



## Dialysis headache: A literature review in the last 30 years

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### Abstract

#### Introduction

According to the International Classification of Headache Disorders (ICHD-3), dialysis headache has no specific characteristics occurring during and caused by haemodialysis. It resolves spontaneously within 72 hours after the haemodialysis session has ended.

#### Objective

To describe the prevalence, clinical features, associated symptoms and risk factors of dialysis headache.

#### Methods

Based on a literature search in the major medical databases and using the descriptors “dialysis headache”, “hemodialysis and headache” and “renal dialysis and headache” we included articles published between 1992 and 2022. Of the 492 articles found, only 9 met the inclusion criteria and were analyzed.

#### Results

We describe 444 patients (53.1% men and 46.9% women) diagnosed with dialysis headache, corresponding to 24.8% of those who underwent hemodialysis. The age ranged from 15 to 75 years. Pain occurred predominantly from the third hour of hemodialysis (65.8%), lasting less than four hours (71.7%), located bilaterally (63.1%), pulsatile (58.5%) and moderate intensity (68.9%). The most frequent associated symptoms were photophobia or phonophobia (71.5%), vertigo (22.3%) and nausea and/or vomiting (16.5%).

#### Conclusion

This review showed a high prevalence of dialysis headache in patients undergoing hemodialysis and that the clinical characteristics, treatment and prevention are still poorly studied.



## Introduction

Headache is one of the most frequently reported neurological symptoms by patients with chronic kidney disease on hemodialysis.<sup>1</sup> This complication deserves attention, given that it increases suffering and worsens the quality of life of patients undergoing this therapy.<sup>2</sup>

The diagnostic criteria for dialysis headache were established by ICHD-3, as shown in Table 1.<sup>3</sup> Pathophysiology and triggering factors of dialysis headache have not yet been fully elucidated. Studies point out as possible mechanisms for this condition the type of dialyzer, difference in serum values of urea, renin, aldosterone, magnesium, sodium and serotonin, changes in blood pressure and reduction in serum osmolality.<sup>1,4,7</sup>

**Table 1.** Diagnostic criteria for dialysis headache according to ICHD-3

- A. At least three episodes of acute headache fulfilling criterion C
- B. The patient on haemodialysis
- C. Evidence of causation demonstrated by at least two of the following:
  1. each headache has developed during a session of haemodialysis
  2. either or both of the following:
    - a. each headache has worsened during the dialysis session
    - b. each headache has resolved within 72 hours after the end of the dialysis session
  3. headache episodes cease altogether after successful kidney transplantation and termination of haemodialysis
- D. Not better accounted for by another ICHD-3 diagnosis.

The prevalence of headache from dialysis headache varies between 27% and 73%.<sup>8</sup> However, despite this high prevalence, it is one of the poorly researched clinical conditions, requiring studies to elucidate its clinical characteristics, epidemiology, pathophysiology, management and prevention.<sup>9</sup>

Some narrative reviews on dialysis headache have already been carried out<sup>8,10</sup>, but they did not specify the methodology or expose the results found in a quantitative way. In this review, we aim to describe the prevalence, clinical features, associated symptoms and risk factors of dialysis headache.

## Methods

This study was an integrative and retrospective review of the articles on dialysis headache published in the last 30 years. The research was performed in the online databases Lilacs, SciELO and PubMed, from May to June 2022, using the descriptors “dialysis headache”, “hemodialysis and headache” AND “renal dialysis and headache”.

Articles published from 1992 to 2022 that addressed the discussion of dialysis headache and written only in English were included. Editorials, comments, letter to the editor,

articles that were not fully available or those who lacked accurate information were excluded. To ensure the validity of these articles, the selected studies were analyzed in detail regarding demographic and clinical characteristics and risk factors associated with dialysis headache in patients with chronic kidney disease undergoing hemodialysis.

Of the 894 articles found in the initial search, those that were repeated or that did not address dialysis headache were eliminated (n=402) and only 492 remained and were analyzed. After reading titles and abstracts, 422 articles were excluded. Of the 70 articles selected, 9 articles (case series) met the inclusion criteria, totaling 444 patients.

Data were analyzed based on demographic and clinical characteristics. They were presented as an arithmetic mean with the standard deviation (SD), or as percentages. The percentages was always related to the total number of patients whose information was available for the specific issue. All collected data were organized in a database. The BioEstat version 5.0 for statistical analysis was used.

## Results

A total of 444 patients were diagnosed with dialysis headache (53.1% men and 46.9% women), corresponding to 24.8% (444/1,792) of those who underwent hemodialysis. The age ranged from 15 to 75 years, as shown in Table 2.

**Table 2.** Distribution of the 444 patients with dialysis headache from 1992 to 2022, according to age and sex

Authors/Year	Country of origin	Number of cases	Average age (years±SD)	Sex	
				male	female
Melo et al. <sup>9</sup>	Brazil	49	45.0	15	34
Chhaya et al. <sup>11</sup>	India	48	47.2±17.3	18	30
Gozubatik-Celik et al. <sup>12</sup>	Turkey	175	57.3±15.7	112	63
Moraes et al. <sup>14</sup>	Brazil	23	53.3±14.7	11	12
Stojimirovic et al. <sup>1</sup>	Serbia	21	NR	16	5
Jesus et al. <sup>15</sup>	Brazil	11	48.8±11.2	10	1
Alessandri et al. <sup>13</sup>	Italy	12	58.0±4.0	7	5
Goksel et al. <sup>7</sup>	Turkey	75	44.9±16.9	35	40
Goksan et al. <sup>6</sup>	Turkey	30	43.0±10.2	12	18

**Note:** NR - Not reported; SD - standard deviation

Pain occurred predominantly from the third hour of hemodialysis (65.8%), lasting less than four hours (71.7%), located bilaterally (63.1%), pulsatile (58.5%) and moderate intensity (68.9%). The most frequent associated



symptoms were photophobia or phonophobia (71.5%), vertigo (22.3%) and nausea and/or vomiting (16.5%). The clinical and epidemiological characteristics of dialysis headache are described in Table 3.

**Table 3.** Clinical and epidemiological characteristics of the 444 patients with dialysis headache

Characteristics	%
Male/Female	53.1/46.9
Timing of headache attacks during dialysis (%)	
First hour	12.0
Second hour	22.2
Third hour	27.8
After the fourth hour	38.0
Duration of attacks (hours)	
<4	71.7
≥4	28.3
Localization of pain	
Unilateral	23.4
Bilateral	63.1
Holocranial/difuse	13.5
Quality of pain	
Dull/pressure	41.5
Throbbing/pulsatile	58.5
Intensity of pain	
Mild (VRS 1 – 4)	16.9
Moderate (VRS 5 – 7)	68.9
Severe (VRS 8 – 9)	9.9
Very severe (VRS 10)	4.3
Concomitant symptoms	
Photophobia or phonophobia	71.5
Vertigo	22.3
Nausea or vomiting	16.5
Osmophobia	3.1
Aura	1.0
Autonomic symptoms	0.3
None	10.3
Not reported	34.5

**Note:** Data are presented in percentages (%) and/or arithmetic mean ± standard deviation (interval in parentheses). Data were not available from all patients for every aspect; VRS - verbal rating scale.

Risk factors associated with dialysis headache were classified into individual factors, health-related factors and hemodialysis-related factors and are described in Table 4.

**Table 4.** Risk factors for dialysis headache

Individual	Younger individuals <sup>8</sup> Higher level of education <sup>8</sup> Women <sup>8,11</sup>
Health related	Biochemical changes <sup>1</sup> Depression <sup>11</sup> Moderate pain <sup>11</sup> Higher concentration of urea nitrogen in the blood <sup>12</sup> Increased pre-dialysis plasma CGRP levels <sup>13</sup> Low serum magnesium level <sup>7</sup> Increased serum sodium levels <sup>7</sup> Increase in serum urea levels pre and post hemodialysis <sup>11</sup> High diastolic and systolic blood pressure pre and post hemodialysis <sup>12</sup> High pre-hemodialysis diastolic blood pressure <sup>11,12</sup> High pre-hemodialysis systolic blood pressure <sup>6,12</sup>
Related to dialysis	Higher frequency of hemodialysis sessions per week <sup>8</sup> Longer time in the hemodialysis program <sup>8,12</sup> Use of hemodialysis compared to OL-HDF <sup>14</sup>

**Note:** CGRP: calcitonin gene-related peptide; OL-HDF: online haemodiafiltration.

## Discussion

In our review, the prevalence of dialysis headache was 24.8%, ranging from 6.6% to 50%<sup>1,11</sup>, but there is a previous review that found a prevalence ranging between 27% and 73%.<sup>8</sup> Although studies use the same diagnostic criteria for dialysis headache, it should be taken into account that updates to these criteria impact this diagnosis.

Several factors can influence the occurrence of dialysis headache. Gender, age and education level are described as individual factors that contribute to the higher frequency of this headache. This multifactorial nature of headache makes it difficult to assess.<sup>9,11</sup>

Studies have shown that women have more risk factors for dialysis headache<sup>9,11</sup>, although no statistical relationship was found between dialysis headache and sex.<sup>1,7,8,12</sup> In our review, we found a predominance of dialysis headache in men (56.5% versus 43.5%), possibly because men more frequently undergo hemodialysis.<sup>15</sup>

Among the health-related factors, changes in blood pressure stand out<sup>6,11,12</sup>, biochemical alterations<sup>1,7,11</sup> and depression.<sup>11</sup> There is a significant decrease in plasma concentrations of CGRP after dialysis, thus, high values of this peptide may contribute to the onset of headache.<sup>13</sup> In turn, factors related to dialysis headache were associated with longer time in the hemodialysis program<sup>9,12</sup> and the frequency of sessions per week.<sup>9</sup> One study described that online haemodiafiltration (OL-HDF) had good results as a preventive method of dialysis headache.<sup>14</sup>



There is a consensus regarding the characteristics related to the type of pain, location, intensity, onset and duration of symptoms. However, there are phenotypic features of migraine<sup>4,5</sup> and, especially, tension-type headache.<sup>9,13</sup>

We found that photophobia, phonophobia, nausea and/or vomiting were associated with dialysis headache. However, nausea and/or vomiting are already part of the complications of hemodialysis<sup>16</sup> and may be associated with intradialytic hypotension, changes in the digestive system, and high serum concentrations of sodium and calcium.<sup>17</sup> In turn, photophobia and/or phonophobia are part of the diagnostic criteria for both migraine and tension-type headache.<sup>3</sup> Photophobia is associated with interactions between the visual system and pain in the path from the retina to the visual cortex<sup>18</sup> and phonophobia is associated with sensitization or inhibition of sensory receptive neurons.<sup>19</sup>

We did not identify studies that addressed the prophylactic or abortive management of dialysis headache, thus requiring controlled clinical trials. In this review, we observed that the management of dialysis headache was limited to information<sup>13,20</sup> or quantify<sup>9,11,21</sup> the administration of analgesics for its control. Thus, clinical approaches, as they present little or no scientific evidence, are considered empirical.<sup>8</sup>

## Conclusion

This review showed a high prevalence of dialysis headache in patients undergoing hemodialysis and that the clinical characteristics, treatment and prevention are still poorly studied.

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