Comparison of Vestibular Functioning among Women with and without the Signs of Vestibular Migraine during Phases of Menstrual Cycle

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This Dissertation is submitted as a part of fulfilment for the

Degree of Master of Science (Audiology)

University of Mysore, Mysuru

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September 2023

CERTIFICATE

This is to certify that this dissertation entitled "**Comparison of Vestibular Functioning among Women with and without the Signs of Vestibular Migraine during phases of Menstrual Cycle**" is a bonafide work submitted as a part of the fulfilment of the degree of Master of Science (Audiology) of the student with Registration Number: P01II21S0082. This has been carried out under the guidance of the 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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CERTIFICATE

This is to certify that this dissertation entitled "**Comparison of Vestibular Functioning among Women with and without the Signs of Vestibular Migraine during phases of Menstrual Cycle**" has been prepared under my supervision and guidance. It is also being certified that this dissertation has not been submitted earlier to any other University for the award of any other Diploma or Degree.

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DECLARATION

This is to certify that this dissertation entitled "**Comparison of Vestibular Functioning among Women with and without the Signs of Vestibular Migraine during phases of Menstrual Cycle**" is the result of my own study under the guidance of Dr. Sandeep M. Assistant professor in Speech Pathology, Department of Speech-Language Pathology, All India Institute of Speech and Hearing, Mysuru and has not been submitted earlier to any other University for the award of any other Diploma or Degree.

Mysuru

September 2023

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Dedicated to my family & my guide

Dr. Sandeep M.

Acknowledgement

At the onset, I would like to thank God for giving me the strength during hard times and kept me going all these years.

I express my deepest gratitude to my guide Dr. Sandeep M. his insights, guidance, and genuine interest in research have been motivating and inspiring me throughout my dissertation. His faith and encouragement to pursue new lines of research has led to this dissertation and made this work a truly rewarding experience. I sincerely thank you for patiently dispelling my doubts and correcting my endless mistakes and making my dissertation a good piece of research.

I am forever grateful for my parent's constant support and I would like to thank them for believing in my abilities and supporting me in all my actions.

My dear sister Sneha R. Kanth, and Pooja R. Kanth for helping me out in my statistical part and making it smooth for me to work in home. And my little brothers Vihaan M. and Prerith M. for keeping me entertained whenever I was under pressure. I might not say it often but you all are the best.

I am thankful for supportive advice from Vinayagar sir and Nirmala ma'am.

I would like to thank to Kriti ma'am, Sanjay sir, Shezeen ma'am, Rajesh sir and Kalai sir for opening the FAAR lab during data collection even after working hours.

I must thank my friends Teenu, Rohini, Kasturi, Sushmitha, Bhoomika and Rashmi for making my Master's program enjoyable.

I would also like to extend my thanks to Harshitha, Vasuki, Rhea, Hima, Divya, Fathima, Archana, and Sudarshana for making up time to be a participant for my dissertation in their busy schedule.

I would like to thank my juniors, for being helpful in all ways. Also, I would like specially thank Aysha Afra and Husna for helping me to complete my data collection.

In addition, I would like to mention Swetha, Sumanth M. C., Ankit, and Mohit for creating fun filled memories in our clinical posting.

I am grateful to Prasad for being there in my all ups and downs during my dissertation.

I would like to specially thank Sanvi Jain for being with me in tough situations.

I would like to highlight two truly exceptional people Manasa N. and Rakshitha N. for being with me like a sister to support me at all point.

I would like to thank Vinu and Anu for their continuous encouragement.

I would like to thank Abhi for his constant moral support.

Thanks to the Spoilers for the memories, we have created - Sumanth M. C., Uday, Prasad, Teenu, and Rohini.

I would like to thank all the participants who have been a part of this study.

I would like to extend a big thanks to one and all who have helped me either directly or indirectly and made this dissertation a success.

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Chapter 1

INTRODUCTION

Vestibular system plays an important role in balancing our body and is a part of the inner ear. It comprises of three semi-circular canals and otolith organs. While the semi-circular canals are sensitive to angular acceleration, the utricle and saccule regulate the linear acceleration. The three semi-circular canals (anterior, posterior & lateral) are in right angle to each other and function in their respective planes. Also, the right and left semi-circular canals are physiologically paired; right anterior canal is functionally paired with the left posterior canal and vice versa; the two horizontal canals are paired functionally (Khan & Chang, 2013).

Migraine is a complex brain disorder (Goadsby et al., 2002). In the recent past, a variant of migraine, called vestibular migraine (VM) is being extensively researched. Recurrent vestibular symptoms, history of migraine, temporal link between vestibular symptoms and migraine symptoms, and the exclusion of other causes of vestibular symptoms contribute to the diagnosis of vestibular migraine. Symptoms of vestibular migraine include various types of vertigo as well as head motion-induced dizziness with nausea. The severity of the symptoms must be moderate or severe. The duration of acute episodes is confined to a range of 5 minutes to 72 hours (Lempert et al., 2022). Headache is the primary symptom reported by the patients with migraine. Migraine patients report considerably greater vestibular symptoms than the tension headache patients (Kayan & Hood, 1984a).

The pathophysiology of migraine involves the dysfunction of subcortical structures (May & Goadsby, 1999a). The basic event that activates the trigemino-vascular system is the firing of first-order peripheral trigeminal neurons in response to nociceptive signals from the meninges. This firing produces pain, which is subsequently directed to the brain (Wilder & Francis, 1959). Continuous activation of these meningeal nociceptors may stimulate first-, second-, and third-order trigemino-vascular neurons, which in turn activates multiple brainstem and forebrain regions, resulting in migrainous symptoms (Burstein & Jakubowski, 2005). The ophthalmic branch of the trigeminal ganglion innervates the inner ear via the basilar artery and the anterior inferior cerebellar artery (Vass et al., 1998a). The superior olivary complex and the cochlear nucleus are likewise innervated by the trigeminal ganglion (May & Goadsby,

1999b). Chemical and electrical stimulation of the trigeminal ganglion causes a rise in inner ear blood flow as well as alterations in vascular permeability with plasma protein extravasation into the inner ear (Vass et al., 1998b). This suggests that the migraine can have an effect on the vestibular system.

One of the common causes of recurrent vertigo is VM. Since the beginning of neurology, it has been known that migraines can cause episodes of vertigo. Numerous case studies have given clear explanations of clinical characteristics of vestibular migraine (Cass et al., 1997; Kayan & Hood, 1984b). There are different types of vertigo that we can observe in participants presenting with vestibular migraine, such as, spontaneous vertigo, positional vertigo, visually induced vertigo, and head motion induced dizziness with nausea (Roberto et al., 2017). In case of acute vestibular migraine, nausea and imbalance might not be a common symptom reported (Lempert & von Brevern, 2019). Patients might have vestibular migraine either associated with headache or without headache. Associated symptoms of vestibular migraine are osmophobia, photophobia, phonophobia, and visual or other auras (Roberto et al., 2017). There are auditory symptoms which is also associated with vestibular migraine including hearing loss, tinnitus, and aural fullness (Tabet & Saliba, 2017). Patients experience dizziness which may be caused by imbalance due to cerebellar dysfunction (Ophoff et al., 1994). Benign paroxysmal positional vertigo and vestibular migraine are two different disorders but they can coexist (Moretti et al., 1980). A person with idiopathic benign paroxysmal positional vertigo is three times more likely to report the presence of migraine symptoms compared to those with known cause such as trauma or surgical procedure (Neuhauser & Lempert, 2009). According to Lempert et al. (2009), it is preferred to use the term 'vestibular migraine' to avoid confusion with other conditions such as motion sickness associated with migraine and non-vestibular dizziness.

Chung and Kim (2008) found life-time prevalence of VM to be 1%, while Kesserwani (2021) found a prevalence of 2.5% over a year. Around 60 to 80% of vertigo prevalence is seen in patients with recurrent vertigo of unknown origin. In contrast, 10% to 20% of patients visiting clinic with headache are reported to experience VM (Lempert & von Brevern, 2019). Although VM is seen in both women and men, its prevalence is shown to be 2-3 times higher in women than in men. Further, in women, the prevalence of migraine is reported to be highest during their reproductive age. Chai

et al. (2014) reported that a significant amount of estrogen levels can trigger acute migraine attacks. One of the frequent triggers of both migraine and vestibular migraine is the hormonal changes that take place during menstruation or hormone therapy. Triggers were more likely to be associated with a more florid acute migraine attack (Kelman, 2007).

Migraine disorders exhibit a higher prevalence among women compared to men. This discrepancy is influenced by the involvement of ovarian neuro-steroids, which play a crucial role in modulating neurotransmitter systems associated with the development of migraines. Unlike the postmenopausal phase, during perimenopause, women experience erratic fluctuations in ovarian neuro-steroid levels. These fluctuations could potentially serve as a specific trigger for initiating migraine episodes. In addition to migraine headaches, dizziness is a frequently reported symptom during perimenopause. A significant portion of this dizziness may be attributed to vestibular migraine, a condition characterized by diverse clinical features encompassing dizziness and/or migraine headaches (Park & Viirre, 2010).

1.1 Need for the Study

The uterus and ovaries are the sites of the regular and organic menstrual cycle. Hormone levels change throughout the menstrual cycle in a healthy female at different times. During the ovarian cycle, the body's levels of estrogen and progesterone are dynamically regulated. Steroid receptors in cochlea are directly affected by estrogen, which is seen both in animals and humans. Since the vestibular and cochlear structures are connected through the ductus reunions, both vestibular and cochlea of the inner ear will have chemical composition changes when a young, healthy woman's menstrual cycle is in progress (Sinha et al., 2021). Sinha and Sahu (2019) compared latency and amplitude of oVEMP in 20 females across the three phases of their menstrual cycle and found no significant difference. Similarly, Sinha et al. (2021) studied VOR (vestibulo-ocular reflex) gain function and the VOR gain asymmetry ratio in 29 young healthy females in various phases of their menstrual cycle. Here again they found no significant changes in either of the parameters. The findings suggest that there is no significant effect of menstrual cycle related change in hormones on the vestibular functioning. However, it is important to note that the participants in both these studies did not report of any vestibular symptoms. In many females, there are signs of vestibular migraine

during their menstrual cycle. In vestibular migraine, both the peripheral and central vestibular functions are known to be deviant (Baier et al., 2009). Therefore, it is necessary to consider females with symptoms of vestibular migraine during their menstrual cycle as a separate cohort to study their vestibular functioning and compare them with those without the symptoms of vestibular migraine during their menstrual cycle. If such comparison does not show group differences in the vestibular functioning, it will further strengthen the conclusions of Sinha et al. (2019, 2021) on the relationship between hormonal changes and vestibular functioning. Hence the present study was taken up.

1.2 Aim of the Study

To explore the influence of menstrual cycle related harmonal changes on the vestibular functioning of young adults.

1.3 Objectives of the Study

The following were the four objectives of the study:

1. To compare the latency and amplitude of cVEMP between persons with symptoms like that of vestibular migraine during their menstrual cycle and those without such symptoms, in their three phases of menstrual cycle.
2. To compare the latency and amplitude of oVEMP between persons with symptoms like that of vestibular migraine during their menstrual cycle and those without such symptoms, in their three phases of menstrual cycle.
3. To compare the VOR gain and VOR gain asymmetry ratios of the three semicircular canal planes between persons with symptoms like that of vestibular migraine during their menstrual cycle and those without such symptoms, in their three phases of menstrual cycle.
4. To compare cVEMP, oVEMP and VOR gain functions across the three phases of menstrual cycle in persons with symptoms of vestibular migraine during their menstrual cycle.

Chapter 2

REVIEW OF LITERATURE

Patients explain vertigo as a to and fro movement when there is no actual movement of the head that is present. At times vertigo is associated with migraine in human population and the link between the vertigo and migraine has been studied right from 19th century. Li., Si., and Ling, et al. (2022) investigated the clinical features of vestibular migraine in 91 participants who had vestibular symptoms associated with migraine. They reported that in 42% of them migraine symptoms occurred before vestibular symptoms; photophobia and phonophobia were commonly encountered. They also found that vestibular migraine is more prevalent in women than in men.

Lempert et al. (2012) gave diagnostic criteria for vestibular migraine that was developed collaboratively by the Barany Society's Committee for Classification of Vestibular Disorders, and the International Headache Society's (IHS) Migraine Classification Subcommittee. Vestibular migraine and suspected vestibular migraine were included in the classification. Recurrent vestibular symptoms, a history of migraine, a temporal link between vestibular symptoms and migraine symptoms, and the exclusion of other causes of vestibular symptoms were reported to be the key consideration to the diagnosis of vestibular migraine. Symptoms of vestibular migraine according to them include, numerous types of vertigo as well as head motion-induced dizziness accompanying nausea. The severity of the symptoms must be moderate or severe, and the duration of acute episodes can range from 5 minutes to 72 hours.

Ishii et al. (2009) reported that hormonal fluctuations during the menstrual cycle can influence labyrinthine fluid homeostasis, potentially leading to balance and hearing issues. They studied 20 women in the age range of 18 to 35 years for their vestibular functioning using tests. The subjects were not using any contraceptives for at least six months and were not having any vestibular or hearing complaints. The results showed that healthy women exhibit differences in vestibular tests results between the premenstrual and postmenstrual periods.

2.1 Prevalence of Vestibular Migraine

Neuhauser et al. (2006) screened a range of German population through a telephone interview to check for the presence of moderate to severe vertigo or dizziness symptoms. They found a life-time prevalence of 1%. The life-time prevalence of vertigo was found to be 7% and that for migraine was 16%. Migraineous vertigo was found to be comparatively more common but underdiagnosed. Similarly, Neuhauser and Lempert (2009), in a community-based study, assessed the life-time prevalence where chance concurrence of migraneous vertigo was found to be 3.2% of the population. Migraineous vertigo was reported to be common among the general population but was often left underdiagnosed.

Chai et al. (2014), in a systematic review analysed how estrogen is related to migraine in women. They found that migraine is more prevalent in women when compared to men and is more during the reproductive age. Smith et al. (2019) found that females are more prone to have vestibular issues than men. The authors attributed hormonal difference, neurochemical difference and higher self-concern of females to be the reason for it.

Cho et al. (2016) studied the prevalence of symptoms of vestibular migraine in patients with symptoms of headache. They assessed for migraine and additional vestibular migraine symptoms using ICHD-3b criteria to classify the symptoms of the same. They found that 10.3% of persons with migraine were diagnosed with vestibular migraine. Most of the associated symptoms were migraine without aura (66.2%), chronic migraine (29.2%) and migraine with aura (4.6%). Most common symptoms in vestibular migraine cases were, head motion induced dizziness and nausea. The authors suggested that applying the criteria for ‘probable vestibular migraine’ can increase the identification of vestibular migraine cases.

Sex hormones, including estrogen, progesterone and androgen play distinct roles in normal auditory function, and their balance is crucial for overall human health and inner ear functions. Estrogen, primarily known as a female hormone, acts as an auditory protectant and is produced in the ovaries, adrenal glands, and fat cells. It is higher in those of reproductive age, supporting bone health and maintaining good cholesterol levels. Estrogens can cause fluid retention, but their impact on inner ear

diseases is still not fully understood. Progesterone, mainly associated with sexual health, is produced in the ovaries and helps balance the effects of estrogen. It aids in energy utilization from fat, supports healthy weight, promotes restful sleep, and offers protection against certain cancers. However, progesterone's influence on hearing is less favourable. Androgen, a male hormone, with testosterone as the primary example, contributes to muscle tone, energy levels, libido, and sperm production in men (Matsumoto, 2002). Women also produce testosterone in the ovaries and adrenal glands, impacting libido, musculoskeletal strength, and energy levels. Proper balance is essential as excessive testosterone can lead to various unwanted effects. Maintaining a balanced level of all three sex hormones is beneficial for both men and women and may offer insights into preventing unwanted inner ear symptoms (He & Ren, 2018).

2.2 Vestibular Test Findings in Persons with Vestibular Migraine

Yollu et al. (2017) studied 100 participants who were scanned using ICHD 3 Beta guidelines for vestibular migraine. There were 21 individuals diagnosed with vestibular migraine, and 20 others who had migraine but were not specifically diagnosed with vestibular migraine, matched in terms of age and gender. Additionally, there was a control group consisting of 20 individuals without migraine. The participants were tested for pure tone audiometry, tympanometry, electrocochleography, computerized dynamic posturography and video head impulse test. The results revealed that there was no difference in the test results of pure tone audiometry and tympanometry. However, EcochG showed significantly higher SP/AP scores in vestibular migraine than those with migraine issues. vHIT results suggested that a significant proportion of vestibular migrane patients had saccadic eye movements, indicating peripheral vestibular involvement.

Boldingh et al. (2011) assessed a group of participants with vestibular migraine and a group of participants with motion sickness. The study involved 99 participants: 37 individuals with 'definite' vestibular migraine, 32 migraine only patients, and 30 healthy controls. They found that 44% of participants with vestibular migraine either had unilateral absence of VEMP response or bilaterally absent at 90dBnHL. On the contrary, only 25% of migraineurs and 3% of healthy controls showed absence of VEMP response. This suggests that vestibular migraine patients have a higher prevalence of impaired VEMP responses compared to both migraine only and healthy

controls. The sound intensity threshold and latencies of VEMP responses were similar across the three groups. This indicates that the sensitivity to sound intensity and the timing of the responses did not significantly differ between vestibular migraine, migraine only, and healthy controls. The results of the study suggested that there might be more abnormalities in the VEMP circuitry among migraineurs, particularly those with vestibular migraine, compared to healthy controls.

Rizk et al. (2020) assessed the effectiveness of VEMPs in distinguishing between Meniere's disease and vestibular migraine, two conditions that can have overlapping symptoms. The study had a retrospective cohort design, involving the analysis of medical records and data from patients who visited a multidisciplinary neurotology clinic between January 2015 and May 2017. Ears affected by vestibular migraine were found to have significantly lower oVEMP amplitudes compared to control ears, while the cVEMP amplitudes were found to be comparable.

Kang et al. (2016) studied 81 patients diagnosed with vestibular migraine diagnosed based on the criteria of the Barany Society and the International Headache Society. The patients underwent several vestibular function tests, including the vHIT, caloric test, VEMPs, and sensory organization test. The results of the study indicated abnormal vHIT and c-VEMP results in 11% and abnormal o-VEMP results in 27% of patients.

ElSherif et al. (2018) compared vHIT results between 80 vestibular migraine patients and 40 healthy controls to identify differences if any in the VOR gain, compensatory saccades, and other parameters. The vestibular migraine group showed a higher rate of saccades (rapid eye movements) compared to the healthy controls. Only a small percentage (7.5%) of the vestibular migraine group displayed low VOR gain along with compensatory saccades, indicating vestibular deficits. The presence of refixation saccades was suggested to be a significant indicator associated with various vestibular issues.

2.3 Effect of Menstrual Cycle on Otolith-Ocular Reflex Pathway

Fluctuation of gonadal hormones have various effects on the human physiology, behaviour, and sensory changes, especially in females. Sinha and Sahu (2019) recorded oVEMP in females during their three phases of menstrual cycle. The latency and

amplitude of N1, P1 and N2 peaks were assessed. The results revealed no significant difference across the three phases and between the ears. The oVEMP was reported to be not affected by the fluctuations in hormones seen across menstrual phases. It was hypothesized that the changes in the metabolic dynamics of the inner ear during the menstrual cycle may not be large enough to show significant alterations in oVEMP responses.

2.4 Effect of Menstrual Cycle on Sacculo-Collic Reflex Pathway

Sinha et al. (2017) recorded cVEMPs in 20 adult females during their three phases of menstrual cycle. The cVEMP response was found to be present in all three phases of menstrual cycle. The findings revealed no significant differences in the mean latency and mean amplitude of cVEMP across the three phases of menstrual cycle. The findings suggested that hormonal changes during the menstrual cycle may not have a significant effect on the cVEMP responses.

2.5 Effect of Menstrual Cycle on VOR Gain Functions

Sinha et al. (2021) investigated the VOR gain function across the three phases of menstrual cycle in adult female. They hypothesized that hormonal changes during the menstrual cycle might affect salt and water retention, leading to symptoms such as dizziness and vertigo. However, these hormonal changes may not affect all women equally or influence all vestibular functions in the same way during the menstrual cycle. The results of the study showed no significant differences across the three phases of menstrual cycle. This suggests that hormonal fluctuations during the menstrual cycle may not have a direct impact on VOR gain and VOR gain asymmetry.

Chapter 3

METHODS

The study aimed to investigate the effect of menstrual cycle related harmonal changes on the vestibular functioning. To do this, adult females with and without vestibular symptoms during their menstrual cycle were compared on various standard tests of vestibular functioning. The outcomes of the tests were statistically compared to draw the inferences. The details of the method adopted is given in the following sections.

3.1 Participants

Thirty-six normal hearing adult females in the age range of 18 to 23 years participated in the study. They were students of undergraduate or postgraduate programs at AIISH. They fulfilled the following participation selection criteria for them to be included in the study:

1. Regular menstrual cycle with no complaints/signs of polycystic ovarian disease or any other medical problems suggestive of menstrual cycle deviations.
2. Not using contraceptives or steroids
3. Normal hearing sensitivity and otological functioning
4. No spontaneous nystagmus, strabismus or any other visual abnormalities that restricts the observation of eye movements.

The participants were divided into two groups based on whether they have vestibular symptoms during their menstrual cycles or not. Accordingly, there were 19 participants in the control group, without any vestibular symptoms, and 17 in the clinical group. The participants of clinical group reported of vestibular symptoms such as vertigo, dizziness, imbalance and light-headedness. The presence of vestibular symptoms was ascertained through a structured interview, using the SO STONED tool (Wuyts et al., 2016). The SO STONED tool (Appendix 1) gives an approximate idea of the symptoms of the vestibular disorders based on the signs that could be present. The tool was named SO STONED as a mnemonic where each letter in the word stands for: Symptoms, often (Frequency), Since, Trigger, Otology, Neurology, Evolution, and Duration.

The participants presenting with the vestibular symptoms during their menstrual cycle were selected for the clinical group while the others were selected for the control group. The participants who have long standing vestibular migraine, which is not related to menstrual cycle were not considered for the study.

All the participants gave a written informed consent for their participation, and the study conformed to the AIISH ethical guidelines prescribed for bio-behavioural research (Venkatesan, 2009).

3.2 Test Environment

All the tests were administered in an acoustically treated, electrically isolated suite wherein the noise levels were within the permissible limits ANSI S3.1-1999 (R2003).

3.3 Test Procedure

The participants were tested thrice, once each during the three phases of their menstrual cycle: follicular phase (1–4 days), a luteal phase (12–15 days), and the menstrual phase (22–25 days). In each session, they were tested for c-VEMP, o-VEMP and vHIT. The test protocols that were used to record c-VEMP, o-VEMP and vHIT are described in the following subsections (3.3.1 to 3.3.3).

A Neuro-audio evoked potential system (Neuro-Audio version, 2010; Neurosoft, Ivanovo, Russia) was used to record c-VEMP and o-VEMP. The electrode site was cleaned using a Nuprep skin preparation gel and the electrodes were placed along with the conduction paste. The placement was stabilized using an adhesive plaster. The absolute impendence was maintained within 5 kOhms and the inter-electrode impedance was maintained within 2 kOhms.

3.3.1 Procedure of c-VEMP

While recording c-VEMP, the participants were instructed to sit straight and turn the neck to the opposite side, so that one side sternocleidomastoid muscle was activated. The participants were asked to keep their head and neck steady and maintain the muscle tension to reduce the artifacts. This was done by giving a biofeedback by the system. The skin of the participant was prepared and silver chloride disc type electrode was

placed. The c-VEMP was recorded in a single channel with three electrodes (positive, negative & ground) placed on the participant. The positive electrode was placed at the upper half of sternocleidomastoid muscle, the negative was placed at the ipsilateral sternoclavicular junction and the ground electrode was placed at Fpz. The stimulus and acquisition parameters used to record c-VEMP are shown in Table 3.1. The c-VEMPs were recorded for the two ears separately.

The averaged responses were analysed by two audiologists, experienced in the analysis of VEMP. The responses were visually inspected to mark the P1 and N1 in them. The latency of the marked peaks was noted down from each waveform. The waveform was then EMG rectified using the default algorithm available in Neuro-audio equipment, and the rectified peak-to-peak amplitude (P1-N1) was noted down for further statistical analysis.

3.3.2 Procedure of o-VEMP

While recording o-VEMP, the participants were instructed to sit erect and then look upward with a gaze angle fixed at 30°. The responses were recorded in a single channel with three recording electrodes: positive electrode placed approximately 1cm below the lower eyelid, negative electrode placed inferior to the non-inverting electrode, and the ground electrode placed at Fpz. The positive and negative electrodes were placed on the contralateral side of the stimulus ear as the response is from the extra ocular muscle on the opposite side. The stimulus and acquisition parameters used to record o-VEMP are shown in Table 3.1. The o-VEMPs were recorded for the two ears separately.

The averaged responses were visually inspected to mark the N1 and P1 in them. The latency of the marked peaks was noted down from each waveform. The waveform was then EMG rectified using the default algorithm available in Neuro-Audio equipment, and the rectified peak-to-peak amplitude (N1-P1) was noted down for further statistical analysis.

Table 3.1: Stimulus and acquisition parameters used to record c-VEMP and o-VEMP

Stimulus & acquisition parameters	**cVEMP**	**oVEMP**
Stimulus	500 Hz tone burst	500 Hz tone burst
Intensity	95 dBnHL	95 dBnHL
Repetition rate	5.1/s	5.1/s
Polarity	Rarefaction	Rarefaction
Tracts	Ipsilateral	Contralateral
Type of electrode	Disc, silver chloride	Disc, silver chloride
Montage	Positive: midpoint or upper half of sternocleidomastoid Negative: sternoclavicular junction Ground: high forehead (Fpz)	Positive: approximately 1 cm inferior to the lower eyelids Negative: inferior to noninverting electrode Ground: high forehead
Filter	10 Hz to 1500 Hz	1 Hz to 1000 Hz
Analysis window	-10 to 40ms	-10 to 64 ms
No. of averages	100	200

3.3.3 Procedure for vHIT

The VHIT was performed for all three semicircular canals and in the two ears. Otometrics ICS Impulse vHIT equipment was used for the purpose. For vHIT test, the participants were seated on a nonadjustable chair at 1 meter away from the target. The target was adjusted to avoid the reflections on the pupil image and was fixed at the eye level. The participants were asked to fix their visual gaze on the target and also to minimize their eye blinks. The examiner would then adjust the soft band of the vHIT goggles to a comfortably tight position on the head of the participant.

To begin with, calibration of the eye baseline movement was carried out using the prescribed procedure (MacDougall et al., 2013). The testing was performed by giving the head thrust for all the six semi-circular canals. vHIT was performed in the lateral plane, left anterior right posterior (LARP) plane, and right anterior left posterior (RALP) plane. The head thrusts were given abruptly 20 times for each pair of canals. The eye movements during the evaluation were recorded with the help of a high-speed

digital infrared camera, in-built in the hardware. Additionally, the gyroscope fixed on the goggle would record the head velocity. The software of the equipment calculated the VOR gain as a ratio of eye to head peak velocity from the average of the 20 head impulses. Mean gain, standard deviation of the gain and the gain asymmetry ratio were noted down as the outcome measures of the test.

3.4 Data Analysis

The data of VEMPs and VHIT were tabulated in Statistical package for social sciences-SPSS (version 26). The data of experimental and control group was loaded in a single file across the different phases of menstrual cycle. The group data was analysed to derive the mean and standard deviation of latency, amplitude, and asymmetry ratio parameters of VEMPs across different phases of menstrual cycle in control and clinical groups. The data were first assessed for their distribution using Shapiro Wilk test of normality. Based on the results of normality test, the decision on parametric versus non-parametric test was made for further statistical analysis.

Chapter 4

RESULTS

In the current study, group and phase of the menstrual cycle were independent variables while the measures of vestibular functioning (response measures of c-VEMP, o-VEMP & vHIT) were the dependent variables.

To begin with, the data were tested for their distribution using Shapiro-Wilk test of normality. The results showed that the data in all the variables of c-VEMP and o-VEMP were normally distributed, while those of vHIT were non-normally distributed. Accordingly, statistical comparisons of c-VEMP and o-VEMP data were made using parametric tests and statistical comparisons of vHIT were made using non-parametric tests. The results obtained are reported under the following headings:

1. Outcomes of the SO STONED questionnaire administration
2. Results of c-VEMP
3. Results of o-VEMP
4. Results of vHIT

4.1 Outcomes of SO STONED Questionnaire Administration

The questionnaire was circulated among 216 adult females, having normal menstrual cycle. Thirty two of them reported vestibular symptoms during their menstrual cycle and 17 of them were randomly selected for the study. Similarly, another 19 of them without any such symptoms were selected for the control group. The results of questionnaire had revealed that all the seventeen participants of the clinical group (participants having vestibular symptoms during their menstrual cycle) had vertigo, dizziness or postural instability associated with headache or symptoms of migraine during their menstrual cycle. Although all of them experienced the reported vestibular symptoms during their menstrual cycle, the first occurrence of such symtpoms, frequency of occurence, and the presence of other associated symptoms varied across the participants. The number of participants of clinical group with different reported symptoms/characteristics is reflected in Table 4.1. The symptoms reported were during the menstrual cycle. On the contrary, none of the participants of the control group reported of experiencing/having experienced any vestibular symptoms during their menstrual cycle.

Table 4.1: Outcomes of SO STONED questionnaire in the clinical group

Questions	Response	No. of participants
Do you experience Vertigo, dizziness, or postural instability during the period of menstrual cycle?	Yes	20
	No	0
Do you experience the symptoms every month?	Yes	5
	No	15
From when do you have vertigo symptoms associated with menstrual cycle?	Months	7
	Years	15
Do you have the symptoms any time other than the menstrual cycle period?	Yes	12
	No	8
Is any of these symptoms associated with vestibular symptoms?	Headache/ migraine	20
	Visual aura	6
	Photophobia	1
	Phonophobia	2
Is any of these symptoms associated with vestibular symptoms?	Aural fullness	6
	Tinnitus	2
For what duration does the symptoms last?	Minutes	16
	Hours	3
	Days	1

4.2 Results of c-VEMP

Table 4.2 gives the mean and standard deviation of P1 latency, N1 latency, P1-N1 amplitude and the rectified EMG of right and left ears in the three phases of menstrual cycle of control and clinical groups. The table reflects prolonged mean latencies and reduced mean amplitudes in the clinical group compared to control group. It also reflects that mean latency and amplitudes varied across the three phases of menstrual cycle. The observations are true in both the ears.

Table 4.2: Mean and standard deviation of P1 latency, N1 latency, P1-N1 amplitude and rectified EMG of right and left ear in the three phases of menstrual cycle of control and clinical groups

Response Measure	Phase	Group	Right ear		Left ear	
			Mean	SD	Mean	SD
P1 latency (in ms)	Follicular	Control	13.49	1.54	13.59	1.58
		Clinical	14.14	1.39	14.17	0.96
	Luteal	Control	13.22	1.34	13.60	1.72
		Clinical	13.70	1.20	13.98	1.13
	Menstrual	Control	13.45	2.04	13.95	2.43
		Clinical	13.72	1.21	13.72	1.21
N1 latency (in ms)	Follicular	Control	22.31	2.01	22.00	2.13
		Clinical	23.84	1.81	22.37	1.57
	Luteal	Control	22.14	1.85	22.55	2.24
		Clinical	22.87	1.88	22.72	1.73
	Menstrual	Control	21.78	2.11	22.31	2.45
		Clinical	22.51	1.81	22.70	1.71
P1-N1 amp (μV)	Follicular	Control	104.93	40.76	113.76	43.92
		Clinical	97.47	55.41	107.60	61.42
	Luteal	Control	125.73	43.90	139.20	59.53
		Clinical	109.35	59.10	107.42	66.79
	Menstrual	Control	111.85	42.53	169.72	44.48
		Clinical	84.15	29.43	94.84	35.39
Rec EMG (μV)	Follicular	Control	1.94	0.53	2.15	0.62
		Clinical	1.85	0.66	2.01	0.79
	Luteal	Control	2.24	0.65	2.54	0.77
		Clinical	1.90	0.76	1.97	0.92
	Menstrual	Control	2.11	0.59	2.31	0.73
		Clinical	1.70	0.47	1.78	0.54

**P1-N1 amp: P1-N1 amplitude, Rec EMG: rectified EMG.*

c-VEMPs of the two groups of participants were compared for their P1 latency, N1 latency, P1-N1 amplitude and the rectified EMG, across the three phases of menstrual cycle. The measures of c-VEMP were analysed on a repeated measures ANOVA, taking phase as the repeating variable and group as between-subject factor. All the four measures of c-VEMP were fit into the same model of ANOVA. Table 4.3 shows the results of repeated measures ANOVA, for the right and left ear. The results showed that there was no significant effect of either the phase of menstrual cycle or the group. Also, there was no significant interaction between phase and group. This was true for all the four measures and for the data of both the ears.

Table 4.3: Results of repeated measures ANOVA, showing the effect of the phase of menstrual cycle and group on the measures of c-VEMP and their interaction, for the right and left ear

Measure	Variable	Right			Left		
		F	df (error)	p	F	df (error)	p
P1 latency	Phase	1.13	2(68)	0.32	0.88	2(68)	0.41
	Group	1.24	1(34)	0.27	0.91	1(34)	0.34
	Phase*Group	0.33	2(68)	0.72	0.12	2(68)	0.88
N1 latency	Phase	1.67	2(68)	0.19	0.280	2(68)	0.75
	Group	2.49	1(34)	0.12	0.638	1(34)	0.43
	Phase*Group	0.06	2(68)	0.94	0.858	2(68)	0.64
P1-N1 amplitude	Phase	3.07	2(68)	0.05	0.96	2(68)	0.38
	Group	2.09	1(34)	0.15	3.25	1(34)	0.08
	Phase*Group	0.72	2(68)	0.49	1.01	2(68)	0.36
Rectified EMG	Phase	2.02	2(68)	0.13	1.556	2(68)	0.21
	Group	2.60	1(34)	0.11	4.362	1(34)	0.04
	Phase*Group	1.48	2(68)	0.23	1.782	2(68)	0.17

Table 4.4 gives the mean and standard deviation of asymmetry ratio in the three phases of menstrual cycle of control and clinical groups. The table reflects increased mean asymmetry ratio in the clinical group compared to control group.

Table 4.4: Mean and standard deviation of asymmetry ratio of c-VEMP in the three phases of menstrual cycle of control and clinical groups

Phase	Group	Mean	SD
Follicular	Control	11.04	9.46
	Clinical	16.12	8.71
Luteal	Control	11.33	9.21
	Clinical	17.51	11.50
Menstrual	Control	10.15	8.25
	Clinical	14.15	8.27

c-VEMPs of the two groups of participants were compared for their asymmetry ratio across the three phases of menstrual cycle and between the two groups using repeated measures ANOVA, taking phase as the repeating variable and group as between-subject factor. Results showed no significant effect of phase [F(2,68)=0.68,

p=0.50] but there was a significant effect of group [F(1,34)=5.80, p=0.02]. There was no significant interaction between phase and group [F(2,68)=0.15, p=0.85].

4.3 Results of o-VEMP

Table 4.5 gives the mean and standard deviation of N1 latency, P1 latency, N1-P1 amplitude and the rectified EMG of right and left ear in the three phases of menstrual cycle of control and clinical groups. The table reflects prolonged mean latencies and reduced mean amplitudes in the clinical group compared to control group. It also reflects that mean latency and amplitudes varied across the three phases of menstrual cycle. The observation was true in both the ears.

Table 4.5: Comparison of control and clinical groups for their latency and amplitude of o-VEMP of right and left ears in follicular, luteal, and menstrual phase of menstrual cycle

RM	Phase	Group	Right ear		Left ear	
			Mean	SD	Mean	SD
N1 latency (in ms)	Follicular	Control	10.55	1.78	10.34	1.08
		Clinical	11.55	2.20	11.19	2.04
	Luteal	Control	10.39	1.33	10.21	1.35
		Clinical	11.90	1.77	11.61	1.56
	Menstrual	Control	10.60	1.24	10.17	1.05
		Clinical	11.59	2.32	11.98	2.89
P1 latency (in ms)	Follicular	Control	15.72	1.90	15.79	1.53
		Clinical	17.62	1.84	17.59	2.08
	Luteal	Control	15.44	1.34	15.64	1.65
		Clinical	17.80	2.25	17.33	1.33
	Menstrual	Control	16.07	1.48	15.73	1.41
		Clinical	16.99	1.74	16.68	3.39
N1-P1 amp (μV)	Follicular	Control	8.75	6.26	11.28	8.19
		Clinical	3.45	1.33	8.60	3.65
	Luteal	Control	9.34	7.98	9.92	7.20
		Clinical	3.41	1.85	5.34	3.13
	Menstrual	Control	9.77	6.88	9.67	8.88
		Clinical	4.16	2.76	5.94	5.10
Rec EMG (μV)	Follicular	Control	1.88	1.50	2.28	1.85
		Clinical	1.11	0.97	2.00	2.56
	Luteal	Control	2.01	1.66	2.08	1.34
		Clinical	0.78	0.39	1.35	0.89
	Menstrual	Control	1.87	1.36	1.90	1.92
		Clinical	0.93	0.53	1.31	0.88

**RM: Response Measure, P1-N1 amp: P1-N1 amplitude, Rec EMG: rectified EMG*

The o-VEMPs of the two groups of participants were compared for their mean N1 latency, P1 latency, N1-P1 amplitude and the rectified EMG, across the three phases menstrual cycle and between the two groups. The measures were analysed on a repeated measures ANOVA, taking phase as the repeating variable and group as between-subject factor. All the four measures of o-VEMP were fit into the same model of ANOVA. Table 4.6 shows the results of repeated measures ANOVA, for the right and left ear.

Table 4.6: Results of repeated measures ANOVA, showing the effect of the phase of menstrual cycle and group on the measures of o-VEMP and their interaction, for the right and left ear

Measure	Variable	Right			Left		
		F	df (error)	p	F	df (error)	p
N1 latency	Phase	0.73	2(68)	0.93	0.51	2(68)	0.60
	Group	0.21	1(34)	0.05	0.37	1(34)	0.10
	Phase*Group	0.27	2(68)	0.14	0.81	2(68)	0.44
P1 latency	Phase	0.93	2(68)	0.39	0.70	2(68)	0.49
	Group	0.11	1(34)	0.73	0.12	1(34)	0.72
	Phase*Group	0.72	2(68)	0.48	1.08	2(68)	0.34
N1-P1 amplitude	Phase	1.45	2(68)	0.24	1.65	2(68)	0.19
	Group	10.90*	1(34)	0.002	2.79	1(34)	0.10
	Phase*Group	0.05	2(68)	0.94	0.22	2(68)	0.79
Rectified EMG	Phase	0.21	2(68)	0.80	1.84	2(68)	0.16
	Group	7.76*	1(34)	0.009	1.40	1(34)	0.24
	Phase*Group	1.11	2(68)	0.33	0.31	2(68)	0.73

The results showed a statistically significant effect of group that was seen in N1-P1 amplitude and rectified amplitude of right ear. There was no significant interaction between phase and group. There was no significant effect of phase of menstrual cycle on the measures of oVEMP.

Table 4.7 gives the mean and standard deviation of asymmetry ratio of o-VEMP in the three phases of menstrual cycle of control and clinical groups. The table reflects that there was no specific trend in the way mean asymmetry ration varied between the groups.

Table 4.7: Comparison of control and clinical groups for their asymmetry ratio of o-VEMP in follicular, luteal, and menstrual phase of menstrual cycle

Phase	Group	Mean	SD
Follicular	Control	25.81	19.72
	Clinical	25.09	17.72
Luteal	Control	29.21	18.63
	Clinical	29.70	22.63
Menstrual	Control	24.64	17.64
	Clinical	20.59	15.13

o-VEMPs of the two groups of participants were compared for their asymmetry ratio across the three phases of menstrual cycle and between the two groups using repeated measures ANOVA, taking phase as the repeating variable and group as between-subject factor. Results showed no significant effect of phase [$F(2,68)=1.62$, $p=0.20$] and group [$F(1,34)=1.10$, $p=0.75$] on the asymmentric ratio of o-VEMP. Also, there was no significant interaction between phase and group [$F(2,68)=1.62$, $p=0.21$].

4.4 Results of VHIT

Table 4.8 gives the median and inter quartile range of mean VOR gain of lateral, anterior and posterior canals of right and left ears in the three phases of menstrual cycle of control and clinical groups. The table reflects differences in the mean gain arranged across 20 thrusts in clinical and control groups.

Table 4.8: Median and interquartile range of mean VOR gain of lateral, anterior, and posterior semicircular canals of right and left ears in follicular, luteal, and menstrual phase of menstrual cycle of control and clinical groups

Semi circular canal	Phase	Group	Right ear		Left ear	
			Median (arbitrary)	Inter quartile range	Median (arbitrary)	Inter quartile range
Lateral	Follicular	Control	1.05	0.16	0.99	0.14
		Clinical	1.00	0.17	0.97	0.17
	Luteal	Control	1.02	0.26	0.97	0.30
		Clinical	1.02	0.21	0.97	0.15
	Menstrual	Control	1.02	0.18	0.97	0.20
		Clinical	1.02	0.11	0.95	0.13
Anterior	Follicular	Control	0.95	0.27	0.89	0.21
		Clinical	0.92	0.28	0.87	0.24
	Luteal	Control	0.96	0.22	0.95	0.18
		Clinical	0.88	0.27	0.87	0.34
	Menstrual	Control	0.84	0.22	0.94	0.15
		Clinical	0.90	0.23	0.93	0.28
Posterior	Follicular	Control	0.93	0.15	0.82	0.10
		Clinical	0.89	0.22	0.85	0.13
	Luteal	Control	0.92	0.21	0.87	0.16
		Clinical	0.94	0.15	0.80	0.14
	Menstrual	Control	0.95	0.16	0.80	0.13
		Clinical	0.86	0.17	0.81	0.14

The median VOR gain across the three phases of menstrual cycle was compared using Friedmann test. This was done separately for the two ears and separately for control and clinical groups. The results (Table 4.9) showed no significant effect of phase on the mean VOR gain. This was true in all the three canals, in both the ears and in both the groups.

Table 4.9: Comparison of mean VOR gain of vHIT of lateral, anterior, and posterior semicircular canals across follicular, luteal, and menstrual phases of menstrual cycle in the two ears and in control and clinical groups

Control group		Right ear			Left ear		
Semicircular canal	Phase	χ^2	df	p	χ^2	df	p
Lateral	Follicular	0.96	2	0.61	0.53	2	0.76
	Luteal						
	Menstrual						
Anterior	Follicular	5.02	2	0.08	0.23	2	0.89
	Luteal						
	Menstrual						
Posterior	Follicular	1.24	2	0.53	3.36	2	0.18
	Luteal						
	Menstrual						
Clinical group							
Semicircular canal	Phase						
Lateral	Follicular	2.35	2	0.30	1.30	2	0.52
	Luteal						
	Menstrual						
Anterior	Follicular	1.08	2	0.58	1.63	2	0.44
	Luteal						
	Menstrual						
Posterior	Follicular	2.41	2	0.29	2.05	2	0.35
	Luteal						
	Menstrual						

The mean VOR gain of vHIT was compared between clinical and control groups using Mann-Whitney U test, separately in the three semicircular canals and in the three phases of menstrual cycle. The results (Table 4.10) showed that there is no significant difference between the two groups in any of the canal and in any of the phase of menstrual cycle.

Table 4.10: Comparison of mean VOR gain of vHIT between clinical and control groups, in the three semicircular canals, in the three phases of menstrual cycle

Follicular		Right ear			Left ear		
Semicircular canal	Phase	MW-U	Z	p	MW-U	Z	p
Lateral	Control / Clinical	175.50	0.66	0.50	185.00	0.40	0.68
Anterior	Control / Clinical	190.00	0.27	0.78	183.00	0.46	0.64
Posterior	Control / Clinical	159.00	1.11	0.26	186.50	0.36	0.71
Luteal							
Semicircular canal	Phase	MW-U	Z	p	MW-U	Z	p
Lateral	Control / Clinical	172.50	0.74	0.45	199.50	0.01	0.98
Anterior	Control / Clinical	140.00	1.62	0.10	129.50	1.90	0.05
Posterior	Control / Clinical	180.00	0.54	0.58	140.00	1.62	0.10
Menstrual							
Semicircular canal	Phase	MW-U	Z	p	MW-U	Z	p
Lateral	Control / Clinical	195.00	0.13	0.89	193.50	0.17	0.86
Anterior	Control / Clinical	172.00	0.75	0.44	160.00	1.08	0.27
Posterior	Control / Clinical	135.50	1.74	0.08	191.50	0.23	0.81

Table 4.11 gives the median and interquartile range of VOR gain asymmetry ratio for the three pairs of canals, in the three phases of menstrual cycle, in control and clinical groups. The median ratio varied across phases and groups. However, the results of Friedman test (Table 4.12) showed no significant differences across the three phases of menstrual cycle, either in control or clinical groups. This was true for all the three pairs of canals.

Table 4.11: Median and interquartile range of VOR gain asymmetry ratio for the three pairs of canals, in the three phases of menstrual cycle, in control and clinical groups

RM	Phase	Group	Median	Inter Quartile
Lateral	Follicular	Control	7.00	10
		Clinical	6.50	10
	Luteal	Control	9.50	12
		Clinical	6.50	4
	Menstrual	Control	8.00	10
		Clinical	6.00	9
LARP	Follicular	Control	9.00	10
		Clinical	9.00	14
	Luteal	Control	7.00	14
		Clinical	9.50	12
	Menstrual	Control	6.50	8
		Clinical	9.50	14
RALP	Follicular	Control	13.00	10
		Clinical	9.00	10
	Luteal	Control	12.00	12
		Clinical	14.50	13
	Menstrual	Control	7.00	8
		Clinical	9.00	10

Table 4.12: Comparison of VOR gain asymmetry ratio across the three phases of menstrual cycle in the three pairs of semicircular canals in control and clinical groups

		Control group			Clinical group		
Pair of semicircular canals	Phase	χ^2	df	p	χ^2	df	p
Lateral	Follicular Luteal Menstrual	1.28	2	0.52	0.11	2	0.94
LARP	Follicular Luteal Menstrual	0.17	2	0.91	1.71	2	0.42
RALP	Follicular Luteal Menstrual	1.69	2	0.42	2.84	2	0.24

Table 4.13 gives the results of Mann-Whitney U test comparing the VOR gain asymmetry ratio of vHIT between clinical and control groups in the three pairs of semicircular canals and in the three phases of menstrual cycle. The results showed no significant difference between the two groups.

Table 4.13: Comparison of mean VOR gain asymmetry ratio of vHIT between clinical and control groups, in the three pairs of semicircular canals, in the three phases of menstrual cycle

Phase	Pairs of semicircular canals	Group	MW-U	Z	p
Follicular	Laterals	Control	188.00	0.32	0.74
		Clinical			
	LARP	Control	191.50	0.23	0.81
		Clinical			
	RALP	Control	184.50	0.42	0.67
		Clinical			
Luteal	Lateral	Control	184.00	0.43	0.66
		Clinical			
	LARP	Control	157.50	1.15	0.25
		Clinical			
	RALP	Control	179.50	0.29	0.76
		Clinical			
Menstrual	Lateral	Control	171.00	0.78	0.43
		Clinical			
	LARP	Control	137.50	1.69	0.09
		Clinical			
	RALP	Control	138.00	1.68	0.09
		Clinical			

**LARP: left anterior right posterior RALP: right anterior left posterior*

Chapter 5

DISCUSSION

The study aimed to determine the influence of menstrual cycle related hormonal changes on the vestibular functioning of young adults. There were 4 hypothesis that were tested in the current study:

1. Participants who report of vestibular symptoms during their menstrual cycle show differences in the c-VEMP response compared to those who do not have such symptoms during their menstrual cycle.
2. Participants who report of vestibular symptoms during their menstrual cycle show differences in the o-VEMP response compared to those who do not have such symptoms during their menstrual cycle.
3. Participants who report of vestibular symptoms during their menstrual cycle show differences in the vHIT response compared to those who do not have such symptoms during their menstrual cycle.
4. The c-VEMP, o-VEMP and VOR gain functions vary across the three phases of menstrual cycle in persons who have vestibular symptoms during their menstrual cycle.

The results of the study showed some interesting findings. The findings are discussed in light of the earlier literature and the underlying physiology in the following sections.

5.1 Effect of Menstrual Cycle related Harmonal Changes on the Sacculo-collic Reflex and the Functioning of Inferior Vestibular Nerve

c-VEMP was recorded in both control and clinical groups across the three (follicular, luteal & menstrual) phases of menstrual cycle. The purpose was to assess the effect of hormonal variations on the sacculo-collic reflex pathway and inferior vestibular nerve. The results showed no significant effect of phase of menstrual cycle on the latency, amplitude and asymmetric ratio of c-VEMP. This was true in control as well as clinical groups. This suggests that harmonal changes secondary to menstrual cycle does not significantly influence the functioning of sacculo-collic reflex and inferior vestibular nerve. The results are in agreement with Sinha et al. (2017), wherein

no significant effect of phase of menstrual cycle on c-VEMP was found. The current study considered subjects who report of vestibular symptoms during menstrual cycle as separate cohort. Even then, there was no significant effect of phase of the menstrual cycle on the cVEMP parameters. The findings further strengthens the inference drawn by Sinha et al. (2017) that there is no noticeable influence of menstrual cycle related harmonal changes on the sacculo-collic reflex.

However, the study found a significant effect of group on the amplitude asymmetry ratio of c-VEMP. The asymmetry ratio was higher in persons with vestibular symptoms compared to those without. This suggests that harmonal changes caused by menstrual cycle results in greater asymmetry in the functioning of sacculo colic reflex in some of the individuals and such individuals are likely to experience vestibular symptoms such as dizziness, nausea and vertigo. The underlying reason may be unilateral hypoperfusion of the labyrinthine artery (Espinosa-Sanchez & Lopez-Escamez, 2015). On the contrary, the control group who did not experience vestibular symptoms during their menstrual cycle had lesser asymmetry in their succulo-collic functioning.

The presence of significant change in the asymmetry ratio of c-VEMP hints at differential effects in the ear wise c-VEMP. However, ear wise c-VEMP findings did not reveal significant differences albeit mean amplitudes being consistently lower in clinical group compared to control group. These results suggest that asymmetry ratio is a more sensitive parameter in identifying the menstrual cycle related vestibular deviations than the c-VEMPs of the individual ears.

Whether the presence of vestibular symptoms during their menstrual cycle can be termed as vestibular migraine is a debatable issue. Typically, vestibular migraine is a diagnosis that is made through the method exclusion. Considering that the participants of clinical group had the vestibular symptoms only during menstrual cycle, not otherwise, one can presumably rule out the other causes of vestibular dysfunction and call this to be the vestibular migraine. Earlier studies have reported normal latency of c-VEMP in persons with vestibular migraine (Baier, Stieber, & Dieterich, 2009) but have reported relatively higher value of asymmetry ratio compared to that of normal (Dlugaiczyk, Habs, & Dieterich, 2020).

Taken together, we can infer that the amplitude and latency parameters are not significantly affected across the phases of menstrual cycle. However, amplitude asymmetry is a sensitive parameter in identifying the cause for vestibular migraine during menstrual cycle. Therefore, the first hypothesis that 'the participants who report of vestibular symptoms during their menstrual cycle show differences in the c-VEMP response compared to those who do not have such symptoms during their menstrual cycle' is accepted.

5.2 Effect of Menstrual Cycle related Harmonal Changes on the utriculo-ocular Reflex and the Functioning of Superior Vestibular Nerve

In the present study o-VEMPs were recorded to assess the effect of phases of menstrual cycle and group on the utriculo ocular pathway and superior vestibular nerve. Results revealed that there was no significant effect of phase of the menstrual cycle on o-VEMP parameters. However, the amplitude (unrectified as well as rectified) of o-VEMP of right ear was significantly lower in clinical group compared to control group. This suggests that the harmonal changes related to the menstrual cycle affects utriculo ocular pathway and superior vestibular nerve to a greater extent in some females than the other. Those in whom the reflex is suppressed to a greater extent are likely to experience vestibular symptoms during their menstrual cycle. Again, whether this can be termed vestibular migraine is debatable.

It may be noted that lower functioning in clinical group compared to control group was observed in one ear (right ear in this case), while the functioning in the other ear remained comparable between the two groups. The exact reason for utriculo-ocular reflex getting suppressed in one ear more than the other ear is not known. The finding hints at the asymmetric functioning of the two ears, but it was not statistically reflected in the asymmetric ratio. One can infer that, those in whom harmonal changes related to menstrual cycle results in asymmetric vestibular functioning are likely to experience vestibular symptoms during their menstrual cycle.

It is also important to note that the observed group effect was present in the absence of effect of phase and significant interaction effect between phase and group. The absence of the phase effect found in the present study is in agreement with the

Sinha et al. (2019). The results showed that the group effect seen is true irrespective of the phase of the menstrual cycle. This suggests that, it is not the harmonal variations across the three phases of menstrual cycle that induces changes in the vestibular functioning. Rather, some females are prone to asymmetric functioning and it is expressed symptomatically during their menstrual cycle.

Based on the results of o-VEMP, the second hypothesis that 'participants who report of vestibular symptoms during their menstrual cycle show differences in the o-VEMP response compared to those who do not have such symptoms during their menstrual cycle' is accepted.

5.3 Effect of Menstrual Cycle related Harmonal Changes on the Vestibulo-Ocular Reflex as seen in Video Head Impulse Test

The results of vHIT showed no significant effect of either the phase of menstrual cycle or the group on the VOR gain and VOR asymmetry ratio. The results are in agreement with Sinha et al. (2021), who had found no significant effect of menstrual cycle related harmonal changes on the VOR. In the current study, those having vestibular symptoms during menstrual cycle were taken as separate cohort as an improvisation to the design of Sinha et al. (2021). Even then, the findings reveal no significant effect of phase of menstrual cycle on the VOR.

Several researchers have proposed direct impact of hormonal fluctuations on inner ear physiology (Charitidi, Meltser, Tahera & Canlon, 2009) and corresponding changes in hearing function during the various phases of the menstrual cycle (Al-Mana, Ceranic, Djahanbakhch, & Luxon, 2008). It is assumed that the harmonal changes influences the inner ear homeostasis in females during the various periods of the menstrual cycle (Darlington, Ross, King & Smith, 2001). There was no observable trend seen in the asymmetry ratio across the different phases and between groups. Hence, it is suggested that vHIT test need not be used to assess the menstrual cycle related changes on vestibular functioning. Based on the results of vHIT, the third hypothesis that 'the participants who report of vestibular symptoms during their menstrual cycle show differences in the vHIT response compared to those who do not have such symptoms during their menstrual cycle' is rejected.

There was no significant change in the c-VEMP, o-VEMP and vHIT across the three phases of the menstrual cycle. The results were true even in a cohort with vestibular symptoms during their menstrual cycle. Therefore, the fourth hypothsis that 'the c-VEMP, o-VEMP and VOR gain functions vary across the three phases of menstrual cycle in persons who have vestibular symptoms during their menstrual cycle' is also rejected.

Chapter 6

SUMMARY AND CONCLUSIONS

In female population one of the very common causes of recurrent vertigo is vestibular migraine. Hormone levels change throughout the menstrual cycle in a healthy female at different phases. This fluctuation of hormones may affect the inner ear physiology. There are evidences to support that the inner ear physiology is altered due to the hormonal variations. Therefore, the present study aimed to determine the effect of the hormonal fluctuations on the vestibular functioning. Sinha et al. in a series of three studies (2017,2019,2021) had shown that there is no significant effect of phase of the menstrual cycle on the c-VEMP, o-VEMP and vHIT. But they had taken those without vestibular symptoms. Therefore, the present study aimed to compare those with and without vestibular symptoms during their menstrual cycle for their c-VEMP, o-VEMP and vHIT, across the three phases of menstrual cycle.

The questionnaire of SO STONED was administered on 216 young women of age 18-23 years. Thirty six among them, who had normal menstrual cycle and no signs of polycystic ovary disorder participated in the study. The participants were divided into control and clinical group having 19 and 17 participants respectively. The clinical group consisted of participants who reported of vestibular symptoms during their menstrual cycle, while the control group had those with no such symptoms. The participants were assessed for c-VEMP, o-VEMP and vHIT thrice during the three phases of their menstrual cycle (follicular, luteal & menstrual phase). The responses were compared across the three phases and between the two groups.

The results showed no significant effect of the phase of the menstrual cycle on the vestibular functioning, as assessed by the three tests. However, there was a significant effect of group on the c-VEMP and o-VEMP. Those who reported of vestibular symptoms during their menstrual cycle had more asymmetric vestibular functioning than those in the control group. There was no significant interaction between phase and group effect, suggesting that those experiencing vestibular symptoms show asymmetric vestibular functioning, irrespective of phase of the menstrual cycle. Based on the results found, it can be concluded that the adult females who experience vestibular symptoms during their menstrual cycle have asymmetric

vestibular functioning and this can be unveiled only if they are taken as a separate cohort. Although they experience symptoms during their menstrual cycle, there is no significant change in their vestibular physiology across the three phases, at least as can be evidenced through c-VEMP, o-VEMP and vHIT.

Implications of Study

Considering that those experiencing vestibular symptoms during their menstrual cycle have higher asymmetry in their vestibular functioning, management strategies can be designed to address their clinical concerns, so as to improve their quality of life during the days of menstrual cycle.

Limitations of the Study

The participants were only assessed using physiological tests. Inclusion of some of the behavioural tests could have been beneficial for better understanding of their behavioural symptoms. Some of the participants of clinical group did not experience the symptoms every month. Restricting to those experiencing symptoms every month probably would have given better picture of the relationship between menstrual cycle and vestibular functioning.

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Appendix I

Questionnaire to Assess the Presence of Symptoms of Vestibular Migraine during Menstrual Cycle

Name:

Age /gender:

Informed consent

'I have been informed about the study titled "Comparison of Vestibular Functioning among Women with and without the signs of Vestibular Migraine during phases of Menstrual Cycle". I understand the purpose and procedure of the questionnaire. I declare that my participation in this study is entirely voluntary and that I may withdraw at any time without incurring a penalty or without being obligated to provide a reason. I understand that my participation in the study will not adversely affect me in any way and that confidentiality will be always maintained about my identity. I also understand that the information given by me will be used only for the purpose of the study. I do not have any financial or non-financial benefitsfrom this study. I hereby give my consent to participate.'

Date: Name:

Place: Signature:

Instructions to the participants

"The questionnaire consists of few questions related to presence of symptoms of vestibular migraine during menstrual cycle. There are nine questions in the questionnaire which you will have to read and select the appropriate symptoms that you experience during the menstrual period."

Questionnaire

a. Do you experience Vertigo, dizziness, or postural instability during the period of menstrual cycle?
   'Yes' 'No'

b. Do you experience the symptoms every month?
   'Yes' 'No'

c. From when do you have vertigo symptoms associated with menstrual cycle?
   If you have the symptoms from several months select 'month' if it is from years select 'year'
   'Month' 'Year'

d. Do you have the symptoms any time other than the menstrual cycle period? If, yes specify.
   The answer needs to be given in a descriptive form. If you experience symptoms then you will have to describe it in few words.
   Answer:

e. Is any of these symptoms associated with vestibular symptoms?
   Select the check box of symptoms that you experience
   - photophobia,
   - phonophobia,
   - visual aura and
   - headache/migraine.

f. Is any of these symptoms associated with vestibular symptoms?
   Select the check box of symptoms that you experience
   - Tinnitus
   - Aural fulness

g. For what duration does the symptoms last?
   Select the option about for what duration the vertigo symptoms last once there is an episode
   - minutes
   - hours
   - days.

h. Are you willing to go through a vestibular evaluation during your next menstrual cycle?
   'Yes' 'No'