



## Hearing Loss in Chronic Renal Failure - An Assessment of Multiple Aetiological Factors

Suja Sreedharan, Vishnu Prasad Jayashree Bhat Mahesh Chandra Hegde Salil agarwal

Cherukattil Waheeda

Kasturba Medical College, Mangalore, Manipal University

### Abstract

**Introduction:** Sensorineural hearing loss in chronic renal failure is believed to be of multifactorial etiology. Associated hypertension and diabetes mellitus, use of ototoxic drugs, hemodialysis and the changes in metabolic parameters are the various reasons quoted for the hearing loss.

**Objectives:** Our study attempts to correlate the hearing thresholds with the multiple parameters like blood levels of urea, serum creatinine, sodium, potassium, calcium and hemoglobin values incriminated in decreased hearing in CRF patients.

**Materials and methods:** Prospective study of 25 patients receiving treatment for CRF. The threshold of the worsen ear was considered for statistical analysis.

**Results:** 18% of the patients at low frequencies (250 and 500 Hz), 32% of the patients at mid-frequencies (1000 and 2000 Hz), and 72% of the patients at high frequencies (4000 and 8000 Hz) had decreased hearing for both bone and air conduction hearing. We found a positive correlation between hearing loss and increasing number of hemodialysis sessions, the levels of blood urea, serum creatinine, serum sodium and use of ototoxic drugs; while serum calcium, serum potassium and hemoglobin levels had a negative correlation.

## Conclusion:

Though the management of CRF including hemodialysis has been refined, hearing loss continues to cause disability in CRF patients.

## Introduction

Renal diseases have been associated with audio-vestibular disorders for a considerable period of time. With the development of hemodialysis, renal patients live longer, and with a better quality of life. Sensorineural hearing loss is frequently reported in patients with chronic renal failure. Many variables may contribute to the pathogenesis of hearing loss in chronic renal failure patients—chronic renal failure per se, the mean age of patients with renal disease, the co-existence of systemic disorders like diabetes and hypertension and even the ototoxic effects of the treatment used to alleviate the condition i.e. the drugs, hemodialysis and renal transplantation<sup>1</sup>.

## Materials and Methods

Our study consisted of twenty five patients with chronic end stage renal disease, receiving medical treatment at the Nephrology Department of Kasturba Medical College, Mangalore. The diagnosis of chronic renal failure was based on history, physical examination, laboratory tests and ultrasonography. Patients were subjected to a full clinical examination including otorhinological examination. Patients with history of ear discharge, decreased hearing or exposure to noise prior to development of chronic renal failure were excluded. Details of the duration of renal failure, number of hemodialysis and use of ototoxic drugs were documented.

Ototoxicity was defined as at least one treatment session with aminoglycosides for seven days of full therapy and/ or treatment with furosemide (>1mg/kg) for more than one week<sup>2</sup>. Blood Pressure, blood sugar levels, hemoglobin, blood urea, serum creatinine, serum sodium, potassium and calcium levels done just prior to the audiological evaluation were recorded in all the patients.

## Audiological evaluation

All patients underwent audiological assessment by Pure Tone Audiometry in an acoustically treated room. Air and bone conduction thresholds were measured. Audiogram was interpreted for the type of loss, degree of loss and frequency distribution. Normal intensity was considered in the range of 0 to 25 dB. Hearing loss intensity was considered mild, in the range 26 to 40 dB; moderate between 41 to 70dB; severe between 71-90dB and profound above 91dB<sup>3</sup>. Measured audio frequencies were documented as low (250 & 500 Hz), middle (1000 & 2000Hz) and high (4000 & 8000 Hz) frequency<sup>2</sup>.

Statistical analysis was performed with Mann Whitney U test and Pearson correlation test after taking the decibel values of the worst ear at each frequency tested for right and left air conduction and bone conduction respectively.

## Results and Observation

25 patients with chronic end stage renal failure were studied. The age range was from 14 to 73 years with a mean age of 49 years. Duration of renal failure at the time of audiological evaluation ranged from 1 month to 72 months. 14 patients of chronic renal failure were treated conservatively. 11 patients underwent hemodialysis, with number of hemodialysis varying from one to 36. Of the 25 patients, 7 had diabetes mellitus, 17 had hypertension and 9 patients were on ototoxic drugs (Figure 1).

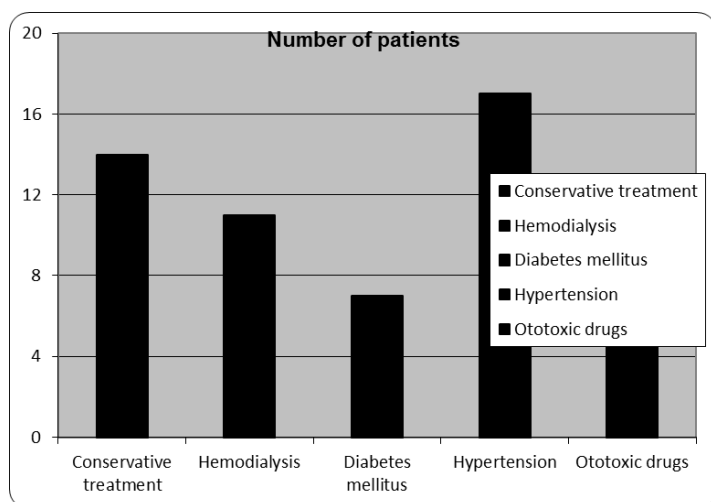


Figure 1: Patient distribution for associated etiological factors

Analysis of air and bone conduction was done for right and left ears separately. The worst ear was taken into consideration for statistical analysis. It was found that for air conduction at low frequencies (250 and 500 Hz), 82% of the patients had normal hearing at low frequencies, 8% had mild hearing loss, 8% had moderate hearing loss and 2% had profound hearing loss.

At mid frequencies (1000 and 2000 Hz), 68% had normal hearing, 8% had mild hearing loss, 22% had moderate hearing loss and 2% had severe hearing loss. At high frequencies (4000 and 8000 Hz), percentage of ears with normal hearing dropped down to 28%; 14% had mild hearing loss, 36% had moderate hearing loss, 18% had severe hearing loss and 4% had profound hearing loss (Table 1).

For bone conduction at low frequencies, 86% of patients had normal hearing, 6% had mild hearing loss and 8% had moderate hearing loss. At mid frequencies, 72% had normal hearing, 16% had mild hearing loss, 10% had moderate hearing loss and 2% had severe hearing loss. At high frequencies, 52% had normal hearing, 22% had mild hearing loss, 24% had moderate hearing loss and 2% had severe hearing loss (Table 2).

Hearing thresholds were compared for both air conduction and bone conduction for patients with chronic end stage renal disease on conservative treatment and patients who underwent hemodialysis. It was found that in hemodialysed patients there was a mild hearing loss at 250, 500, 1000 & 2000Hz and moderate hearing loss at 4000 & 8000 Hz. In patients with CRF on conservative treatment, hearing threshold was normal at 250 & 500 Hz while there was a mild hearing loss at 1000 & 2000 Hz and moderate hearing loss at 4000 & 8000 Hz.

No statistically significant difference was found between the two groups (Figures 2 and 3). Comparison of the number of hemodialysis sessions a patient underwent with the hearing thresholds revealed a significant correlation ( $p < 0.05$ ) of the number of sessions with hearing loss at 250 and 500 Hz, for both air and bone conduction.

	Low frequency	Mid frequency	High frequency
NORMAL HEARING	82%	68%	28%
MILD LOSS	8%	8%	14%
MODERATE LOSS	8%	22%	36%
SEVERE LOSS	-	2%	18%
PROFOUND LOSS	2%	-	4%

Table 1: Air conduction for the worse ear: patient distribution:

	Low frequency	Mid frequency	High frequency
NORMAL HEARING	86%	72%	52%
MILD LOSS	6%	16%	22%
MODERATE LOSS	8%	10%	24%
SEVERE LOSS	-	2%	2%
PROFOUND LOSS	-	-	-

Table 2: Bone conduction for the worse ear: patient distribution:

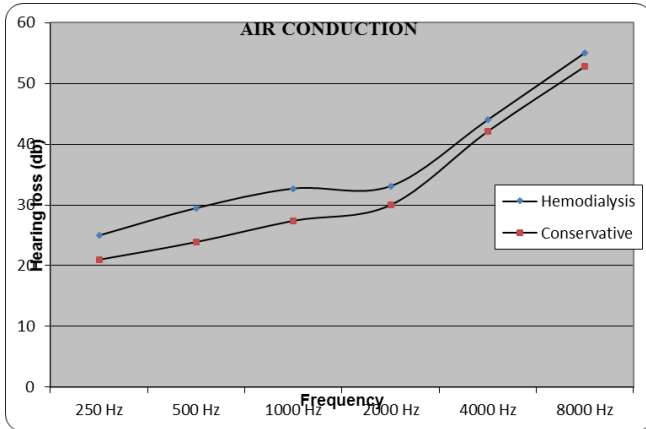


Figure 2: Air conduction thresholds for CRF patients on conservative management and those on hemodialysis.

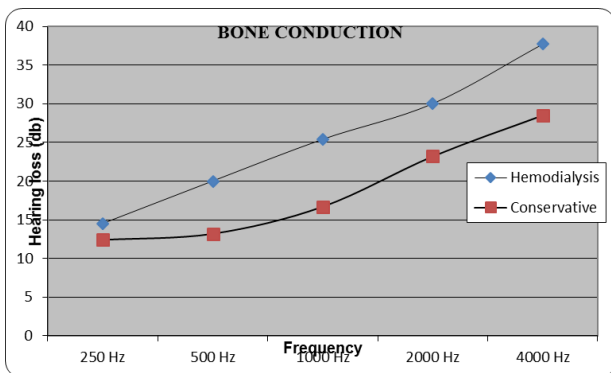


Figure 3: Bone conduction thresholds for CRF patients on conservative management and those on hemodialysis.

Comparison of chronic renal failure patients with and without diabetes showed that both the groups had normal hearing threshold at low frequencies; mild hearing loss at middle frequencies and moderate hearing loss at high frequencies. No significant difference was observed between the two groups on statistical analysis. Similarly no significant difference was found when hypertension was considered the variable between groups. Hence hypertension alone does not seem to worsen the hearing of chronic renal failure patients.

A significant difference was observed between the group of patients treated with ototoxic drugs and the group which was not, with patients on ototoxic drugs having poorer hearing threshold (Figures 4 and 5). The results hereby show that in addition to chronic renal failure, if patients are put on ototoxic drugs, they are likely to have worse hearing.

The serum creatinine values had a positive correlation with hearing thresholds in air conduction which was not significant ( $p > 0.05$ ), but in bone conduction there was significant correlation at 500 and 1000 Hz with the hearing loss ( $p < 0.05$ ). In case of blood urea also there was a positive correlation with hearing loss but it was not statistically significant ( $p > 0.05$ ).

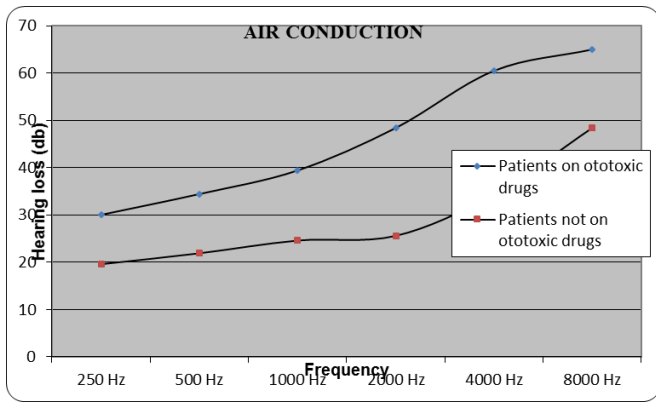


Figure 4: Air conduction thresholds for CRF patients with and without ototoxic drugs.

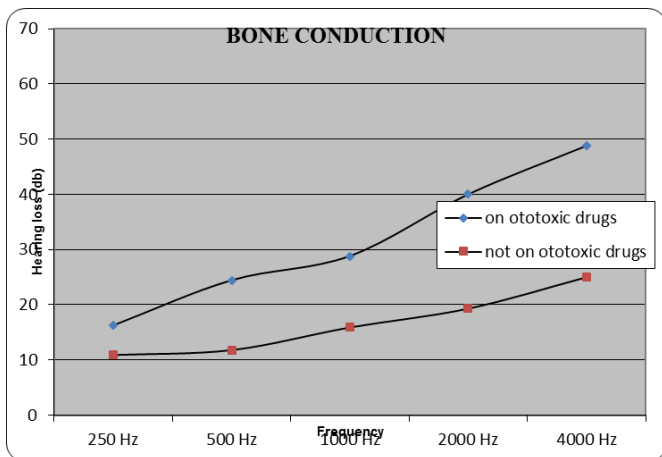


Figure 5: Bone conduction thresholds for CRF patients with and without ototoxic drugs.

The serum sodium levels had a positive correlation with the hearing thresholds for both air and bone conduction. Using Pearson's correlation test we found significance with hearing loss at 250, 500, 1000 and 2000Hz ( $p < 0.05$ ). On the other hand, serum potassium levels and blood hemoglobin levels correlated negatively with the hearing thresholds. However,  $p$  was  $> 0.05$  in both cases.

The serum calcium values when compared with the hearing thresholds for air and bone conduction using Pearson Correlation test revealed a significant negative correlation at 4000 and 8000 Hz ( $p < 0.05$ ).

#### Discussion

Although the gross anatomy of the kidney and cochlea differ, a very many similarities exist between the nephron and the stria vascularis at the anatomical, physiological, pharmacological, pathological and ultra structural levels. All this may make the nephron and the stria vascularis susceptible to the same type of haemodynamic or pharmacological insults<sup>4</sup>.

Many studies have documented the association between the hearing loss and chronic renal failure. Accelerated presbycusis, duration of renal failure, hemodialysis, ototoxic drugs, hypotension, circulating uremic toxins, anemia, electrolytic imbalances and metabolic disturbances are some of the causes listed in literature as possible causes for hearing loss in patients with chronic renal failure<sup>1</sup>.

In fact Oda et al has even suggested a quantitative relationship between treatment, degree of impairment, and temporal bone pathology<sup>5</sup>.

The documented hearing loss in chronic renal failure patients vary from 20% to 87% mostly depending on the different criteria for sample selection<sup>2</sup>. Though all frequencies can be affected in chronic renal failure, the susceptibility of high frequency to renal damage is well known<sup>6,7</sup>. The overall prevalence of hearing loss in our study was 80% of which 80% had high frequency hearing impairment. But a significant 44% had middle and 20% had low frequency hearing impairment. Statistical tests to correlate the duration of chronic renal failure to hearing loss proved negative.

Accelerated presbycusis has been mentioned in the literature as a probable cause of hearing loss in patients with renal failure<sup>6</sup>. The audiometric pattern of the loss in old age varies from a sloping high tone loss to a flatter audiogram with a loss for all frequencies<sup>8</sup>. In our study, though there was a positive correlation between the age and the hearing thresholds, we were unable to demonstrate a statistical significance, probably because the maximum numbers of patients were in the fourth and fifth decade with a mean age of 49 years.

No significant correlation has been proved previously between blood pressure and hearing loss. Similarly there is no evidence of atherosclerosis occurring in any of the smaller vessels of the ear<sup>9</sup>. However Kligerman et al suggested that patients with chronic renal failure are at risk for premature cardiovascular aging, and the potential for the development of clinically significant hearing loss always exists<sup>7</sup>.

Moreover hypotension is one of the possible complications of hemodialysis. We did not find any significant difference in hearing thresholds of renal failure patients with hypertension and without hypertension. Diabetics, as a whole, are deafer particularly in the lower frequencies and diabetes may be associated with accelerated sensorineural hearing loss in CRF but at present the evidence is inadequate<sup>10</sup>. We did not find any significant difference between CRF patients with and without diabetes with respect to the hearing thresholds.

Uremia affects the function of various organ systems and patients with chronic renal failure suffer widespread complications that are either the result of the chronic renal failure or the adaptive mechanism of the body in response to the disturbed homeostasis<sup>11</sup>.

Pathological changes in the cochlea range from mild loss of outer hair cells and spiral ganglion to complete absence of the organ of Corti<sup>5</sup>. The presence of an unidentified uremic toxin, which leads to uremic nephropathy of the eighth cranial nerve, leading to hearing loss has also been suggested<sup>11</sup>. In our study we found that with increasing urea levels, hearing loss of the patient with chronic renal failure increased. But this was not of statistical significance. We also found that patients with chronic renal failure had worsening hearing thresholds as their serum creatinine values increased. This correlation was proved statistically for bone conduction values at low frequencies.

Chronic renal failure is characterized by disturbed Na<sup>+</sup>, K<sup>+</sup> blood levels. This may result in poor coupling of energy from the footplate of stapes to the hair cells<sup>11</sup>. In fact some researchers have suggested that the degree of hearing loss in CRF is directly related to the degree of hyponatremia<sup>12</sup>. But in our study we found that hypernatremia worsened the hearing thresholds with significant correlation at lower and middle frequencies. However serum potassium did not demonstrate any significant correlation with hearing thresholds.

Patients with chronic renal failure after long term hemodialysis, suffer from deranged calcium-phosphorus metabolism, accelerated atherosclerosis, bone disease and metastatic calcification in soft tissues and vasculature<sup>13</sup>. But cochlear stria deposits of calcium seen in CRF patients may bear little relationship to the disturbed calcium metabolism though the size may be related to presence of hearing loss<sup>13</sup>. In our study the serum calcium levels showed a significant correlation with hearing thresholds, with hearing loss present at higher frequencies.

The extension of life with the development of hemodialysis has brought new problems. Hemodialysis has been implicated both in the development of high frequency loss<sup>7</sup> and also in improvement of low frequency losses in CRF<sup>14</sup>. Though the role of dialysis is unclear, adverse factors possibly related to hemodialysis are acute hypotension, reduction in blood osmotic pressure, acute clearance of urea, increased red blood cell mass and immunologic reaction to dialyzer membranes<sup>15</sup>. Further, it has been proposed that long term hemodialysis may cause electrolyte, osmotic and biochemical alterations leading to sensorineural hearing loss<sup>2</sup> though a single session may not have significant effect on hearing<sup>15</sup>.

Statistically we did not find a significant significance in the hearing thresholds of patients of chronic renal failure who were on conservative treatment and patients who were undergoing hemodialysis but we found a significant correlation between the increasing number of hemodialysis to the hearing loss. Many pharmacological agents act both on the inner ear and the kidney<sup>14</sup>. Patients with renal insufficiency are conservatively managed with antihypertensive drugs, diuretics, beta blockers and calcium antagonists and antibiotics; all of which may be potentially ototoxic. Ototoxicity may be defined as "the tendency of certain therapeutic agents and other chemical substances to cause functional impairment and cellular degeneration of the tissues of the inner ear, and especially of the end organs and neurons of the cochlear and vestibular divisions of the eighth cranial nerve"<sup>16</sup>. In our study nine patients with chronic renal failure were on ototoxic drugs as part of the medical treatment. The audiograms of these patients revealed mild hearing loss at low frequencies and moderate hearing loss at middle and high frequencies and a significant difference between the two groups was observed.



## Conclusions

In our study, we have made certain conclusions regarding the effect of various etiological factors on the hearing thresholds in patients with chronic renal failure based on a single audiological evaluation. Patients with CRF are subject to wide fluctuations in hemodynamic and metabolic parameters over time. Though we have arrived at certain broad conclusions based on our results, we cannot presume to identify the exact etiological factors responsible for hearing loss. Further studies are required wherein weekly or perhaps biweekly audiometric evaluations are carried out in these patients and correlated with the metabolic as well as therapeutic events that have taken place in the interval.

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