Research Article

Comparison of Hearing Abnormalities in Non-Diabetic and Diabetic End-Stage Renal Disease Patients Undergoing Hemodialysis

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Highlights

- More prevalence of hearing loss was observed in hemodialysis patients with diabetes
- No significant difference in hearing loss prevalence, mean thresholds between groups
- There was no significant effect of diabetes on hearing

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ABSTRACT

Background and Aim: Hearing loss is a highly prevalent symptom in patients with chronic kidney diseases (CKD). Comorbidities such as Diabetes Mellitus is known as the most common cause of CKD and a significant risk factor for sensorineural hearing loss (SNHL). The aim of this study was to compare SNHL among diabetic with non-diabetic hemodialysis patients.

Methods: In this study, 33 diabetic patients on hemodialysis were selected from Hami center, Arak, Iran. Non-diabetic subjects were 31 hemodialysis patients without diabetes were matched for age, duration of CKD and hemodialysis. Data were obtained via questionnaire, patients' files, physical examination, otoscopy and tympanometry. Hearing was analyzed using pure-tone audiometry for both groups.

Results: In the study, 66.2% of diabetic patients and 52.1% of non-diabetic subjects had SNHL. Results showed that diabetic patient has 1.3 times more likely to have hearing impairment. This difference was not statistically significant. Bilateral mild SNHL was the most prevalent in both groups. No significant difference was reported in SNHL prevalence, mean thresholds of hearing and ear laterality between the groups. Gender and age had a significant effect on hearing loss after adjusting covariables. No significant association was found between diabetes and hearing loss.

Conclusion: SNHL was more common in hemodialysis patients with diabetes. Patients with diabetes had poorer hearing thresholds compared to non-diabetic group, with no significant difference between groups. The periodical assessment of hearing and extending audiological care in this high-risk population is recommended due to long-term irreversible symptoms of the disease.

Keywords: Diabetes mellitus; hearing loss; end-stage renal disease

Introduction

In the current advanced world, Diabetes Mellitus (DM) tops the list of end-stage renal disease (ESRD) causes [1, 2]. Taking into account the cumulative effect of rapid growth of aging as well as increasing rate of life-style related disease such as hypertension, obesity and DM globally, prevalence, annoyance and consequences of ESRD will inevitably continue to rise in the near future [3, 4]. Multisystem diabetes-related complications would negatively impact the treatment of ESRD [5]. About 30% to 40% of diabetic patients are affected by Diabetic kidney disease which progresses to ESRD in one-third of cases [6, 7]. The pathological changes include hypertrophy, inflammation and renal fibrosis in endothelial, tubulointerstitial cells, podocytes, and mesangial cells [8, 9]. It is well known that diabetic nephropathy with type 2 DM and hypertensive nephropathy, are the leading causes of rising ESRD incidence in developed and developing countries, reflecting the catastrophic consequences of these two silent killers [10]. In addition, diabetic nephropathy has been found to be associated with hearing impairment in DM patients [1].

Hearing impairment has been established as a highly prevalent complication in patients with ESRD [11, 12]. It is strongly associated with physical, emotional symptoms and negatively impacts effective communication, quality of life leading to both medical and non-medical costs [13]. The etiology of hearing loss in patients with renal failure is multifactorial. Neurologic and microvascular alterations led to complications in auditory system including reduction in velocity conduction of auditory nerve, neuropathy and microangiopathy. Oxidative stress and hemodialysis are other risk factors for developing sensorineural hearing loss (SNHL) in chronic kidney disease (CKD) patients. Moreover, organ crosstalk between CKD and DM, hypertension have been found to increase developing SNHL in ESRD patients [12]. Some risk factors are shared by diabetes, chronic renal failure and hearing loss [14]. As SNHL is usually irreversible, its prevention is considered a major clinical and public health goal [15]. Review of literature addresses the complex relationship between DM and SNHL as well [14, 16]. The association of hearing loss with DM, however, is still controversial [8, 17, 18].

Considering high prevalence of hearing loss in ESRD patients and controversial effect of its comorbid DM as a chronic disease in the etiology of hearing impairment, this study was taken up to compare hearing in hemodialysis patients with and without DM. The second goal is to evaluate the association of other related variables and pure tone thresholds.

Methods

This cross-sectional study was conducted in 2019 among hemodialysis patients aged 20-60 years in the Hami hemodialysis center, Arak, Iran. All patients had ESRD according to the patient's diagnostic history. Inclusion criteria for diabetic group were hemodialysis patients with known DM as diagnosed by American Diabetes Association (ADA) criteria. Exclusion criteria were: otologic diseases, hearing loss from childhood, history of trauma or exposure to loud noise, previous ear surgery, kidney transplantation, use of ototoxic medication, psychiatric disorders, conductive hearing loss and temporary hemodialysis. All subjects underwent hemodialysis with a Bellco (formula plus model, Italy), three times per week for four hours per session. The demographic, clinical characteristics of all patients are summarized in Table 1.

Collecting data

After approval of the Research by the Ethics Committee, subjects willing to give written informed consent were included. Demographic characteristics included age, gender, occupation, education was extracted using a researcher-made questionnaire and patients' files. The criteria for DM were based on laboratory test results in their medical files, clinical findings and confirmation by a specialist. After physical examination by a specialist, otoscopy, and tympanometry were performed by an experienced audiologist to eliminate pathologies of the outer and middle ear, and essentially conductive hearing loss. Then, subjects were classified as diabetic and non-diabetic groups. Age, duration of CKD and hemodialysis duration were adjusted. All patients underwent pure tone audiometry (PTA) using the diagnostic audiometer (Itera II Madsen, GN Otometrics, USA). Pure tone audiometry thresholds via air conduction (AC) and bone conduction (BC) were determined in both ears at 250 to 8000 Hz and 250 to 4000 Hz, respectively. The average of 4 Bureau International D'Audiophonologie (BIAP) frequencies (0.5, 1, 2, 4 kHz) for each patient was calculated in each ear separately. Hearing thresholds ≥25 dB were considered as hearing impairment [2]. The mean thresholds of low frequencies (250 and 500 Hz), middle frequencies (1000 and -2000 Hz) and high frequencies (4000 and 8000Hz) were also calculated. Then, the prevalence, degree and laterality of hearing loss were determined in both patients' groups. Finally, we analyzed all patients (33 diabetic patients and 31 non-diabetic patients).

Statistical methods

SPSS version 17 was used for all statistical analyses. We used Independent t-test, chi-square and, Fisher's exact tests for analyzing data.

Significance level was considered>0.05. Generalized estimating equations (GEE) method was used to analyze the correlated data and to consider association of the two observations (two ears) for each individual. GEE logistics model was conducted for the dual auditory (normal and abnormal) as the dependent variable and the ear as the repetitive variable. First model was included gender, age, occupation, education, duration of dialysis, DM, ear. Then non-significant variables (occupation, education, duration of dialysis) exception DM and ear were eliminated. The final model was included gender, age, DM and ear.

Results

Demographic and clinical characteristics of diabetic and non-diabetic cases have been indicated in Table 1. The mean age of diabetic and non-diabetic groups±SD was 56.54±5.63 and 52.19±10.75 years respectively with no significant difference (p>0.05).

All diabetic subjects were affected by type 2 DM. After adjusting age, duration of CKD and hemodialysis, results showed higher prevalence of hearing loss (66.2%) in the diabetic group (63.6% in right ear (RE), 68.8% in left ear (LE)) than (52.1%) in non-diabetic ones (56.1%in RE, %48.1% in LE). It means that diabetic patients are more at risk of developing hearing loss, compared with non-diabetic subjects. But this difference was not statistically significant between groups in both ears using chi-square test (p=0.330 in RE vs. p=0.074 in LE).

We characterized hearing loss in hemodialysis patients in 3 groups according to frequency: low-, mid- and high-frequency range. According to Table 2, the mean of hearing thresholds in diabetic group were higher (poorer) at all frequency ranges than that in non-diabetic ones in both ears. Differences at high frequency were statistically significant in the right ear (p=0.033) and at low frequencies in the left ear according to independent t-test (p=0.034).

Out of 47 patients with hearing loss, 34 (72.3%) had bilateral loss (20 patients (58.8%) in the non-diabetic group vs. 14 cases (41.2%) in the diabetic group) with no statistically significant difference with regard to the laterality of ear involvement between the groups (p<0.05) (Table. 1).

The prevalence rate of mild hearing loss was prominent in diabetic patients (30.3% in RE vs. 36.4% in LE) followed by moderate degree (21.2% in RE vs. 30.3% in LE), with no statistically significant difference between groups in both ears (p>0.05). Although half of non-diabetic group had normal hearing, there was no significant association between hearing of both ears and DM according to Fisher's exact test (p=0.117 in RE and p=0.066 in LE) (Table 3).

Risk of affecting by abnormal hearing was much higher in females than males. This difference was statistically significant using chi-square test (p=0.014) (Table 1). Illiteral, Unemployed- housewives and retired cases had the highest prevalence rate of DM. Number of Unemployment, retired and housewives' cases was two times more in diabetic group than non-diabetic group but these differences were no statistically significant between groups using chi-square test (p>0.05).

According to the final GEE logistics model and adjusting variables, gender (p=0.016) and age (p=0.001) had a significant effect on hearing loss, but diabetes had no significant effect on hearing. (p=0.886). The odds of abnormal hearing in females was 3.7 higher compared with males. The odds of abnormal hearing for every one-year increase in age is 1.1 times larger. (Table 4).

In addition, three GEE linear models with hearing frequency ranges (low, mid and, high) as response were confirmed. The gender and DM had no significant effect on hearing at low- and high-frequency ranges (p>0.05). Gender had a significant impact on hearing at mid-frequency range (p=0.007). The average of hearing thresholds was 9.12 Hz higher at mid-frequency range in females than males. DM had no significant effect on hearing in the mid-frequency range (p>0.05).

Discussion

The relationship between DM, ESRD and SNHL is complex and not well understood yet [19]. In the present study, we found higher prevalence of SNHL among hemodialysis cases with diabetes (66.2%) compared with non-diabetic group. Previous studies reported prevalence of hearing loss in diabetic patients from 44.0% to 60.2% [8, 18] which is lower than that in our study (66.2%). Our findings are in line with Bainbridge et al. reported SNHL in 67% of cases than in 30% in controls [20]. The possible explanation for the divergent results

Table 1. Demographic and clinical characteristics of the study participants (n=64)

Variables		No. (%)		p
		Diabetic group (n=33)	Non-diabetic group (n=31)	
Gender	Male	17 (40.50)	25 (59.50)	0.014*
	Female	16 (72.70)	6 (27.30)	
Occupation	Unemployed-house-hold	15 (65.20)	8 (34.80)	0.080
	Retired	8 (61.50)	5 (38.50)	
	Employee	10 (35.70)	18 (64.30)	
Education	Illiterate	15 (53.60)	13 (46.40)	0.317
	under diploma	11 (43.20)	15 (56.80)	
	Diploma and higher	7 (70.00)	3 (30.00)	
Hearing loss	Yes	27 (57.40)	20 (42.60)	0.120
	No	6 (35.30)	11 (64.70)	
Age (years)		56.54±5.63	52.19±10.75	0.060
Mean hemodialysis duration (years)		3.13±3.24	3.96±4.06	0.310

Data are expressed as mean±SD or frequency.

* p<0.05

could be higher age of participants and multimorbidity in our study. Meta-analysis of 13 eligible studies between diabetic and non-diabetic cases by Horikawa et al. showed higher prevalence of hearing impairment in diabetic patients regardless of age [21]. Mozaffari et al. studied 160 patients (80 DM cases vs. 80 age and gender-matched controls) 45% of diabetic cases had SNHL. They concluded that DM is a risk factor of SNHL regardless of age and smoking [16]. A previous study found that SNHL was significantly higher in cases (74%) compared to controls (18%) [22]. The possible hypothesis for SNHL in diabetic subjects was attributed to microvascular disease of stria vascularis affecting hair cells in the cochlea [23].

According to our data, diabetic patients are approximately 1.07 times more likely to develop hearing loss

Table 2. Comparison of the mean hearing thresholds at different frequency ranges in diabetic and non-diabetic groups

Groups	Ear					
	Mean±SD					
	RE			LE		
	LF	MF	HF	LF	MF	HF
Diabetic group (n=33)	26.13±11.74	38.18±18.21	52.12±20.78	27.65±16.04	47.57±22.12	59.92±22.93
Non-diabetic group (n=31)	22.25±10.96	29.83±15.598	41.29±18.729	22.17±8.50	36.69±18.69	49.11±22.04
p	0.178	0.054	0.033*	0.034*	0.077	0.082

RE; right ear, LE; left ear, LF; low frequency (0.25 and 0.5 kHz), MF; middle frequency (1 and 2 kHz), HF; high frequency (4 and 8 kHz)

* p<0.05 as significant

Table 3. Hearing status for each ear in both group

Ear	Groups	Hearing degree					p*
		No. (%)					
		Normal	Mild	Moderate	Moderate–to-severe	Severe	
RE	DM	12 (36.40)	10 (30.30)	7 (21.20)	4 (12.10)	0 (0.00)	0.117
	Non-DM	15 (48.40)	12 (38.70)	3 (9.70)	0 (0.00)	1 (3.20)	
LE	DM	7 (21.20)	12 (36.40)	10 (30.30)	3 (9.10)	1 (3.00)	0.066
	Non-DM	13 (41.90)	13 (41.90)	2 (6.50)	3 (9.70)	0 (0.00)	

RE; right ear, DM; diabetes mellitus, LE; left ear

* Chi-square test

than the non-diabetic ones, although this difference was not significantly different (p=0.880). This finding was slightly lower than the odds ratio of 1.82 for low/mid-frequency hearing loss in Bainbridge et al. [20], and 1.41 in Helzner and Contreara study [24]. Comorbidities such as DM appeared to be associated with increased risk of getting SNHL in patients with CKD [25]. Previous studies reported increased odds of hearing loss in diabetics compared with non-diabetics [8, 26]. Demographic characteristics of participants and clinical profile might affect these different results.

The predominant rate of hearing loss severity was mild. Similar results were reported in Ren et. al. study [27]. Hearing impairment was most often bilateral similar to findings of Pillay et al. study [28].

Study revealed greater mean PTA thresholds at all frequency ranges in diabetic patients than those in non-diabetic ones. These observations are consistent with the report of higher thresholds in Bainbridge study. Hearing thresholds were most affected in the high frequency in right ear compared with low frequencies in the left ear. These findings are in accordance with DM-related hearing loss predominantly affects thresholds of higher frequencies [27, 29]. In contrast, Austin et al found low and mid-range frequencies were more likely to impaired [17]. This discrepancy may be due to difference in age and noise exposure level of population between studies. There are still controversies about what frequencies are the affected indeed. It is likely that high frequency is affected initially progressing to low frequency loss with long-term complications of exposure to hyperglycemia. Another explanation would be related to other comorbid conditions including cardiovascular disorders such as hypertension.

Table 4. Results of generalized estimating equations logistics model

Variable	Category	Estimated coefficient	SE	OR	95% Confidence interval for odds ratio		p
Sex	Female	1.31	0.54	3.70	1.27	10.73	0.016*
	Male	-	-	1.00			
DM	No	-0.06	0.43	0.93	0.40	2.20	0.886
	Yes	-	-	1.00			
Ear	Left	0.60	0.42	1.82	0.80	4.18	0.153
	Right	-	-	1.00			
Age		0.10	0.031	1.10	1.03	1.17	0.001*

SE; standard error, OR; odds ratio, DM; diabetes mellitus

* p<0.05 as significant

Findings indicated no association between DM and hearing impairment in hemodialysis patients. This is similar to findings reported by Shargorodsky et al. [30] and contrary to the findings of Kim et al. [8]. To our knowledge, no study has investigated the possible effect of DM -as a main comorbidity-on developing hearing loss in hemodialysis patients.

It was reported that organ interaction between CKD and type 2 DM could increase the possibility of developing SNHL in these patients [2]. So, patients with diabetic renal failure are more prone to experience SNHL resulting from combined contributions of cochlear microangiopathy, neuropathy, hyperglycemia of the cerebrospinal fluid or perilymph, contributing to auditory system damage [24]. Further, we explored the risk factors contributing to developing hearing impairment in hemodialysis patients with diabetes. Gender and age have been shown to affect predisposition of diabetic group to hearing loss, older female diabetics being more affected. On the contrary, findings of Mishra and Poorey indicated age as a significant predictor of hearing loss in diabetic patients but not gender [22].

We observed the highest prevalence rate of DM in illiterate, Unemployed-housewives and retired hemodialysis cases, but no association between education, occupations with risk of hearing loss was found. On contrary, a study found the relationship between lower education and higher risk of developing hearing loss [22]. Nearly identical life-style in hemodialysis patients and smaller sample size would be an explanation for this controversial result.

This study had potentialities and limitations. This is the first study evaluating hearing status in hemodialysis patients with DM. The main limitation of this study was limited sample size and hence another study with larger population is required for identifying the proper predictors of hearing loss. Secondly, there was lack of comparison for other systemic dysfunction including cardiovascular disorders such as hypertension.

Conclusion

This study indicated higher incidence of mild bilateral sensorineural hearing loss in hemodialysis patients with diabetes than non-diabetic ones. Patients with type 2 diabetes had poorer hearing thresholds compared to the non-diabetic group, but no significant difference was reported between groups. Gender and age had significant impacts on developing hearing loss. In addition, having chronic kidney disease combined with diabetes seems to increase the interaction of developing hearing impairment, periodic evaluation of the auditory system is proposed in such patients. Extending audiological care using otoacoustic emissions, high frequency audiometry and speech perception in noise is also recommended. to provide better health care and living conditions for these high-risk patients. Further studies with larger sample sizes are needed for proper evaluation and prediction of hearing dysfunction in this high-risk population.

Ethical Considerations

Compliance with ethical guidelines

This study was conducted in accordance with the ethical principles approved by the Research Council of Arak University of Medical Sciences (Code No: IR.ARAKMU.REC.1397.37).

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Authors' contributions

BK: Study design, acquisition of data, interpretation of the results; NS: Study concept, design, supervision; designed the study. AM: Statistical analysis of data, interpretation of the results; LP: Study concept supervision; MHB: Acquisition of data, all authors discussed the results and contributed to the final manuscript.

Conflict of interest

The authors declare that there are no conflicts of interest.

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