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OTHER ARTICLES

A Systematic Review on Hearing and Balance in Patients with Chronic Kidney Disease with and Without Hemodialysis

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Abstract

Objective Exploring the auditory and vestibular manifestations associated with chronic kidney disease (CKD) has been growing in recent years. Understanding these complaints in CKD patients is crucial for comprehensive patient care. This review aimed to investigate the audiological findings and profiles across various stages of CKD and guide for informed decision-making in their management.

Methods Relevant articles from PubMed, ScienceDirect, EBSCO Medline, SCOPUS, Google Scholar, and Clinical Key were identified for review. The selected articles were published from 2008 to 2023 and written in English language. A total of 41 articles on auditory and vestibular assessments in CKD were eligible for review.

Results Pure tone audiometry (PTA), immittance audiometry (IA) and otoacoustic emissions (OAEs) were the most commonly employed hearing tests respectively, with a higher frequency of utilization in hemodialysis cases compared to non-hemodialysis ones. Also, vestibular evoked myogenic potentials (VEMPs) emerged as the most popular vestibular test among hemodialysis patients while questionnaires were frequently employed in CKD patients. Moreover, our analysis suggests a potential association between the duration of hemodialysis and the development of tinnitus and vertigo. Abnormalities were also observed in auditory brainstem response (ABR), speech audiometry, central auditory processing tests and videonystagmography (VNG) assessment in hemodialysis and non-hemodialysis patients.

Conclusion CKD patients, particularly those undergoing hemodialysis, face a higher risk of hearing loss, tinnitus, and vestibular complaints. Performing otoacoustic emissions and vestibular-evoked myogenic potentials along with PTA on CKD patients, regardless of the disease stage is recommended to more effective management of audiovestibular complaints in these population.

Keywords Chronic kidney disease · Hemodialysis · Hearing loss · vertigo · Tinnitus

Introduction

Chronic Kidney Disease (CKD) is a widespread and often silent condition affecting millions of people worldwide [1]. It is characterized by a gradual decline in renal function over time [2]. The rising prevalence of CKD has become a major public health concern leading to various health complications and socio-economic challenges [3]. CKD is classified into five stages based on glomerular filtration rate, which is regarded as the best measure of kidney function. Lower GFR values indicate more advanced CKD stages [4]. According to data, the reported prevalence of CKD was 13.4% in Stages 1 to 5, while it was 10.6% in stages 3 through 5 [5]. Lifestyle factors and rising prevalence of kidney problems contribute to the growing incidence of auditory and vestibular issues [6].

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One of the lesser-known consequences of CKD is its potential impact on the auditory and vestibular systems. Individuals with CKD may experience sensorineural hearing loss (SNHL), tinnitus, and balance disorders [7]. Studies have shown that CKD patients are at a higher risk of auditory and vestibular dysfunction compared to the general population [1, 8–11]. Therefore, understanding these manifestations in CKD patients is crucial for early identification, intervention and overall well-being [7]. Various audiological assessments like Pure Tone Audiometry (PTA), Otoacoustic Emissions (OAEs), impedance audiometry and vestibular tests have been used to evaluate hearing and vestibular system in these patients [12–16].

The mechanisms behind auditory and vestibular dysfunction in CKD are not yet fully understood. CKD's impacts on ear system can be divided into three categories: disease process, medication side effects and treatment [17, 18]. Factors contributing to these impairments include electrolyte imbalance, metabolic acidosis, disruption of calcium metabolism, hypertension and accumulation of uremic toxins, oxidative stress and vascular abnormalities [19]. The similarities between the nephron and the cochlea's stria vascularis suggest a potential link between CKD and auditory and vestibular impairments [20]. furthermore, the use of ototoxic drugs in managing the CKD patients such as aminoglycoside antibiotics and loop diuretics can potentially harm the audio-vestibular system [21].

However, despite the increasing prevalence of CKD, its potential impact on the auditory and vestibular system remains understudied. Furthermore, studies exploring the association between CKD and vestibular dysfunction are scarce. Therefore, this paper aims to address the existing gaps in knowledge and contradictories in previous studies by comprehensively examining auditory and vestibular assessments in CKD patients, both in hemodialysis and non-hemodialysis settings (Fig. 1).

Methods

A literature search was conducted using electronic databases, including PubMed, Scopus, Medline, Web of Science, and Google Scholar in line with PRISMA guidelines. The keywords used for searching were: " Chronic Kidney Disease", "Chronic Renal Failure ", "Hearing Loss", "Audiometry", "tinnitus", "vestibular function", "auditory system", "central auditory processing" and "hemodialysis". This current paper focused on research articles published in English from 2008 to 2023 that investigated the auditory and vestibular status of CKD patients, reported audiologic findings and provided insights into the potential causes and management of hearing problems in this population. Initially, 760 original articles were identified. All identified articles were reviewed by all authors independently. After a title and abstract screening, 152 articles were retrieved for full-text review. Finally, according to the eligibility criteria, 41 articles were considered for review (Fig. 1). Two independent members of the research team evaluated the quality of each article to assess any potential bias.

Results

In this review article, a total of 41 articles were finally selected and examined. Diverse study methods were applied in the studies, including cross-sectional and case-control designs. The majority of these studies were conducted in Asia (73%) mostly in India (39%) followed by Iran (12%) and Iraq (10%) respectively. Also, the most common type of studies was cross-sectional. 15 studies were conducted in the past 5 years, suggesting the burgeoning interest in this particular research domain. Notably, the largest portion of the studies focused on hemodialysis patients, comprising 65% of all studies.

Auditory Abnormalities in CKD Patients: Prevalence, Characteristics and Assessment

An overview of the studies included in this review including their details and indicators are shown in Table 1.

Table 2 presents research studies investigating the prevalence and distinctive diagnostic vestibular observations among CKD cases. Based on the reviewed articles, a wide range of audiological assessment has been employed to examine the auditory function of CKD patients. Among these assessments, PTA emerged as the most commonly utilized hearing test, accounting for 88.62% of the studies (87.50% in HD cases vs.93.75% in non-HD cases). Other assessments such as Immittance Audiometry, Otoacoustic Emissions, ABR and central auditory processing tests were also frequently utilized respectively in both groups. Speech audiometry, Hearing Handicap Inventory for Adults (HHIA) and Dynamic Range (DR) test were used only in HD group.

The prevalence of hearing loss among CKD patients was found to be over 50%, with a higher rate observed in HD patients compared to non-HD patients. Hearing loss predominantly affected high frequencies and tended to manifest as bilateral Sensorineural Hearing Loss (SNHL) in both groups. Notably, only one study investigated the hearing characteristics of diabetic HD patients compared to non-diabetic HD patients and found no significant difference in the prevalence of SNHL or mean thresholds between the two groups.

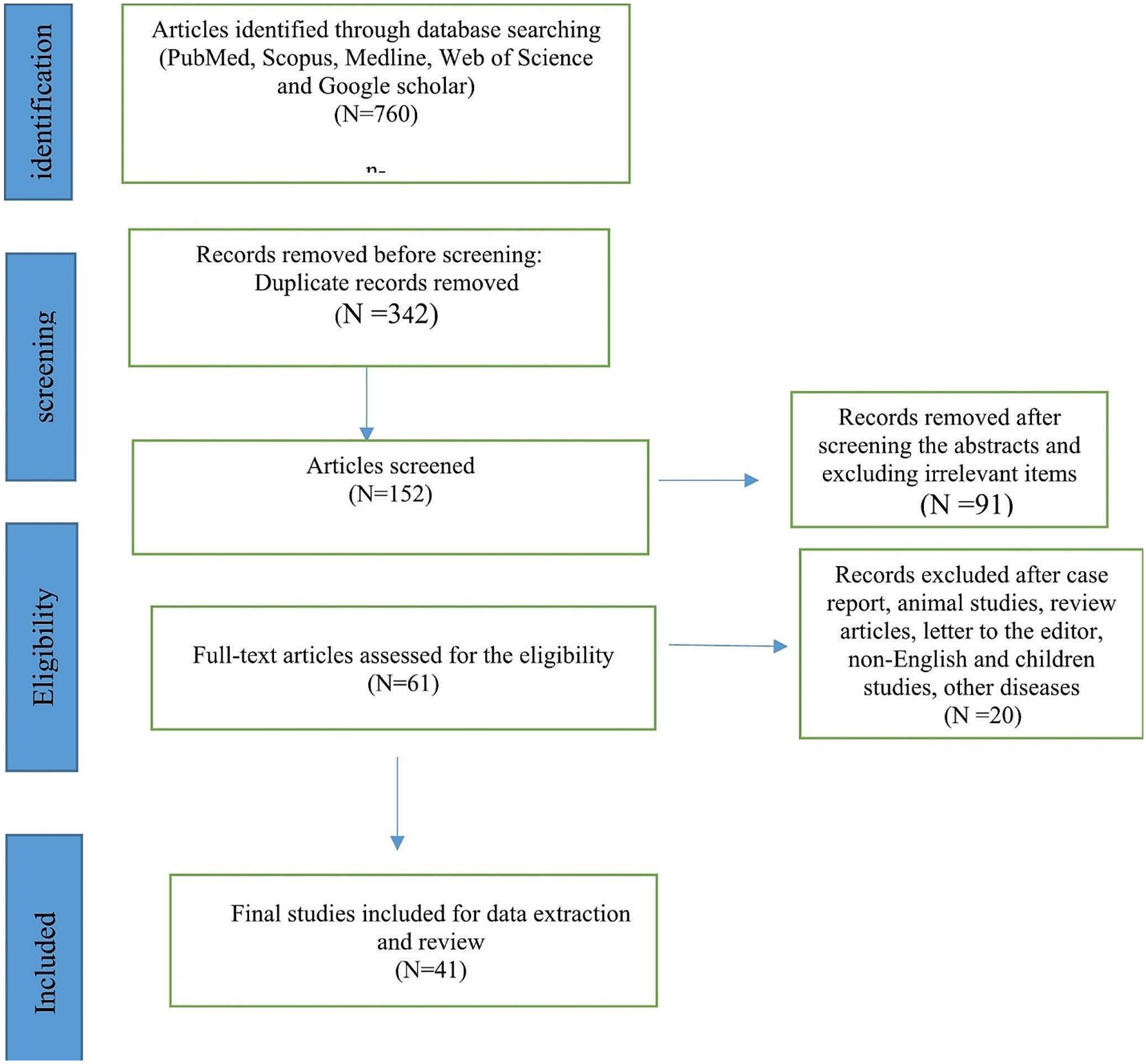

Fig. 1 PRISMA flow diagram of the study selection

While seven out of 35 studies indicated an association between SNHL in CKD patients and the duration of the disease, two studies found no relationship. Interestingly, one study demonstrated that hemodialysis could improve hearing loss in CKD patients. Two studies reported good speech discrimination scores in the majority of HD patients, irrespective of hearing loss. No study investigated speech discrimination scores in non-HD patients. The prevalence of tinnitus among CKD patients ranged from 10.22 to 19.23% according to three studies.

Abnormal findings were observed in Otoacoustic Emissions (OAEs), including decreased reproducibility and levels of OAEs in both HD and non-HD patients. Notably, a significant proportion (62.5%) of CKD patients with normal hearing exhibited absent Transient-evoked OAEs. On the other hand, CKD patients exhibited significant delays in absolute latencies and increased Inter-Peak Latencies (IPLs), along with poorer morphology, when compared to healthy controls. However, one study reported that the prolongation of absolute latencies and IPLs remained within the normal range in non-HD cases.

HD cases demonstrated poorer performance in GDT, amplitude modulation detection and Speech Recognition Threshold in noise compared to normal subjects. No studies were conducted on non-HD patients in this area. Only one study investigated hearing handicaps in HD patients and

Table 1 Studies on prevalence, characteristics of auditory diagnostic tests findings among CKD patients

Author(s)	Year	Type of study	Country	Subjects	Tests	Key finding (s)
Primadewi et al. [22]	2022	Cross-sectional	Indonesia	HD $N=45$	OAE PTA	-Strong positive association between duration of CKD and degree of SNHL
Kotian, et al. [13]	2022	Cross- sectional	India	CKD $N=90$	PTA	-A significant correlation between hearing loss with CKD duration
Kohansal, et al. [23]	2022	Cross- sectional	Iran	diabetic HD $N=33$ nondiabetic HD $N=31$	PTA	-Mostly bilateral mild SNHL in both groups. -No significant difference in SNHL prevalence and mean hearing thresholds between groups.
Zamani et al. [24]	2022	Cross-sectional	Iran	CKD $N=30$ Controls $N=29$	CV test SSQ	-Lower score in in three subscales of the SSQ in patients than normal group with no statistically significant difference between groups.
Kumar et al [25]	2021	NA	India	HD $N=14$ non- CKD $N=14$	MDT, GDT, SRT in noise	-Poorer GDT, MDT, and SRT in noise in HD cases
Saeed & Alabbasi [26]	2021	Cross-sectional	Iraq	HD $N=59$	PTA IA	- Significant relation between duration of HD with the development of tinnitus and vertigo
Kohansal et al. [27]	2020	Cross sectional	Iran	HD $N=64$	PTA	- No significant difference in hearing thresholds and audiogram shape among different vascular access groups.
Jain et al. [8]	2020	Cross-sectional	India	CKD $N=100$ Controls $N=50$	PTA ABR	- Increase in hearing threshold in both groups particularly at higher frequencies - Delayed absolute latencies and increased IPLs in ABR in CKD patients compared with healthy controls
Lara-Sa´nchez et al. [10]	2020	Cross-sectional	Spain	CKD $N=51$ Healthy $N=51$	PTA TEOAE DPOAE ABR	- SNHL specially at high frequencies - Decrease in the TEOAEs reproducibility and in the DPOAEs level. -Enhancement of the V wave absolute latency and III -V and I- V IPLs in the ABR waves but within normal range.
Boateng et al. [1]	2019	Case-control	Ghana	HD $N=50$ Control $N=50$	IA PTA	-Higher prevalence of SNHL with higher hearing thresholds among the case group than the control group -No significant association between SNHL and duration of CKD
Mudhol & Jahnavi [28]	2019	Cross-sectional	India	CKD $N=30$	PTA	-High prevalence of SNHL in CKD patients -High correlation between severity of SNHL and CKD duration.
Tamae et al. [29]	2018	NA	Japan	CKD $N=5$ HD $N=7$ Controls $N=80$	MFT	- Significantly greater G width of the HD group than other groups with no significant difference in the conductance width among groups
Singh et al. [15]	2018	NA	India	CKD and HD $N=55$	PTA TEOAE	-Absent of TEOAE with normal hearing in 62.5% of CKD patients
Saeed et al. [18]	2018	Cross-sectional	Iraq	HD $N=59$	PTA	-Mostly Mild to moderate SNHL at high frequencies - Poorer hearing threshold with increasing duration of dialysis.
Reshma et al. [30]	2017	cross-sectional	India	HD $N=30$ controls $N=30$	PTA	- Higher prevalence of hearing loss in HD cases than in CKD patients

Table 1 (continued)

Author(s)	Year	Type of study	Country	Subjects	Tests	Key finding (s)
da Costa et al. [12]	2017	Cross sectional	Brazil	HD $N = 80$	IA PTA Speech Audiometry HHIA.	-High prevalence of SNHL - handicap perception in 43.75% of cases with greater impairment in high frequencies using HHIA - Moderate correlation of BIAP with the total score of HHIA and its social domain.
Bawa et al. [31]	2017	NA	India	HD $N = 15$ controls $N = 15$	PTA	- Mild hearing loss in CKD patients -Higher prevalence of SNHL in CKD patients than healthy ones with significant difference
Acharya et al. [32]	2017	Cross-sectional	India	CKD $N = 70$	PTA	-Mild hearing loss mainly in higher frequencies in half of CKD patients with hearing loss - Correlation between hearing loss with duration of illness and HD in the group with hearing loss
Reddy et al. [33]	2016	Cross sectional	India	HD $N = 200$	PTA IA	- Mostly mild SNHL at high frequencies -Association between hearing loss degree with CKD duration
Rahman. and Akhtar [34]	2016	Cross sectional	Bangladesh	HD $N = 50$	PTA	-Ameliorating effect of HD on SNHL in CKD patients
Somashekara et al. [35]	2015	Cross-sectional	India	CKD $N = 60$	PTA	-High-frequency hearing loss in CKD patients related to disease duration and HD sessions
Jamaldeen et al [36]	2015	Case-control	India	HD $N = 120$ control $N = 120$	PTA IA	-Mild SNHL at high and low frequencies in CKD cases, inversely related to the number of HD sessions. -More prevalence of bilateral hearing loss in CKD patients than controls.
Bendo et al. [37]	2015	NA	Albania	HD $N = 36$ CKD $N = 15$ control $N = 10$	IA PTA, DPOAE	-High-frequency hearing loss in patients with CKD. -Worsen hearing loss in patients with CKD one year after the first evaluation.
Sreedharan et al. [38]	2015	NA	India	HD $N = 25$	PTA	-High frequency hearing loss in most patients -A positive correlation between hearing loss and increasing number of HD sessions
Sarafraz et al. [39]	2015	NA	Iran	HD $N = 58$	PTA SDS DR	-SNHL mostly in high frequencies -Abnormal DR results in high and low frequencies
Sam et al. [40]	2014	Cross-sectional	India	CKD $N = 40$ HD $N = 40$ Controls $N = 40$	PTA	-Bilateral moderate to moderately severe SNHL in most CKD patients, especially in higher frequencies compared with control group
Lopez et al. [14]	2014	Experimental	Brazil	HD $N = 35$ dialysis $N = 15$ CKD $N = 51$ controls $N = 27$	PTA ABR, TEOAE	-poorer results in audiological tests in conservative treatment group than that of the HD groups with no significant differences in the percentage of hearing loss between the various types of treatment.
Peyvandi and Roozbahany [17]	2013	Cross sectional	India	HD $N = 70$	PTA SRT SDS IA	-Increased severity of SNHL with increasing CKD duration, mostly in higher frequencies. -Good SDS in majority of patients
Govender et al. [41]	2013	Cross sectional	South Africa	$N = 50$	PTA, DPOAE	-Significant differences between PTA and DPOAEs findings in the high-frequency range in stages 3 through 5 with DPOAEs

Table 1 (continued)

Author(s)	Year	Type of study	Country	Subjects	Tests	Key finding (s)
Adekwu et al. [42]	2012	Cross sectional	Nigeria	CKD $N = 118$ healthy $N = 98$	PTA	-More prevalence of hearing loss in both speech frequencies and high frequencies in CKD patients
Sharma et al. [43]	2011	NA	India	$N = 52$	PTA	-Mild to moderate Hearing loss in most CKD patients. -poorer hearing threshold at 250 Hz with increasing CKD duration
Aloubaide et al. [44]	2011	NA	Iraq	HD $N = 92$ CKD $N = 8$	PTA	-Increasing incidence of SNHL with CKD duration but not directly relevant to the number of HD sessions
Jakić et al. [9]	2010	NA	Croatia	HD $N = 66$	PTA	-Mostly mild SNHL among HD patients in high frequencies -No significant difference in hearing thresholds for speech frequencies between subgroups.
Lasisi et al. [45]	2009	NA	Nigeria	CKD $N = 33$	PTA	-No significant difference in the mean pure tone pre- and post – treatment with systemic steroid.
Aspris et al. [46]	2008	NA	Greece	HD $N = 31$ Control $N = 31$	ABR	- Overall significant difference between the absolute latencies and IPLs prior to and following HD

HD: Hemodialysis; OAEs: OtoAcoustic Emissions; PTA: Pure Tone Audiometry; CKD: Chronic kidney disease; SNHL: Sensorineural Hearing Loss; CV: consonant-vowel;SSQ: speech, spatial and qualities of hearing scale questionnaire;NA:Not Applicable; MDT: modulation detection threshold; GDT: Gap Detection Threshold; SRT: Speech Recognition Threshold; IA: Immittance Audiometry; ABR: Auditory Brainstem Response; IPL:Interpeak Latencies; TEOAE: Transient-Evoked Otoacoustic Emissions; DPOAE: Distortion Product Otoacoustic Emissions; HHIA: Hearing Handicap Inventory for Adults; BIAP: Bureau International d' audiophonologie; SDS: Speech Discrimination Score; DR: Dynamic Range

found 43.57% handicap in high frequencies using HHIA, while CKD patients obtained lower scores in certain subscales of Speech, Spatial, and Qualities of Hearing Scale questionnaire than normal subjects in a study, with no statistically significant difference.

Vestibular Abnormalities in CKD Patients: Prevalence, Characteristics and Assessment

Vestibular evoked myogenic potentials (VEMPs) were the most common test used in evaluating vestibular function of HD patients (66.66%). Questionnaires, VNG and bedside tests were also employed to vestibular assessment in CKD patients. However, VNG and bedside tests were not applied in assessing HD patients. Approximately 13.63–16.95% reported experiencing vertigo, while dizziness was reported by 23% of individuals with CKD. Other symptoms observed among studies were dizziness and imbalance. The duration of hemodialysis was found to have a significant adverse impact on the vestibular system.

Regarding vestibular function, CKD cases exhibited various abnormalities including reduced tracking ability, prolonged saccade latency, decreased nystagmus velocity in optokinetic test and VEMPs abnormalities in non-HD group. Additionally, the severity of CKD was associated with an increased risk of vestibular dysfunction compared to individuals without CKD. Absent VEMPs in 28–44% of HD cases with negative correlation was reported between VEMP amplitude and disease duration. However, no significant difference was found in VEMP responses based on underlying disease or CKD duration. Significant correlation was observed between HD duration and development of vertigo using questionnaire in two studies (Table 2).

Discussion

The reviewed articles provide valuable insights into the audiological profile of CKD patients in both HD and non-HD patients. It is the first review to provide a comparative perspective on auditory and vestibular dysfunction characteristics, and relevant profile in this population.

Regarding auditory assessments, PTA emerged as the most commonly utilized hearing test in both HD and non-HD cases which aligns with previous study emphasizing the prominence of this method in evaluating ear function in these patients [42]. Immittance audiometry and otoacoustic emissions were also frequently utilized respectively. Speech audiometry, Hearing Handicap Inventory for Adults (HHIA), and Dynamic Range (DR) tests were used only in the HD group. The prevalence of hearing loss among CKD patients was found to be over 50%, with a higher rate in

Table 2 Studies on prevalence, characteristics of diagnostic vestibular findings among CKD patients

Author(s)	Year	Type of study	Country	Subjects	Tests	Key finding(s)
Rosario et al. [47]	2023	Observational study	India	$N=88$ CKD, HD	questionnaire	-significant correlation between the duration of HD and the onset of vertigo
Varghese et al. [16]	2021	Cross- sectional	India	HD $N=25$ Non-CKD $N=25$	oVEMPs, cVEMPs	- Absent cVEMPs and oVEMPs in 28% and 44% of subjects with CKD, respectively -A negative correlation between disease duration and VEMPs amplitude.
Saeed & Alabbasi [26]	2021	Prospective study	Iraq	$N=59$ HD	Questionnaire	-significant relation between the duration of hemodialysis and the development of vertigo
Gabr et al. [7]	2019	Cross-sectional	Egypt	$N=60$ CKD,HD	VNG VEMPs	-Low gain tracking, prolonged saccade latency, reduced nystagmus velocity in optokinetic and VEMPs test in CKD cases
Jung et al [11].	2017	Cross-sectional	Korea	$N=7{,}799$ CKD	Bedside test	-increased risk of vestibular dysfunction with increasing CKD severity compared to the participants without CKD
Sazgar et al. [48]	2008	NA	Iran	HD $N=20$ controls $N=16$	VEMPs	- Significant difference in VEMPs responses between HD subjects and controls. -No significant difference in response of VEMP according to underlying disease and CKD duration

CKD: Chronic Kidney Disease; HD: Hemodialysis; oVEMPs: ocular Vestibular Evoked Myogenic Potentials; cVEMP: cervical Vestibular Evoked Myogenic Potentials; VNG: Video Nystagmo Graphy

HD patients compared to CKD patients. Hearing loss was mostly bilateral mild SNHL, particularly at high frequencies in both groups. However, it is worth mentioning that there was normal hearing function in patients with type 1 and 2 CKD. This discrepancy may be attributed to the heterogeneity of CKD patients in terms of disease severity, comorbidities and hemodialysis. Long-term CKD has been shown to increase susceptibility to hearing loss [22, 28, 49], possibly due to imbalances in serum electrolytes and nitrogen metabolism end products, which are crucial for homeostasis. Hemodialysis has been shown to play a significant role in the occurrence of SNHL, potentially due to accumulation of amyloid materials in the inner ear [17], although one study demonstrated that hemodialysis can improve hearing loss in CKD patients [34]. CKD and hemodialysis can affect the inner ear leading to increased inner ear pressure or endolymphatic hydrops, which may contribute to otologic symptoms experienced by these individuals [29].

Abnormal findings in otoacoustic emissions were decrease in reproducibility and levels. Some CKD patients with normal hearing exhibited absent transient-evoked otoacoustic emissions, supporting the notion that OAEs can detect early cochlear pathology before noticeable increases in hearing thresholds occur [7]. Additionally, CKD patients exhibited delays in absolute latencies and increased interpeak latencies, along with poorer morphology, compared to healthy controls. Although in one study, prolongation of ABR waves latencies fell within the normal range. The prolongation of ABR wave latency indicates reduced neural synaptic transmission due to CKD or hemodialysis [46, 50]. Poorer performance in auditory processing in CKD patients undergoing hemodialysis such as gap detection threshold and speech recognition threshold in noise may be attributed to dysfunction in the nervous system caused by uremia [51]. Mazumder et al. discovered a reduced overall acetylcholine activity, a neurotransmitter, in the brains of mice with CKD, suggesting a potential mechanism for these auditory processing deficits [52].. Furthermore, tinnitus was almost prevalent (16.95% to19.23%) in CKD cases, providing further evidence of the link between CKD and auditory complications.

Regarding vestibular function, vestibular evoked myogenic potentials (VEMPs) were the most commonly utilized test to evaluate vestibular system in HD patients while questionnaires, videonystagmography (VNG), and bedside tests were employed in CKD patients. Vertigo and dizziness were reported by a significant proportion of CKD patients. However, the duration of hemodialysis had an adverse effect on the vestibular system. Abnormalities in tracking ability, saccade latency, optokinetic nystagmus velocity, and VEMPs were observed in CKD cases. The severity of CKD was associated with an increased risk of vestibular dysfunction compared to individuals without CKD [7, 16, 48]. However, the underlying disease or duration of CKD did not significantly impact VEMP responses. Several factors contribute to the development of vertigo in CKD, including disease severity, electrolyte imbalances, ototoxic drugs, age, and hemodialysis [26].

Given the limited number of studies investigating vestibular and central auditory functions in this population, further research is warranted to elucidate the full spectrum of these complications and develop targeted interventions to mitigate the impacts in CKD patients. Considering that CKD can affect both auditory and vestibular functions, the use of PTA and other advanced tests including OAE and vestibular tests might complement each other for identifying changes across different levels of the audiovestibular pathways in CKD patients regardless of the disease stage.

Conclusion

CKD patients, especially those undergoing hemodialysis, face higher risk of experiencing hearing loss, tinnitus, and vestibular complaint. The prevalence, severity, and patterns of these impairments differ between hemodialysis and non-hemodialysis patients. Hemodialysis patients, for instance, may exhibit a higher incidence of sensorineural hearing loss and abnormal vestibular findings compared to non-hemodialysis ones. The severity and patterns of these impairments are influenced by factors such as the duration and severity of CKD, presence of comorbidities, and the individual's overall health status in both groups.

However, the impact of hemodialysis on the rate of SNHL remains inconclusive due to conflicting results from various studies. Further research is needed to better understand the underlying mechanisms and implications of these differences, allowing for the development of tailored management for specific needs of both hemodialysis and non-hemodialysis CKD patients and enhancing the comparability and generalizability of results across studies.

Given the association between CKD and vestibular dysfunction, it is recommended to closely monitor individuals with CKD for potential audiovestibular impairments. Conducting otoacoustic emissions and vestibular-evoked myogenic potentials on CKD patients, regardless of the disease stage, holds promise as valuable diagnostic tools.

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