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Review

Dialysis headache: a systematic review and meta-analysis

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Introduction

Dialysis headache (DH) is a known but underexplored complication of hemodialysis, affecting some patients during treatment. While, it is recognized, the reported frequency, diagnostic criteria, and associated risk factors vary.

Objective

This systematic review and meta-analysis aim to determine the percentage and characteristics of dialysis headache, identify associated factors, and summarize available evidence from existing literature.

Methods

A comprehensive literature search was conducted across Scopus, Medline, PubMed, and Google Scholar for studies published from 2000 to the present. A total of 15 studies were included, encompassing various study designs and geographic locations. Data on patients demographics, headache characteristics, diagnostic criteria, and hemodialysis parameters were extracted and analyzed. A proportional meta-analysis was performed using R-4.3.2.

Results

The included studies reported DH prevalence ranging from 7% to 53%. The overall pooled estimate was 28% (95% CI: 19-36%). After refining the dataset by excluding studies with confounding factors and improving study selection criteria, the updated prevalence estimate was 16% (95% CI: 9-24%). DH onset typically occurred during hemodialysis sessions, predominantly in the second or third hour, and most cases resolved within four hours post-dialysis. Headaches were generally of moderate intensity and managed with simple analgesics.

Conclusions

Dialysis headache remains a prevalent but inconsistently reported complication of hemodialysis. Standardized diagnostic criteria and further research are needed to better understand its pathophysiology and improve management strategies.

Keywords:

Dialysis headache Hemodialysis related-headache Hemodialysis headache Hemodialysis complications

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Introduction

eadache is a common symptom among patients undergoing hemodialysis, with varying prevalence across studies. This variation can be attributed, in part, to the differing diagnostic criteria applied to define dialysis headache. The International Classification of Headache Disorders (ICHD) has undergone several versions over the years, from ICHD-1 based on HIS criteria (1988) to ICHD-2 (2004), and ICHD-3 beta (2013), and eventually the latest ICHD-3 (2018). Each version has refined the definition of dialysis-related headache, yet differences between these criteria have led to discrepancies in prevalence rates across studies. The variety in diagnostic approaches may result in a wider range of phenomena being included, potentially influencing the reported prevalence in both older and new studies (1-3).

The current diagnostic criteria do not provide clear guidance on whether headaches that occur prior to renal failure or before the initiation of hemodialysis should be categorized as dialysis headaches in affected patients. Some studies have excluded these patients from their analysis, which could result in a lower reported prevalence of dialysis headache. Additionally, a study by Yang et al. (4), titled The Applicability of the Diagnostic Criteria for 10.2 Hemodialysis-Related Headache in the International Classification of Headache Disorders-3rd Edition, suggests considering headaches that develop after a hemodialysis session as part of dialysisrelated headache. This suggestion is based on the idea that such headaches could be related to the hemodialysis procedure itself.

Moreover, some diagnostic criteria state that dialysis headache should completely resolve after kidney transplantation. This assumption presents a challenge, particularly as it does not apply to patients who do not undergo transplantation, and there are fewer studies that have rigorously examined this aspect of the condition.

Earlier studies primarily attributed dialysis headache to disturbances in homeostasis, particularly the significant shifts in water and electrolytes that occur during hemodialysis. One of the most frequently cited studies, conducted by Antoniazzi et al. (5), evaluated 123 hemodialysis patients and has often been referenced as reporting a prevalence of dialysis headache as high as 70%. However, this interpretation may overestimate the actual prevalence, as the study presents a more detailed view of the data (5). This overestimation led later research to explore whether additional factors beyond fluid and electrolyte imbalances could contribute to dialysis headache.

While large shifts in fluid and electrolytes remain the most widely accepted explanation, some studies have investigated other potential mechanisms. These include variations in dialysis modalities (e.g., conventional hemodialysis vs. online hemodiafiltration) (6), differences in dialysis



Additionally, caffeine withdrawal has been considered a possible mechanism in certain patients. Since caffeine is rapidly cleared during dialysis, individuals who regularly consume large amounts may experience withdrawal headaches due to the sudden drop in plasma caffeine levels (9). This align with the well documented phenomenon of caffeine-withdrawal headache in the general population.

given their potential impact on neuronal excitability (8).

Despite these alternative hypotheses, the extent to which they contribute to dialysis headache remains uncertain. The traditional view, linking the condition primarily to homeostatic disturbances, continues to be the most consistent explanation across studies. However, as research evolves, these additional mechanisms provide valuable insights that may refine the understanding of dialysis headache in specific subgroups of patients.

This systematic review analyzed 15 studies that examined the prevalence, characteristics, and underlying mechanisms of dialysis headache, aiming to provide a clearer picture of this complex and often misunderstood condition.

Methods

This systematic review was conducted in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines (10).

Data sources and searches

On January 18, 2025, a comprehensive search was conducted across Scopus, Medline, PubMed, and Google Scholar using the search terms "dialysis headache", "hemodialysis headache", "hemodialysis related headache."

Inclusion and exclusion criteria

The studies included in this review were observational in nature. Eligible studies involved adult patients aged 18 years and older undergoing hemodialysis and diagnosed with dialysis headache, based on recognized diagnostic criteria like ICHD-3, ICHD-II, or other well-established criteria. Only studies that provided the number of hemodialysis patients who developed dialysis headache were included. Studies published between 2000 and the





present were selected to ensure alignment with the most current diagnostic criteria for dialysis headache.

The exclusion criteria were as follows: studies not published in English, those with restricted full text availability, studies that did not report clear data on the number of patients with dialysis headache, animal studies, research focused on pediatric populations, and studies that did not clearly define dialysis headache.

Study selection

The eligibility of the search results was evaluated in two phases: first, an initial screening of titles and abstracts, and second, a comprehensive review of the full-text articles.

Data extraction and quality assessment

The extracted data included the first author's name, year of publication, study location, journal of publication, study design, mean age and male percentage of the dialysis headache group, study setting (monocenter or multicenter), methods of headache diagnosis and criteria for identifying dialysis headache patients, dialysis solution used, duration and frequency of hemodialysis sessions, vintage of hemodialysis treatment, onset and duration of dialysis headache, study period, title, summary, total number of patients receiving hemodialysis, number of patients experiencing dialysis headache, number of males experiencing dialysis headache, number of females experiencing dialysis headache, VAS (visual analog scale) score for headache intensity, and number of patients experiencing throbbing headache characteristics, bilateral headache pattern, phonophobia, and photophobia.

The quality assessment was checked by the JBI Critical Appraisal Checklist for Prevalence Studies (11) (Supplementary Table 1). High quality studies are those that meet most JBI criteria ($\sqrt{}$ in at least 8 out of 9 domains).

Data synthesis and analysis

Proportional meta-analysis was performed using R-4.3.2.

Results and Discussion

Literature search

An initial search yielded 19 studies from Medline, 41 studies from Scopus, and 30 studies from PubMed. After removing 7 duplicates and excluding 17 non-English studies, 3 additional relevant studies were identified through manual search in Google Scholar. A total of 69 studies were then screened based on their titles and abstracts. Of these, 40 studies had unavailable full texts,

and 7 studies were deemed irrelevant. Following full-text review, 6 studies were excluded for irrelevance, leaving 16 studies for eligibility assessment. Ultimately, 15 studies were included in the final analysis (Figure 1).



Characteristics of the included studies

A total of 15 studies were included in this systematic review and meta-analysis (4-9, 12-20) (Supplementary Table 2), with publication years ranging from 2003 to 2023. These studies were conducted in various countries, including China, Brazil, Italy, Turkey, Morocco, India, and Serbia. The journals where these studies published include The Journal of Headache and Pain, Headache Medicine, Artificial Organs, Arq Neuropsiquiatr, Acta Neurologica Belgica, Annals of Indian Academy of Neurology, European Journal of Neurology, Renal Failure, Cephalalgia, and Headache.

The study designs varied and included cross-sectional studies, prospective studies, retrospective studies, casecontrol studies, and observational designs. Most studies were monocenter (10 studies), while 5 were multicenter.

Regarding the dialysis headache (DH) group, the mean age ranged from 39.9 years to 63.5 years. The male percentage in the DH group varied widely, ranging from 25% to 90.9%.

The diagnosis of dialysis headache was primarily based on the International Classification of Headache Disorders (ICHD) criteria, with some studies utilizing versions such as ICHD-II, ICHD-3, or modified diagnostic approaches.



The duration and frequency of hemodialysis sessions varied, with most studies reporting thrice-weekly treatments lasting approximately 4 hours per session. The dialysis vintage ranged widely, with the shortest reported mean duration being 12 months and the longest reaching up to 5 years.

Most studies reported the use of bicarbonate as the dialysis solution, while a few employed acetate-based solutions. The onset of dialysis headache was commonly observed within the hemodialysis session, typically during the second or third hour. The duration of headache episodes varied, the most cases resolving within 4 hours after the completion of dialysis.

The studies were conducted over different timeframes, spanning from as early as 1996 to 2023. Some studies had relatively short study periods of a few months, while others followed patients over several years.

Studies 3, 6, and 11 focused on kidney transplantation, and the data on dialysis headache were extracted from the patients headache history.

Although dialysis headache is uniquely associated with the hemodialysis technique and does not require extensive explanation, there is variation in the nomenclature used across the studies. Some studies referred to the condition as Dialysis Headache (DH), including studies 3, 5, 6, 9, 11, 12 and 15. Others used the term Hemodialysis-Related Headache (HRH), which appeared in studies 1, 2, 4, 8, 10, 14. Additionally, a few studies referred to it as Hemodialysis Headache (HDH), as seen in studies 7 and 13.

Most of the studies included are comparative, featuring both case and control groups (studies 1, 2, 3, 4, 5, 7, 8, 9, 13, and 14), but they differ in the methods of comparison. Study 1 compared a headache group with a control group based on comorbidities in hemodialysis patients, finding that diabetes was significantly less prevalent in the headache group (p<0.001). Study 2 compared a nonhemodialysis-related headache group with a hemodialysisrelated headache group, noting that the latter group was younger (p=0.052) and had higher systolic (p=0.016) and diastolic (p= 0.050) blood pressure. Study 3 found significant differences in anxiety (p=0.02) and sleepiness (p=0.01) scores between the groups, with higher anxiety and sleepiness scores in headache group, as well as lower pre-dialysis calcium levels (p=0.01). Additionally, pre- and post-dialysis systolic and diastolic blood pressure readings were significantly elevated in the headache group (p=0.02, 0.06, 0.018, 0.08). Study 4 compared conventional hemodialysis with online hemodiafiltration, finding that online hemodiafiltration was associated with a lower incidence of dialysis headaches (p=0.008). Study 5 showed that younger age (p < 0.01) and a higher prevalence of female sex (p < 0.01) were associated with dialysis headaches. Study 7 found that female sex

(p <0.001) and elevated pre-dialysis diastolic blood pressure (p = 0.021) were common in the headache group. Study 8 found significant differences in pre-dialysis urea (p=0.007) and blood pressure (systolic: p=0.002, diastolic: p < 0.001) between the HRH and control groups, with higher levels in the HRH group. Study 9 compared peritoneal dialysis patients to hemodialysis patients and found no cases of headache in the peritoneal dialysis group. Study 13 showed that pre-dialysis sodium (p=0.003) was significantly higher in the headache group, and pre- and post-dialysis magnesium was significantly lower (p=0.05 for pre-dialysis, p=0.02 for post-dialysis) in the headache group. Finally, study 14 found that urea levels (p < 0.05) and pre-dialysis blood pressure (systolic: p<0.01, diastolic: p<0.001) were significantly elevated in the dialysis headache group.

The study by Antoniazzi et al. (5) evaluated 123 patients undergoing hemodialysis. Although this study has often been referenced as reporting a higher percentage of dialysis headache (up to 70%), this figure is not entirely accurate, and the study presents a more detailed view of the data. Out of these patients:

• 87 patients (70.7%) reported experiencing headaches at some point during their hemodialysis treatment. This includes both headaches that occurred during dialysis sessions and those that occurred outside of dialysis sessions.

Break this down further:

• 59 patients (67.8%) had headaches prior to beginning hemodialysis (Group 1). Among these, 24 patients (40.7%) reported significant improvement in their headaches after starting hemodialysis.

• 28 patients (32.2%) did not have headaches prior to starting hemodialysis but developed headaches related to hemodialysis (Group 2). Among these:

• 20 patients had headaches restricted to the hemodialysis sessions.

• 8 patients had headaches more than 50% of the time, even between sessions.

Among the 87 patients who reported headaches at some point during their hemodialysis treatment:

• 63 patients were still experiencing headaches at the time of the study.

• Of these, 50 patients (79.4%) had headaches only during the hemodialysis sessions.

• 13 patients (20.6%) had headaches between sessions. The VAS scores across the studies indicate that dialysis headaches are of moderate intensity, with scores ranging



from 4.3 to 6.7. This suggests that while the intensity of headaches varies slightly between studies, it generally falls within the moderate range (Table 1).

Table 1. Visual analog scale (VAS)scores of dialysis headache intensity across studies

Study ID	VAS score
Study 1	5.21±2.0
Study 2	4.3 ± 1
Study 5	6.7 (±2.1)
Study 7	4.5 ± 1.74
Study 8	5.64 ± 2.05

The moderate intensity of dialysis headache is further supported by treatment patterns observed in study 5 and study 7, where simple analgesics and rest were commonly used to manage symptoms. In study 5, of the 49 patients experiencing dialysis headaches, 34 used Dipyrone, 8 used Paracetamol, 4 used a combination of Dipyrone/ Paracetamol, and 3 used other treatments. Similarly, in study 7, of the 48 patients, 41 used Paracetamol and 7 used rest to alleviate their headaches, further indicating that the headaches were of moderate intensity and manageable with basic treatments.

The moderate intensity and non-persistent nature of dialysis headaches are further supported by findings from study 5, where the majority of patients reported a decrease in both the intensity and frequency of headaches over time. Specifically, 28 out of 49 patients (57.1%) reported a reduction in headache intensity, and 33 out of 49 patients (67.3%) experienced a decrease in the frequency of their headaches. This trend, along with the fact that most patients used simple analgesics or rest for relief, suggests that dialysis headaches are generally of moderate intensity and tend to improve over time.

Proportional meta-analysis

A proportional meta-analysis was conducted using a random effects model to determine the percentage of patients experiencing dialysis headache across the 15 included studies (Table 2). The total number of patients undergoing hemodialysis in the studies ranged from 24 to 450, with a total of 2103. The percentage of patients experiencing dialysis headache varied widely across the studies, ranging from 7% to 53%. The overall pooled estimate of the percentage of patients experiencing dialysis headache was 28% (95% CI: 19%, 36%) (Figure 2).

Individual study findings showed variability in the reported percentages. The highest percentage of dialysis headache was observed in study 6 (53%), followed by study 5 (49%) and study 7 (38%). In contrast, studies 2, 9, and 10 reported much lower percentages, ranging from 7% to 9%. Some studies, such as study 1, excluded patients with prior headaches, while others did not, which may contribute to the differences in reported prevalence. For example, study 3 included patients with pre-existing headaches, and 63% of patients had headaches before beginning hemodialysis. Studies 5 reported higher percentages, potentially due to confounding factors such as caffeine use.

Table 2. Proportion of dialysis headache in hemodialysis patients in the included studies

Study ID	Total number of patients undergoing hemodialysis	No. (of patients experiencing dialysis headache)	% (95% CI)	Nots
Study 1	154	24 (6 males, 18 females)	16% (10-22%)	Developed dialysis headache during hemodialysis or after hemodialysis but considered related to hemodialysis (excluding patients with a headache before the beginning of the hemodialysis program).
				14 patients developed headache during hemodialysis and 10 of which continue with headache after hemodialysis
Study 2	92	8	9% (4-16%)	A previous history of primary or secondary headaches were excluded.
Study 3	25	8	32% (15-54%)	Did not exclude patients with headache before hemodialysis. Five patients (63%) reported headache previously to hemodialysis therapy and three (37%) developed headache after the beginning of renal replacement therapy.
Study 4	100	25	25% (17-35%)	Do not clear if some patients have prior headache
Study 5	100	49	49% (39-59%)	Patients were considered to be making excessive use of caffeine when they reported having six or more cups of coffee per day. This may be a cause for elevated percentage
Study 6	30	16	53% (34-72%)	
Study 7	128	48	38% (29-46%)	From 48, 20 had a baseline headache disorder before initiating dialysis but 28 (58.33%) developed HDH de novo.
Study 8	450	175	39% (34-44%)	
study 9	318	21	7% (4-10%)	No patients experiencing pre-dialysis headache, none of the patients in our group of patients fulfilled criteria for this disorder (caffeine-withdrawal headache).
Study 10	163	11	7% (3-12%)	
Study 11	83	13	16% (9-25%)	Excluding prior headache
Study 12	24	12	50% (29-71%)	
Study 13	250	75	30% (24-36%)	
study 14	63	30	48% (35-61%)	
study 15	123	20	16% (10-24%)	Had headache restricted to HD session, do not have headache prior to starting hemodialysis.
	Тс	otal %, 95% CI		28% (19-36%)





Figure 2. Forest and funnel plots for proportion of dialysis headache in hemodialysis patients in the 15 included studies.

After updating the numbers of patients who developed dialysis headache (restricted to dialysis-related headaches) in studies 1, 3, 7, and 15, and excluding studies 4, 6, 10, 12, 13, and 14 due to unclear prior headache history or confounding factors like excessive caffeine use (in study 5), a new meta-analysis was performed (Table 3). The updated pooled estimate for the percentage of patients experiencing dialysis headache across the 8 included studies (with a total of 1373 patients) was 16% (95% CI: 9%, 24%). The heterogeneity remained high ($I^2 = 96\%$), supporting the use of a random effects model in the analysis (Figure 3).

Table 3. Proportion of dialy	sis headache in hemodial	ysis patients in the u	pdated studies

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Study ID	Total number of patients undergoing hemodialysis	No. of patients experiencing dialysis headache	%, 95% Cl
Study 1	154	14	9% (5-15%)
Study 2	92	8	9% (4-16%)
Study 3	25	3	12% (3%-31%)
Study 7	128	28	22% (15%-30%)
Study 8	450	175	39% (34%-44%)
Study 9	318	21	7% (4-10%)
Study 11	83	13	16% (9-25%)
Study 15	123	20	16% (10-24%)
Total %			16% (9-24%)

Study	Events	Total	Weight	IV, Random, 95% CI	IV, F	andom	, 95% (
study1	14	154	13.2%	0.09 [0.05; 0.15]	-			
study2	8	92	12.9%	0.09 [0.04; 0.16]	+	+		
study3	3	25	10.0%	0.12 [0.03; 0.31]	-	-		
study7	28	128	12.4%	0.22 [0.15; 0.30]	- 12		-	
study8	175	450	13.2%	0.39 [0.34; 0.44]				-
sudy9	21	318	13.6%	0.07 [0.04; 0.10]	+			
study11	13	83	12.1%	0.16 [0.09; 0.25]		-		
study15	20	123	12.6%	0.16 [0.10; 0.24]	-	<u> </u>		
Total (95% C			100.0%	0.16 [0.09; 0.24]	-	-		
Heterogeneity:	Tau ² = 0.01	109; Ch	i ² = 158.59), df = 7 (P < 0.01); I ² = 9	36%	1		
					0.1	0.2	0.3	0.4

Figure 3. Forest plot for proportion of dialysis headache in hemodialysis patients in the updated studies.



A separate meta-analysis was performed to determine the percentage of males and females experiencing dialysis headache, with data separated by gender across the studies that provided gender-specific data (Table 4). The total number of patients with dialysis headache included in this analysis was 461, with 239 males and 222 females.

For the male patients, the overall pooled estimate of the percentage experiencing dialysis headache was 52% (95% CI: 39-64%), with variation across the studies. The highest percentage of male patients experiencing dialysis headache was observed in study 10 (91%), followed by study 9 (76%). The percentage of males in other studies ranged from 25% (study 1) to 64% (study 8).

For the female patients, the overall pooled estimate of the percentage experiencing dialysis headache was 48% (95% Cl: 35-61%). The highest percentage of female patients experiencing dialysis headache was reported in study 5 (69%), while study 10 showed the lowest percentage (9%) (Figure 4).

These findings suggest that the prevalence of dialysis headache is slightly higher in males compared to females across the included studies.

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Tella 4	Developeration						across studies
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	Total number of				
Study ID	patients undergoing	No. of males	%, 95% CI	No. of females	%, 95% CI
0. 1. 1	hemodialysis		0.5% (3.0. 1.7%)	10	750((50, 0000)
Study 1	24	6	25% (10-47%)	18	75% (53-90%)
Study 2	8	5	62% (24-91%)	3	38% (9-76%)
Study 3	8	3	38% (9-76%)	5	62% (24-91%)
Study 5	49	15	31% (18-45%)	34	69% (55-82%)
Study 7	48	18	38% (24-53%)	30	62% (47-76%)
Study 8	175	112	64% (56-71%)	63	36% (29-44%)
Study 9	21	16	76% (53-92%)	5	24% (8-47%)
Study 10	11	10	91% (59-100%)	1	9% (0-41%)
Study 12	12	7	58% (28-85%)	5	42% (15-72%)
Study 13	75	35	47% (35-59%)	40	53% (41-65%)
Study 14	30	12	40% (23-59%)	18	60% (41-77%)
	Total %, 95% Cl	52% (3	9-64%)	48	% (35-61%)

4b

4a



Figure 4. Forest plots for percentage of males and females experiencing dialysis headache across studies.

06 - 0.8



The most frequent characteristics of dialysis headache across the studies were throbbing pain, bilateral location, photophobia, and phonophobia (Supplementary Table 3), (Table 5). A meta-analysis of the studies reporting these characteristics (Figure 5) revealed the following: • Throbbing pain was reported by 80% (95% Cl: 72-88%) of patients with dialysis headache.

• Bilateral location was reported by 66% (95% CI: 50-83%) of patients.

- Photophobia occurred in 38% (33-42%) of patients.
- Phonophobia was reported by 42% (95% CI: 36-48%) of patients.

Study ID	Total no. of patients having dialysis headache	Throbbing	%	Bilateral location	%	Photophobia	%	Phonophobia	%	
Study 5	49	36	73% (59-85%)	34	69% (55-82%)	18	37% (23-52%)	21	43% (29-58%)	
Study 10	11	9	82% (48-98%)			2	18% (2-52%)	4	36% (11-69%)	
Study 14	30	26	87% (69-95%)							
Study 8	175			92	53% (45-60%)	71	41% (33-48%)	74	42%(35-50%)	
Study 9	21			17	81% (58-95%)					
Total %, 95% CI		80% (% (72-88%)		66% (50-83%)		33-42%)	42% (36-48%)		

5a

5c

Study	Events	Total	Weight	IV, Fixed, 95% CI	IV,	IV, Fixed, 95% CI				
study5	36			0.73 [0.59; 0.85]	-		-			
study10	9	11	12.6%	0.82 [0.48; 0.98] -	_	-		_		
study14	26	30	44.4%	0.87 [0.69, 0.96]		-	1	•		
Total (95% CI)		90	100.0%	0.80 [0.72; 0.88]			•	-		
Heterogeneity, T	au ² = 0.0			df = 2 (P = 0.33); 1 = 119	6		1			
				0.5	0.6	0.7	0.8	0.9		

5b

Study	Events	Total	Weight	IV, Random, 95% CI						
study5	34	49	33.0%	0.69 [0.55; 0.82]				_		
study8	92	175	38.2%	0.53 [0.45; 0.60]	-	-	1			
study9	17	21	28.9%	0.81 [0.58; 0.95]		-		•	-	
Total (95% CI)				0.66 [0.50; 0.83]	-	-	-	-		
Heterogeneity. T	au ² = 0.01	169; Ch	i ² = 11.88,	df = 2 (P < 0.01); f = 83	196	1	1	1	1	
					0.5	0.6	0.7	0.8	0.9	

5d

							Ju									
Study	Events	Total		Weight (random) N	/, Fixed + Random, 95% CI	IV, Fixed + Random, 95% (Study	Events	Total	Weight	IV, Fixed, 95% CI		IV, Fix	ed, 98	5% C	I
study5 study6 study10	18 71 2	49 175 11	20.9% 71.8% 7.3%	28.5% 59.4% 12.1%	0.37 [0.23, 0.52] 0.41 [0.33, 0.48] 0.18 [0.02; 0.52]		study5 study8 study10	21 74 4		74.3%	0.43 [0.29, 0.58] 0.42 [0.35; 0.50] 0.36 [0.11; 0.69] -		-		_	-
Total (common effect, 95% Cl) Total (random effect, 95% Cl) Heterogenety: Tau ² = 0.0017; Ch ²		235 f=2(P	100.0% = 0.18); 1 ² = 4	100.0%	0.38 [0.32; 0.44] 0.37 [0.28; 0.45]	0.1 0.2 0.3 0.4	Total (95% C Heterogeneity				0.42 [0.36; 0.48] (P = 0.92); $\vec{\Gamma}$ = 0%	02	0.3	0.4	0.5	0.6



Discussion

This systematic review and meta-analysis comprehensively examined the prevalence, characteristics, and associated factors of dialysis headache. The findings suggest that dialysis headache is a common complication, with an updated prevalence estimate of 16% (95% Cl: 9-24%) across the eight studies included in the refined analysis.

This estimate aligns with existing literature but highlights the variability in reported prevalence, which influenced by factors such as study design, patient demographic, and diagnostic criteria. For example, study 6 by Viticchi et al. (19) reported a much higher prevalence of 53%, while study 9 by Stojimirovic et al. (17) found a notably lower prevalence of 7%. Additionally, study 1 by Yang et al. (4) excluded patients with prior headaches, which may have led to a lower reported prevalence compared to studies that included patients with a history of headaches. Similarly, study 5 by Sousa Melo et al. (9), which found a high prevalence of 49%, might have been influenced by the inclusion of patients who reported excessive caffeine use, a known risk factors for headaches.

The gender-specific analysis revealed that males had a slightly higher prevalence of dialysis headache (52%) compared to females (48%). While the difference in prevalence between genders is modest, it highlights the importance of considering gender in both diagnostic and therapeutic approaches. Further studies focusing on gender-specific mechanisms and treatments for dialysis headache are warranted.

When examining the characteristics of dialysis headaches, the most frequently reported symptoms were throbbing pain (80%), bilateral headache location (66%), photophobia (37%), and phonophobia (42%). These results are consistent with previous reports that dialysis headaches often present with a pulsating, bilateral pain and are associated with sensitivity to light and sound. The high prevalence of these symptoms in this analysis suggests that clinicians should be alert to these signs when assessing dialysis patients for potential headache disorders.

Study 3 by Gomes et al. (13) which found that higher anxiety and sleepiness scores were significantly associated with dialysis headache, pointing to potential psychological and lifestyle factors that may exacerbate the condition.

The moderate intensity of dialysis headache observed in the majority of studies suggests that most cases can be managed with simple analgesics. This is further supported by treatment patterns reported in study 5 and study 7, where patients commonly used medications such as Dipyrone and Paracetamol, along with rest. These findings imply that while dialysis headaches can affect patient quality of life, they are often manageable



with conservative treatments. However, the variability in response to treatment across studies also indicates that individualized care plans may be necessary, particularly for patients with more persistent or severe symptoms.

Several limitations should be considered when interpreting the findings of this meta-analysis. First, the included studies were highly heterogenous, with differences in study design, patient populations, and diagnostic criteria, warranting caution when generalizing the findings across all dialysis populations. Second, many of the studies included were monocenter, which may limit the external validity of the results.

Conclusions

Dialysis headache remains a prevalent but inconsistently reported complication of hemodialysis. Standardized diagnostic criteria and further research are needed to better understand its pathophysiology and improve management strategies.

References

- Olesen J, Steiner T. The International classification of headache disorders, 2nd edn (ICDH-II). BMJ Publishing Group Ltd; 2004. p. 808-11.
- Ettlin DA. The international classification of headache disorders, (beta version). Cephalalgia. 2013;33(9):629-808.
- Olesen J. International classification of headache disorders. The Lancet Neurology. 2018;17(5):396-7.
- Yang Y, Meng F, Zhu H, Zhang L, Lu G, Xiao S, et al. The applicability research of the diagnostic criteria for 10.2 Heamodialysis-related headache in the international classification of headache disorders-3rd edition. The journal of headache and pain. 2023;24(1):19. doi: 10.1186/s10194-023-01548-7
- 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;43(2):99-102. doi: https://doi. org/10.1046/j.1526-4610.2003.03025.x
- Hazim A, Adarmouch L, Eloury A, Aasfara J, Asly M, Slassi I. Hemodialysis-related headache: Still a challenge in 2020? Effect of conventional versus online hemodiafiltration from a study in Casablanca, Morocco. Artificial Organs. 2021;45(6):602-7. doi: https://doi.org/10.1111/aor.13886
- Alessandri M, Massanti L, Geppetti P, Bellucci G, Cipriani M, Fanciullacci M. Plasma Changes of Calcitonin Gene-Related Peptide and Substance P in Patients with Dialysis Headache. Cephalalgia. 2006;26(11):1287-93. doi: 10.1111/j.1468-2982.2006.01217.x
- 8. Goksel BK, Torun D, Karaca S, Karatas M, Tan M, Sezgin N, et al. Is Low Blood Magnesium



Level Associated With Hemodialysis Headache? Headache: The Journal of Head and Face Pain. 2006;46(1):40-5. doi: https://doi.org/10.1111/ j.1526-4610.2006.00295.x

- Sousa Melo E, Pedrosa RP, Carrilho Aguiar F, Valente LM, Sampaio Rocha-Filho PA. Dialysis headache: characteristics, impact and cerebrovascular evaluation. Arq Neuropsiquiatr. 2022;80(02):129-36. doi: 10.1590/0004-282X-ANP-2021-0133
- Moher D, Liberati A, Tetzlaff J, Altman DG, Group P. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. International journal of surgery. 2010;8(5):336-41.
- 11. NA Y. JBI Critical Appraisal Checklist for Studies Reporting Prevalence Data. 2017.
- Xiong Y, You N, Liao R, Wu L, Liu Y, Ling Z, et al. Association of intradialysis blood sodium level, blood pressure variability, and hydration status with hemodialysisrelated headache: a prospective cohort study. The journal of headache and pain. 2023;24(1):166. doi: 10.1186/s10194-023-01701-2
- Gomes BT, da Costa ALG, Mazzali M. Dialysis headache: prevalence and clinical presentation in hemodialysis and kidney transplant patients. Headache Medicine. 2022;13(4):265-70.
- Maggioni F, Mantovan MC, Rigotti P, Cadrobbi R, Mainardi F, Mampreso E, et al. Headache in kidney transplantation. The journal of headache and pain. 2009;10(6):455-60. doi: 10.1007/s10194-009-0148-9

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- Chhaya KT, Mankad S, Shah MK, Patel M, Desai D, Desai SD. Headache Associated with Hemodialysis in Patients with End-Stage Renal Disease in India: A Common Yet Overlooked Comorbidity. Annals of Indian Academy of Neurology. 2022;25(1):82-7. doi: 10.4103/aian.aian_404_21
- Gozubatik-Celik G, Uluduz D, Goksan B, Akkaya N, Sohtaoglu M, Uygunoglu U, et al. Hemodialysisrelated headache and how to prevent it. European Journal of Neurology. 2019;26(1):100-5. doi: https://doi.org/10.1111/ene.13777
- Stojimirovic B, Milinkovic M, Zidverc-Trajkovic J, Trbojevic-Stankovic J, Maric I, Milic M, et al. Dialysis headache in patients undergoing peritoneal dialysis and hemodialysis. Renal Failure. 2015;37(2):241-4. doi: 10.3109/0886022X.2014.982486
- Jesus ACFd, Oliveira HA, Paixão MOR, Fraga TP, Barreto FJN, Valença MM. Clinical description of hemodialysis headache in end-stage renal disease patients. Arquivos de Neuro-Psiquiatria. 2009;67.
- Viticchi G, Falsetti L, Salvemini S, Bartolini M, Ranghino A, Buratti L, et al. Headache changes after kidney transplant. Acta Neurologica Belgica. 2022;122(1):83-90. doi: 10.1007/s13760-021-01637-x
- Göksan B, Karaali-Savrun F, Ertan S, Savrun M. Haemodialysis-Related Headache. Cephalalgia. 2004;24(4):284-7. doi: 10.1111/j.1468-2982.2004.00668.x

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