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ORIGINAL ARTICLE

Changes in middle ear transmission characteristics secondary to altered bone remodelling

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Abstract

Summary Alteration in the process of bone remodelling results in conditions like osteopenia and osteoporosis in which the bones become susceptible to fracture. The functioning of middle ear bones in such individuals were assessed in this study and it was found that the middle ear bones are equally susceptible to micro-fractures and can cause reduction in the transmission of sound energy.

Introduction Alteration in the process of bone remodelling or increase in the number of osteoclasts cells as it occurs in osteoporosis and osteopenia are likely to affect the middle ear bones in the same way it affects the skeletal bones. Whether these micro-structural changes occurring at the level of the middle ear secondary to altered bone remodelling cause any significant impairment in its functioning is not explored. Thus, the present study aimed at assessing the different aspects of middle ear functioning in individuals with reduced BMD.

Methods The study included 25 normal, 39 osteopenic and 40 osteoporotic participants. The participants underwent pure-tone audiometry, otoscopic examination, conventional immittance evaluation using a 226 Hz probe tone, multi-component and multi-frequency tympanometry and acoustic reflex threshold testing. None of the participants had any current or previous history of middle ear effusion.

Results A significantly higher proportion of participants in the clinical group had hearing loss compared to the normal group. The clinical group participants also had reduced middle ear resonance frequency, elevated static compliance values and elevated or absent acoustic reflexes compared to the normal participants. There was no difference among the three groups for the proportion of participants having conductive hearing loss.

Conclusions There is a detrimental impact of reduction in bone mineral density on middle ear transmission characteristics which may go unnoticed initially. Treatment of osteoporosis may potentially mitigate hearing loss from middle ear fractures due to reduced bone mineral density. Absence of significant air-bone gap with the presence of reduced middle ear resonance frequency may be early signs of reduced BMD.

Keywords Middle ear · Osteopenia · Osteoporosis

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Introduction

The normal metabolic balance of bone is maintained by relatively equal bone formation and bone resorption, which are maintained by osteoblasts and osteoclasts respectively [1]. When bone resorption occurs at a faster rate compared to bone formation, the volume of the bone remains the same; however, its density decreases and the bone becomes brittle which makes the bones more susceptible to fractures [2]. Early diagnosis of such condition becomes important in order to prevent adverse consequences. DXA (dual energy x-ray absorptiometry) bone mineral density (BMD) has been reported to correlate well with the total bone strength. The reduction in BMD is measured using T-scores. WHO criteria defines T-score of more than − 1 as normal, − 1 to − 2.5 as osteopenia, and less than − 2.5 as osteoporosis [3]. Osteopenia is a milder form of bone loss and it is thought to be a precursor of osteoporosis. In osteoporosis, the amount of cortical and cancellous bone is decreased, haversian canals are widened, and the rate of bone resorption exceeds the rate of bone formation [4]. The decrease in the density of bone is often progressive and there are no symptoms. However, the bones become susceptible to fracture.

The ossicles in the middle ear are bony structures and are responsible for transmitting sound energy from outer ear to the inner ear. Any alteration in the process of bone remodelling or increase in the number of osteoclasts as occurs in osteoporosis and osteopenia is likely to affect middle ear structures [5–7]. A study by Kanzaki and colleagues in 2006 showed thinning of the manubrium of the malleus and incus in mice with altered bone remodelling [5]. Other authors showed that individuals with altered bone remodelling are at 1.31 times greater risk of acquiring cholesteatoma [6] and middle ear fractures [7]. A study of the effect of osteoporosis on middle ear ossicles reported that a reduction in BMD leads to multiple micro-fractures at different foci of the middle ear ossicles [7]. Structural changes (intraosseous micro-fracture) in the middle ear ossicles secondary to altered bone remodelling may also change the normal sound transmission characteristics of the middle ear.

Changes in middle ear transmission characteristics might result in a reduction in the intensity of sound reaching the inner ear, thereby causing hearing loss. Excess of osteoclast cells may also result in thinning of middle ear bones at various sites [7]. They can also reduce the overall stiffness of the middle ear which may cause alteration in the middle ear admittance, susceptance, conductance and resonance frequency.

Adequate calcium is necessary for normal bone remodelling [8], but calcium is also responsible for the neurotransmission of impulses between synapses [9]. Hence, any alteration in the optimal functioning of calcium might result in abnormality in the acoustic reflex threshold. Various studies have shown an association between altered bone remodelling and hearing loss [10–15]; however, most of them have reported an association between reduced BMD and sensorineural hearing loss [10, 12, 13]. Although few studies have assessed middle ear functioning in these individuals and have reported abnormal findings, the research in this aspect is sparse and is less comprehensive [11, 14]. Thus, the present study aimed to understand the effect of reduced bone mineral density on various aspects of middle ear functioning and its characteristics.

Method

Participants

The study included 104 participants, 57 females and 47 males, who underwent DXA BMD under the supervision of an orthopaedic surgeon. The density of the total hip is recommended for BMD measurement due to its high precision, reproducibility and correlation with the risk of fractures [16]. The BMD measurements obtained from the lumbar spine are also highly reproducible, but the chances of artefacts are relatively high [17]. As an optional measure, the BMD can also be estimated from the forearm, especially when it is not possible to measure it from the hip or spine; however, these measures are confounded by the differences in BMD between the dominant and the non-dominant hands [17]. BMD at the hip is the single most reliable factor for predicting hip fracture risks, and spinal bone mineral density can be used for monitoring treatment outcomes, if at all [18]. Therefore, the present study used BMD measurements from the hip utilising the total hip BMD. The patients were classified into normal (T-score ≥ -1.0), osteopenia (T-score between − 1.1 and − 2.4) and osteoporosis (T-score ≤ -2.5) [3]. The present study had 25 individuals with normal BMD (mean age = 54.9 years, SD = 12.24; 13 female and 12 male), 39 participants with osteopenia (mean = 56.2 years, SD = 13.32; 22 female and 17 male) and 40 participants with osteoporosis (mean age = 59.4 years, SD = 9.4; 22 female and 18 male). There was no significant difference in the age of the participants of the three groups on administration of Kruskal-Wallis *H* test. Otoscopic examination was done to rule out otitis media and effusion. All participants in the study were native south Indians dwelling in the state of Karnataka, and there were no cultural or ethnic differences among them.

Instrumentation and test environment

A calibrated two-channel clinical audiometer (Inventis Piano with TDH-39 supra-aural headphones, housed in MX-41/AR ear cushions [Telephonics, Farmingdale, NY, USA]) was used for finding air-conduction thresholds and carrying out speech audiometry. Radio ear B-71 bone vibrator (Radio ear, KIMMETRICS, Smithsburgh, Maryland, USA) along with the same audiometer was used for measuring bone-conduction thresholds. A calibrated middle ear analyser (Grason-Stadler Incorporated [GSI] Tympstar [GSI VIASYS Healthcare, WI, USA]) was used for obtaining the tympanogram type and static compliance at 226 Hz, acoustic reflex threshold and resonance frequency of the middle ear. Multi-component tympanometry at 226 Hz, 678 Hz and 1000 Hz was done to find the susceptance and the conductance component.

Procedure

A detailed case history was obtained from all participants including any complaint or history of hearing loss, otorrhoea, otalgia, recent upper respiratory tract infection and tinnitus. Individuals having a history of conductive pathology caused by middle ear effusions (otitis media) were excluded from the study. All participants underwent pure tone audiometry from 250 to 8 kHz using the preferred method for clinical determination of pure tone thresholds modified by Carhart and Jerger, 1959 [19]. A 226 Hz probe-tone frequency was used for obtaining ear canal volume, admittance at the tympanic membrane and tympanometric peak pressure. For obtaining tympanograms, the pressure in the ear canal was swept from + 200 daPa to − 400 daPa at the rate of 200 daPa/s. For obtaining susceptance and conductance tympanograms, the probe-tone frequencies of 678 Hz and 1000 Hz were used and the pressure in the ear canal was swept at the rate of 200 daPa/s. The obtained tympanograms were classified into 'XBYG' at each of these probe-tone frequencies and groups, where 'X' and 'Y' represent the number of extremes (positive and negative peaks are both counted as extremes) observed in susceptance and conductance tympanograms, respectively. The 226 Hz probe-tone was also used for recording acoustic reflex thresholds elicited using ipsilateral and contralateral (only one at a time) presentation of the reflex triggering tones of 500, 1000, 2000 and 4000 Hz. The lowest stimulus level resulting in a compliance change of 0.03 mmho was considered as acoustic reflex threshold. For obtaining the resonance frequency of middle ear, the probe-tone was swept from 200 to 2000 Hz at the rate of 50 Hz. The frequency at which the susceptance curve first showed a notch was considered resonance frequency.

Statistical analyses

The data analysed included T-score, age, four frequency pure-tone average (PTA), static admittance at tympanic membrane, resonance frequency of middle ear and acoustic reflex thresholds (ART). Shapiro-Wilk's test for normality was administered to understand the distribution of the data. Most of the parameters analysed showed non-normal distribution ($p < 0.05$). Hence, non-parametric statistical techniques were used for within and between group comparisons of data as well as correlation analyses. The Wilcoxon signed rank test was done to investigate ear differences for PTA, static admittance, resonance frequency and ART. There was no significant effect of ear for any parameter ($p > 0.05$); hence, the data of the two ears were combined. The Kruskal-Wallis H test was administered for between group comparisons of various measures described above. The Mann-Whitney U test was done for pair-wise comparisons between groups in case there was a significant group difference on the Kruskal-Wallis H test. Spearman's correlation analyses were done to examine the relationships between the variables.

Results

Pure tone audiometry

PTA > 15 dB HL was considered as presence of hearing loss as per the modified classification for degree of hearing loss [20]. Using this criterion, 40% of ears in the normal group, 62% in those with osteopenia and 90% of ears in the osteoporosis group had hearing loss. The equality of test for proportion was administered to check for differences between groups for the presence of hearing loss. The details are described in Table 1. Figure 1 shows the PTA of participants of all three groups in the form of a bee swarm plot. Hearing loss greater than a mild degree can pose subtle or obvious difficulties in real life communicative situations [21]; hence, the number of participants having hearing loss greater than 25 dB HL was also analysed. It was found that 22% of individuals in the control group, 33% in osteopenia group and 64% in the osteoporosis group had hearing loss of mild or higher degree. The outcomes of equality of test for proportions for this parameter are shown in Table 1. A difference of more than 15 dB between two ears at any frequency was operationally defined as significant asymmetry in hearing loss. No participant in the present study showed significant asymmetry in hearing loss.

The presence of conductive pathology was evident in 18.75% of ears in osteoporosis group and 14% each in osteopenia group and group with normal BMD. There was no significant difference in the proportion of participants having conductive pathology among the groups ($p > 0.05$, equality of test for proportions).

Static compliance

The normative range for static compliance is 0.5 to 1.75 mmho [22]. Abnormal static compliance (reduced or increased beyond the normative data) was observed in 23/80 (28.75%; 16 abnormally high and 7 abnormally low) ears in osteoporosis group, 18/78 (23.07%; 16 abnormally high and 2 abnormally low) in osteopenia group and 5/50 (10%; 3 abnormally high and 2 abnormally low) in normal BMD group. The outcomes

Table 1 Results of 'equality of test for proportion' for various test outcomes

Test out comes	Normal and osteopenia	Normal and osteoporosis	Osteopenia and osteoporosis
PTA > 15	$Z = 2.52$, $p = 0.01$*	$Z = 6.3$, $p = 0.000$*	$Z = 4.25$, $p = 0.000$*
PTA > 25	$Z = 1.38$, $p = 0.16$	$Z = 6.25$, $p = 0.000$*	$Z = 3.82$, $p = 0.001$*
Abnormal SC	$Z = 2.03$, $p = 0.04$*	$Z = 2.5$, $p = 0.01$*	$Z = 0.62$, $p = 0.5$
Abnormal RF	$Z = 3.39$, $p = 0.007$*	$Z = 5.46$, $p = 0.000$*	$Z = 5.19$, $p = 0.000$*
Absent ART	$Z = 0.72$, $p = 0.47$	$Z = 2.23$, $p = 0.03$*	$Z = 1.81$, $p = 0.07$*

PTA pure tone average, *SC* static compliance in mmho, *RF* resonance frequency in Hz, *ART* acoustic reflex threshold

*mark indicates significant difference between groups for the presence of abnormality

of statistical comparison using equality of test for proportions are shown in Table 1.

Resonance frequency of middle ear

The normative range for resonance frequency of the middle ear is 800 to 1200 Hz [23]. In the control group, 6/48 (12.5%) ears showed abnormal resonance frequency. Out of those, 1 ear had increased resonance frequency and 5 ears had reduced resonance frequency. In the osteopenia group, 32/78 (41.02%) ears showed abnormal resonance frequency out of which 14 had increased and 18 had reduced resonance frequency. In the osteoporosis group, 65/80 (81.25%) ears had abnormal resonance frequency, out of which 16 had increased resonance frequency and 49 had reduced resonance frequency. The outcomes of statistical comparison using equality of test for proportions are shown in Table 1.

The Kruskal-Wallis *H* test revealed presence of significant difference in resonance frequency of middle ear among the groups [$\chi^2 = 15.01$, $p = 0.001$]. The Mann-Whitney *U* test for pair-wise comparisons revealed significantly lower middle ear resonance frequency in osteoporosis than osteopenia [$Z = 2.18$, $p = 0.05$] and the group with normal BMD [$Z = 2.99$, $p = 0.008$]. Further, middle ear resonance was also significantly lower in osteopenia than the group with normal BMD [$Z = 3.54$, $p = 0.001$]. Figure 2 shows the individual resonance frequency data depicted in a beeswarm plot with overlapped box-plot.

Multi-component tympanometry

Multi-component tympanometry could be done in only 13, 19 and 21 individuals in normal BMD, osteopenia and osteoporosis groups, respectively. This was due to the test being a late introduction to the protocol. Equality of test for proportion was done for between group comparisons of these proportions for 678 Hz and 1000 Hz probe-tone frequencies. A significantly larger proportion of ears in the

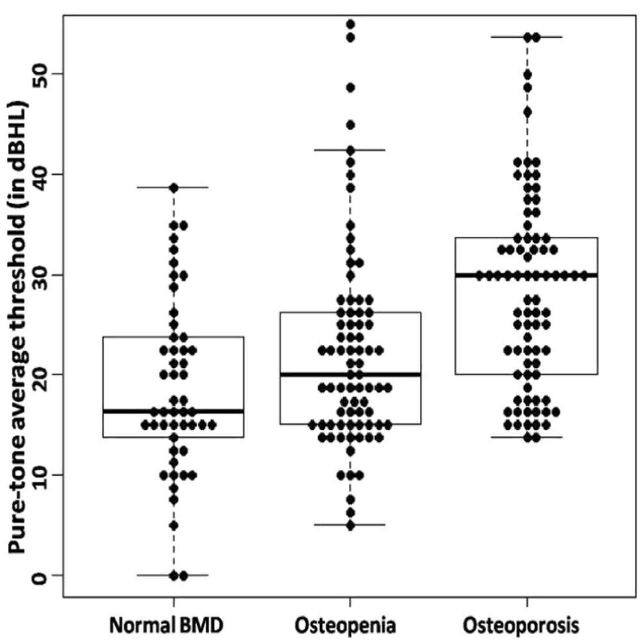

Fig. 1 Pure-tone average thresholds of individuals with normal bone mineral density, osteopenia and osteoporosis

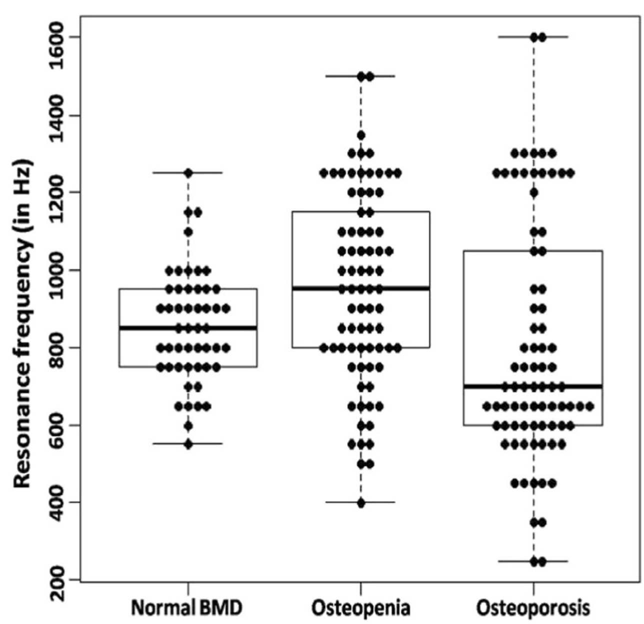

Fig. 2 Resonance frequency of middle ear of individuals with normal bone-mineral density, osteopenia and osteoporosis

Table 2 Percentage of ears having various types of susceptance and conductance tympanograms when using 678 and 1000 Hz probe-tone frequencies in various groups

Groups	Probe-tone frequency = 678 Hz				Probe-tone frequency = 1000 Hz			
	1B1G	3B1G	3B3G	5B3G	1B1G	3B1G	3B3G	5B3G
Normal ($N = 26$)	80.77^{ψ}	19.23	$0^{\delta\psi}$	0	3.84	$92.30^{\delta\psi}$	3.84^{ψ}	0^{ψ}
Osteopenia ($N = 38$)	84.21^{ψ}	0^{ψ}	15.79	0	10.52	$57.89^{€\psi}$	21.05	10.52^{ψ}
Osteoporosis ($N = 42$)	$33.33^{€\delta}$	30.95^{δ}	35.71	0	11.90	$21.42^{€\delta}$	$38.09^{€}$	$28.57^{€\delta}$

N no. of participants in that group

ψ statistically significant difference from osteoporosis group ($p < 0.05$)

δ statistically significant difference from osteopenia group ($p < 0.05$)

€ statistically significant difference from normal BMD group ($p < 0.05$)

osteoporosis group revealed a 3B3G pattern for the 678 Hz probe tone frequency and 5B3G pattern for 1000 Hz probe-tone frequency than the osteopenia and normal BMD groups ($p < 0.05$). The percentage of ears with various patterns of susceptance and conductance tympanograms and outcomes of equality of tests for proportions are shown in Table 2.

Acoustic reflex thresholds

Both ipsilateral and contralateral acoustic reflexes were absent in more participants at each frequency in the two clinical groups than in the control group; however the absence of acoustic reflex at all four frequencies was operationally defined as an abnormal result. The osteoporosis group had 28.75% of individuals with absence of reflexes, whereas the osteopenia group and control group had 16.67% and 12% individuals with absent reflexes respectively. The Kruskal-Wallis *H* test showed significant differences in ipsilateral as well as contralateral acoustic reflex thresholds among the groups ($p < 0.05$). The Mann-Whitney *U* test revealed no significant difference for acoustic reflex threshold between normal BMD and osteopenia group ($p > 0.05$). However there were significant differences between normal BMD and osteoporosis groups and between the osteopenia and osteoporosis groups ($p < 0.05$). The outcomes of the Mann-Whitney *U* test for pair-wise comparisons are shown in Table 3.The relationship between T-score and acoustic reflex threshold was investigated using Spearman's rank correlation and the results revealed significant negative correlation between the two variables ($p < 0.05$). This means that a higher level of stimulation was required to elicit acoustic threshold in those who had reduced 'T' scores.

Vitamin D values were available for 19 participants of which 12 were in the osteoporosis group and 7 in osteopenia group. The correlation between BMD scores (i.e. T-score) and Vitamin D levels was moderately positive yet significant ($r_s = 0.479$, $p = 0.038$) in these participants (Supplement Fig. 1 shows the scatter plot of this correlation). However, among these participants, there was no significant correlation between Vitamin D levels and any of the other parameters used in the present study. Supplement Table 1 shows the outcomes of correlation between vitamin D levels and various parameters used in the present study.

Discussion

The current study was aimed at assessing alterations in middle ear sound transmission characteristics due to decreased BMD. The study showed that a higher proportion of participants with reduced BMD had hearing loss compared to the individuals with normal BMD. Alterations in bone remodelling may affect the middle ear bones in a similar manner to the bones of the skeletal system. Studies have shown alterations in the middle ear ossicles secondary to reduced bone mineral density [5, 7]. Osteoprotegrin (OPG) is a regulator of bone metabolism as it inhibits the differentiation, survival and fusion of osteoclastic precursor cells and promotes apoptosis of osteoclasts. Kanzaki et al. [5] observed erosion of the malleus, incus and the stapedial fixation in adult mice deficient with OPG. Thus normal OPG is necessary for equilibrium of osteoblasts and osteoclasts cells and maintenance of healthy middle ear bones. Thus any alteration in the bone mineral metabolism would result in structural changes at the level of the middle ear and might also cause attenuation of sound travelling to the inner ear thereby resulting into hearing loss.

Demineralisation of the cochlear capsule can affect the hearing system both structurally [24–26] and functionally [10–15]. Reduced intestinal absorption of calcium may play a role in some cases of osteoporosis [8, 27]. Calcium and other ions are necessary for the electro-motility of outer hair cells

Table 3 Median ipsilateral and contralateral acoustic reflex thresholds at 500, 1000, 2000 and 4000 Hz in groups with normal BMD, osteopenia and osteoporosis and outcomes of Mann-Whitney *U* test for between group's comparisons of acoustic reflex thresholds

Frequency (in Hz)	Normal BMD		Osteopenia		Osteoporosis	
	Ipsi ART	Contra ART	Ipsi ART	Contra ART	Ipsi ART	Contra ART
500	90^{ψ}	95^{ψ}	85^{ψ}	97.5^{ψ}	$95^{\delta€}$	$100^{\delta€}$
1000	90^{ψ}	97.5^{ψ}	90^{ψ}	97.5	$95^{\delta€}$	$100^{€}$
2000	95^{ψ}	100^{ψ}	95^{ψ}	100	$100^{\delta€}$	$105^{€}$
4000	100	100^{ψ}	100	100	100	$105^{€}$

BMD bone-mineral density, *Ipsi ART* ipsilateral acoustic reflex threshold, *Contra ART* contralateral acoustic reflex threshold

ψ statistically significant difference from osteoporosis group ($p < 0.05$)

δ statistically significant difference from osteopenia group ($p < 0.05$)

€ statistically significant difference from normal BMD group ($p < 0.05$)

and energy transmission at the level of the cochlea [9]. The findings from our study could also be attributed to alterations of the cochlea both structurally and functionally due to metabolic changes subsequent to altered bone remodelling. The results from our study are consistent with previously reported studies that have found associations between hearing loss and bone mineral density [10–15]. There have also been reports that the individuals with reduced bone mineral density are at higher risk for developing hearing loss [13].

In the osteoporosis group, approximately 90% of ears had more than minimal hearing loss, and 64% had hearing loss of greater than mild degree but those having conductive pathology was only around 19%. For the osteopenic group, only 14% had conductive pathology, which was much less compared to the proportion of those who had hearing loss. The above findings indicate that though there is significant impairment in the detection of sound, the functional abnormality is more at the level of the cochlea and less at the level of middle ears. Though there are studies showing thinning and structural changes of the middle ears [5, 7], these initial microdeterioration may not necessarily result in hearing loss. Also the above studies were done on animals and generalisation to humans is difficult. Initial deterioration in the structure due to reduced bone mineral density might result in more subtle problems which may not cause a functional air bone gap in these participants.

A significantly higher number of participants in the osteoporosis group showed abnormal static compliance compared to the control group. There were no significant differences between the two clinical groups. Static compliance is the measure of transmission of longitudinal sound waves via the middle ear. The findings indicate that obvious difference in the functioning of transmission occurs only when the bone mineral density values are very different. Initial microdeterioration of the middle ear structures [5, 7] may not result into noticeable differences in the static compliance characteristics; however, an increase in severity might lead to the significant differences seen in our study.

Middle ear resonance frequency was seen to be increased as well as reduced in a significantly higher proportion of the clinical groups compared to the normal BMD group. There have been a few studies which have shown an association between reduced BMD and otosclerosis [28, 29]. Atan and colleagues evaluated BMD levels in patient who had underwent exploratory tympanotomy after being diagnosed with otosclerosis. The authors found that patients with otosclerosis had reduced BMD compared to normal; however, the reduction in BMD was not severe enough to categorise the pathological population either into osteopenia or osteoporosis [28]. Tonuk and colleagues reported increased BMD levels in patients with otosclerosis [30]. In the present study, a very high participation of individuals with osteopenia and osteoporosis had reduced resonance frequency. Microfractures in the middle ear bones secondary to reduction in bone mineral density [5, 7] might result in reduction of resonance frequency.

Resonance frequency is inversely proportional to the root of the mass, and as the density of the bone decreases as seen in osteoporosis without any changes in the volume, the resonance frequency also reduces. The findings also suggest that the middle bones may be more susceptible to fracture with alteration in BMD, which is consistent with Swinnen's studies [31]. Alteration in bone remodelling would thus definitely affect the transmission characteristics the middle ear due to structural changes.

The present study also showed that as BMD decreases, the acoustic reflex threshold increases. This could be related to the reduction in middle ear resonance frequency and presence of middle ear problems. Subtle middle ear abnormalities will in turn necessitate higher energy to elicit the stapedial reflex. The degree of hearing loss increases with the decrease in BMD. Changes in middle ear functioning probably due to intraosseous fractures in the middle ear bones result in reduced resonance frequency. Alteration in the functioning of middle ear is silent as the reduction in the resonance frequency does not result in a significant air bone gap.

However, with increasing severity, there could be attenuation of sound transmission resulting in an air-bone gap and higher acoustic reflex threshold.

There was a significant positive correlation between T-score and Vitamin D levels in a small number of participants for whom both these values were available. This is in agreement with reports of a positive association between BMD and Vitamin D levels, especially when the levels of Vitamin D are 30 ng/ml [32] or less. However, we found no significant correlation between vitamin D levels and any audiological measure in the present study. This may be due to the small sample size for which vitamin D levels were known. Future studies could look at evaluating the correlation using larger numbers of subjects.

Conclusion

There is a detrimental impact of reduction in BMD on the middle ear transmission characteristics which may go unnoticed initially. Treatment of osteoporosis may potentially ameliorate hearing loss due to middle ear fractures from reduced BMD. The absence of a significant air-bone gap with the presence of reduced middle ear resonance frequency may be early signs of reduced BMD.

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Compliance with ethical standards

Conflicts of interest None.

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