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ORIGINAL RESEARCH

Hearing thresholds and patterns of hearing loss in patients with Chronic Kidney Disease

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Abstract

Background: This study determined the prevalence and pattern of hearing loss in CKD patients

Methods: A cross-sectional, hospital-based study conducted from July 2010 to June 2011.

Results: There were 100 subjects and 100 controls, their ages ranged between 18 and 69 years. Stages of CKD show that 44 were stage III, 34 were stage IV while 22 were stage V. In the right ear, 59% of subjects had hearing loss compared with 7% among the controls. In the left ear, 66% of subjects had hearing loss compared with 15% among the controls ($p < 0.001$). The mean ± SD air conduction hearing threshold levels was, in the right ear (subjects) = 31.1 ± 16.1 and (controls) = 11.913 ± 8.023 ($p < 0.001$), in the left ear (subjects) = 34.6 ± 12.2 and (controls) = 15.9 ± 11.5 ($p < 0.001$)*;* air – bone gap for subjects and controls were 2.9 ± 2.7 and 1.7 ± 1.8 which indicated sensorineural hearing loss. There is a significant association between decreasing e-GFR and severity of hearing loss ($r = -1.000$; $p = 0.01$ (normal hearing), ($r = -0.698$; $p = 0.518$ (mild/moderate HL) & ($r = -0.000$; $p = 0.010$ (severe /profound HL). While 50% of patients in stage III CKD had normal hearing, 13.6% of patients in stage V had normal hearing.

Conclusion: There is a high prevalence of sensorineural hearing loss in chronic kidney disease, with a statistically significant association between worsening stage of disease and severity of hearing loss.

Keywords: Audiometric assessment, Chronic Kidney Disease, Prevalence, Rehabilitation, Sensorineural hearing loss

Introduction

Chronic kidney disease (CKD) is defined as abnormalities of kidney structure or function, present for at least 3 months, with health implications. [1] CKD is classified based on cause, glomerular filtration rate (GFR) category, and albuminuria category. [1] The disease affects multiple organ systems, and its effect on the ear could cause hearing impairment. [2, 3] Various studies have associated hearing loss, especially sensorineural type, with chronic kidney disease. [4,5] The reported prevalence of HL among patients with chronic kidney disease in previously published studies ranged between 28% – 100%. [6, 7] The complications of chronic renal failure (CRF) may be due to the progression of the disease process or effects of medications used for its treatment. There are many anatomical, physiological, pharmacological and pathological similarities between the nephron, which is the functional unit of the kidney and the stria vascularis of the cochlea. [8,9] Both the nephron and ear contain epithelial structures in close contact with their vascular supply, and basement membrane-lined intercellular channels also exist in both the glomerulus and the stria.[9] In both, epithelial cells show features known to be associated with active transport of fluid and electrolytes. [10,11] Various pharmacological agents act on both the kidney and inner ear. Such medications like aminoglycoside antibiotics, non-steroidal anti-inflammatory drugs and frusemide can be both nephrotoxic and ototoxic. [12] Similarly, there are various hereditary conditions that combine both renal pathology as well as hearing loss.[13, 14] Hearing loss could cause considerable disability both for learning and communication. Considering the importance of hearing loss in CRF, and the paucity of data on CKD and its effect on hearing, this stimulated our interest to carry out a study on the condition. This study aims to determine the hearing thresholds, the prevalence and patterns of hearing loss in patients with Chronic Kidney Disease that presented at the nephrology unit of our hospital. We also hope to recommend relevant modifications to the usual care of patients with CKD that can lead to improvement in their quality of life and lead to a better management of underlying conditions which could, in turn, potentially preserve their hearing function.

Methods

This was a one-year cross-sectional hospital-based study conducted between July 2010 and June 2011. It involved consenting patients aged 18years and above with estimated glomerular filtration rate (eGFR) of $\leq$ 60 mL/min/1.73m^2. The control group was matched with the test

group for age and sex and were recruited from healthy volunteering hospital staff, students of different training programmes of the hospital and patients' relatives. Informed written consent was obtained from consecutive eligible participants in the best understood language, following which interviewer-administered structured questionnaires (in sections A and B) were administered to each participant. Section A contained patients' demographic and clinical data. Diagnosis of CKD was based on history, clinical, biochemical and kidney ultrasonography evaluation. The estimated glomerular filtration rate (eGFR) was calculated using the Modification of Diet in Renal Disease (MDRD) equation.[1] The stage of disease was determined using the estimated glomerular filtration rate (eGFR). The stage of the disease was classified as stage I (eGFR > 90 mL/min/1.73m^2), stage II eGFR (60 – 89mL/min/1.73m^2), Stage III eGFR (30-59 mL/min/1.73m^2), stage IV eGFR (15 - 29mL/min/1.73m^2), stage V eGFR (< 15 mL/min/1.73m^2). Patients in stages III, IV and V were recruited for the present study. Section B contained detailed general clinical and otological examinations using the head mirror with a good lighting system and otoscope. Any impacted wax was removed manually with wax hook or by instilling wax softener before syringing. Pure tone audiometry was performed in a soundproof booth using a diagnostic Audiometer (MA 65) (calibrated to ISO standard) on each patient, for both the air and bone conduction standard measurements. Hearing loss is threshold > 25dB pure tone average (PTAv) of air conduction on the pure tone audiogram. The pure tone average for each patient was calculated, hearing loss was determined, and its degree was based on the World Health Organisation (WHO) standard classification. [15, 16] Normal hearing is defined as threshold ≤ 25dB PTAv, mild hearing loss is defined as threshold > 25dB but ≤ 40dB PTAv, moderate hearing loss is defined as threshold > 40dB but ≤ 60dB PTAv, severe hearing loss is defined as threshold > 60dB but ≤ 80dB PTAv and profound hearing loss is defined as threshold >80dB but ≤ 100dB PTAv. Conductive hearing loss is defined as an air-bone gap > 10 dB when the air conduction threshold > 25dB and bone conduction threshold ≤ 25dB. Sensorineural hearing loss is defined as PTAv threshold > 25 dB with air-bone gap < 10dB. The pure tone average for both air conduction and bone conduction were calculated by finding the average of the hearing threshold for frequencies (0.5 kHz, 1 kHz, 2 kHz and 4 kHz). The air – bone gap was calculated by subtracting the bone conduction threshold from the air conduction threshold to determine whether the hearing loss was sensorineural or conductive. Excluded from the study were CKD patients with

congenital ear anomalies, infective/inflammatory ear lesions, inner ear disease conditions like vestibular schwannoma, labyrinthitis etc, past history of head injury, presence of comorbidities like diabetes mellitus and Sickle cell anaemia and patients with history of occupational or social exposure to excessive noise. The control subjects were apparently healthy adults who did not have any form of kidney disease as assessed or confirmed from their electrolyte, urea and creatinine results. The same protocol used for patients was duplicated in the control patients. Ethical approval for this study was obtained from the Ethical Review Committee of Ladoke Akintola University of Technology Teaching Hospital, Osogbo (approval number LTH/HC/2010/12/0080). *Statistical analysis*: Data collected were entered into a spreadsheet and presented in descriptive format, tables, diagrams and graphs where appropriate. The dependent variable was the pure tone average of the subjects, while the independent variable was estimated glomerular filtration rate (eGFR). Student's t–test was used to determine differences in prevalence of hearing loss between the study and the control group and the level of statistical significance set at 0.05. It was also used to test differences in severity of hearing loss between the test and control subjects, while correlation coefficient was used to assess the association between pure tone average and estimated glomerular filtration rate (eGFR). Analysis was done using Statistical Package for the Social Sciences (SPSS) version 14 (Illinois, USA).

Results

There were 100 patients (test subjects) and 100 controls that participated in the study, and their ages ranged between 18 and 69 years (mean ± SD = 43.25 ± 15.47 and 39.1 ± 12.3 respectively). Among the test subjects, there were 52 males and 48 females (male: female = 1.1: 1), while among the controls, there were 55 males and 45 females (male: female =1.2:1). The age group 31 – 50 years was the predominant age among both the test subjects and the controls. Table I show the age and sex distribution among the subjects and the controls. Distribution of stages of chronic kidney disease among the subjects shows that 44 were in stage III, 34 were in stage IV, while 22 were in stage V.

Table I: Clinical and Renal Parameters of the Subjects

Variables	Subjects	Control	T-test	P-value
Age group (years)				
18-30	23	35	4.536	0.292
31-50	41	40		
51-70	36	25		
Mean age (years)	43.25 ± 15.47	39.13 ± 12.33	12.036	0.024
Mean weight (Kg)	62.83 ±13.09	65.65 ± 15. 49	27.248	0.265
Mean serum creatinine (mmo	4.323 ± 4.191	0.996 ± 0.103	5.039	0.862
Mean e-GFR (mL/min/1.73m	28.34 ± 14. 84	108.99 ± 19.53	21.053	0.046

All the patients in stage V were undergoing renal replacement (dialysis) during the period of this study. Table II depicts the pure tone averages for frequencies 0.125, 0.25, 0.5, 1, 2, 4 and 8 KHz in both ears among the test subjects and the controls.

Table II: Hearing thresholds at different frequencies among the Subjects and the Controls

Frequency	Subjects N = 100	Controls N = 100	T- test	P-value	Subjects N = 100	Controls N = 100	T-test	P-value
	RIGHT				**LEFT**			
0.125	16.25	1.85	82.792	0.000	18.00	7.45	39.26	0.001
0.25	18.25	3.00	88.763	0.000	20.30	9.05	32.03	0.001
0.50	25.25	8.25	73.481	0.001	30.30	13.45	52.81	0.000
1.0	29.60	10.70	72.138	0.000	31.85	15.20	78.24	0.000
2.0	31.95	13.05	73.481	0.000	35.15	18.40	52.21	0.000
4.0	37.55	15.65	82.792	0.000	41.15	18.65	89.03	0.000
8.0	46.20	18.90	73.481	0.000	46.95	23.60	75.18	0.000

There is statistically significant hearing loss across all the tested frequencies among the subjects when compared with the controls. Pure tone averages were calculated for low (0.125 – 0.25 KHz), middle (speech) frequency (0.5 – 4 KHz) and high frequencies (8 KHz). Among the subjects and the controls in the right ear; hearing loss were 59% and 7% respectively in the speech frequency. Also, high-frequency hearing loss (subjects and controls) were 69.0% and 12 % and low-frequency hearing loss (subjects and controls) were 30.0% and 1% respectively. In the left ear; among the subjects, 66.0% had hearing loss compared with 15% among the control group in the speech frequency observed. In the high and low frequencies, hearing loss was 77% and 34% among the subjects compared with 20% and 10% among the controls respectively as shown in Table III.

Table III: Comparative analyses of the hearing thresholds at different frequency ranges in the ears between the two Groups of Subjects

Variable		Right ear				Left ear			
Threshold (d	Frequenc	Subjects	Control	X^2	P- Value	Subjects	Controls	X^2	P- Value
0 – 25	Low	70	99			66	90		
26 – 60		24	1	32.199	0.000	26	10	19.60	0.000
≥ 60		6	0			8	0		
0 – 25	Middle	41	93			34	85		
26 – 60		49	7	62.44	<0.001	48	11	62.44(	<0.001
≥ 60		10	0			18	4		
0 – 25	High	31	88			24	85		
26 – 60		47	12	72.707	0.000	51	15	85.54	0.000
≥ 60		22	0			25	0		

Notes: 0 – 25 dB = Normal hearing; 26 - 60 dB = Mild to moderate hearing impairment, >60 dB = Severe to profound hearing impairment. Low frequency = 0.125 – 0.25 kHz; Middle frequency = 0.5 – 4 kHz; High frequency = 8 kHz

The type of hearing loss noted was mainly sensorineural. The mean air – bone gaps for test subjects and controls were 2.92 ± 2.70 and 1.67 ± 1.80dB. Association between the estimated glomerular filtration rate (e-GFR) and hearing threshold was determined among the test subjects (Table IV). While 50.0% of all patients in stage III CKD had normal hearing, only 13.6% of all patients in stage V had normal hearing(r = -1.000; p = 0.01). Also while only 6.8% of all patients in stage III disease had severe to profound hearing loss, 45.4 % of all patients in stage V disease had developed severe to profound hearing loss ((r = -0.000; p = 0.010). As the e-GFR decreases (worsening stage of CKD), the hearing threshold of the affected patients increased i.e. hearing got worse.

Table IV:Association between estimated Glomerular Filtration Rate and Pure Tone Average

Pure Tone Average (dB)	Stages of CKD			r	p-value
	III	IV	V		
Normal hearing (0 – 25)	22	6	3	- 1.000	0.010
Mild – moderate hearing loss (26 – 60)	19	18	9	- 0.698	0.518
Severe – profound hearing loss (> 60)	3	10	10	- 1.0000	0.010
Total	44	34	22		

Estimated Glomerular Filtration Rate (e-GFR ml/min/1.73m^2)

Discussion

The prevalence of hearing loss among patients with chronic renal failure, as found in the present study, is considerably higher than what is found in the general population. Hearing loss has been a common finding in studies investigating effects of renal failure on auditory function. [17] Despite differences in methodologies and indices of auditory function, the existence of hearing loss has been a common trend. The clinical significance of the effect of CKD on hearing acuity requires attention more so as hearing impairment is considered a societal problem. Our finding in the present study of a significantly high prevalence of hearing loss of 66.0% among patients with chronic kidney disease resonates with reported prevalence of 20-80% from previous research. [7,17]

A researcher opined that the presence of hearing loss and the estimation of the type and the degree constitute one of the most common methods used to investigate the effects of renal disease on the auditory system.[18] The degree of hearing loss (that ranges from mild to profound) in the present study was similar to the findings of Lasisi et al.[2] While most other studies did not report various degrees of hearing loss and the proportion of patients affected, Vilayur et al.[19] however stratified degree of hearing loss into mild and high with 40dB being the cut-off point. They reported 43.5% mild hearing loss compared with 21.9% in the control group and 29.7% severe hearing loss compared with 10.3% in the control group among patients with moderate CKD. The degree of hearing loss may give an indication of the extent of damage to auditory function. [17] Preponderance of mild to moderate degree of hearing loss (with gradual course) coupled with the compensatory mechanisms among the patients may be the reason the disability may not be noticed in the early course of the disease. [8]

The type of hearing loss may distinguish between lesion affecting the outer or middle ear (conductive hearing loss) or the cochlear and the neural pathways (sensorineural hearing loss). Preponderance of SNHL among patients with CKD in this study agrees with the findings of previous researchers. [8, 17] A study had reported that, CRD had significantly longer wave I – III inter-peak latency difference in ABR; the difference reflects conduction time from the cochlear to the level of the cochlear nucleus which indicated a subclinical dysfunction of the VIII nerve caused by axonal uraemic neuropathy. [20] The findings indicated neural involvement in the auditory dysfunction associated with renal failure and dialysis.[19] Similarly Baldini et al.[21] reported ABR measures from patients on chronic dialysis in comparison with a control group. They found significant prolongations of waves III & V among the patients. Orendorz-Fraczkowska et al.[22] reported that latencies of ABR wave I, III, V and inter-peak latencies I – III – V were longer than the control, indicating a retrocochlear involvement in addition to cochlear dysfunction. This shows that auditory function is affected by CRF, which involves cochlear as well as retrocochlear lesions, giving rise to sensorineural hearing loss.

Our findings also showed that hearing loss in CKD cuts across all frequencies, from low frequencies to high frequencies, with 30%, 66% and 76% hearing loss in the low, middle (speech) and high frequencies respectively, among the subjects. This finding indicated that

the threshold of hearing progressively worsens as frequencies increase. Previous researchers had noted a consensus in audiometric findings among patients with CRF of a preponderance of high-frequency hearing loss.[17,20] The implication of this is that the majority of CKD patients with impaired hearing might not be aware until hearing loss encroaches on the speech frequencies. [23] Therefore, the gradual course of hearing loss in CKD calls for routine audiometric assessment of all patients with CKD for early detection and rehabilitation. A similar study showed that, although hearing loss in CKD cuts across all frequencies, low and high frequencies were more affected than the speech frequency.[24] The low-frequency hearing loss they observed, however, improved with hemodialysis. This led them to suggest that low-frequency hearing loss might be due to endolymphatic hydrops, which was influenced by fluid balance.[24] Other relevant studies implied that the discrepancy in cochlear dysfunction among children with CKD was generally observed in the low-frequency area, whereas the consensus among adults with CRF points to a high-frequency hearing loss.[25,26] Apparently, our findings of progressive hearing deterioration as frequencies increase might be related to the fact that our study centred more on the adult population.

Another major finding from our study is the significant direct relationship between stages of chronic kidney disease and severity of hearing loss. This was similar to the findings by Vilayur et al. [19] Other researchers had reported that hearing loss among patients with CRF seems to deteriorate as the disease progressed years after the initial evaluation. [17] Hearing loss had been observed to worsen with greater renal damage. [27] An insidious destruction of the cochlea, attributable to the uraemic process, might be responsible for the worsening of hearing as the renal failure progressed. Therefore, findings from the present study, which are in tandem with reports from the previous studies, call for early and periodic hearing assessment with appropriate audiological testing among all patients with chronic kidney disease. [17, 19, 27] This will facilitate early intervention for those affected, which could preserve hearing function, as well as the amplification mechanism in form of hearing aids, and lead to improvement in their quality of life

In this study, the peak age of presentation was the age group (31 – 50) years (mean 43.3 ± SD years). This was similar to findings from previously published studies.[28–30] Other reports found mean age to range between 47 - 58 years, with more males affected than females (M: F 1.4 – 2: 1).[28,30] Lasisi et al. [8] reported two patients with chronic kidney

disease aged 35years and 36years that developed profound sensorineural hearing loss during the course of their treatment. The majority of the Nigerian population suffering from chronic kidney disease are middle-aged, with its negative effect on the economy of the family and the nation as a whole; hence, CKD is gaining increasing recognition as a global public health problem.

The mechanisms proposed to cause hearing loss in CKD include: ototoxicity, axonal uraemic neuropathy, degradation of cellulose acetate dialyser membrane, anaemia, infection, and renal replacement therapy such as haemodialysis. [31 – 33] Some researchers have reported rapid ultrafiltration with subsequent neuronal ischemia, hypotension and vascular collapse, which could predispose to embolism as factors for hearing loss in haemodialysis.[25,34,35] Therefore, every effort that can potentially preserve the hearing function of patients with CKD, such as monitoring of ototoxic medication, should be undertaken.

Conclusion

There is a high prevalence of sensorineural hearing loss in CKD with a statistically significant association between worsening stage of disease and severity of hearing loss. Effective management of these patients will necessitate collaborative effort with the Nephrologists and Otorhinolaryngologists.

Efforts to preserve the hearing function of patients with CKD, like monitoring of ototoxic medication, should be instituted. Early and periodic clinical hearing assessment is imperative. Prompt and appropriate interventions and rehabilitative process like fitting of hearing aids for effective utilisation of residual hearing function, will lead to improvement in the quality of life of patients with chronic kidney disease.

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