. A narrative review by Sousa Melo and colleagues found that the prevalence of dialysis headache varies between 27% and 73%, with characteristics including frontal location, moderate to severe intensity, and onset a few hours after dialysis initiation [18]. The reduction in headache burden after kidney transplantation, as shown by Elron et al. [12] and confirmed in a recent Italian study where headache improved substantially within three months post-transplant [19], strongly indicates that the uremic milieu – with its metabolic imbalances, osmotic shifts, and accumulation of uremic toxins – is a direct promoter of migraine. Taken together, these data establish that in advanced CKD stages 4 5 and especially in ESRD on hemodialysis, migraine prevalence is substantially higher than the 10 14% typically reported in the general population, and kidney transplantation offers significant symptomatic relief. In contrast to the high prevalence observed in advanced CKD, large population based studies in community dwelling adults with predominantly mild to moderate CKD have produced conflicting or even inverse associations. Kwon and colleagues analysed a Korean nationwide health insurance database including 15,443 CKD patients and 61,772 matched controls followed for up to 16 years [14]. After overlap weighted Cox regression adjustment for multiple confounders, they found that CKD was associated with an 11% reduction in the hazard of newly diagnosed migraine (adjusted hazard ratio = 0.89; 95% confidence interval 0.81–0.97). The preventive effect was particularly significant in those aged ≥70 years, females, overweight adults, non-smokers, and those without hypertension or diabetes [14]. This apparently

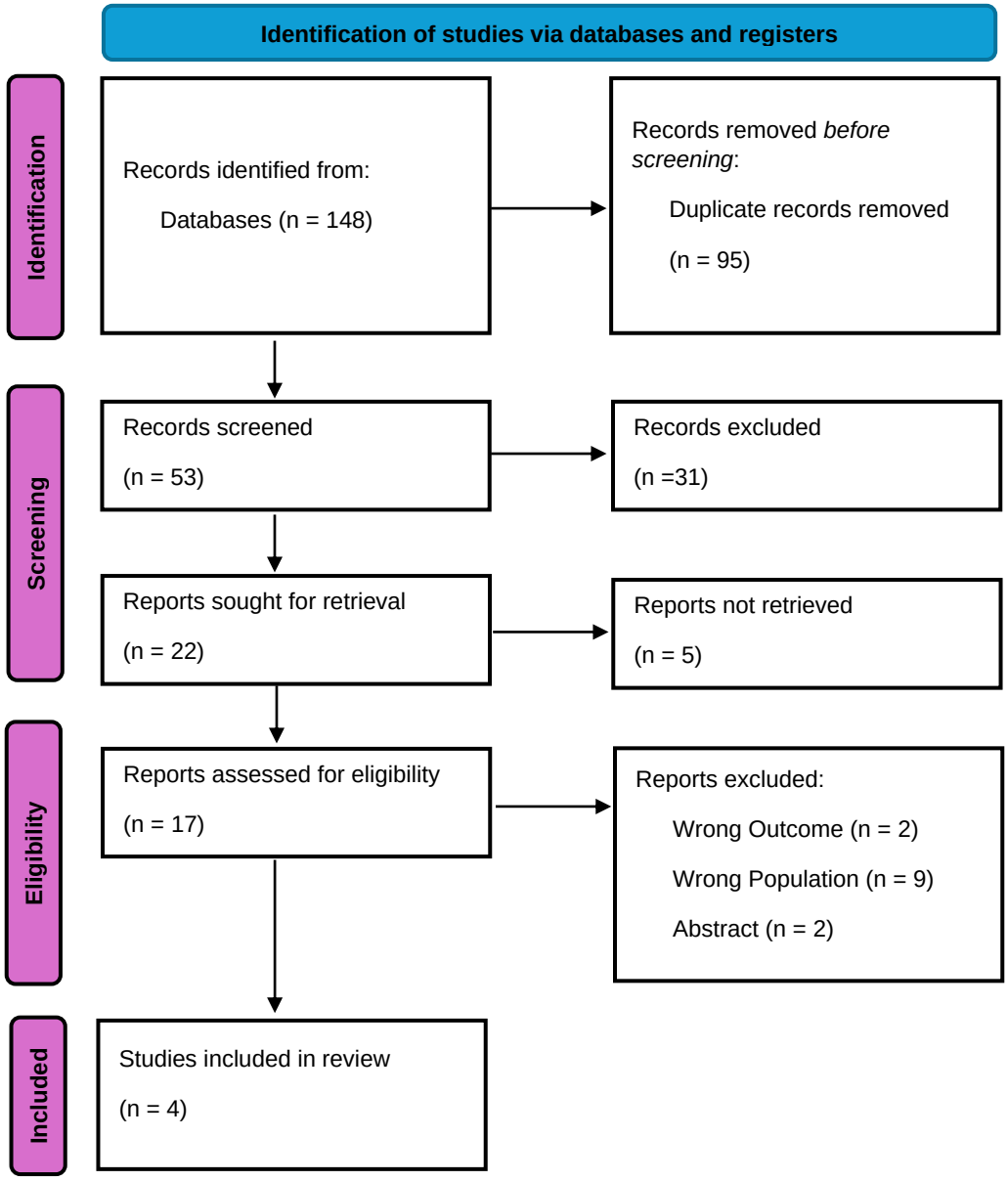


Figure 1: PRISMA 2020 Flow Diagram of Study Selection Process.

Table 1: Demographic and Study Characteristics of Included Studies.

Study (Author, Year) [Reference]	**Location**	**Study Design**	**Sample Size**	**Sample Type**	**Population**	**Age Range (years)**	**Female (%)**	**CKD Definition**	**Key Inclusion/Exclusion Criteria**	**Data Source / Time Period**
He et al., 2025 [11]	USA	Retrospective cohort	12,605 patients with PRES	Adult patients non-electively admitted with PRES	Adult CKD patients with PRES	NM (adults)	NM	Different stages of CKD vs. no kidney disease (ICD-10 codes)	Inclusion: Adult patients non-electively admitted with PRES (2016-2019). Exclusion: NM	Nationwide Inpatient Sample Database (NIS), 2016-2019
Elron et al., 2022 [12]	Israel	Comparative cross-sectional	87	Pediatric patients with CKD or kidney transplant	Pediatric CKD and kidney transplant patients	NM (children and adolescents)	52.9% (46/87)	eGFR < 60 mL/min/1.73m² or structural kidney disease	Inclusion: Children and adolescents with CKD or transplanted kidney. Exclusion: NM	Hospital charts and interviews, NM
Zhang et al., 2023 [13]	Multi-center (UK Biobank)	Observational and genetic (GWAS, MR)	48,975 migraine cases / 540,381 controls; 41,395 CKD cases / 439,303 controls; eGFR N=567,460; UACR N=547,361	European ancestry individuals	General population (European ancestry)	Adult (NM)	NM	eGFR < 60 mL/min/1.73m² and/or UACR ≥ 30 mg/g	Inclusion: European ancestry. Exclusion: NM	UK Biobank, GWAS consortia (NM)

Kwon et al., 2024 [14]	South Korea	Population-based longitudinal cohort	15,443 CKD patients, 61,772 matched controls	Adults with/without CKD	Korean adults	45.9 ± 14.4 (CKD group)	42.3% (CKD group)	eGFR < 60 mL/min/1.73m² or proteinuria (≥1+) for ≥3 months	Inclusion: Adults with/without CKD. Exclusion: Prior migraine diagnosis	Korean National Health Insurance Service (NHIS) database, 2002-2019

Abbreviations: *CKD = chronic kidney disease; eGFR = estimated glomerular filtration rate; GWAS = genome-wide association study; MR = Mendelian randomization; N = sample size; NM = not mentioned; PRES = posterior reversible encephalopathy syndrome; UACR = urinary albumin-to-creatinine ratio; USA = United States of America.*

Table 2: Migraine-Related Findings and Outcomes of Included Studies.

Study (Author, Year) [Reference]	**Primary Objective of Study**	**Migraine-Related Findings**	**Key Effect Measures**	**Subgroup/Sensitivity Analysis**	**Adjustment for Confounders**	**Main Conclusion on Migraine-CKD Link**	**Additional Notes / Limitations**
He et al., 2025 [11]	Evaluate incidence, outcomes, and risk factors of PRES in CKD patients	Migraines identified as a key risk factor for PRES in CKD patients (mentioned in risk factor list)	NM	NM	Multivariate logistic and linear regression	CKD is strongly associated with PRES; migraines are one of several risk factors	Large national cohort; migraine is one factor among many; use of administrative data limits clinical detail
Elron et al., 2022 [12]	Compare headache prevalence and characteristics between pediatric CKD and kidney transplant patients	25.3% (22/87) reported headaches, 68% (15/22) of these had migraine. Prevalence in CKD group: 36.6% vs. transplant group: 15.2%, p=0.03	Prevalence (%), p-value	NM	Glomerular filtration, phosphate level	Headaches (mostly migraine) associated with lower GFR and higher phosphate; lower after transplantation	Small sample; single center; subjective interview data

Zhang et al., 2023 [13]	Investigate phenotypi-c and genetic relationships between migraine, CKD, and kidney function	No causal effect of migraine on CKD (OR=1.03, 0.98-1.09, p=0.28). Migraine on UACR: log-scale-beta=0.02 (0.01-0.04, $p=1.92\times10^{-3}$). No global genetic correlation, but four shared genomic regions. 28 shared expression-trait associations	OR, HR (1.13, 0.85-1.50), log-scale-beta, p-value	Cross-trait meta-analysis; transcriptome-wide association; MR with pleiotropy correction	Multivariable; MR with pleiotropy adjustment	No causal association; significant biological pleiotropy between migraine and kidney function	Large GWAS; European ancestry only; potential residual confoundi-ng
Kwon et al., 2024 [14]	Assess correlation between CKD and migraine developme-nt	11% reduction in migraine occurrence in CKD patients (aHR=0.89, 0.81-0.97). Incidence: 2.26% in CKD vs. 3.08% in controls	aHR (0.89), incidence rate (5.36 per 1000 person-years)	Aged ≥70, females, overweight, nonsmokers, without hypertension/diabetes	Age, sex, income, residence, lifestyle, comorbidit-ies	CKD associated with modestly lower migraine risk in Korean adults	Large Korean database; residual confoundi-ng possible; migraine diagnosis based on claims

Abbreviations: *aHR = adjusted hazard ratio; CI = confidence interval; CKD = chronic kidney disease; GFR = glomerular filtration rate; GWAS = genome-wide association study; HR = hazard ratio; MR = Mendelian randomization; NM = not mentioned; OR = odds ratio; PRES = posterior reversible encephalopathy syndrome; UACR = urinary albumin-to-creatinine ratio.*

Table 3: Risk of Bias Assessment of Included Studies**.**

Study [Reference]	**Assessm-ent Tool**	**Selection (max 4)**	**Comparability (max 2)**	**Outcome/Exposure (max 3)**	**Total Score / Max**	**Risk of Bias Judgement**	**Key Limitations**
He et al., 2025 [11]	Newcastle-Ottawa Scale (cohort)	3/4	1/2	3/3	7/9	Moderate	Administrative data, no adjustment for migraine severity, potential residual confounding
Elron et al., 2022 [12]	JBI Checklis-t for Prevalence Studies	3/5 (domain-specific)	N/A	3/4	6/9	Moderate	Small sample size, single center, no validation of headache/migraine diagnosis by neurologist
Zhang et al., 2023 [13]	MR-BASE / GRADE-MR	4/4 (genetic instruments)	2/2 (pleiotropy sensitivity)	2/3	8/9	Low to Moderate	European ancestry only, possible horizontal pleiotropy for UACR finding
Kwon et al., 2024 [14]	Newcastle-Ottawa Scale (cohort)	4/4	2/2	2/3	8/9	Low	Migraine diagnosis based on claims (may underestimate), no data on headache frequency or medication use

Abbreviations: JBI = Joanna Briggs Institute; GRADE-MR = Grading of Recommendations Assessment, Development and Evaluation for Mendelian randomization; N/A = not applicable; UACR = urinary albumin-to-creatinine ratio.

paradoxical "protective" association may be attributed to the routine use of renin-angiotensin aldosterone system (RAAS) blockers – such as angiotensin converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs) – in CKD patients for blood pressure control and proteinuria reduction. RAAS inhibitors, particularly candesartan and lisinopril, have shown efficacy in migraine prevention [20]. Furthermore, beta blockers (such as metoprolol and propranolol) are first-line treatments for migraine prophylaxis and are frequently administered to CKD patients with hypertension or coronary artery disease. Therefore, the pharmacological management of CKD may inadvertently lower the incidence of new onset migraine, representing an example of "collateral benefit." However, the Korean study [14] relied on diagnostic codes from insurance claims, which may underestimate migraine because patients with multiple serious comorbidities might be less likely to seek medical attention for headache or have their headache attributed to their kidney disease rather than coded separately. Indeed, a nationwide Taiwanese cohort study by Weng and colleagues found the opposite: after adjusting for covariates, migraine patients had a 1.22 fold higher risk of developing CKD compared to non-migraine controls (95% CI 1.13–1.31) [21]. This discrepancy underscores the importance of genetic background, healthcare system differences, and potential residual confounding, and it highlights the need for standardized, prospective studies with neurologist confirmed migraine diagnoses. The most robust evidence on causality comes from the comprehensive observational and genetic analysis performed by Zhang and colleagues [13]. Using UK Biobank and large-scale GWAS summary data (48,975 migraine cases/540,381 controls; 41,395 CKD cases/439,303 controls; eGFR N=567,460; UACR N=547,361), they first found no significant observational association between migraine and incident CKD (hazard ratio = 1.13; 95% CI 0.85–1.50). They then leveraged large scale genome wide association study (GWAS) data for migraine (48,975 cases / 540,381 controls), CKD (41,395 cases / 439,303 controls), eGFR (N = 567,460), and urinary albumin to creatinine ratio (UACR, N = 547,361). Global genetic correlation analysis revealed no significant genome wide correlation between migraine and CKD. However, cross trait meta-analysis identified four specific genomic regions showing significant local genetic correlation between migraine and eGFR. A putative functional variant, rs1047891 (located in the CPS1 gene), was implicated across migraine, CKD, and renal function. Transcriptome wide association analysis identified 28 shared expression trait correlations between migraine and kidney function, demonstrating strong biological pleiotropy [13]. Most significantly, Mendelian randomization (MR) analysis indicated no causal influence of migraine on CKD (odds ratio = 1.03; 95% CI 0.98–1.09; p = 0.28). A putative causal effect of migraine on UACR was noticed (log scale beta = 0.02; $p = 1.92 \times 10^{-3}$), but this impact reduced to null after adjustment for both correlated and uncorrelated pleiotropy, suggesting it was likely driven by shared biological pathways rather than a direct causal mechanism [13]. These findings are consistent with a large MR study by Larsson and colleagues, who also found no evidence of a causal effect of migraine on eGFR or CKD risk using independent genetic instruments [22]. Similarly, a recent MR analysis by Hamed and colleagues reported no causal relationship between migraine and kidney function measures, reinforcing the conclusion that the observed epidemiological associations are likely due to confounding or pleiotropy rather than direct causation [23]. The shared biological mechanisms underlying this pleiotropy may include endothelial dysfunction, systemic inflammation, oxidative stress, and abnormal neurovascular coupling, all of which are implicated in both migraine pathogenesis and CKD progression [24]. Beyond prevalence and causality, the study by He and Gillespie [11] adds another important dimension: migraines were identified as a risk factor for PRES among CKD patients. In their nationwide cohort of 12,605 individuals with PRES, the authors concluded that migraines, along with hypertension, metastatic cancer, solid organ transplantation, and rheumatologic illnesses, were important risk factors for developing PRES. Moreover, kidney failure was independently related with in hospital mortality (adjusted odds ratio = 5.12; 95% CI 2.09–12.53; $p < 0.001$) [11]. This finding is clinically significant because PRES is an acute neurological emergency that can lead to intracerebral hemorrhage, status epilepticus, and death if not promptly recognized and treated. The link between migraine and PRES in CKD patients may reflect shared vascular vulnerability: both conditions involve cerebral autoregulation dysfunction and endothelial activation. A systematic review on PRES in CKD by Dos Santos and colleagues confirmed that CKD is a major risk factor for PRES and that the majority of affected patients have underlying hypertension or autoimmune disease, but they also noted that migraine as a specific risk

factor has been understudied [11]. Therefore, while migraine does not cause CKD, its presence in a CKD patient should raise clinical suspicion for potentially serious neurological complications such as PRES, especially when acute severe headache, altered mental status, or seizures occur. The role of non-steroidal anti-inflammatory drugs (NSAIDs) in linking migraine and CKD deserves comment, although no study in our systematic review directly addressed this. Migraine patients often use NSAIDs for acute attack treatment, and overuse of NSAIDs is a well-established cause of CKD, particularly analgesic nephropathy. A meta-analysis by Garg and colleagues found that regular use of NSAIDs was associated with a 30 50% increased risk of CKD [25]. In patients who already have CKD, NSAIDs can accelerate progression. Thus, the clinical intersection of migraine and CKD requires careful medication management: while migraine itself may not harm the kidneys, the drugs used to treat it can. None of the four included studies accounted for NSAID or analgesic overuse, which is a notable limitation. Future research should specifically examine whether migraine patients with high NSAID consumption have a higher incidence of CKD than those who use non NSAID acute treatments.

Another important consideration is the distinction between migraine and other headache types in CKD patients. Many studies, including some cited in this discussion, have used the term “headache” without subtyping, or have used questionnaire based rather than neurologist administered ICHD criteria. In the pediatric study by Elron et al. [12], headache was assessed by interview, and migraine was diagnosed using a standardized questionnaire based on ICHD 2 criteria, which is a strength. In contrast, the Korean study [14] used diagnostic codes from insurance claims, which cannot distinguish migraine from other headache disorders and may have low sensitivity. Similarly, the genetic study [13] used GWAS summary statistics where migraine cases were defined by physician diagnosis or self report, which is acceptable for large scale genetics but may introduce misclassification. For future studies, standardized headache phenotyping using ICHD 3 criteria is essential to accurately estimate migraine prevalence and incidence in CKD populations. In summary, the literature on CKD and migraine shows three distinct patterns when integrated with previous research. First, in children and adults with advanced CKD (stages 4 5) and especially in ESRD on hemodialysis, migraine prevalence is markedly elevated (approaching 40 50% in some series), and it improves after kidney transplantation, indicating a reversible, uremia driven phenomenon [12, 15- 17]. Second, in community dwelling adults with milder CKD, large observational studies show either no association or a modest inverse association, possibly due to the protective effects of RAAS blockers and beta blockers used in CKD management [14, 21]. Third, genetic evidence consistently demonstrates no causal effect of migraine on CKD, but instead reveals substantial biological pleiotropy – shared genetic variants and molecular pathways that predispose to both conditions [13, 22]. Clinically, these findings reassure migraine patients that their condition does not directly cause kidney disease, but they also warn that in advanced CKD, migraine is very common and should be actively sought and treated. Furthermore, in CKD patients who develop acute severe headache with neurological symptoms, migraine may be a risk marker for PRES, requiring prompt neuroimaging [11]. Limitations: This systematic review highlights significant limitations, including heterogeneity among studies, lack of neurologist-confirmed migraine diagnoses in most cases, and restricted geographic and ancestral scopes. Additionally, overuse of NSAIDs or analgesics was not adequately adjusted for, and some studies relied on administrative coding that may introduce residual confounding.

Conclusion

The relationship between chronic kidney disease (CKD) and migraine varies by CKD stage, showing high prevalence in advanced CKD and end-stage renal disease, with improvements post-transplantation. Mild CKD lacks a consistent association with migraine. Genetic studies indicate no causal link, suggesting biological pleiotropy. While migraine screening in advanced chronic kidney disease (CKD) warrants consideration, migraines themselves should be recognized as a clinical warning sign for potential neurological complications. Management should avoid nephrotoxic medications. Future studies with standard diagnostic criteria and comprehensive medication records are needed to clarify the CKD-migraine connection and guide clinical practices.

Conflict of Interest

None

Funding

None

References

1. Bikbov B, Purcell CA, Levey AS, Smith M, Abdoli A, Abebe M, et al. Global, regional, and national burden of chronic kidney disease, 1990–2017: a systematic analysis for the Global Burden

of Disease Study 2017. The lancet. 2020 Feb 29;395(10225):709-33.
2. Kovesdy CP. Epidemiology of chronic kidney disease: an update 2022. Kidney international supplements. 2022 Apr 1;12(1):7-11.
3. Mark PB, Stafford LK, Grams ME, Aalruz H, Abd ElHafeez S, Abdelgalil AA, et al. Global, regional, and national burden of chronic kidney disease in adults, 1990–2023, and its attributable risk factors: a systematic analysis for the Global Burden of Disease Study 2023. The Lancet. 2025 Nov 22;406(10518):2461-82.
4. Caturano A, Galiero R, Rocco M, Tagliaferri G, Piacevole A, Nilo D, et al. The dual burden: exploring cardiovascular complications in chronic kidney disease. Biomolecules. 2024 Oct 31;14(11):1393.
5. Steiner TJ, Stovner LJ. Global epidemiology of migraine and its implications for public health and health policy. Nature Reviews Neurology. 2023 Feb;19(2):109-17.
6. Almadani AH, Alghamdi AH, Bashandi AA, et al. Prevalence of migraine among adults with mood disorders: a Saudi cross-sectional study. BMC Psychiatry. 2025;25(1):1132. Published 2025 Nov 27. doi:10.1186/s12888-025-07601-w
7. Alazem A, Abobakr E, Galal RE, Hammady MM, Selim A. The Prevalence and Severity of Headaches in Hemodialysis Children: A Comparative Study. The Egyptian Journal of Hospital Medicine. 2022 Oct 1;89(1):5258-65.
8. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:n71. doi: 10.1136/bmj.n71.
9. Wandscher K, Helbach J, Pieper D, Hoffmann F. "We used standard Cochrane methods"–observational study on reporting according to PRISMA-A in Cochrane review abstracts between 2016 and 2023. Journal of Clinical Epidemiology. 2025 May 1;181:111713.
10. Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan—a web and mobile app for systematic reviews. Syst Rev. 2016;5(1):210. doi: 10.1186/s13643-016-0384-4.
11. He M, Gillespie A. Posterior Reversible Encephalopathy Syndrome in Chronic Kidney Disease: Incidence, Outcomes, and Risk Factors in a National Cohort. Kidney Medicine. 2025 Jul 1;7(7):101022.
12. Elron E, Davidovits M, Eidlitz Markus T. Headache in pediatric and adolescent patients with chronic kidney disease and after kidney transplantation: a comparative study. Journal of Child Neurology. 2022 May;37(6):497-504.
13. Zhang W, Zhang L, Yang L, Xiao C, Wu X, Yan P, et al. Migraine, chronic kidney disease and kidney function: observational and genetic analyses. Human Genetics. 2023 Aug;142(8):1185-200.
14. Kwon MJ, Kim JK, Kim MJ, Yoo DM, Lee NE, Han KM, et al. Associations between Chronic Kidney Disease and Migraine Incidence: Findings from a Korean Longitudinal Big Data Study. Journal of Personalized Medicine. 2024 Mar 28;14(4):356.
15. Davidovits M, Eidlitz Markus T. Headache in pediatric and adolescent patients with chronic kidney disease, with and without hemodialysis: a comparative cohort study. Cephalalgia. 2018 Apr;38(5):883-91.
16. Antoniazzi AL, Bigal ME, Bordini CA, Tepper SJ, Speciali JG. Headache and hemodialysis: a prospective study. Headache: The Journal of Head and Face Pain. 2003 Feb;43(2):99-102.
17. Jesus AC, Oliveira HA, Paixão MO, Fraga TP, Barreto FJ, Valença MM. Caracterização clinica da cefaléia da diálise em pacientes renais crônicos. Arquivos de Neuro-Psiquiatria. 2009;67:978-81.
18. Sousa Melo E, Carrilho Aguiar F, Sampaio Rocha-Filho PA. Dialysis headache: a narrative review. Headache: The Journal of Head and Face Pain. 2017 Jan;57(1):161-4.
19. Viticchi G, Falsetti L, Salvemini S, Bartolini M, Ranghino A, Buratti L, et al. Headache changes after kidney transplant. Acta Neurologica Belgica. 2022 Feb;122(1):83-90.
20. Wang HB, Yang J. The role of renin-angiotensin aldosterone system related micro-ribonucleic acids in hypertension. Saudi Medical Journal. 2015 Oct;36(10):1151.
21. Weng SC, Wu CL, Kor CT, Chiu PF, Wu MJ, Chang CC, et al. Migraine and subsequent chronic kidney disease risk: a nationwide population-based cohort study. BMJ open. 2017 Dec 1;7(12):e018483.
22. Larsson SC, Burgess S. Appraising the causal role of smoking in multiple diseases: a systematic review and meta-analysis of Mendelian randomization studies. EBioMedicine. 2022 Aug 1;82.
23. Hamed SA. Neurologic conditions and disorders of uremic syndrome of chronic kidney disease: presentations, causes, and treatment strategies. Expert review of clinical pharmacology. 2019 Jan 2;12(1):61-90.
24. Paolucci M, Altamura C, Vernieri F. The Role of Endothelial Dysfunction in the Pathophysiology and Cerebrovascular Effects of Migraine: A Narrative Review. *J Clin Neurol*.

2021;17(2):164-175.
doi:10.3988/jcn.2021.17.2.164

25. Soliman S, Ahmed RM, Ahmed MM, Attia A, Soliman AR. Non-steroidal anti-inflammatory drugs: what is the actual risk of chronic kidney disease? A systematic review and meta-analysis. *Rom J Intern Med*. 2025;63(1):3-27.