

**Effect of Degree of Acquired Cochlear Hearing Loss on Ocular Vestibular
Evoked Myogenic Potential**

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14AUD020



**This Dissertation is submitted as part fulfillment
for the Degree of Master of Science in Audiology
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Certificate

This is to certify that this dissertation entitled “**Effect of degree of acquired cochlear hearing loss on Ocular Vestibular Evoked Myogenic Potential**” is the bonafide work submitted as part fulfillment for the Degree of Master of Science in Audiology of the student with Registration No. 14AUD020. This has been carried out under the guidance of a faculty of this institute and has not been submitted earlier to any other University for the award of any other diploma or degree.

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Declaration

This dissertation entitled “Effect of degree of acquired cochlear hearing loss on Ocular Vestibular Evoked Myogenic Potential” is the result of my own study under the guidance of Dr. Niraj Kumar Singh, Lecturer in Audiology, Department of Audiology, All India Institute of Speech and Hearing, and has not been submitted earlier in any other University for the award of any Diploma or Degree.

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Abstract

Vestibular deficits frequently co-exist with hearing loss and there could be a possibility of one having an impact on the other. However, effect of hearing loss on ocular vestibular evoked myogenic potential (oVEMP) has sparsely been explored. Even the studies that have investigated this aspect, have mainly concentrated on the congenital and only severe to profound degree of hearing loss, notwithstanding the fact that the vestibular pathologies are quite often acquired in origin. Thus the present study aimed at examining the effect of the degrees of acquired cochlear hearing loss on oVEMP response parameters. Ocular VEMPs elicited by 500 Hz tone-bursts were recorded from 50 ears of adults with hearing loss ranging from mild to profound degree (sub-grouped into mild, moderate to moderately severe & severe to profound) and 50 ears of individuals with normal hearing. The results revealed significant reduction in response rate, prolongation of latencies and decrease in peak-to-peak amplitude of oVEMP with increase in severity of hearing loss ($p < 0.05$). Further, there was significant correlation of hearing thresholds and duration since the onset of hearing loss with oVEMP response parameters ($p < 0.05$). Thus, the use of a correction factor for the degree of hearing loss is recommended when interpreting the results of oVEMP.

Key words: *Hearing loss, oVEMP, correction factor*

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At each stage of life from each person there will be something to learni have learnt that no end for learning , sharing knowledge, and being humble.... I thank nite sir and srikar sir for their kindness and support to me and to all my classmates during our study.

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CHAPTER 1

INTRODUCTION

Vestibular evoked myogenic potential (VEMP) is a modulation within the electromyographic (EMG) activity which is caused by a high intensity acoustic (Singh & Barman, 2013), vibratory (Wang, Weng, Jaw, & Young, 2010) or electrical stimulation (Basta, Todt, Eisenschenk, & Ernst, 2005) of the ear. It can be obtained from various muscles including trapezius muscle (Duclaux, Colleaux, & Dubreuil, 1997), triceps (Cherchi et al., 2009), soleus muscle (Cristina, Cunha, Labanca, Campelo, & Utsch, 2014), gastrocnemius muscle (Rudisill & Hain, 2008), sternocleidomastoid muscle (Cherchi et al., 2009), and inferior oblique muscle (Rosengren et al., 2005; Weber et al., 2012) using the surface electrodes placed on the skin overlying them.

A VEMP recorded from the sternocleidomastoid muscle is commonly termed as cervical VEMP (cVEMP) and that recorded from inferior oblique muscle is referred as ocular VEMP (oVEMP). While cVEMP is clinically used for the assessment of the functional integrity of saccule, inferior vestibular nerve and the sacculocollic pathway (Colebatch, Halmagyi, 1992; Colebatch, Halmagyi, & Skuse (1994), oVEMP has proven its utility in the assessment of utricle and the superior vestibular nerve (Todd et al., 2009a,b).

Ocular VEMP reflects the functioning of the utriculo-ocular reflexes to sound (Piker et al., 2013), vibration (Curthoys, Vulovic, & Manzari, 2012), or galvanic stimulus (Cheng, Chen & Young, 2009). A successful recording of oVEMP requires the utricular afferents to project to the vestibular nuclei via the superior vestibular nerve. Further, the neurons in the vestibular nuclei project to the inferior oblique

muscle via the contralateral oculomotor nucleus after crossing the medial longitudinal fasciculus (Weber et al., 2012). Therefore, oVEMP can be recorded using surface electrodes placed beneath the contralateral eye (Chihara et al., 2007, 2009; Weber et al., 2012). Most recent literature also shows the presence of ipsilateral pathway, although less robust than the contralateral one for oVEMP (Singh, Valappil, & Mithlaj, 2015).

Clinically, oVEMP is recorded from the surface electrodes beneath the contralateral eye when gaze is directed upward (Singh & Barman, 2013). This is mainly owing to two significant changes that occur in inferior oblique muscle when the gaze is directed upwards- (1) activation of the inferior oblique muscle (Iwasaki et al., 2009, Rosengren et al., 2013) and (2) increased proximity of the otherwise deeply placed inferior oblique muscle to the skin surface beneath the eyes (Weber et al., 2012; Rosengren et al., 2013). This biphasic response is recorded at the median latencies of around 10 ms (negative peak) and 15 ms (positive peak). It is for this reason that a number of studies refer these peaks as n10 and p15 (Todd, Rosengren, & Colebatch, 2003; Rosengren et al., 2005). Other studies call these peaks as n1 and p1 (Singh, & Barman, 2013, 2014, 2016 a, b).

1.1. Need for the study

The inner ear consists of auditory and vestibular structures responsible for hearing and balance function. The cochlea and the vestibular apparatus are in close proximity to each other, not only anatomically but also embryologically and physiologically. The development of the inner ear starts at the beginning of the fourth week and is completed by 25 weeks; by this time the vestibular apparatus also

achieves adult form and size (O’Rahilly, 1963). Further, in both the systems, the sensory epithelium consists of mechanoreceptor hair cells whose stereocilia are embedded in an overlying mesh-gel layer (Arwing 1955; Brookhouser, 1982; Potter, 1984; Sanderg, 1965). The variation between the systems exists only in the nature of the overlying layer and the organization of the hair cells within the sensory epithelium. Since both auditory and vestibular structures of the inner ear are derived in a similar manner embryologically and they share the same fluid environment and blood supply, it might be possible that a disorder of one may normally include a disorder of the other. Further, the studies on the effects of various factors like noise (Kumar, Vivarthin & Bhatt, 2010) and ototoxicity (Hsu, Cheng & Young, 2015) have shown the co-occurrence of hearing loss and vestibular defects; thus confirming the assumption from the above discussion. However, the literature on the effect of degree of hearing loss on oVEMP is sparse.

In a study exploring the association between hearing loss and VEMP, Bansal, Sahni, & Sinha, (2013) obtained oVEMP from 23 individuals (45 ears) with congenital severe to profound hearing loss in the age-range 15-30 years. oVEMP was recorded for tone-burst of 500 Hz with 2-0-2 blackmann weighted function at repetition rate of 5.1/s. The stimuli were presented monaurally and the responses were filtered using a band-pass filter of 10-1000 Hz. Their results demonstrated significantly lower oVEMP amplitudes in the group of individuals with hearing loss than the healthy controls. Similar results were reported by Niu et al (2016). Although these were well planned and executed studies, the authors only investigated the effect of congenital hearing loss and not the acquired hearing loss. Since most of the disorders of vestibular system are acquired and have hearing loss as a co morbid symptom, it is important to understand if hearing loss has any impact on the outcome

of oVEMP; however there are no studies to demonstrate this. As they (Bansal et al., 2013; Niu et al., 2016) showed that hearing loss had caused an alteration of oVEMP amplitude, it appears logical to believe that the extent of hearing impairment may have varying degree of impact on oVEMP. Therefore it is important to study the effect of hearing loss on the outcome of oVEMP, not only in the severe and profound degrees but also in the lesser degrees of hearing loss.

1.2 Aim of the study of the study

The present study aimed to investigate the effect of various degrees of cochlear hearing loss on oVEMP response parameters.

1.3 Objectives

In order to fulfill the aim of the study, the following objectives were formulated

1. To compare the response rate, individual peak latencies and peak-to-peak amplitude of oVEMP between healthy individuals and those with cochlear hearing loss.
2. To compare the response rate, individual peak latencies and peak-to-peak amplitude of oVEMP between various degrees of cochlear hearing loss.
3. To examine the correlation between hearing thresholds and the various oVEMP parameters (n1 latency, p1 latency, & peak-to-peak amplitude).
4. To examine the correlation between the duration of onset of the cochlear hearing loss and various oVEMP parameters.

1.4 Hypotheses

The study began with four null hypotheses, each pertaining to an objective. These hypotheses are as follows:

1.4.1. There is no significant difference in response rate, individual peak latencies and peak-to-peak amplitude of oVEMP between healthy individuals and those with cochlear hearing loss.

1.4.2. There is no significant difference in response rate, individual peak latencies and peak-to-peak amplitude of oVEMP between various degrees of cochlear hearing loss.

1.4.3. There is no significant correlation between hearing thresholds and the various oVEMP parameters (n1 latency, p1 latency, & peak-to-peak amplitude).

1.4.4. There is no significant correlation between the duration since the onset of cochlear hearing loss and various oVEMP parameters.

CHAPTER 2

Review of Literature

VEMP is one of the most recent diagnostic tests for assessment of otolith function (Kumar, Bhat, Sequeira, Bhojwani, & Pathology, 2015) They are short latency reflexes elicited by high energy signals like loud acoustic (Singh, & Barman, 2013), vibratory (Wang et al., 2010) or galvanic stimuli (Basta et al., 2005). They can be recorded by placing electrodes on activated muscles like sternocleidomuscle and the ocular muscles. When recorded using electrodes placed over the sternocleidomuscle they are called cVEMP and when obtained from electrodes placed over inferior oblique muscle, they are termed as oVEMP (Colebatch et al., 1994; Todd et al., 2007).

cVEMP assess the sacculocollic pathway and is characterized by a biphasic response with an early positive peak at average latency of 13 ms called P13 and later negative peak at about 23 ms namely N23 (Colebatch, et al. 1994). oVEMP is said to be of utricle origin and assess the integrity of superior vestibular nerve and vestibular ocular reflex pathway mediated by them (Weber et al., 2012). It is characterized by biphasic response with an initial negative peak of average latency of about 10 ms called n1 and a later positive peak with an average latency of about 15 ms named p1 (Piker, Jacobson, & Hood, 2013).

Literature is abundant with several stimuli, acquisition and subject related factors that affect the response parameters of oVEMP. The literature search for various subject related factors like age, gender, body position, gaze elevation angle and hearing loss was done using various search engines like google, google scholar,

pubmed central and research gate and the findings have been discussed below in the subsequent section.

2.1 Effect of maturation on oVEMP

Maturation is process by which an innate ability, skill or reflex develops and becomes adult-like, Most of the abilities and reflexes are present at birth but they gradually evolve and sharpen to take adult proportions, and this happens for almost all aspects. Vestibulo-ocular pathway is also said to be mature with age and is linked to the development of walking skills in children (Wang, Hsieh, & Young, 2013). There are only few studies that have looked at studying the maturation of oVEMP.

Wang et al (2013) studied the development of oVEMP in healthy children who were grouped into 3 sub-groups based on age , twenty full term neonates were classified as group A, 15 children in the age range of 1-3 years as group B and 15 children 4-13 years as group C. Tone bursts of 500 Hz were generated using blackman-gated 1 ms rise/ fall time and plateau of 2 ms was used and delivered to the ears at 123 dB pSPL. oVEMP were recorded in eyes closed method for group A and B whereas for subjects in group C were asked to fix eye gaze on a target making 30⁰ elevation. Response were band-pass filtered between 1 to 1000 Hz and analysed for 50 ms. Response rate was found to be 0% in neonates, 40% in group B and 100% in group C. In group B except for 9 children < 2yrs of age, others had peak latencies and peak-to-peak amplitude similar to those found in C. Based on these results, the authors concluded that the maturation of oVEMP is complete by 2 years of age. However, the basic problem with this study was the way in which oVEMP were recorded up to 3 years of age (eyes closed). Studies have shown that oVEMPs are

absent even among high proportion of adults when recorded using closed eye position.

Kumar & Sinha (2014) also investigated development of oVEMP on subjects in the age range of 9–30 years by sub-grouping them into 3 groups. Group I consisted of 15 children in the age range of 9-11 years, group II had 15 children in the age range of 11-13 years and group III had 15 adults in the age range of 18-30 years. Tone burst of 2-0-2 cycles of rarefaction polarity at 125 dB SPL with a repetition rate of 5.1/ s were used and response were analysed for 70 ms and band pass-filtered between 1 to 1000 Hz. Peak latencies were significantly longer in group I when compared to group II and group III. However, there was no difference between group II and III. Furthermore, the peak-to-peak amplitude was significantly larger for group II and did not significantly differ between group I and III. They concluded that the oVEMPs become adult-like by 11-13 years of age.

2.1 Effect of advancing age on oVEMP

With age all the reflexes have a tendency to reduce and the muscle reflexes to acoustic stimulation like VEMP should be no different. In fact, they have been found to be reduced with increase in age (Piker & Hood, 2013; Nyguyen et al., 2010; Tseng et al., 2010). Several researchers have studied the effects of age on the oVEMP parameter like response rate, latency, peak-to-peak amplitude, asymmetry ratio, and frequency tuning and frequency amplitude ratio of oVEMP and have reported the findings

2.1.1 Effect of age on response rate of oVEMP.

Tseng et al (2010) studied the effect of age on oVEMP on 70 healthy individuals in the age range of 24–76 years using a 500 Hz bone-conduction stimulus.

They found response rate of 100% upto 59 years and the response rate significantly reduced thereafter. Similar findings were reported by (Singh, 2014) Kumar, Bhatt, Sequeria & Bhojwani (2015). They included 90 participants with either normal hearing or sensorineural hearing loss, who were divided into 3 sub-groups as young adults (21-40 years), middle aged adults (41-60 years) and older adults (> 60 years). Tone burst of 500 Hz were presented at 100 dB nHL, responses were averaged for 200 sweeps and filtered using 1-1000 Hz band-pass filter. Subjects were asked to maintain an upward eye gaze on a visual target at 30-35° from the horizontal. They reported decrease in response rate for oVEMP with increase in age and observed response rate of about 98% in the younger group which declined to 60% in the older group.

Piker et al (2013) studied the effect of age on oVEMP and cVEMP. They included 39 participants with symmetrical hearing who had presence of oVEMP at 500 Hz, 750 Hz and 1000 Hz. Subjects were equally divided into 3 groups – young adults (18 – 39 years), middle age (40 – 59 years), and old adult (\geq 60 years). oVEMPs were recorded for 7 frequencies ranging from 125 Hz to 2000 Hz at 3 levels – 117, 122 and 127 dB pSPL. Stimuli were blackman-gated (2 ms rise / fall time and 2 ms plateau time) and presented at the rate of 5.1/s. Subjects were in semi-recumbent position with gaze fixed on a visual target at \sim 30° vertically from the center. Response rate was also reduced with increase in age and this effect of advancing age was more profound in the lower and higher frequencies than the mid-frequencies of 500, 750 and 1000 Hz.

Similarly, Husna & Singh (2016) studied the effect of age on response rate of oVEMP on 50 healthy individuals in the age range of 20- 80 years, who were divided into sub-groups covering a span of 10 years. oVEMP were recorded from

contralateral side using alternating polarity tone-bursts (2 ms rise/fall time and 1 ms plateau time) at octave and mid-octave frequencies from 250 Hz to 2000 Hz and presented using an intensity of 125 dB pSPL. Subjects were instructed to fix gaze at about 30° in the superior medial plane. Responses were acquired for duration 64 ms and were band-pass filtered from 1 to 1000 Hz. Response rates were found to be significantly larger in groups up to 50 years of age and smaller in the older aged group. However they reported of no significant difference on response rates in the groups above 50 years and also among groups below 50 years.

2.1.2 Effect of age on peak latencies.

Nguyen et al (2010) investigated the age related characteristic of oVEMP on 53 healthy individuals in the age range of 20-70 years who were sub-grouped as 20-30years, 31-50 years and > 50 years. They used both air-conduction and bone-conduction mode in four conditions- (1) click of 0.1 ms duration, at an intensity of 105 dB nHL with positive polarity at a repetition rate of 5/s, (2) 500 Hz tone burst, with a linear envelope of (1ms rise/fall time, 2 ms plateau time) presented at an intensity of 125 dB SPL with a positive polarity at a repetition rate of 5/s, (3) manual taps of vibration delivered at Fz and (4) mini taps of vibration delivered at Fz. Subject lay in semi recumbent position with an elevation of 30° from the horizontal and were instructed to maintain maximum upward eye gaze. They also ensured symmetrical recording from both eyes by recording 20° saccade tests. They observed no significant association between age and peak latencies of oVEMP.

On the contrary, Kumar et al (2015) found a significant difference in both n1 and p1 latency between the older adults (> 60 years) and the younger adults (21-40 years) and middle aged adults (41-60 years). Although there was no significant

difference between younger and middle aged adults for both n1 and p1 latencies of oVEMP.

2.1.3 Effect of age on peak-to-peak amplitude of oVEMP.

Nguyen et al (2010) observed significant reduction in peak-to-peak amplitude for individuals > 50 years of age when compared to lower age groups (20-30 years). Stimulus and response parameters for this study have been discussed above. Similar findings were observed by Piker et al (2013) and also by Kumar et al (2015). However, Husna & Singh (2016) did not observe significant reduction in peak-to-peak amplitude in older age groups, although a trend of reduction in peak-to-peak amplitude with increase in age was noticed.

2.1.4 Effect of age on asymmetry ratio of oVEMP.

Study by Nguyen (2010) on effect of age on oVEMP included subjects in the age range of 20–70 years. The other stimulus and response parameters have been discussed above. They found no association between age and the asymmetry ratio of oVEMP, probably owing to the fact that age is a symmetrical process.

2.1.5 Effect of age on frequency tuning of oVEMP.

Piker et al (2010) studied the affect of age on frequency tuning of oVEMP and reported a response peak to be at 750 Hz for younger adults (18-39 years) and 1000 Hz for older adults (> 60 years), although there was no significant interaction between age and frequency tuning. Similar results were observed by Husna & Singh (2016). They reported as greater proportion of frequency tuning at 500 Hz or 750 Hz in younger age group compared to older age group (> 60 years) who had higher proportion of frequency tuning at 1000 Hz.

2.1.6 Effect of age on Frequency amplitude ratio of oVEMP.

Frequency amplitude ratio (FAR) is defined as the ratio of peak-to-peak amplitude between two frequencies. Although it is most popularly studied for 1000 Hz and 500 Hz frequency pairs, above frequency pairs have also been studied.

Singh & Barman (2016), studied frequency amplitude ratio of oVEMP on 36 healthy individuals in the age range of 15-50 years. Tone-burst of 500 Hz, 750 Hz, 1000 Hz and 1500 Hz with 2 ms rise/fall time and 1 ms plateau time were used. The responses were recorded for 64 ms epoch and were band-pass filtered between 1-1000 Hz. They found significant correlation between age and FAR for frequencies pairs 750/500, 1000/500 as well 1500/500.

From all the above studies of effect of age on oVEMP, it can be noticed that response rate and peak-to-peak amplitude of oVEMP reduce and peak latencies prolong with increase in age. The less often studied parameters like frequency tuning and frequency amplitude ratio are also impacted by advancing in age with difference in frequency tuning to higher frequency and increase in FAR with increasing age.

2.2 Effect of body position on oVEMP

Anatomically, the orientation of utricle haircells are nearly vertically and with change in body positions its orientation changes, thus generates different gravitational forces on the otoconial membrane (O'Neil & Monroe, 2011). Furthermore, different agonist and antagonist muscles activate with change in position. Thus, body position could affect oVEMP parameters like latencies and peak-to-peak amplitude.

O'Neil and Monroe (2011) investigated the effect of body positioning on oVEMP on 30 healthy adults. Subjects were positioned in four different head and

body alignments- (1) sitting upright with head held straight, (2) lying in supine position with chin tucked in towards chest by making an angle of 30° , (3) turning towards right side and chin tucked in towards chest by making an angle of 30° , (4) turning towards left side and chin tucked in towards chest by making an angle of 30° from supine position. 500 Hz tone burst stimuli, ramped with blackman window of 2 cycle plateau and 1 cycle rise/fall time, were used and intensity was varied from 75-90 dB nHL. Using rarefaction polarity the stimulus was delivered at a rate of 5 Hz. Responses were band-pass filtered between 1-1000 Hz. Subjects were asked to fix a gaze at 20° vertical elevation for position (1) and on premarked points on the wall for other 3 positions. The response rate was reported to be higher in sitting upright and lying supine position and it was to be 98% in these positions compared to turning towards right/left side of the body where it was 86%. The best threshold was found for sitting in upright position. Based on these findings, the authors recommended sitting upright position for clinical recording of oVEMP.

2.3 Effect of gaze elevation on oVEMP

oVEMP have been found to be best recorded from surface electrode over inferior muscle. The inferior muscle, unlike the sternocleidomastoid muscle, is positioned deep below the epithelial layer and comes closer to surface only when activated during upward gaze (Rosengren, 2013). Owing to this knowledge about the inferior oblique muscle, several studies investigated the effect of gaze position on parameters of oVEMP.

Murnane, Akin, Kelly, and Byrd, (2011) studied the effects of changing in gaze elevation angle on 24 subjects in age range of 18-32 years. Using 500 Hz presented at 125 dB pSPL which were delivered at a repetition rate of 5.1 Hz, they

obtained oVEMPs for gaze elevation angles of 0° , 15° and 30° . The peak latencies were found to be earlier with increase in elevation of eye, however it was statistically earlier for p1 latency for 15° and 30° compared to 0° elevation. Peak-to-peak amplitude was found to be significantly larger with increase in elevation.

Rosengren, Colebatch, Strauman and Weber (2013) studied the effect of gaze elevation and electrode positioning on oVEMP on 10 healthy individuals using 500 Hz, 4 ms bursts of vibration held at Fz, delivered at rate of 7 Hz by a handheld minishaker. Responses were sampled for 10000 Hz for 70 ms and were band-pass filtered between 5 Hz to 2000 Hz. Eye gaze were maintained at 0° , 24° upward and 24° downward gaze. They observed that the prolonged latencies with gaze downward than the gaze in neutral and upward direction and reduction in peak-to-peak amplitude with downward gaze. Response rate and peak-to-peak amplitude was found to be higher with upward gaze and reduced significantly with gradual lower elevations.

Kanther and Gurkov (2014) also examined effect of gaze elevation on 32 healthy individuals in the age range of 18-43 years. They obtained recordings with 500 Hz tone burst which was blackman gated for 2 ms rise/fall time and 2 ms plateau time and presented at 100 dB nHL using a 5.1 Hz repetition rate. Responses were recorded for 70 ms epoch and band-pass filtered between 10-750 Hz. Subjects were asked to maintain gaze at an elevation of 30° and 35° at a distance of 80 cm. Results revealed similar response rate and peak latencies for both elevation; however, significant larger amplitude was observed with 35° than 30° .

Ayesha & Singh (2016) did a similar study on 50 healthy individuals in the age range of 18-35 years. Tone burst of 500 Hz at 125 dB pSPL with rarefaction polarity was used. Stimulus was presented at 5.1/s repetition rate and was blackman-

gated (2 ms rise/fall time, 1 ms plateau time). Responses were band-pass filtered between 1-1000 Hz. Subjects were asked to fix their gaze on pre-marked points ranging from -5° to $+30^{\circ}$ elevation in 5° steps on wooden scale. Results revealed significantly lower response rate for -5° to $+10^{\circ}$ than for elevation from 15° to 30° . Shortening of peak latencies and increase in peak-to-peak amplitude was observed with increase in elevation up to 20° elevation.

The findings from the above studies suggest increase in response rate, peak-to-peak amplitude and earlier latencies with increase in gaze elevation. However few studies suggest significant changes only up to 20° elevation. Nonetheless, there is a unanimous agreement for use of gaze elevation in the midline in order to obtain best and most reliable recordings of oVEMPs

2.5 Effect of hearing loss on oVEMP

Cochlea and vestibule are in close proximity to each other and are embryologically and physiologically related (O’Rahilly, 1963). They share similar fluid environment and blood supply and hence an abnormality in cochlea might also lead to abnormalities in vestibular system. Thus hearing loss due cochlear damage could affect various oVEMP parameters.

Bansal et al (2013) investigated cervical and ocular vestibular evoked myogenic potentials in individuals with severe to profound hearing loss. They studied 46 participants, 23 with normal hearing and 23 with bilateral severe to profound hearing loss. oVEMP was recorded with 500 Hz tone-burst that was blackman-gated (2 ms rise/fall time and 1ms plateau time) and presented at 95 dB SPL at repetition rate of 5.1/s. Responses were band-passed filtered between 10-1000 Hz. Results showed response rate of 100 % in control group and 66% in the experimental group.

Further, no significant difference was found for peak latencies. Peak-to-peak amplitude was significantly larger in the control group than the experimental group.

Similarly study was carried out by Niu et al (2016) on 29 individuals in the age range of 18-63 years, diagnosed as having congenital severe to profound hearing loss. oVEMP were recorded with 500 Hz tone-burst stimuli, blackman-gated (2 ms rise/fall time and 2 ms plateau time) and at 125 dB pSPL, which was varied in 5 dB step. Responses were band-pass filtered between 10-1500 Hz. They found a response rate of 100% in the control group and 38.94% in the study group (congenital profound hearing loss). Furthermore, significantly smaller peak-to-peak amplitude was found in the study group compared to the control group ($p < 0.05$). Peak latencies and peak-to-peak amplitude was significantly between the two groups.

All the above studies reports of abnormal findings on oVEMP in individuals with hearing loss. However all the above studies were done in individuals with congenital hearing loss group and they were restricted to only severe to profound hearing loss group. There are no published reports of effects of mild, moderate or moderately severe degrees of hearing loss on parameters of oVEMP.

CHAPTER 3

Method

The study included two groups of participants, both in the age range of 18-50 years. The group of participants with normal hearing sensitivity were classified as group I and the group of participants with cochlear hearing loss were termed as group II. The participants were nominated to the two groups based on the fulfilment of certain criteria. Each of the participants in the study were explained about the experiment, and signed the informed written consent. Further none of them were paid for their participation in the study.

3.1.1 Selection criteria to Group I.

Group I consisted of 50 ears of 25 healthy individuals with normal audio-vestibular system. The raw data of various oVEMP of healthy individuals was obtained by randomly selecting the subjects used in the previously published studies (Singh, Kadisonga, & Ashitha, 2014); (Singh & Barman, 2013) Singh & Barman, 2013, 2014, 2015). As per these studies, the group of healthy individuals had PTA < 15 dB, 'A' type tympanogram and reflexes present at 100 dB. Further they also had normal results on auditory brainstem responses and otoacoustic emissions.

3.1.2 Selection criteria to Group II.

Group II consisted of 50 ears of 27 participants with acquired cochlear hearing loss with the degree ranging from mild to profound. They were further equally sub-grouped into 3 groups (mild, moderate to moderately severe & severe to profound) based on the degree of hearing loss classified by Goodman (1965). As per this guideline, individuals with a PTA of 26-40 dBHL, 41-55 dBHL, 56-70 dBHL,

71-90 dBHL and >90 dBHL are classified as having mild, moderate, moderately severe, severe and profound hearing loss, respectively.

A detailed structured case history, otorhinolaryngological investigation and audiological evaluation ensured non-inclusion of participants in whom the hearing impairment is known to coexist with the vestibular deficits such as Meniere's disease, ototoxicity, noise induced hearing loss, labyrinthitis and presbycusis. All the participants in this group had speech recognition threshold (SRT) within 12 dB HL of the pure tone average (PTA) and the degree appropriate speech identification scores (SIS). The normal middle ear function was ascertained by the finding of 'A' type tympanogram and a lack of history suggestive of a conductive component to their hearing loss. Furthermore, participants with signs and symptoms of retrocochlear pathology were excluded. This was ensured through normal results on auditory brainstem responses (ABR) using the site of lesion testing protocol (except severe to profound hearing loss sub-group) and/or the case history. A lack of vestibular involvement was further ascertained through normal results on behavioural balance screening techniques such as Romberg test, Fukuda stepping test, tandem gait test and past pointing test.

3.2. Test environment

All the tests were carried out inside the well-illuminated, sound treated rooms with ambient noise levels within the permissible limits (ANSI S3.1, 1999). Pure-tone audiometry and speech audiometry were carried out in a double room set-up whereas the immittance evaluation, ABR and oVEMP were obtained in a single room set-up.

3.3. Instrumentation

A calibrated Grason-Stadler Incorporated 61 (GSI-61) clinical audiometer with impedance matched TDH-50 supra-aural headphones was used for air-conduction testing like pure-tone audiometry and speech audiometry. The same audiometer with Radioear B-71 bone vibrator was used to obtain bone-conduction thresholds. A calibrated GSI-Tympstar clinical immittance meter was used for tympanometry and reflexometry. Biologic Navigator Pro evoked potential system version 7.2.1 with impedance matched SINSER insert earphones was used to record and analyze auditory brain stem responses and oVEMP.

3.4. Procedure

A detailed structured case history was taken from all the participants before the commencement of the audiological evaluation. Pure-tone audiometry was obtained using modified Hughson-Westlake procedure (Carhart & Jerger, 1959) for the octave frequencies from 250 to 8000Hz for air-conduction stimuli and from 250 to 4000Hz for bone-conduction stimuli. SRT were obtained using spondee word lists and SIS were obtained using phonetically balanced word lists in the participant's native language. Immittance evaluation was administered in order to rule out the middle ear pathology in all the participants. This included tympanometry as well as acoustic reflex testing. Tympanometry was carried out using a probe-tone frequency of 226 Hz by varying air pressure from -400 daPa to +200 daPa inside the ear canal at a rate of 50 daPa/s. Using the same probe-tone frequency, both ipsilateral and contralateral acoustic reflex thresholds were obtained for stimulus frequency of 500 Hz, 1000 Hz and 2000 Hz. Auditory brainstem responses (ABR) were obtained to rule out retrocochlear pathology. For this, a two-channel recording was obtained using click stimuli of rarefaction polarity and a blackman gating for stimulation rate of 11.1/s and

90.1/s at a level 90 dB nHL. The other stimulus and acquisition related parameters for ABR recording are mentioned in the Table 3.4.1.

Table 3.4.1.

Stimulus and recording parameters for obtaining auditory brainstem responses

Stimulus Parameters		Recording parameters	
Stimulus	Click	Gain	100000
Intensity	90 dB nHL	Epoch	16 ms
Rate of stimulation	90.1/s and 11.1/s	Filter	30 to 3000
Sweeps	1500	Electrode Montage	Non inverting – Cz, Inverting - mastoid
Polarity	Rarefaction		Ground – Fz

Behavioural vestibular tests were done to rule out the vestibular pathology. Romberg test was carried out by instructing participants to stand with their feet together and arms stretched forward so that they were parallel to the ground. The test was carried out in both eyes open and closed condition and any sway or imbalance was considered abnormal. In the Fukuda stepping test, participants were instructed to march 50 steps at a place with their eyes closed and arms stretched forward, similar hand positioning to Romberg test. Deviation of greater than 45⁰ towards, either side and/or distance of >1m from original standing point was considered abnormal (Harit & Singh, 2012). Tandom gait test was performed with the participants walking heel-to-toe for about 5 metres with head held straight on an imaginary straight line.

Presence of sway or imbalance was considered abnormal. In past pointing test the participants were asked to touch their nose tip and the clinician's finger tip alternating with their index finger. The positioning of the clinician's finger was altered regularly and unpredictably both in terms of direction and distance. Undershoot or overshooting of the target or presence of tremors was considered abnormal.

For recording oVEMP, participants were instructed to sit in an upright position. A commercially available skin preparing gel was used to scrub the electrode sites and gold plated disc electrodes were placed on these sites with the help of a commercially available conduction paste and surgical plaster. The non-inverting electrode was placed 1 cm below the centre of the lower eye lid, the inverting electrode 2 cm below the non-inverting and the ground electrode on the forehead. This electrode site selection is same as that used in the previous oVEMP publications (Chihara et al., 2009; Singh & Barman, 2013, 2014, 2016 a,b). The absolute and inter-electrode impedance were maintained below 5 k Ω and 2 k Ω respectively. The contralateral ear stimulation was achieved through the use of default SINSER insert earphones. During the recording, the participants were instructed to maintain constant eye gaze at a point kept at an angle of 30° in the supero-medial plane. Further, the participants were instructed to avoid any movements of head, neck and jaw in order to avoid adulteration of responses through muscle artifacts. The ocular VEMPs were recorded using monaural stimulation. Alternating polarity short tone-bursts of 500 Hz were presented at an intensity of 125 dB peSPL. The stimuli were ramped using blackman gating with rise/fall and plateau times of 2 ms and 1 ms respectively and were presented at a repetition rate of 5.1 Hz as these parameters were reported to be best suited to clinical recording of oVEMP (Joshi & Singh, 2013; Singh et al., 2014). The responses were band-pass filtered between 1 and 1000 Hz and were amplified by

a factor of 30000. An epoch time of 75 ms, inclusive of pre-stimulus recording of 10.5 ms, was used and 200 sweeps were averaged per recording.

3.5 Response analyses

A present oVEMP was operationally defined as a waveform that consisted of initial negative peak (n1) occurring at a latency of about 10 ms (range = 8-13 ms) with a subsequent positive peak (p1) occurring at about 15 ms (range = 14-18 ms). The responses were analysed by two experienced audiologists for presence/absence. They also identified and marked the appropriate peaks in case of a present oVEMP. The inter-judge agreement for peak identification and response prevalence was excellent [$\alpha > 0.9$, $K = 0.95$].

3.6. Statistical analyses

The data were analysed using Statistical package for social sciences (SPSS) software version 17.0. Shapiro-Wilks test of normality revealed non-normal distribution of the data ($p < 0.05$) and therefore non-parametric statistics were used. Descriptive statistics were done separately for the groups and for each of the subgroups (mild, moderate-moderately severe and severe to profound hearing loss) within group II to find out the mean, median, standard deviation and range for the various oVEMP parameters. A free public domain software Smith's statistical package (SSP) was used for equality of test for proportion in order to compare the response rates between the groups. Kruskal-Wallis test was used to determine differences between the groups and whenever there was significant difference; Mann-Whitney U test was done for pairwise comparison between the groups for individual latencies (n1 & p1) and peak-to-peak amplitude.

Spearman's correlation was done to find correlation between hearing threshold and oVEMP parameters and also between the duration since the onset of hearing loss and oVEMP parameters. Further, linear regression analysis was done in case of any significant correlation between the variables, in order to generate linear regression curves and equations.

CHAPTER 4

Result

In the present study, oVEMPs were recorded from 50 ears with hearing loss and their findings were compared against randomly drawn data of 50 ears with normal hearing. Ears with hearing loss were sub-divided into 3 groups based on the degree of hearing loss as mild ($PTA = 26-40$ dBHL), moderate to moderately severe ($41 > PTA < 70$ dBHL) and severe to profound ($PTA > 71$ dBHL) for the fulfilment of one of the objectives of the present study. Figure 4.1 show the representative oVEMP waveforms obtained from one individual with normal hearing and three individuals with hearing loss, one each from the above mentioned three sub-groups. Figures 4.2, 4.3 and 4.4 show individual data for n1 latency, p1 latency and peak-to-peak amplitude across the groups and sub-groups used in the present study.

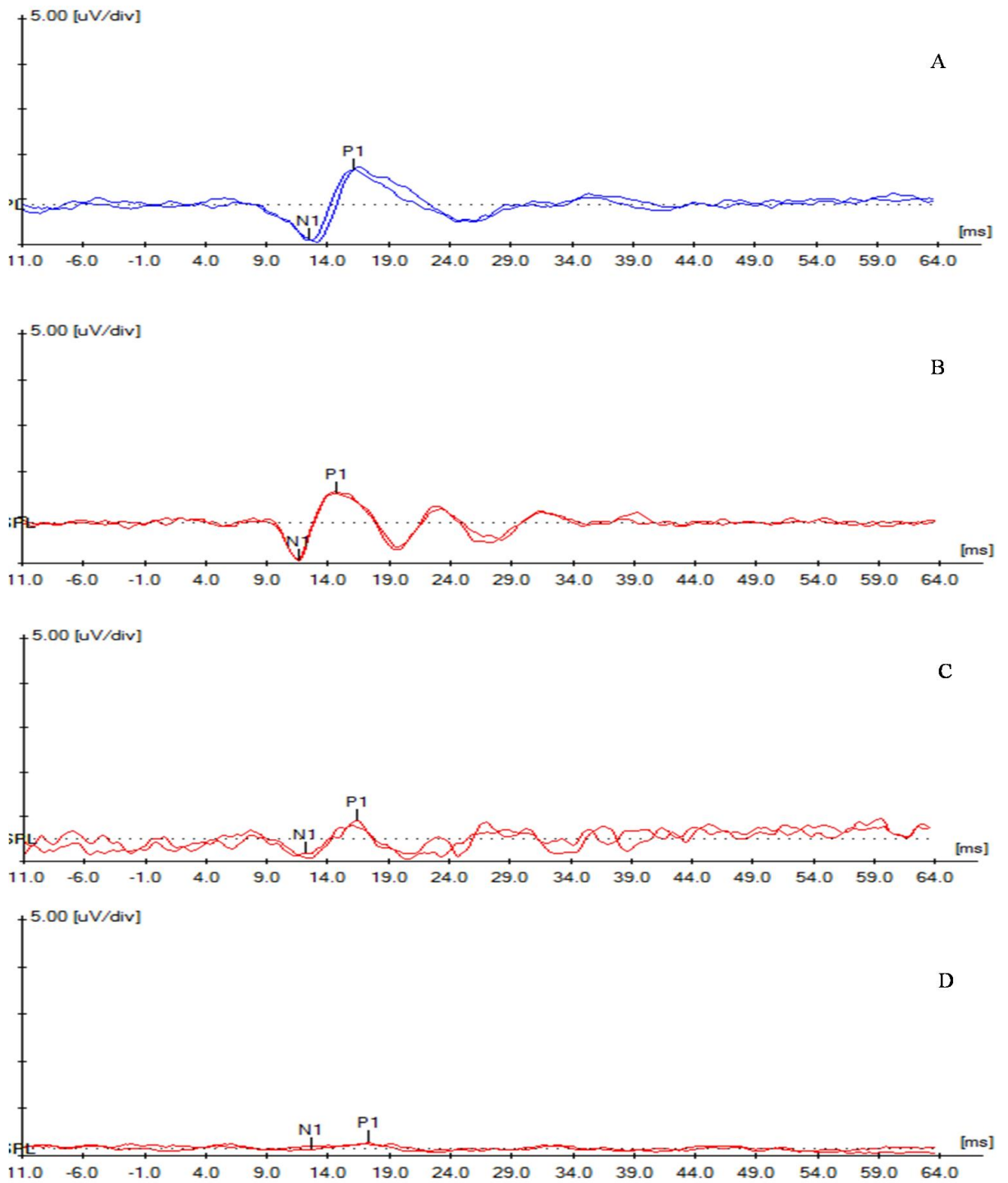


Figure 4.1: Representative oVEMP waveforms of one individual each from normal hearing (A), mild hearing loss (B), moderate to moderately severe hearing loss (C) and severe to profound hearing loss (D) groups.

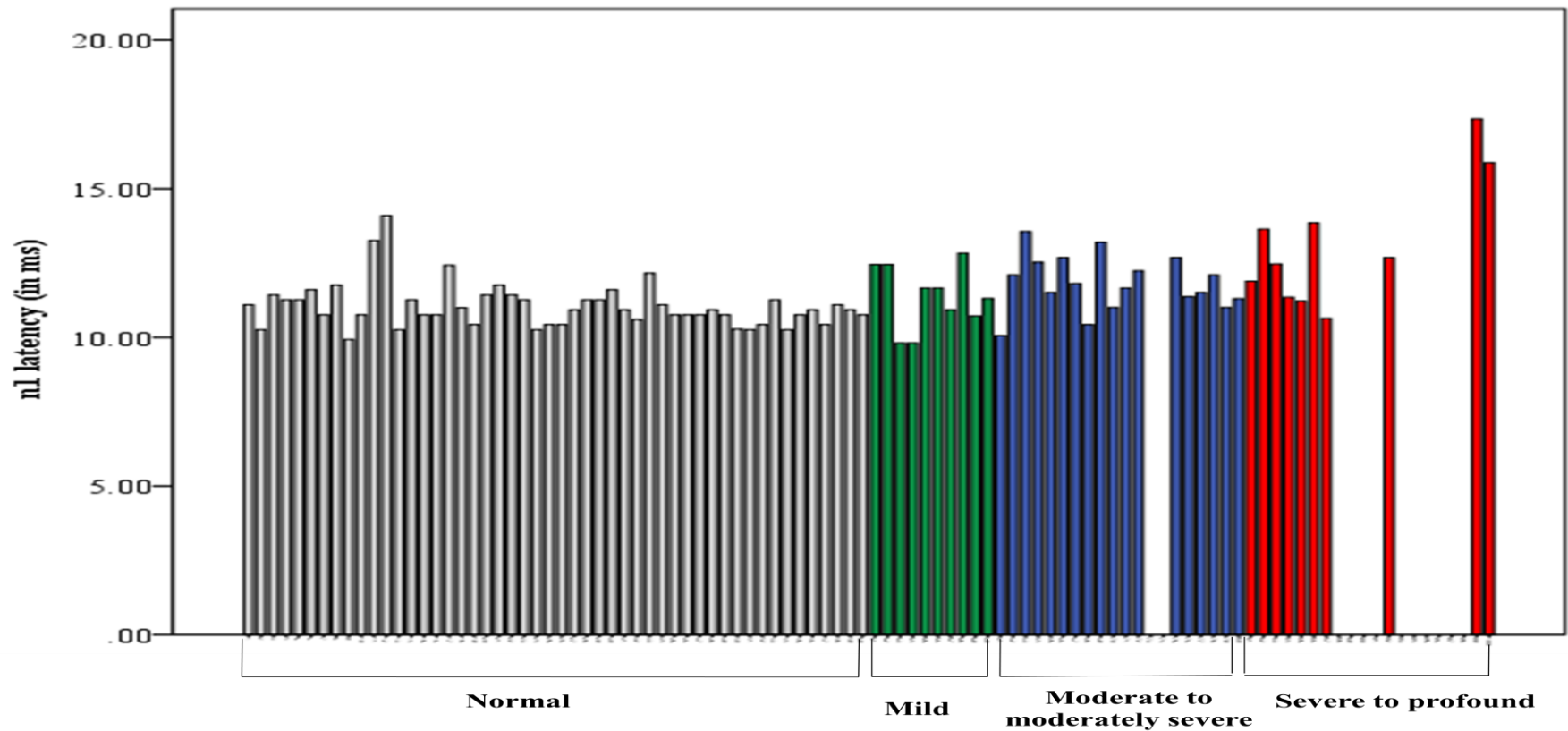


Figure 4.2: nI latency of oVEMP for all the subjects included in the study

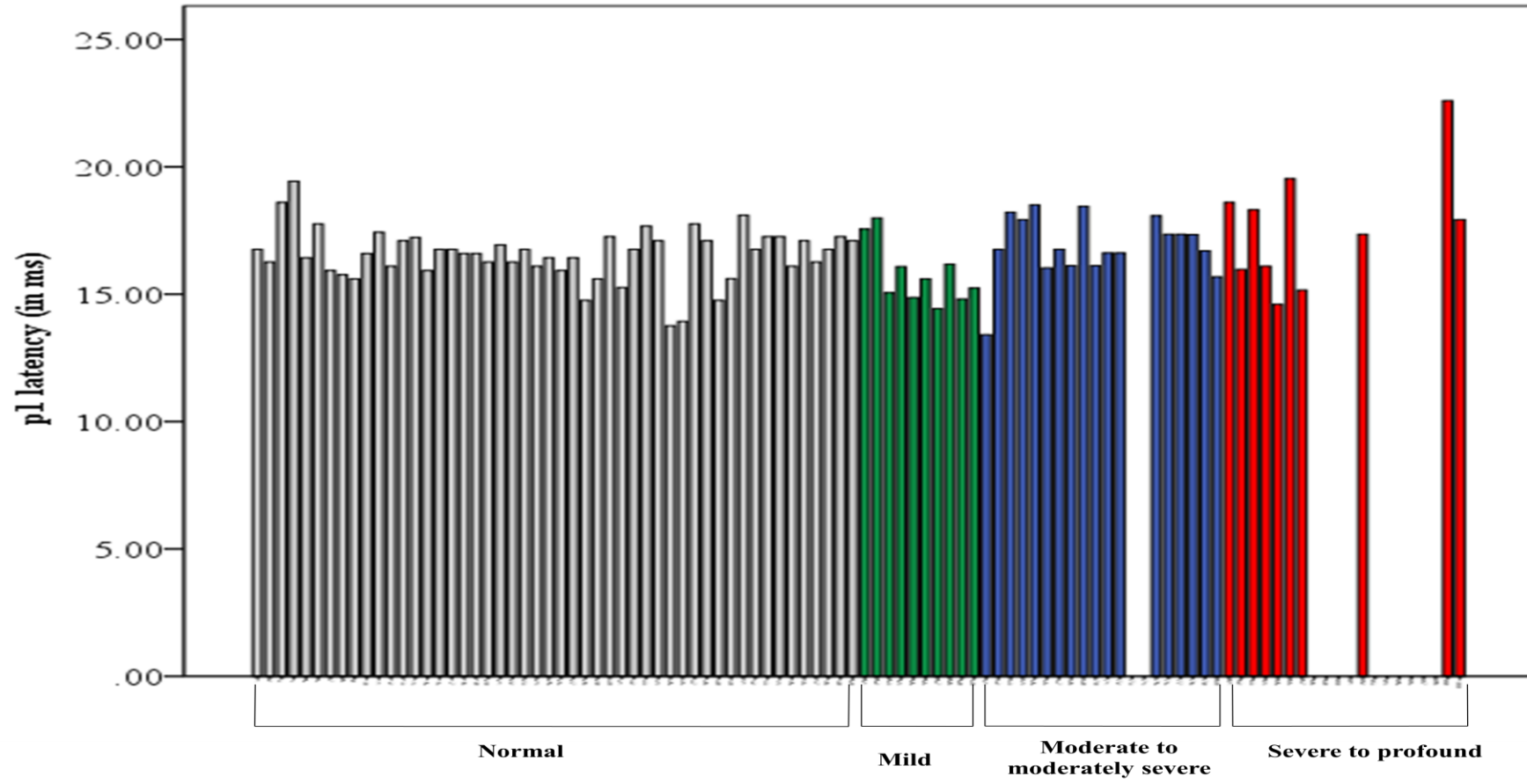


Figure 4.3: p1 latency of oVEMP for all the subjects included in the study

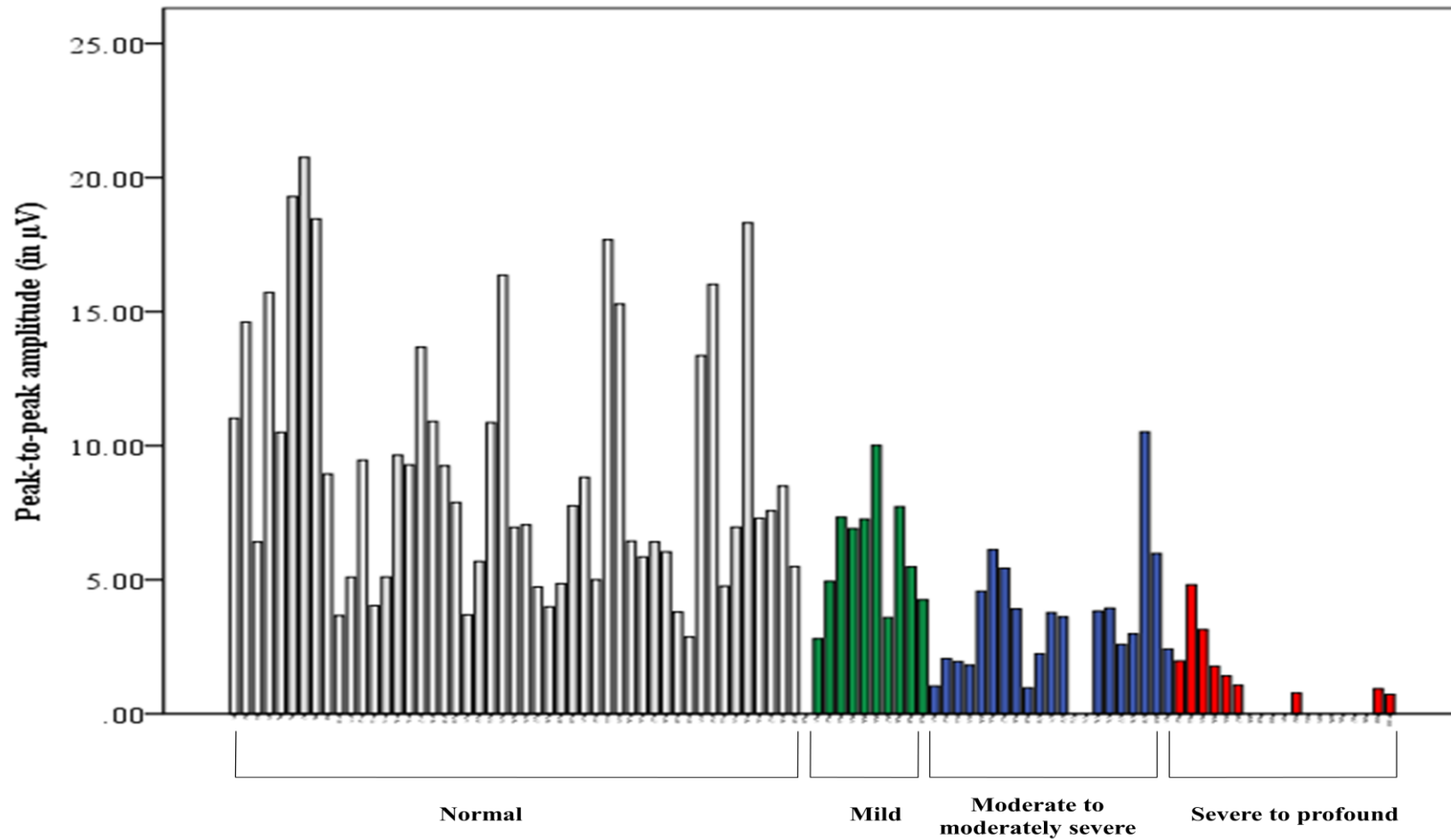


Figure 4.4: Peak-to-peak amplitude of oVEMP for all the subjects included in the study

The study began with four null hypotheses. The results are discussed below for each of the hypotheses in order to prove or disprove them.

4.1 Hypothesis 1

The first hypothesis of the present study stated, “there is no significant difference in response rate, individual peak latencies and peak-to-peak amplitude of oVEMP between healthy individuals and those with cochlear hearing loss”. The statement comprised of three different parameters and therefore the results under this hypothesis are discussed under each of these parameters.

4.1.1 Effect of hearing loss on response rate of oVEMP.

oVEMPs were found to be present in all 50 ears of individuals with normal hearing and 38 out of the 50 ears of individuals with hearing loss, thereby producing response rates of 100% and 76% in healthy ears and ears with hearing loss, respectively. Equality of test for proportions was done in order to find the statistical significance of the above mentioned observations and the results revealed significantly lower response rates in the ears with hearing loss than the ears with normal hearing [$Z = 3.69, p < 0.001$]. Figure 4.1.1 shows the response rates of oVEMP in ears with normal hearing and those with hearing loss and also the outcome of the equality of test for proportions for statistical comparison between the two groups.

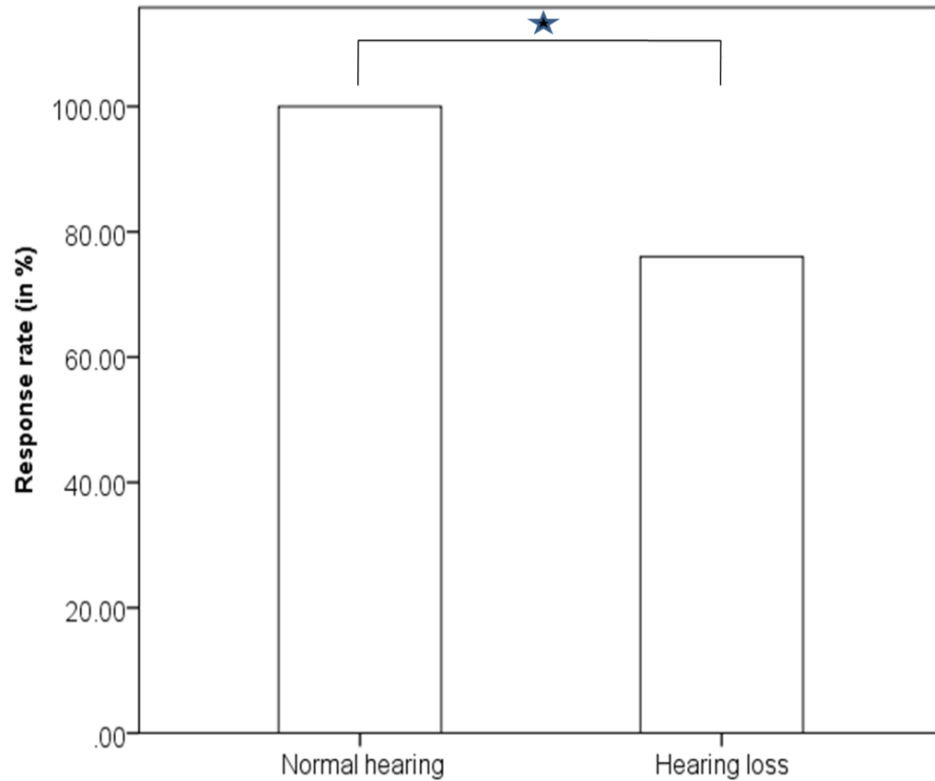


Figure 4.1.1: Response rates of oVEMP in ears with normal hearing and ears with hearing loss. The star-marked comparison is statistically significant ($p < 0.001$).

4.1.2 Effect of hearing loss on peak latencies of oVEMP.

The biphasic oVEMP responses were analyzed in terms of n1 and p1 latencies. Mean, standard deviation, median and range of n1 and p1 latencies were obtained which are shown in Table 4.1.2. It can be noticed from the table that the latencies were longer in ears with hearing loss than the ears with normal hearing.

Table 4.1.2.1.

Mean, median, standard deviation and range of n1 and p1 latency in normal hearing ears and ears with hearing loss

Group	N	n1 latency (in ms)				p1 latency (in ms)			
		Mean	Median	SD	Range	Mean	Median	SD	Range
Ears with normal hearing	50	11.05	10.93	0.75	9.93-14.10	16.56	16.68	1.03	13.76-19.43
Ears with hearing loss	50	12.03	11.73	1.49	9.81-17.35	16.79	16.66	3.60	13.41-22.60

Note: ‘SD’ – standard deviation; ‘N’- number of ears.

Mann-Whitney *U* test was carried out to investigate the statistical significance of the above mentioned observations for latencies. The results revealed significantly longer n1 latency in ears with hearing loss than ears with normal hearing [$Z = -4.083$, $p < 0.01$]. However, there was no significant difference between the groups for p1 latencies [$Z = -0.49$, $p > 0.05$]. Figure 4.2.1.1 shows mean and 95% confidence intervals of n1 and p1 latencies in both the groups and the outcome of Mann-Whitney *U* test for between groups comparison.

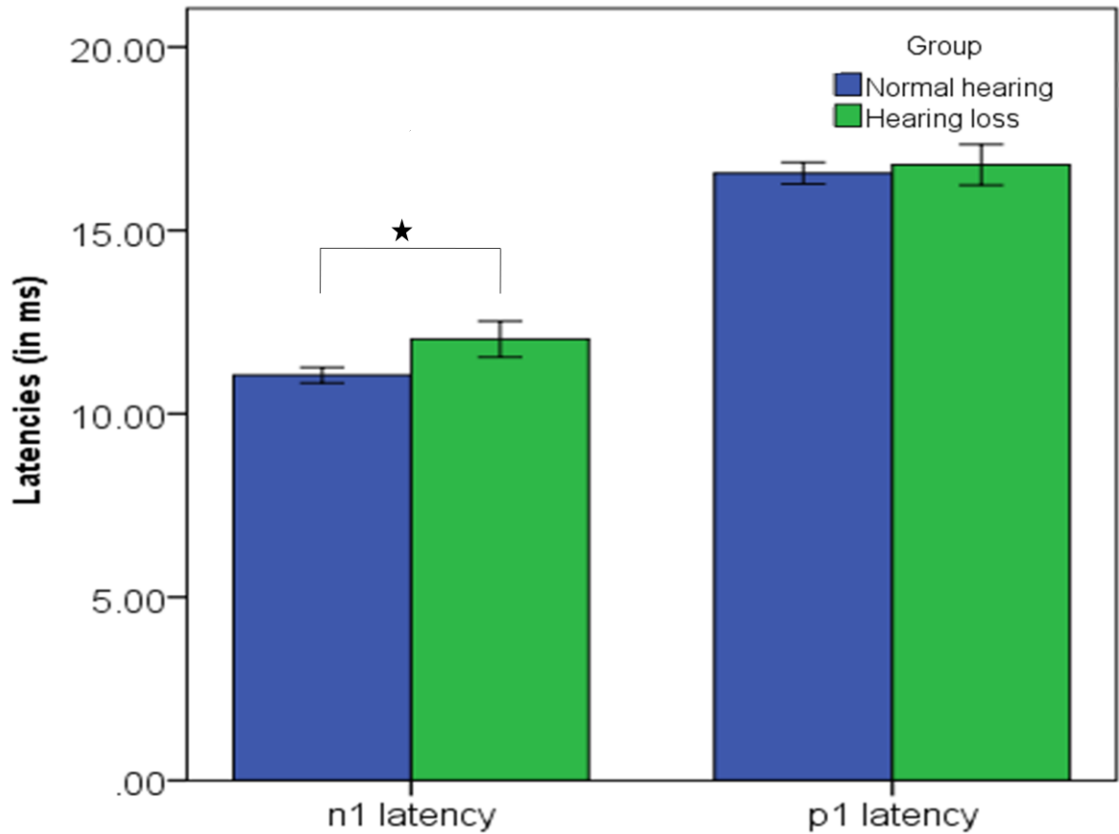


Figure 4.1.2.1: Mean and 95% confidence intervals of n1 and p1 latencies in ears with normal hearing and those with hearing loss and the outcome of Mann-Whitney *U* test for between groups comparison. Star-marked comparisons are statistically significant ($p < 0.01$)

4.1.3 Effect of hearing loss on peak-to-peak amplitude of oVEMP.

The biphasic oVEMP responses were analysed for peak-to-peak amplitude. Amplitudes were measured from n1 peak to p1 peak and not for deviation from the baseline. Mean, median, standard deviation and range of peak-to-peak amplitude were obtained and are shown in Table 4.1.3.1. It can be noticed that the peak-to-peak amplitude in the ears with hearing loss were smaller than the ears with normal hearing.

Table 4.1.3.1. *Mean, median, standard deviation and range of peak-to-peak amplitude (in μV) of oVEMP in ears with normal hearing and ears with hearing loss*

Group	N	Mean	Median	SD	Range
Ears with normal hearing	50	9.18	7.66	4.78	2.86-20.75
Ears with hearing loss	50	3.85	3.60	2.51	0.72-10.51

Note: ‘N’ – number of participants, ‘SD’ – standard deviation.

Further, non-parametric statistical analysis was done using Mann-Whetney *U* test in order to investigate the statistical significance of the above mentioned observations pertaining to the peak-to-peak amplitude of oVEMP. The results revealed significantly smaller peak-to-peak amplitude in ears with hearing loss than in ears with normal hearing [$Z = -5.804, p < 0.001$]. Figure 4.1.3.1 shows the mean and 95% confidence intervals of peak-to-peak amplitude of oVEMP in both groups of participants and the outcome of Mann-Whitney *U* test for between groups comparison.

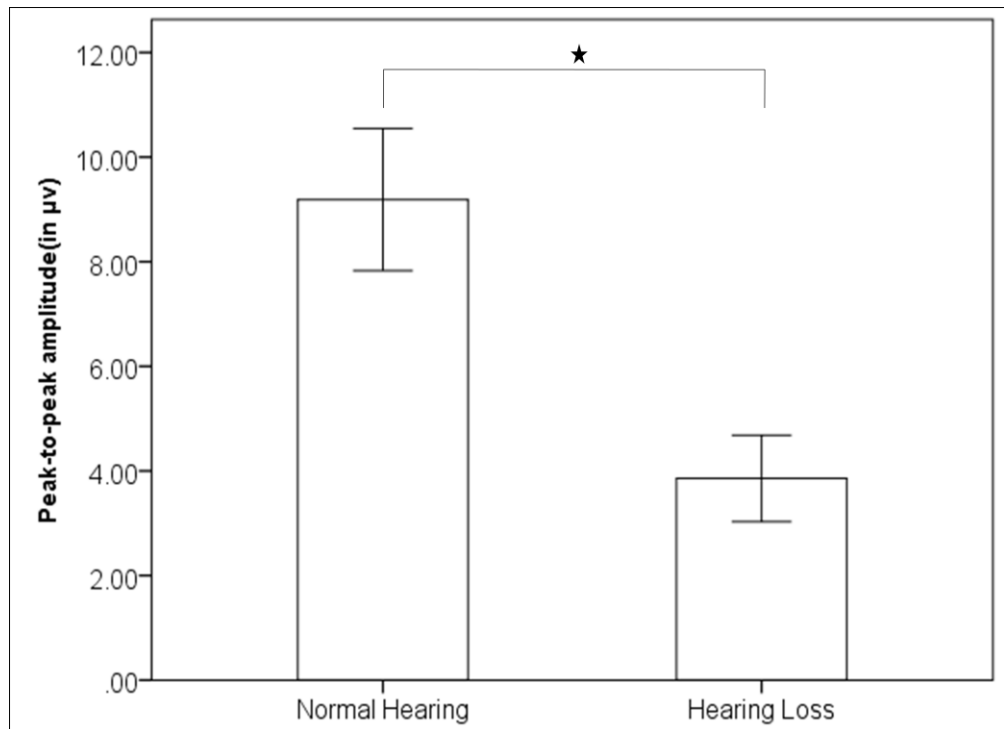


Figure 4.3.1.1: Mean and 95% confidence intervals of peak-to-peak amplitude in ears with normal hearing and those with hearing loss and the outcome of Mann-Whitney U test. Star-marked comparison is statistically significant ($p < 0.001$).

The null hypothesis 1 that there is no significant difference in response rate, peak latencies and peak-to-peak amplitude of oVEMP between normal hearing ears and ears with hearing loss is therefore rejected expect for p1 latency for which it was accepted. Thus, the alternate hypothesis 1 is that there is a significant difference in response rate, n1 latencies and peak-to-peak amplitude of oVEMP between normal hearing ears and ears with hearing loss.

4.2 Hypotheses 2

The second hypothesis of the present study stated, “there is no significant difference response rate, individual peak latencies and peak-to-peak amplitude of oVEMP between various degrees of cochlear hearing loss”. Since the hypothesis

statement had three different parameters, it was tested separately for each of these and the results are therefore discussed under each of these parameters.

4.2.1 Effect of degree of hearing loss on response rate.

Hearing loss group comprised of 50 ears. These were further grouped into 3 sub-groups as mild, moderate to moderately severe and severe to profound. oVEMP was present in all 10 ears in the mild hearing loss group producing a response rate of 100%. Among the 20 ears with moderate to moderately severe hearing loss, oVEMP was present in 18 ears and among the 20 ears with severe to profound hearing loss group, oVEMP was present in 10 ears, thereby producing a response rates of 90% and 50% in moderate to moderately severe and severe to profound hearing loss groups, respectively. Equality of test for proportions was done to compare the response rates of oVEMP between the various hearing loss sub-groups and the results revealed significantly lower response rate in severe to profound hearing loss group when compared to mild hearing loss group [$Z = 2.73, p < 0.01$] and moderate to moderately severe hearing loss group [$Z = 2.76, p < 0.01$]. However, there was no significant difference in response rate of oVEMP between mild hearing loss group and moderate to moderately severe hearing loss group [$Z = 1.03, p > 0.05$]. Figure 4.2.1.1 shows the response rates across the sub-groups among ears with hearing loss and the outcome of the equality of test for proportions for between groups comparisons of response rate of oVEMP.

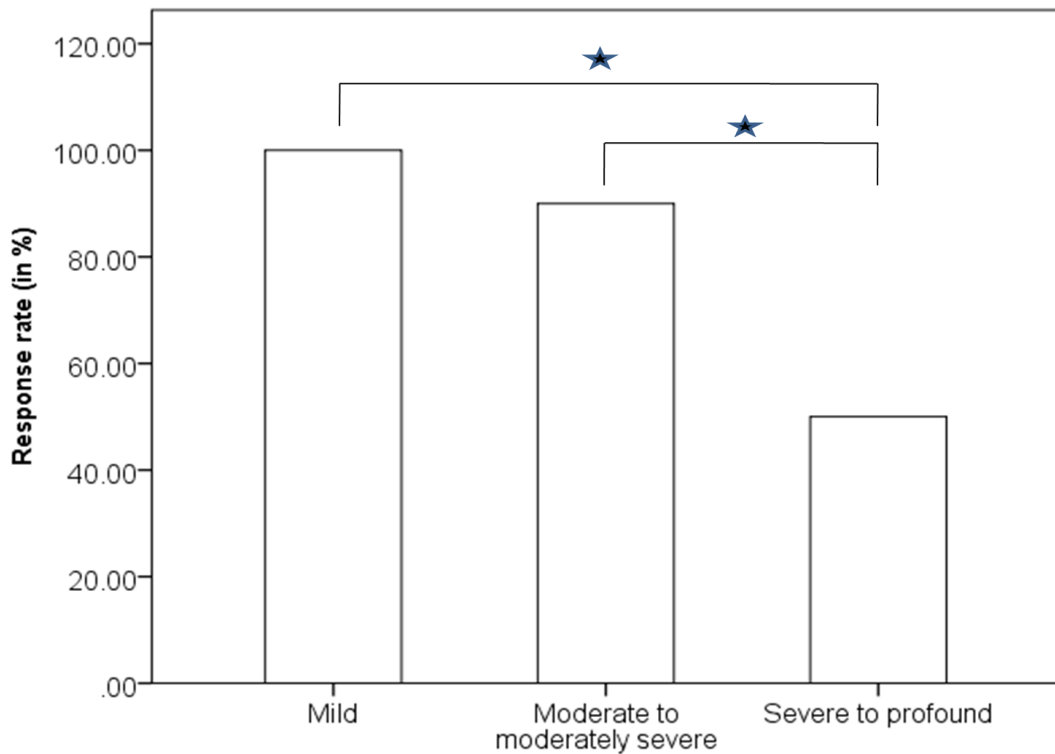


Figure 4.2.1.1: Response rate of oVEMP in ears with mild, moderate to moderately severe and severe to profound hearing loss and the outcome of the equality of test for proportions for comparison of response rates between the groups of ears with various degrees of hearing loss. The star-marked comparisons are statistically significant ($p < 0.05$).

4.2.2 Effect of degree of hearing loss on peak latencies of oVEMP.

The biphasic oVEMP responses were analysed in terms of n1 and p1 latencies. Mean, median, standard deviation and range of n1 and p1 latencies were calculated and are shown in the Table 4.2.2.1. It can be noticed from the table that the n1 latency was longer in severe to profound hearing loss group compared to mild hearing loss and moderate to moderately severe hearing loss groups, with no difference between mild and moderate to moderately severe hearing loss groups. The p1 latencies though

showed progressive prolongation of latencies with the smallest values observed in the mild hearing loss group and the largest in the severe to profound hearing loss group.

Table 4.2.2.1.

Mean, median, standard deviation and range of n1 and p1 latencies of oVEMP in ears with mild, moderate to moderately severe and severe to profound hearing loss

Groups	n1 latency (in ms)				p1 latency (in ms)			
	Mean	Media	SD	Range	Mean	Median	SD	Range
Mild	11.36	11.48	1.06	9.81-12.83	15.78	15.42	1.1	14.43-17.99
Moderate to moderately severe	11.36	11.73	1.06	8.34-14.38	16.89	16.76	1.2	12.22-19.34
Severe to profound	13.09	12.57	2.14	10.06-13.56	17.61	17.64	2.3	14.622.60

Note: ‘SD’ – standard deviation.

A Kruskal-Wallis test was carried out to investigate the statistical significance of the above mentioned observations for latencies of oVEMP peaks. The results revealed no significant group difference for n1 latencies [$\chi^2(2) = 4.53, p > 0.05$], whereas there was a statistically significant difference among group for p1 latencies [$\chi^2(2) = 6.17, p < 0.05$]. This necessitated for further statistical pair-wise comparison between the three sub-groups of hearing loss in order to find out the specific pairs of groups that were significantly different from each other.

Mann-Whitney U test was done for pair-wise comparison of p1 latencies between the groups. The results revealed significantly longer p1 latencies in severe to profound hearing loss group than the mild hearing loss group [$Z = -1.89, p > 0.05$] and moderate to moderately severe hearing loss group [$Z = -0.60, p < 0.05$]. However there was no significant difference in p1 latencies of oVEMP between mild and moderate to moderately severe hearing loss groups [$Z = -2.351, p > 0.05$]. Figure 4.2.2.1 shows mean and 95% confidence intervals of n1 and p1 latencies in the groups of ears with various degrees of hearing loss and the outcome of Mann-Whitney U test for between groups comparison.

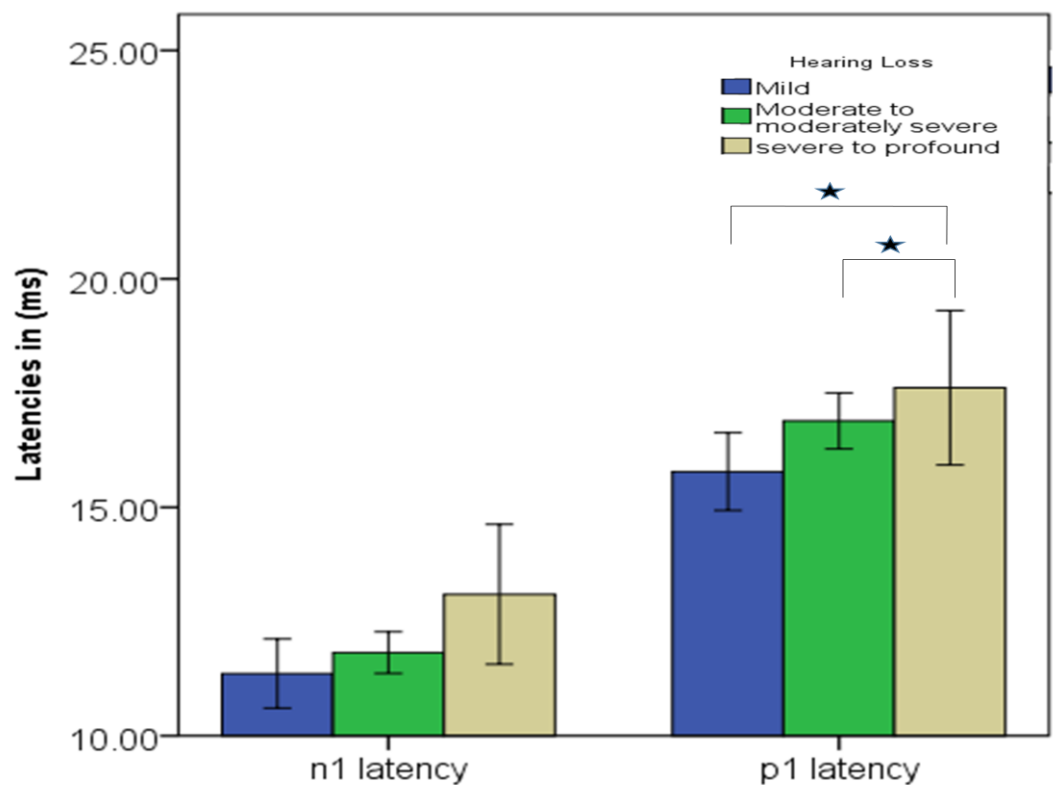


Figure 4.2.2.1: Mean and 95% confidence intervals of n1 and p1 latencies of oVEMP in ears with mild, moderate to moderately severe and severe to profound hearing loss and the outcome of Mann-Whitney U test for between groups comparison. Star-marked comparisons are statistically significant ($p < 0.05$).

4.2.3 Effect of degree of hearing loss on peak-to-peak amplitude.

The biphasic oVEMP responses were analysed for peak-to-peak amplitude. Mean, median, standard deviation and range of peak-to-peak amplitude were obtained and are shown in Table 4.2.3.1. It can be noticed from the table that the largest peak-to-peak amplitude values corresponded to the mild hearing loss group whereas the smallest values of peak-to-peak amplitude were pertaining to the severe to profound hearing loss group. The moderate to moderately severe group portrayed the in between value for peak-to-peak amplitude of oVEMP.

Table 4.2.3.1.

Mean, median, standard deviation and range of peak-to-peak amplitude (in μ V) of oVEMP in ears with mild, moderate to moderately severe and severe to profound hearing loss

Group	N	Mean	Median	SD	Range
Mild	10	6.02	6.19	2.2	2.80-10.01
Moderate-Moderately severe	20	3.73	3.69	2.2	0.97-10.51
Severe- profound	20	1.89	1.59	1.28	0.72-4.81

Note: ‘SD’ – standard deviation, ‘N’ – no of ears.

Further, non-parametric statistical analysis was done using Kruskal-Wallis test to determine the significant difference, if any, among the groups. The results revealed a significant difference in peak-to-peak amplitude of oVEMP among the groups [$\chi^2(2) = 15.53, p < 0.01$]. Therefore further statistical analysis was done using Mann-Whitney *U* test for pair-wise comparison. The results revealed significantly smaller peak-to-peak amplitude in severe to profound hearing loss group when compared to mild hearing loss [$Z = -3.47, p < 0.01$] and moderate to moderately severe hearing loss

group [$Z = -2.49, p < 0.01$]. Furthermore, the peak-to-peak amplitude in moderate to moderately severe hearing loss group was also significantly smaller than the mild hearing loss group [$Z = -2.49, p < 0.01$]. Figure 4.2.3.1 shows the mean and 95% confidence intervals of peak-to-peak amplitude of oVEMP in sub-groups of participants with hearing loss and the outcome of Mann-Whitney U test for between groups comparison.

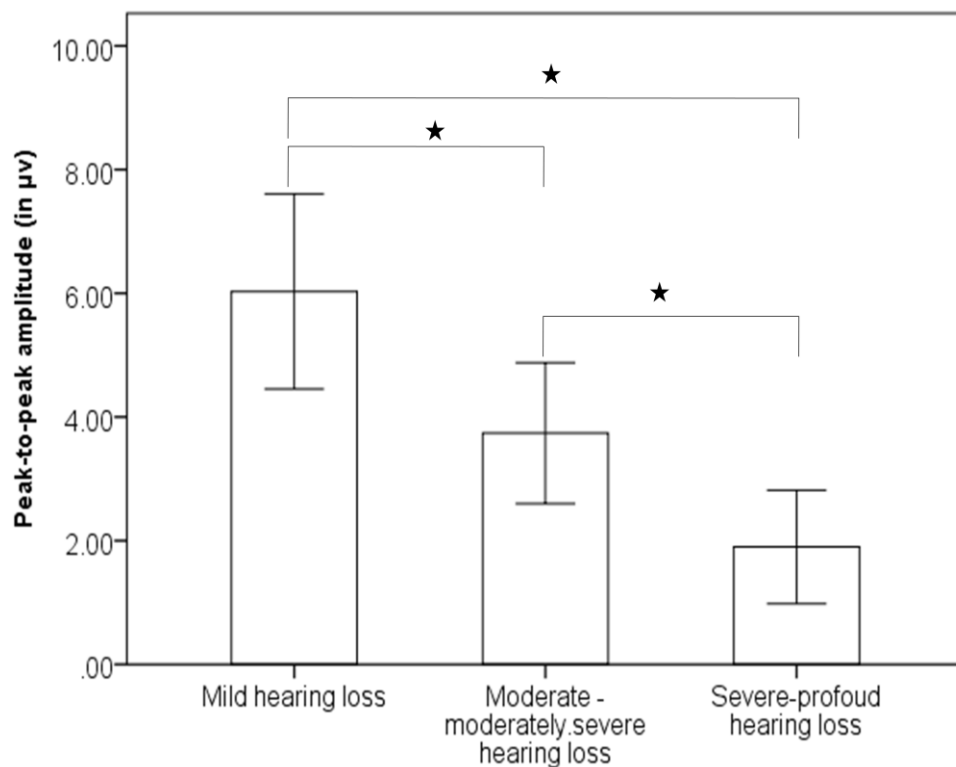


Figure 4.2.3.1: Mean and 95% confidence intervals of peak-to-peak amplitude of oVEMP in ears with mild, moderate to moderately severe and severe to profound hearing loss and the outcome of Mann-Whitney U test for comparison between the groups. Star-marked comparisons are statistically significant ($p < 0.01$).

The null hypothesis 2 that there is no significant difference in response rate, individual peak latencies and peak-to-peak amplitude of oVEMP between various degrees of cochlear hearing loss is therefore rejected, except for n1 latency for which it was accepted. Thus, the alternate hypothesis 2 is that there is a significant difference

in response rates, p1 latency and peak-to-peak amplitude of oVEMP between subgroups of hearing loss.

4.3 Hypothesis 3

The third hypothesis of the present study stated “there is no significant correlation between hearing thresholds and the various oVEMP parameters (n1 latency, p1 latency, & peak-to-peak amplitude). Since the hypothesis statement had two different parameters, it was tested separately for each of these and the results are therefore discussed under each of these parameters.

4.3.1 Correlation between hearing threshold and latencies of oVEMP.

Spearman’s correlation analysis was carried out to find correlation between hearing threshold and latencies of oVEMP. A positive correlation was found between hearing threshold and n1 latency, although it was not significant [$r = 0.20, p > 0.05$]. Further, a positive correlation was also found between hearing threshold and p1 latency but it was not significant [$r = 0.30, p > 0.05$]. Figure 4.3.1.1 shows the scatter plots depicting the correlation between hearing thresholds of individuals with hearing loss and latencies of oVEMP.

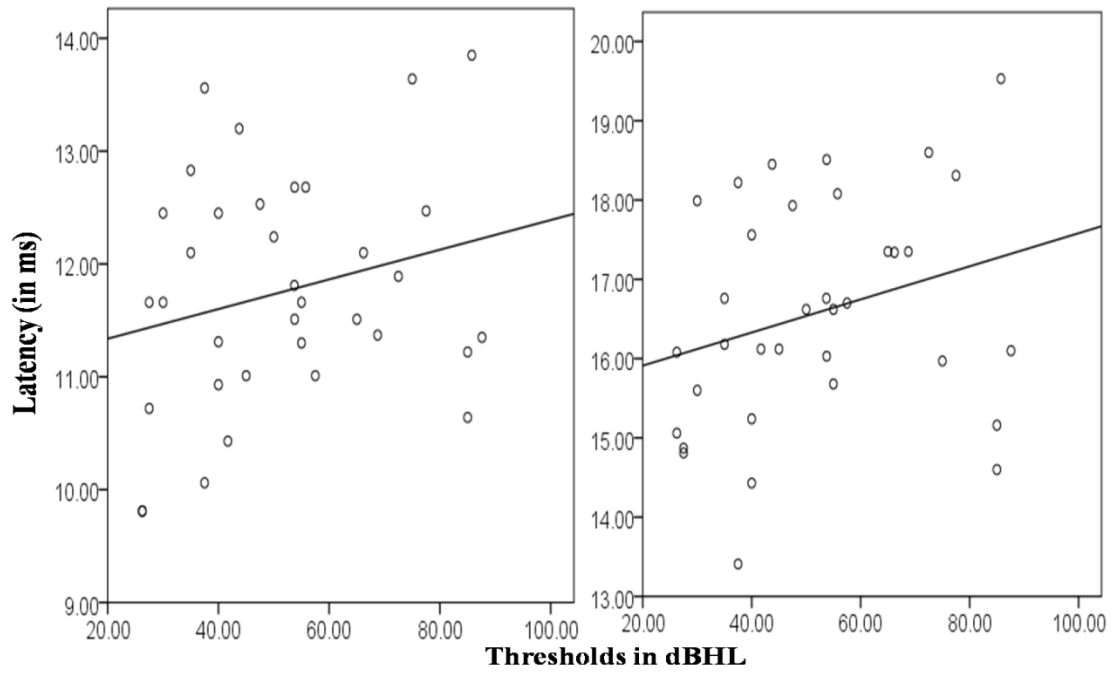


Figure 4.3.1.1: Correlation between hearing threshold and n1 latency (left panel) and p1 latency (right panel) of oVEMP. The diagonal line represents the linear regression curve.

4.3.2 Correlation between hearing threshold and peak-to-peak amplitude.

Spearman's correlation analysis was carried out to find correlation between hearing threshold and peak-to-peak amplitude. A significant negative correlation was found between the two [$r = -0.39$, $p < 0.05$]. Figure 4.3.2.1 shows the scatter plot depicting the relationship between hearing threshold and peak-to-peak amplitude of oVEMP.

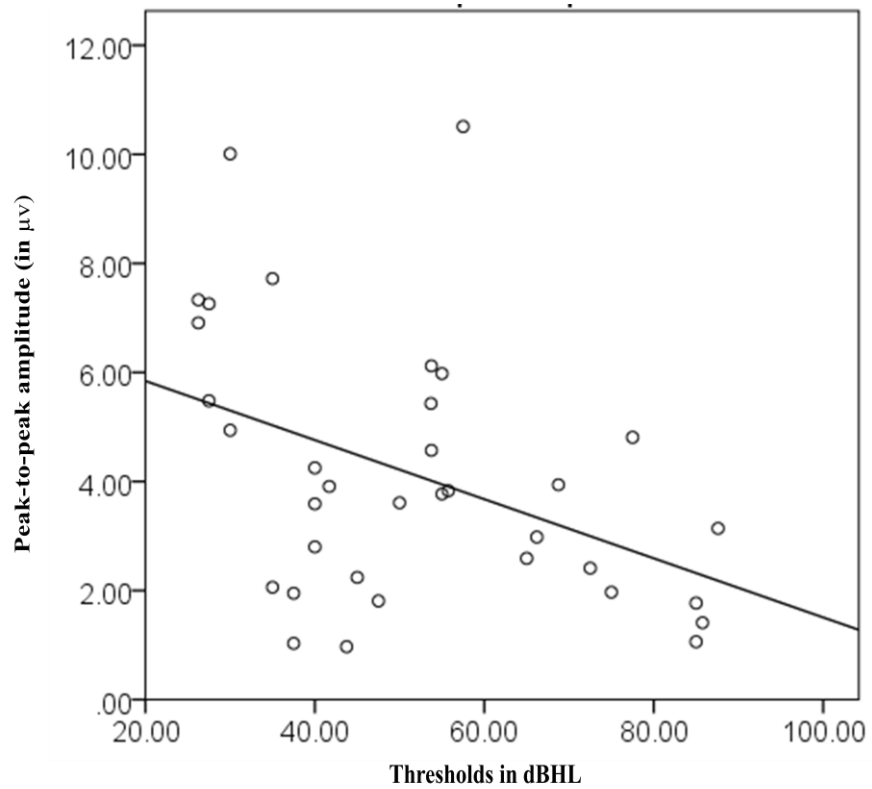


Figure 4.3.2.1: Correlation between hearing threshold and peak-to-peak amplitude of oVEMP. The diagonal line depicts the linear regression curve.

Since there was a significant correlation between hearing threshold and peak-to-peak amplitude, a linear regression analysis was done in order to generate a linear regression equation which is as shown in equation 4.3.2.1.

$$A = 0.418 (T) + 0.12 \dots \dots \dots \text{Eq}$$

4.3.2.1

where A is the peak to peak amplitude in µV and T is the hearing threshold in dBHL.

The null hypothesis 3 that there no significant correlation between hearing thresholds and the various oVEMP parameters is therefore accepted, except for peak-to-peak amplitude for which it is rejected. Thus, the alternate hypothesis 3 is that there is a significant correlation between hearing threshold and peak-to-peak amplitude.

4.4 Hypothesis 4

The fourth hypothesis of the present study stated, “there is no significant correlation between the duration since the onset of the cochlear hearing loss and various oVEMP parameters (latencies and peak-to-peak amplitude). Since the hypothesis statement had two different parameters, it was tested separately for each of these and the results are therefore discussed under each of these parameters.

4.4.1 Correlation between the duration since the onset of hearing loss and oVEMP latency.

Spearman’s correlation was done to find the correlation between the duration since the onset of hearing loss and latencies of oVEMP. A significant positive correlation was found between duration since the onset of hearing loss and n1 latencies [$r = 0.33, p < 0.05$]. Further, a significant positive correlation was also found between the duration since the onset of hearing loss and p1 latency [$r = 0.35, p < 0.01$]. Figure 4.4.1.1 shows the scatter plots depicting the correlation between the duration since the onset of hearing loss latencies of oVEMP.

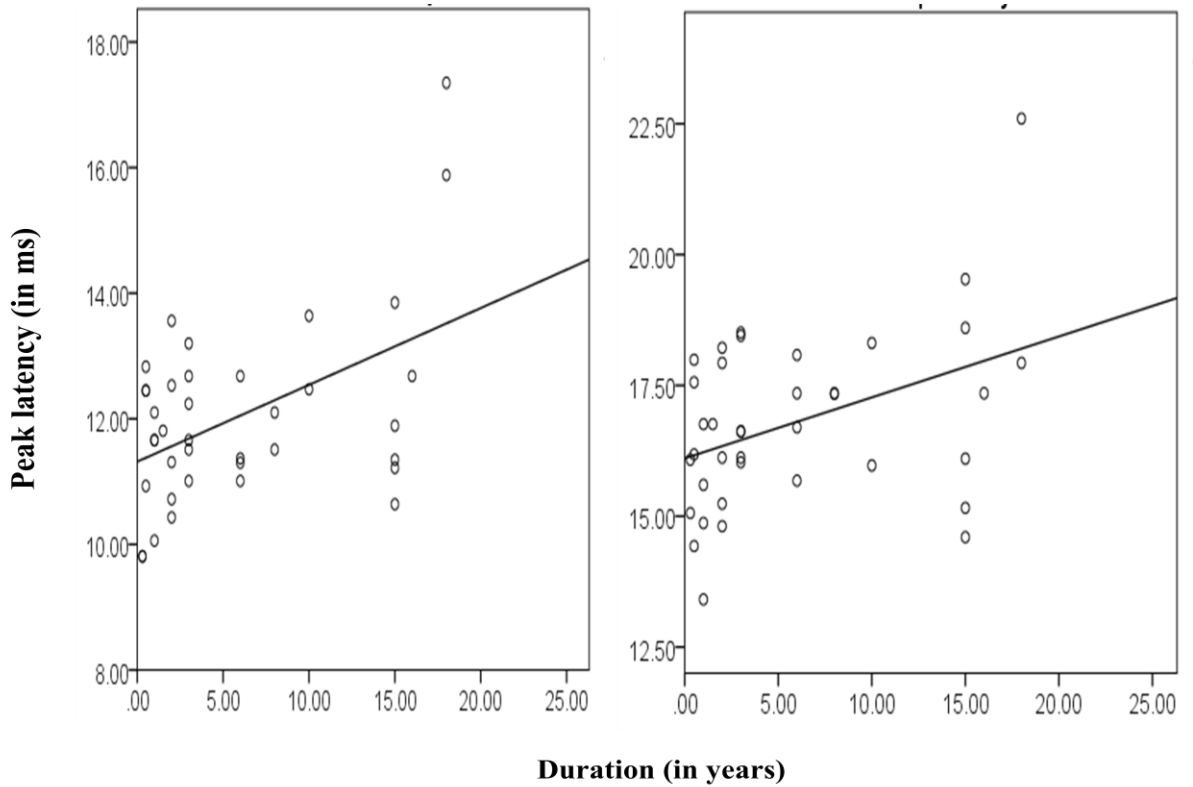


Figure 4.4.1.1: Correlation between the duration since the onset of hearing loss and n1 latency (left panel) and p1 latency (right panel). The diagonal lines depict the linear regression curves.

Since there was a significant correlation between the duration since the onset of hearing loss and latencies of oVEMP, linear regression analyze was done in order to generate linear regression equations which is as shown in equations 4.4.1.1 and 4.4.1.2 for n1 and p1 latencies, respectively.

$$n1 = 0.481(d) + 0.02. \dots \dots \dots \text{Eq}$$

4.4.1.1

$$p1 = 0.404(d) + 0.012. \dots \dots \dots \text{Eq}$$

4.4.1.2

where ‘n1’ is the latency of n1 in ms, ‘p1’ is the latency of p1 in ms and ‘d’ is the duration since the onset of hearing loss in years.

4.4.2 Correlation between the duration since the onset of hearing loss and peak-to-peak amplitude of oVEMP.

Spearman's correlation was carried out to find the correlation between the duration since the onset of hearing loss and peak-to-peak amplitude of oVEMP. A significant negative correlation was found between the two [$r = 0.53$, $p < 0.01$]. Figure 4.4.2.1 shows the scatter plot depicting correlation between the duration since the onset of hearing loss and peak-to-peak amplitude of oVEMP.

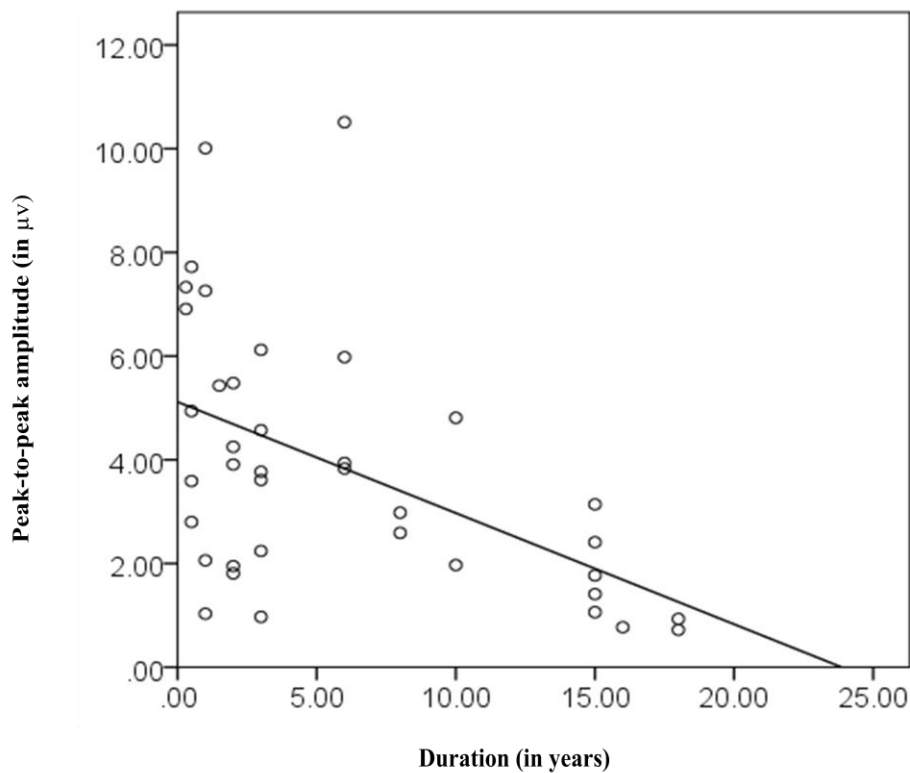


Figure 4.4.3.1: Correlation between duration since the onset of hearing loss and peak-to-peak amplitude. The diagonal line represents linear regression curve.

Since there was a significant correlation between the duration since the onset of hearing loss and peak-to-peak amplitude of oVEMP, a linear regression analysis

was done in order to generate a linear regression equation which is shown in equation 4.4.2.1.

$$A = 0.501(d) + 0.001 \dots \dots \dots \text{Eq 4.4.2.1}$$

where 'A' is the peak to peak amplitude in μV and 'd' is the duration since the onset of hearing loss in years.

The null hypothesis 4 that there is no significant correlation between the duration since the onset of the cochlear hearing loss and various oVEMP parameters (n1 latency, p1 latency and peak-to-peak amplitude) is rejected. Therefore, the alternating hypothesis is that there is significant correlation between the duration since the onset of hearing loss and oVEMP parameters (n1 latency, p1 latency and peak-to-peak amplitude).

Overall, the findings of the present study showed significantly reduced response rates, prolonged latencies and stunted peak-to-peak amplitude of oVEMP in ears with hearing loss than the normal hearing ears. Furthermore, there was progressive but significant reduction in response rates, prolongation of latencies and reduction of peak-to-peak amplitude of oVEMP with increase in degree of hearing loss from mild to profound degree. Lastly, while the peak-to-peak amplitude was significantly correlated with the degree of hearing loss, latencies as well as peak-to-peak amplitude were significantly correlated with the duration since the onset of hearing loss.

CHAPTER 5

Discussion

The present study aimed at investigating the effect of degree of hearing loss on oVEMP parameters like response rates, peak latencies and peak-to-peak amplitude. The study included 50 ears with normal hearing and 50 ears with hearing loss. The comparisons were made between normal hearing ears and ears with hearing loss and also between various degrees of hearing loss. Further, correlation of oVEMP parameters with hearing threshold and duration since the onset of hearing loss was investigated.

5.1 Effect of hearing loss on response rate of oVEMP

The response rate was found to be significantly smaller in the hearing loss group when compared to the normal hearing group. These findings were in agreement with Niu et al (2016), who found a response rate of 100% in the control group and 38.94% in the hearing loss group (congenital profound hearing loss). These findings were also similar to those reported in an Indian study by Bansal et al (2013) who observed reduced response rate of 66% in the experimental group (severe to profound hearing loss) as against 100% in the control group.

These findings could be attributed to the close relationship of the otolith organs with cochlea (Tribukait et al., 2014). The cochlea and otolith organs are derived embryologically from the same otic placodes and share similar cellular structures, fluid environments and blood supply (Arwing 1955; Brookhouser, 1982; Potter, 1984; Sanderg, 1965). Further, they also show sensitivity to sound and vibration (Bickford et al., 1969; Colebatch et al., 1994). Thus co-existence of cochlear and vestibular pathologies could be likely. This assumption is further supported by the

findings of poorer VEMP response rates in pathologies like ANSD (Singh et al., 2016), noise induced hearing loss (Madappa & Mamatha, 2009) and ototoxicity (Kumar et al., 2010) that are primarily the pathologies of the hearing mechanism.

5.2 Effect of hearing loss on peak latencies of oVEMP

The n1 and p1 latencies of oVEMP were found to be prolonged in ears with hearing loss than the ears with normal hearing, although statistically significant group difference was obtained only for the n1 latency. These findings were in disagreement with the findings of Bansal et al (2011), who found no difference in peak latencies of oVEMP between the control (normal hearing) and the experimental (severe to profound hearing loss) groups. The discrepancy between the findings of the present study and that by Bansal et al (2011) could be due to difference in the subject selection criteria, as the later study had subjects with congenital hearing loss as against acquired hearing loss in the present study.

Longer latencies are believed to be markers of neural pathologies involving the vestibular nerve, vestibular nuclei or the pathway to the ocular muscles, as in cases of auditory neuropathy spectrum disorders (Singh et al., 2016), multiple sclerosis (Gabelic, Magdalena, Velimir & Mario, 2013), vestibular schwannoma (Iwasaki, Murofushi, Chihara & Ushio, 2010) or age related decline (Tseng et al., 2010). All the participants of the pathological group were within 50 years of age and age related prolongation of latencies has been reported to be significant only after 60 years of age (Tseng et al., 2010). Therefore aging process cannot explain the finding of longer latencies in the ears with hearing loss than the ears with normal hearing. Furthermore, the participants in the hearing loss group were devoid of any obvious neuronal pathologies like ANSD, multiple sclerosis or vestibular schwannomas as

this was ensured through a structured case history, a battery of audiological tests including auditory brainstem responses, oto-acoustic emissions and immittance and a neurological screening. Therefore, these pathologies were also not present in the participants with hearing loss. The case history in a large percentage of individuals with hearing loss demonstrated the presence of slowly progressive hearing loss. There might be a possibility that the idiopathic factor that was causing hearing loss to progress was also causing a slow steady decline in otolith organs functioning which was not being revealed by the behavioral test results or case history because slowly progressive pathologies usually show good central compensations (Kamath & Pfaltz, 1970). The steady decline in the peripheral function would however also steadily cause a neural deprivation of higher structures thereby causing a slowly declining vestibular nerve function. This in turn might have caused prolongation of latencies of oVEMP. Similar damage patterns have been shown for the acoustic branch of the 8th cranial nerve and higher auditory structures through auditory deprivation due to peripheral hearing loss (Silman et al., 1984; Hurley et al., 1991).

5.3 Effect of hearing loss on peak-to-peak amplitude of oVEMP

In the present study, the peak-to-peak amplitude of oVEMP was found to be significantly smaller in ears with hearing loss than the ears with normal hearing. These findings were in agreement with those reported previously (Bansal et al., 2010; X-Niu et al., 2016). They also found significantly smaller amplitude in the study group compared to the control group.

The finding of smaller peak-to-peak amplitude of oVEMP in ears with hearing loss than the ears with normal hearing could be attributed to slow progressive status of the vestibular pathology, as discussed above, which could have led to the

central compensation which in turn would have eliminated any obvious vestibular symptoms from being reflected in the case history. This assumption finds support from the studies of oVEMP in ANSD population (Sinha et al., 2013; Singh et al., 2016). While Sinha et al (2013) found absence of oVEMP in 100% of their subjects with ANSD Singh et al (2016) observed absence of oVEMP in the majority of individuals with ANSD. However, the complaint pertaining to the vestibular symptoms were sparse among these subjects despite the absence of oVEMP. Further, the present study included the behavioural balance screening tests like the Fukuda stepping test, Romberg test, past-pointing test and tandem gait test in order to exclude the subjects with positive results on these tests from the present study. Therefore, none of the subjects in the present study had positive results on these tests. Absent or reduced oVEMP in significantly high number of ears with hearing loss despite normal results on these tests suggest towards paradoxical results and questions the sensitivity of oVEMP and the behavioural balance assessment tests in identifying vestibular pathologies. Honaker et al (2009) reported poor sensitivity of about 25-30 % for the behavioural balance assessment tests in detecting vestibular deficits. Therefore, there appears to be a scenario where subtle and slow onset sub-clinical vestibular deficits that possibly co-occurred with a slowly progressing hearing loss might have been missed by the behavioural tests, yet were resulting in reduced amplitude of oVEMP.

5.4 Effect of degree of hearing loss on response rate.

The results of the present study demonstrated significantly reduced response rate of oVEMP in the severe to profound hearing loss group compared to the mild and moderate to moderately severe hearing loss group. There are no previous studies investigating the effect of various degrees of hearing loss on oVEMP. The lower response rate in the severe to profound hearing loss than the lesser degrees of hearing

losses could be attributed to the embryological and physiological similarities between the cochlea and vestibular system (Arwing 1955; Brookhouser, 1982; Potter, 1984; Sanderg, 1965), as discussed above. The factors causing hearing loss possibly lead to otolith damage thereby causing absence of oVEMP. Since higher amount of cochlear damage is associated with higher degree of hearing loss, it was probably also associated with higher otolith structure damage and therefore absence of oVEMP in more percentage of individuals with higher degree of hearing loss.

5.5 Effect of degree of hearing loss on peak latencies of oVEMP

The peak latencies were prolonged in severe to profound hearing loss group compared to mild and moderate to moderately severe hearing loss group, with no significant difference between mild and moderate to moderately severe hearing loss group. As discussed earlier, neural pathologies are likely to affect the latencies of oVEMP (Singh et al., 2016; Tseng et al., 2010) and larger neural pathologies could possibly affect the latencies to a greater extent than lesser degrees of neural involvements. It has also been discussed earlier that a slowly growing vestibular pathology associated with slowly growing hearing loss could increasingly cause neural deprivation and therefore prolongs the latencies. Since the degree of hearing loss is more in severe to profound hearing loss, going by the above understating, the neural deprivation caused by symptomatically well compensated but deficient inputs would further prolong latencies of oVEMP peaks.

5.6 Effect of degree of hearing loss on peak-to-peak amplitude

Peak-to-peak amplitude of oVEMP showed a trend of reduction with increase in degree of hearing loss. This trend was further found to be significant, with progressively significantly reducing oVEMP amplitudes with increase in the degree of

hearing loss from mild to severe to profound. As discussed earlier, central compensation due to slow progressive nature of the vestibular deficits that might be associated with slow progressive nature of hearing loss might have resulted in vestibular pathologies going undetected. However, progressively growing vestibulopathies might have caused progressive reduction in the functioning of otolith organs thereby progressively reducing the peak-to-peak amplitude of oVEMP. This would have happened even though the individuals were asymptomatic and results on behavioral balance assessments were well within the normal limits because of a combination of central compensation and poor sensitivity of the behavioral balance assessment tools used in the present study (Honaker et al., 2009; Pfaltz & Kamath, 1970).

5.7 Correlation between hearing threshold and oVEMP parameters

Pearson's correlation analysis between hearing threshold and oVEMP parameters revealed significant reduction of oVEMP amplitude with increasing hearing threshold. There are no previous studies to compare the findings of the present study against. However, this significant correlation is further testimony to the above discussion regarding slowly progressive nature of vestibular damage associated with possibly a common causative factor for hearing loss and vestibular damage. As discussed above, this could be because of several common aspects, anatomically, physiologically as well as embryologically, that exist between the vestibular system and the auditory system (Arwing 1955; Brookhouser, 1982; Potter, 1984; Sanderg, 1965).

5.9 Correlation between duration since the onset of hearing loss and oVEMP

There was a significant correlation between duration since the onset of hearing loss with the peak latencies (n1 and p1) and with peak-to-peak amplitude of oVEMP. While the latencies prolonged, the amplitude reduced with increasing duration since the onset of hearing loss. There are no previous studies to again compare the findings of the present study against. However, these findings could be attributed to slow progressive hearing loss associated with undetected compensated vestibular deficits which would have obscured the vestibular symptoms in the case history, yet showed up in progressive prolongation of latencies caused by deprivation and reduction in oVEMP amplitude, as discussed above.

CHAPTER 6

Summary and conclusion

The oVEMP reflects the functioning of the utriculo-ocular reflexes. This reflexes are sensitive to sound (Piker et al., 2013), vibration (Curthoys et al., 2012) or galvanic stimulus (Cheng et al., 2009) and can be recorded using surface electrodes beneath the contralateral eye when gaze is directed upward (Singh, & Barman, 2013). The obtained response in persons with normally functioning utricle mediated VOR pathway is characterized characterised by negative peak at around 10 ms peak and a later positive peak at around 15 ms (Singh & Barman, 2014).

Literature shows anatomical and physiological similarities between the cochlea and vestibular organs. Hence a damage of cochlea resulting in hearing loss have shown abnormalities in VEMP reflecting damage to the vestibular organs (Bansal et al., 2013; X-Niu et al., 2016). However, the above studies were conducted on individuals with congenital hearing loss group and were restricted to only severe to profound hearing loss group. Therefore, the present study aimed at investigating the effect of various degrees of hearing loss ranging from mild to profound loss on oVEMP response parameters.

In order to fulfil the objectives, the present study incorporated 50 ears with cochlear hearing loss and 50 ears with normal hearing of individuals in the age range of 18-50 years. The ears with hearing loss were further divided into three sub-groups as mild, moderate to moderately severe and severe to profound hearing loss. The non-inverting electrode was placed 1cm below the centre of the lower eye lid, the inverting electrode was placed 2 cm below the non-inverting electrode and the ground electrode was placed on the forehead. The participants were instructed to fix eye gaze

at 30⁰ elevation in the superior-medial plane was were asked to avoid movements. oVEMPs were recorded using tone burst of 500 Hz, presented at a intensity of 125 dB peSPL using a repetition rate of 5.1/s. Two hundred averages were obtained for each recording. Responses were recorded for 75 ms which included 10.5 ms pre-stimulus duration. The responses were band-pass filtered between 1 to 1000 Hz and were amplified by 30000. Presence of oVEMP was defined as an initial negative at about 10 ms followed by a positive peak at around 15 ms. oVEMP responses were analysed for response rate, n1 latency, p1 latency and peak-to-peak amplitude.

Kruskal-Wallis test was done whenever the comparison was attempted among 3 or more groups and this was followed by Mann-Whitney *U* test for pair-wise comparison in case of a significant difference among groups on Kruskal-Wallis test. In case of comparison between 2 groups, a Mann-Whitney *U* test was done. For comparison of response rates, equality of test for proportions was done. Further Spearman's correlation was done between degree of hearing loss and oVEMP parameters and also between duration since onset of hearing loss and oVEMP parameters.

The comparison between ears with normal hearing and those with hearing loss (irrespective of the degree of hearing loss) revealed significantly lower response rates, longer latencies and smaller peak-to-peak amplitude of oVEMP in the clinical group than the ears with normal hearing. Further, the results revealed progressively lower response rates, longer latencies and smaller peak-to-peak amplitudes with increase in the degree of hearing loss from mild to severe to profound hearing loss. There was also significant correlation of oVEMP parameters with degree of hearing loss and the duration since onset of cochlear hearing loss. These findings could be attributed to the possibility of a co-existence of slowly growing vestibular pathologies that remained

asymptomatic due to ease with which central vestibular compensation occurs for slowly developing vestibular disorders (Pfaltz & Kamath, 1970). Further, they also went undetected by behavioural balance assessment tests, possibly because of their inherently poor sensitivity (Honaker, Boismier, Shepard, & Shepard, 2016).

Thus, the findings of the present study show alterations of oVEMP parameters in individuals with acquired cochlear hearing loss and increase in the effect on oVEMP with increasing degree of hearing loss. This implicates that one needs to be careful when using oVEMP for evaluating vestibular function in individuals with co-existing cochlear hearing loss and use appropriate correction factor in latencies and amplitude values of oVEMP for the degree of hearing loss.

The findings of present study have high implications as hearing loss and vestibular pathologies often co-exist. Therefore, a clinician needs to adjust for the effects of degree of hearing loss on oVEMP response parameters before deciding on normal or abnormal functioning of the utricle mediated vestibulo-ocular reflex pathway. Further, the regression equations generated in the present study would be helpful in predicting the outcomes on oVEMP testing, possibly after validating these equations in routine clinical practice.

The present study's findings could be limited by the use of only a small size in each of the hearing loss groups and non-use of objective measures like electronystagmography (ENG) / videonystagmography (VNG) for eliminating subjects with vestibular problems. Therefore future studies could use these tests to eliminate the subjects with even subtle vestibulopathies and then evaluate the effect of degree of hearing loss on oVEMP response parameters.

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