

Case Studies

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Do neuropathy and hypertension associated with increased risk of hearing loss among type 2 diabetic patients?

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Abstract

Aim: The aim of this study was to investigate the relation between neuropathy and hearing loss among type 2 diabetes mellitus (T2DM) patients.

Methods: Cross sectional study carried on subjects aged between 20 and 60 years who visited the Ear Nose Throat (ENT), diabetic metabolic syndrome, and Endocrinology outpatient clinics registry of the Medipol International School of Medicine, Medipol Hospital during the study period from February 2015 to May 2017. Of the total 850 diabetic patients approached, 610 (71.9%), gave their consent. During the study period, prevalence, hearing, audiological test, family history and medical problems associated with hearing impairment in middle aged patients were recorded. Two audiometers Grason Stadler GSI 61 and Interacoustics AC40 Clinical audiometer were used to evaluate the hearing loss.

Results: The mean age (\pm SD, in years) for neuropathy with hearing loss versus normal subjects was 47.7 ± 10.2 vs. 48.5 ± 9.1 . The associated risk factors were significantly higher in T2DM with hearing loss, hypertension, (32.6% vs 15.7%), tinnitus (40.0% vs 18.0%), vertigo (59.7% vs 26.8%) and headache (54.9% vs 45.3%), than in normal hearing diabetes. There were statistically significant differences between hearing impairment versus normal hearing for vitamin D [18.09 ± 7.65 ng/ml vs 22.85 ± 9.00 ng/ml; $p < 0.001$], calcium ($p < 0.001$), magnesium ($p < 0.001$), phosphorous ($p < 0.001$), creatinine ($p = 0.007$), cholesterol [$p < 0.001$], HDL ($p < 0.001$), LDL ($p < 0.001$), albumin ($p = 0.010$), systolic blood pressure [129.75 ± 10.60 Hg vs 126.73 ± 12.39 Hg; $p = 0.017$] and, diastolic blood pressure [81.09 ± 9.2 mm Hg vs 79.29 ± 7.95 mm Hg; $p = 0.012$] and microalbuminuria ($p = 0.001$). Multivariable logistic regression analysis revealed that variables for predictors of hearing loss with neuropathy among diabetic patients were vertigo ($p < 0.001$), numbness ($p < 0.001$), hypertension ($p < 0.001$), duration of DM ($p < 0.001$), head ache ($p < 0.001$), Vitamin D deficiency ($p < 0.001$), sleeping disturbance ($p = 0.012$), BMI ($p = 0.033$), and cigarette smokers considered at higher risk as a predictors of neuropathy with hearing loss among diabetic patients.

Conclusion: The current study results suggests a strong positive association between neuropathy and hearing impairment among T2DM. The study confirms that the Hypertensive and diabetic patients have moderately increased risk of future hearing loss.

Key Words: premature; newborn with asphyxia; neonatal hypoxia; perinatal anoxia; (fetal distress), absence of oxygen at birth.

Introduction

Type 2 diabetes mellitus (T2DM), one of the main threats to ageing population health in the 21st century, is described as a worldwide epidemic as it affects the health and economy of almost all countries regardless of socioeconomic status or geographic location [1]. It is based on high blood glucose, insulin resistance and relative insulin deficiency. T2DM leads to an increase in the risk of future cardiovascular disease [2-4] and is the primary reason of mortality and morbidity in most high-income and developing countries [3-5]. Lifestyle factors, sleep duration, physical activity, regular exercise and healthy-balanced diet are essential components in prevention of pre-diabetes [4-5].

Hearing loss and its complications reveal commonly in type 2 diabetes mellitus (T2DM) [6-8]. A number of studies have attempted to identify the source of hearing loss in those with DM [9-14]. Several studies investigated that T2DM leads to side effects of hyperglycemia which may be retinopathy, neuropathy, nephropathy, vascular diseases. The several studies reported that hearing impairments can affect even the simplest tasks of daily life [4,9,17]. The relation between hearing loss and T2DM among middle aged population and patients are documented and reported in detailed [11-17]. The aim of this study was to investigate the relation between neuropathy and hearing loss among type 2 diabetes mellitus (T2DM) patients.

Subjects and Methods

Cross sectional study carried on subjects aged between 20 and 60 years who visited the Ear Nose Throat (ENT), diabetic metabolic syndrome, and Endocrinology outpatient clinics registry of the Medipol International School of Medicine, Medipol Hospital during the study period from February 2015 to May 2017. IRB ethical approval for this study was obtained from the Medipol International School of Medicine, Istanbul Medipol University, and informed written consent was obtained from patients before the start of the study.

The current sample size was determined by considering prevalence rate of 10%-12% impaired hearing loss among diabetes patients in Istanbul [1,7] assuming 99% confidence interval and 2% bound on the error of estimation. The minimum sample size detected as 850 subjects. Finally, of the 850 registered with diagnosed diabetes and showed indications, only 610 (71.7%). agreed to participate this study at the Medipol International School of Medicine, Istanbul Medipol University.

Laboratory measurements

The patients were considered to have DM if they have a history of DM and are currently taking oral medications for diabetes. The World Health Organization (WHO) [2] and International Diabetes Federation (IDF) [3] Bener et al. [4-5] defined DM when fasting venous blood glucose concentration is equal or higher than 7.0 mmol/L and/or for a 2 hour post-glucose tolerance test (GTT) venous blood glucose concentration is higher than 11.1 mmol/L. A glucose meter used to measure fasting blood glucose of all patients. Oral glucose tolerance test (OGTT) was carried out only if blood sugar was less than 7 mmol/l. The inclusion criteria comprised of diagnosis of T2DM in conformity with international standards by WHO and IDF [2-3], fasting plasma glucose (FPG) higher than 7.0 mmol/L and/or 2 hours postprandial plasma glucose (PPG) or ran-

dom plasma glucose higher than 11.1 mmol/L (5). Furthermore, having regular anti-diabetic drug treatment for at least 3 year, aged between 20 and 60 years, residence in a city of Istanbul for more than 3 years-period.

Questionnaire

The questionnaire, included socio-demographic, age, gender, nationality, education level, lifestyle habits, BMI, co-morbid symptoms, diabetic complications, systolic and diastolic blood pressures, Clinical biochemistry serum triglyceride, total cholesterol, high-density lipoprotein (HDL) cholesterol, low density lipoprotein (LDL) cholesterol, Hemoglobin A1c (HbA1c) and fasting glucose levels (FPG) were collected.

Physical examination and measurements

BMI was calculated as; weight in kilogram divided by the square of height in meters. According to WHO criteria [15], if it is greater than 25 kg/m², the subjects were assumed as overweight and greater than to 30 kg/m², the subjects were considered as obese [4-5]. WHO [15] International Society of Hypertension Writing Group defined standardized criteria of hypertension when Systolic Blood Pressure (SBP) \geq 140 mmHg or Diastolic Blood Pressure (DBP) \geq 90 mmHg or using anti-hypertensive medication. Patients who walking or cycling for more than 30 minutes/day were classified as physically active.

Hearing assessment method:

Pure-tone audiometry is a behavioral test used to measure hearing sensitivity. This measure involves the peripheral and central auditory systems [5, 16]. Two clinical digital audiometers (Garson Stadler GSI 61 and Interacoustics AC40 Clinical audiometer) are used to be a device for diagnosing hearing loss that are regularly calibrated to international standards were perform by pre-trained technicians to test patients' hearing level. Hearing loss evaluation described as follows [5,16]: normal (\leq 26 dB) and 26 dB above, hearing loss.

Nerve conduction studies

Motor nerve conduction, F response, and sensory nerve conduction studies are important methods of documentation and follow up of nerve functions in Diabetic neuropathy (DN) [17]. Motor nerve conduction studies are affected in a small subset of DN (large fibre neuropathies). Even in large diameter fibre neuropathy nerve conduction velocity (NCV) is insensitive for many pathological changes known to be associated with DN. The nerve conduction changes are non specific and key to the diagnosis lies in excluding other causes or those superimposed on DN. Entrapment neuropathies are common in diabetic patients and result in unilateral NCV changes, especially across the entrapped segment of the nerve. The commonest abnormality in diabetes is reduction in the amplitude of motor or sensory action potentials because of axonopathy. Pronounced slowing of NCV suggests demyelinating neuropathy, which is rarely associated with diabetes; therefore pronounced slowing of NCV in a diabetic patients should prompt investigations for an alternative diagnosis. However, the likelihood of chronic inflammatory demyelinating neuropathy (CIDP) occurring in diabetic patients is 11 times higher than the normal population [17]. The NCV is gradually diminished in DN, with esti-

mates of a loss of about 0.5 m/s/y [18].

The statistical analysis was performed by using the Statistical Package for Social Sciences [SPSS]. Student's t test was used to ascertain the significance of differences between mean values of two continuous variables and non-parametric Mann-Whitney tests were used to determine if the results differed, indicating lack of normal distribution of the variable. Chi-square test Fisher's exact test (two-tailed) were performed to test for differences in proportions of categorical variables between two or more groups. A multivariate logistic regression model was performed to evaluate the relation between selected lifestyle factors, neuropathy, and presence of hearing loss. Confounders were assessed statistically through change in beta coefficient (crude β -adjusted β), and if the change was more than 10%, the variable was considered as a confounder and retained in the final model. Model fit was assessed through the Hosmer-Lemeshow goodness of fit test. An insignificant p value for Hosmer-Lemeshow indicated that model was good

fit. The cut-off value for significance was chosen as 0.05.

Results

Table 1 shows the socio-demographic characteristics of subjects with hearing impairment and subjects with normal hearing. Majority of the hearing loss observed at the age above 45 years old. Over 90% of the studied patients were frequent users of mobile phones and approximately 88% of subjects with hearing loss were watching TV. The mean duration of diabetes was 9.54 ± 5.31 years, duration of sleep was 5.88 ± 1.25 Hours, 27.8% had positive family history of diabetes. Subjects with hearing impairment had worst risk factor profile than T2DM patients with normal hearing: hypertension, (32.6% vs 15.7%), tinnitus (40.0% vs 18.0%), vertigo (59.7% vs 26.8%) and headache (54.9% vs 45.3%), than in normal hearing diabetes. There was a statistically significant differences between hearing impairment and normal hearing among T2DM regarding smoking ($p=0.047$) and sleeping disturbances ($p<0.001$).

Table 1: Comparison of socio-demographic and clinical characteristics between diabetic neuropathy patients with and without hearing loss (N=610)

	Neuropathy		Odds Ratio 95%CI	P value
	Hearing Loss ≥ 26 dB n=144	Normal Hearing < 26 dB n=466		
Age groups (in years):				
<40	37(25.7)	120(25.8)	1	
40-49	33(22.9)	90(19.2)	1.18(0.69-2.04)	0.531
50-59	33(22.9)	107(23)	1.00(0.58-1.71)	0.999
60 and above	41(28.5)	149(32)	0.89(0.53-1.47)	0.658
Gender:				
Male	55(38.2)	180(40.3)	0.91(0.62-1.34)	0.645
Female	89(61.8)	278(59.7)	1	
Level of education:				
Primary	20(13.9)	57(12.2)	1.18(0.65-2.14)	0.584
Intermediate	42(29.2)	111(23.8)	1.27(0.79-2.03)	0.310
Secondary	30(20.8)	123(26.4)	0.82(0.49-1.36)	0.440
University	52(36.1)	175(37.6)	1	
BMI (kg/m²):				
Normal (< 25)	43(29.9)	110(23.6)	1	0.130
Overweight/obese	101(70.1)	356(76.4)	1.17(0.90-2.08)	
Physical activity:				
Yes	28(19.4)	145(31.1)	1	0.007
No	116(80.6)	321(73.5)	1.41(1.05-1.24)	
Smoking status:				
Yes	30(20.8)	63(13.5)	1.68(1.04-2.73)	0.033
No	114(79.2)	403(86.5)	1	
Sheeh Smoking status:				
Yes	28(19.4)	57(12.2)	1.73(1.10-2.85)	0.029
No	116(80.6)	409(87.8)	1	
Do you use mobile phone				
Yes	130(90.3)	381(81.8)	2.07(1.13-3.77)	0.015
No	14(9.7)	85(18.2)	1	
Do you hear TV sounds:				
Yes	101(70.1)	386(82.8)	1.21(1.06-1.39)	0.001
No	43(39.9)	90(17.2)	1	
Family history of DM:				
Yes	39(27.1)	76(16.3)	1.90(1.22-2.97)	0.005
No	105(72.9)	390(83.7)	1	
Hypertension				
Yes	47(32.6)	73(15.7)	2.69(1.70-4.0)	0.001
No	97(67.4)	393(84.3)	1	
Tinnitus				
Yes	58(40.3)	84(18.0)	3.06(2.03-4.61)	0.001
No	86(59.7)	382(82.0)	1	
Vertigo				
Yes	86(59.7)	42(9.0)	14.96(9.45-23.70)	0.001
No	58(49.3)	424(91.0)	1	
Headache				
Yes	79(54.9)	211(45.3)	1.46(1.00-2.13)	0.044
No	65(45.1)	255(54.7)	1	
Duration of diabetes (in years)	9.54 \pm 5.31	8.19 \pm 4.42	1.02(0.99-1.05)	0.003
Sleeping (in hrs)	5.88 \pm 1.25	6.39 \pm 1.24	1.02(0.99-1.05)	0.003

Table 2: Clinical biochemistry baseline value among neuropathy hearing loss and normal hearing subject among T2DM patients

Variables	Neuropathy with Hearing Loss ≥ 26 dB n=144 Mean \pm SD	Normal Hearing with diabetic <26 dB N = 466 Mean \pm SD	P value
Vitamin D (ng/ml)	18.09 \pm 7.42	22.41 \pm 9.90	<0.001
Hemoglobin (g/dL)	12.80 \pm 2.30	12.96 \pm 2.25	0.282
Magnesium (mmol/L)	0.78 \pm 0.09	0.89 \pm 0.08	<0.001
Potassium (mmol/L)	4.41 \pm 0.47	4.46 \pm 1.18	0.365
Calcium (mmol/L)	2.09 \pm 0.38	2.25 \pm 0.26	0.038
Phosphorous (mmol/L)	1.42 \pm 0.30	1.56 \pm 0.26	<0.001
Creatinine(mmol/L)	69.61 \pm 14.43	65.01 \pm 18.72	0.007
Fasting Blood Glucose(mmol/L)	7.60.13 \pm 1.29	7.09 \pm 0.88	0.010
HbA1c	8.31 \pm 1.00	7.36 \pm 0.86	<0.001
Cholesterol (mmol/L)	3.36 \pm 0.67	3.07 \pm 0.84	0.002
HDL (mmol/L)	1.43 \pm 0.90	1.21 \pm 0.37	0.030
LDL (mmol/L)	1.97 \pm 0.92	1.72 \pm 0.69	0.025
Albumin (mmol/L)	40.01 \pm 4.34	38.31 \pm 7.93	0.002
Billirubin (mmol/L)	7.16 \pm 1.49	5.86 \pm 1.56	0.001
Triglyceride (mmol/L)	1.82 \pm 0.41	1.67 \pm 0.35	0.010
Uric Acid (mmol/L)	276.8 \pm 89.82	287.9 \pm 84.43	0.295
Systolic Blood Pressure mm Hg	129.75 \pm 10.60	126.73 \pm 12.73	0.009
Diastolic Blood Pressure mm Hg	81.09 \pm 9.20	79.30 \pm 7.75	0.023
Microalbuminuria	14.75 \pm 2.31	7.20 \pm 0.96	<0.001
	n(%)	n(%)	
Vitamin D Level			
Deficiency			
25(OH)D <20 ng/ml	90(62.5)	236(50.6)	
Insufficiency			
25(OH)D 20-29 ng/ml	41(28.5)	140(30.0)	0.007
Optimal			
25(OH)D 30-80 ng/ml	13(9.0)	90(19.3)	

Table 2 shows baseline chemistry biomarker values among the two groups. There were statistically significant differences between hearing impairment versus normal hearing for vitamin D [18.91 \pm 7.65 ng/ml vs 22.85 \pm 9.00 ng/ml; p<0.001], calcium [2.19 \pm 0.38 ng/ml vs 1.96 \pm 0.14 mmol/L; p<0.001], magnesium [0.81 \pm 0.08 mmol/L vs 0.87 \pm 0.14 mmol/L ; p<0.001], phosphorous [1.42 \pm 0.30 mmol /L vs 1.56 \pm 0.26 mmol/L; p<0.001], ceatinine [69.61 \pm 14.43 mmol/L vs 75.1 \pm 18.72 mmol/L; p=0.007], cholesterol [3.36 \pm 0.67 mmol/L vs 3.07 \pm 0.84 mmol/L ; p<0.001], HDL(1.43 \pm 0.90 mmol /L vs 1.21 \pm 0.30 mmol/L; p=0.001), LDL [1.97 \pm 0.91 mmol /L vs 1.72 \pm 0.70 mmol/L; p=0.001], albumin [40.0 \pm 4.34 mmol/L vs 38.31 \pm 3.96 mmol/L; p=0.010], systolic blood pressure [129.75 \pm 10.60 Hg vs 126.73 \pm 12.39 Hg; p=0.017] and, diastolic blood pressure [81.09 \pm 9.2 mm Hg vs 79.29 \pm 7.95 mm Hg; p=0.012] and microalbuminuria [14.75 \pm 2.51 mmol /L vs 7.29 \pm 0.96 mmol /L p=0.001].

Table 3 presents multivariable logistic regression analysis of variables for predictors of hearing loss with neuropathy among diabetic patients. Vertigo (OR 10.90 95% CI (8.77-12.81); p<0.001), numbness (OR 4.60 95%CI (2.48-8.50); p<0.001), hypertension (OR 2.57 95%CI (1.58-4.29); p<0.001), duration of DM (OR 2.83 95%CI 1.75-4.98; p<0.001), head ache (OR 2.26 95%CI 1.60-

3.12; p<0.001), Vitamin D deficiency (OR 2.05; 95%CI 1.89-2.23, p<0.001), sleeping disturbance (OR 2.64; 95%CI 2.46-2.84, p=0.012), BMI (OR 3.10 95%CI 2.50-4.10; p=0.033), and cigarette smokers (OR 1.90; 95%CI 1.31-2.73, p=0.042) were considered at higher risk as a predictors of neuropathy with hearing loss among diabetic patients.

Table 3: Multivariate stepwise logistic regression analysis for predictors of hearing loss for neuropathic among T2DM patients (N=638)

Variables	Adj. OR (95%CI)	P value
Vertigo	10.90(8.77-12.81)	<0.001
Numbness in hand	4.60(2.48-8.50)	<0.001
Hypertension	2.57 (1.58-4.29)	<0.001
Duration of DM	2.83(1.75-4.98)	<0.001
Head ache	2.26(1.60-3.12)	<0.001
Vitamin D deficiency	2.05(1.89-2.23)	0.010
Sleep disturbance	2.64 (2.46-2.84)	0.012
BMI (kg/m ²)	3.1 (2.50-4.10)	0.033
Smoking (yes)	1.90 (1.31-2.73)	0.042

Discussion

The present study has revealed hearing loss as an important consequence of diabetes associated with the metabolic syndrome and can be used as a tool for diagnosing patients presenting hearing loss. Diabetes mellitus is an incurable disease and its management should be focused on preventing chronic complications associated with diabetes. Although, hearing loss is usually recognized complication of diabetes. Therefore, effective control of diabetes is essential to reduce the incidence of hearing loss in the middle age group and may affect the quality life.

More recently, Bener et al. [5,6] studied 1,633 diabetic patients and reported an overall prevalence of peripheral neuropathy was 9.5 % among them. The analysis showed that the condition was significantly associated age, being male, consanguinity, family history of DM and having high blood pressure were significant predictors of diabetic neuropathy. Similarly, more recently Unmar et al [9] determined the prevalence of diabetic peripheral neuropathy (DPN) and subclinical DPN (sDPN) in 240 patients with T2DM using nerve conduction study (NCS) as a diagnostic tool. The results showed that 50.8% of the participants had DPN, and among them, 17.1% had sDPN. sDPN showed significant independent associations with age, height, HbA1c, presence of atherosclerosis and diabetic retinopathy.

The current study results are in concordance with previous reported T2DM is related to high-frequency sensorineural hearing loss [18] and impaired auditory brainstem responses [9,13]. These results are in support of the fact that diabetes mellitus may have very complex repercussion on the auditory pathways.

Usually, the chronic hyperglycemia of diabetes may affect its metabolic balance and function leading to hearing impairment and several reported studies have indicated that hearing impairment is associated with DM (3,9,12). Also, angiopathy and neuropathy of

diabetes have been considered as reasons for hearing impairment as well [3]. Furthermore, Kang et al [12] reported that HbA1c level was associated with hearing impairment in the non-diabetic participants of current study and the high HbA1c levels might be closely monitored for hearing loss. A recent meta-analysis concluded that mild hearing loss is more prevalent in participants with DM [14].

The correlation between hearing loss and hypertension can be considered as an important risk factors. There a number of studies have indicated the strong association between hypertension-related hearing loss [6,11,14,19-20]. Most previous studies reported that hypertension was associated with high-frequency hearing impairment, and likewise, in this study, we found a positive association between these variables [6,18-23].

The current study revealed strong association between high prevalence of hearing impairment, vertigo and tinnitus in T2DM patients (5-6,20-22). The results of the present study indicate that neuropathy, hypertension and hearing impairment are commoner in T2DM patients.

Conclusion

The current study results supports a strong positive association between neuropathy and hearing impairment among T2DM. The study confirms that the Hypertensive and diabetic patients have moderately increased risk of future hearing loss. Meanwhile, hyperglycemia could be considered as a modifiable risk factor for diabetic neuropathy, the regularly glycemic control may be the most effective and important therapy for reducing the incidence or slowing the progression of neuropathy and improving quality of life in T2DM patients.

Contributors

AB designed and supervised the study and was involved in data collection, statistical analysis the writing of the paper. MÖ, LH,

MG and HC were involved in data collection, interpretation of data and writing manuscript. RAD and MAG reviewed and revised the manuscript. All authors approved the final version.

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Competing Interests: None to declare

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