Association of age, gender and duration of diabetes with distortion product otoacoustic emissions in type 2 diabetes mellitus

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Abstract
Introduction: Screening of outer hair cells is necessary in identification of undetected hearing loss. Objectives: Present study is focused on functional analysis of outer hair cells by distortion product otoacoustic emissions (DPOAEs) in type 2 diabetes with and without hearing impairment.

Materials and Methods: This is a cross-sectional study, two groups i.e. WoHI (n=50) and WHI (n=50) of either sex with an age group of 35-55 were included. DPOAE screening is a non-invasive test protocol that assists to detect the accuracy of cochlear outer hair cell functioning and hearing at frequencies ranging from 1000Hz-4000Hz.

Statistical Analysis: The data were analyzed by Chi-square test to see the association between DPOAE screening of both the ears in WoHI and WHI groups with age, gender, duration of diabetes.

Results: The association of age with DPOAEs in WoHI and WHI groups, fail percentage of the right ear DPOAE in the age group 35-44 years were 11.5% and 16.6% respectively, it was not statistically significant (P=0.891). The association of gender with DPOAE screening in WoHI and WHI groups, fail percentage of the right ear DPOAE in the male group were 12% and 15% respectively and in the female group were 6.3% and 20% respectively, it was not statistically significant (P=0.435).

Conclusion: OAE alone does not assess the entire auditory pathway in diabetic persons. A thorough case history including duration of disease, age of onset and frequency of HbA1C monitoring and OAE screening is a quick noninvasive clinically feasible procedure for potentially identifying or detecting hearing impairment.

Keywords: Type 2 diabetes, DPOAEs, Duration of diabetes, WHI, WoHI.

Introduction
Screening of outer hair cells is necessary in identification of undetected hearing loss and provides information, whether the individual has higher potential to develop hearing loss or not. In the present study the OHCs are screened by distortion product otoacoustic emissions which are participated in the amplification process of hearing.1

DPOAEs are sounds generated in the cochlea and recorded in the ear canal and are produced through the nonlinear interaction of two closely spaced, external primary tones of frequencies f1 and f2 with f2 greater than f1. When the normal ear is stimulated simultaneously by two primary tones (f1 and f2), low-level, inter modulation distortion products (DP) can be measured in the ear canal. This distortion is a by-product of the amplification process of the outer hair cell active mechanism.2

Glucose metabolism has greater influence on the inner ear because it has higher metabolic activity so any disruptions in the glucose metabolism alter the hair cell function1. In diabetes the microvascular disease affects the stria vascularis which is responsible for the production of endolymph and driving force for mechanical transduction of hair cells.4,5 Hyperglycaemia is associated with increased blood viscosity in the cochlear micro circulation especially involving the stria vascularis. The associated tissue ischemia and hypoxia can cause damage to single or multiple cells. The high dependence on glucose as the source for its high energy consumption makes the cochlea a target of damage in DM6. The above reasons are initiated to study the changes in DPOAE screening in T2DM subjects with and without hearing impairment in the present study.

Materials and Methods
Study Design: It is a cross-sectional study.
Inclusion Criteria: The present study was carried out after getting the ethics committee approval (FWA00002084; dated 16/03/2015). In the present study two groups i.e. Without hearing impairment (WoHI) (n=50) and with hearing impairment (WHI) (n=50) of either sex with an age group of 35-55 were included. The participants were enrolled in the study after acquired the informed consent.

Exclusion Criteria: Participants who had a history of immune/ metabolic diseases like hyperbilirubinaemia/kernicterus, polyarteritis nodosa, type 1 diabetes, paraproteinaemias, anoxia /hypoxia, sarcoidosis, rheumatoid arthritis, uraemia, Guillain-Barré Syndrome, chronic infections like Leprosy, AIDS, Borreliosis, Ramsey Hunt syndrome, using heavy metals like lead, cobalt, mercury; drugs like carboplatin, methyldopa and reserpine; neoplasma /intracranial cystic lesions, chronic middle ear diseases, cranial trauma, ear surgeries, recent surgeries, congenital problems, noise exposure, smoking, alcoholism, hypertension, stroke and hepatic encephalopathy were excluded from the study.

Methods
Screening of DPOAEs: DPOAE screening is a conventional objective, non-invasive test protocol that
assists to detect the accuracy of cochlear outer hair cell functioning and hearing at frequencies ranging from 1000Hz-4000Hz. The DPOAEs are screened with instrument Biologic Scout Sport system (Natus, USA).

The subject is seated comfortably with relaxation; a probe wire is inserted in the patient’s ear. The stimulus used is click sound, with an intensity of 65-70 dB Sound Pressure Level (SPL) and test frequencies include 1000Hz-4000 Hz. The subject is instructed to stay still as the instrument would collect the responses automatically with no specific participation of the subject. The results thus obtained are numerical representations for the formula 2f1-f2. Results obtained with a noise floor of more than 6 dB are noted as no response. Thus, after the compilation using the formula, the final results of the test are displayed as Pass or Refer, which in turn explain the outer hair cell functioning. Pass means normal functioning and Refer means abnormal, and requires further investigation with brainstem auditory evoked potentials. OAEs would be present in neural pathology while absent in cochlear pathology. In the present study if the subject result of OAEs is “pass”, considered it as 0 and if the result is “refer or fail” then it is considered as 1.

**Statistical Analysis**

All the data were expressed as frequency distribution. The data were analyzed by Chi-square test to see the association between DPOAE screening of both the ears in WoHI and WHI groups with age, gender, duration of diabetes values. For all the statistics and graph plotting, Sigma Plot 13.0 (Systat software, USA) was used. P <0.05 was considered as significant.

**Results**

The association of age with DPOAE screening in WoHI and WHI groups were given in table 1. The WoHI and WHI groups, fail percentage of the right ear DPOAE in the age group 35-44 years was 11.5% and 16.6% respectively and in the age group 45-55 years were 8.3% and 23% respectively, it was not statistically significant (P=0.891). The fail percentage of the left ear DPOAE in the age group 35-44 years were 8.3% and 23% respectively and in the age group 45-55 years were 4.2% and 23% respectively, it was also found to be not statistically significant (P=0.484). This showed that there was no association between the age and DPAOE of both ears in WoHI and WHI groups.

The association of gender with DPOAE screening in WoHI and WHI groups were given in table 2. The WoHI and WHI groups, fail percentage of the right ear DPOAE in the male group were 12% and 15% respectively and in the female group were 6.3% and 20% respectively, it was not statistically significant (P=0.435). The fail percentage of the left ear DPOAE in the male group were 15% and 18% respectively and in the female group were 6.3% and 30% respectively, it was also found to be not statistically significant (P=0.340). This showed that there was no association between the gender and DPAOE of both ears in WoHI and WHI groups.

The association of duration of diabetes (DOD) with DPOAE screening in WoHI and WHI groups were given in table 3. The WoHI and WHI groups, fail percentage of the right ear were 6% and 10% respectively, it was not statistically significant (P=0.891). The fail percentage of the WoHI and WHI groups left ear were 4% and 12% respectively, it was statistically significant (P=0.003). This showed that there was no association between the DOD and DPAOE in the right ear and there was association in the left ear of WoHI and WHI groups.

The association of gender with DPOAE screening in both the ears in WoHI and WHI groups.

**Table 1: Association of age with DPOAE screening in WoHI and WHI groups**

<table>
<thead>
<tr>
<th>Ear</th>
<th>Age (years)</th>
<th>WoHI group</th>
<th>WHI group</th>
<th>X^2 value and p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Pass</td>
<td>Fail</td>
<td>Pass</td>
</tr>
<tr>
<td>Right</td>
<td>35-44</td>
<td>23</td>
<td>3</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>45-55</td>
<td>22</td>
<td>2</td>
<td>20</td>
</tr>
<tr>
<td>Left</td>
<td>35-44</td>
<td>24</td>
<td>2</td>
<td>22</td>
</tr>
<tr>
<td></td>
<td>45-55</td>
<td>23</td>
<td>1</td>
<td>20</td>
</tr>
</tbody>
</table>

Values are number of subjects with pass or fail of DPOAE.

**Table 2: Association of gender with DPOAE screening in WoHI and WHI groups**

<table>
<thead>
<tr>
<th>Ear</th>
<th>Gender</th>
<th>WoHI group</th>
<th>WHI group</th>
<th>X^2 value and p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Pass</td>
<td>Fail</td>
<td>Pass</td>
</tr>
<tr>
<td>Right</td>
<td>Male</td>
<td>30</td>
<td>4</td>
<td>33</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>15</td>
<td>1</td>
<td>8</td>
</tr>
<tr>
<td>Left</td>
<td>Male</td>
<td>29</td>
<td>5</td>
<td>33</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>15</td>
<td>1</td>
<td>7</td>
</tr>
</tbody>
</table>

Values are number of subjects with pass or fail of DPOAE.
Table 3: Association of duration of diabetes (DOD) with DPOAE screening in WoHI and WHI groups

<table>
<thead>
<tr>
<th>Ear</th>
<th>DOD (years)</th>
<th>WoHI group</th>
<th>WHI group</th>
<th>$X^2$ value and p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Pass</td>
<td>Fail</td>
<td>Pass</td>
</tr>
<tr>
<td>Right</td>
<td>5-15</td>
<td>47</td>
<td>3</td>
<td>45</td>
</tr>
<tr>
<td>Left</td>
<td>5-15</td>
<td>48</td>
<td>2</td>
<td>44</td>
</tr>
</tbody>
</table>

Values are number of subjects with pass or fail of DPOAE.

Discussion

The standard pure tone audiometry tests up to 8 kHz frequency, but evaluating hearing status at higher frequencies may be crucial in such cases as monitoring noise exposure or ototoxicity. High frequency hearing loss affects OAEs at lower frequencies, and therefore OAEs can be good indicators for predicting preclinical changes in the cochlea. DPOAEs are used to determine the cochlear pathology associated with the sensorineural hearing loss. If the DPOAEs are normal they evidenced that outer hair cell function is normal regardless of the audiometric data. This finding strongly supports the present study because the subjects are having higher pure tone average values in WHI group but they showed normal DPOAE.

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In the present study the DPOAE screening of both right and left ears of the study groups did not show association with age, gender, duration of diabetes, BMI and Hba1c values. In T2DM patients the amplitude of DPOAEs at all frequencies decreased, it suggests that the functioning of the outer hair cells are impaired but the medial olivocochlear efferent system was not affected. As the age advances both OHC loss and reduced EP result in elevated hearing thresholds on distortion threshold levels (HTL). Reduced EP affects the inner hair cell responses in two ways: as a result of the reduced voltage across the transduction channels and from the reduced output of the cochlear amplifier. The medial olivocochlear fibres (MOC) inhibit the function of outer hair cells, when these fibres are disrupted and lost their inhibition on OHCs. In the present study, association between age and DPOAE is not present in WoHI and WHI groups for both the ears. Ottaviani et al (2002) did not found any association among the duration of diabetes, Hba1c and OAE amplitudes in their regression analysis. The present study is in line with this previous research reported.

Conclusion

DPOAEs result “Pass” means the outer hair cellular functioning is normal and “Fail or Refer” means the outer hair cellular function is abnormal and the subject is referred for further investigations with PTA and BAER. Age, gender, duration of diabetes, BMI and Hba1c are not associated with results of DPOAEs in both the ears of WoHI and WHI groups. OAE alone does not assess the entire auditory pathway in diabetic persons. A thorough case history including duration of disease, age of onset and frequency of Hba1c monitoring and OAE screening is a quick non-invasive clinically feasible procedure for potentially identifying or detecting hearing impairment.

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Conflict of Interest: NIL

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