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Prevalence and Patterns of Hearing Loss among Chronic Kidney Disease of Various Stages in Bangladeshi Patients

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Abstract **Objectives**: This study was designed to evaluate the association between chronic kidney disease and sensorineural hearing impairment. Early detection of sensorineural hearing imapirment in CKD patient will allow appropriate treatment which will improve quality of hearing. **Hypothesis:** Sensorineural hearing impairment is more prevalent in chronic kidney disease patients than control group. **Setting:** The work was done at a tertiary level hospital in the central part of country. **Participants:** The subjects were divided into a case group consisting of 55 CKD patients and a control group of 50 people. Subjects with age below 18 years and above 60 years, AKI, audiometric evidence of conductive hearing loss & past medical or surgical treatment of otologic conditions were excluded from the study. **Results**. Prevalence of sensorineural hearing loss in CKD patients was found to be 54% and the prevalence of hearing loss in control subjects was found to be 16%. Comparison of hearing loss between CKD and the control groups was found to be statistically strongly significant (p value was 0.0004). In CKD patients, 10 % had mild loss of hearing impairment, 30 % had moderate loss, severe loss was present in 40% patients and 20% had profound loss of hearing. By disease stage, the prevalence of hearing loss in CKD patients was as follows: stage III, 6.6%; stage IV, 33.3% and stage V 60 %. **Conclusion:** The present study showed the relationship between chronic kidney disease and sensorineural hearing impairment to be statitistically significant (P<0.05) which signifies that that hearing loss is relatively prevalent in patients with CKD.

Keywords: *CKD, hearing loss*

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1. Introduction

The kidney and the cochlea of the inner ear have some very similar membranes which are held together with a substance called collagen. These membranes are similar in function and in structure. In both cases, these membranes help to maintain the chemical balance of the fluids of the kidney and inner ear. Because of similar molecular structure, they can be damaged by the same drugs, such as overdose of diuretics. Reports over many years also have shown associations between various other chronic kidney conditions and hearing loss. Sensorineural hearing loss is increasingly found in chronic kidney disease irrespective of the cause of CKD. Hearing disorders usually begin in the high frequency portion of the sound spectrum. It has been suggested that common physiologic mechanisms involving fluid and electrolyte shifts in stria vuscularis of cochlea and glomerulus might explain the association between hearing loss and CKD [1]. There also are certain anatomic similarities at an ultra structural level and evidence for similar antigenicity of the cochlea and kidney [2]. Several small studies have indicated an increased prevalence of high-frequency hearing loss in patients with CKD [3].

2. Rationale

Early detection and management of complications of Chronic Kidney Disease is an important component of CKD management plan. Hearing impairment in CKD patient could be an easily overlooked complication of CKD. Early detection of sensorineural hearing impairment in CKD patient will help to reduce exposure to risk factors and taking appropriate measures can improve the hearing function as well as the quality of life of CKD patients.

Nephrologists' usually don't evaluate the CKD patient for hearing function. Sensorineural hearing impairment can affect the quality of living in CKD patient. This study will investigate whether there is any relationship between chronic kidney disease and sensorineural hearing impairment & early detection of sensorineural hearing

imapirment in CKD patient will allow appropriate treatment to improve quality of hearing.

3. Methods

It was a cross sectional study. The study was carried out during July 2013 to June 2014.

The samples of the cases were collected from Department of Nephrology, Bangabandhu Sheikh Mujib Medical University, Dhaka. The samples of the control subjects were collected from ophthalmology outdoor patients Department (OPD) of Bangabandhu Sheikh Mujib Medical University, Dhaka .The study subjects were broadly divided into two groups, the case or CKD (stage III to V) group and the control group whose age, sex and confounding factors(Diabetes mellitus and Hypertension)were matched. The sample number was 55 in case group and 50 in control group.

So, the total sample was 105 in number. Prior to commencement of this study, the research protocol was approved by Institutional review board (IRB) of Bangabandhu Sheikh Mujib Medical University, Dhaka.

Detailed general and systemic examinations were done. e-GFR was calculated. And according to the e-GFR, patients were grouped into different stages of CKD following K/DOQI 2002 guidelines. Then the patients were assessed with routine laboratory investigations (CBC, urine R/M/E), renal function tests (blood urea, serum creatinine, serum calcium, serum inorganic phosphate, serum uric acid e.t.c.), specific laboratory tests (UTP, FBS or RBS, serum fasting lipid profile) as per data sheet. Renal USG was done to measure kidney size and to see any structural abnormality.

The patients were then evaluated for their hearing function. Hearing-related questions included family history of hearing loss, past medical or surgical treatment of otologic conditions, diseases associated with hearing loss was asked as per data sheet. Otoscopic examination was performed by the investigator to rule out any problem in external ears or in tympanic membrane. Rinne's test, Weber's test and Absolute bone conduction tests were done and their findings were noted. The tuning fork tests were carried out by vibration of tuning forks of frequency: 512 Hz.

Those who had normal otoscopic finding were further evaluated by pure tone audiometry.

Pure-tone audiometry was performed by audiologists in sound-treated booths using standard TDH-39 earphones and Equnix AT235 audiometers. A total of 75 patients were evaluated by pure tone audiometry and 20 of these patients showed evidence of high frequency mild conductive deafness and thus excluded from the study..A total of 55 CKD patients (stage III to V) who had normal hearing and showed audiometric evidence of sensorineural deafness (both pure & mixed) were taken for data analysis. Hearing impairment was determined according to WHO grades of hearing impairment (WHO, 2014).

4. Statistical Analyses

1. After processing of all available data, statistical analysis was done.
2. Obtained datas were expressed in frequency, percentage, mean and standard deviation as applicable.
3. Continuous variables were expressed as means ± SD.
4. Comparisons between groups were done by the Student's t-test where appropriate for continuous variables.
5. Categorical datas were analyzed by chi-square est.
6. The whole analyses were done with the help of computer based SPSS (Statistical Programme for Social Science) programme version 17.0 for windows.
7. A two-tailed P-Value of<0.05 was considered as significant.

5. Results

Case group consist of 55 CKD patients. Data obtained are summarized in Table 1

Table 1. Different baseline clinical characters of patients with chronic kidney disease

Baseline characteristics	**CKD group (n=55)**
Age, y	43.44±13.75
Sex (female/male)	33/22
Diabetes Mellitus	18
Hypertension	38
Duration of CKD (in Months)	20.6±18.9
BMI (kg/m^2)	21.54±4.21
Systolic BP(mm Hg)	163.9±19.8
Diastolic BP(mm Hg)	93.8±8.36
Hb % (gm/dl)	9.33±1.92
Serum creatinine(mg/dl)	6.72±4.22
Serum Calcium (mmol/l)	1.89±0.13
Serum Phosphate (mmol/l)	2.12±0.23
Current smoker (%)	27.27

Table 2. Distribution of risk factors between the patients with chronic kidney disease and healthy control

Risk factor	**CKD group (n=55)**		**Control group (n=50)**		**P value**
	n	%	n	%	
Diabetes Mellitus					
Yes	18	33	16	32	> 0.05
No	37	67	34	68	
Hypertension					
Yes	38	69	34	68	> 0.05
No	17	31	16	32	
Smoking					
Current smoker	15	27	15	30	> 0.05
Non-smoker / Ex smoker	40	73	35	70	

Analysis was done by chi (X^2) test to compare statistical difference between two groups.

There was no statistically significant difference between the groups (P>0.05, analysis done by chi (X^2) test).

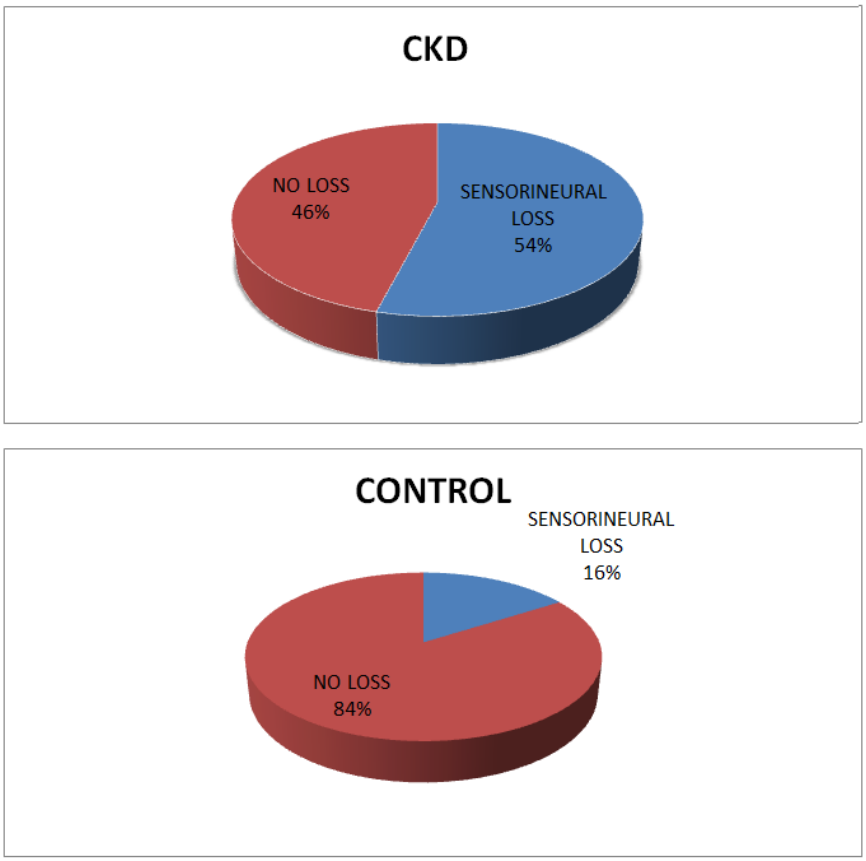

Figure 1. Comparison of hearing loss between CKD patients and control

The pie chart (Figure 1) shows the prevalence of sensorineural hearing loss in CKD patients which was found to be 54% and the prevalence of hearing loss in control subjects which was found to be 16%. Comparison between two groups for hearing loss was done by chi (X^2) test. p value was 0.0004***. There is strongly significant difference between CKD and Control group. This signifies that CKD is associated with sensorineural hearing loss.
***= Significant at P < 0.001.

Table 3 shows by disease stage, the prevalences of hearing loss in CKD patients were as follows: stage III, 6.6%; stage IV, 33.3% and stage V 60 %.

The prevalence of sensorineural and mixed hearing loss in CKD patients was found to be 14%, 40% respectively. The prevalence of sensorineural and mixed hearing loss in control subjects was found to be 4%, 12% respectively.

Table 3. Prevalence of hearing loss in various stages of chronic kidney disease

With CKD(n=30)	n	%
StageIII	2	6.6%
Stage1V	10	33.3%
StageV (predialysis)	18	60%

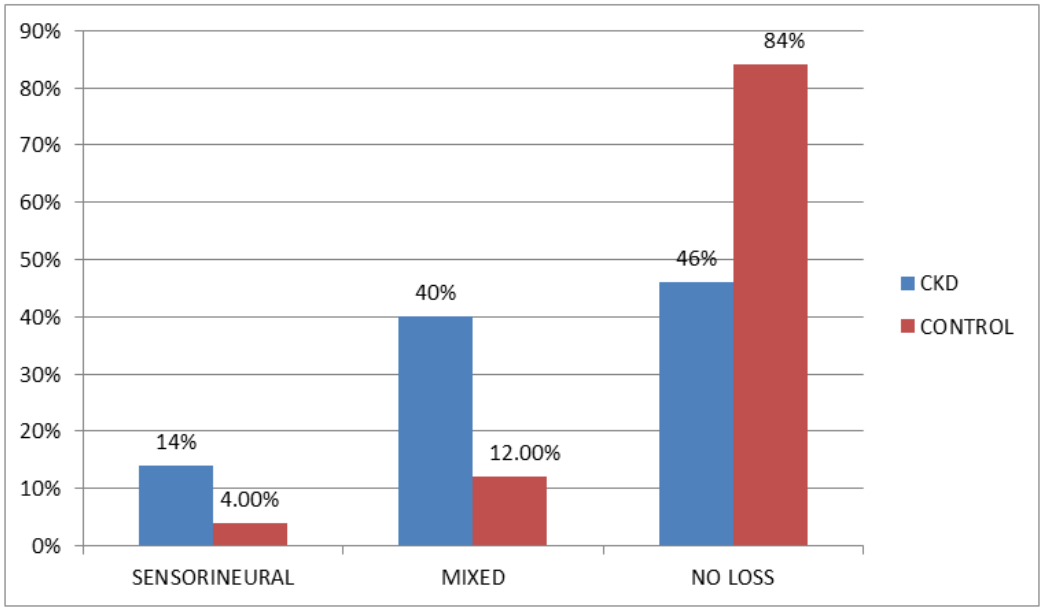

Figure 2. Prevalence of different types of hearing loss in CKD patients (n=55) and control (n=50)

In CKD patient with hearing impairment, 10 % had mild loss, 30 % had moderate loss, severe loss was present in 40% patients and 20% had profound loss of hearing.

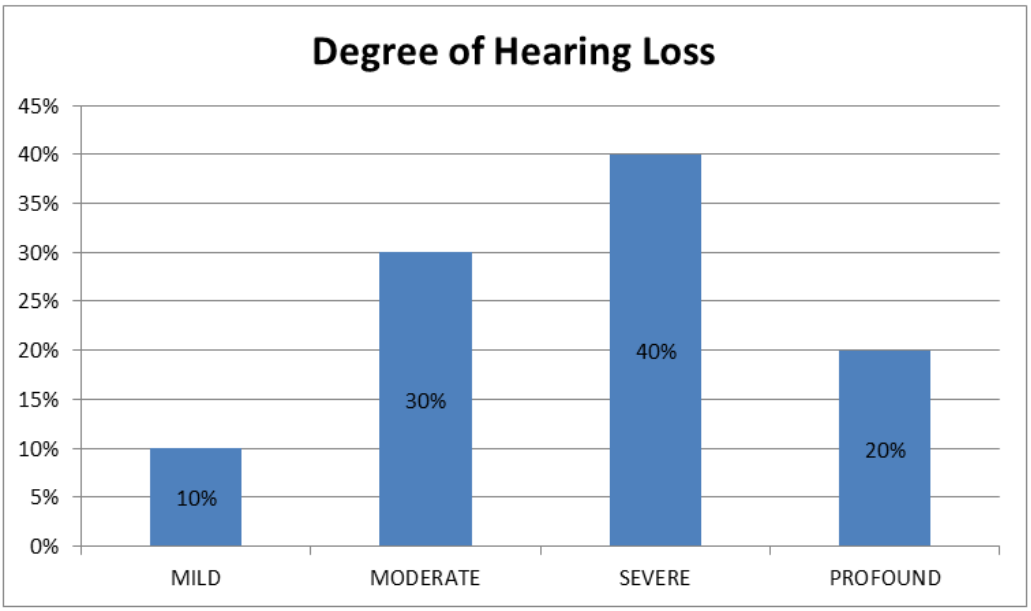

Figure 3. Degree of hearing loss based on pure tone audiometry (n= 30)

6. Discussion

This study was conducted to evaluate the association between chronic kidney disease and sensorineural hearing impairment. Prevalence of hearing loss in chronic kidney disease was seen and compared with control group. Prevalence of hearing loss was also seen according to stages of kidney disease.

Nephron and stria vascularis of the cochlea share physiologic, ultrastructural, and antigenic similarities that could underlie the link between CKD and hearing loss [1]. The cochlea and kidney have similar physiological mechanisms, namely the active transport of fluid and electrolytes accomplished by the stria vascularis and the glomerulus, respectively [4]. It has been suggested that common physiologic mechanisms involving fluid and electrolyte shifts in stria and kidney might explain the association between hearing loss and CKD [1]. The aetiopathogenetic mechanisms reported included osmotic alteration resulting in loss of hair cells, collapse of the endolymphatic space, oedema and atrophy of specialized auditory cells and in some, complications of haemodialysis have been hypothesized. [5]. There also are certain anatomic similarities at an ultrastructural level and evidence for similar antigenicity of the cochlea and kidney. Although the gross anatomy of the kidney and cochlea differs greatly, there are many similarities at the ultrastructural level. Both contain epithelial structures in close contact with their vascular supply. Basement membrane is found closely opposed to capillary endothelium in both Bowman's capsule and the proximal renal tubule of the kidney and also around the capillaries of the stria vascularis. In addition, basement membrane-lined intercellular channels exist in both the glomerulus and the stria vuscularis. These may account for similar effects of medications (i.e. nephrotoxic and ototoxic effects of aminoglycosides) and immunological factors on the two organs. Inner ear and kidney development are both influenced by similar genetic factors in hereditary conditions such as Alport's syndrome and Branchio-Oto-Renal syndrome. Presence of hearing loss and estimation of type and degree constitute one of the most common methods used to investigate the effects of renal disease on the auditory system. Severity of hearing loss may give an indication of the extent of damage to auditory function, whereas the type of hearing loss may distinguish between lesions in the outer and middle ear (conductive hearing loss) or the cochlea and the neural pathways (sensorineural hearing loss). A smaller comparison of the hearing loss in older patients with CKD with an age-matched control population was made by Antonelli et al (1991), who also found a difference between the study and the control groups; they attributed the hearing loss to a subclinical uremic axonal neuropathy shown by the alteration of ABR response. Changes in ABR pattern were also reported in other studies, [7] and their coincidence with alterations in otoacoustic emissions backs up the inference that repeated biochemical and electrolytic disturbances can act on the cochlea, the acoustic nerve and the brainstem. The auditory brainstem response (ABR) is an auditory evoked potential extracted from ongoing electrical activity in the brain and recorded via electrodes placed on the scalp. The resulting recording is a series of vertex positive waves of which I through V are evaluated [8,9,10].

The association between inner ear and kidney affections was also described in a paediatric age group, in which the alterations were more commonly observed in transient otoacoustic emissions than in audiogram, [11] thus witnessing an early cochlear involvement. Actually, the involvement of young people is even reported by other authors, [5] and otoacoustic emissions are considered a more sensitive tool to detect incipient cochlear damage than behaviour thresholds.

This was a cross sectional study. A group of 55 patients with chronic kidney disease (stage III-V). and another group consisting of 50 persons (not known to have any

previous kidney disease and had normal renal function) were included as control group. The studied groups were matched for age, sex, hypertension status, diabetes status to minimize the effects of these confounding variables on the studied markers.

The mean age in the CKD group and the control group was 43.44±13.75 and 41.36±12.23 respectively. The age range was 18-60 years. In the present study, 60% was male and 40% was female in CKD group and 66% was male and 34% was female in the healthy control group. There were no statistically significant differences between two groups for the ages and sexes. Diabetes Mellitus was found 33% in CKD group and 32% in the control group respectively. Hypertension was found 69% and 68 % in CKD group and in the control group respectively. There were no statistically significant differences between two groups for the Diabetes Mellitus and Hypertension. Thus the effect of confounding variables like Diabetes Mellitus and Hypertension had been minimized.

The mean body index (mean±SD) in the patient group was 21.54±4.21. The mean systolic blood pressure (mean ± SD) & the mean diastolic blood pressure in the patient group was 163.9±19.8. & 93.8±8.36 respectively. The mean duration of CKD (in Months), Hb %, serum creatinine(mg/dl),serum calcium and serum phosphate were 20.6±18.9, 9.33±1.92, 6.72±4.22, 1.89±0.13 and 2.12±0.23 respectively. 27% of CKD patient were current smoker. Among the CKD participants, highest percentage had hypertension (69%) and 33% had diabetes mellitus. In patients with established CKD, multiple risk factors have been hypothesized to cause hearing loss, including use of ototoxic medications, hypertension, and diabetes [12,13] particularly in association with hypertension [14], electrolyte disturbances, and hemodialysis itself. Multiple shared risk factors for CKD and hearing loss include age, diabetes, hypertension, and medications that are both ototoxic and nephrotoxic. [15] Starting from an attempt to explain the origin of "idiopathic" sudden sensorineural hearing loss in young subjects without vascular risk factors [16], some observations were reported over the years by few researcher about the possibility that a hemodynamic imbalance can represent a causal factor, that was subsequently confirmed by a series of studies, [17] some unexplained inner ear disorders or sufferance can depend on a sharp reduction of blood pressure values followed by an abnormal peripheral sympathetic vasomotor response; the inner ear circulation, due to its terminal type, can thus be jeopardized by a more or less transient condition able to generate an acute local ischemia and subsequent hypoxia. This mechanism is likely to act both under physiological conditions that must deal with a generic exaggerated sympathetic reactivity [18] and under pathological conditions as treated hypertension and or chronic heart failure. [17] According to this statement, researcher has hypothesized and supported a common origin for different inner ear disorders that have never found a completely satisfactory explanation, including Meniere's Disease. [19] As stated above, a complicate structure that accomplishes a complicate function is common to kidney and labyrinth; moreover, their blood supply may be conditioned by particular factors that can yield additional difficulties in maintaining a stable perfusion: namely, the pressure of inner ear fluids [20] and the postglomerular vasomotor tone [21] respectively.

In our study, sensorineural hearing loss was found in 54% of CKD and 16% of control group. T Alport (1927) first described the classical genetic syndrome named after him that established a connection between hearing loss and renal insufficiency. Other observations followed which indicated the presence of hearing loss in many renal diseases, including disorders in which there was no indication of genetic disease. Some of the other rare conditions or syndromes in which hearing loss is closely linked to CKD includes HDR (hypoparathyroidism, deafness, and renal dysplasia) syndrome, [23] Brachio-Oto Renal syndrome, [24] Fabry disease [25], and MELAS (mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke) syndrome. [26] Prevalence of sensorineural loss in our study result almost match with Eswari et al. (2010). In a recent community-based study, Eswari et al. (2010) showed an association between nonsyndromal CKD and hearing loss. They mentioned with moderate CKD, 54.4% had measured hearing loss compared with 28.3% with eGFR ≥60 mL/min/1.73 m^2. Author established in their study moderate CKD as a independent risk factor for hearing loss. Shing (2012) showed 28% prevalence of sensorineural hearing impairment in CKD patient when compared to 6% in healthy control.

The prevalence of pure sensorineural and mixed hearing loss in CKD patients was found to be 14%, 40% respectively. The prevalence of pure sensorineural and mixed hearing loss in control subjects was found to be 4%, 12% respectively. In CKD patient with hearing impairment, 10 % had mild loss, 30 % had moderate loss, severe loss was present in 40% patients respectively and 20% has profound loss of hearing.

The prevalences of hearing loss in CKD patients by disease stages were 6.6%, 33.3%, 60 % in stage III, stage IV, and stage V respectively. This indicates incidence of sensorineural loss was highest when eGFR <15 ml/min/1.73m^2. Eswari et al. (2010) found that participants with eGFR <45 mL/min/1.73 m^2 had the highest prevalence of hearing loss (73%) but in our study we found prevalence of hearing loss is 60% only when eGFR is less than 15 ml/min/1.73m^2.

7. Conclusion

The present study showed that hearing loss is relatively prevalent in patients with CKD. So, we recommend screening for hearing function in patients mostly with CKD (stage V). Our results have confirmed a link between CKD and hearing loss in adults, and these data suggest that earlier clinical hearing assessment with appropriate audiologic testing and interventions such as the appropriate fitting of hearing aids could preserve hearing function in patients with CKD.

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