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Systematic Review

Is Type 2 Diabetes Mellitus Associated With Alterations in Hearing? A Systematic Review and Meta-Analysis

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Objectives/Hypothesis: The aim of this study was to systematically and quantitatively review the available evidence on the effects of type 2 diabetes mellitus on hearing function.

Data Sources and Review Methods: Eligible studies were identified through searches of eight different electronic databases and manual searching of references. Articles obtained were independently reviewed by two authors using predefined inclusion criteria to identify eligible studies. Meta-analysis was performed on pooled data using Cochrane's Review Manager.

Results: Eighteen articles fulfilled the inclusion criteria. Hearing loss (HL) was defined by all studies as pure tone average greater than 25dB in the worse ear. The incidence of HL ranged between 44% and 69.7% for type 2 diabetics, significantly higher than in controls (OR 1.91; 95% confidence interval 1.47–2.49). The mean PTA (pure tone audiometry) thresholds were greater in diabetics than in controls for all frequencies [test or overall effect $Z = 3.68$, $P = 0.0002$]. Auditory brainstem response (ABR) wave V latencies were also statistically significantly longer in diabetics when compared to control groups [OR 3.09, 95% CI 1.82– 4.37, $P < 0.00001$].

Conclusions: Type 2 diabetic patients had significantly higher incidence for at least the mild degree of HL when compared with controls. Mean PTA thresholds were greater in diabetics for all frequencies but were more clinically relevant at 6000 and 8000 Hz. Prolonged ABR wave V latencies in the diabetic group suggest retro-cochlear involvement. Age and duration of DM play important roles in the occurrence of DM-related HL.

Key Words: Type 2 diabetes, hearing function, systematic review, meta-analysis.

Level of Evidence: 3a.

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INTRODUCTION

The prevalence of type 2 diabetes mellitus (DM) has increased progressively over the last 2 decades, with over 21 million people diagnosed with type 2 DM in the United States alone.[1,2] Complications from this disease are common and are said to be due to hyperglycemia-induced microangiopathy.[3–6] Clinical and animal research both point to the deleterious effects of hyperglycemia on retinal and renal tissues,[7–10] and other tissues of the body.[11–13] Hyperglycemia leads to microangiopathy through various pathways, which in turn have been shown to be the pathology behind many complications associated with type 2 DM.[14,15] Previous research works on both human temporal bone and experimental animals have shown thickening of the basement membrane of the capillaries within the stria vascularis on the lateral wall of the cochlea, similar to what has been described for diabetes-related microangiopathy.[16–18] Other aspects of the cochlea such as the organ of Corti and spiral ganglion neurons were equally shown to be affected.[16–18]

Therefore, it is not surprising that for many years a number of clinical researchers have also studied the effects of diabetes on hearing function.[19–22] However, clinical studies have not always shown a positive association between type 2 DM and hearing loss (HL). While some authors report an association between type 2 DM and HL,[23,24] others have shown no difference.[25,26] In a recent review, Horikawa et al. showed an association between DM in general and HL.[27] In their review, they compared the incidence of HL amongst diabetic adults (regardless of type) and nondiabetic adults. However, it is known that type 2 DM constitutes up to 90% of all diabetes cases[28] and differs from type 1 DM with regard to etiology, pathogenesis, clinical features, and predisposition to complications. In actual fact, the occurrence of complications may be the first presentations in type 2 DM, with direct impact on quality of life of patients. There is currently no consensus on whether or not HL complicates type 2 DM.

The primary aim of this study is to conduct a systematic review in order to explore the effects of type 2 DM on

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TABLE I.
Search Terms and Key Words.

I. Ovid Medline/Medline in Process	
1. Diabetes	Exp Diabetes Mellitus/
	(Diabet* OR MODY OR NIDDM OR T2DM OR IDDM OR DM 1 OR DM 2).ti,ab.
2. Hearing	Exp Hearing/OR Exp Diagnostic Techniques, Otological/OR Exp ear/
	(Hearing OR ear OR ears OR hear OR hears OR aural OR auditor* OR auditi* OR cochl* OR Audial OR audiol* OR ototox* OR oto-tox* OR Deaf* OR Hypoacus* OR Hypo-acus OR otolog*).ti,ab.
	Random Allocation/OR Placebos/OR Follow-Up Studies/OR prospective Studies/OR Cross-Over Studies/OR Double-Blind Method/OR Single-Blind Method/
II. Biosis	
1. Diabetes	(Diabet* OR MODY OR NIDDM OR T2DM OR IDDM OR DM 1 OR DM 2).ti,ab.
2. Hearing	Hearing OR ear OR ears OR hear OR hears OR aural OR auditor* OR auditi* OR cochl* OR Audial OR audiol* OR ototox* OR oto-tox* OR Deaf* OR Hypoacus* OR Hypo-acus OR otolog*).ti,ab.
	1 AND 2
	(Placebo* OR random* OR blind* OR mask* OR crossover* OR cross over* OR cross-over* OR assign* OR allocat* OR volunteer* OR groups OR latin square* OR Meta-analys* OR Meta analys*).ti,ab.
	((systematic* OR quantitativ* OR methodologic*) adj (review* OR overview* OR synthes*)).ti,ab.
	3 AND (4 OR 5)

the hearing function by performing a quantitative analysis of currently available published data on this subject. We compared the incidence of HL among type 2 diabetics with age-matched nondiabetic controls. We also examined pure tone audiometry (PTA) thresholds and auditory brainstem-evoked response (ABR) wave latencies in persons with type 2 DM, comparing these values with those of controls. PTA testing is a behavioral hearing test used to determine the degree and type of HL. It provides the thresholds for hearing at different frequencies, usually ranging from 250 Hz to 8000 Hz. Normal hearing has thresholds between −10 to 15 dB.[29] On the other hand, ABR is an electrophysiological test that assesses the transmission of sound impulses at the brainstem level. It provides the threshold for hearing as well as the speed of sound conduction from the eighth cranial nerve through the cochlear nuclei, olivary nucleus, lateral lemniscus, and inferior colliculi,[30,31] which are represented as waves I, II, III, IV, and V, respectively.[32]

It is anticipated that the results of this review will provide an insight into the possible relationship between type 2 DM and HL.

MATERIALS AND METHODS

Search Strategy

Eligible articles were identified through a comprehensive search of the following electronic databases: Ovid Medline, Ovid Medline in Process, PubMed, Ovid Embase, Biosis Preview, ISI Web of Science, and Scopus. A search of the reference lists from relevant studies was also performed. The search strategy included medical subject headings, subheadings, and text words such as "Diabetes Mellitus," "NIDDM OR Type 2 Diabetes OR IDDM OR DM type 1 OR DM type 2," "Hearing," "auditory system," "hearing loss," "hearing disorder," "deaf," and "ear." Articles published from database inception up to April 2013 and written in English, French, or Spanish were eligible for evaluation. Search words and keywords in the search strategies for Ovid Medline/Medline in process are cited in Table I. Full search strategies of the other databases can be obtained from the authors.

Inclusion and Exclusion Criteria

Studies describing hearing assessment in type 2 diabetic patients using either PTA or ABR were included. Only prospective cohort or cross-sectional or case-controlled studies were eligible. Studies that did not exclude other risk factors for HL, those that considered HL in both types 1 and 2 DM, or those that did not clearly state the type of DM patients that they studied were excluded. Also excluded were studies in which control subjects were not subjected to similar hearing tests as the DM patients, the diagnosis of DM was based on self-report, or the hearing assessment was not standardized. In addition, when the same data was presented in various publications, only one fitting the criteria of this review was included. Authors were contacted via e-mail if more information was needed to help with the categorization of the article. Finally, letters, commentaries, conference abstracts, and case reports were not eligible for evaluation.

Study Selection

The first two authors (OVA and MMM) preset the criteria for study eligibility and independently screened the titles and abstracts retrieved by the electronic search to obtain a list of relevant articles. This list was jointly reviewed and a common list was generated. Authors were e-mailed for clarifications if important details were missing. This constituted the first-stage review. All relevant citations for second-stage review were reviewed in hard copies and as full texts to justify inclusion or exclusion, initially independently and later jointly by the first two authors. All divergence among reviewers was resolved by consensus.

Quality Assessment

The articles considered eligible were further subjected to quality assessment using the modified Downs and Black scale.[33] Articles obtaining a score greater than 14 out of 19 possible points were included in the final analysis. Two investigators independently rated the selected articles in a blinded fashion, and scores were then compared using the Pearson correlation coefficient to determine the inter-rater reliability. Correlation coefficient greater than 0.8 was considered acceptable for a significance level of $\alpha < 0.05$.

Data Extraction and Analysis

The data extracted are shown on Table II. Meta-analysis of the data was conducted using Cochrane Review Manager Software (RevMan version 5.1, Cochrane IMS, Denmark). Data were entered in either continuous or dichotomous formats. The pooled OR for the incidence of HL was obtained using a Mantel-Haenszel random effect model; whereas the pooled standardized mean of difference (SMD) for the PTA thresholds and ABR wave latencies were obtained using inverse variance and random effect analysis model.

TABLE II.
Characteristics of the Included Studies.

Author/(Year)	Level of Evidence	Participants (Diabetics/Controls)	Mean DM Duration (years)	Mean Age (years)	Method of Hearing Assessment	Incidence of Hearing Loss (%) (DM vs. Controls)	*P* Value
Incidence							
Bemanie (2011)	III	109/87	10.52	47.9/45.7	PTA	69.7 vs. 39.1	0.005
Mozaffari (2010)	III	71/80	9.28	45/45.1	PTA	45.1 vs. 20	<0.001
Aladag (2009)	III	63/37	7.86	46.58/47.51	PTA	44 vs. 48.6	NS
Mitchelle (2009)	III	210/1648	</>10	70.5/69.7	PTA	50 vs. 38.2	NS
Sakuta (2007)	III	103/442	NS	51–59	PTA	60.2 vs. 45.2	*0.048
Dalton (1998)	III	344/3029	NS	69.6/65.1	PTA	59 vs. 44	<0.02
Pure Tone Audiometry Thresholds							
Swaminatham (2011)	III	30/30	NS	40–50	PTA	NA	0.0002
Austin (2009)	III	88/137	5.45	26–49/26–49*	PTA	NA	<0.01
Panchu (2008)	III	41/41	NS	35–55	PTA	NA	<0.01
Diaz-de Leon (2005)	III	94/94	7.2 ± 5.4	50/50	PTA/ABR	NA	<0.05
El Nagger (2003)	III	39/39	NS	42.7/41.8	PTA	NA	>0.05
Kurt (2002)	III	75/45	14.6	58.3/56.8	PTA	NA	0.001
Acuña-Garcia (1997)	III	40/34	NS	58.8/60.9	PTA	NA	>0.05
Auditory Brainstem Evoked Responses							
Gupta (2013)	III	126/106	5.68 ± 3.16	35–50	ABR	NA	0.01
Gupta (2010)	III	25/25	>5	48.8/45.7	ABR	NA	<0.001
Talebi (2008)	III	31/69	8.74	54.2/50.87	ABR	NA	0.007
Diaz-de Leon (2005)	III	94/94	7.2 ± 5.4	50/50	PTA/ABR	NA	<0.05
Sasso (1999)	III	110/106	8.1	48.4/47.9	OAE/ABR	NA	<0.05
Pozessere (1988)	III	14/20	2.9	48.9/51	ABR	NA	NS

ABR= auditory brainstem evoked responses; DM = Diabetes mellitus; NA = not applicable (These studies did not provide incidence of hearing loss; rather they provided the thresholds for PTA or ABR wave latencies.); NS = not specified; OAE = otoacoustic emissions; PTA = pure tone audiometry.

Heterogeneity and Publication Bias

Statistical heterogeneity was explored using the chi-squared (χ^2) at the 5% significance level ($P < 0.05$). I^2 statistic was used to quantify variation across studies results. Between-study variance was also estimated using tau-squared (τ^2) statistic and funnel plot used to investigate publication bias visually.

RESULTS

A total of 2,650 articles were identified through the search; 16 additional articles were identified through a search of the references of selected articles. Following independent and joint review of titles and abstracts, 67 articles were selected for full articles review, 38 of these was excluded (Fig. 1). Twenty-nine (29) articles were therefore assessed for quality using the modified Down and Black scale. Eighteen (18)[34–51] of these obtained adequate scores and were thus included for data extraction and further review. The inter-rater agreement for this review was acceptable as per preset criteria with correlation coefficient 0.87 and $P < 0.01$. The descriptive characteristics of the included studies are shown in Table II.

Incidence of Hearing Loss

Six studies gave overall incidence of HL among type 2 diabetics and controls as a percentage of total number in each group. The incidence ranged from 44% to 69.7% for diabetic subjects; and from 20% to 48.6 % for nondiabetic controls (Table II). The definition for HL was pure tone average greater than or equal to 25dB at selected frequencies in the worse ear. One study[52] was not included in this analysis because the ages of controls were not matched with diabetics.

The duration of DM for four of these six studies were below 10 years; a higher incidence of HL occurred in the study where the duration of DM was greater than 10 years (Table II).[46] Table III shows a trend of higher incidence in older diabetic groups as compared to relatively younger groups.[34–36,43,45,46]

The studies included did not provide separate data for males and females. However, the percentages of males in each study was compared with the OR obtained for each study (Table IV). The results are inconclusive, but showed a high OR in the study with only males.[34] Mitchell et al. reported a multivariate adjusted OR of 1.41 for the male sex.[36]

Analysis of pooled odds ratio (OR) showed the incidence of HL to be 1.91 times higher in type 2 DM group than in control group [OR = 1.91 (95% CI, 1.47, and 2.49)] (Fig. 2a). Test for overall effect Z = 4.81, $P < 0.00001$, and $I^2 = 55\%$ (Fig. 2a). Analyses were performed with groups divided by age above and below 65 years. The OR was 2.10 and 1.75 for the groups, with mean age below and above 65 years, respectively.

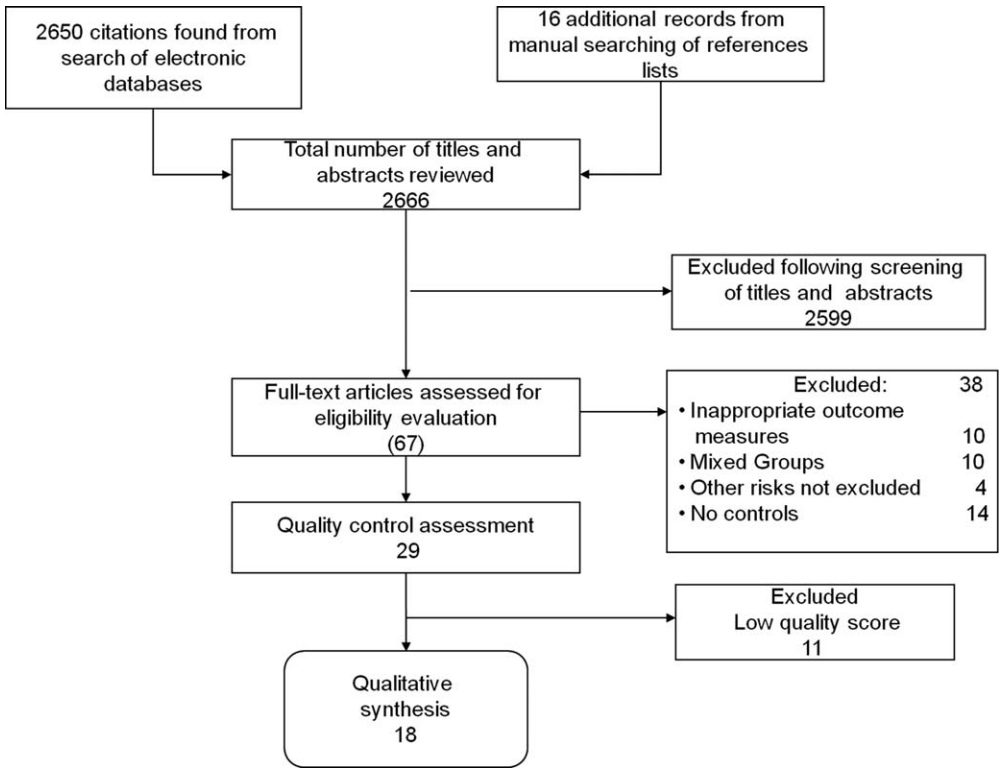


Fig. 1. Flow diagram for study selection of studies looking at effects of type 2 diabetes mellitus on hearing function.

Pure Tone Audiometry Threshold at Different Frequencies

Seven studies provided data on mean PTA thresholds for both diabetic and control subjects at various frequencies.[44,47–50] We pooled PTA averages at 500 Hz for 453 diabetics and 1,910 controls,[36,42,44,47,48] at 1000 Hz for 493 diabetics and 1,944 controls. Analyses at 2000 Hz and 4000 Hz were for 523 diabetics and 1,974 controls,[36,42,44,47–49] while for 8000 Hz, 454 diabetics and 1,905 controls were analyzed.[36,42,44,47,50] The means of differences between diabetics and controls were large at all frequencies, for example, 4.56, 4.46, 4.98, 6.92, 7.59, and 7.99 for 500, 1000, 2000, 4000, 6000, and 8000 Hz, respectively (Fig. 3). The greatest values were shown for 6000 and 8000 Hz.

It is interesting to note that, although the mean PTA thresholds for diabetics were higher than those for controls, they were still in the range for slight to mild HL, based on the classification of degree of HL of the American Speech-Language-Hearing Association.[29] The PTA thresholds increased with increasing frequencies for both diabetic and control groups, with SMDs being very significant at high frequencies.

ABR Wave Latencies

Waves III and V latencies were significantly longer for diabetic participants ($Z = 3.66$, $P = 0.0003$, $I^2 = 48\%$; $Z = 4.65$, $P < 0.00001$, $I^2 = 98\%$, respectively).[37–41] However, waves I latencies were not significantly different among the two groups ($Z = 031$, $P = 0.76$, $I^2 = 0\%$) (Fig. 4).

TABLE III.
Relationship Between Mean Age of Diabetics/Controls and Hearing Loss.

Author/(Year)	Diabetics Mean Age (years)	Diabetics Incidence of HL	Controls Mean Age (years)	Controls Incidence of HL
Mozaffari et al. (2010)	45	45.1%	45.1	20%
Aladag et al. (2009)	46.58	44%	47.51	48.6%
Sakuta et al. (2007)	51–59	60.2%	NS	45.2%
Dalton et al. (1998)	69.6	59%	65.1	44%
Mitchell et al. (2009)	70.5	50%	NS	38.2%
Bamanie and Al-Noury (2011)	47.9	69.7	45.7	39.1

HL = hearing loss.

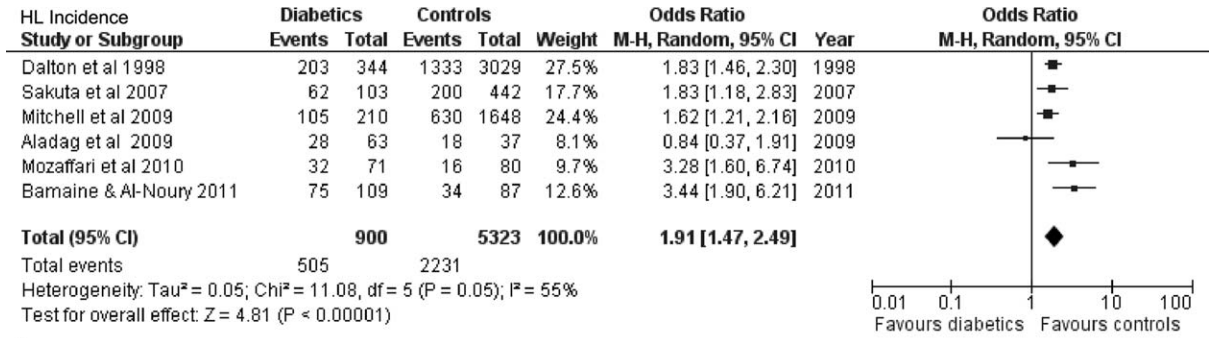
TABLE IV.
Relationship Between the Proportion of Males in Each Study and the OR for Hearing Loss.

	% Male	OR
Mozaffari et al. (2010)	36.3	1.83
Mitchell et al. (2009)	42.9	0.84
Dalton et al. (1998)	43.3	3.44
Bamanie & Al-Noury (2011)	50	1.83
Aladag et al. (2009)	57	1.62
Sakuta et al. (2007)	100	3.28

Studies are arranged in order of increasing male proportion.
OR = odds ratio.

DISCUSSION

Results from this review shows that individuals with type 2 DM have a greater association with HL when compared to control subjects. The odds ratio of 1.91 is slightly lower than that shown by Horikawa et al., who evaluated HL among individuals with DM without separating them into types.[27] As the criterion used by all the studies to diagnose HL was PTA thresholds greater than 25 dB, it may be argued that the degree of HL in these subjects, although not precisely stated, may possibly be mild. Therefore, it is safer to infer that diabetics are more likely to have hearing thresholds above 25 dB when compared to nondiabetic subjects, or that mild degree of HL occur more in diabetics than controls. It is not clear if type 2 DM increases the risk of developing moderate to severe HL from these data. This is important because most cases of mild HL may not produce sufficient clinical symptoms to warrant aggressive treatment, whereas moderate to severe HL would.[53] In addition, the PTA thresholds among type 2 diabetics were mostly below 30dB, although slightly higher at higher frequencies. This implies that the possibility of having HL impact the quality of life is not very high in the diabetics. However, these mild degrees of HL may be easily worsened when superimposed upon by other conditions that affect the hearing organ.



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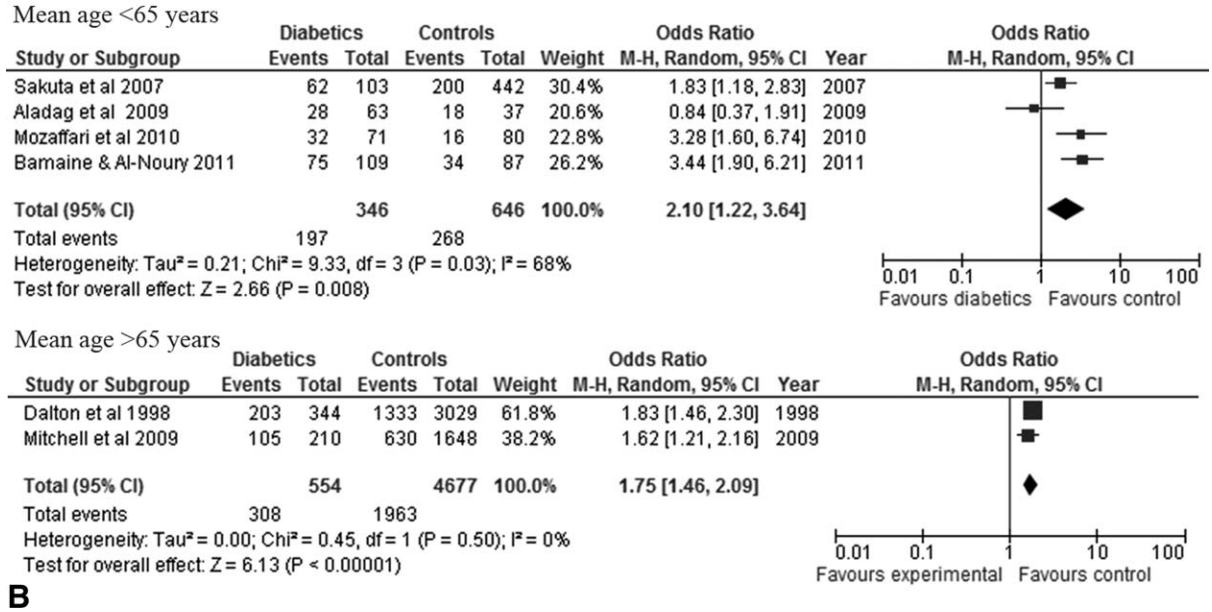

B

Fig. 2. A. Forest plot of six studies that compared the incidence of hearing loss among diabetics and controls. Outcome is odds ratio (OR) for the incidence of hearing loss bars indicate 95% confidence interval. The weights of each study in the meta-analysis are indicated. Analysis model = random effect; effect measure is OR; M-H = Mantel-Haenszel. B. Forest plot of studies comparing the incidence of hearing loss among diabetics and controls with mean ages above and below 65 years. The odds ratio for the two age groups (above and below 65 years) are shown.

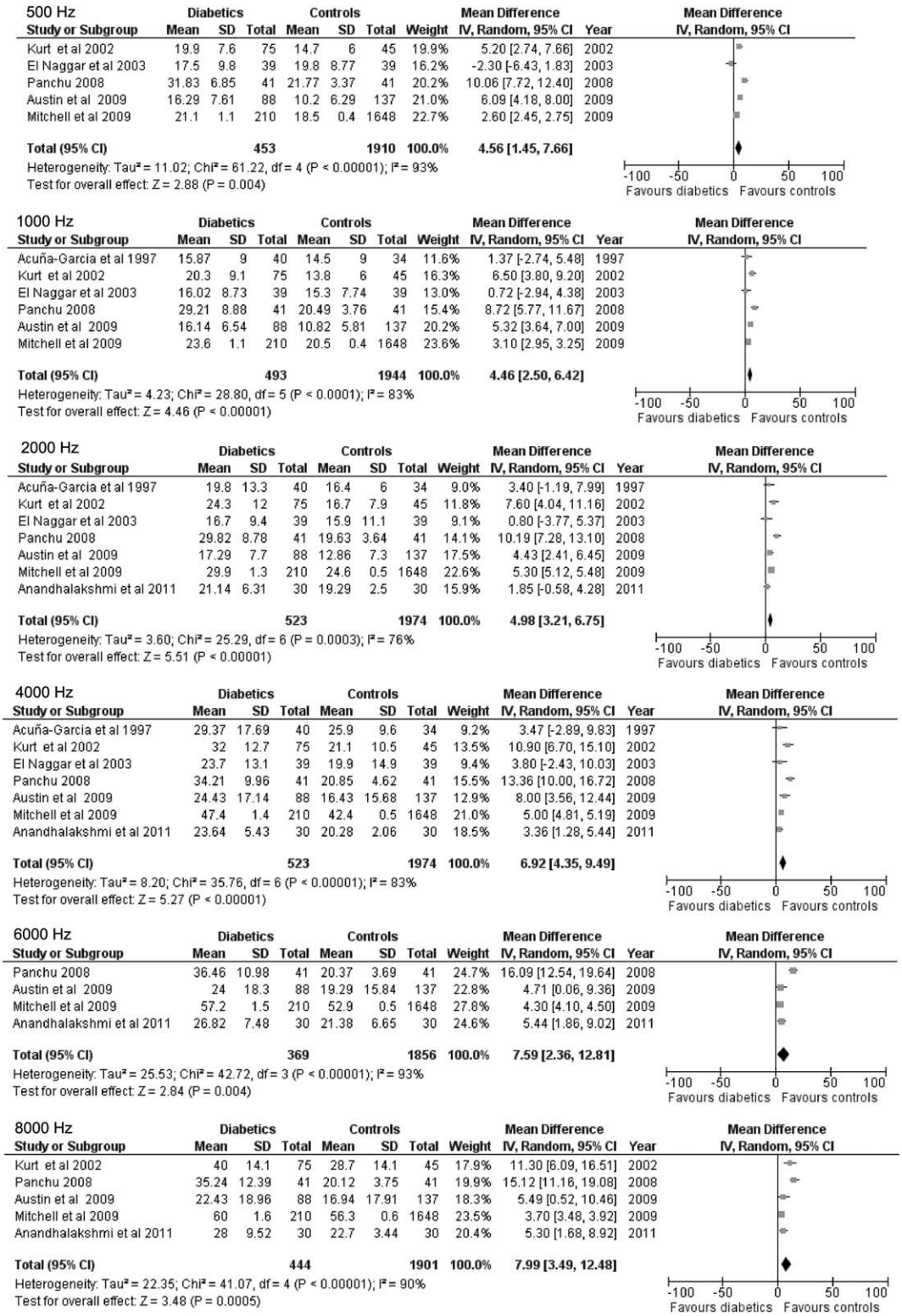

Fig. 3. Forest plots of studies showing standardized mean difference for pure tone audiometric thresholds in diabetics and controls at 500, 1000, 4000, 6000, and 8000 Hz. Bars and diamonds indicate 95% confidence intervals (Cis). The weights of each study in the meta-analysis are indicated. IV = inverse variance; analysis model = random effect; effect measure is mean of difference.

Hearing thresholds were higher in diabetics at every frequency when compared with nondiabetic controls with increasing magnitude as the frequencies got higher. It is interesting to note that the pure tone audiometric thresholds at the lower frequencies for both diabetics and controls were mostly within the normal or slight HL range

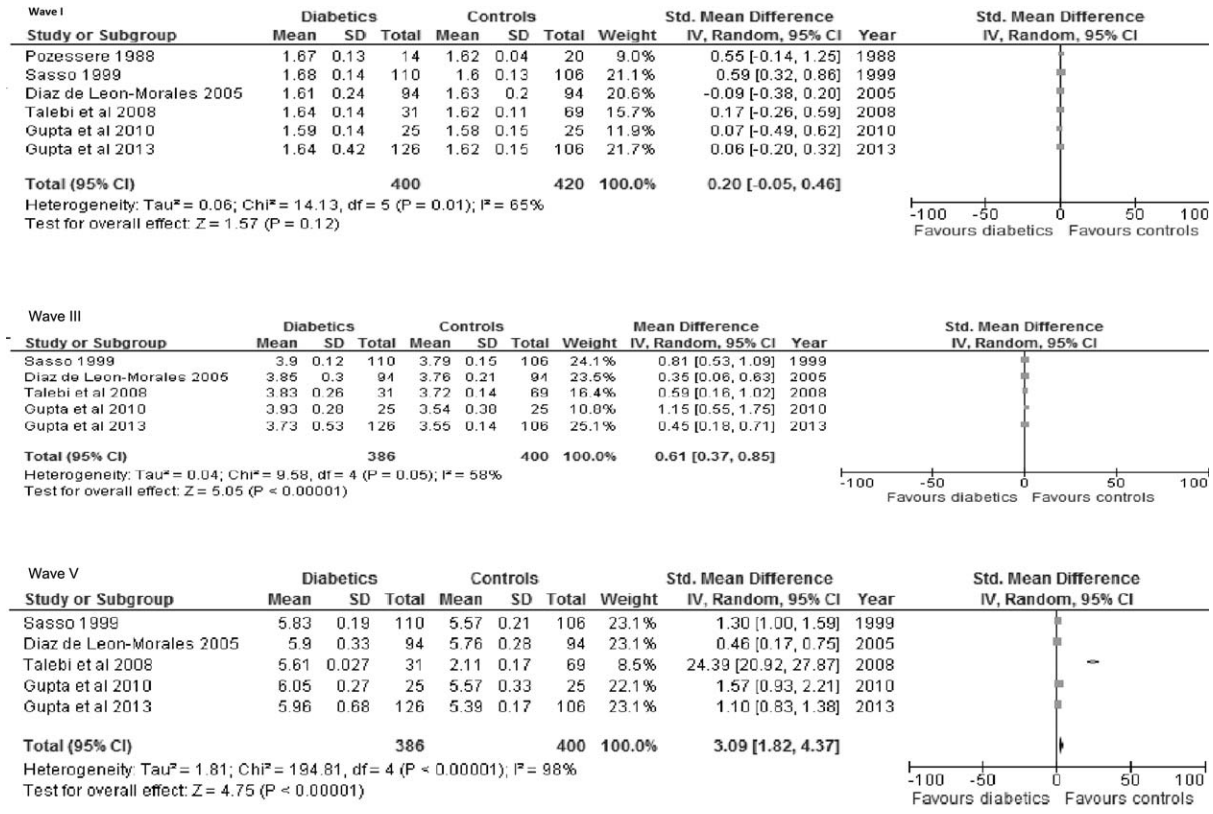

Fig. 4. Forest plots of studies showing standardized mean of difference for auditory brainstem-evoked responses (ABR) waves' latencies (a: wave I, b: wave III, c: wave V) for both diabetics and controls. Bars and diamonds indicate 95% confidence interval. The weights of each study in the meta-analysis are indicated. IV = inverse variance; analysis model = random effect; effect measure is SMD (standardized mean difference).

and may therefore not produce significant impact clinically. Conversely, at higher frequencies, the values for the mean thresholds were greater. Higher thresholds were presented by the Mitchell et al. study, which is probably because they studied older diabetics.[36] A number of studies have earlier reported that HL among diabetics was more predominant at the high frequencies.[23,24,54] This finding is comparable to what is seen with age-related HL, where high frequencies are the first to be affected.[55,56] Loss of sensory cells at the basal turn of the cochlea and loss of cochlear neurons are two of the reasons purported for age-related HL.[16,57] Similar degeneration of cells at the cochlear basal turn (the area representing high frequencies) was observed in an animal model of DM by Nakae et al.[16] In as far back as 1964, Falbe Hansen[20] showed that glycogen granules were more abundant at the apical turn of diabetic rats and decreased progressively toward the basal turn. High frequency HL may have negative impact on the quality of life as individuals with this problem often have difficulty understanding speech.[58]

The incidence of HL appeared to be higher for older diabetics[34–36] (Table III). Control subjects also showed an increase in incidence of HL with increasing age; however, the increase was more among the diabetic group (Table III). Higher thresholds were observed in the study that looked at elderly diabetics (Fig. 3).[36] In addition, stratification of the incidence of HL according to the mean age (below and above 65 years) revealed that the odds of HL occurrence was higher among the diabetic group regardless of age group (Fig. 2b). However, the difference that type 2 DM made on the incidence of HL was greater among the younger group when compared to the older age group. This is not surprising, given the fact that aging could predispose the control group to HL when the mean age is above 65 years.[55] Pathological similarities have been shown in the cochlea with aging and DM, particularly at the basal part of the spiral canal and the basement membrane in the capillaries within the stria vascularis.[59] Diabetic state was previously shown to make worse identifiable arteriosclerotic changes induced by aging.[59] This may suggest that the diabetic state potentiates the mechanisms responsible for age-induced HL. Considering that individual variations exist with regard to susceptibility to age-induced HL,[58] it is a possibility that DM accelerates or increases the likelihood of developing age-induced HL. Albeit, separating age-induced HL and DM-related hearing effects in elderly diabetics is a potentially challenging task. Both pathologies have been suggested to share a common pathway; their effects may therefore be additive.[55]

In our results, a conclusive remark cannot be made on how the sex of the diabetic subjects affects their predisposition to HL due to insufficient data on this.

However, we noticed a trend of high OR in the study that investigated only male diabetics[34] (Table IV). Gender has been shown to have an effect on the occurrence of age-induced-HL with the male sex being more affected.[60,61] Further studies are required to elucidate the possible role that gender plays in the occurrence of HL among type 2 diabetics.

Analyses of wave latencies and inter-peak latencies with pooled data analyses revealed significantly longer latencies for diabetic groups, particularly for wave V (Fig. 4).[37–41,51] Remarkably, the duration of DM for the patients who showed this finding were all below 10 years (between 2.9 and 8.74 years). This shows that retrocochlear effects from diabetic conditions might be occurring 10 ten years of DM diagnosis. The latencies produce information on how fast electrical sound signals are transmitted through various parts of the auditory brainstem.[32] Hence, the elongation of these latencies would suggest that there is a delay in the conduction of auditory signals within the brain stem with diabetes. Neuronal involvement is prominent among diabetic complications.[62] It is therefore not surprising that neurons at the brainstem would show significant changes with the diabetic condition. Very early studies showed changes occurring in the vasa nervorum of the seventh and eighth cranial nerves.[63] Pronounced neuronal damage and microglial activation occurred in the presence of hyperglycemia in the hippocampus and frontal cortex.[64] Reduced dendritic branching and spine density was observed in the presence of hyperglycemia of 8 weeks duration in Wistar rats.[65] Therefore, it is suggested here that the prolongation in waves latency observed in this review is due to hyperglycemia-induced changes in the neurons of the auditory brainstem. Brain-derived neurotrophic factor (BDNF) was found to be significantly reduced in the retina of STZ-diabetic rats when compared to controls,[66] and has been suggested as one factor in the pathogenesis of diabetic neuropathy/retinopathy. BDNF has also been shown to play a role in the development of auditory neurons and innervations,[67,68] and was reduced in the serum of diabetic patients.[69,70] It may play a role in neuronal pathology at the brainstem level in the diabetic state.

Oxidative stress has equally been implicated in the pathogenesis of diabetic neuropathy.[71] The presence of high glucose leads to the formation of free radicals through the defective functioning of the inner membrane of the mitochondria. This eventually results in excessive production of reactive oxygen species leading to neuronal cell death.[72–74] Treatment with antioxidants has been shown to reverse the effect of diabetes on nerve conduction velocities.[74] Therefore, delayed ABR latencies may in fact be preventable or reversible by antioxidant treatment. Further research in this area will improve our understanding of the pathogenesis of HL induced by the diabetic state and possible ways to prevent it.

We could not establish a statistical relationship between DM-induced HL and duration of DM from combined data analysis as there was not enough spread of the data for DM duration. However, through multivariate regression analysis, some studies showed that duration of DM had little effect on the incidence of HL seen in diabetic subjects.[35,37,42] This was corroborated by other studies.[75–77] Mean duration of type 2 DM was found to be longer among diabetic individuals with sensorineural HL when compared with their counterparts without sensorineural HL.[78] Gupta et al. also showed that with longer duration of DM, more diabetics had delayed ABR wave latencies.[38] Positive correlation between duration of DM and severity of DM were supported by other authors.[24,78] Similarly, the incidence of diabetic neuropathy was higher with increasing DM duration.[79] While it may appear that the observations regarding relationship of DM duration and occurrence of HL are divergent, logistic regressions was more in support of no association, four of the studies included in this review statistically showed no relationship, while only one did show a relationship. It appears that in the older age groups, HL incidence among control subjects approaches that in diabetic subjects. Austin et al. 2009[44] showed age-group–dependent differences in the incidence of HL when comparing diabetics to controls: In the older age groups HL was more among control subjects, it was almost the same for both groups in the middle age group, while in the younger age groups more DM than control subjects had HL.

There are a few limitations which could be potential sources of bias in this meta-analysis. Exclusion of publications in languages other than English, Spanish, and French could have eliminated studies with important results. Also, the inclusion of both ABR and PTA as tests of hearing would possibly give different results since ABR specifically assesses the retrocochlear pathway of hearing, while PTA is a behavioral test that encompasses the perception of hearing in its totality.[80] Some heterogeneity existed with the results provided by the included studies. This can be attributed to the number of studies included, variations in the sample sizes of the studies, differences in population, disparity in the proportions of diabetic to control participants in the included studies, and differences in the incidence of HL among control subjects across the included. Establishing a causal relationship between type 2 DM and HL is still intricate because the hearing levels of these individuals prior to the onset of DM are unknown, properly conducted prospective studies are required to study the progressive changes in hearing function in diabetics and matched controls and possibly establish a causal relationship. Diabetics show variations in many ways, among which are the treatment modalities and the level of glycemic controls that may have a potential for influencing the hearing thresholds. Randomizing patients to treatment groups in prospective studies will be helpful in assessing the effects of these covariables. Last, different population groups are presented in the studies; although age matched, it is not known how environmental effects can aggravate the effects of DM on hearing.

Nevertheless, this review provides some new information about the relationship between type 2 DM and HL, including: a) combined data analysis to obtain summary measure of odds ratio estimates relating to the effect of DM on hearing; b) the finding that at least mild

forms of HL are more common among diabetic individuals; c) PTA thresholds demonstrating slight to mild degree of HL at lower frequencies and mild to moderate degree of HL at higher frequencies; and (d) the impact of type 2 DM on ABR wave latencies, particularly wave V.

CONCLUSION

The results of this meta-analysis suggest that mild HL is more prevalent among diabetic subjects compared to nondiabetic subjects. A trend for (clinically significant) increased hearing thresholds for high frequency sounds among type 2 diabetics, especially in the older group, is also shown. ABR waves' latencies (particularly wave V) similarly showed a tendency for significant differences between diabetic and nondiabetic groups.

List of Abbreviations

Auditory brainstem evoked responses (ABR); decibels (dB); diabetes mellitus (DM); hearing loss (HL); hertz (Hz); odds ratio (OR); pure tone audiometry (PTA); standardized mean difference (SMD).

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