



Dialysis headache: a systematic review and Meta-Analysis

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Supplementary Table 1. Quality assessment of included studies using JBI Checklist

Study ID	Appropriate Sample Frame	Proper Recruitment	Adequate Sample Size	Detailed Description	Sufficient Data Coverage	Valid Diagnostic Criteria	Standardized Measurement	Proper Statistical Analysis	Response Rate Adequate	Overall Quality
Study 1	√	√	√	√	√	√	√	√	√	9
Study 2	√	√	X	√	√	√	√	√	√	8
Study 3	√	√	X	√	√	√	√	√	√	8
Study 4	√	√	√	√	√	√	√	√	√	9
Study 5	√	√	√	√	√	√	√	√	√	9
Study 6	√	√	X	√	√	√	√	√	√	8
Study 7	√	√	√	√	√	√	√	√	√	9
Study 8	√	√	√	√	√	√	√	√	√	9
Study 9	√	√	√	√	√	√	√	√	√	9
Study 10	√	√	√	√	√	√	√	√	√	9
Study 11	√	√	X	√	√	√	√	√	√	8
Study 12	√	√	X	√	√	√	√	√	√	8
Study 13	√	√	√	√	√	√	√	√	√	9
Study 14	√	√	X	√	√	√	√	√	√	8
Study 15	√	√	√	√	√	√	√	√	√	9



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Supplementary Table 2. Characteristics of the included studies

Study ID	Author	Year	Country	Journal	Study design	Mean age for DH group	Sex(male%) of DH group	Multicenter or monocenter
Study 1	Ying Yang	2023	China	The Journal of Headache and Pain	randomized cross-sectional study	57.45±10.75 years	25%	monocenter
Study 2	Yuqin Xiong	2023	China	The Journal of Headache and Pain	prospective cohort	47.9 ± 12.8	5 (62.5%)	monocenter
Study 3	Bruno Teixeira Gomes	2022	Brazil	Headache Medicine	Observational study	39.9 ± 12.9	3 (38%)	monocenter
Study 4	Asmaa Hazim	2021	Morocco	Artificial Organs	A descriptive, cross-sectional	63.52 (14.32) for all HD patients	45% for all HD patients	multicenter
Study 5	Eduardo Sousa Melo	2021	Brazil	Arq Neuropsiquiatr	cross-sectional	45 (39–58.9)	30.60%	multicenter
Study 6	Giovanna Viticchi	2021	Italy	Acta Neurologica Belgica	retrospective study	-	-	monocenter
Study 7	Kishti T. Chhaya	2021	India	Annals of Indian Academy of Neurology	cross-sectional	47.2 (17.3)	37.50%	monocenter
Study 8	G. Gozubatik-Celik	2018	Turkey	European Journal of Neurology	prospective study	57.3 (15.7)	64%	multicenter
Study 9	Biljana Stojimirovic	2014	Serbia	Renal Failure	prospective study	318 on HD (119 females and 199 males, mean age 59.90 ± 12.73 years)	76%	multicenter
Study 10	Alan Chester Feitosa de Jesus	2009	Brazil	Arq Neuropsiquiatr	prospective descriptive study	48.8±11.2	90.90%	monocenter
Study 11	Ferdinando Maggioni	2009	Italy	The Journal of Headache and Pain	retrospective study			monocenter
Study 12	Alessandri M	2006	Italy	Cephalalgia	case-control	58(4)	58.30%	monocenter
Study 13	Basak Karakurum Goksel	2006	Turkey	Headache	case-control	44.9 ± 16.9	46.70%	monocenter
Study 14	B Gökşan	2004	Turkey	Cephalalgia	retrospective	43 ± 10.2	40%	monocenter
Study 15	Ana L. Antoniazzi	2003	Brazil	Headache	Prospective	-	-	multicenter



Supplementary Table 2. Characteristics of the included studies, continued

Study ID	Method of headache diagnosis and criteria for identifying dialysis headache patients	Dialysis solution	Duration, frequency of hemodialysis session, vintage of HD treatment	Onset and duration of dialysis headache	Study period
Study 1	ICHD-3, this study suggest modification to include headache developed after HD session and considered related to HD.	bicarbonate	4 hours, three weekly dialysis treatments, The mean duration of chronic dialysis therapy was 6.38±5.40 years.	at a mean of 2.33±0.79 h after dialysis commenced. The average headache duration was 6.56±1.57 h (median=3.0 h), with 66.67% of the patients reporting a duration of ≤4 h.	January 2022 to September 2022
Study 2	HRH is defined as having at least three headache episodes that begin during HD and resolve within 72 h of HD session completion.	acetate	2-3 acetate HD treatments per week. The median dialysis vintage was 27.1 (12-46.2) months.	headache occurred 100.3 ± 69.5 min after the start of dialysis. The intra-dialysis headache duration and the whole headache duration were 98.8 ± 68.1 and 120 (65-217.5) minutes, respectively.	October 17, 2022 to February 24, 2023
Study 3	ICHD-3	-	3h30 to 4h, three sessions weekly. Dialysis length (months) 56.2.	-	December 2021 to May 2022
Study 4	ICHD3□	bicarbonate	thrice per week 4-hour hemodialysis sessions for at least 6 month. Dialysis vintage of 50.28 ± 48.31 months	-	-
Study 5	ICHD-3	bicarbonate	4 hours. dialysis vintage was of 54 (±59.3) months	Duration of headache 215.2 (±429.2) minutes.	September 2015 to January 2016. Included patients undergo HD not less than 6 months.
Study 6	IHS 2018 criteria (ICHD-3)	-	-	-	All patients who underwent kidney transplantation for ESKD in the previous 5 years
Study 7	ICHD3□	-	4 h, except one patient 3hr. 53 patients undergoing HD thrice a week while 75 twice a week.	mostly starts less than 60 minutes of HD session for 71% (n=34) of patients.	3 months follow-up
Study 8	ICHD-II	bicarbonate	4 h, thrice weekly.	Headache was started a mean of 2.90 ± 0.86 h after the HD. The mean duration of headache was 6.22 ± 7.8 h, with a duration of ≤4 h reported by 64.0% of patients.	1 May 2015 to 31 December 2015
Study 9	ICHD-II	bicarbonate	4 h, thrice weekly.	during the third hour of HD session, less than four hours duration.	Time on dialysis ranged from 3 to 60 months in PD patients and from 3 to 240 months in HD patients.
Study 10	ICHD II, 2004	-	-	-	November 2007 to January 2008
Study 11	ICDH-II, 2004	-	-	-	-
Study 12	criteria of HIS, and it is defined by the following diagnostic criteria: (i) at least three attacks of acute headache fulfilling criteria iii and iv; (ii) the patient is on hemodialysis; (iii) headache develops during at least half of hemodialysis sessions; (iv) headache resolves within 72 h after each hemodialysis session and/or ceases altogether after successful transplantation.	bicarbonate	3 times a week.	-	-
Study 13	according to the revised International Headache Society criteria for 2003 (headache that starts during an HD session and resolves within 72 hours after the session, Headache develops during at least half of hemodialysis sessions)	bicarbonate	three times weekly. The duration of each session was 4 to 5 hours.	-	-
Study 14	the criteria of the International Headache Society 1988, 2003	acetate in 35 patients and bicarbonate in 28 patients	4 h, vintage (years) 5 ± 3.8.	often starting during the third hour of hemodialysis and lasting less than four hours.	1996 to 2000.
Study 15	International Headache Society criteria, Patients with chronic renal failure attending 3 HD services in Ribeirão Preto, São Paulo, Brazil, from January of 1998 to December of 1999, were evaluated.	-	Mean duration of chronic HD therapy was 42.4 months.	-	January of 1998 to December of 1999



Supplementary Table 2. Characteristics of the included studies, continued

Study ID	Title	Summary
Study1	The applicability research of the diagnostic criteria for 10.2 Hemodialysis-related headache in the international classification of headache disorders-3rd edition	The study by Ying Yang et al. investigates the applicability of the diagnostic criteria for hemodialysis-related headache (HRH) in the International Classification of Headache Disorders, 3rd Edition (ICHD-3). It aims to evaluate how well these criteria can identify HRH in patients undergoing maintenance hemodialysis.
Study 2	Association of intradialysis blood sodium level, blood pressure variability, and hydration status with hemodialysis-related headache: a prospective cohort study	The study by Yuqin Xiong et al. investigates the relationship between intra-dialysis blood sodium levels, blood pressure variability, and hydration status with hemodialysis-related headache (HRH) in a prospective cohort study. The research found that younger age, lower pre-ultrafiltration blood sodium levels, increased overhydration to dry weight ratio, and greater variability in systolic blood pressure during dialysis are significantly associated with a higher risk of HRH.
Study 3	Dialysis headache: prevalence and clinical presentation in hemodialysis and kidney transplant patients	The study by Bruno Teixeira Gomes et al. investigates the prevalence and clinical presentation of headache in patients undergoing hemodialysis and those who have had kidney transplants. It found that 32% of hemodialysis patients and 20% of kidney transplant patients experienced dialysis headache. The headaches were predominantly pulsating, accompanied by photophobia, phonophobia, and nausea or vomiting. Patients with headache had higher anxiety and sleepiness scores.
Study 4	Hemodialysis-related headache: Still a challenge in 2020? Effect of conventional versus online hemodiafiltration from a study in Casablanca, Morocco	The study by Asmaa Hazim et al. investigates whether online hemodiafiltration (OL-HDF) is more effective than conventional hemodialysis in reducing the prevalence of hemodialysis-related headache (HRH). The study was conducted in Casablanca, Morocco, and found that 60% of patients reported headache, with 41.6% (n=25) experiencing it during hemodialysis. The research suggests that OL-HDF may be more effective in reducing the incidence of HRH compared to conventional hemodialysis.
Study 5	Dialysis headache: characteristics, impact and cerebrovascular evaluation	The study by Eduardo Sousa Melo et al. investigates the characteristics, impact, and cerebrovascular evaluation of dialysis headache. The research found that dialysis headache is common, occurring in 49% of the 100 patients studied. It typically starts after the second hour of hemodialysis and is most often a tension-type headache. The headache has a significant negative impact on quality of life, particularly in the domains of pain and general health. Women, younger individuals, and those with higher education levels are more likely to experience dialysis headache. Transcranial Doppler ultrasonography revealed a pattern of cerebral vasodilatation among patients with dialysis headache, suggesting a failure of compensatory cerebral self-regulation mechanisms.
Study 6	Headache changes after kidney transplant	The study by Giovanna Viticchi et al. investigates how headache characteristics change after kidney transplantation in patients with chronic kidney disease (CKD). The research found that 65.5% of patients experienced headache before transplantation, with 38.2% reporting migraine and 14.5% (n=16) reporting dialysis headache. After transplantation, 53.6% of patients reported changes in headache characteristics, with 27.3% experiencing complete resolution, 19.1% showing improvement, and 7.2% experiencing worsening. The study suggests that kidney transplantation significantly impacts headache frequency and severity, and targeted treatments could improve patients' quality of life. The study enrolled 110 patients who had undergone kidney transplantation in the previous 5 years (30 was on hemodialysis, 80 was on peritoneal dialysis) to investigate changes in headache characteristics before and after the transplant.
Study 7	Headache Associated with Hemodialysis in Patients with End-Stage Renal Disease in India: A Common Yet Overlooked Comorbidity	The study by Chhaya et al. included 128 patients undergoing hemodialysis in India. The researchers found that 48 patients (37.5%) experienced headache during hemodialysis. From 48, 20 had a baseline headache disorder before initiating dialysis but 28 developed HDH de-novo. 25% (n=12) of patients experiencing headache within the first 60 minutes, 27% (n=13) between 60-120 minutes, 21% (n=10) between 120-180 minutes, and 27% (n=13) after 180 minutes. The duration of hemodialysis-related headache was mostly less than 60 minutes for 71% (n=34) of patients, while 25% (n=12) had headaches lasting 60-120 minutes, and only 2% (n=2) had headaches lasting 120-180 minutes or more than 180 minutes.
Study 8	Hemodialysis-related headache and how to prevent it	The study by G. Gozubatik-Celik et al. included 175 patients developed DH of a total of 450 potential subjects. It discusses the prevalence of hemodialysis-related headache (HDH) and provides recommendations for its prevention. The study highlights that HDH is a common issue among patients undergoing hemodialysis and suggests strategies such as adjusting dialysis protocols.
Study 9	Dialysis headache in patients undergoing peritoneal dialysis and hemodialysis	The study by Biljana Stojimirovic et al. evaluated 318 individuals undergoing hemodialysis, and found that 21 patients (6.6%) experienced dialysis headache, while no cases of headache were reported among the peritoneal dialysis patients. This indicates that dialysis headache is predominantly associated with hemodialysis and not peritoneal dialysis.



Supplementary Table 2. Characteristics of the included studies, continued

Study ID	Title	Summary
Study 10	Clinical description of hemodialysis headache in end-stage renal disease patients	The study by Alan Chester Feitosa de Jesus et al. aimed to determine the frequency and clinical characteristics of headache in patients undergoing hemodialysis. The study found that 76.1% of the patients reported experiencing headache, with 6.7% diagnosed with isolated hemodialysis headache (HDH) without a previous history of primary headache. The study found that the time elapsed between the beginning of the dialysis session and the onset of headache varied among patients. Specifically, no patients (0%) experienced headache within the first hour, 27.3% (3 patients) experienced headache between 1–1.9 hours, 36.4% (4 patients) between 2–2.9 hours, and 27.3% (3 patients) between 3–4 hours.
Study 11	Headache in kidney transplantation	The study by Ferdinando Maggioni et al. investigated the prevalence and characteristics of headache in kidney transplant patients. The study included 83 consecutive kidney transplant patients who underwent neurological examination and a detailed headache history was taken. The researchers found that 44.5% of the patients experienced headache after kidney transplantation, which is higher than the rates reported for the general population and in comparable studies on liver transplant patients. The data about dialysis headache extracted from the headache history.
Study 12	Plasma changes of calcitonin gene-related peptide and substance P in patients with dialysis headache	The study by M Alessandri et al. investigated the levels of calcitonin gene-related peptide (CGRP) and substance P (SP) in patients experiencing dialysis headache. The study found that CGRP levels were significantly higher in patients with dialysis headache compared to those without, both before and after hemodialysis. Substance P levels were also higher in patients with dialysis headache, but the difference was not statistically significant. The data about dialysis headache extracted from the headache history.
Study 13	Is low blood magnesium level associated with hemodialysis headache?	The study by Basak Karakurum Goksel et al. investigated whether low blood magnesium levels are associated with hemodialysis headache (HDH). The researchers enrolled 250 patients undergoing hemodialysis and found that 75 of them experienced HDH. The study revealed that patients with HDH had significantly lower levels of magnesium compared to those without HDH. The findings suggest that low blood magnesium levels may be a contributing factor to HDH, and magnesium supplementation could potentially help alleviate these headaches.
Study 14	Haemodialysis-related headache	The study by B Göksan et al. investigated the prevalence and clinical characteristics of hemodialysis-related headache (HDH) in patients undergoing hemodialysis. The study included 63 patients with chronic renal failure who were on regular dialysis for at least 6 months. The researchers found that 48% of the patients experienced HDH. The headaches were typically bilateral, pulsating, and moderate in intensity, often starting during the third hour of hemodialysis and lasting less than four hours. Associated symptoms included photophobia or phonophobia, vertigo, and nausea or vomiting. The study highlights the significant impact of HDH on patients' quality of life and underscores the need for further research into its management and prevention.
Study 15	Headache and Hemodialysis: A Prospective Study	The study by Ana L. Antoniazzi et al. evaluated 123 patients undergoing hemodialysis. Out of these patients: <ul style="list-style-type: none"> · 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. <p style="text-align: center;">To further break down the data:</p> <ul style="list-style-type: none"> · 59 patients (67.8%) had headaches prior to beginning hemodialysis (Group 1). #24 patients (40.7%) in this group 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). #20 patients had headaches restricted to the hemodialysis sessions. #8 patients had headaches more than 50% of the time, even between sessions. <p style="text-align: center;">Among the 87 patients who reported headaches at some point during their hemodialysis treatment:</p> <ul style="list-style-type: none"> · 63 patients were still experiencing headaches at the time of the study. #50 patients (79.4%) had headaches only during the hemodialysis sessions. #13 patients (20.6%) had headaches between sessions. <p>The study highlights the significant prevalence of headache in patients undergoing hemodialysis, with a notable portion experiencing headaches specifically during dialysis sessions.</p>



Supplementary Table 3. Characteristics of dialysis headache across the included studies

Study ID	Start	Characteristic of headache	Signs	Location	Treatment	Behavior of headache intensity over the months	Behavior of headache frequency over the months
Study 5	*Insidious 39/49 *Sudden 10/49	*Throbbing 36/49 *Pressing 11/49 *Stabbing 2/49	*Photophobia 18/49 *Phonophobia 21/49	*Bilateral 34/49 *Unilateral 9/49 *Sometimes unilateral and sometimes bilateral 6/49	*Dipyrene 34/49 *Paracetamol 8/49 *Dipyrene/paracetamol 4/49 *Others 3/49	*Same as in the beginning 12/49 *Becoming more intense 9/49 *Becoming less intense 28/49	*Same as in the beginning 7/49 *Becoming more frequent 9/49 *Becoming less frequent 33/49
Study 7				*Frontotemporal 22/48 *Frontal 18/48 *Temporal 3/48 *Parietal 3/48 *Occipital 2/48	*Paracetamol 41/48 *rest 7/48		
Study 8			*Phonophobia 74/175 *Photophobia 71/175	*Bifrontal 73/175 *Vertex 24/175 *Generalized 45/175 *Bitemporal 19/175 *Occipital 14/175			
Study 9				*Bilateral 17/21			
Study 10		*Dull 2/11 *Throbbing 9/11	*Photophobia 2/11 *Phonophobia 4/11	*Vertex 1/11 *Diffuse 3/11 *Frontal 1/11 *Temporal 3/11 *Occipital 2/11 *Occipitotemporal 1/11			
Study14		*Dull 4/30 *Throbbing 26/30		*Frontotemporal 15/30 *Occipital 8/30 *Diffuse 7/30			