Research

Correlation between duration of chronic renal failure patients undergoing hemodialysis and sensorineural hearing loss

Novi Primadewi, Dewi Pratiwi, Taufani Dewi
Department of Otorhinolaryngology Head and Neck Surgery,
Faculty of Medicine, Sebelas Maret University, Surakarta

ABSTRACT

Background: Along with the increasing incidence of chronic renal failure patients receiving hemodialysis, recently, the incidence of sensorineural hearing loss (SNHL) among patients with end-stage kidney disease undergoing hemodialysis had also increased. The cochlea and kidney have many anatomical, physiological, pharmacological and pathological similarities. Dialysis sometimes causes worsening of hearing function. **Objective:** To determine the correlation between the duration of renal failure patients undergoing hemodialysis and the degree of sensorineural hearing loss. **Method:** A retrospective study using cross sectional method, conducted from August–September 2018. The study began by identifying patients with chronic renal failure and then continued with Oto Acoustic Emission (OAE) examination and pure tone audiometry. **Result:** The results of the Spearman rank statistical test for the correlation between duration of hemodialysis and the degree of SNHL in the right and left ears in patients with chronic renal failure found a significant positive correlation r= 0.498 and p=0.001 (right) , and r= 0.400 and p=0.006 (left). **Conclusion:** There was a significant correlation between the length of hemodialysis and the degree of sensorineural hearing loss.

Keywords: chronic renal failure, duration of hemodialysis, sensorineural hearing loss

ABSTRAK

Latar belakang: *Seiring dengan peningkatan angka kejadian pasien gagal ginjal kronik yang mendapatkan hemodialisa, akhir-akhir ini didapati peningkatan angka kejadian* Sensorineural Hearing Loss (SNHL) *di antara pasien dengan penyakit ginjal stadium akhir yang menjalani hemodialisa. Koklea dan ginjal memiliki banyak kesamaan anatomis, fisiologis, farmakologis dan patologis. Dialisa terkadang menyebabkan memburuknya fungsi pendengaran.* ***Tujuan:*** *Untuk mengetahui hubungan lama pasien gagal ginjal yang menjalani hemodialisa dengan derajat gangguan pendengaran tuli sensorineural.* ***Metode:*** *Penelitian retrospektif dengan metode potong lintang, dilakukan dari Agustus-September 2018. Penelitian dimulai dengan mengidentifikasi pasien gagal ginjal kronik kemudian dilanjutkan dengan pemeriksaan tes* Oto Acoustic Emission (OAE) *dan audiometri nada murni.* ***Hasil:*** *Hasil uji statistik Spearman rank untuk korelasi lama hemodialisa dengan derajat* SNHL *telinga kanan dan kiri pada pasien gagal ginjal kronik didapatkan korelasi positif yang signifikan: r= 0,498 dan p=0,001 (kanan) dan r= 0,400 dan p=0,006 (kiri).* ***Kesimpulan:*** *Terdapat korelasi yang bermakna antara lama hemodialisis dengan derajat tuli sensorineural.*

Kata kunci: *gagal ginjal kronik, lama hemodialisa, tuli sensorineural*

Correspondence address: dr. Novi Primadewi, Department of Otorhinolaryngology Head and Neck Surgery, Faculty of Medicine, Sebelas Maret University, Surakarta. Email: noviprimadewi@staff.uns.ac.id

INTRODUCTION

Sensorineural hearing loss (SNHL) is often defined as loss of hearing sensitivity due to peripheral tissue injury and/or cell death in the auditory organ, the cochlea. In addition, the central auditory central auditory structures of the brain could also have an independent role in the development of SNHL. SNHL disorders might occur in cases of chronic kidney disease (CKD) or CKD undergoing hemodialysis.[1,2]

The prevalence of CKD is continuously increasing. Data from the US National Health and Nutrition Examination Survey showed that in the period of 1999 to 2004 the prevalence of stage 1 to 4 CKD increased significantly when compared to the survey period of 1988 to 1994 (13.1% versus 10.0%). At the same time, this high prevalence and increasing incidence are largely found in the aging population. Meanwhile, this is also associated with an increase in the incidence of hypertension and diabetes mellitus.[3]

Along with the increasing incidence of CKD patients receiving hemodialysis, the incidence of SNHL among hemodialysis patients with end-stage renal disease (ESRD) has recently increased.[4] The prevalence of SNHL, especially high frequency in patients with CKD or ESRD can be up to 85% higher than the general population.[5]

Peyvandi et al.[6] stated that sensorineural hearing loss had a significant prevalence in CKD patients. Although there was no correlation between the severity of hearing loss and age or gender, it did rise with the patient's renal failure duration. Higher frequencies were typically affected by this hearing loss, which had no impact on hearing discrimination. Hearing loss is an aspect to consider in the management of patients with CKD, and these patients need to undergo routine hearing screening tests.

Hearing loss (HL), especially with cochlear disorder is found in a high percentage of patients with CKD.[7] Jamaldeen et al.[8] found out that almost every CKD patient undergoing second or third hemodialysis experienced some degree of hearing loss. Etiopathogenetic mechanisms include osmotic disturbances that result in loss of hair cells, collapse of the endolymphatic space, edema and atrophy of hearing-specific cells thought to be due to hemodialysis.[9]

CKD is a risk factor for inner ear disease based on endothelial dysfunction, one of the various mechanistic processes occurring in nephropathy. The association between renal failure and vestibulo-cochlear injury is supported by the observation that nephropathy patients have an increased risk of cardiovascular complications. From this point of view, CKD and inner ear pathology are effects of the same mechanistic process, mainly due to vascular injury. In addition, CKD can be considered as an independent risk factor for hypoxia because it is specifically associated with inflammation and oxidative stress.[10]

The study by Peyvandi et al.[6] analyzed the correlation between the duration of patients having suffered from CKD with the length of time patients had undergone hemodialysis (in months), by dividing the duration of CKD and hemodialysis in three ranges, 6-12 months, 1-2 years and 2-5 years.

Cochlear sensory dysfunction due to electrolyte imbalance is an important cause factor of hearing loss. Recently, Meena et al.[11] showed that the incidence of sensorineural hypoxia was higher in patients with chronic renal failure than in the healthy group.

CKD patients with hypertension and diabetes mellitus were associated with SNHL, but not correlated with the degree of hearing loss. Individuals with and without this disease had the same frequency of mild hearing loss.[12] On the other hand, Saeed et al.[13] showed that hearing impairment at the high frequency is more common in patient with chronic renal

failure (CRF) on hemodialysis. The longer the duration of hemodialysis will reduce the hearing threshold.

The aim of this study was to determine the correlation between the duration of renal failure patients undergoing hemodialysis with the degree of sensorineural hearing loss.

METHOD

This was an analytic retrospective study. Research observations were carried out with a cross sectional approach.

The study population came from patients with kidney failure who came to undergo hemodialysis at the Hemodialysis Unit of Dr. Moewardi General Hospital, Surakarta from August-September 2018. Patients included in the study were those who met the inclusion criteria and did not meet the exclusion criteria. Inclusion criteria were: a) outpatients with a glomerular filtration rate <15ml/min/1.73m2 in at least the last three months, with or without known kidney injury; b) routinely undergo hemodialysis twice a week; c) willing to become a research subject by signing a consent form after receiving an explanation (informed consent).

Meanwhile, the exclusion criteria were as follows: a) age older than or equal to 60 years; b) patients who had a history of excessive noise exposure, stroke, autoimmune disease, and taking ototoxic drugs.

The number of samples taken was determined based on the eligibility guidelines for multivariable analysis. In this study, the number of samples determined was 15 observations per independent variable. With 3 independent variables, the number of samples taken was 15 × 3 = 45 subjects.

The variables used in this study were independent and dependent variables. The independent variable was the length of time patients with chronic kidney failure underwent hemodialysis, while the dependent variable was the degree of SNHL. Confounding variables were diabetes mellitus and hypertension.

The data obtained from the research subjects were collected and analyzed using the contingency coefficient test and the Spearman rank test.

RESULT

Table1. Characteristic of subjects

Variable	Frequency (n=45)	(%)
Age		
20-30 years old	3	6.7%
>30-40 years old	8	17.8%
>40-50 years old	10	22.2%
>50-60 years old	24	53.3%
Gender		
Male	27	60.0%
Female	18	40.0%
Duration of hemodialysis		
<6 month	0	0.0%
>6-12 month	8	17.8%
>12-18 month	6	13.3%
>18-24 month	3	6.7%
>24 month	28	62.2%

History of DM		
Yes	28	62.2%
No	17	37.8%
History of HT		
Yes	18	40.0%
No	27	60.0%
Degree of SNHL		
Right ear		
Mild	7	15.6%
Moderate	6	57.8%
Moderate-severe	11	24.4%
Severe	21	2.2%
Left ear		
Mild	12	26.7%
Moderate	19	42.2%
Moderate-severe	11	24.4%
Severe	3	6.7%

Table 2. The correlation between diabetes mellitus and the degree of SNHL in the right ear of chronic renal failure patients

DM	Right ear				Total	r	p
	Mild	Moderate	Moderate-Severe	Severe			
Yes	3	15	9	1	28	0.277	0.290
	6.7%	33.3%	20.0%	2.2%	62.2%		
No	4	11	2	0	17		
	8.9%	24.4%	4.4%	0.0%	37.8%		
Total	7	26	11	1	45		
	15.6%	57.8%	24.4%	2.2%	100.0%		

Based on Table 1, it was known that most of the patients were >50-60 years old. Patients with CRF were mostly male, namely 60.0%, and the majority of patients undergoing hemodialysis was for > 24 months as many as 62.2%. Patients with a history of DM were 62.2% and patients with a history of hypertension were 40.0%. The degree of SNHL in the right ear was mostly moderate (57.8%) as well as in the left ear the majority was also moderate (42.2%).

Table 2 showed that most patients with chronic renal failure with DM had moderate degree of SNHL in the right ear, which was 33.3%. Similar results were also obtained in the right ear of CRF patients without DM, mostly moderate grade SNHL, which was 24.4%. The results of the statistical test of the contingency coefficient obtained the value of r = 0.277 and p = 0.290, which meant that there was no significant correlation between a history of DM and SNHL in the right ear, with close correlation in weak category.

Table 3. The correlation between diabetes mellitus and the degree of SNHL in the left ear of chronic renal failure patients

DM	Left ear				Total	r	p
	Mild	Moderate	Moderate-Severe	Severe			
Yes	7	11	8	2	28	0.130	0.857
	15.6%	24.4%	17.8%	4.4%	62.2%		
No	5	3	3	1	17		
	11.1%	17.8%	6.7%	2.2%	37.8%		
Total	12	19	11	3	45		
	26.7%	42.2%	24.4%	6.7%	100.0%		

Table 3 showed that most CRF patients with DM had moderate degree SNHL in the left ear, which was 24.4%. Similar results were also obtained in the left ear of CRF patients without DM, mostly moderate grade SNHL, which was 17.8%. The results of the statistical test of the contingency coefficient obtained values of r = 0.130 and p = 0.857, which meant that there was no significant correlation between a history of DM and SNHL in the left ear, with close correlation in weak category.

Table 4. The correlation between hypertension and the degree of SNHL in the right ear of chronic renal failure patients

HT	Right ear				Total	r	p
	Mild	Moderate	Moderate-severe	Severe			
Yes	4	8	6	0.	18	0.266	0.332
	8.9%	17.8%	13.3%	0%	40.0%		
No	3	18	5	1	27		
	6.7%	40.0%	11.1%	2.2%	60%		
Total	7	26	11	1	45		
	15.6%	57.8%	24.4%	2.2%	100.0%		

Table 4 showed that most CRF patients with hypertension had moderate degree of SNHL in the right ear, which was 17.8%. Similar results were also obtained in the right ear of CRF patients without hypertension, mostly moderate grade SNHL, which was 40.0%. The results of the statistical test of the contingency coefficient obtained values of r = 0.266 and p = 0.332, which meant that there was no significant correlation between hypertension and the degree of SNHL in the right ear, with close correlation in weak category.

Table 5. The correlation between hypertension and the degree of SNHL in the left ear of chronic renal failure patients

HT	Left ear				Total	r	p
	Mild	Moderate	Moderate-severe	Severe			
Yes	5	8	4	1	18	0.060	0.983
	11.1%	17.8%	8.9%	2.2%	40.0%		

No	7	11	7	2	27
	15.6%	24.4%	15.6%	4.4%	60%
Total	12	19	11	3	45
	26.7%	42.2%	24.4%	6.7%	100.0%

Table 5 showed that most CRF patients with hypertension had moderate degree of SNHL in the left ear, which was 17.8%. Similar results were also obtained in the left ear of CRF patients without hypertension, mostly moderate grade SNHL, which was 24.4%. The results of the statistical test of the contingency coefficient obtained values of r = 0.060 and p = 0.983, which meant that there was no significant correlation between hypertension and the degree of SNHL in the left ear, with close correlation in very weak category.

Table 6. The correlation between duration of hemodialysis and the degree of SNHL in the right ear in chronic renal failure patients

Duration of hemodialysis	Right ear				Total	r	p
	Mild	Moderate	Moderate-severe	Severe			
<6 months	0	0	0	0	0	0.498	0.001
	0.0%	0.0%	0.0%	0.0%	0.0%		
>6-12 months	4	4	0	0	0		
	8.9%	8.9%	.0%	.0%	17.8%		
>12-18 months	2	3	0	1	6		
	4.4%	6.7%	.0%	2.2%	13.3%		
>18-24 months	0	3	0	0	3		
	0.0%	6.7%	.0%	.0%	6.7%		
>24 months	1	16	11	0	28		
	2.2%	35.6%	24.4%	.0%	62.2%		
Total	7	26	11	1	45		
	15.6%	57.8%	24.4%	2.2%	100.0%		

Table 7. The correlation between duration of hemodialysis and the degree of SNHL in the left ear of chronic renal failure patients

Duration of hemodialysis	Left ear				Total	r	p
	Mild	Moderate	Moderate-Severe	Severe			
<6 month	0.0%	0.0%	0.0%	0.0%	0.0%	0.400	0.006
>6-12 month	5	3	0	0	8		
	11.1%	6.7%	.0%	.0%	17.8%		
>12-18 month	1	4	1	0	6		
	2.2%	8.9%	2.2%	.0%	13.3%		
>18-24 month	0	3	0	0	3		
	.0%	6.7%	.0%	.0%	6.7%		

>24 month	6	9	10	3	28
	13.3%	20.0%	22.2%	6.7%	62.2%
Total	12	19	11	3	45
	26.7%	42.2%	24.4%	6.7%	100.0%

Based on Table 6, it was known that the highest proportion of SNHL degrees in the right ear of CRF patients with hemodialysis duration of 6-12 months obtained mild and moderate degrees (8.9%), hemodialysis duration>12-18 months obtained moderate degrees of SNHL (6.7%). For >18-24 months in the right ear the degree of SNHL was moderate, which was 6.7%, and >24 months in the right ear was moderate grade SNHL (35.6%).

The results of the Spearman rank statistical test showed that the value of r = 0.498 and p = 0.001 which meant that there was a positive and significant correlation between the duration of CRF patients undergoing hemodialysis and the degree of SNHL in the right ear, with close correlation in moderate category.

Based on Table 7, it was known that the highest proportion of SNHL degrees in left ear of CRF patients with hemodialysis duration of 6-12 months obtained mild degrees (11.1%), while >12-18 months moderate degrees of SNHL (8.9%). For >18-24 months in the left ear, the degree of SNHL was moderate, which was 6.7%, and patients >24 months in the left ear had moderate to severe SNHL (22.2%). These results indicate that there was a tendency that the longer hemodialysis, the more severe the degree of SNHL.

Spearman rank statistic test results obtained values of r = 0.400 and p = 0.006 which meant that there was a positive and significant correlation between the duration of CRF patients undergoing hemodialysis and the degree of SNHL in the left ear with a close correlation in moderate category.

The multivariate analysis in this study was not carried out because the confounding variable in this study obtained a p value >0.25 , and multivariate requirement was a p value <0.25.

DISCUSSION

In this study, CKD patients who underwent hemodialysis were asked about their early medical histories. Tinnitus symptoms were often present, but many patients chose to disregard them. In accordance with a study by Jamaldeen et al.[8] early symptoms such as tinnitus which were sometimes ignored, need to be watched out in patients undergoing hemodialysis. If SNHL could be detected early, the progression of hearing loss to a more severe condition might be prevented.

The prevalence of CKD continues to increase. In some ways the high prevalence of this incidence is partly due to the aging process, meanwhile it is also associated with an increased incidence of hypertension and diabetes mellitus.[2] The results of our study showed that the majority of patients had a history of diabetes mellitus (62.2%) and a history of hypertension (40%).

According to several studies, vascular occlusion brought on by an embolism, hemorrhage, or vasospasm causes microcirculatory insufficiency that leads to age-related sensorineural hearing loss. This condition is also known as microangiopathy or hyperviscosity syndrome caused by diabetes or hypertension.[14] Although hypertension and diabetes mellitus are associated with hearing loss but there is no association with the degree of SNHL. Individuals with and without this

disease have the same frequency of mild hearing loss.[10,12]

There are similarities in the structure and function of glomerular basement membrane and the stria vascularis of the cochlea. CKD disease affects multiple organs. Complications of CKD could be caused by the disease itself or the effects of the medications used to treat it. The auditory system and many other organ tissues might be impacted by the buildup of uremic toxins and prolonged hemodialysis. The hearing loss is generally of a sensorineural type and had been diagnosed in many patients with long-term CKD, which worsened over time.

During embryogenesis, the inner ear and kidney show similar genetic regulation, and the genes responsible for genetic abnormalities when mutated play an important role in ear and kidney differentiation, although they are expressed in different phases of morphogenesis.[14] In addition, according to El-Anwar et al.[7], the cochlea and the kidney have similar physiological mechanisms in the form of an active transport of fluids and electrolytes carried out by the stria vascularis in the cochlea with the glomerulus in the kidney. Although the gross anatomy of the kidney and cochlea is distinctly different, there are similarities at the ultrastructural level. Both contain epithelial structures that are closely related to their vascular supply. The basement membrane is found in close proximity to the capillary endothelium both in Bowman's capsule and the proximal renal tubules of the kidney, as well as in the vicinity of the capillaries of the stria vascularis. The basement membrane lines the intercellular channels found in both the glomerulus and the stria vascularis. Furthermore, epithelial cells in both cochlea and kidney exhibit features associated with fluid and electrolyte transport, namely microvilli containing large numbers of mitochondria.

In the middle ear, the microcirculation is characterized by the presence of selective transport mechanisms to maintain a chemical gradient of ions between the blood, perilymph and endolymph. In particular, the capillary network within the stria vascularis consists of specialized vascular epithelium that is important for regulating endocochlear potential, ionic transport and endolymph. The major constituent in ionic homeostasis is potassium ion which is responsible for sensory transduction and maintenance of endocochlear potential. In the endolymph that fills the scala media of the cochlea, potassium ions are pushed toward the sensory hair cells where they trigger signals and then travel to the perilymph via the basolateral canals where a new potassium ion cycle will begin. Transport of potassium ions in the endolymph through the epithelium is an active process mediated by Na-K ATPase. This pump is expressed on the cell membrane in marginal cells of the stria vascularis as well as in secretory cells regulated by mineralocorticoid hormones.[14]

Injury to the stria vascularis of the inner ear with consequent loss of endocochlear potential is one possible after-effect of hypoxia in patients with cardiovascular disease. Inner ear disease may also be associated with altered vasomotor reactivity, often seen in patients with nephropathy. Indeed, the overactivity of the sympathetic nervous system, resulting from neurohormonal mechanisms in the failing kidney and the morphological similarities between the cochlear and renal microcirculation strongly support the idea that sensorineural hypoxia in chronic nephropathy is associated with vasomotor defects.[14]

In patients with CKD, the level of ICAM-1 (Intercellular Adhesion Molecule 1) and VCAM-1 (Vascular Cell Adhesion Molecule 1) are progressively increased before hemodialysis, during hemodialysis or after kidney transplantation. Another pathogenic consequence of endothelial dysfunction in both hearing loss and CKD

is impaired vasodilation. In the ear, altered availability of nitric oxide (NO) is often the result of endothelial NO synthetase (eNOS) polymorphisms. This genetic modification reduces eNOS activity, with low NO levels and increased blood viscosity that can induce microcirculatory injury. Elevated levels of asymmetrical dimethylarginine (ADMA), a competitive inhibitor of eNOS, and the presence of excess reactive oxygen species (ROS) reduce NO production and result in impaired endothelial vasodilation in CKD.[14]

According to Peyvandi et al.[6], SNHL had a significant prevalence in CKD patients. The degree of SNHL increased with the length of time the patient had had renal failure, but was not correlated with age or gender. The results of our study indicated that there was a significant correlation between the length of time patients undergoing hemodialysis and the degree of SNHL. The longer time underwent hemodialysis, the higher the degree of SNHL.

Meena et al.[11] showed that the incidence of sensorineural hearing impairment was higher in patients with chronic renal failure than in the healthy group. Sensorineural hearing in the high frequency range was symmetrical and bilateral and was associated with the total number of hemodialysis, the long duration of the patient suffering from kidney failure, hypertension and electrolyte imbalance, but was not associated with an increase in serum creatinine, blood urea and macroscopic kidney morphological changes.

The limitation of this study was the difficulty of getting chronic renal failure patients undergoing hemodialysis for a period of <6 months. In the sample, there were more patients who had undergone hemodialysis for more than 24 months. This was related to the type of hospital where the study was located, which was a type A hospital or tertiary reference which often received patients who had had hemodialysis from other health care facilities.

The group of patients who had undergone hemodialysis for more than 24 months reached 62.2% or more than half of the study population, so it should be limited to reduce research bias. Researchers put a limit on the length of patients on hemodialysis more than >24 months but under 5 years. The bias which might arise because there were more patients on hemodialysis more than 24 months was also a limitation of this study.

In addition, hearing loss could also be influenced by the speed sound of the machine (rotation) and the type of hemodialysis machine, so that it could become a bias in this study. Further research is needed to determine the effect of these factors on the incidence of SNHL.

Our study found that there was a positive and significant correlation between the duration of chronic kidney failure patients undergoing hemodialysis with the degree of sensorineural hearing loss.

REFERENCES

1. Ouda, L., Profant, O., and Syka, J. Age-related changes in the central auditory system. Cell Tissue Res. 2015; 1: 007-014.
2. Ulfa L, Muyassaroh, Naftali Z, Arwanto A, Murbani I. Pengaruh hemodialisis terhadap kejadian kurang pendengaran sensorineural pada penderita gagal ginjal kronik. MKB. 2016; 48:2.
3. Hill NR, Fatoba ST, Oke JL, et al. Global Prevalence of Chronic Kidney Disease – A Systematic Review and Meta-Analysis. PLoS ONE. 2016; 11 (7): e0158765
4. Wu RX, Chen CC, Wang CH, Chen HC. Intratympanic steroid injection for sudden sensorineural hearing loss in a patient on hemodialysis. Hemodialysis International. 2014; 18: 192-214Dsad
5. Wang IK,Wang CY, Muo CH et al. Risk of sudden sensorineural hearing loss in patients with end-stage renal disease undergoing dialysis. 2016; 22(5): 397-402

6. Peyvandi A, Roozbahany NA. Hearing Loss in Chronic Renal Failure Patient Undergoing Hemodialysis. Indian J Otolaryngol Head Neck Surg. 2013; 65(3): S537-S540

7. El-Anwar MW, Elsayed H, Khater A, Nada E. Audiological findings in children with chronic renal failure on regular hemodialysis. Egyptian Journ Otol. 2013; 29: 182-88.

8. Jamaldeen J, Basheer A, Sarma AC, Kandasamy R. Prevalence and patterns of hearing loss among chronic kidney disease patients undergoing hemodialysis. Australas Med J. 2015; 8(2): 41-6.

9. Muyassaroh,Ulfa L. Gangguan pendengaran sensorineural pada gagal ginjal kronis yang dilakukan hemodialisis. ORLI. 2013; 43: 2.

10. Vilayur E, Gopinath B, Harris DC. The association between reduced GFR and hearing loss: a cross-sectional population-based study. Am J Kidney Dis. 2010; 56: 661-9.

11. Meena RS, Aseri Y, Singh BK. Hearing loss in patients of chronic renal failure: a study of 100 cases. Indian J Otolaryngol Head Neck Surg. 2012; 64: 356-9

12. De Moraes Marchiori LL, de Almeida Rego Filho E, Matsuo T. Hypertension as a factor associated with hearing loss. Braz J Otorhinolaryngol. 2006; 72: 533-40.

13. Saeed HK, Al-Abbasi AM, Al-Maliki SK, Al-Asadi JN. Sensorineural hearing loss in patients with chronic renal failure on hemodialysis in Basrah, Iraq. Ci Ji Yi Xue Za Zhi. 2018 Oct-Dec; 30(4): 216-20.

14. Cuna V, Battaglino G, Capelli I, Sala E, Donati G, Cianciolo G, Manna GL. Hypoacusia and Chronic Renal Dysfunction: New Etiopathogenetic Prospective. Therapeutic Apheresis and Dialysis. 2015; 19(2): 111-18.