Hearing and Kidney: Effects of Chronic Kidney Disease on Various Auditory Parameters – Results from a Tertiary Care Hospital in India

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Abstract:

Background*: An association between chronic kidney disease (CKD) and hearing loss was first described in patients with Alport syndrome. Patients with CKD develop sensorineural hearing loss with the progression of the disease. Studies using BAER as an index of auditory function among patients with CKD showed evidence of various degrees of auditory dysfunction.*

Materials and methods*: 100 adult CKD patients (stage 3 – 5 and 5D) and 50 controls were included in the study. Clinical and biochemical parameters were assessed and all the patients and controls underwent Pure Tone Audiometry (PTA) and Brainstem Auditory Evoked Response (BAER) evaluation.*

Results*: When hearing thresholds were compared between the patients and controls PTA showed an increase in hearing threshold in all patient groups. This increase was more noticeable at higher frequencies (4 and 8 kHz). Compared with healthy controls, a highly significant delay was observed in CKD patients in both absolute and interpeak latencies in BAER in the present study.*

Conclusion*: The present study provides a concrete evidence to the otherwise disputed relation of auditory function in CKD proving that hearing is permanently affected by ESRD at all levels of the auditory neural pathway.*

Key Words*: chronic kidney disease, sensorineural hearing loss, Pure Tone Audiometry, Brainstem Auditory Evoked Response.*

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Introduction:

Contrary to common belief the incidence and prevalence of hearing loss, both subclinical and overt, is high in patients with Chronic Kidney Disease (CKD). Patients with CKD develop sensorineural hearing loss with the progression of the disease. The etiology for this hearing loss is not well defined although the pathophysiologic and biochemical changes associated with CKD are believed to cause auditory pathway damage, both at the sensory organ and neuronal levels. Ototoxic drugs, diabetes, infection, noise exposure and congenital otonephropathies are the known etiologic factors that account for the majority of hearing losses occurring in CKD, with the most common being ototoxic diuretics and antibiotics.

Cochlear dysfunction in kidney disease was first established as "Hereditary Familial Congenital Hemorrhagic Nephritis".[1] This syndrome is characterised by nephropathy, bilateral symmetric sensorineural hearing loss, ocular abnormalities and hereditary origin. The association of hereditary nephritis and deafness was established by examination of hearing with controlled audiometry and the structural abnormalities between glomerulus and stria vascularis showed that both the kidney and cochlea were concerned with electrolyte transport.[2,3] Changes in the outer hair cells and spiral ganglia do occur in CKD as witnessed in different temporal bone

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sections and audiovestibular changes result from the water and electrolyte imbalance accompanying CKD.[4] The function of both the kidney and the cochlea includes complex processes of water and ion regulation which are dependent on the functioning of different proton pump systems which maintain homeostasis of pH and ions.[5,6]

The Brainstem Auditory Evoked Response is an early evoked response that reflects neural function along the ascending auditory pathway, from the cochlea to the inferior colliculus. Studies using BAER as an index of auditory function among patients with CKD showed evidence of various degrees of auditory dysfunction.

The present study is done to explore the potential usefulness of electrophysiologic indices for evaluating the physical status of patients being treated for end stage CKD. These indices can be helpful in early diagnosis and management of CNS dysfunction, cognitive impairment, and sensorineural hearing loss in patients of chronic kidney disease.

Material and methods:

This prospective observational study was conducted on 100 adult patients of CKD and 50 healthy controls on regular follow up of Kidney and Dialysis Clinic at Pandit Bhagwat Dayal Sharma Post Graduate Institute of Medical Sciences, Rohtak. This study was duly approved by the Ethical committee and the Post graduate board of studies of the institution. The inclusion criteria of the CKD patients were age between 18 and 75 years, CKD stage 3, 4 and 5, and patients on maintenance hemodialysis for at least 3 months. Patients excluded were those who had congenital hearing loss or middle ear alterations, history of excessive exposure to noise, history of use of ototoxic medications, patients using any type of hearing aids, and post renal transplant patients.

The study participants were divided into two groups:

Group I consisted of 100 patients of CKD (stage 3 to 5D).

Group II consisted of 50 healthy controls.

Group I was further subdivided into 4 groups A, B, C and D based on CKD staging by NKF-K/DOQI.[7]

Group A consisted of 25 patients with eGFR between 30-59 ml/min/1.73m^2 (CKD Stage 3).

Group B consisted of 25 patients with eGFR between 15-29 ml/min/1.73m^2 (CKD Stage 4).

Group C consisted of 25 patients with of eGFR <15 ml/min/ 1.73m^2,not on hemodialysis (CKD stage 5).

Group D consisted of 25 patients with of eGFR <15 ml/min/ 1.73m^2 on hemodialysis (CKD stage-5 D).

After accounting for the inclusion and exclusion criteria patients and controls included in the study underwent a battery of investigations which included a complete blood count, blood urea, serum creatinine, blood sugar, serum calcium and phosphorus, serum uric acid, seum albumin, serum electrolytes, urine routine examination, 24 hour urine for proteinuria, viral markers (HIV/HBsAg/Anti HCV), ECG, Chest X-ray PA view, and ultrasound abdomen for bilateral kidney size and echotexture. All the patients and controls underwent Pure Tone Audiometry (PTA) and Brainstem Audiometry Evoked Response.

At the end of the study, the data was expressed as mean±1SD or range. Probability values <0.05 were considered to be significant in all the analyses. Independent t-test and ANOVA test were used to analyze differences in quantitative variables between the groups. The correlations were tested using Pearson correlation coefficient analysis. All statistical calculations were carried out using SPSS 21.0 software.

Results:

The mean age of group I and II was 53 years and 46 years respectively. Out of the 100 patients 64 were male and 36 were female while out of the 50 controls 26 were male and 24 were female. The comparison of mean hearing threshold between group I and group II is shown in table 1a with the difference being statistically significant ($p<0.0001$). This shows that patients with CKD have sensorineural hearing loss which is grater at higher frequencies. However on further subgroup analysis (table 1b) there was no significant difference among any of the subgroups. Hearing loss, defined as hearing threshold greater than 25dB, was found in 19 out of 25 patients each (76%) in group A and B, 20 out of 25 patients (80%) in group C and 17 out of 25 patients (68%) in group D. Comparing between the dialysed and non-dialysed group of stage-V patients shows significant difference at all frequencies except 2 and 4 kHz with the dialysed patients having more severe hearing loss.

The BAER latencies for group I and II are given in table IIa with all the differences being statistically significant between the two groups ($p<0.0001$). The latencies for the subgroups A, B, C, and D are given in table IIb. The difference among the subgroups was statistically significant for waves I and III, and interpeak III-V latency ($p<0.05$). In addition the difference between the non-dialysed and the dialysed groups was significant only for wave I, and interpeak latencies III-V and I-V. Comparing between the dialysed and non-dialysed group of stage-V patients show significant difference at all frequencies except 2 and 4 kHz with the dialysed patients having more severe hearing loss. Similar comparison for the BAER latencies showed significant difference only for wave I, and interpeak latencies III-V and I-V.

Table Ia: *Comparison of hearing threshold of cases vis-à-vis controls*

Pure Tone Audiometry	Group I (N=100) Mean±S.D	Group II (N=50) Mean±S.D	P Value*
0.25kHz	11.59 ± 3.24	8.54 ± 2.28	<.0001
0.5kHz	12.59 ± 3.24	8 ± 1.95	<.0001
1.0kHz	13.56 ± 3.37	7.58 ± 2.29	<.0001
2.0kHz	14.98 ± 3.41	7.02 ± 2	<.0001
4.0kHz	19.33 ± 4.55	8.6 ± 2.33	<.0001
8.0kHz	28.96 ± 5.97	10.82 ± 2.37	<.0001

*Analyzed by Independent t-test

Table Ib: *Comparison of hearing threshold in different groups of CKD patients*

Pure Tone Audiometry	Group A (N=25) Mean±S.D	Group B (N=25) Mean±S.D	Group C (N=25) Mean±S.D	Group D (N=25) Mean±S.D	P value*
0.25kHz	12.12 ± 3.14	11.92 ± 3.35	12.24 ± 3.11	10.08 ± 3.07	0.059
0.5kHz	13.12 ± 3.14	12.92 ± 3.35	13.24 ± 3.11	11.08 ± 3.07	0.059
1.0kHz	14.12 ± 3.14	13.92 ± 3.35	14.24 ± 3.11	11.96 ± 3.52	0.051
2.0kHz	15.12 ± 3.14	14.92 ± 3.35	15.24 ± 3.11	14.64 ± 4.12	0.933
4.0kHz	19.08 ± 4.04	18.8 ± 4.27	19.28 ± 4.03	20.16 ± 5.8	0.840
8.0kHz	29.96 ± 4.97	29.68 ± 5.23	30.32 ± 4.98	25.88 ± 7.55	0.218

*Analyzed by ANOVA

Table IIa: *Comparison of Brainstem Evoked Response Audiometry latencies (absolute and interpeak) of cases vis-à-vis controls*

Brainstem Evoked Response Audiometry	Group I (N=100) Mean±S.D	Group II (N=50) Mean±S.D	P value*
I	1.82 ± 0.11	1.73 ± 0.07	<.0001
III	4.02 ± 0.13	3.8 ± 0.11	<.0001
V	5.81 ± 0.16	5.53 ± 0.09	<.0001
I-III	2.2 ± 0.1	2.07 ± 0.07	<.0001
III-V	1.8 ± 0.12	1.73 ± 0.07	<.0001
I-V	4 ± 0.15	3.8 ± 0.07	<.0001

*Analyzed by Independent t-test

Table IIb: *Comparison of Brainstem Evoked Response Audiometry latencies (absolute and interpeak) among different groups of CKD patients*

Brainstem Evoked Response Audiometry	Group A (N=25) Mean±S.D	Group B(N=25) Mean±S.D	Group C(N=25) Mean±S.D	Group D (N=25) Mean±S.D	P value*
I	1.79 ± 0.12	1.81 ± 0.12	1.81 ± 0.1	1.87 ± 0.07	0.037
III	3.98 ± 0.12	3.99 ± 0.12	4.03 ± 0.13	4.09 ± 0.11	0.005
V	5.82 ± 0.16	5.78 ± 0.2	5.83 ± 0.14	5.8 ± 0.14	0.656
I-III	2.19 ± 0.11	2.18 ± 0.11	2.22 ± 0.11	2.22 ± 0.09	0.437
III-V	1.85 ± 0.13	1.83 ± 0.12	1.81 ± 0.12	1.71 ± 0.07	0.0003
I-V	4.04 ± 0.16	4.01 ± 0.14	4.02 ± 0.13	3.93 ± 0.13	0.065

*Analyzed by ANOVA

Discussion:

An association between chronic kidney disease and hearing loss was first described in patients with Alport syndrome.[1] However, anatomical, physiological, pathological, and pharmacological similarities between the nephron and stria vascularis of the cochlea may explain this association in cases that are not related to syndromes or genetic diseases.[8] There is physiologic, ultrastructural and antigenic analogies between the kidney and the cochlea which permit to infer that the link between inner ear damage and kidney failure is likely to be much more than a coincidental finding.[9] The similarities of labyrinthine and renal function are well exemplified by the shared essential importance of aquaporins, specific cellular water channels, and by the presence of an ion transport system that to date has been demonstrated only in the rat and in the human endolymphatic sac beside the kidney. Furthermore it has been shown that there is an immunological connection between the kidney and inner ear in that antibodies raised against the nephron also deposit in the stria vascularis.[10] Sensorineural hearing loss at high frequencies is the most common type in patients with chronic kidney disease, and includes both cochlear impairment and lesions to particular portions of the auditory pathway.[11]

When hearing thresholds were compared between the patients and controls PTA showed an increase in hearing threshold in all patient groups. The hearing loss was bilaterally symmetrical, involving all frequencies, particularly the higher ones. The results of the present were similar to those of Bains et al. who showed a definite deterioration of audiologic functions among CKD patients. In that study the incidence of sensorineural hearing loss among the non-dialysed group of CKD patients was 70% while in the dialysed group it was 60%.[12] Bazzi et al. found an incidence of 77% including patients with mild and very mild hearing loss. Similar to the findings of the present study hearing loss in this study also occurred mainly in the high frequency band (4 and 8 kHz). The observation of hearing loss found to be more at higher frequencies in our study are also in accordance with the observations made by Wigand et al.,[13] Kopsa et al.,[14] Mitschke et al.,[15] and Johnson and Mathog.[16] Hearing loss was found to be around 40% among CKD patients on hemodialysis in one study.[2]

Compared with healthy controls, a highly significant delay was observed in CKD patients in both absolute and interpeak BAER latencies in the present study. This is in agreement with Rossini et al., who reported prolongation of all ABR waves following wave I.[19] Pagani et al. also noted the prolongation of ABR wave III and V latencies among patients with ESRD.[17] According to Gafter et al., patients with ESRD had prolonged wave III and V latency and I-V interpeak latency prior to and following hemodialysis.[18]

The present study showed correlation of the absolute latencies of peaks I and III, and of interpeak latencies III to V and I to V with blood urea levels. However only the absolute latency of peak III, and interpeak latency III to V were found correlated with serum creatinine values. Blood urea nitrogen was the unique chemical index to correlate with BERA parameters in the study by Rossini et al.[19] These findings are in contrast with various other studies which found no correlations between biochemical measures and changes in ABR absolute and interpeak latencies.[18,20-22] There was no correlation of absolute or interpeak latencies with serum calcium or albumin levels in the present study. However Antonelli et al. reported that ABR wave latency was correlated to albumin and calcium levels.[23] In addition, Pratt et al. reported changes in absolute and interpeak latency that were correlated to calcium ion changes prior to and following hemodialysis.[24]

The present study did not show improvement of BAER absolute wave latencies of the dialysed group compared to the non-dialysed group. The latencies for waves I and III were even worse in the dialysed group. There was a poor correlation of serum creatinine and BAER latencies in the present study. Serum urea and creatinine are nonspecific indicators of renal failure and may have a weak relationship to the pathophysiological processes which result in CNS dysfunction in uremia. It is possible that middle molecules or other uremic toxins may correlate better with uremic neurotoxicity. Non-dialysed patients have a higher residual GFR which may result in better clearance of middle molecules than patients on hemodialysis with a lower residual GFR, since it is believed that hemodialysis does not result in efficient removal of these middle molecules. This results in shorter delay in neural conduction in non-dialysed patients.

The limitation encountered in the present study is the absence of any intervention to treat the hearing dysfunction encountered on either PTA or BAER in these patients of CKD.

Conclusions:

The present study provides a concrete evidence to the otherwise disputed relation of auditory function in CKD proving that hearing is permanently affected by ESRD at all levels of the auditory neural pathway. BAER can prove useful in the early detection of hearing impairment in patients of CKD, even in the subclinical stage. However, further studies are required to devise specific therapies to halt as well as reverse this auditory dysfunction.

Conflict of interest: None.

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