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Hearing impairment in relation to vitamin D status in type 2 diabetic patients: A cross-sectional study

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ABSTRACT

Objectives: To evaluate the association of serum 25 hydroxy vitamin D (25OHD) and hearing impairment type 2 diabetes mellitus (T2DM) patients. In addition, we aimed to examine whether T2DM-associated hearing impairment is correlated with the severity of diabetes.

Methods: The present case-control study recruited adult patients with T2DM and healthy controls. Using pure-tone stimuli, we used an audiometer to assess the hearing thresholds of air conduction in each ear separately.

Results: 84 patients and 32 volunteers were included. The serum 25OHD was lower in T2DM patients than in healthy control (12.24±1.3 versus 23.19±5.69, respectively; p<0.001). The prevalence of vitamin D deficiency was 100% in the T2DM group, compared to 25% in the control group (p=0.001). T2DM patients exhibited higher hearing thresholds at all tested frequencies compared to the control group (p<0.001). Diabetic patients with hearing impairment had a significantly lower serum 25OHD than the normal hearing group (11.7±1.2 versus 12.6±1.2 ng/d; p=0.02). The multivariate analysis demonstrated that serum 25OHD level was an independent predictor of hearing loss among diabetic patients (β=-0.605; p=0.041).

Conclusions: The present study highlights the potential role of vitamin D deficiency in developing hearing impairment in the setting of T2DM. We found a negative correlation between serum 25OHD level and air conduction thresholds at low-mid and high frequencies amongst patients with T2DM.

Keywords: 25 hydroxy vitamin D (25OHD), cholesterol, triglyceride, hearing loss

INTRODUCTION

Diabetes mellitus (DM) is a major cause of global mortality and morbidity; up to 463 million adults worldwide suffer from DM worldwide, which is expected to reach 700 million adults in the next two decades [1, 2]. In addition, DM accounts for up to 1.6 million global deaths annually [3]. Type 2 DM (T2DM), the commonest type of diabetes, results from chronic hyperglycemia due to insulin resistance and β-cell dysfunction. It affects mainly adults over 45 years old [4, 5]. Patients with T2DM are at increased risk of a wide range of complications (broadly classified according to nature of affected vessels into micro and macrovascular groups), including cardiovascular diseases, diabetic neuropathy, retinopathy, chronic kidney disease (CKD), and cerebrovascular disorders [6, 7]. Also, risk factors such as prolonged and uncontrolled hyperglycemia, chronic hypertension, dyslipidemia, and obesity significantly increase risk of diabetes-related complications [8].

Previous observational studies have linked T2DM and hearing impairment, though the current data are controversial [9, 10]. Patients with T2DM exhibited a higher risk of hearing impairment and incidental hearing loss [9, 11-13]. Nonetheless, the exact pathogenic mechanism by which T2DM affects the vestibular and auditory systems has not been fully understood yet.

Previous reports showed a significant impairment in the conduction of vestibulocochlear nerve among T2DM patients with sensorineural hearing loss (SNHL) [13]. Microangiopathy and pathological changes in the cochlea were also implemented to develop hearing impairment among diabetes patients [14]. Notably, a subclinical hearing impairment was noted in patients with an early form of diabetes who did not develop microvascular complications [15].

On the other hand, vitamin D deficiency is prevalent in T2DM patients, especially in patients with prolonged, uncontrolled hyperglycemia [16, 17]. This high prevalence is thought to stem from the regulatory function of vitamin D in the insulin section. Previous animal studies demonstrated that pancreatic tissues carry a number of vitamin D receptors, which, in return, play a critical role in insulin synthesis and release [18, 19].

In addition, vitamin D is critical for innate immunity; hence, a vitamin D deficiency can precipitate infection and release inflammatory cytokines, potentially contributing to DM pathogenesis [20, 21]. On the other hand, vitamin D deficiency is a reported risk factor for cochlear impairment and SNHL, owing to the associated disruption in calcium metabolism [22].

Nevertheless, there is little data about vitamin D deficiency's role in developing hearing impairment in T2DM. Thus, we conducted the present study in order to examine the association of serum 25 hydroxy vitamin D (25OHD) and hearing impairment in the setting of T2DM. In addition, we aimed to examine whether T2DM-associated hearing impairment is correlated with the severity of diabetes.

MATERIAL AND METHODS

We confirm that the present study was obliged to the standards of the Declaration of Helsinki. In this cross-sectional study, adult patients (aged over 18 years old) with T2DM, as confirmed by the American Diabetes Association's criteria [23], were recruited from April to December 2019 at endocrinology and audio-vestibular units of Al-Zahraa University Hospital.

In addition, a control group was included that consisted of healthy volunteers. We excluded patients who refused to sign the written informed consents as well as patients with middle ear diseases, past history of otologic disease or ototoxic drug intake, ear/head trauma, occupational exposure to noise, systemic or neurological diseases, immunological diseases, metabolic bone diseases, cognitive function disability, and/or Meniere's disease or labyrinthitis. We also excluded patients who were on vitamin D replacement therapy or drugs that affect vitamin D metabolism.

Data Collection

Eligible patients underwent full history taking and clinical/otological examination. In addition, the following laboratory investigations were collected: complete lipid profile, fasting, and post-prandial blood glucose profile, glycated hemoglobin (HbA1c), renal functions, serum calcium and phosphorus levels, and serum 25-hydroxy vitamin D (25OHD). The serum 25OHD was measured using Chemiluminescence immunoassay (IDS Ltd., Boldon Colliery, Tyne & Wear, UK). The cut-offs for vitamin D insufficiency and deficiency were <30ng/dL and <20ng/dL, respectively.

Pure-tone audiometry

We used two channel diagnostic audiometer (Piano Plus). to assess the thresholds of air conduction and bone conduction in each ear separately by using pure-tone stimuli at frequencies of 250 Hz to 8,000 Hz for air conduction and 500 Hz to 4,000 Hz for the bone conduction threshold. The mean hearing threshold was calculated for all the tested frequencies and was used to obtain each ear's hearing loss degree.

The cut-off for hearing impairment was diagnosed when the mean of the hearing threshold was more than 25 dBHL. In addition, mild, moderate, moderately severe, severe, and profound hearing loss was defined if the mean hearing threshold is 26-40, 41-55, 56-70, 71-90, and more than 90 dBHL, respectively.

Table 1. Comparison of patients & control according to baseline data

Baseline data	Patients (n=84)	Control (n=32)	p-value
Age (years)	54.35±6.70	54.17±8.10	0.140
Male, No. (%)	26 (31.0%)	14 (43.8%)	0.400
Disease duration (year)	11.36±3.83	-	-
SBP (mmHg)	129.76±13.62	115.63±9.48	<0.001
DBP (mmHg)	83.33±7.81	76.25±7.07	0.003
BMI (Kg/m^2)	33.85±5.61	26.29±4.34	<0.001
WC (cm)	113.57±11.16	79.69±13.91	<0.001
FBS (mg/dL)	209.64±12.82	97.50±8.14	<0.001
PPBS (mg/dL)	275.71±15.93	112.06±13.10	<0.001
HbA1c (%)	9.61±1.76	5.14±0.32	<0.001
Creatinine (mg/dL)	0.91±0.023	0.68±0.012	<0.001
Calcium	9.06±0.57	9.47±0.42	0.013
Phosphorus	4.53±0.49	4.01±0.62	0.500
Albumin (g/dL)	4.14±0.36	4.19±0.35	0.600
Cholesterol (mg/dL)	191.79±16.88	157.81±26.51	<0.001
Triglyceride (mg/dL)	195.07±34.00	123.50±24.49	0.004
HDL	41.18±9.34	43.38±3.64	0.400
LDL	110.55±18.25	89.13±25.92	0.100
25OHD (ng/dL)	12.24±1.30	23.19±5.69	<0.001

Note. SBP: Systolic blood pressure; DBP: Diastolic blood pressure; BMI: Body mass index; FBS: Fasting blood sugar; HDL: High-density lipoprotein; & LDL: Low-density lipoprotein

Statistical Analysis

Data analysis was done using SPSS version 28.0 (SPSS Inc., Chicago, IL, USA). The quantitative mean, standard deviation (SD), and frequency (percentages) were used to describe the continuous and dichotomous data. Independent-sample t-tests were used to examine the comparison between the two groups. To test the hypotheses in categorical variables, the chi-squared test was used. Finally, the results of the linear regressions were shown using the coefficient values (β) and related p-values [24].

RESULTS

84 patients (54.1±6.73 years old; males=69%) and 32 controls (54±8.1 years; males=56.3%). The mean disease duration was 11.36±6.83 years. Compared between patients and control groups were non-significant differences regarding age and gender. In terms of clinical examination findings, T2DM patients had significantly higher body mass index and blood pressure.

Likewise, diabetic patients exhibited significantly higher serum creatinine, cholesterol, triglyceride, and LDL values. The serum 25OHD was lower in T2DM patients than in healthy control (12.24±1.3 versus 23.19±5.69, respectively). The prevalence of vitamin D deficiency was 100% in the T2DM group, compared to 25% in the control group (**Table 1**).

Regarding audiometer findings, the hearing thresholds of both ears were higher in T2DM patients at all tested frequencies (250, 500, 1,000, 2,000, 4,000, and 8,000 Hz) (**Table 2**).

26 (42.9%) diabetic patients had hearing impairment in at least one ear (**Figure 1**).

The degree of the hearing loss ranged from mild to severe, and moderate hearing loss was noted in 4.8% and 1.9% of the

Table 2. Comparison between diabetic patients with & without hearing loss according to air conduction (n=84)

Frequency (Hz)	Right ear			Left ear		
	Patients without hearing loss (n=52)	Patients with hearing loss (n=32)	p-value	Patients without hearing loss (n= 54)	Patients with hearing loss (n=30)	p-value
250	18.7±4.30	32.6±7.30	0.011*	18.0±5.50	33.0±4.80	0.009*
500	19.5±4.90	35.0±14.90	0.012*	18.7±4.10	33.0±13.60	0.006*
1,000	19.3±7.02	37.0±15.40	0.007*	19.4±3.20	32.0±11.20	0.011*
2,000	19.6±5.40	37.0±11.66	0.015*	19.1±5.40	35.3±14.30	0.002*
4,000	21.1±60	46.0±12.70	0.001*	20.4±5.70	46.7±15.70	0.000*
8,000	22.8±9.70	54.0±15.90	0.000*	22.2±8.20	52.0±21.40	0.000*

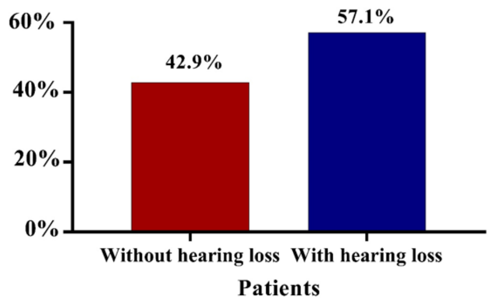

Figure 1. Distribution of hearing loss among T2DM patients (Source: Authors' own elaboration)

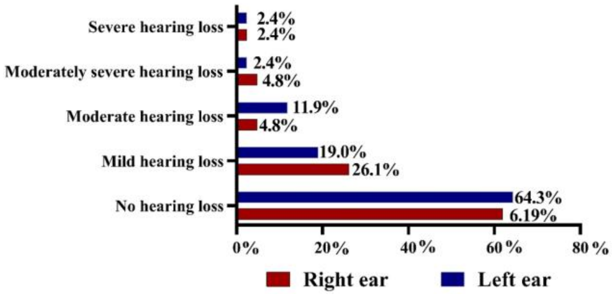

Figure 2. Degree of hearing loss in right & left ear among T2DM patients (Source: Authors' own elaboration)

patients in the right and left ears, respectively (**Figure 2**). Patients with hearing loss were more likely to be males and older than patients without hearing impairment.

On the other hand, the HbA1c level was comparable between (9.5±1.7 versus 9.8±1.8, respectively). Likewise, other laboratory parameters were comparable between patients with and without hearing impairment.

Diabetic patients with hearing impairment had a significantly lower level of serum 25OHD than patients with no hearing impairment (11.7±1.2 versus 12.6±1.2 ng/dL, respectively (**Table 3**).

Although, apart from the hearing loss, there were some additional otologic symptoms in the T2DM group, like tinnitus, vertigo, and headache, as demonstrated in (**Figure 3**), the symptoms were equally distributed between T2DM patients with or without hearing loss.

The multivariate analysis demonstrated that serum 25OHD level was an independent predictor of hearing loss among diabetic patients (β=-0.605; p=0.041; **Table 4**).

Table 3. Comparison of general, clinical, & laboratory baseline data between diabetic patients with & without hearing loss

Baseline data	Patients without HL (n=48)	Patients with HL (n=36)	p-value
Sex (n [%])			0.02*
Male	8 (16.7%)	18 (50.0%)	
Female	40 (83.3%)	18 (50.0%)	
Age (years)	51.0±5.9	58.0±5.9	<0.001*
Disease duration (years)	11.1±4.8	11.6±3.1	0.20
SBP (mmHg)	127.0±12.3	133.0±15.0	0.40
DBP (mmHg)	82.0±6.5	85.0±9.2	0.20
HTN (n [%])			0.20
Yes	4 (8.3%)	8 (22.2%)	
No	44 (91.7%)	28 (77.8%)	
BMI (Kg/m^2)	34.0±5.4	32.5±5.9	0.80
WC (cm)	112.3±10.2	115.2±12.2	0.20
FBS (mg/dL)	201.0±64.5	220.0±61.1	0.70
PPBS (mg/dL)	266.0±81.0	288.0±70.0	0.80
HbA1c (%)	9.5±1.7	9.8±1.8	0.10
Creatinine (mg/dL)	0.9±0.07	1.0±0.06	0.90
Calcium	9.0±0.6	9.1±0.6	0.30
Phosphorus	4.6±0.5	26.4±7.5	0.20
Albumin (g/dL)	4.1±0.4	4.1±0.3	0.70
Cholesterol (mg/dL)	190.0±50.31	193.0±44.1	0.60
Triglyceride (mg/dL)	186.0±98.6	206.0±90.41	0.40
HDL	40.8±8.6	41.7±10.5	0.30
LDL	115.0±46.35	105.0±31.14	0.40
25OHD (ng/dL)	12.6±1.2	11.7±1.2	0.02*

Note. SBP: Systolic blood pressure; DBP: Diastolic blood pressure; BMI: Body mass index; FBS: Fasting blood sugar; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; & HL: hearing loss

DISCUSSION

The role of vitamin D in the pathogenesis of T2DM and hearing impairment appears; nonetheless, the published literature is scarce regarding whether vitamin D deficiency exaggerates hearing impairment in diabetic patients [25]. Our results demonstrated that patients with T2DM are at higher risk of vitamin D deficiency and hearing impairment than the general population. In T2DM, serum 25OHD level correlated negatively with right and left hearing thresholds at low-mid and high frequencies. Moreover, patients with hearing loss had a significantly lower level of serum 25OHD than patients with normal hearing.

Vitamin D is a key player in the process of physiological hearing through its regulation of calcium metabolism within the vestibule, mineralization of the otic capsule, and its role in maintaining the normal histology of neurosensory epithelium [22]. Thus, deficient levels of vitamin D can precipitate the development of cochlear impairment and hearing loss [26]. Previous reports demonstrated that vitamin D deficiency and genetic alterations in VDRs were correlated significantly with impaired ear development, incidental cochlear hearing loss, SNHL, otosclerosis, and vestibular disorders [27, 28].

Thus, it is logical to consider vitamin D deficiency as a critical contributor to hearing impairment in T2DM patients,

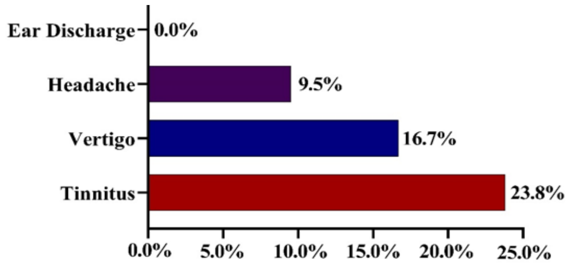

Figure 3. Distribution of ENT symptoms loss among T2DM patients (these symptoms were equally distributed in those with & without hearing loss) (Source: Authors' own elaboration)

given the high prevalence of vitamin D deficiency in the setting of diabetes.

Such theory is supported by the findings of our study in which we found a significant correlation between serum 25OHD level and degree of impairment in T2DM patients; patients with hearing impairment exhibited a lower level of serum 25OHD than patients with normal audiometer findings. Our findings are in line with the results in [29, 30] that conducted in T2DM; in both reports, the degree of hearing impairment was positively correlated with lower levels of vitamin D. Other reports demonstrated similar findings [30].

As mentioned before, vitamin D deficiency is prevalent in diabetic patients [16]. Various theories have tried to explain the association between vitamin D deficiency and diabetes. Vitamin D participates in the process of insulin secretion and sensitivity and maintains normal innate immunity response. Dysregulation in both factors is a known contributor to the pathogenesis of diabetes [31]. Notably, our analysis demonstrated that all diabetic patients had vitamin D deficiency. This prevalence was in line with previous reports from Saudi Arabia, the United Arab Emirates, and Kuwait, which showed a prevalence rate of 98%, 83%, and 80%, respectively [32, 33]. However, such prevalence is notably higher than other reports from Asia and North America [34, 35]. These differences may be attributed to ethnic variability.

On the other hand, patients with T2DM exhibited a higher risk of hearing impairment and incidental hearing loss [11-13]. The present study found that almost one-third of the patients had a moderate-to-severe hearing impairment. Our findings align with a large-scale survey study that demonstrated a hearing impairment prevalence of 48% among diabetic patients [36]. Other studies reported similar findings [37, 38].

The present study is one of the first few studies addressing vitamin D's role in T2DM-associated hearing loss. Nonetheless, a number of limitations exist. The sample size of the present study was not pre-planned, and our findings' statistical power is unclear. The sample was from a single center, and the sampling technique was based on non-probability consecutive sampling methods, which may affect the generalizability of our findings. Another limitation is the lack of data about the chronicity of vitamin D deficiency and history of vitamin D supplementation among the included patients. Owing to the cross-sectional nature of the present study, it was difficult to establish a definite temporal dimension of the association between vitamin D deficiency and hearing loss. The lack of long-term data did not allow us to correlate between serum 25OHD and long-term sequels of diabetes.

Table 4. Multivariate stepwise logistic regression analysis for predictors of hearing loss among T2DM patients (n=84)

Variables	B	Wald	p-value
Vertigo	-0.535	0.254	0.615
Headache	1.430	0.123	0.725
Tinnitus	0.709	0.735	0.391
Low Vit D	-0.605	4.169	0.041*
HbA1c	0.130	0.419	0.518

CONCLUSIONS

The current investigation emphasizes the possible contribution of vitamin D insufficiency to the developing hearing impairment in T2DM. The research findings showed a negative connection between serum 25OHD levels and low-mid and high-frequency hearing thresholds. Additionally, it was shown that diabetic individuals with hearing loss also had low blood levels of 25OHD. Therefore, when vitamin D deficiency is present in T2DM patients, endocrinologists and audiologists should be concerned, and a thorough audiological evaluation is required. But bigger sample size investigations should be conducted in order to corroborate our results.

Author contributions: All authors have sufficiently contributed to the study and agreed with the results and conclusions.

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Ethical statement: Authors stated that the study was approved by the Ethics Committee of the Faculty of Medicine for Girls, Al-Azhar University Cairo, Egypt, with reference No RHDIRB202001092. All participants signed collection informed consent.

Declaration of interest: No conflict of interest is declared by authors.

Data sharing statement: Data supporting the findings and conclusions are available upon request from the corresponding author.

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