

Deafness and Diabetes Mellitus : A Systematic Literature Review

<https://doi.org/10.47210/bjohns.2021.v29i3.554>

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ABSTRACT

Introduction

Diabetes mellitus cases are increasing worldwide. It affects almost all systems of the body including audio-vestibular system. Diabetic otopathy (DO) is the presence of symptoms and signs of vestibular and auditory disorders in patients with diabetes mellitus after the exclusion of other causes. In this review we aimed to study the mechanism of development of hearing loss in diabetes, the relationship between duration and severity of diabetes, and association of other complications with hearing loss.

Materials and Methods

We searched the MEDLINE & PubMed database using terms 'diabetic otopathy' and 'diabetes & hearing loss' for the articles published since 1970. Twenty articles were selected and reviewed.

Results

The mechanism of development of DO is not yet clearly known. But it is suggested to be multifactorial. This review of literature suggested that hearing impairment is two times more prevalent in subjects with diabetes as compared to those without diabetes. The relationship between diabetic otopathy and diabetic kidney disease is most commonly noticed.

Conclusion

The higher prevalence of hearing impairment in diabetic patients compared with nondiabetic patients was consistent. It is necessary to establish a screening and monitoring strategy for patients with diabetes mellitus to prevent the development of hearing loss and its consequences on life quality.

Keywords

Diabetes Mellitus; Diabetic Otopathy; Deafness

Diabetes mellitus (DM) is a metabolic disorder with uncontrolled sugar level which affects all systems of the body. According to the International Diabetes Federation (IDF), 463 million people in the world and 88 million people in the Southeast Asia region have diabetes in 2020. Out of this 88 million people in the Southeast Asia, 77 million belong to India.¹ As we know, Diabetes mellitus lead to development of several complications like retinopathy, peripheral neuropathy, nephropathy and accelerated atherosclerosis.^{2,3,4,5} But what is not well known is, it may also lead to hearing loss. The reason may be that the patients with hearing loss visit ENT surgeon and not the physician who is treating their diabetes. Secondly it is not included in the list of complications of diabetes mellitus in any textbook till now.

Diabetic otopathy (DO) is defined by the presence of symptoms and signs of vestibular and auditory

disorders in patients with diabetes mellitus after the exclusion of other causes. Its clinical manifestations include dizziness, vertigo, tinnitus and hearing loss.^{6,7} Diabetic otopathy has an impact on the quality of life, affecting the communication and cognitive functions. In this review we aimed to study the mechanism of development of hearing loss in diabetes, the relationship between duration & severity of diabetes, and association of other complications with hearing loss.

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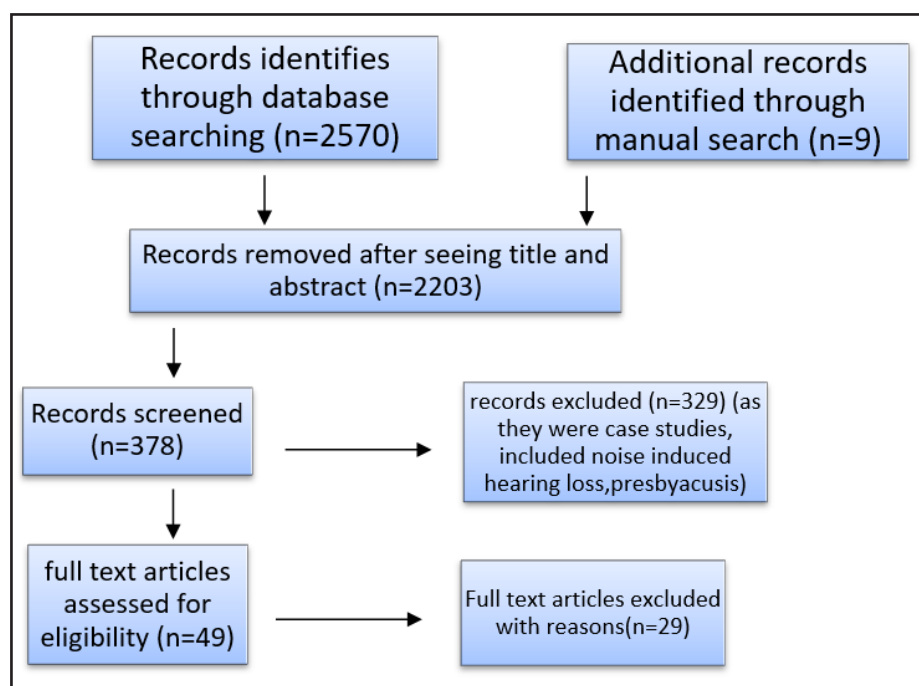


Fig. 1. Flow diagram of Data search done for this systematic review.

Materials and Methods

We made a review of the literature by searching the MEDLINE & PubMed database for the articles published since 1970. The search terms that we used were “diabetes otopathy” and “diabetes & hearing loss”. Twenty articles published in medical journals were selected depending on following criteria (Fig. 1):

- 1) Observational study using a cross-sectional design,
- 2) Adult subjects included, and
- 3) Hearing impairment objectively assessed using pure-tone audiometry.

Review

Mechanism of development of hearing loss

The mechanism of development of DO is not yet clearly known. But it is suggested to be multifactorial.⁸ The auditory neuropathy, microangiopathy of the cochlea and encephalopathy are thought to be the few factors responsible for development of hearing loss.^{9,10}

The first mechanism described in the literature for development of hearing impairment in diabetes, is increased polyol pathway flux reported in 1977.¹¹ High blood glucose increases the intracellular accumulation of sorbitol which is an important chemical of the polyol pathway. Sorbitol slows down nerve conduction velocity¹² and is related to the immune, ischemic and metabolic changes seen in diabetes.¹³ Aladag in 2009 reported that the protein oxidation as part of oxidative stress appears to be more important than lipid peroxidation in the pathogenesis of DO.¹⁴

Microangiopathy seen in diabetes is another factor responsible in the development of hearing loss. Increased glucose exposure initiates a metabolic cascade that could disrupt the cochlea both anatomically and physiologically. Studies have reported increased basement membrane thickening and porosity of the endothelium which is due to the upregulation of vascular endothelial growth factor and increased vascular permeability factor. This leads to changes in auditory electrolyte homeostasis within the endolymph and interfere with hair cell transduction and signal transmission. The cochlea contains Na/K/ATPase enzyme, but in diabetes, hyperglycemia down-regulates this enzyme, causing elevated intracellular Na⁺ and

extracellular K^+ and Ca^{++} .^{15, 16}

One more factor responsible for hearing loss in diabetes is Nitric oxide. It plays a role in regulation of the vascular endothelium of the auditory system. The metabolic changes seen in diabetes impair the production of nitric oxide and cause vasodilatations. This limits blood supply to certain areas of the auditory organ.¹⁷ Once ischemia sets in, excitotoxicity and apoptosis occurs, due to elevated intracellular Ca^{++} and damaged DNA.¹⁸

The metabolic changes of diabetes mellitus also results in deposits of collagen (advanced glycation end-products) in many areas of the peripheral auditory system.¹⁹ This results in abnormal post-translational protein modifications, leading to difficulty in articulation of the hair cells and deficits in sound transduction.¹⁸

Endolymph is a medium wherein the intracellular environment depends on glucose for cellular function. Utilizing other substrates as alternative source of energy to maintain the endolymph during diabetes mellitus may be the one more important cause of hearing loss.¹⁹

Literature research and study characteristics

Table I shows details of the literature search done by us. Nineteen studies included both males and females but only one study involved males only. In a large number of included studies (14 studies), the mean age of participants was 60 yr or less. Eleven studies were done in Asian region and nine studies of other regions. In eleven studies, participants were hospital based, and in nine studies participants were from the general population. All studies described the method for assessment of hearing impairment as pure tone audiometry though the hearing threshold taken for deafness varied in different studies. But the threshold levels were almost consistent with that of hearing impairment defined by WHO. Most studies used 25 dB for the hearing impairment threshold with the exception of three studies that used 26, 30, and 20 dB, respectively, as the threshold. Fifteen of twenty studies identified the type of diabetes but the mean duration of diabetes was given in only nine studies.

Relation between duration & severity of diabetes and hearing loss

The association between hearing loss and diabetes mellitus was first reported by Jorden in 1857.³⁹ In 1864, the first scientific documentation connecting glucose metabolism disorders to inner ear diseases was done.⁴⁰ It showed the relation between sensorineural deafness and diabetes, thus establishing the link between hearing loss and hyperglycemia.

Kim et al have done the prospective cohort study on a large group of young adults and middle-aged men and women. These participants were subjected to regular auditory tests and screenings from 2002 to 2014. The conclusion was that the participants with normal glucose levels, pre-diabetes and diabetes mellitus have a rate of hearing loss of 1.8, 3.1 and 9.2 per 1000 person respectively. That means hearing loss was 7 times higher in diabetics as compared to non-diabetics.³⁹ Jin Lin also in his paper reported that number of type 2 diabetes patients suffered from hearing loss is much more as compared to pre-diabetes patients or the control group.¹¹ Recently in 2018, Cruickshank et al., reported that hearing loss is more common in patients with HbA1c >12.5%. This shows that a patient with uncontrolled sugar levels than the one with controlled sugar levels is more likely to be associated with the diabetic otopathy.¹³ Similar study done in south India, in Karnataka by Dr Tiwari & Dr Mudhol showed that 76.8% diabetics in the age group 30 to 65 were suffering from sensorineural hearing loss irrespective of age 21. In the study done by Makwana et al in Jaipur, India Oct 2019, prevalence of mild sensorineural hearing loss was found to be 80%. According to them longer duration and uncontrolled diabetes are the factors which had higher risk of developing hearing loss.²⁰

This review of literature suggested that hearing impairment in subjects with diabetes is two times more prevalent as compared to those without diabetes. The significant association between hearing impairment and diabetes was maintained throughout the analysis. It is well known that aging is associated with both prevalence of hearing impairment and diabetes. However, a stronger association was observed in studies of younger

Table I: Characteristics of studies included in this review

SI NO	AUTHOR	YEAR	COUNTRY	STUDY SETTING	TYPE OF DIABETES	MEAN DURATION OF DIABETES (YR)	AGE RANGE (YR) (MEAN)	PREVALENCE OF DIABETES %
1	Makwana AV et al. ²⁰	2019	India	Hospital	DM2	NA	55.5	80
2	Tiwari and Mudhol et al. ²¹	2018	India	Hospital	DM2	>3	55.52	78.6
3	Yikawe, et al. ²²	2017	Nigeria	Hospital	DM2	7.81 ± 5.34	46.49	71.8
4	Jerico Gutierrez, et al. ²³	2016	Philippine	Hospital	DM 1 & 2	>5	57.52	45.31
5	Konrad-Martin et al. ²⁴	2015	US	Population	DM2	NA	47.7	NA
6	Krishnappa and Naseeruddin ²⁵	2014	India	Hospital	NA	NA	50-80	73.58
7	Kim M B et al. ²⁶	2014	Korea	Hospital	DM2	NA	44.1	NA
8	Bamania et al. ²⁷	2011	Saudi Arabia	Hospital	T2DM	10.5	29-69	40.3
9	Mozaffari et al. ²⁸	2010	Iran	Population	9T1DM 71 T2DM1	9.3	20-60 (45.0)	36.3 21.2
10	Uchida et al. ²⁹	2010	Japan	Population	FPG_126 mg/dl, HbA1c _6.5%	NA	40-86	50.1
11	Cheng et al. ³⁰	2009	US	Population	NA	4.8	25-69 (44.3) 25- 69 (44.9)	49.1
12	de Sousa et al. ³¹	2009	Brazil	Hospital	NA	6.1	40- (50.5)	85.4
13	Aladag et al. ³²	2009	Turkey	Population	T2DM	NA	-46.9	57
14	Mitchell et al. ³³	2009	Australia	Population	T2DM	NA	55- (69.8)	42.9

Table I: Characteristics of studies included in this review

SINO	AUTHOR	YEAR	COUNTRY	STUDY SETTING	TYPE OF DIABETES	MEAN DURATION OF DIABETES (YR)	AGE RANGE (YR) (MEAN)	PREVALENCE OF DIABETES %
15	Sakuta et al. ³⁴	2006	Japan	Population	T2DM	<10	51–59 (52.8)	39.5
16	Helzner et al. ³⁵	2005	US	Population	NA	>10	73–84 (77.5)	47.3
17	Huang. ³⁶	2004	China	Hospital	T2DM	NA	23– (56.1)	54.2
18	Dalton et al. ⁶	1998	US	Population	T2DM	NA	43–84	43.3
19	Marumo et al. ³⁷	1984	Japan	Hospital	Primary DM	NA	18–75	72.8
20	Minami et al. ³⁸	1977	Japan	Hospital	NA	NA	15–79	61.1

participants (mean age of participants, approx 45 yr) compared with studies of older participants. This means that hearing impairment associated with diabetes is not dependent of age.

Several studies are published to analyze the link between diabetic complications and hearing loss. Tay in his survey showed that hearing impairment was correlated with the duration of diabetes, but not with other complications of the disease such as retinopathy.⁴⁰ Bayazit analysed hearing loss in patients with complications of diabetes in comparison with a group of patients without complications and concluded that diabetic neuropathy and encephalopathy are involved in etiology.⁴¹ The relationship between diabetic otopathy and diabetic kidney disease is most commonly noticed. Dalton et al emphasized an association between severe diabetic nephropathy (patients with proteinuria, kidney transplant or dialysis) and hearing loss in their study. The glomerular filtration rate was used as an indicator of renal function and it was shown that hearing loss occurs from the early stages of chronic kidney disease.⁴² Same results were demonstrated from a study conducted in Korea, that is patients with chronic renal disease stage 2 (eGFR 60-90ml/min/1.73m²) had a severe

auditory disorder. Independent of diabetes, lowering the glomerular filtration rate is associated with hearing loss of moderate severity among the analysed population. Hearing loss is not seen in non diabetic patients with severely reduced kidney function.¹⁵

In addition to above factors, the hearing loss caused by diabetes Mellitus is also affected by Triglyceride levels, Smoking & Alcohol consumption as stated below.

Conclusions

Current review suggests that the higher prevalence of hearing impairment in diabetic patients compared with nondiabetic patients was consistent regardless of age. The micro vascular lesions, atherosclerosis of the large vessels and even direct damage of the acoustic-vestibular nerve are the causes. Other elements that correlate with hearing impairment in DM are nephropathy, hypertriglyceridemia, increased alcohol consumption and hypertension. The influence of glycemic control (HbA1c) on hearing is uncertain. It is necessary to establish a screening and monitoring strategy for patients with diabetes mellitus to prevent the development of hearing loss and its consequences

on life quality.

Ethics approval and consent to participate – Not applicable.

Consent for publication – Not Applicable

Availability of data and material – Library, D. Y. Patil Medical College, Kolhapur:

Competing interests - NIL

Funding- Non Funded Study

Authors' contributions – Each Author contributed to the article during data acquisition, analysis & interpretation. They also contributed towards drafting the article and revisiting it critically for more intellectual content. Final approval of the version to be published was sought from all the authors.

Acknowledgements – Audiology department & staff of D.Y.Patil Medical College Library.

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