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Review Article

The effect of hemodialysis on hearing in chronic kidney disease patients – A systematic review

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ABSTRACT

Hemodialysis as a treatment modality for Stage V chronic kidney disease (CKD) has significantly decreased mortality. However, there have been several studies reporting sensorineural hearing loss (SNHL) in these patients which affects their quality of life. The role of hemodialysis in its etiology has been widely debated and the strength of available evidence has not yet been evaluated. A systematic literature review was conducted to identify a possible association of hemodialysis to hearing loss and guide in making informed decisions in the management of CKD patients. Relevant articles from PubMed, ScienceDirect, EBSCO Medline, SCOPUS, Google Scholar, and Clinical Key were identified using Preferred Reporting Items for Systematic Review and Meta-Analyses framework. Studies that were published since the inception of the database to May 2020 and written in the English language were analyzed. A total of 36 articles on hemodialysis and sudden or SNHL were retrieved. Many were observational (13 cohorts, 10 case-control, seven case series, and six cross-sectional) studies involving 99,020 participants with ages ranging from 1 to 80 years. This review elucidates the occurrence of SNHL in CKD patients on hemodialysis. Yet, the available literature fails to provide conclusive evidence on hemodialysis as a causative agent for SNHL. Audiological assessment of all CKD patients before hemodialysis and regular follow-up may help in early diagnosis and better management of hearing loss.

Keywords: Hemodialysis, Sensorineural hearing loss, Sudden hearing loss, Sudden deafness, Chronic kidney disease patients

INTRODUCTION

Chronic kidney disease (CKD) is a multisystem disorder characterized by a gradual impairment of kidney function culminating in chronic kidney failure which is now termed as Stage V CKD characterized by glomerular filtration rate below 15 ml/min/1.73 m^2 and reduction in creatinine clearance of 10 ml/min/1.73 m^2.[1] It is one of the leading causes of mortality and morbidity in the elderly. According to health statistics, the global prevalence of CKD in 2017 was 9.1% of the population (697.5 million cases).[2] The all-age global prevalence of CKD increased by 29.3% between 1990 and 2017.[2] An aging population worldwide may account for this upswing. CKD patients require renal replacement therapy in the form of either renal transplantation, peritoneal dialysis, or hemodialysis as treatment.[3]

Willem Kolff from the Netherlands pioneered modern hemodialysis therapy in 1943.[4] Hemodialysis is the process of the removal of unwanted substances and extra fluid from the blood using a dialyzer. It is a complex life support system that has helped reduce mortality from CRF.[5] The all-age and age-standardized global incidence of dialysis have increased between 1990 and 2017 by 43.1% and 10.7%, respectively.[2] However, there have been many reports of CKD patients developing complications such as cardiovascular accidents, infection, protein anabolism, anorexia, fatigue, breathlessness, as well as sensorineural hearing loss (SNHL) which compromise the quality of life of these patients.[5,6] Any pathology in the cochlea, vestibular cochlear nerve, or central auditory pathways can lead to SNHL.[7] A SNHL of more than 30 dB at three sequential frequencies occurring within a period of 72 h is called sudden SNHL (SSNHL).[8]

Hemodialysis is a long-term treatment that is quite expensive. Hence, the quality of life a patient enjoys is the key yardstick to measure its effectiveness in addition to its role in maintaining homeostasis. According to a recent study by Li (2020), approximately 30–40% of patients under regular hemodialysis experienced SNHL.[9] Although numerous studies documented hearing loss in renal failure patients on hemodialysis, the exact cause for this hearing loss remains controversial.[10,11] It is not clear whether the hearing loss reported in CKD patients is due to the disease process or due to the intervention. A recent study showed that there was an

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increased risk of mortality with atherosclerotic complications in hemodialysis patients with new-onset SNHL.[12] As the number of CKD patients is increasing at an alarming rate, the number of people requiring hemodialysis is bound to increase. This systematic review makes an effort to answer the research question "*Does Hemodialysis cause sensorineural hearing loss?*"

MATERIAL AND METHODS

This systematic review was conducted using Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) framework.[13] All primary articles relevant to the research question were searched from the available literature.

Search strategy

The search engines used to extract the data were PubMed, Science Direct, SCOPUS, Clinical key, EBSCO Medline, and Google Scholar. The electronic search was performed using different combinations of the terms, namely, hemodialysis, SNHL, sudden hearing loss, sudden deafness, chronic renal disease, CKD, and chronic renal failure. All the literature available from database inception till May 31, 2020, was included in the study. The selected articles were exported to Mendeley (Desktop version 1.19.4). These records were screened for duplication, by titles and abstracts, inclusion-exclusion criteria, and availability of full text. The entire process of screening and reviewing the full texts of eligible articles was done independently by two groups of three authors.

Inclusion criteria

This study attempted to investigate the association of SNHL and hemodialysis in CKD patients. The experimental studies, as well as observational studies such as case reports, cross-sectional studies, case–control studies, and cohort studies (prospective and retrospective), were included as the source of data. The inclusion and exclusion criteria were clearly defined. The articles needed to be in the English language. The study population was CKD patients. The intervention should be hemodialysis. Comparators included were CKD patients on other treatment modalities such as conservative treatment, peritoneal dialysis, and renal transplantation or age- and sex-matched healthy controls. The outcome observed in all the incorporated studies was the development of SNHL or SSNHL. Confirmed hearing loss with either pure tone audiometry (PTA), distortion product otoacoustic emissions (DPOAE), transitory evoked otoacoustic emission (TEOAE), or impedance audiometry was included in the study. The WHO classification or ASHA classification used to quantify the degree of hearing loss was reported in this study.[14]

Exclusion criteria

Studies on CKD patients who had undergone hemodialysis but developed complications other than hearing loss were excluded from the study. Besides, patients with conductive hearing impairment or having known causes for hearing loss such as ototoxic drug intake and noise exposure were also eliminated from this review.

Quality assessment

The studies with keywords in the title and abstract were selected, full text retrieved, and critically appraised independently by two groups of three authors to assess for its relevance, validity, and potential risk of bias using the Critical Appraisal Skills Programme Checklist (CASP). Separate checklists were used for case-control and cohort studies.[15]

Data extraction

In the included studies, several characteristics such as publication year, the country where the study was conducted, study design, the target population (age and gender distribution), type of treatment for Stage V CKD (hemodialysis, peritoneal dialysis, renal transplantation, or conservative treatment), duration of hemodialysis, duration of follow-up, and criteria to evaluate hearing levels were extracted. The results of the study were appraised for the quality of evidence and bias if any were reported.

Statistical analysis

Descriptive analysis was done and the characteristics of individual studies were compiled in a tabular form.

RESULTS

Search results

This systematic review was guided by the PRISMA framework [Figure 1]. A total of 1584 articles were retrieved and imported to Mendeley to be reviewed independently by two groups of three authors. One hundred and thirty-eight duplicates were removed. On screening for relevance with the titles and abstracts, 1265 articles were excluded (1195 articles were irrelevant, 49 articles were not in the English language, and 21 articles were not available in full text). A total of 181 full-text eligible articles were screened based on inclusion/exclusion criteria and 145 articles were eliminated as the CKD patients had exposure to one or more factors that could also cause hearing loss such as radiation, noise, ototoxic drugs, Alport syndrome, or Fabry's disease. Finally, 36 scientific articles were included for qualitative synthesis. The 36 articles extracted were from 1973 to 2020 and came from 16 different countries. The details are shown in [Table 1].

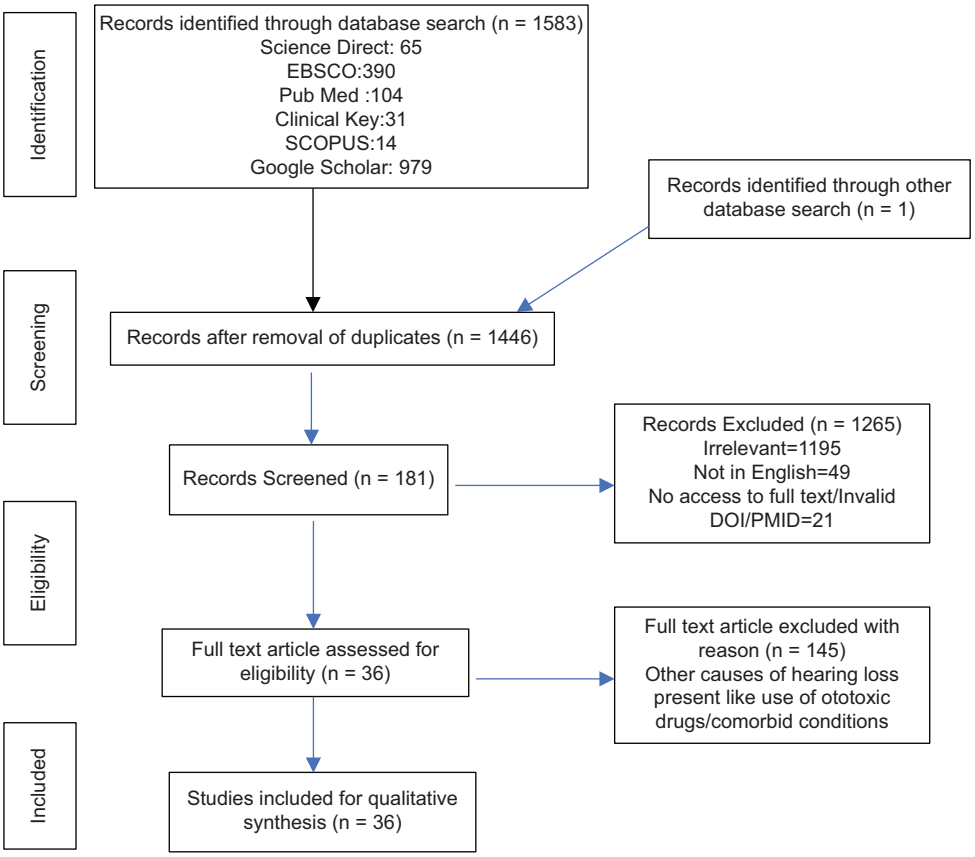

Figure 1: Preferred Reporting Items for Systematic Review and Meta-Analyses flowchart.

Study population

The study population comprised 99,020 individuals (43,143 males and 55,877 females). Their ages ranged from 1 year to 80 years. Among them, 21,787 were CKD patients while 77,233 were healthy controls. Among the CKD patients, the mean duration of the disease was 5 years.[9,10,16-35] The different treatment modalities for CKD reported were hemodialysis in 15,007 and peritoneal dialysis in 6443 while 195 were on conservative treatment and 142 participants had undergone renal transplantation.

Audiological tests used

It was observed that different researchers used varied audiological tests to detect and quantify the hearing loss. The most common being PTA used in 61.1% of the studies as a single assessment tool while it was combined with DPOAE in four studies,[22,24,33,36] with TEOAE in three studies[23,32,37] while all three hearing assessment tools; PTA, DPOAE, and TEOAE were used in one.[38] In two studies, impedance audiometry was used along with PTA,[20,30] while in one study, impedance audiometry was used with PTA and DPOAE.[25] Speech audiometry was used along with PTA in one study.[7] A single study incorporated Brainstem Evoked Response Audiometry (BERA) as a hearing assessment tool.[38]

Study design

The varying study design was encountered in this systematic review with 13 cohort studies, 10 case-control studies, seven case reports, and six cross-sectional studies [Figure 2]. Among the cohort studies, there were 12 prospective studies and one retrospective study with a total of 96,040 participants. Cohort studies on this topic from 1977[40] to 2018[27] were obtained. There are conflicting results with six articles[24,27,35,37,40] reporting hemodialysis as the cause for the development of SNHL while the remainder refuted it.[21,22,29,33,41,43]

The earliest case-control study on this topic was in 1992[10] while the most recent was in 2020.[16] The total sample from case-control studies was 1656. Case-control studies helped to compare the audiological results of the target population (patients on hemodialysis) with healthy, age- and gender-matched controls[10,16,20,23,25,28,44,45] or with CKD patients receiving conservative treatment.[17,20,32] Six among them reported a positive association between hemodialysis and occurrence of SNHL,[16,23,28,32,44,45] while four were

Table 1: Characteristics of included studies.

No.	Author	Year	Study design	Sample size (*n*)	Duration of hemodialysis (in years)	Comparators	Hearing assessment employed	Correlation of hemodialysis with hearing loss
1	Saeeda	2018	Cohort (prospective)	59	1	None	PTA	There is a significant correlation
2	Mancini *et al.*	1996	Cross sectional	68	8.75	Conservative and renal transplant	PTA, impedance audiometry	There is a significant correlation
3	Singh *et al.*	2018	Case control	55	>1/12	Conservative	PTA, TEOAE	There is a significant correlation
4	Fidan *et al.*	2012	Cohort (prospective)	119	Unspecified	Peritoneal dialysis and healthy control	PTA, TEOAE	There is a significant correlation
5	Kusakari *et al.*	1992	Case control	37	8.75	None	PTA	There is no significant correlation
6	Ozturan and Lam	1998	Cohort (prospective)	19	7	Healthy control	PTA, DPOAE	There is no significant correlation
7	Okwuonu *et al.*	2017	Case report	1	Unspecified	None	PTA	There is a significant correlation
8	Saha *et al.*	2020	Case control	1000	5	Healthy control	PTA	There is a significant correlation
9	Jakić *et al.*	2010	Case report	66	30	None	PTA	There is a significant correlation
10	Sam	2014	Cross sectional	119	2	Conservative and healthy control	PTA	There is a significant correlation
11	Wang *et al.*	2017	Cohort (retrospective)	95,425	0.4	Healthy control	PTA	There is a significant correlation
12	Mwangi	2012	Case control	78	4/52	Conservative	PTA	There is no significant correlation
13	Jamaldeen *et al.*	2015	Case control	120	Unspecified	Healthy control	PTA	There is a significant correlation
14	Reshma *et al.*	2017	Cross sectional	60	Unspecified	Healthy control	PTA	There is no significant correlation
15	Makita *et al.*	1995	Case report	6	5	None	PTA	There is a significant correlation
16	Akeem O. Lasisi	2007	Case report	61	Unspecified	Healthy control	PTA	There is a significant correlation
17	Lavonne Rergsthom	1973	Case report	224	Unspecified	None	PTA	There is no significant correlation
18	Cedric A. Quick	1976	Case report	602	7	None	PTA	There is no significant correlation
19	M.M. Ghasemi	2004	Case control	62	18	Conservative and control	PTA, impedance audiometry	There is no significant correlation
20	D. Gatland	1991	Cohort (prospective)	66	Unspecified	None	PTA	There is no significant correlation
21	Syed S. Rizvi	1980	Case report	1	Unspecified	None	PTA	There is a significant correlation

(Contd...)

Table 1: *(Continued).*

No.	Author	Year	Study design	Sample size (*n*)	Duration of hemodialysis (in years)	Comparators	Hearing assessment employed	Correlation of hemodialysis with hearing loss
22	A. Barbara Klingerman	1981	Cohort (prospective)	67	1	Healthy control	PTA, tympanometry	There is no significant correlation
23	Joseph O. Boateng	2019	Case control	100	Unspecified	Healthy control	PTA, tympanometry	There is a significant correlation
24	P. Stavroulaki	2001	Cohort (prospective)	18	8.75	Healthy control	PTA, DPOAE	There is no significant correlation
25	Bendo *et al.*	2015	Cohort (prospective)	61	1	Conservative and control	PTA, DPOAE	There is a significant correlation
26	Lent	2001	Cohort (prospective)	19	5.6	None	PTA	There is no significant correlation
27	Lasisi *et al.*	2006	Case control	61	10	Healthy controls	PTA	There is a significant correlation
28	William	1977	Cohort (prospective)	20	Unspecified	None	PTA	There is a significant correlation
29	Nikolopoulos *et al.*	1997	Cohort (prospective)	46	Unspecified	None	PTA	There is no significant correlation
30	Bendo *et al.*	2015	Case control	53	Unspecified	Healthy control	PTA, impedance audiometry, DPOAE	There is no significant correlation
31	Aspris *et al.*	2008	Cohort (prospective)	62	24	Healthy control	PTA	There is no significant correlation
32	Li *et al.*	2020	Cross sectional	26	21.67	None	PTA	There is a significant correlation
33	Gabr *et al.*	2019	Cross sectional	60	Unspecified	Conservative and control	PTA, DPOAE, TEOAE	There is a significant correlation
34	El-Anwar	2013	Case control	30	>2	Healthy control	PTA, TEOAE	There is a significant correlation
35	Singh *et al.*	2016	Cohort (prospective)	50	2	None	PTA, DPOAE	There is a significant correlation
36	Esfahani	2004	Cross sectional	30	1	None	PTA	There is no significant correlation

unable to demonstrate a clear association of SNHL and hemodialysis.[10,17,20,25]

Case reports constituted a total sample of 962. The earliest case report dates back to 1973[47] while the latest was in 2017.[6] The majority of these articles demonstrated a significant association between hemodialysis and SSNHL.[6,18,26,28,46,48]

Cross-sectional studies formed 16.7% of the selected articles from 1996[30] to 2020[9] with a sample population of 363. Similar to case reports, cross-sectional studies linked hemodialysis to the occurrence of SSNHL.[9,30,34,38,49]

Hemodialysis and hearing loss

High-frequency SNHL was reported in 89% of the studies while 11% did not specify the frequency affected. The time period of hemodialysis was mentioned in only 63.9% of studies with the mean duration of hemodialysis being 5.6 years. Although all studies reported the occurrence of SNHL, only 22% of studies reported an association of hearing loss with the duration of dialysis.[17,27,28,35,37,44,46] The follow-up period after hemodialysis varied from 3 months to 12 years. About 5.5% of participants reported SNHL after the very first session of hemodialysis.[24,28] Pre-dialysis hearing assessment

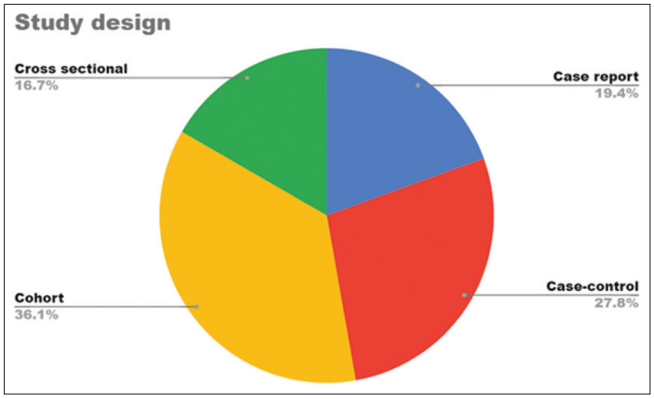

Figure 2: Distribution of the study design employed.

to detect any pre-existing hearing impairment was mentioned in only 13 (38%) of the 36 studies.[16,19,22,24,27,28,33,36,37,40,43,44,46]

DISCUSSION

Case reports linking hemodialysis to the occurrence of SNHL in CKD patients have existed for a significant period of time. Since 1973, there have been several published articles that referred to this topic without drawing any conclusion on the specific cause for the hearing loss.[7] This systematic review comprehensively encapsulated the published evidence on the association of hemodialysis with SNHL in CKD patients. In the present review of 36 articles on the topic, numerous variations were encountered concerning the methodologic design employed, the patient population selected, the duration of hemodialysis, duration of follow-up after hemodialysis, and the methods used for the assessment of hearing loss. Many were observational studies such as cohort studies, case-control studies, case reports, case series, and cross-sectional studies which are placed at a lower level at the hierarchy of evidence-based medicine.[50] Researchers seemed to prefer prospective over retrospective studies to minimalize bias and for better precision in determining the association of the intervention to the outcome. Selection bias was manifested by a few studies which focused on one specific group, namely, the younger age group[22,51] or patients already undergoing hemodialysis in the hospital for a varied duration.[19,33] Absence of homogeneity in the study population in the various studies limited the generalizability of the results to represent a wider population. In this systematic review, 22 out of 36 studies documented an association between hemodialysis and SNHL. Majority of the case studies and cross-sectional studies reported a positive correlation. Similarly, six out of 10 case-control studies confirmed a positive association of hemodialysis with SNHL when compared to the control group. The 13 cohort studies served as the focal point of this systematic review as they contributed to the largest sample population and allowed evaluation of the relationship of intervention to an outcome. Six of these studies too reported a positive association between SNHL and hemodialysis. It proved to be a reliable provider of relevant data due to a lack of randomized controlled trials. These findings show that hemodialysis has a significant role in the causation of SNHL.

Although the majority of the studies reported SNHL in CKD patients on hemodialysis, some degree of ambiguity regarding its etiology was revealed by this review. The key to understanding this unique complication of SNHL in CKD patients may lie in the basic anatomical and physiological properties of the kidney and cochlea. Literature states that the underlying mechanism responsible for SSNHL in CKD patients may be fundamentally due to the stria vascularis of the cochlea and basement membrane of the kidney glomeruli functioning primarily through the Na+-K+-activated ATPase. Although the underlying mechanism is not known, the hypothesis suggested that the cochlea is vulnerable to changes in electrolyte concentration and osmolality which may, in turn, result in loss of hair cells, the collapse of endolymphatic space, edema, and atrophy of specialized auditory cells leading to SNHL.[16,51] Reshma *et al.* in their study on patients with CKD on hemodialysis related the occurrence of SNHL to decreased total antioxidant capacity and increased oxidative stress.[52] On the other hand, some other researchers claim that the uremia, anemia, and osmotic alteration brought about hemodialysis were to be blamed for the development of SNHL.[48]

CONCLUSION

The data collected for this literature review from a pool of studies elucidate that hemodialysis may have a pivotal role in the mechanism of SNHL in CRF patients. However, there is a lack of concrete evidence indicating hemodialysis as the sole cause for SNHL. Therefore, routine otological examination with audiological assessment of CRF patients before hemodialysis is recommended. Further research on this topic with longitudinal study design, well-defined study population, and objective measurements is suggested to draw a valid conclusion on the causal effect of hemodialysis to SNHL in CRF patients.

Recommendations of the study

All CRF patients need to undergo thorough pre-hemodialysis otologic and audiometric evaluation followed by repeated audiological assessments at regular intervals of hemodialysis to identify patients who may develop hearing impairment during treatment. This may prove to be the stepping stone in early detection as well as lead to a better understanding of the etiology of SSNHL in patients on hemodialysis. Further, a randomized controlled trial on this topic would help provide a stronger level of evidence to expand scientific knowledge and contribute to making conclusions about the effect of hemodialysis on hearing.

Limitations of the study

Inability to access some of the full-text articles might have affected this literature review.

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Declaration of patient consent

Patient consent is not required as there are no patients in this study.

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Conflicts of interest

There are no conflicts of interest.

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