Audiological and Vestibular Assessment in Individuals with Osteopenia and Osteoporosis

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LIST OF ABBREVIATION

BMD: Bone Mineral Density

DEXA: Dual X-ray Absorptiometry

PTA: Pure tone Audiometry

SRT: Speech recognition threshold

SIS: Speech identification score

RF: Resonance frequency

SC: Static compliance

ECV: Ear canal Volume

OAE: otoacoustic emission

TEOAE: Transient Evoked Otoacoustic emission

DPOAE: distortion Product Otoacoustic emission

ABR: Auditory Brainstem Response

FST: Fukuda Stepping Test

SVV: Subjective Visual Vertical

cVEMP: Cervical Vestibular Evoked Myogenic Potential

oVEMP: Ocular Vestibular Evoked Myogenic Potential

vHIT: Video Head Impulse Test

RALP: Right Anterior Left Posterior

LARP: Left Anterior Right Posterior

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ABSTRACT

Excess of bone resorption compared to formation results in conditions like osteopenia and osteoporosis consequently making the bone brittle and more susceptible to fractures. The optimal functioning of calcium is altered in this pathology. Ear being primarily composed of skeletal structures and the requirement of optimal level of calcium for its normal functioning right from the pinna to the inner hair cells and vestibule makes it important to assess the function of auditory and vestibular system holistically in patients with altered bone remodeling. The present study included 122 participants, out of which 43 osteoporotic, 41 osteopenic and 38 age matched individuals with normal bone mineral density (BMD). All the participants underwent detailed audiological and vestibular assessment. The detailed audiological and vestibular evaluation includes pure tone audiometry (PTA), immittance evaluation, transient evoked otoacoustic emission, click evoked ABR (threshold estimation and at varying repetition rates), Fukuda stepping test, Subjective visual vertical test, cVEMP , oVEMP and vHIT. The present study showed that the participants with reduced bone mineral density have poorer hearing thresholds as evidenced on PTA and click evoked ABR. The osteopenic and osteoporotic participants also had reduced middle ear resonance frequency and elevated and absent acoustic reflexes. The vestibular functioning was also seen to be affected in comparison to the age matched normal BMD individuals based on subjective and objective vestibular tests. The metabolic changes at the level of the cochlea secondary to sub-optimal functioning of calcium might be a probable reason behind the significant consequences of reduced bone mineral density. Vestibular abnormality could be attributed to the changes of the calcium carbonate otoconia particles possibly secondary to altered bone remodeling. One can also presume vestibular problems in individuals with reduced bone mineral density are consequent to

sympathetic remodeling; nonetheless it is difficult to state with any degree of certainty whether altered bone remodeling lead to vestibular problems or vice versa. The present study provides the evidence of involvement of audio-vestibular system in participants with osteopenia and osteoporosis and shreds the need of their holistic assessment in order to rehabilitate them better and earlier.

Key Words: *Osteopenia, Osteoporosis, Auditory system, Vestibular system,*

Introduction

Osteoporosis is a clinical state associated with increased brittleness and fragility of bones due to loss of tissue, typically as a consequence to hormonal changes, deficit of calcium and/or paucity of vitamin D (WHO, 2004). Osteopenia is lesser severe clinical form than osteoporosis, also associated with reduction in protein and mineral content of bone tissue (WHO, 2004). These two conditions thus represent the array of clinical forms of reduced bone mineral density.

Demineralization of bones is a universal phenomenon for the entire human race. Demineralization is usually counterbalanced by remineralization for appropriate preservation of the bone strength (IOF, 2015). When this balance tilts in the favour of excessive bone mineral resorption, bones become weak, brittle and more susceptible to fractures over the years. This continuous demineralization and remineralization, often referred to as bone remodeling, explains the pathophysiology of osteoporosis (IOF, 2015).

The metabolic balance between the activities of the osteoclasts and osteoblasts determines the equilibrium between demineralization and remineralization (Hwang & Putney, 2011). The changes in the intracellular calcium ion (Ca^{2+}) concentrations control the differentiation and functions of osteoclasts (Hwang & Putney, 2011). Further, the alterations in concentrations of the intracellular calcium ions are believed to act as the common triggers of diverse signaling pathways, including enzyme activation, cell survival and cell differentiation (Huang & Putney, 2011). This would mean that a decline in the calcium ion concentration is directly linked to not only the cell differentiation and survival but also the performance of various neural pathways. All this in unison augments the brittleness of various bones of the body.

According to the International Osteoporosis Foundation (IOF), 40% of women in the world have fracture due to osteoporosis during their lifetime. Fractures are associated with increased morbidity/mortality and diminished quality of life in a variety of ways, including decline in physical and emotional functioning (Randel et al, 2000). Over 90% of the hip fractures are resultants of falls and such falls rank among the top six causes of death among individuals aged ≥ 65 years or older (Baraff et al, 1999). Mortality is a grave issue; however other lethal end results of falls include mobility restriction, disability, social isolation, insecurity and fear, which form a cascade of events that are damaging to health and quality of life in these individuals (Lachman et al, 1998; Legters, 2002). Studies have observed that a high correlation exists between balance deficit and incidence of falls, and loss of body balance is the greatest contributor towards falls in the elderly (Lynn et al, 1997; Silsupadol et al, 2006). Furthermore, the balance rehabilitation programs have been found to be effective in avoidance of falls among the elderly (Rogers et al, 2001), many of whom could be potentially suffering from bone mineral density.

It is well documented that intercellular Ca^{2+} plays a pivotal role in the regulation of nerve impulses and is also absolutely essential for the functioning of the hair cells, and generation and propagation of a nerve impulse (Chan & Hudspeth, 2005; Huang & Putney, 2011). Thus, reduced calcium could lead to improper release of neurotransmitter even at the auditory and vestibular periphery, leading to hearing, balance and postural deficits. Further, a study reported that the older adults who experienced falls had impaired balance function (Madureira et al., 2010). Since old age is linked with reduction in calcium ion concentration, there is a possibility that balance function impairment might have been caused by the decreased calcium concentration (osteopenia/osteoporosis) in them. Therefore it seems logical to accept a relationship between

calcium deficiency and body balance of an individual. However, this phenomenon has been sparingly examined.

The altered bone mineral density causes bone structure changes such as kyphosis (Sinaki et al, 2005), which can also cause balance issues. Osteoporotic women, when compared against non-osteporotic women, have been found to demonstrate worst balance and maximum oscillation in evaluation of balance using the Polhemus system in four upright postural situations (Abreu et al., 2010). Further, when evaluated using the computerized dynamic posturography (CDP), Lynn et al (1997) observed larger sway amplitudes and inappropriate use of balance maintenance strategies in a group of patients with osteoporosis than the controls. Recent evidences also advocate the finding of reduced otoconia density in adult female osteoporotic rats (Vibert et al, 2008). Now that otoconia are found in the utricle and saccule and that utricle and saccule are responsible for generation of vestibular evoked myogenic potentials (Colebatch & Halmagyi, 1992; Curthoys et al, 2011), it would be hard to disagree that abnormal of absent VEMPs would be expected in these patients.

Decrease in the bone mineral density is also known to cause absorption of bones in the middle ear further causing thinning of them, and changing the middle ear characteristics. Changes can also occur due to altered stiffness in the soft tissue elements of the middle ear, epitympanic spurs and proliferation of fibrous tissue adjacent to the ossicles. The process of bone demineralisation, which causes osteopenia and osteoporosis, can also affect the temporal bone in which the cochlea is housed. It can result in mechanisms which can cause sensorineural hearing loss. It can also result in compression of the auditory nerve, obstruction of vascular shunts and narrowing of the auditory canal. It has been seen that as the bone fragility increases, the hearing loss (degree & prevalence) increases. Individuals affected with osteopenia or osteoporosis, the

alterations of bone density, mass, and dampening of the finely tuned motion mechanics of the middle ear could potentially induce conductive hearing loss, whereas transformations in the otic capsule and the temporal bone might affect the inner ear, thereby causing sensorineural hearing loss. Furthermore, the transduction process in the cochlea is an end result of the efficient release of neurotransmitters. The Ca^{2+} is also vital to the recycling of K^{+} ions, especially their removal from the hair cells. A deficiency of Ca^{2+}, which is the case with individuals suffering from osteopenia and osteoporosis, could therefore potentially hamper the K^{+} recycling and result in dysfunctional neurotransmitter release, which in turn would cause sensorineural hearing loss. However, there is clear lack of published reports on audiological test findings in osteoporosis and osteopenia (Ozkiris et al, 2013; Kahveci e al, 2014; Yeh et al, 2015; Gargeshwari et al, 2017a).

Reduction in the density of otoconia in the vestibular end organs due to osteopenia and osteoporosis can consequently result in falls and fractures thereby reducing the quality of life of an individual. Also, there have been very few studies which have explored the effect of reduced bone mineral density on hearing mechanism (Ozkiris et al, 2013; Kahveci et al, 2014; Yeh et al, 2015; Gargeshwari et al, 2017). However, these studies have looked into only one aspect of audiological testing and have not done a comprehensive audiological and vestibular evaluation in the same set of individuals. To the best of our knowledge, there have been only two preliminary studies which have assessed the effect of reduced bone mineral density on audiological and vestibular test findings (Gargeshwari et al, 2017a; Gargeshwari et al, 2017b). The study included 12 osteopenic, 11 osteoporotic, and 12 age-matched controlled groups and found that there occurs increase in the hearing threshold with reduction in bone mineral density, they also reported abnormal results (poorer performance) on subjective and objective vestibular tests.

However the results cannot be generalized due to small sample size and thus there was a need to evaluate more number of osteopenic and osteoporotic individuals on similar grounds to ascertain the previous findings. Therefore, the aim of the present study was to investigate the effect of osteopenia and osteoporosis on the results of behavioral and objective audiological and vestibular assessment tests.

Method

Participants

A total of 122 participants who underwent Dual energy x-ray absorptiometry bone mineral density (DEXA BMD) testing under a supervision of an orthopedic surgeon were included in the study. According to the WHO (2004) recommendation the participants were classified as being osteopenic if their T-score (outcome of bone mineral density test) was between -1.1 to -2.5 and osteoporotic if their T-score was≥-2.6 (in the negativity). Those having T-scores better than -1.1 (towards positivity) were considered to have normal bone mineral density. Out of 122 participants, 41 participants were included in osteopenic group (Mean = 54 years, 22 females & 19 males), 43 participants in osteoporotic group (Mean age = 56.8 years, 23 females & 20 males) and 38 age matched normal BMD participants were included (Mean age = 53.63 years, 21 females & 17 males), according to the WHO (2004) recommendation, in the study.

Instrumentation and Environment

A calibrated two channel clinical audiometer with TDH-39 headphones housed in MX-41/AR ear cushions were used for finding air-conduction thresholds and doing speech audiometry. Radio ear B-71 bone vibrator along with the same audiometer was used for

measuring bone conduction thresholds. A calibrated middle ear analyzer was used for obtaining tympanogram, static compliance, ear canal volume, acoustic reflex threshold and middle ear resonance frequency. The Otodynamics ILO V6 was used for recording TEOAEs and DPOAEs. Biologic navigator pro with ER3A insert earphones along with gold plated disc electrodes were used to assess click evoked auditory brainstem response (ABR), cervical and ocular vestibular evoked myogenic potentials (cVEMP & oVEMP). All the tests were carried out in acoustically treated air-conditioned rooms with permissible noise level as per the guidelines recommended by the American National Standards Institute (2008).Video head impulse test (V-HIT) was carried out using OTO-SUITE software. The patient had to wear Frenzel glasses provided by the manufacturer of the OTO-SUITE software. The behavioural vestibular tests like Fukuda stepping test (FST), tandem gait test (TGT) and subjective visual vertical (SVV) test were also done.

Procedure

Air conduction and bone conduction threshold were tracked using modified ascending technique (Hughson & Westlake, 1944) to assess the hearing sensitivity of the subject. Pure tone average was calculated by averaging thresholds obtained at 0.5 kHz, 1 kHz, 2 kHz and 4 kHz. Speech audiometry includes calculation of speech recognition threshold, speech identification scores and uncomfortable level. Tympanometry was done using 226 Hz probe tone to rule out any middle ear pathology. Ipsilateral as well as contralateral reflexes were checked at 0.5 kHz, 1 kHz, 2 kHz and 4 kHz. Transient evoked OAEs were recorded using clicks at 80 dB peakSPL for both ears in a non-linear mode. Distortion product OAEs were recorded using two tones with the ratios of their frequency being 1.2 (f2/f1 =1.2) and the level of lower frequency (L1) being 65dB SPL and that of the higher frequency (L2) being 55 dB SPL. Responses were obtained at 1 kHz, 1.5 kHz, 2 kHz, 3 kHz, 4 kHz and 6 kHz. Both TEOAEs and DPOAEs were considered to be

present at any frequency if emissions were at least 6 dBSPL greater than two standard deviations above the mean noise floor (Starr et al, 1996).

Auditory Brainstem responses was recorded using gold plated electrodes in biologic navigator pro instrument. The threshold for clicks was calculated to find the effect of reduced bone mineral density on hearing sensitivity. The responses were also recorded for varying stimulation rate of 11.1/s, and 90.1/s at 90 dBnHL. The electrode placement sites were scrubbed using a commercially available abrasive gel in order to achieve absolute and inter-electrode impedance below 5 kΩ and 2 kΩ respectively before recording the evoked potentials. The disc type surface electrodes were placed using commercially available conduction paste and secured in place using surgical plaster.

For the Fukuda stepping test, the participants stood with both their arms outstretched in front and marched at the same place for 50 steps at a rate of 1 step/s while keeping their eyes closed throughout. As per the recommendations of Harit and Singh (2012), the angle of deviation exceeding 45º in either direction and/or distance of deviation beyond 1 meter were deemed abnormal findings. For the TGT, the participants were instructed to walk heel-to-toe on an imaginary straight line for 10 meters. Loss of balance or raising of arms to ensure balance sustenance were considered abnormal results (Rumalla et al, 2015).

The bucket test was used for evaluation of SVV. The bucket consisted of a bright strip placed inside it on the diameter. The participant placed his/her head as inside the bucket as comfortable and aligned the strip position to his/her perceived vertical. The angle at which the bucket was handed differed across observations. The angles of deviation of the perceived vertical from the true vertical were noted by a pointer indicating the angles on a 180º protractor attached

to the back of the bucket. Deviation of perceived vertical by >3º from the true vertical was considered as an abnormal result (Karlberg et al, 2002; Hafstrom et al, 2004).

For the cVEMP recordings, the non-inverting electrode was placed the ipsilateral sternocleidomastoid muscle at a point located at about 1/3rd of its length from the superior side, the inverting electrode at the sternoclavicular junction and common electrode at the forehead. In order to activate the sternocleidomastoid muscle, the participants were asked to rotate their head away from the ear receiving acoustic stimuli. The tone-burst frequencies used for recording cVEMP were 500 Hz, 750 Hz and 1000 Hz, one at a time. The intensity of each of these tone-bursts was 125 dB peSPL while the repetition rate used for stimulus delivery was fixed to 5.1 Hz. The response were band-pass filtered using a high filter of 10 Hz and a low-pass filter of 1500 Hz. Responses corresponding to 200 tone-bursts were averaged to produce the final cVEMP waveform. The pre-stimulus rectification protocol of the Biologic Navigator evoked potential system was used to minimize the consequences of changes in the electromyographic activity between the recordings within and between individuals.

The contralateral oVEMP was obtained using single channel recording. The non-inverting electrode was secured on the skin surface approximately 1 cm below the centre of the lower eye-lid, inverting electrode 2 cm below the non-inverting and ground on the forehead. Similar electrode placement sites have been used previously (Rosengren et al, 2005; Singh & Barman, 2013). The participants were instructed to keep a constant 30º upward centre gaze by maintaining visual fixation over a strip placed at the appropriate elevation. Like cVEMPs, oVEMPs were also recorded fortone-burst frequencies of 500 Hz, 750 Hz and 1000 Hz. The intensity and repetition rates used were 125 dB peSPL and 5.1Hz, respectively. The band-pass filter constituted by a low-pass filter of 1000 and a high-pass filter of 1 Hz was used for

eliminating unwanted frequencies from the response spectra. The responses were recorded and averaged for 200 sweeps of tone-bursts at each frequency.

vHIT was administered using otosuite vestibular software. Frenzel glasses were used. A target was placed at the distance of 1 metre and the subject was asked to gaze at the target. A head thrust were given 20 times in pitch, roll and yaw plane and VOR gain were calculated as ratio of eye acceleration to head acceleration in all the planes. Saccades at the time of head thrust i.e., covert saccades and after the head thrust i.e., overt saccades were looked for. Responses were checked for the stimulation in the Lateral, RALP (Right anterior and left posterior) and LARP (Left anterior and right posterior planes).

Statistical analyses

Shapiro Wilks test for normality was used to check the distribution of the data, as the data was not distributed normally, non- parametric tests were used to analyse the findings statistically. Wilcoxon signed rank test was used to check whether there exist any differences within individuals for two conditions. Kruskal Wallis H test was administered to check if their existed any difference across groups. Mann Whitney U test was done to check if the difference between any two groups for the various parameters. Spearman's Correlation coefficient was calculated to check if there existed any sort of correlation between 'T' score and any other parameters. Equality of test for proportion was administered to check if there was any difference between groups for the proportion of participants having abnormal results.

RESULTS

The present study assessed different aspects of auditory and vestibular peripheral functioning in individuals with reduced bone mineral density. Kruskal Wallis H test revealed that there was no significant difference for age of individuals across groups ($\chi 2 = 4.78$, $p = 0.09$). Wilcoxon signed rank test revealed no significant effect of ear for the participants across groups for all the parameters analyzed ($p > 0.05$), hence the data of the two ears were combined.

Outcomes of audiological evaluation

The audiological evaluation included were pure-tone audiometry (PTA), speech audiometry and immittance evaluation. Pure-tone audiometry was done to assess participant sensitivity for pure-tones, speech audiometry was administered to find their understanding of speech and immittance evaluation was done to ascertain the functioning of the middle ear.

Pure-tone and speech audiometry

It is reported across studies that hearing loss greater than mild degree poses subtle problems in communicative environmental situations; hence individuals having pure-tone average (Average of hearing thresholds at 500 Hz, 1000 Hz, 2000 Hz & 4000 Hz) greater than 25 dBHL were considered to have abnormal hearing sensitivity. It was found that 63%, 22% and 18% of participants in the osteoporosis, osteopenia and normal BMD group respectively had abnormal hearing sensitivity. Test of equality for proportion was done to analyze whether there was any significant difference between groups for the proportion of participants having abnormal results. It was found that significantly higher proportion of participants in the osteoporosis group had abnormal hearing sensitivity compared to osteopenia ($Z = 5.37$, $p = 0.000$) and normal BMD group ($Z = 5.72$, $p = 0.000$). There was no significant difference for the proportion of participant

having abnormal hearing sensitivity between normal BMD and osteopenia group. Hearing threshold greater than 15 dBHL is classified as minimal hearing loss, 89%, 66% and 60% in the osteoporosis, osteopenia and normal BMD group had minimal hearing loss and greater degree. Significantly higher proportion of participant in the osteoporosis group had hearing loss greater than 15 dBHL compared to osteopenia ($Z = 3.54$, $p = 0.000$) and normal BMD group ($Z = 4.3$, $p = 0.000$). No significant difference was seen between osteopenia and normal BMD group.

Kruskal Wallis H test revealed significant increase (poorer thresholds) in the pure tone average ($\chi2 = 20.39$, $p = 0.000$) and speech recognition threshold ($Z = 15.09$, $p = 0.001$) across groups. Mann Whitney U test showed that osteoporosis group had significantly increased (poorer) hearing thresholds compared to osteopenia ($Z = 3.36$, $p = 0.001$) and normal BMD ($Z = 4.2$, $p = 0.000$) group. There was no significant difference between the normal BMD and osteopenic individuals ($Z = 1.2$, $p = 0.23$). Figure 1 shows the mean hearing thresholds and the 2 standard deviation for the three groups across frequencies. The figure 1 shows that the osteoporosis group had poorer thresholds compared to osteopenia and normal BMD group. The osteopenia group had hearing thresholds better than osteoporosis group but poorer than normal BMD individuals. It was also found that the osteoporosis group had significantly poorer SRT compared to the osteopenia ($Z = 3.47$, $p = 0.01$) and normal BMD group ($Z = 3.17$, $p = 0.002$). There was no significant difference across groups for speech identification scores ($\chi2 = 4.8$, $p = 0.08$).

Spearman's correlation showed significant negative correlation between T score and PTA ($r_s = -0.42$, $p = 0.000$) and SRT ($r_s = -0.28$ $p = 0.002$). As the T score decreased i.e. with the reduction in the BMD there occurred an increase (poorer) in the pure tone average and speech recognition threshold.

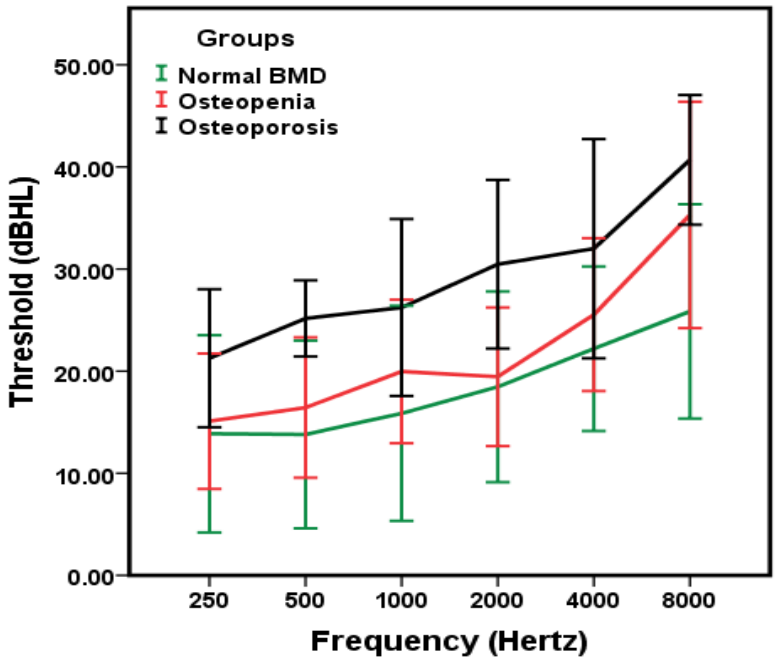

Figure 1: Mean hearing thresholds and 2 S.E. for the three groups across frequencies

Immittance evaluation

Kruskal Wallis H test revealed significant difference across groups for static compliance ($\chi 2 = 14.4$, $p = 0.001$) and resonance frequency ($\chi 2 = 6.7$, $p = 0.03$) of the middle ear. Mann Whitney U test revealed significantly lesser static compliance value in the normal BMD group compared osteopenia ($Z = 2.92$, $p= 0.004$) and osteoporosis group ($Z = 3.64$, $p = 0.000$). There was no significant difference between osteopenia and osteoporosis ($Z = 0.32$, $p = 0.75$) group for the static compliance values. Osteoporosis group had significantly lesser resonance frequency compared normal BMD group ($Z = 2.54$, $p = 0.01$). There was no significant difference between normal BMD and osteopenia group ($Z = 1.3$, $p = 0.2$) and between osteopenia and osteoporosis group ($Z = 1.4$, $p = 0.16$).

Spearman's correlation was done to check if their existed any correlation between T scores and acoustic reflex threshold. It was found that there occurred increase (poorer) in the acoustic reflex threshold with decrease in the bone mineral density. Table 1 shows the

Spearman's correlation between T score and acoustic reflex threshold values across frequencies for ipsilateral as well as contralateral stimulation.

Table 1. Spearman's Correlation results between 'T' score and Acoustic reflex threshold

	Ipsilateral stimulation (Hz)				Contralateral stimulation (Hz)			
	500	1000	2000	4000	500	1000	2000	4000
r_s	-0.243	-0.224	-0.45	-0.399	-0.51	-0.5	0.43	0.58
p	0.01	0.03	0.000	0.001	0.000	0.000	0.000	0.000

Note: r_s = spearmans correlation coefficient, p = significance value at 95% confidence limit

Both ipsilateral and contralateral acoustic reflexes were absent in more number of participants at each frequency in the two clinical groups than the control group, however the absence of acoustic reflex at all the four frequencies was considered an abnormal result (absent reflexes). 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 equality of test for proportions revealed absence of acoustic reflexes in significantly higher proportion of individuals in osteoporosis group than the group with normal BMD levels [Z = 2.23, p = 0.03]. There was no significant difference between osteopenia and normal BMD group [Z = 0.72, p = 0.47] and also between osteopenia and osteoporosis groups [Z= 1.81, p = 0.07].

Otoacoustic evaluation

TEOAEs were obtained from 500 Hz to 4 kHz and DPOAEs from 1 kHz to 8 kHz. Both DPOAEs as well as TEOAEs was considered to be present only if the signal-to-noise ratio was greater than 6 dB at three consecutive frequencies. For the TEOAEs it was found that 72% of the

participant in the normal BMD group had presence of OAEs as against 50% in the osteopenia and 31% in the osteoporosis group. Equality of proportion revealed significantly higher proportion of participant in the osteoporosis group had absence of TEOAE compared to osteopenia ($Z = 2.46$, $p = 0.01$) and normal BMD ($Z = 5.21$, $p = 0.000$) group. The osteopenia group also showed significantly lesser proportion of participants having presence of TEOAEs as compared to the normal BMD individuals ($Z = 2.88$, $p = 0.004$). DPOAEs were present in 82%, 70% and 38% of participants in the normal BMD individuals, osteopenia and osteoporosis group respectively. It was seen that the higher number of participants in the osteoporosis group had absence of DPOAE as against osteopenia ($Z = 4.04$, $p = 0.000$) and normal BMD ($Z = 5.6$, $p = 0.000$) groups. There was no significant difference for the proportion of participants having absence of DPOAEs between normal BMD and osteopenic participants ($Z = 1.76$, $p = 0.08$).

Auditory brainstem responses

ABR was done at 11.1/s, and 90.1/s repetition rates for 90 dBnHL and it was found that there occurred increased in the latency of peak I, peak III and peak V with increase in repetition rates for the participants of all the three groups. Also peak I was not seen in higher number of participants at 90.1/s across groups ($p > 0.05$). On administration of Kruskal Wallis H test, it was found that there was no significant difference for the latency of peak I and peak III across groups at 11.1/s and 90.1/s repetition rates ($p > 0.05$). However, there occurred significant increase in the latency of peak V across groups with decreasing BMD at 11.1/s ($\chi2 = 6.6$, $p = 0.04$) and 90.1/s ($\chi2= 12.4$, $p = 0.002$). Mann Whitney U test revealed significant difference between normal BMD and osteoporosis group for latency of peak V at 11.1/s. There also occurred significant difference between normal BMD group and osteopenia and between normal BMD

and osteoporosis group for the latency of peak V at 90.1/s. Table 2 shows the Mann Whitney U test results of peak V between groups.

Table 2. Mann Whitney U test results between groups for clicks at varying repetition rates

Between groups	Repetition Rates	
	11.1/s	90.1/s
1 & 2	(Z = 1.39, p = 0.16)	(Z = 3.6, p = 0.000)*
2 & 3	(Z = 1.32, p = 0.19)	(Z = 0.23, p = 0.82)
1 & 3	(Z = 2.5, p = 0.01)*	(Z = 2.5, p = 0.011)*

Group 1: Normal BMD; Group 2: Osteopenia; Group 3: Osteoporosis

Spearman's Correlation showed significant increase in the latency of peak V with decrease in the BMD levels at 11.1/s (r_s = -0.19, p = 0.04). There was marginally significant increase of peak V at 90.1/s (r_s = 0.18, p = 0.058). There was no significant correlation for latency of peak I and peak III at any repetition rates with 'T' score (p > 0.05). Figure 2 represents waveform from each group at 11.1/s and 90.1/s repetition rates. We can see that the latency of peak V is delayed in figure c which represents osteoporosis group.

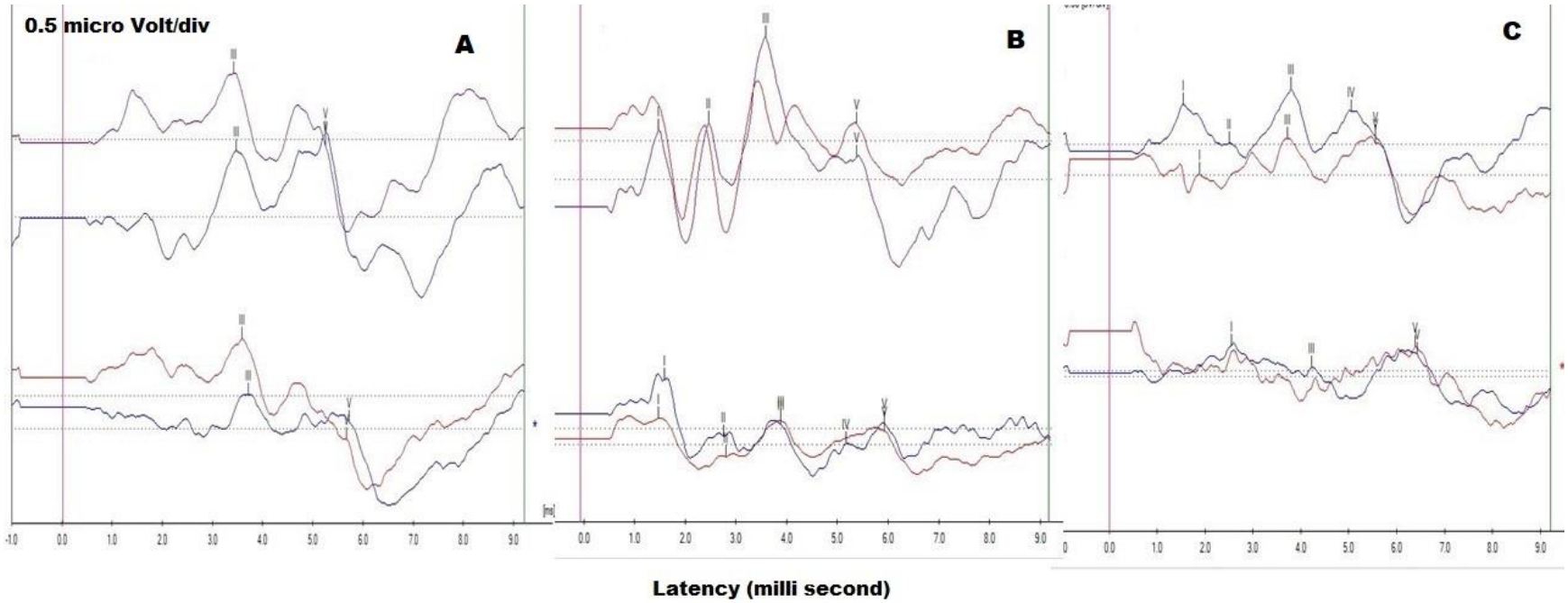

Figure 2: Representative waveforms from each groups. A. represents the normal BMD group. B. represents the osteopenia group. C. represents Osteoporosis group. The upper waveform in each group represents 11.1/s and the lower one represents 90.1/s

Subjective vestibular evaluation

Fukuda stepping test (FST), Subjective visual vertical test (SVV) and Sharpened Romberg test was done as a part of subjective vestibular evaluation. For Fukuda stepping test a rotation of greater than $45^0$and a deviation of greater than 1 meter in the forward direction was considered to be abnormal. It was seen that 8/38, 25/41 and 29/43 participants in the normal BMD, osteopenia and osteoporosis group respectively had abnormal results on FST. On administering equality of proportion it was found that significantly lesser proportion of participants in the normal BMD group had abnormal results on FST compared to osteopenia ($Z = 3.59$, $p = 0.000$) and osteoporosis ($Z = 4.42$, $p = 0.000$). There was no significant difference between osteopenia and osteoporosis group ($Z = 0.93$, $p = 0.35$).

Presence of either self- perceived sway by the participant or observed by the clinician and a tendency to fall was considered to be abnormal finding on Sharpened Romberg test. Results revealed that 7/38, 16/41 and 21/43 participants in the normal BMD, osteopenia and osteoporosis group respectively had abnormal results on Sharpened Romberg Test. Equality of proportion revealed significantly lesser proportion of participant having abnormality for normal BMD compared to osteopenia ($Z = 2.01$, $p = 0.04$) and osteoporosis ($Z = 3.04$, $p = 0.002$). There was no significant difference for test results between osteopenia and osteoporosis ($Z = 1.1$, $p = 0.27$).

Subjective visual vertical test was administered to test ones perception of verticality. Deviation of greater than 3^0 was considered to be abnormal. 10/38, 22/41 and 23/43 participants in the normal BMD, osteopenia and osteoporosis group respectively had abnormal results on SVV test. Significantly lesser proportion of participants in the normal BMD group had abnormality on SVV compared to osteopenia ($Z = 2.47$, $p = 0.01$) and osteoporosis ($Z = 2.68$, $p =$

0.007). There was no significant difference between proportion of participants having abnormal results on SVV between osteopenia and osteoporosis group ($Z = 0.22$, $p = 0.82$).

Objective vestibular evaluation

Objective vestibular evaluation included cVEMP and oVEMP to assess the functioning of sacculo-collic and utriculo-occular pathway functioning respectively and Video head Impulse test was done to assess the functioning of the lateral, anterior and posterior semicircular canal in three planes. The objective vestibular evaluation aimed to assess and compare the functioning of all the vestibular end organs (Utricle, Saccule and Semicircular canals) in the participants in the three groups.

Cervical vestibular evoked myogenic potential (cVEMP)

The descriptive data of absolute latency P1 and N1 and peak to peak amplitude P1N1 is given in the Table 3. From the table we can see that there occurred reduction in the amplitude of P1N1 with reduction in the bone mineral density. Also as the frequency increased the absolute latency of both peak P1 and N1 decreased in all the three groups.

Table 3. Descriptive data of the parameters analyzed for cVEMP

		Normal BMD			Osteopenia			Osteoporosis		
		X	M	SD	X	M	SD	X	M	SD
500 Hz	P1 latency (in ms)	15.25	15.2	1.45	15.16	15.1	0.9	15.5	15.44	1.08
	N1 latency (in ms)	23.9	23.5	2.36	22.8	22.9	1.73	23.2	23.5	2.38
	Amplitude (in µV)	15.16	12.8	7.96	11.3	10.9	6.1	8.6	7.3	4.6
750 Hz	P1 latency (in ms)	14.82	14.85	1.34	14.89	14.72	1.35	14.82	14.93	1.25
	N1 latency (in ms)	23.4	23.3	1.9	23.0	22.9	1.9	23.3	23.2	2.2
	Amplitude (in µV)	13.5	11.48	7.07	11.22	10.31	5.8	8.9	7.21	5.0
1 kHz	P1 latency (in ms)	14.53	14.6	1.3	14.6	14.6	1.22	14.5	14.4	2.2
	N1 latency (in ms)	23.0	22.9	2.1	22.23	22.3	1.7	22.5	22.6	1.9
	Amplitude (in µV)	15.7	13.8	8.4	11.46	10.6	4.87	8.55	8.13	4.28

Note: X = Mean, M = Median, SD = standard deviation.

On administration Test of Equality for proportion it was found that significantly higher number of participants in the osteoporosis group had absent cVEMP compared to osteopenia group at 500 Hz, ($Z = 2.20$, $p = 0.02$), 750 Hz ($Z = 2.4$, $p = 0.02$), 1000 Hz ($Z = 2.7$, $p = 0.008$). It was also seen that higher proportion of participants in the normal BMD group had present cVEMP compared to osteoporosis at 500 Hz (2.02, $p = 0.05$), 750 Hz ($Z = 2.98$, $p = 0.003$) and 1000 Hz ($Z = 2.56$, $p = 0.01$). There was no significant difference for the presence or absence of cVEMP between the normal BMD and osteopenia group at any of the three frequencies ($p > 0.05$). The details of the percentage of participants having presence and absence of responses in each of the three groups and each of the three frequencies are mentioned in figure 3.

On administration of Kruskal Wallis H test it was found that there was no significant effect of groups on the absolute latency of P1 ($\chi2= 3.43$, $p = 0.18$) and N1 ($\chi2= 6.9$, $p = 0.32$) at 500 Hz, absolute latency of P1($\chi2= 0.43$ $p = 0.81$) and N1($\chi2= 2.82$ $p = 0.243$) at 750 Hz and absolute latency of P1 ($\chi2= 0.19$, $p = 0.9$) and N1 ($\chi2= 5.76$, $p = 0.56$) at 1000 Hz. However it was seen that there occurred significant reduction in the P1N1 amplitude of the cVEMP as the severity of bone mineral deficiency increased across groups at 500 Hz ($\chi2= 32.98$, $p = 0.000$), 750 Hz ($\chi2= 24.42$, $p = 0.000$), 1000 Hz ($\chi2= 32.3$, $p = 0.000$). Figure 4 shows the cVEMP representative waveform of one participant from each group.

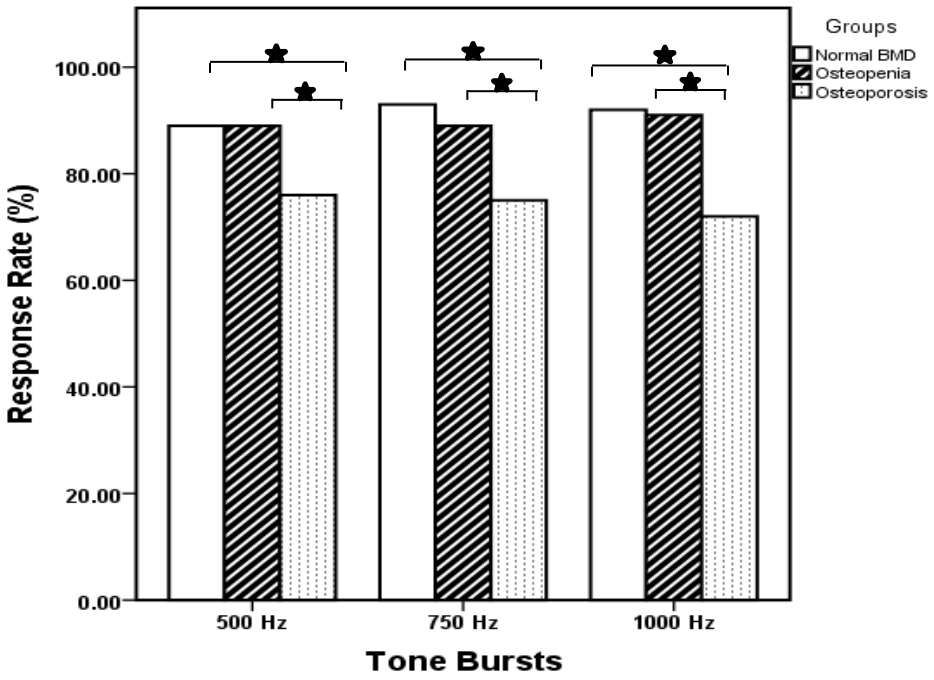

Figure 3: The response rates of cVEMP at three frequencies across groups. The * mark indicate significance difference on test of equality for proportion at $p<0.05$ level

Mann Whitney U test was done to find out if there existed any difference between any two groups for amplitude P1N1 at all the frequencies. At 500 Hz there was significant difference between normal BMD and osteopenic group ($Z = 2.8$, $p = 0.005$), between osteopenia and osteoporosis group ($Z = 3.3$, $p = 0.001$) and between normal BMD and osteoporosis group ($Z = 5.66$, $p = 0.000$). At 750 Hz there was significant difference between normal BMD and Osteopenic group ($Z = 2.01$, $p = 0.045$), between osteopenia and osteoporosis group ($Z = 3.07$, $p = 0.002$) and between normal BMD and osteoporosis group ($Z = 4.88$, $p = 0.000$). At 1000 Hz there was significant difference between normal BMD and Osteopenic group ($Z = 2.84$, $p = 0.005$), between osteopenia and osteoporosis group ($Z = 4.1$, $p = 0.000$) and between normal BMD and osteoporosis group ($Z = 4.97$, $p = 0.000$).

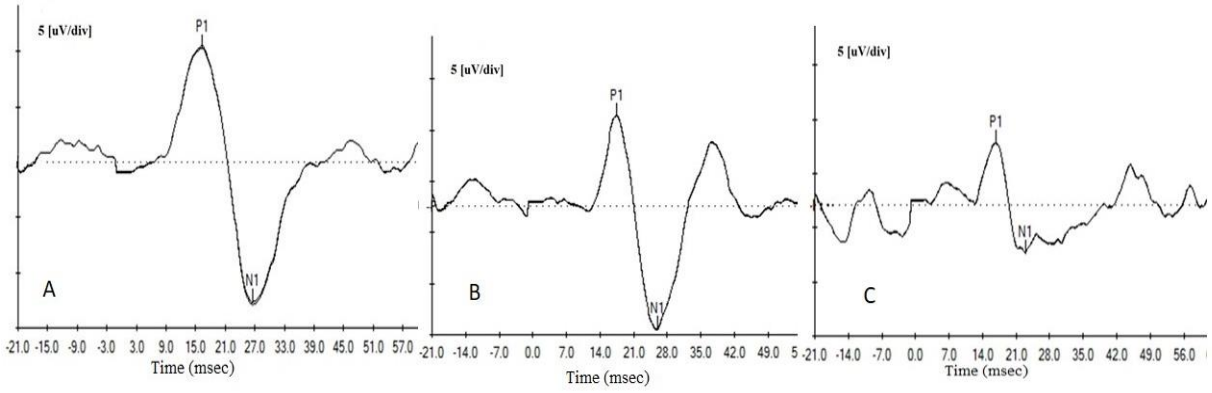

Figure 4: Rectified cVEMP from a participant representing mean from each of the group. A. Normal BMD, B. Osteopenia, C. Osteoporosis

Spearman's correlation coefficient was calculated to find out if there was any significant correlation between 'T' score and the cVEMP parameters. There was no significant correlation between 'T' score and the latency of P1 or N1 however there was a significant correlation between the amplitude of cVEMP and 'T' score at 500 Hz (r_s = 0.292, p = 0.000), 750 Hz (r_s = 0.270, p = 0.000), and at 1000 Hz (r_s = 0.335, p = 0.000).

Frequency amplitude ratio (FAR) was calculated by dividing the amplitude P1N1 at 1000 Hz by amplitude P1N1 at 500 Hz. Kruskal Wallis H test revealed that there was no significant difference between groups for frequency amplitude ratio and frequency tuning (p > 0.05). Table 4 shows the descriptive analyses of FAR for the three groups. Thus there was no significant effect of frequency among the three groups. Also there was no significant effect of frequency within individuals within groups. Frequency tuning was calculated for each of the participant. Highest amplitude obtained among the three frequencies was termed as the tuned frequency for that individual. There was no significant difference between the proportions of participants for tuning frequency between groups.

Table 4. The descriptive statistics for frequency amplitude ratio for all the three groups.

	Normal BMD			Osteopenia			Osteoporosis		
	X	M	SD	X	M	SD	X	M	SD
cVEMP	1.77	1.07	0.69	1.76	1.04	2.15	1.61	1.25	1.56
oVEMP	1.3	1.11	0.59	1.25	1.13	0.58	1.47	1.13	0.58

Note: X = Mean, M = Median, SD = standard deviation.

Ocular vestibular evoked myogenic potential (oVEMP)

oVEMP was done to assess the functioning of the utriculo-ocular pathway in these participants and the parameters like absolute latency of N1 and P1 and peak to peak amplitude N1P1 were analyzed. Table 5 shows the descriptive statistics of the parameters analyzed for oVEMP. It can be seen that there occurs increase in the absolute latency of N1 and P1 with decrease in BMD (across groups). The peak to peak amplitude N1P1 is least (poorer) in the osteoporosis, and the amplitude is lesser in the osteopenia group compared to the normal BMD group at all the three frequencies. There also occurred decrease in the absolute latencies of N1 and P1 with increasing frequencies.

Table 5. Descriptive data of the parameters analyzed for oVEMP

Freq. (Hz)	Parameters	Normal BMD			Osteopenia			Osteoporosis		
		X	M	SD	X	M	SD	X	M	SD
500	P1 latency (in ms)	11.42	11.22	0.95	11.94	12.16	1.32	12.29	12.6	1.14
	N1 latency (in ms)	16.71	16.7	1.45	16.53	16.64	1.83	17.27	17.30	1.0
	Amplitude (in µV)	4.93	4.11	2.84	3.25	2.41	2.63	2.52	2.0	1.9
750	P1 latency (in ms)	10.79	10.85	0.79	11.37	11.1	0.99	11.65	11.60	0.94
	N1 latency (in ms)	15.90	15.8	1.12	15.76	15.6	1.3	16.8	16.9	1.1
	Amplitude (in µV)	6.6	6.4	3.8	4.9	2.7	4.35	3.3	2.6	3.62
1000	P1 latency (in ms)	10.12	10.3	0.7	10.6	10.5	1.77	11.24	10.85	1.6
	N1 latency (in ms)	15.3	15.2	1.08	15.2	15.41	1.43	16.4	15.9	1.43
	Amplitude (in µV)	6.59	5.87	4.88	4.05	3.99	2.29	3.41	2.4	2.53

Note: N1 = absolute latency of peak N1 (ms), p1 = absolute latency of peak P1 (ms), N1P1 = Amplitude N1P1 (microvolt), X = Mean, M = Median, SD = standard deviation.

Among the participants in the normal BMD group, absence of oVEMP was seen in 23% of ears at 500 Hz, 24% of ears at 750 Hz, and 24% of ears at 1000 Hz. In the osteopenia group the absence of oVEMP was seen in 34 % of ears at 500 Hz, 20% of ears at 750 Hz and in 27% of ears at 1000 Hz. The osteoporosis group had absence of oVEMP in 56% of ears at 500 Hz, 49% at 750 Hz and in 46% at 1000 Hz. On administration of equality of test for proportion it was found that there was a significant difference for the response rates among osteopenia and osteoporosis group at 500 Hz ($Z = 2.88$, $p = 0.004$), 750 Hz ($Z = 3.98$, $p = 0.0000$) and at 1000 Hz ($Z = 2.53$, $p = 0.01$). Also significantly higher number of participants in the osteoporosis group had absence of oVEMP compared to the normal BMD group at 500 Hz ($Z = 4.17$, $p = 0.0000$), at 750 Hz ($Z = 3.18$, $p = 0.002$) and 1000 Hz ($Z = 2.77$, $p = 0.005$). Figure 5 shows the response rates for oVEMP for different groups at different frequencies and their significant difference.

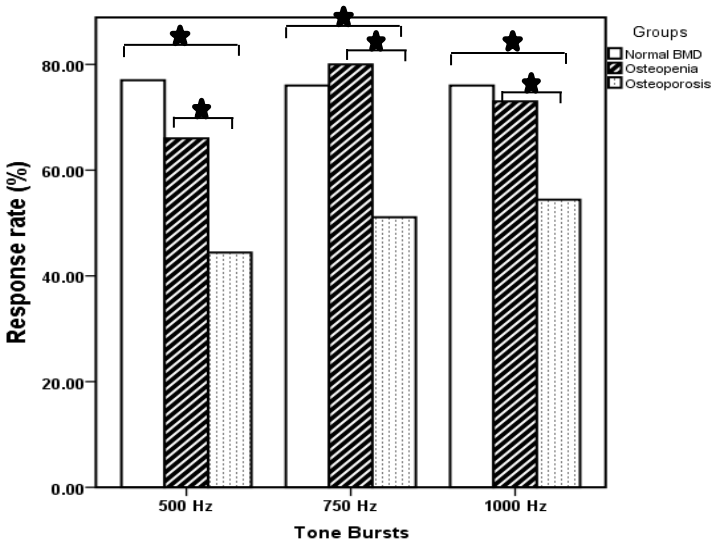

Figure 5: *Response rates of oVEMP at different frequencies for the groups. The * mark indicate the significance difference between groups*

On administration of Kruskal Wallis H test it was found that there was significant difference across groups for latency N1 ($\chi2 = 12.42$, $p = 0.002$), for latency of P1 ($\chi2 = 10.28$, $p = 0.006$) and peak to peak amplitude of N1P1 ($\chi2 = 23.77$, $p = 0.000$) at 500 Hz. There was also significant difference seen at 750 Hz for latency N1 ($\chi2 = 20.94$, $p = 0.000$), for latency P1 ($\chi2 = 27.35$, $p = 0.000$) and peak to peak amplitude of N1P1 ($\chi2 = 29.74$, $p = 0.000$). At 1000 Hz as well it was seen that there was increase in latency of N1 ($\chi2 = 25.2$, $p = 0.000$), increase in latency of P1 ($\chi2 = 24.5$, $p = 0.000$) and reduction in the amplitude of N1P1 ($\chi2 = 29.9$, $p = 0.000$) across groups (as BMD decreased).

Mann Whitney U test showed no significant difference between normal BMD group and osteopenia group and between osteopenia and osteoporosis group for the latency of N1 and latency of P1 at 500 Hz, 750 Hz and at 1000 Hz ($p > 0.05$). However there was significant difference between normal BMD and osteoporosis group for latency N1 ($Z = 3.61$, $p = 0.000$) and latency P1 ($Z = 2.8$, $p = 0.005$) at 500 Hz, for latency of N1 ($Z = 4.47$, $p = 0.000$) and latency of P1 ($Z = 4.8$, $p = 0.000$) at 750 Hz and also latency of N1 ($Z = 4.9$, $p = 0.000$) and latency of P1 ($Z = 5.18$, $p = 0.000$) at 1000 Hz. For the amplitude of N1P1 there was no significant difference between osteopenia and osteoporosis group at all three frequencies ($p > 0.05$). The amplitude N1P1 was significantly lower in the osteopenia group compared to normal group at 500 Hz ($Z = 3.43$, $p = 0.001$), 750 Hz ($Z = 4.5$, $p = 0.000$) and also at 1000 Hz ($Z = 4.4$, $p = 0.000$). Further significant reduction in amplitude was seen in osteoporosis group compared to the normal BMD individuals at 500 Hz ($Z = 4.7$, $p = 0.000$), 750 Hz ($Z = 5.1$, $p = 0.000$) and also at 1000 Hz ($Z = 4.5$, $p = 0.000$). The representative waveform of one of the participant in each group is mentioned in figure 6.

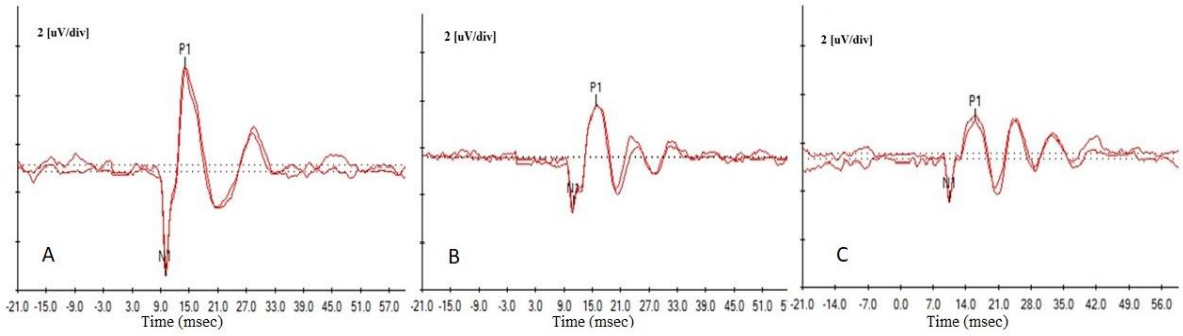

Figure 6: oVEMP from a participant representing mean from each of the group. A. Normal BMD, B. Osteopenia, C. Osteoporosis

Spearman's correlation coefficient was calculated to find out if there was any significant correlation between T score and the oVEMP parameters. There was no significant correlation for 'T' score and latency of N1 and P1 at any frequencies ($p > 0.05$). However, there was a significant positive correlation between the amplitude of oVEMP and 'T' score at 500 Hz ($r_s = 0.317$, $p = 0.000$), 750 Hz ($r_s = 0.34$, $p = 0.000$), and at 1000 Hz ($r_s = 0.28$, $p = 0.000$) i.e. there occurred significant reduction in the amplitudes of oVEMP with reduction in bone mineral density. Frequency amplitude ratio was calculated by dividing the amplitude N1P1 at 1000 Hz to amplitude N1P1 at 500 Hz. There was no significant difference between the three groups ($p > 0.05$). Table 4 shows the descriptive analyses of frequency amplitude ratio for the three groups.

Video Head Impulse Test

Vestibular ocular reflex was calculated as the ratio of eye velocity upon head velocity. Refixation of saccades was observed and its presence was considered positive only if at least 5 head movements had saccades out of 20 head movements. It was seen that the VOR gain was

reduced in the vertical planes in the osteoporosis group. The descriptive statistics of the VOR gain is mentioned in table 6.

Table 6. Descriptive statistics of VOR gain in all 6 planes across groups.

	Normal BMD			Osteopenia			Osteoporosis		
Canals	X	M	SD	X	M	SD	X	M	SD
RL	0.96	0.94	0.1	0.95	0.94	0.13	0.9	0.91	0.12
LL	0.89	0.88	0.04	0.88	0.88	0.09	0.88	0.84	0.13
RA	0.87	0.85	0.18	0.92	0.93	0.22	0.76	0.75	0.11
LA	0.81	0.82	0.09	0.78	0.82	0.12	0.71	0.7	0.09
RP	0.8	0.78	0.08	0.82	0.8	0.11	0.73	0.68	0.15
LP	0.88	0.82	0.13	0.82	0.86	0.15	0.7	0.69	0.16

Note: RL: Right Lateral, LL = Left Lateral, RA = Right Anterior, LP = Left Posterior, LA = Left Anterior, RP = Right Posterior, X = Mean, M = Median, SD = Standard deviation.

Kruskal Wallis H test revealed significant difference across groups only for the right posterior ($\chi2 = 13.8$, $p = 0.001$) and left posterior ($Z = 30.2$, $p = 0.000$) planes and right anterior ($\chi2 = 15.6$, $p = 0.000$) and left anterior planes ($\chi2 = 20.4$, $p = 0.000$). Mann Whitney U test revealed no significant difference between normal BMD and osteopenia group ($Z = 4.48$, $p = 0.11$). However the osteoporosis group had significantly reduced VOR gain in the right posterior ($Z = 3.25$, $p = 0.001$), left anterior ($Z = 4.5$, $p = 0.000$), left posterior planes ($Z = 5.52$, $p = 0.000$) and right anterior planes ($Z = 3.35$, $p = 0.001$) compared to normal BMD. Osteopenia group also showed significantly higher VOR gain in the right posterior ($Z = 3.12$, $p = 0.002$), left anterior ($Z = 2.9$, $p = 0.004$), left posterior planes ($Z = 3.74$, $p = 0.000$) and right anterior planes ($Z = 3.3$, $p = 0.001$) compared to osteoporosis group. There was no significant difference in the VOR gain between osteopenia and osteoporosis group for any of the planes. Equality of test for proportion

revealed that the osteoporosis group showed higher proportion of participants having re-fixation of saccades in the vertical planes compared to the normal (Z = 4.04, p = 0.000) and osteopenia (Z = 2.2, p = 0.04) group. However there was no significant difference in the proportion of participants showing re-fixation of saccades in the lateral planes between any two groups (Z = 1.45, p = 0.96). Figure 7, 8, 9 shows the representative VOR waveforms from the normal BMD, osteopenia and osteoporosis group respectively.

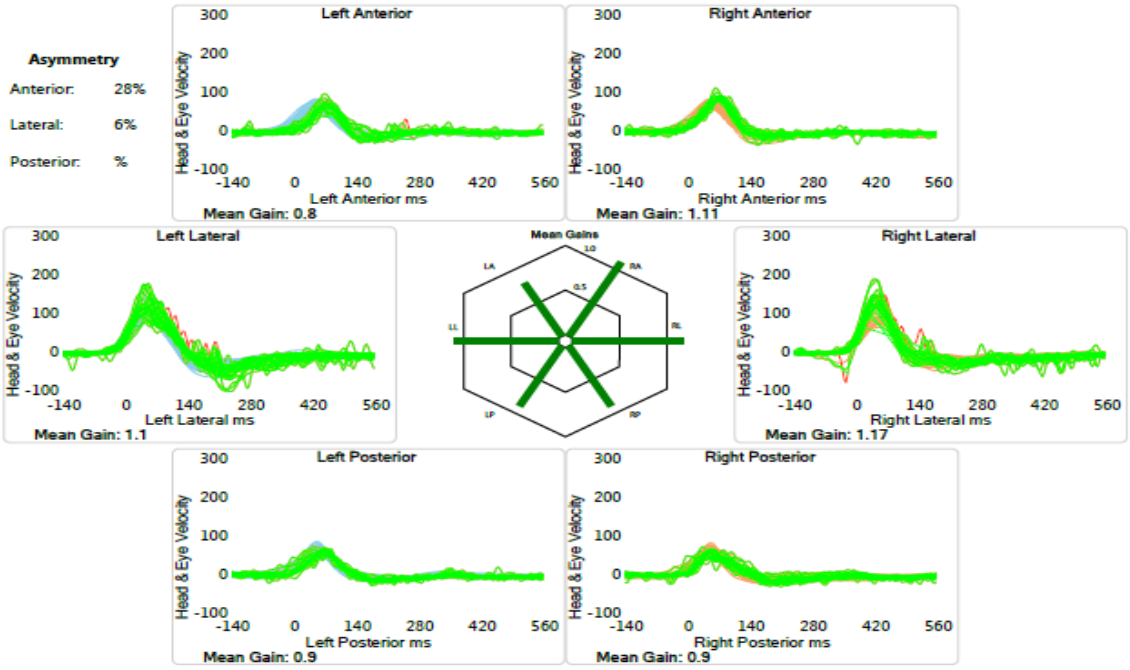

Figure 7: *VOR waveform of a participant with normal BMD showing normal VOR gain and no presence of refixation of saccades*

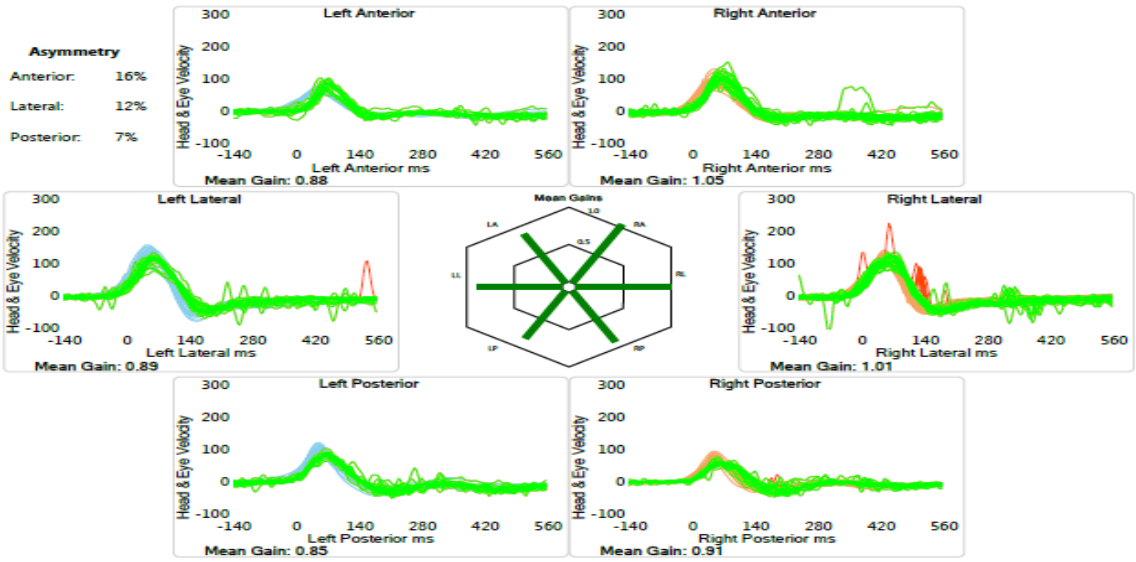

Figure 8: *VOR waveform of a participant with osteopenia showing normal VOR gain and presence of refixation of saccades only in one plane*

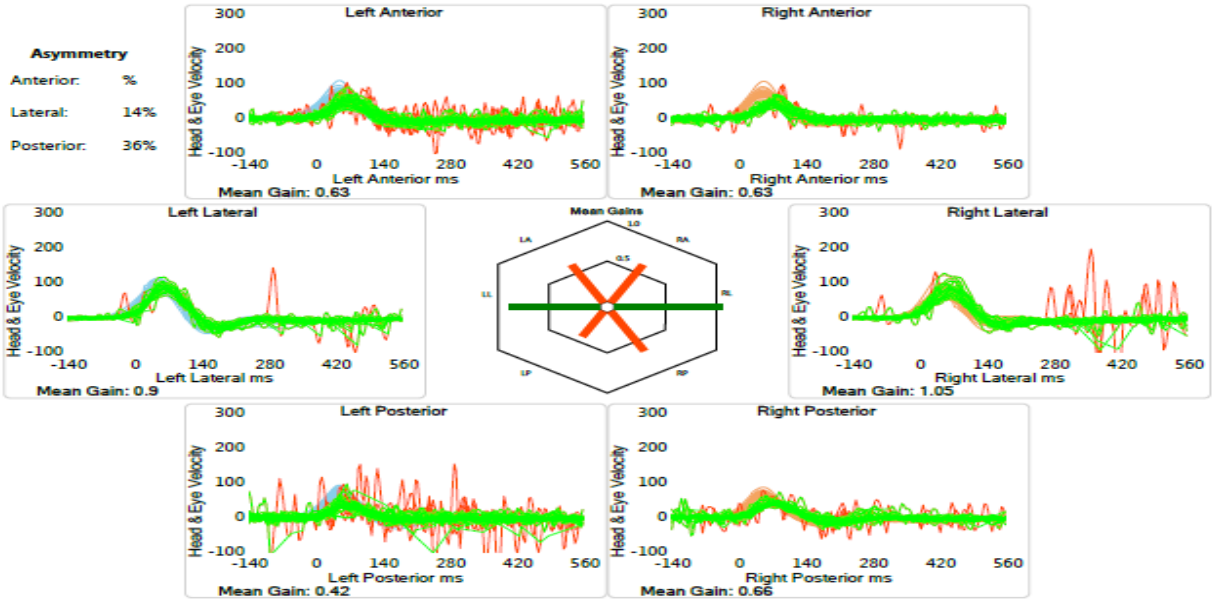

Figure 9: *VOR waveform of a participant with osteoporosis showing reduced VOR gain and presence of refixation of saccades majorly in the vertical planes.*

DISCUSSION

Pure-tone and speech audiometry

It was found that prevalence of hearing loss and poorer speech understanding scores was seen in the osteoporotic patients as compared to the normal BMD and the osteopenic individuals. Association between hearing loss with reduced BMD has been widely reported in literature (Clark et al, 1995; Ozakiris et al, 2013; Yeh et al, 2014; Gargeshwari et al, 2017a). Histopathological studies by various authors have reported alteration in the functioning of auditory periphery secondary to paget's disease right at the level of the middle ears (Khetarpal & Schucknect, 1990), to the internal auditory meatus (Applebaum & Clemis, 1977). Clarke et al, 1995, reported that hearing loss could be associated with decrease in bone mineral density secondary to demineralisation of the cochlear capsule. The possible evolution of the theory could be from the studies on the patients with paget's disease in which there is increased number of osteoclastogenic cells causing demineralisation of the temporal bone. Also alteration in bone remodeling affects the homeostasis of calcium thereby affecting its optimal functioning at the level of cochlea resulting into elevated hearing thresholds and poorer speech understanding.

Immittance evaluation

Static compliance and resonance frequency

Static compliance at the level of the tympanic membrane was higher in the osteoporosis group followed by osteopenia and normal BMD individuals. Also the reduction in the resonance frequency was seen with reduction in the bone mineral density. The static compliance is the measure of transmission of longitudinal sound waves via the middle ear. Various studies have reported changes occurring at the middle ear level secondary to reduction in bone mineral

density (Kanzaki et al, 2006; Swinnen et al, 2012; Gargeshwari et al, 2017). Thinning of manubrium in low BMD mice was reported by Kanzaki et al in year 2006. In addition, Swinnen et al, 2012 reported that individuals with altered bone remodeling are more susceptible to microfractures of bones and reduction in BMD which could result in intra-osseous microfracture, thereby change the normal sound transmission characteristic of middle ear. Similar findings were reported by Gargeshwari et al, 2017. Thus as resonance frequency is directly proportional to the root of the stiffness and as the density of the bone reduces as seen in osteoporosis without any changes in the volume, the resonance frequency also reduces. Thus intra-osseous changes at the level of middle ear bone might result in higher static compliance and reduced middle ear resonance frequency.

Acoustic reflex threshold

The results of the present study also showed that as the bone mineral density decreases the acoustic reflex threshold increases which have been reported previously (Swinnen et al, 2012; Gargeshwari et al, 2017). This could be related to the reduction in middle ear resonance frequency and presence of middle ear problem. Subtle middle ear changes will in turn necessitate higher energy so as to elicit the stapedial reflex. Also the absorption of calcium is altered with reduction in bone mineral density. For efficient release of the neurotransmitter, optimal functioning of calcium is necessary. Reduction in the intestinal absorption of calcium might alter the neurotransmission of the impulse which would cause absence or elevation of acoustic reflex threshold.

Otoacoustic evaluation

The OAEs in the present study was completely absent in a significantly higher proportion of the clinical groups than the control group. Absence of OAEs in individuals with reduced bone mineral density may be either due to increased calcium levels causing damage to the outer hair cell which are the source of otoacoustic emissions or due to reduced utility of calcium ions as calcium has been shown to be vital for the recycling of potassium ions outside of the hair cell (Jagger & Ashmore, 1999). Reduction in the bone mineral density is likely to cause alteration in the metabolism at the level of the cochlea could be due to alteration in the optimal functioning of calcium. And hence result in reduced electro-motility and thereby reduced or absent OAEs in a higher proportion of individuals in the clinical groups than the control groups.

Auditory Brainstem response

The present study showed prolonged latencies at higher repetition rates in individuals with significant altered bone remodeling. ABR is a time locked responses and recorded from different generating sites right from the distal part of cochlear nerve to the lateral lemniscus. The auditory evoked potentials developed at these sites are a result of transmission of sound between cell bodies of the neurons and the axons. Calcium is very vital for the efficient release of impulse between cells and neurons and also between neurons. Reduction in the optimal functioning of calcium which is the outcome of alteration in bone remodeling could cause lesser neurotransmission release between neurons at higher repetition rates (in more taxed situation) resulting in prolonged latency of peak V.

Subjective Vestibular Tests

Subjective visual vertical test

The outcomes of SVV in the present study confirmed significantly larger proportion of abnormal results in the two clinical groups than the control group. SVV as a test is sensitive for detecting pathologies of utricule (Kumagami et al, 2009). Hence the findings indicate towards the existence of utricular pathology in cases with osteopenia and osteoporosis. The maculae within the utricular macula are composed of large volumes of calcium carbonate crystals (otoconia) which not only contributes majorly to its mass but also plays vital roles in the processes of depolarization and hyperpolarization (Eatock & Songer, 2011). A study on lower animals with osteoporosis Vibert et al (2008) showed ultra-structural metamorphosis in the otoconia of the utricle. Although there are no reports to this extent on human beings, a similar ultra-structural metamorphosis in otoconia might be expected. Since utricle is vital to identification of the absolute verticality of a visual target, the ultra-structural changes in the utricle associated with osteoporosis and osteopenia could have possibly lead to more deviances in the perceived vertical.

FST and Sharpened Romberg

The results on FST and Sharpened Romberg tests revealed abnormal results in significantly larger proportion of individuals with osteoporosis than osteopenia and the healthy controls. There are no published reports regarding the findings of these tests in individuals with osteopenia and osteoporosis. However, higher sway amplitudes and more abnormal results in individuals with osteoporosis than healthy controls has been reported on computerized dynamic posturography and standing balance tests (Lynn et al, 1997; Mendy et al, 2014; Gargeshwari et

al, 2017). Therefore, these results confirm the presence of vestibular pathology in individuals with osteoporosis. As mentioned above, the ultra-structural changes in the peripheral vestibular system could be possible elicitor of such responses on these tests.

Objective vestibular evaluation

cVEMP and oVEMP

Significantly reduced VEMP amplitudes and higher proportion of participants having abnormal responses in individuals with reduced bone mineral density might be attributed to reduction in the optimal functioning of calcium. Since osteopenia and osteoporosis are more associated with older age groups, some people might think of age-related changes in vestibular periphery as the reason for the findings of VEMP in these individuals. While it is true that the process of aging causes reduction in amplitude and absence of cVEMP (Jha & Sujeet, 2016) and oVEMP (Jha & Sujeet, 2016), this is probably not a significant contributor to the findings as there was no significant difference in age between the three groups of the present study. Conductive pathology is another factor often associated with osteopenia and osteoporosis and could have possible affect on cVEMP and oVEMP results (Wang & Lee 2007). However, the subject selection criteria used in the present study guarded against this as the individuals with conductive hearing loss were excluded from the present study. Therefore it also improbable that lower response rates of cVEMP and oVEMP in the osteoporosis group was caused by conductive hearing loss. Studies have shown that microstructural changes occur at the level of the maculae in the rats with osteoporosis (Vibert et al 2008). Such changes in human if occurring might also result in abnormal vestibular test results. The alteration in the functioning of calcium which is the essence of these pathologies might have resulted in the significant prolongation of absolute

latencies for oVEMP in individuals with reduced BMD. As the neural impulses for oVEMP are mediated along the utriculo-occular pathway, and those for cVEMP travel along the sacculo-collic pathway, the abnormally prolonged latencies for oVEMP but not for cVEMP in individuals with osteoporosis points towards lesser susceptibility and more robustness of saccule and inferior vestibular nerve to the detrimental effects of pathology than the utricle and superior vestibular nerve. The same has been established through the results of cVEMP and oVEMP in other vestibulopathies like benign paroxysmal positional vertigo (Singh et al, 2014), vestibular neuritis (Moon et al, 2012) and auditory neuropathy spectrum disorders.

Video Head Impulse Test

There was significant reduction of VOR gain in osteoporotic patients only in the vertical planes, which could be attributed to the property of otoconia requiring optimal calcium homeostasis to dissolve itself into the endolymphatic fluid (Yamanaka et al, 2013. However as there occurs alteration in the level of calcium, the otoconia are more susceptible of getting dislodged and creating symptoms like Benign paroxysmal positional vertigo. Studies have shown multiple canalith repositioning requiring for symptom cessation in the patients with osteopenia/osteoporosis having giddiness (Jang & Kang, 2009). Thus, probable dislodging of the crystals in the more common posterior semicircular canal might have resulted in abnormal gain in the two posterior planes. The anterior planes function in conjunction with the posterior planes and any changes in the movement of fluid in one would affect the functioning of the other. Thus the gain of anterior planes would have been reduced probably because of its complementary function with the posterior planes which are more susceptible for dislodging of the otoconia crystals in the canal.

Other aspects

An alternate thought worth discussing here is that the majority of studies suggest towards reduced BMD as the probable cause of balance impairment in individuals with osteoporosis and osteopenia; however, a small section of researchers are showing research evidences in support of vestibular impairment being one of the causes of osteoporosis (Levasseur et al, 2004; Vignaux et al, 2015; Bigelow et al, 2016). This could be due to the fact that vestibular system plays a pivotal role in regulation of bone homeostasis. Hence an impairment of the vestibular system has a potential to alter the bone homeostasis.

The otolith system has symmetrical location on either side of the skull in the petrous bone. The otolith organs are the main sensory organs for sensing gravity and linear acceleration. Its role in the regulation of posture, respiration, heart rate, and blood pressure is well established (Yates, 1992; Yates & Miller, 1998). These are supported by anatomical projections from vestibular nuclei to autonomic centers of the brainstem (Yates & Bornstein, 2005). The inputs from the vestibular system aid in the changes in sympathetic nerve outflow during movements and postural changes. These inputs cause stimulation of vestibule sympathetic system and help in further elicitation by the vestibule sympathetic reflex. The vestibular system also receives sympathetic nervous system projections (Balaban, 1996) which plays a pivotal part in the formation of bones and muscles (Dimitri & Rosen, 2016).

SUMMARY AND CONCLUSION

The present study aimed at assessing the auditory and vestibular functioning of patients with reduced bone mineral density. The study assessed various aspects of hearing and balance at the various levels in the auditory system. The findings revealed that patients with osteoporosis suffered from hearing and balance problems both at the peripheral as well as at the higher centers. These patients do report difficulties listening in adverse environments and do exhibit problems in balancing on administration of tests. Thus the study shreds the importance of evaluating auditory and vestibular system in patients with osteoporosis and osteopenia in order to rehabilitate them earlier and better.

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