Section: Nephrology

Original Research Article

EPIDEMIOLOGY AND RISK FACTORS OF HEADACHE IN CHRONIC KIDNEY DISEASE PATIENTS UNDERGOING HAEMODIALYSIS IN A TERTIARY CARE CENTER A CROSS SECTIONAL STUDY

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ABSTRACT

Background: Headache is common but least addressed problem among chronic kidney disease (CKD) patients on Haemodialysis (HD). The aim is to find the epidemiology of headache and the proportion of Dialysis Related Headache (DRH)in CKD patients undergoing HD. To find the risk factors of headache in these patients.

Materials and Methods: A cross sectional study was carried out amongst 99 consenting CKD patients on HD in our institution. Structured questionnaire was used to record demographic, clinical profile, dialysis frequency, shift, VAS score, quality, and site of headache. Haemoglobin, BP during headache, treatment and imaging details were taken from dialysis records. Data was entered in EXCEL sheet and analysed using SPSS version 19.

Results: Among 99 patients 43 (43.43%) had headache with 27(62.79%) males and 16 (37.21%) females. 7 out of 43 (16.27%) had DRH. Headache was bifrontal throbbing in most patients and highest in 4th hour. Mean Hb was 9.51, SD+/-1.43. Mean VAS score was 4.14, SD+/_1.08. Hypertension was found be significant risk factor for headache (n=36 OR 2.85 with 95% CI 1.07 to 7.5, p value 0.01). Anaemia and dialysis frequency had no statistically significant association. Headache subsided without medication in half (n=23, 53.5%). Oral Paracetamol 500 mg was commonly used as treatment (n=13, 30.23%). CT taken in 4 cases, one had posterior reversible encephalopathy. Dialysis terminated in 2 cases.

Conclusion: This study shows nearly half of HD patients have headache (43.43%) with hypertension as a significant risk factor. More studies are needed to understand the pathophysiology of the same.

Keywords: Chronic kidney disease, headache, haemodialysis.

INTRODUCTION

Chronic Kidney Disease (CKD)is a common problem in our country and many people end up in end stage renal disease (ESRD) requiring renal replacement therapy in the form of hemodialysis (HD) or renal transplant. Majority of these patients undergo HD as renal replacement therapy since renal transplant is not feasible for many in a resource poor country like India. Headache in CKD patients on HD is a least addressed problem but it adds significant burden to the patients by affecting their quality of life. This study aims to find the epidemiology and etiology of headache and the proportion of dialysis related headache in CKD patients undergoing HD in our institution.

A brief review: International Headache Society (IHS) defines a headache attack as: Headache that builds up, remains at a certain level for minutes, hours or days, then wanes until it has resolved completely4 CKD patients receive HD mostly twice or thrice weekly as advised by the Nephrologist.

Headache is a common problem among dialysis patients with prevalence ranging from 27% and 73% as per study done by Antoniazzi et al.[1] One Indian study recently published by by Chayya et al in 2022 gives a headache prevalence of 38% among dialysis patients on HD.[2]

Hemodialysis headache (HDH) was first described by Bana et al in 1972.[3] In ICHD 3 it is classified under Headache related to Homeostasis. According to International Headache Society (IHS) Classification ICHD 3 10.2, dialysis headache is described as Headache with no specific characteristics occurring during and caused by haemodialysis and that resolves spontaneously within 72 hours after the haemodialysis session has ended.

Diagnostic criteria of Dialysis Headache (IHS ICHD 3rd editon)

A. At least three episodes of acute headache fulfilling criterion C
B. The patient is on haemodialysis
C. Evidence of causation demonstrated by at least two of the following:
   - each headache has developed during a session of haemodialysis
   - 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
C. Headache episodes cease altogether after successful kidney transplantation and termination of haemodialysis
D. Not better accounted for by another ICHD-3 diagnosis.

The mechanisms being proposed for headache in CKD patients undergoing dialysis are many Variations in urea, sodium and magnesium levels, and in blood pressure and body weight, may be risk factors for developing Dialysis headache.4

Objectives

Primary

1. To estimate the proportion of headache in chronic kidney disease (CKD) patients undergoing haemodialysis in Department of Nephrology, Government Medical College, Thrissur
2. To determine the proportion of Dialysis related headache among these patients

Secondary

To determine the risk factors of headache in chronic kidney disease patients undergoing hemodialysis in Department of Nephrology, Government Medical College, Thrissur.

MATERIALS AND METHODS

Study design: Cross sectional study

Study setting: Dialysis unit of Department of Nephrology, GMC, Thrissur

Study subjects: All consenting patients undergoing hemodialysis in the dialysis unit of Department of Nephrology.

Inclusion Criteria

- Patients above the age of 18
- Patients undergoing maintenance Hemodialysis for ESRD in the institution

Exclusion Criteria

- Patients who don't give consent for including in the study.
- Patients already diagnosed with primary or secondary headache disorders

Sample size: Calculated with formula 4 pq/d2 Prevalence of headache in dialysis P =38% as per the recent study by Chhaya2 et al from western part of India. Q=100-P=62. d(precision) was kept at 25% and sample size =104. Of the 104 hemodialysis cases 3 got slot outside and 2 went for transplant to higher center. Hence remaining 99 cases were included.

Method All ESRD patients undergoing maintenance HD in the dialysis unit of Department of Nephrology Government Medical College Thrissur who satisfy inclusion and exclusion criteria will be included in the study by census sampling method

Study period: 1 year after obtaining ethical clearance.

Methodology: A structured questionnaire was be used to enter demographic details and clinical details like duration of dialysis, comorbidities, hemoglobin level, presence or absence of headache, whether satisfies ICHD 3 10.2 criteria for dialysis related headache, duration of headache, severity as per visual analog scale, shift in which patient was taken for dialysis, associated features of headache like vomiting, location of headache, nature of headache. BP during headache episode and medications given if any were also recorded by reviewing dialysis notes of the patient. Details of imaging if any done for headache was also documented by reviewing dialysis records.

Data analysis: Data was entered in Excel sheet and master chart was prepared. Statistical analysis was done using SPSS version 19. Mean and standard deviation were calculated for quantitative variables . Descriptive statistics (frequencies and percentages) were calculated for age, gender, clinical features, and prevalence of dialysis related headache. Odds ratio was calculated for each parameter assessed. Chi square test was applied to find out the significance of the variable. A P value less than 0.05 was considered significant.

Ethical aspect: Study was started after obtaining clearance from institutional ethics committee. Name or any revealing features of the persons would not be published. No interventions were planned in this study. No financial implications for the study participants.

Expected outcome of the study: The demographic and clinical profile of ERSD patients with headache will be analyzed and proportion of dialysis related

headache may be found out and risk factors may be identified for the same. This study may help in better understanding of the problem and to find preventive measures like adequate blood pressure control or usage of prophylactic treatment etc.

RESULTS

A total number of 99 patients who were undergoing hemodialysis were included in the study. Of which 68.69% were males (n=68) and 31.31 % were females (n=31). Median age was 49years with Interquartile range of 40 to 56. Proportion of patients with headache among the 99 patients undergoing hemodialysis was 43.43% %(95%CI=34.09-53.76) (n=43) out of which 62.79% were males (n=27) and 37.21% were females (n=16). Of the 43 cases 37.2% had onset of headache towards the end of HD session ie in the 4th hour. Median duration of headache 30 minutes with interquartile range of 30-120 minutes. Headache was bifrontal in location in 86% of cases (n=37) and Throbbing in nature in 65% of cases (n=28). Mean (SD) severity of headache pain using Visual analog scale Score was 4.18±1.08 Mean (SD) Hemoglobin was 9.15 gm/dl±1.43. Headache was self-limiting in 53.5% (n =23), relieved by coffee in 16%(n=7) and local application of pain balm in 11%(n=5). 30.23%of cases (n=13) required Paracetamol as treatment. Out of 43 cases 7 cases (16.27%) satisfied the criteria for dialysis related headache. Hypertension was found to be a significant risk factor for headache (n=36 OR 2.85 with 95% CI 1.07 to 7.5, p value 0.03). BP >160 /100 in 74.4% (n=32) CT head was done in 4 cases and one patient had Posterior reversible encephalopathy syndrome (PRES). Dialysis was terminated in 2 cases.

Table 1: Demogarphic and clinical profile of study population n=99 and Headache cases n=43.

Variable	Total Cases n=99	Headache case n=43
Mean Age	48.03 yrs	47.18yrs 447447.18yrs
Male	68	27
Female	31	16
Mean duration of dialysis	40.61	37.09+/-30.45
Mean HB	9.41, SD=1.52	9.51, SD=1.43
Twice weekly HD	60	25
Thrice weekly HD	39	18
Anemia	87	37
Hypertension	72	36
CAD	13	5
DM	26	12
Dialysis shift 1st	32	13
Dialysis shift 2nd	29	12
Dialysis shift3rd	29	15
Dialysis shift4th	9	3

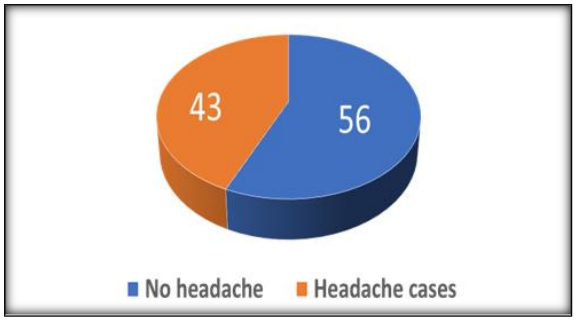

Figure 1: Headache proportion among Hemodialysis Patients (n=99)

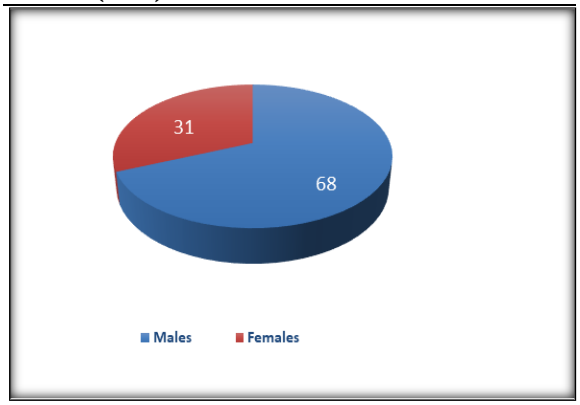

Figure 2 Gender Distribution of study population n=99

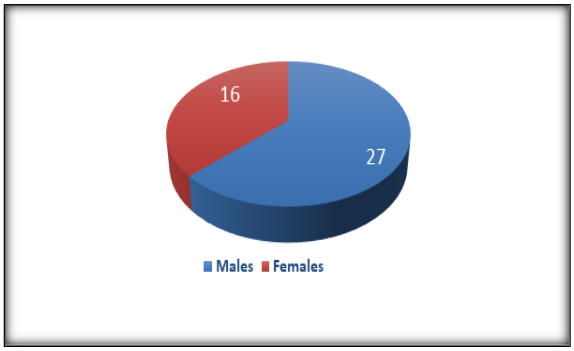

Figure 3: Gender distribution of headache cases n=43

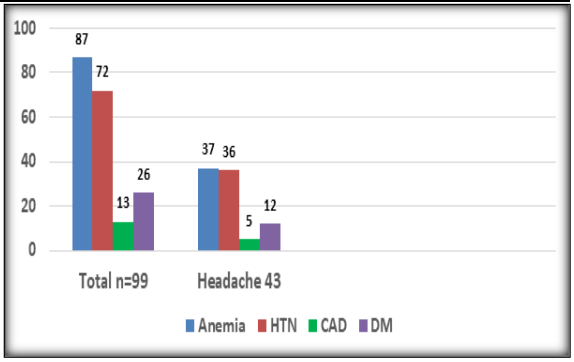

Figure 4: Comorbidities in study sample and headache cases

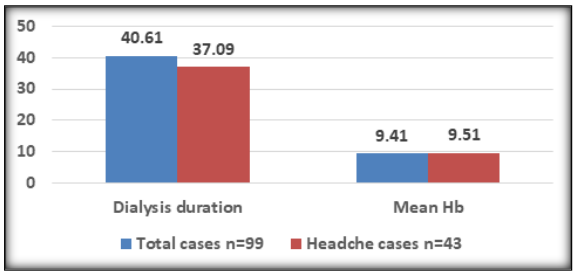

Figure 5: Mean duration of dialysis and mean HB values

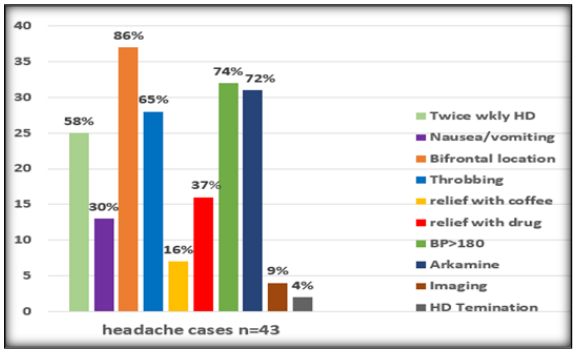

Figure 6: Clinical Profile of headache cases

Table 2: Association of headache with parameters

Sl No	Factors		Headache		Chisquare & p value
			Yes	No	
1	Gender	Male	27(39.7%)	41(60.3%)	Chi sq= 1.23
		Female	16(51.6%)	15(48.4%)	p = 0.26
2	Age	<47	18(50%)	18(50%)	Chi Sq=0.993
		>47	25(39.7%)	38(50.3%)	p=0.31
3	HTN	Yes	36(50%)	36(50%)	Chi sq= 4.632
		No	7(25.9%)	20(74.1%)	**p=0.03**
4	Anemia	Yes	37(42.5%)	50(57.5%)	Chi Sq 0.240
		No	6(50.0%)	6(50.0%)	p=0.625
5	HD duration	<41 mths	27(46.6%)	31(53.4%)	Chi Sq=0.554
		>41 mths	15(39%)	25(61%)	p=0.457
6	Weekly HD frequency	twice	25(41.7%)	35(58.3%)	Chi Sq=0.194
		thrice	18(46.2%)	21(53.8%)	p=0.660

DISCUSSION

Nearly half of the study population of chronic kidney disease patients undergoing hemodialysis had headache as per our study. Of this nearly two thirds were male. A study conducted by Chhaya et al in 2020 in India also has 38% as headache prevalence in their dialysis study sample.2 When the gender distribution was analyzed our study showed two third of patients with headache were males (63% n=43) which may be explained by the fact that the study sample also has two third males(69% n=99). Similar results regarding gender distribution is seen in study conducted by Alan et al with 58.9% males having headache in their study population undergoing hemodialysis.[5] Around 37.2% of cases had onset of headache during 4th hour of dialysis session. Study by Alan et al also shows 56.6 % had headache during the last hour of dialysis session.[5] The median duration of headache was30 minutes with interquartile range of 30-120 minutes Headache was bifrontal in location in 86% of cases (n=37) and Throbbing in nature in 65% of cases (n=28). Mean (SD) severity of headache pain using Visual analog scale (VAS)Score was 4.18±1.08. Study by Chhaya et al also has similar findings with duration less than 60 minutes in 71% of cases, bifrontal in location in 46% of cases, mean (SD) severity of headache pain on VAS was 4.54 ± 1.742. Regarding headache relief, it was self-limiting in 53.5% (n =23), relieved by coffee in 16% (n=7) and local application of pain balm in 11%(n=5). 30.23%of cases (n=13) required Paracetamol as treatment. Out of 43 cases 7 cases (16.27%) satisfied the ICH 3criteria for dialysis related headache4. Hypertension was found to be a significant risk factor for headache (n=36 OR 2.85 with 95% CI 1.07 to 7.5, p value 0.03). BP >160 /100 in 74.4% (n=32). Arkamine was the most common drug used to treat BP in 72% of cases (n=31). Antoniazzi et al. demonstrated HD headache in 70.7% of 123 HD patients. The cause of headache was shown to be arterial hypertension in 23.7%of these patients.[1] A study done by Xiong et al also states hypertension as a risk factor for hemodialysis related headache with higher systolic and diastolic BP6 Gozubatik-Celik et al in their study also found that high BP was a risk factor for dialysis headache with significantly higher mean systolic and diastolic blood pressure pre-dialysis values (systolic, P = 0.002; diastolic, P < 0.001).[7] CT head was done in 4 cases and one patient had Posterior reversible encephalopathy syndrome (PRES). Dialysis was terminated in 2 cases.[6-8]

The possible mechanisms proposed for dialysis related headache are low magnesium levels, plasma changes in substance P and Calcitonin G related peptide (CGRP), fluctuation in BP with intra dialysis hypertension, fluctuating urea levels, Caffeine withdrawal and Dialysate related.

A study done by Goskel et al shows that Pre and post hemodialysis Mean Magnesium levels were lower in the Headache group.[7] Reduced magnesium in serum is a risk factor for migraine (menstrual migraine in particular), tension-type headaches, cluster and posttraumatic headaches. Substance P and CGRP variation as a cause of dialysis related headache is described by Alessandri et al 8. Goskan et al studied the role of urea in dialysis related headache and found that difference between pre- and post-dialysis urea values in patients with Dialysis headache was statistically significant (P < 0.05).[9] Nikic et al describes caffeine withdrawal headache in their article.[10] 16 % of our dialysis headache also had relief of headache within 15 minutes of consumption of coffee. The mechanism proposed being fall in caffeine level during dialysis due to removal.[11]

CONCLUSION

Headache is common in chronic kidney disease patients undergoing hemodialysis. Renal impairment limits the treatment options for headache in such patients as NSAIDs are contraindicated and dialysis alters the pharmacodynamics, dosing and efficacy of

drugs. Most get relief with local applications. Hypertension was found to be a significant risk factor hence adequate BP control may be helpful in preventing headache in dialysis patients. Headache increases the morbidity of the patients who are already suffering with their renal impairment related complications. More studies are needed to understand the pathophysiology and risk factors of headache in dialysis patients to provide adequate treatment options for them

Limitations

This was a cross sectional study and hence no control group to compare risk factors of headache. Serum Magnesium levels were not done due to limitation of test availability.

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