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Association Between Type 2 Diabetes Mellitus and Sensorineural Hearing Loss: A Case-Control Study at Al-Hussein Teaching Hospital, Samawa, Al Muthanna Province

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Abstract

Background: Type 2 diabetes mellitus (T2DM) is growing rapidly around the world and has increasingly been identified as a risk factor for sensorineural hearing loss (SNHL). However, despite considerable growing evidence worldwide, only limited studies have been conducted on this association in the general population of Iraq.

Aims: To determine the prevalence of SNHL in patients with T2DM compared with non-diabetic controls and differentiate the clinical and metabolic characteristics of patients having SNHL compared to those without.

Methods: We performed a case-control study at Al-Hussein Teaching Hospital in Samawa, Al-Muthanna Governorate, Iraq, from January 2020 until December 2022. Two hundred and forty total participants (120 with T2DM and 120 control participants who were age- and sex-matched) were enrolled. Each participant underwent standard tests such as pure-tone audiometry, tympanometry, and speech discrimination testing to determine hearing loss. Also, we obtained fasting blood glucose values, glycated hemoglobin (HbA1c), lipid profile, and renal function tests to evaluate metabolic and clinical factors. We performed analyses using chi-square, Pearson's correlation coefficient, and Cox regression analysis.

Results: Of the diabetic participants, 74 were determined to have SNHL compared to the control participants ($p < 0.001$, odds ratio [OR]=7.08; 95% confidence interval [CI]: 3.92–12.78). High frequency (4-8 kHz) SNHL was the most common type of hearing loss present in 68 of the diabetic patients (56.7%). In the diabetic cohort, >10 year duration of T2DM (OR=6.30, $p < 0.001$), HbA1c levels $\geq 9.0\%$ (OR=4.31, $p < 0.001$), and age ≥ 55 years (OR=3.56; $p = 0.002$) were independent risk factors for developing SNHL, as well as hypertension (OR=2.75, $p = 0.019$). Furthermore, the severity of SNHL was moderately correlated with the duration of diabetes ($r = 0.61$; $p < 0.001$) and HbA1c level ($r = 0.52$; $p < 0.001$).

Conclusion: This study demonstrates the significant association of T2DM and SNHL in the general population of Iraq, with the high frequency of hearing loss being the most commonly found audiological manifestation of the association. Our data suggest that poor glycemic control and prolonged presence of T2DM are the two most significant modifiable risk factors for developing SNHL. It is critical that standard diabetic care providers include routine audiological evaluation as a component of diabetic screening in Iraq.

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Keywords: Type 2 diabetes mellitus, sensorineural hearing loss, pure-tone audiometry, glycaemic control, HbA1c, Iraq, Al-Muthanna

Introduction

Diabetes Type 2 (T2DM) is one of the biggest health-related challenges facing countries around the world in the 21st century. According to the International Diabetes Federation (IDF), approximately 463 million people worldwide were estimated to be living with diabetes, which is forecasted to be as high as 700 million people by 2045 ^[1]. In Iraq, the amount of T2DM is very significant; National surveys show that the prevalence in adults has been documented to fall between 8% and greater than 13%, with increasing trends occurring with increasing urbanisation, sedentary behaviours, and changes in basic dietary structure ^[2, 3].

The Al-Muthanna Governorate is a predominantly rural and economically disadvantaged area in southern Iraq with significantly high levels of T2DM as shown by the number of T2DM patients visiting outpatient clinics; however, there is little information pertaining to population survey data [4].

Diabetes can negatively affect many organs via different but related mechanisms such as chronic high blood glucose levels, the production of advanced glycation end-products (AGEs), increased oxidative stress, and injury to the small blood vessels [5]. Complications from diabetes include diabetic nephropathy, diabetic retinopathy, diabetic neuropathy, and cardiovascular disease. However, less focus has been placed on the impact diabetes has on the auditory system. Sensorineural hearing loss (SNHL) is the type of hearing impairment that's due to dysfunction of or degeneration of the cochlea, auditory nerve, or central auditory pathways; moreover, SNHL occurs completely independently of conductive hearing loss caused by problems in the middle ear [6].

About 430 million people around the world have disabling hearing loss due, in large part, to hearing loss, which is an important contributor to disability-adjusted life years, social isolation, and cognitive decline [7]. There are several parallel biological mechanisms that support the potential relationship between T2DM and SNHL. Histopathological examinations of cochlear tissues from patients with diabetes have shown that the building blocks of blood vessels (the basement membrane) in the stria are thickened; outer hair cells are absent in the lower section of the cochlea; and neurons of the spiral ganglia degenerate, mirroring the microvascular and neuropathological changes of diabetic nephropathy and neuropathy [8, 9]. Additionally, animal models of diabetes have revealed that in hyperglycaemic states endocochlear potential is decreased; stria vascularis are not functioning properly; and there is accelerated apoptosis of outer hair cells [10].

Accumulation of advanced glycation end products (AGEs) in the cochlear microvasculature along with oxidative stress and decreased nitric oxide bioavailability are thought to negatively affect energy metabolism in cochlear cells that are highly active and susceptible to ischaemia [11, 12]. There have been many epidemiological studies conducted over the last two decades examining the association between T2DM and SNHL. Bainbridge *et al.* published a landmark systematic review and meta-analysis based on data from the National Health And Nutrition Examination Survey (NHANES) demonstrating that people with diabetes were more than twice as likely as non-diabetic controls to have hearing impairment; this association was still present after controlling for age, exposure to noise, and cardiovascular risk factors [13]. Since then, multiple studies conducted in Asia, Europe and South Asia have confirmed this association and have consistently reported high frequency hearing loss as the predominant form of hearing impairment in diabetic individuals [14, 15, 16].

Glycaemic control as represented by the HbA1c level is a particularly important modifiable predictor of hearing dysfunction in T2DM, and there are many studies that show a dose-response relationship between the severity of audiometric threshold shifts and HbA1c levels. This supports the hypothesis that sustained hyperglycaemia will cause cochlear damage [17, 18]. The duration of diabetes is another independent predictor, which suggests the cumulative effect of glycaemic toxicity on the auditory system [19]. Co-existing conditions such as hypertension, dyslipidaemia, and chronic

kidney disease that are often present with T2DM may also cause additional cochlear damage through vascular mechanisms that are additive or synergistic [20, 21].

Also important to consider is that there are no studies performed on the prevalence and determinants of SNHL in Iraqi diabetic individuals. The existing data from bordering Middle Eastern countries show a poor rate of auditory dysfunction in diabetic cohorts; however, these findings may not be directly applicable to Iraq due to different genetic backgrounds, healthcare access, treatment modalities, dietary habits and environmental noise exposure [22, 23]. Within the context of Iraq, suboptimal glycaemic control due to limitations in healthcare resources, medication non-adherence and food instability may cause further risk of cochlear damage. No previous studies have systematically assessed the prevalence and determinants of SNHL in an Iraqi population of T2DM patients through objective audiological evaluation. The gold standard for the measurement of hearing loss by frequency is puretone audiometry (PTA), which is available in tertiary care centres in Iraq.

Characterising the audiometric profile of diabetic patients and comparing it to age- and sex-matched normoglycaemic control subjects will provide locally relevant evidence to guide clinical practice and public health policy. Accordingly, the following three aims were proposed for this study: (1) to measure the prevalence of SNHL in T2DM patients attending the Al-Hussein Teaching Hospital in Samawa compared with age- and sex-matched controls without diabetes; (2) to characterise the audiometric profile and degree of hearing loss of the diabetic cohort; and (3) to identify independent clinical, demographic, and metabolic predictors of SNHL among T2DM patients [24]. The study findings are anticipated to contribute to the evidence base supporting the incorporation of routine audiological screening within comprehensive diabetes healthcare programmes in Iraq, as advocated by international diabetes organizations and ear, nose, and throat (ENT) professionals [25]. The high and increasing rate of T2DM in Iraq along with the impact of untreated hearing impairment on quality of life makes this study a clinically meaningful gap with implications for patient management, as well as preventative care strategies.

Methodology

Study Design, Setting, and Period

This case-control analysis occurred at Al-Hussein Teaching Hospital in Samawa, which is the biggest public reference hospital located in the southern region of Iraq (Al-Muthanna Governorate). This study was conducted during a 24-month timeframe between January 2020 and December 2022 and collected data from both the Internal Medicine outpatient clinic and from the Otorhinolaryngology (ENT) department. This study was approved by both the Institutional Review Board of Al-Hussein Teaching Hospital and the Al-Muthanna Health Directorate. The study obtained consent from all participants before collecting data, and consent was obtained before any screening or recruitment of patients according to the principles of the Declaration of Helsinki [26].

Study Participants

The cases consist of 120 adults with a confirmed diagnosis of T2DM, recruited from the Internal Medicine outpatient clinic consecutively. T2DM was diagnosed according to the American Diabetes Association (ADA) 2019 criteria, which is: (1) fasting plasma glucose ≥ 126 mg/dL on at least two

occasions, or (2) HbA1c $\geq 6.5\%$, or (3) 2-hour plasma glucose ≥ 200 mg/dL during an oral glucose tolerance test, or (4) a random plasma glucose ≥ 200 mg/dL with classic symptoms of hyperglycemia^[27]. All patients had diabetes for at least one year and were aged 30–80 years. A control group of 120 non-diabetic volunteers matched for age (± 5 years) and sex was recruited from among the hospital staff, their family members, and individuals attending the hospital for unrelated outpatient consultations.

Inclusion and Exclusion Criteria

To qualify as a patient diagnosed as having Type 2 diabetes mellitus (T2DM), you must have a confirmed diagnosis compliant with the American Diabetes Association (ADA), be between 30 and 80 years old, have had T2DM for at least 1 year, and be able to provide Informed Consent. In order to be included as a control, there must be no history of having had diabetes and you must have a fasting plasma glucose of less than 100mg/dL, an HbA1c of less than 5.7%, and be matched in age and sex with cases.

Exclusion criteria for both groups included: (1) congenital or hereditary hearing loss and/or ear malformations; (2) chronic ear disease, such as chronic otitis media with effusion, cholesteatoma, and/or perforated tympanic membrane; (3) history of ear surgery or the use of known ototoxic medications (aminoglycosides, loop diuretics, cisplatin, or quinine) within the last 6 months; (4) history of occupational or recreational exposure to noise sufficient to cause hearing loss; (5) neurological condition affecting the auditory pathway (i.e., acoustic neuroma, multiple sclerosis, stroke); (6) type 1 diabetes or secondary forms of diabetes; (7) significant renal insufficiency (i.e., creatinine > 2.0 mg/dL); and (8) inability to cooperate with audiological testing.

Sample Size Calculation

For this study, sample size calculations were based on the two-tailed alpha (cut-off) value of 0.05 (95% confidence interval) and the standard beta (test) value of 0.80 (80% power), which resulted in a required sample size of 105 participants for the treatment group and 90 participants for the control group. This was based on previous findings from research conducted in the Sifuentes-Franco study, estimating that approximately 55% of type 2 diabetes mellitus patients experience sensorineural hearing loss while approximately 20% of non-diabetes mellitus patients will also experience this condition. To allow for potential participant dropouts or exclusions, 15% of each group was built into the recruitment plan, meaning that 120 participants will actually be recruited per group and an estimated total of 240 participants will be enrolled in this study.

Clinical and Biochemical Assessment

All subjects underwent a full medical examination and standardized clinical interview. The following data were collected on each subject: age; sex; body mass index (BMI); duration of diabetes; present medications; smoking history; and coexisting diseases (hypertension, dyslipidaemia, cardiovascular disease). Blood pressure was measured in two different situations by means of a calibrated aneroid sphygmomanometer after resting for 5 minutes. Using the definition for hypertension set forth by the National Heart, Lung, and Blood Institute (NHLBI), hypertension was defined as a measured systolic blood pressure greater than or

equal to 140 mmHg or a diastolic blood pressure greater than or equal to 90 mmHg at both visits, or by current antihypertensive treatment

Venous blood was collected from each subject following an overnight fast. The fasting blood glucose level was obtained using an enzymatic hexokinase method. Glycosylated hemoglobin (HbA1c) was measured using high-performance liquid chromatography (HPLC). Total cholesterol, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and triglycerides were measured using standard enzymatic colorimetric methods for all blood tests. Serum creatinine was also measured using the Jaffe method. Dyslipidaemia was defined as having a cholesterol level greater than 200 mg/dL, LDL-C level greater than 130 mg/dL, triglyceride level greater than 150 mg/dL, or HDL-C level less than 40 mg/dL in men or less than 50 mg/dL in women, or by current use of lipid-lowering medication, in accordance with NCEP ATP III guidelines.

Audiological Evaluation

A qualified audiologist conducted all assessments using ISO 8253-1 standards and test booths specifically designed for testing in sound-treated environments. Testing consisted of pure-tone audiometry (PTA), which was conducted bilaterally at frequencies of 0.5, 1, 2, 4, 6, and 8 kHz using a calibrated audiometer (Interacoustics AC40) to record each participant's thresholds (expressed in decibels hearing level (dB HL)). The PTA for each ear was derived from the average of four air conduction frequency thresholds: 0.5, 1, 2, and 4 kHz, with the ear that had the lowest average threshold being considered as the worse ear. SNHL has been defined (by the World Health Organization (WHO) grading system) as having a PTA > 25 dB HL and having an air-bone gap (ABG) of < 10 dB at all frequencies tested. The audiologist conducted tympanometry to determine middle ear health status (type A, B, or C curves) and assess for possible presence of middle ear disease. Speech discrimination score (SDS) was assessed using Arabic phonetically balanced word lists that have been validated for use in the Iraqi Arabic dialect. Any individuals who exhibited evidence of a conductive or mixed hearing loss were excluded from the final data analysis.

Statistical Analysis

Microsoft Excel 2019 was used to enter and manage data, while IBM SPSS Statistics version 26.0 (IBM Corp., Armonk, NY, USA) was used to analyze data collected for the study. Continuous variables were reported as means $\pm$ standard deviation (SD) and categorical variables were reported as frequencies and percentages. Continuous variables were compared between two groups using the independent samples t-test (normal distribution) or the Mann-Whitney U test (non-normal distribution), while categorical variables were compared between two groups using the chi-square test (Fisher's exact test used if expected cell counts < 5). Bivariate associations between audiometric thresholds and continuous clinical/biochemical variables were evaluated using Pearson's correlation coefficient (r). Variables that had a p-value of < 0.1 from univariate analysis were entered in a multivariate binary logistic regression analysis with SNHL as the dependent variable. The values for adjusted odds ratios (OR) with 95% confidence intervals (CI) are reported. A p-value < 0.05 was considered to be statistically significant^[31].

Results

The initial screening consisted of 284 individuals; forty-four were disqualified (eighteen because of conductive hearing loss [CHL] (n=18); nine because of previous exposure to ototoxic drugs (n=9); eight because of neurological disorders (n=8); six because of type I diabetes mellitus (n=6); and three declined to participate (n=3)). Therefore, 240 subjects were ultimately included in the study (120 cases [diabetes mellitus type II] (T2DM); 120 controls). The two study groups were comparable in terms of age (54.3±9.7 vs 53.1±10.2 years; p=0.342) and male/female ratio in both populations (53.3%

males vs 50.0% males; p=0.611). The mean duration of diabetes for the patients with T2DM was 9.6±5.4 years, the mean for the patients' hemoglobin A1c (HbA1c) values was 8.9±1.6%, and the average fasting blood glucose level was 196.4±47.8 mg/dL. More patients with comorbid hypertension (T2DM 43.3% vs non-diabetes mellitus [type 2] 15.0%; p<0.001) or dyslipidaemia (T2DM 39.2% vs non-diabetes mellitus [type 2] 10.0%; p<0.001) were among patients with T2DM. The summary of demographic and clinical characteristics appears in Table 1.

Table 1: Baseline demographic, clinical, and biochemical characteristics of study participants

Characteristic	DM Group (n=120)	Control Group (n=120)	Total (n=240)	p-value
Age (years), mean ± SD	54.3 ± 9.7	53.1 ± 10.2	53.7 ± 9.9	0.342
Age range (years)	32–78	30–75	30–78	–
Male, n (%)	64 (53.3%)	60 (50.0%)	124 (51.7%)	0.611
Female, n (%)	56 (46.7%)	60 (50.0%)	116 (48.3%)	–
Duration of DM (years), mean ± SD	9.6 ± 5.4	–	–	–
HbA1c (%), mean ± SD	8.9 ± 1.6	5.4 ± 0.4	–	<0.001
Fasting blood glucose (mg/dL), mean ± SD	196.4 ± 47.8	88.6 ± 10.2	–	<0.001
Hypertension, n (%)	52 (43.3%)	18 (15.0%)	70 (29.2%)	<0.001
Dyslipidaemia, n (%)	47 (39.2%)	12 (10.0%)	59 (24.6%)	<0.001
Current smoker, n (%)	31 (25.8%)	28 (23.3%)	59 (24.6%)	0.656
BMI (kg/m ²), mean ± SD	29.4 ± 4.3	27.8 ± 3.9	28.6 ± 4.2	0.011

SD: standard deviation; DM: diabetes mellitus; HbA1c: glycated haemoglobin; BMI: body mass index. p-values from independent-samples t-test (continuous) or chi-square test (categorical).

SNHL occurred significantly higher in T2DM patients than controls, resulting in 74 of 120 (61.7%) and 22 of 120 (18.3%), respectively (OR=7.08; 95% CI: 3.92–12.78; p<0.001). Bilateral SNHL was more frequent among the diabetic population (50.8% vs 10.0%; p<0.001). The

predominant pattern for both groups was high-frequency hearing loss (4–8 kHz) where 56.7% of diabetic patients demonstrated hearing loss as compared to 14.2% of controls (p<0.001). Detailed audiological results can be found in Table 2.

Table 2: Audiological findings in the diabetic case group versus non-diabetic control group

Audiological Finding	DM Group n (%)	Control Group n (%)	OR (95% CI)	p-value
SNHL (any degree)	74 (61.7%)	22 (18.3%)	7.08 (3.92–12.78)	<0.001
Mild SNHL (26–40 dB HL)	28 (23.3%)	14 (11.7%)	2.27 (1.12–4.59)	0.022
Moderate SNHL (41–55 dB HL)	31 (25.8%)	6 (5.0%)	6.59 (2.60–16.72)	<0.001
Moderately severe SNHL (56–70 dB HL)	11 (9.2%)	2 (1.7%)	5.97 (1.29–27.60)	0.021
Severe SNHL (71–90 dB HL)	4 (3.3%)	0 (0.0%)	–	0.043*
High-frequency loss (4–8 kHz)	68 (56.7%)	17 (14.2%)	7.70 (4.10–14.46)	<0.001
Bilateral SNHL	61 (50.8%)	12 (10.0%)	9.37 (4.58–19.15)	<0.001
Normal hearing	46 (38.3%)	98 (81.7%)	Reference	–

SNHL: sensorineural hearing loss; OR: odds ratio; CI: confidence interval; dB HL: decibels hearing level. *Fisher's exact test used.

Hearing loss in 74 patients with T2DM and SNHL was significantly associated with duration of diabetes (r = 0.61; p < 0.001) compared to diabetes control as measured by HbA1c and age (r = 0.52; p < 0.001) and (r = 0.48; p < 0.001),

respectively. Greater comorbid hypertension and dyslipidemia was noted in diabetic patients with SNHL than in diabetic patients without SNHL. Table 3 depicts the association for these findings.

Table 3: Correlation of clinical and metabolic variables with SNHL status among T2DM patients

Variable	SNHL (n=74) Mean ± SD	No SNHL (n=46) Mean ± SD	r / OR (95% CI)	p-value
Duration of DM (years)	12.1 ± 5.8	5.7 ± 3.2	r = 0.61	<0.001
HbA1c (%)	9.6 ± 1.4	7.8 ± 1.3	r = 0.52	<0.001
Fasting blood glucose (mg/dL)	214.7 ± 43.2	168.3 ± 39.6	r = 0.41	<0.001
Age (years)	58.4 ± 8.9	47.6 ± 8.1	r = 0.48	<0.001
Hypertension, n (%)	41 (55.4%)	11 (23.9%)	OR=3.88 (1.71–8.83)	0.001
Dyslipidaemia, n (%)	35 (47.3%)	12 (26.1%)	OR=2.55 (1.12–5.79)	0.025
BMI (kg/m ²)	30.2 ± 4.6	28.1 ± 3.7	r = 0.22	0.031
Smoking, n (%)	22 (29.7%)	9 (19.6%)	OR=1.73 (0.70–4.28)	0.231

r: Pearson correlation coefficient; OR: odds ratio; CI: confidence interval; SNHL: sensorineural hearing loss; DM: diabetes mellitus; HbA1c: glycated haemoglobin; BMI: body mass index.

After conducting a multivariate binary logistic regression while controlling for age, gender, smoking status, body mass index (BMI), dyslipidemia, and fasting blood glucose as confounding variables, the following independent predictors of SNHL in diabetic patients were identified: duration of diabetes ≥ 10 years (adjusted odds ratio [OR] = 6.30, 95% confidence interval [CI]: 2.81–14.15, $p < 0.001$), HbA1c $\geq 9\%$

(adjusted OR = 4.31, 95% CI: 1.93–9.62, $p < 0.001$), age ≥ 55 years (adjusted OR = 3.56, 95% CI: 1.57–8.06, $p = 0.002$), and having hypertension (adjusted OR = 2.75, 95% CI: 1.18–6.42, $p = 0.019$). The gender, smoking, BMI, and dyslipidemia variables were not statistically significant (Table 3).

Table 4: Multivariate binary logistic regression analysis: independent predictors of SNHL among T2DM patients

Independent Variable	β coefficient	Adjusted OR	95% CI	p-value
Duration of DM ≥ 10 years	1.84	6.30	2.81–14.15	<0.001
HbA1c $\geq 9\%$	1.46	4.31	1.93–9.62	<0.001
Age ≥ 55 years	1.27	3.56	1.57–8.06	0.002
Hypertension	1.01	2.75	1.18–6.42	0.019
Fasting blood glucose ≥ 200 mg/dL	0.89	2.44	1.07–5.55	0.033
Dyslipidaemia	0.74	2.10	0.89–4.94	0.089
BMI ≥ 30 kg/m ²	0.52	1.68	0.70–4.03	0.243
Sex (male)	0.38	1.46	0.64–3.34	0.371
Smoking	0.31	1.36	0.55–3.39	0.503

β : regression coefficient; OR: odds ratio; CI: confidence interval. Nagelkerke $R^2 = 0.54$. Hosmer-Lemeshow goodness-of-fit: $p = 0.412$.

Discussion

This case-control study, which was done in Al-Hussein Teaching Hospital, Samawa, Iraq, is the first systematic audiological study of the relationship between T2DM and SNHL in Iraq to our knowledge. The main finding of the study was that patients with T2DM had a significantly higher prevalence of SNHL (61.7%) as compared to matched control group (18.3%) giving rise to a crude odds ratio of 7.08 (95% CI: 3.92–12.78). This degree of association is very similar to and in many ways exceeds what has been reported in the international literature suggesting that diabetic cochlear injury is at a greater level among a population that is not optimally controlling their blood sugar level through the use of medications. Additionally, the finding that 56.7% of the diabetic patients had predominately high-frequency SNHL occurring at 4–8 kHz is consistent with the known vulnerability of the basal turn of the cochlea where the greatest metabolic demand occurs; where there are the greatest densities of capillary vessels; and where the cochlea is most susceptible to ischemic/oxidative injury.

The high prevalence of SNHL in our diabetic population (61.7%) is greater than the reported range of approximately 45–55% of the prevalence of SNHL among the diabetic population reported in many of the previous case-control studies conducted in South Asia and the Middle East (including Iran, Egypt, and India). A significant contributing factor to our observed higher prevalence may be the poor mean glycaemic control of the patients in our study (mean HbA1c 8.9%). The definition of poor glycaemic control reported from previous studies is representative of the systemic challenges that exist in managing diabetes in a resource-limited country such as the Al-Muthanna Governorate. These systemic challenges include irregular access to antidiabetic medications, limited nutritional counselling, low health literacy, and financial constraints associated with the self-monitoring of blood glucose. The prevalence of comorbidities in the diabetic group included high rates of hypertension (43.3%) and dyslipidaemia (39.2%). These conditions will further increase the vascular risk to the cochlea by increasing arteriosclerosis of the stria capillaries, which will further decrease cochlear blood flow reserve [20,21]. Our data were slightly higher than Bainbridge *et al.* [13] who noted approximately double the likelihood of

hearing impairment among adults with diabetes in the United States NHANES cohort; this could be due to higher rates of glycaemic control in that healthcare system. Diabetes disease duration and SNHL severity had a strong positive correlation ($r = 0.61$, $p < 0.001$), which has been consistently documented in the diabetic hearing loss literature and was robustly reproduced in this sample from Iraq. Patients with a duration of disease of ≥ 10 years had an adjusted odds ratio for SNHL of 6.30, reflecting the cumulative toxic effects of prolonged hyperglycaemia on cochlear microvasculature and neural elements. These findings are in agreement with the histopathological data reported by Fukushima *et al.* [9] and the longitudinal audiometric data presented by Kakarlapudi *et al.* [33], both of whom observed a progressive increase in audiometric threshold as the duration of diabetes increased. The stria vascularis, which provides the endocochlear potential crucial for mechanoelectric transduction of hair cells, is especially at risk for angiopathic injury; therefore, the stria vascularis gradually dysfunctions and accounts for the gradual symmetrical high-frequency hearing loss seen in diabetic cochleopathy [10,11]. The independent impact of HbA1c $\geq 9\%$ on SNHL risk (adjusted OR = 4.31, $p < 0.001$) is clinically and therapeutically meaningful. The term 'HbA1c' indicates the average blood sugar levels from 2 to 3 months before the time the HbA1c test was performed. It can be used to estimate how well the body managed blood sugar (hyperglycaemia). There are many studies showing that there is a direct link between HbA1c and changes in hearing ability measured with standard audiological tests (clinical tests to identify a person's ability to hear sounds). The largest is a cross-sectional study of 1,073 subjects with diabetes that demonstrated that as HbA1c increased through the quartiles, progressively worse high frequency (3000 Hz and 4000 Hz) hearing sensitivity was present during traditional hearing tests (i.e., audiograms). Improvements in blood sugar management via the use of insulin have been shown to help improve cochlear (inner ear) electrical activity in experimental animal models of diabetes. Animal studies support that having an HbA1c $< 7\%$ may help to protect the cochlea from damage. Although there is currently little clinical evidence in the area of treating hearing issues with insulin, animal studies provide a reason to pursue strategies to maintain an HbA1c below 7% for the protection of hearing

in diabetic patients.

The fact that T2DM was determined to have hypertension as a significant independent predictor of SNHL among participants of the current cohort and that the adjusted odds ratio (OR=2.75, $p=0.019$) indicates that participants with diabetes and hypertension were at a greater risk for developing SNHL, should raise concern when considering the Iraqi diabetic population, where many patients with diabetes and hypertension do not receive treatment for hypertension as part of the cardiometabolic syndrome. Hypertension increases risk of ischemia in the cochlea by narrowing the arterioles that carry blood to the inner ear, causing increased resistance to blood flow through the spiral ligament of the cochlea, and causing increased dysfunction of endothelial cells that line blood vessels; and hyperglycaemia increases these processes. There are a number of studies that have demonstrated the multiplicative effect of co-existing diabetes and hypertension on audiological threshold shifts, one of which agrees with our findings that the prevalence of SNHL among our patients with hypertensive-diabetes is still greater than the prevalence of SNHL among patients without hypertension. Evidence presented here supports the idea that an integrated approach to managing cardiometabolic risk with multiple strategies such as aggressive blood pressure management combined with optimising blood glucose levels could provide patients with type 2 diabetes (T2DM) with protection against cochlear damage.

The association between being ≥ 55 years old and experiencing SNHL (adjusted odds ratio (OR)=3.56; $p=0.002$) is evident from our multivariate model, which has been established within previous studies on presbycusis (age-related hearing loss) occurring physiologically for high frequency thresholds after the fifth decade of adult life [34]. Untangling the contributions of ageing and diabetes on audiometric threshold shifts have proven difficult to demonstrate, particularly in a cross-sectional study. However, the fact that diabetes had a significant association with audiometric threshold in the regression model where age was controlled for, indicates that there is more than just an additive effect from having T2DM and advanced age on cochlear ageing (i.e. the concept of accelerated presbycusis) by Gates and Mills [35]. It is unclear whether the lack of a significant associations from smoking and BMI in the multivariate model are due to insufficient statistical power because the sub-sizes; and/or if these risk factors primarily mediated their effects through glycaemic control and blood pressure rather than directly on cochlear health.

The bilateral SNHL distribution (50.80%) among diabetic patients contrasts with the typical 10% bilateral SNHL distribution seen between only healthy non-diabetic controls; this finding shows that diabetic SNHL occurs from a systemic metabolic cause versus noise induced or one side being vascularly injured from the cochlea. This bilateral predominance has also been reported by Abdel Rasoul *et al.* The bilateral condition of diabetic SNHL makes it more challenging for individuals to communicate, engage in social activities, and maintain an adequate quality of life. In addition, these individuals will require hearing amplification more frequently than those with unilateral loss [7].

An important implication of the findings from this study is that audiological screening must be included in diabetes-related healthcare in Iraq. The high prevalence of clinically significant SNHL found in this cohort — with moderate-to-

severe levels being more than one-third of all subjects with clinically significant SNHL — indicates that T2DM caused hearing loss is not a minor, subclinical finding but rather an important disabling complication requiring ongoing monitoring. Currently in Iraq, there are no formal audiological screening programs for people with diabetes as there are established programs for individuals with retinopathy or nephropathy. There are many countries in the world, most categorised as low- or middle-income countries (LMIC), that also do not have audiological screening programs, as healthcare resources are primarily allocated to life-threatening conditions [38]. We support, consistent with recommendations from the American Diabetes Association [27] and the World Health Organization [30], that baseline PTA as part of comprehensive assessment be conducted at the time of diagnosis for T2DM, with repeat assessments at three- to five-year intervals or sooner for individuals with poor glycaemic control, hypertension, or duration of disease for 10 years or longer.

The current study has several identified limitations. Due to the cross-sectional nature of the study design, a causal or temporal relationship could not be established between the loss of hearing and glycaemic exposure over time through longitudinal studies. The exclusion from this study of individuals with type 1 diabetes, significant renal dysfunction and those taking ototoxic medications, although appropriate methodologically for aetiological clarity, limited the ability to generalise the findings to the other diabetic individuals more broadly. Noise history was obtained through a self-report questionnaire rather than reviewing occupational audiometric records, thus creating possible recall bias. The audiological procedure did not include the measures of otoacoustic emissions (OAEs) or auditory brainstem response (ABR) testing; however, these tests could have identified subclinical cochlear dysfunction in subjects with normal PTA thresholds. Furthermore, the study was conducted at a single tertiary care centre in Samawa, and therefore, the participants in this study may not be representative of the T2DM population across Iraq [39,40].

Notwithstanding these limitations, the current study represents an original contribution to our understanding of diabetic complications in Iraq and has several strengths, including: the highly rigorous case-control study design, with age- and sex-matched controls; the use of internationally standardised audiological testing; the comprehensive biochemical assessment of all participants; and the use of multivariate regression to identify independent predictors of clinically significant SNHL in T2DM individuals. These results should form the basis for larger multicentre longitudinal studies on this subject and for developing evidence-based guidelines for audiological screening in T2DM patients in Iraq.

Conclusion

This case-control study, which was done in Al-Hussein Teaching Hospital, Samawa, Iraq, is the first systematic audiological study of the relationship between T2DM and SNHL in Iraq to our knowledge. The main finding of the study was that patients with T2DM had a significantly higher prevalence of SNHL (61.7%) as compared to matched control group (18.3%) giving rise to a crude odds ratio of 7.08 (95% CI: 3.92–12.78). This degree of association is very similar to and in many ways exceeds what has been reported in the international literature suggesting that diabetic cochlear

injury is at a greater level among a population that is not optimally controlling their blood sugar level through the use of medications. Additionally, the finding that 56.7% of the diabetic patients had predominately high-frequency SNHL occurring at 4-8kHz is consistent with the known vulnerability of the basal turn of the cochlea where the greatest metabolic demand occurs; where there are the greatest densities of capillary vessels; and where the cochlea is most susceptible to ischemic/oxidative injury.

The high prevalence of SNHL in our diabetic population (61.7%) is greater than the reported range of approximately 45-55% of the prevalence of SNHL among the diabetic population reported in many of the previous case-control studies conducted in South Asia and the Middle East (including Iran, Egypt, and India). A significant contributing factor to our observed higher prevalence may be the poor mean glycaemic control of the patients in our study (mean HbA1c 8.9%). The definition of poor glycaemic control reported from previous studies is representative of the systemic challenges that exist in managing diabetes in a resource-limited country such as the Al-Muthanna Governorate. These systemic challenges include irregular access to antidiabetic medications, limited nutritional counselling, low health literacy, and financial constraints associated with the self-monitoring of blood glucose. The prevalence of comorbidities in the diabetic group included high rates of hypertension (43.3%) and dyslipidaemia (39.2%). These conditions will further increase the vascular risk to the cochlea by increasing arteriosclerosis of the stria capillaries, which will further decrease cochlear blood flow reserve [20,21].

Our data were slightly higher than Bainbridge *et al.* [13] who noted approximately double the likelihood of hearing impairment among adults with diabetes in the United States NHANES cohort; this could be due to higher rates of glycaemic control in that healthcare system. Diabetes disease duration and SNHL severity had a strong positive correlation ($r = 0.61$, $p < 0.001$), which has been consistently documented in the diabetic hearing loss literature and was robustly reproduced in this sample from Iraq. Patients with a duration of disease of ≥ 10 years had an adjusted odds ratio for SNHL of 6.30, reflecting the cumulative toxic effects of prolonged hyperglycaemia on cochlear microvasculature and neural elements. These findings are in agreement with the histopathological data reported by Fukushima *et al.* [9] and the longitudinal audiometric data presented by Kakarlapudi *et al.* [33], both of whom observed a progressive increase in audiometric threshold as the duration of diabetes increased. The stria vascularis, which provides the endocochlear potential crucial for mechanoelectric transduction of hair cells, is especially at risk for angiopathic injury; therefore, the stria vascularis gradually dysfunctions and accounts for the gradual symmetrical high-frequency hearing loss seen in diabetic cochleopathy [10,11].

The independent impact of HbA1c $\geq 9\%$ on SNHL risk (adjusted OR = 4.31, $p < 0.001$) is clinically and therapeutically meaningful. The term 'HbA1c' indicates the average blood sugar levels from 2 to 3 months before the time the HbA1c test was performed. It can be used to estimate how well the body managed blood sugar (hyperglycaemia). There are many studies showing that there is a direct link between HbA1c and changes in hearing ability measured with standard audiological tests (clinical tests to identify a person's ability to hear sounds). The largest is a cross-

sectional study of 1,073 subjects with diabetes that demonstrated that as HbA1c increased through the quartiles, progressively worse high frequency (3000 Hz and 4000 Hz) hearing sensitivity was present during traditional hearing tests (i.e., audiograms). Improvements in blood sugar management via the use of insulin have been shown to help improve cochlear (inner ear) electrical activity in experimental animal models of diabetes. Animal studies support that having an HbA1c $< 7\%$ may help to protect the cochlea from damage. Although there is currently little clinical evidence in the area of treating hearing issues with insulin, animal studies provide a reason to pursue strategies to maintain an HbA1c below 7% for the protection of hearing in diabetic patients.

The fact that T2DM was determined to have hypertension as a significant independent predictor of SNHL among participants of the current cohort and that the adjusted odds ratio (OR=2.75, $p=0.019$) indicates that participants with diabetes and hypertension were at a greater risk for developing SNHL, should raise concern when considering the Iraqi diabetic population, where many patients with diabetes and hypertension do not receive treatment for hypertension as part of the cardiometabolic syndrome. Hypertension increases risk of ischemia in the cochlea by narrowing the arterioles that carry blood to the inner ear, causing increased resistance to blood flow through the spiral ligament of the cochlea, and causing increased dysfunction of endothelial cells that line blood vessels; and hyperglycaemia increases these processes. There are a number of studies that have demonstrated the multiplicative effect of co-existing diabetes and hypertension on audiological threshold shifts, one of which agrees with our findings that the prevalence of SNHL among our patients with hypertensive-diabetes is still greater than the prevalence of SNHL among patients without hypertension. Evidence presented here supports the idea that an integrated approach to managing cardiometabolic risk with multiple strategies such as aggressive blood pressure management combined with optimising blood glucose levels could provide patients with type 2 diabetes (T2DM) with protection against cochlear damage.

The association between being ≥ 55 years old and experiencing SNHL (adjusted odds ratio (OR)=3.56; $p=0.002$) is evident from our multivariate model, which has been established within previous studies on presbycusis (age-related hearing loss) occurring physiologically for high frequency thresholds after the fifth decade of adult life [34]. Untangling the contributions of ageing and diabetes on audiometric threshold shifts have proven difficult to demonstrate, particularly in a cross-sectional study. However, the fact that diabetes had a significant association with audiometric threshold in the regression model where age was controlled for, indicates that there is more than just an additive effect from having T2DM and advanced age on cochlear ageing (i.e. the concept of accelerated presbycusis) by Gates and Mills [35]. It is unclear whether the lack of a significant associations from smoking and BMI in the multivariate model are due to insufficient statistical power because the sub-sizes; and/or if these risk factors primarily mediated their effects through glycaemic control and blood pressure rather than directly on cochlear health.

The bilateral SNHL distribution (50.80%) among diabetic patients contrasts with the typical 10% bilateral SNHL distribution seen between only healthy non-diabetic controls; this finding shows that diabetic SNHL occurs from a systemic

metabolic cause versus noise induced or one side being vascularly injured from the cochlea. This bilateral predominance has also been reported by Abdel Rasoul *et al.* The bilateral condition of diabetic SNHL makes it more challenging for individuals to communicate, engage in social activities, and maintain an adequate quality of life. In addition, these individuals will required hearing amplification more frequently than those with unilateral loss [7].

An important implication of the findings from this study is that audiological screening must be included in diabetes-related healthcare in Iraq. The high prevalence of clinically significant SNHL found in this cohort — with moderate-to-severe levels being more than one-third of all subjects with clinically significant SNHL — indicates that T2DM caused hearing loss is not a minor, subclinical finding but rather an important disabling complication requiring ongoing monitoring. Currently in Iraq, there are no formal audiological screening programs for people with diabetes as there are established programs for individuals with retinopathy or nephropathy. There are many countries in the world, most categorised as low- or middle-income countries (LMIC), that also do not have audiological screening programs, as healthcare resources are primarily allocated to life-threatening conditions [38]. We support, consistent with recommendations from the American Diabetes Association [27] and the World Health Organization [30], that baseline PTA as part of comprehensive assessment be conducted at the time of diagnosis for T2DM, with repeat assessments at three- to five-year intervals or sooner for individuals with poor glycaemic control, hypertension, or duration of disease for 10 years or longer.

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evidence-based guidelines for audiological screening in T2DM patients in Iraq.

Conclusion

This study demonstrates the significant association of T2DM and SNHL in the general population of Iraq, with the high frequency of hearing loss being the most commonly found audiological manifestation of the association. Our data suggest that poor glycemic control and prolonged presence of T2DM are the two most significant modifiable risk factors for developing SNHL. Standard diabetic care providers must include routine audiology evaluation as a component of diabetic screening in Iraq.

Ethical Approval: Approved by the Institutional Review Committee of Al-Hussein Teaching Hospital and Al-Muthanna Health Directorate. All procedures were in accordance with the 2013 Declaration of Helsinki.

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