# "VARIATIONS OF NEUTROPHIL LYMPHOCYTE RATIO AND POTENTIAL ASSOCIATION OF SERUM URIC ACID LEVELS IN PATIENTS WITH PERIPHERAL VESTIBULAR DISORDERS: A CROSS-SECTIONAL STUDY IN KLES DR. PRABHAKAR KORE HOSPITAL, BELAGAVI."


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# LIST OF ABBREVIATIONS

| GLOSSARY | ABBREVIATIONS |
|---|---|
| BPPV | Benign Paroxysmal Positional Vertigo |
| ENT | Ear Nose and Throat |
| DHI | Dizziness handicap inventory |
| NLR | Neutrophil lymphocyte ratio |
| SCC | Semi-Circular Canal |
| SSCD | Superior semicircular canal dehisence |
| CSF | cerebrospinal fluid |
| RALP | Right anterior left posterior plane |
| CRP | C-reactive protein |
| CNS | central nervous system |
| WBC | white blood cell |
| $CaCO_3$ | Calcium carbonate |
| BPPV | benign paroxysmal positional vertigo |
| VOR | Vestibulo-occular reflex |
| MD | Meniere's disease |
| MV | migrainous vertigo |
| VN | vestibular neuronitis |
| IL-1 | interleukin-1 |
| IL-1β | interleukin-1 beta |
| IL-6 | interleukin-6 |
| IL-33 | interleukin-33 |
| E2 | 17β-estradiol |

| GLOSSARY | ABBREVIATIONS |
|---|---|
| ER | estrogen receptor |
| TNF-alpha | tumor necrosis factor-alpha |
| TH 2 | T helper 2 |
| PLR | Platelet to lymphocyte ratio |
| SGOT | Serum glutamic oxaloacetic transaminase |
| HDL | High density lipoprotein |
| MHR | Monocyte to high density lipoprotein ratio |
| IAC | Internal auditory canal |
| TSLP | thymic stromal lymphopoietin |
| MS | multiple sclerosis |
| SIRS | systemic inflammatory response |
| CAP | community-acquired pneumonia |
| ED | emergency department |
| UA | Uric acid |
| IR | Insulin resistance |
| NSE | neuron specific enolase |
| SUA | Serum uric acid |
| ROS | reactive oxygen species |

# ABSTRACT

**Background:** Dislodging otoconia, endolymphatic hydrops, inner ear virus infection, or trauma to the oval and round windows or bone labyrinth are the most common causes of peripheral vestibular vertigo. Dizziness, nausea, vomiting, nystagmus, and unsteadiness are just a few of the symptoms that can indicate vertigo. BPPV is the most common peripheral vestibular disorder in adults, and is the commonest ENT diagnosis associated with vertigo.

**Objectives:**

- To study the variations of neutrophil to lymphocyte ratio and potential association of serum uric acid level in patients with Peripheral vestibular disorders

**Methodology:** This cross sectional study was conducted in the department of Otorhinolaryngology and Head and Neck Surgery of KAHER's Jawaharlal Nehru Medical College and KLES Dr. Prabhakar Kore Hospital and Medical Research Center, Belagavi from 27th September 2023 to 26th October 2023, to examine the variations of neutrophil to lymphocyte ratio and potential association of serum uric acid levels in patients with peripheral vestibular disorders. A total of 51 patients who were confirmed cases of peripheral vestibular disorders that came to the department of otorhinolaryngology were included in the study.

**Results:** Neutrophil lymphocyte ratio and serum uric acid levels were shown to be associated with peripheral vestibular disorders in our investigation. 41.18% of the students in the study were male, while 58.82% of the students were female. In terms of numbers, it was discovered that the mean age of females (50.97) exceeded the

mean age of males (48.43). The DHI score indicated a severe impairment in 58.82% of the study subjects, who had an average serum uric acid level of 9.51. 39.22% of study participants had a mean blood uric acid level of 8.42, indicating a moderate impairment. There was a highly significant difference in the means of serum uric acid between the moderate and severe handicap groups.

**Conclusion:** Based on our results, we have concluded that hyperuricemia plays a major role in the development of peripheral vestibular diseases. With the majority of patients exhibiting mild to moderate stress levels and moderate to severe handicap on the DHI, it was determined that the neutrophil to lymphocyte ratio was a significant parameter in assessing the inflammatory status of peripheral vertigo patients. This finding led to the conclusion that peripheral vertigo may be a consequence of anxiety-induced release of stress hormones and inflammatory markers.

**Conclusion Key Words:** neutrohil lymphocyte ratio, NLR, Benign Paroxysmal Positional Vertigo, BPPV, serum uric acid

# TABLE OF CONTENTS

# LIST OF TABLES

# LIST OF GRAPHS

# LIST OF FIGURES

# INTRODUCTION

An illusion of movement- 'Vertigo', pertains to dysfunctions in semicircular canals or their central nervous system (CNS) connections.[1] Vertigo can be 'rotational' or 'true vertigo' wherein rotational vertigo equates to vestibular vertigo. Vestibular vertigo in itself can be with 'illusion of motion of objects or self - known as rotational vertigo; changes of position of head instigating dizziness or vertigo i.e. positional vertigo, or recurrent dizziness or imbalance with nausea and oscillopsia.[1]

While 7.4% was the all time prevalence of vertigo among 18-79 years of age, 4.9% was the one year prevalence and 1.4% the incidence over one year.[1] Dysfunctioning vestibular system, semicircular canals, and vestibular nerves together work in the advent of peripheral vestibular vertigo.[2] Its occurence can be attributed to varying causes ranging from the dislodgement of otoconia, development of endolymphatic hydrops, viral infection of inner ear, trauma to the oval and round window or bony labyrinth.[2]

About 80% of vertigo is peripheral, of which the most common is benign paroxysmal positional vertigo followed by less common causes like Ménière's disease, vestibular neuritis, labyrinthitis, acoustic neuroma, herpes zoster, perilymphatic fistula, viral infections, aminoglycoside toxicity.[3] Nausea, vomiting, dizziness, nystagmus and unsteadiness are collective presenting features of vertigo.[2]

While vertigo presents with varying presenting features it also acts as a catalyst for stress and anxiety, thereby, causing release of elevated levels of stress hormones. This provokes various symptoms, probably through autonomic nervous system disorders, aggravated by elevated stress-hormone levels and inflammatory

markers. The three most often utilized indicators of inflammation are C-reactive protein (CRP), ESR, and white blood cell (WBC) count. The neutrophil-to-lymphocyte ratio, or NLR, is a quick and easy way to gauge a subject's level of inflammation.[4]

The otolith organs of the inner ear, which include the utricle and saccule situated along the elliptical recess and spherical recess respectively; play key roles in vestibular mechanism. They act as gravity receptor organs which sense gravitational acceleration and linear acceleration of the head and drive the translational vestibulo-ocular reflex. Specialized epithelia called macula are contained in the bilateral utricles and saccules. The macula encompasses an array of hair cells and their stereocilia project into the otolithic membrane. The otolithic membrane also known as statoconial membrane encompasses an otoconial layer, a gelatinous layer, -with a mean thickness of 50micrometers, and contain calcium carbonate crystals(otoconia). This membrane is rich in mucopolysaccharides-also known as glycosaminoglycans which serves as a supportive structure. The travel of these $CaCO_3$ crystals into lumen of the semi-circular canals, premeditated by any degeneration of the macula, is what precipitates benign paroxysmal positional vertigo.

These crystals dissolve in endolymph of utricle on being permitted to return there by a series of re-positioning maneuver. One of the many bodily fluids referred to as extracellular fluids that are not found inside of cells is the endolymphatic fluid. A person's body is composed of these fluids to an extent of around 25%. The body solely contains water as a solvent, hence all bodily fluids are aqueous solutions. The labyrinthine artery, which splits off from the basilar artery and becomes the anterior vestibular artery and posterior vestibular artery, connects the endolymphatic fluids to

the arterial blood supply. The superior, horizontal, and utricle canals are fed by the anterior branch. The cochlea, saccule, and posterior canal are fed by the posterior branch.[5]

Despite being insoluble in water, calcium carbonate (CaCO3) dissolves readily in water containing carbon dioxide because it is converted to calcium hydrogen carbonate or calcium bicarbonate.[5]

The two main waste products of tissue cell metabolism are carbon dioxide and hydrogen ions (H+), which help release oxygen from hemoglobin and give the cells the oxygen they require. Hemoglobin and about 25% of the total carbon dioxide the cells make mix to form carbamino hemoglobin, which is transported to the lungs and released in return for oxygen. The enzyme carbonic anhydrase in red blood cells converts about 70% of carbon dioxide to carbonic acid. A significant amount of this carbonic acid is returned to the lungs, where carbonic anhydrase transforms it into carbon dioxide and releases it. The remaining carbonic acid contributes to one of physiology's most significant inorganic buffers, which keeps the pH of human blood at 7.4.[5]

Similar to the intramembranous ossification of the skull, which is the structure of calcium salts in the preformed fibrous matrix, saccules and utricles contain a pattern of embedded otoliths in the fibrous mesh (otoconial membrane). Phosphate of calcium makes up our bones. However, unlike calcium phosphate, otoliths are made of calcium carbonate and have a weaker ionic interaction. As a result, when otoliths are subjected to inflammation, infection, or low pH, they can readily slip off the otoconial membrane and produce BPPV. Strong muscular activity was maintained by aerobic respiration in later vertebrates, but infrequent oxygen shortages caused lactate

from anaerobic respiration to build up and lowered pH, raising the possibility of melting calcium carbonate bones. Since calcium phosphate has a stronger ionic bond than calcium carbonate, all vertebrates have converted from calcium carbonate to boost bone strength. Otoliths, or ear stones without muscle connection, do, on rare occasions, nevertheless use calcium carbonate. While the organic components of otoliths vary between species, the minerals that make up their organs for measuring linear acceleration and gravity are comparable. Otoliths are 95% calcium carbonate crystals that vary in size by 6 micrometers and take the forms of cylinders, barrels, and aragonite. Otoliths begin to grow at either day 4 or 6 of embryonic development. By day 7 of postnatal development, they are fixed to fibrous mesh (otoconial membrane) and cease to regenerate. Low pH can have an impact on otoliths, just as calcium carbonate limestones easily disintegrate in acidic rainfall. Compared to calcium phosphate, calcium carbonate has a weaker ionic bonding. Put another way, it melts easily in low pH environments. Otoliths in the utricle are more likely to melt if the pH drops because the endolymph fluid has an acidity of 7.38 pH in the saccule and 7.87 pH in the utricle.[6]

Sometimes metabolic acidosis in the blood and low pH in the endolymphatic fluids are caused by diabetes mellitus or hyperuricemia, which will speed up the disintegration of calcium carbonate otoliths. Because the chemoreceptor's sensitivity to carbon dioxide is slightly reduced while we sleep, the blood typically experiences minor respiratory acidosis at night. Even though they are not as severe as metabolic acidosis, low pH and mild respiratory acidosis during sleep can lead to the active remodeling of inner ear otoliths, which can lead to the development of faulty otoliths. After being readily broken down and rolled into the semicircular canals, these faulty otoliths give rise to vertigo in the morning.

Peripheral vestibular disorders account for the majority of cases of vertigo; these include benign paroxysmal positional vertigo (BPPV), Meniere's disease (MD), migrainous vertigo (MV), and vestibular neuronitis (VN). Vertigo and dizziness symptoms can have a significant impact on daily activities and quality of life. Many people with vestibular vertigo get subsequent psychological illnesses over the course of their illness.[7] The etiopathogenesis of depression may involve increased production of the primary proinflammatory cytokines, including interleukin-1 (IL-1), interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-alpha), and acute phase reactants, according to reports. Furthermore, depression and stress can lead to a decrease in lymphocytes and an increase in neutrophils and leukocytes.[8]

Increased IL-1 stimulates T-cells and monocytes, which results in the generation of IFN-gamma. This is favorably correlated with increases in the total leukocyte count. Furthermore, elevated leukocyte-neutrophil ratios and acute phase proteins appear to be substantially correlated with elevated IL-6 releases from activated monocytes in depressed patients. Uric acid crystal deposition during acute arthritis attacks has been shown to activate neutrophils, synovial cells, macrophages, and IL-8 to produce a variety of inflammatory chemokines and cytokines, such as TNF-α, IL-8, IL-1β, IL-6, and monocyte chemotactic factor, for the induction of acute joint inflammation.[9]

Hence, in our study we have analysed the association of neutrophil to lymphocyte ratio in subjects with vertigo which was peripheral.

The xanthine oxidase enzyme catalyzes the formation of uric acid, which is a biomarker for peripheral vertigo that is derived from xanthine molecules. By adhering to a loose interotoconial filament matrix and the gelatinous matrix with surface

adhesion, otoconia are bonded and joined. Elevated levels of uric acid create an inflammatory reaction in this matrix through an immunopathological mechanism that is triggered, akin to what happens in gout joints. This leads to progressive harm commensurate with exposure to elevated uric acid levels over the course of an adult's life.[10]

Increased blood uric acid levels can create reactive oxygen species (ROS), which can harm blood vessels and obstruct the inner ear's blood supply. For this reason, peripheral vertigo associated with vestibular neuritis, BBPV, and Meniere's disease may result from blockage of the vertebrobasilar artery, which provides blood to the inner ear.[11]

Gout and concomitant conditions like BPPV and Meniere's disease are associated by a number of pathophysiological pathways. One theory suggests that BPPV in gout patients may be brought on by the accumulation of purine crystal deposits from floating otoconial debris in the semicircular canals.[11] Moreover, increased blood uric acid levels have been related to otoconia by inducing inflammation of the gelatinous matrix. Furthermore, increased uric acid levels trigger the production of damaging reactive oxygen species (ROS) through the release of inflammatory mediators. ROS generation has the potential to harm blood vessels and disrupt blood flow. Consequently, a comprehensive analysis of the correlation between gout and cardiovascular disease has been conducted, and additional data has demonstrated that gout increases the risk of various vascular disorders. Thus, peripheral vertigo may result from blockage of the vertebrobasilar arteries supplying the inner ear, and this theory may help to explain the correlation between gout and peripheral vertigo (e.g., BPPV and Meniere's disease). Histopathological temporal

bone studies have demonstrated that aberrant endolymph balance in Meniere's illness may be caused by circulatory abnormalities. The cochlear lateral wall, which includes the capillary network, is squeezed against the bone labyrinth due to an increased amount of endolymphatic fluid. This increase in cochlear outflow resistance might result in ischemia reperfusion damage. Consequently, those who already have gout-related issues with their microvascular systems may be more susceptible to endolymphatic hydrops-related inner ear damage.[11]

Because of the uricosuric effects of estrogen, women often have lower amounts than men.[10] The function of estrogen in controlling the kidneys' increased excretion of uric acid via raising renal clearance. Furthermore, URAT1 (Urate Transporter 1), a uric acid transporter, decreases in the presence of estrogen, hence lowering the amount of uric acid that the kidneys reabsorb. It has been demonstrated that high estrogen levels in women of reproductive age support the kidneys' regular production of uric acid through urine.[10]

It is commonly recognized that the female sex hormone estrogen 17β-estradiol (E2) carries out a wide range of functions and plays a part in many diverse roles, including memory functions, bone metabolism, and the differentiation and function of reproductive organs. Clinically, BPPV-affected women had significantly lower levels of progesterone and E2.[12] By binding to nuclear hormone receptors like estrogen receptor(ER)α and β, estrogen affects target cells. As a result, one key factor influencing how estrogen signals to the cell is the ER level. As people age, there is a reduction in the expression of ERα and β. ERα and β were discovered to be usually co-expressed in the inner ear in a prior double-staining research. ERβ, however, is

predominant in inner ear strial marginal cells or type II spiral ganglion neurons. These results lend credence to estrogen's function in the inner ear.[12]

Hence, women in premenopausal and menopausal stages with decline in hormone estrogen levels and associated elevated serum uric acid levels have an increased preponderance to develop the most common peripheral vertigo - BPPV.

The three most often utilized indicators of inflammation are C-reactive protein (CRP), ESR, and white blood cell (WBC) count. The neutrophil-to-lymphocyte ratio (NLR) is an easy-to-use metric for determining a subject's level of inflammation. NLR has been suggested as a potential marker of inflammation in cardiac and non-cardiac illnesses as well as a dependable predictor of the host's inflammatory condition.[4] NLR is an easily measured, reproducible marker of inflammation. In patients with breast carcinoma, NLR was shown to have the potential to predict poor prognosis. NLR along with Monocyte-to- Lymphocyte ratio (MLR) has also been shown to have a clinical significance in diagnosing SLE thus paving way for importance of NLR in autoimmune diseases.[4] Hence neutrophil to lymphocyte ratio was taken as a parameter for assessing the inflammatory status of subjects in our study.

A very limited number of studies have been conducted, especially in India, correlating the association of uric acid levels in serum and NLR in subjects with peripheral vestibular disorders and most of the studies were conducted among BPPV patients. Therefore, in our study we will be studying the association of neutrophil lymphocyte ratio and serum uric acid level in subjects with Peripheral vestibular disorders.

# OBJECTIVE

To study the variations of neutrophil to lymphocyte ratio and potential association of serum uric acid level in patients with Peripheral vestibular disorders.

# REVIEW OF LITERATURE

Vertigo, affects approximately 15% to over 20% of adults each year. Vestibular vertigo accounts for approximately a quarter of these cases, with a 12-month prevalence of 5% and an annual incidence of 1.4%. Prevalence increases with age and is about two to three times that of men in women.[7]

A common cause of recurrent vertigo, characterized by perception of movement of the surrounding objects with attacks; is benign paroxysmal positional vertigo.[13]

The literature describes 3 lines of evidence on association of serum uric acid level and NLR with peripheral vestibular disorder patients : (1)The NLR levels were significantly higher in peripheral vestibular disorders and the values rise with increase in vertigo severity. (2) Women had a higher BPPV percentage than men related to hormonal factors in women. They tend to have lower uric acid levels than men because of the uricosuric effects of estrogen. Hence, women in premenopausal and menopausal stages with decline in hormone estrogen have elevated serum uric acid levels and serve as an independent risk factor.[10] (3) Serum uric acid levels were higher in patients with BPPV and independently associated with the same.

Abdul Azeez Vallur, in his study in 2017 studied the ESR, NLR, PLR, MHR and Bilirubin levels in BPPV patients for a period of 1 year. In this one year cross sectional study he found that pathogenesis of BPPV is connected to inflammation.[13]

In a study conducted by Abir Omara et al., a statistically significant positive correlation was noted between anxiety, depression scores, total Dizziness handicap

inventory scores and vestibular vertigo.[7] Hence, in our study patients presenting with peripheral vestibular disorders were evaluated for neutrophil lymphocyte ratio along with assessment of dizziness handicap inventory scoring.

In elderly patients , the BPPV incidence is significantly higher, but it occurs in any age. Venkata Kasyapi V et al., in their study in 2018 found a positive correlation with age and the median NLR was raised in patients with BPPV.[2]

The Dizziness handicap inventory consists of 25 items designed to assess the self-perceived level of handicap due to dizziness. The items are grouped into emotional (9 items), functional (9 items), and physical (7 items) domains. Each item has three response options (yes, sometimes, and no), which were 4, 2, and zero points, with a total score ranging from 0 to 100, with 0 indicating no perceived disability and 100 indicating the maximum perceived severity of dizziness.[7]

Abir Omara et al., in 2022 has reported a significant positive correlation between anxiety, depression scores and dizziness handicap inventory score among vertigo patients presenting the need for screening and treatment of co-morbid mental health disorders.[7]

Andi Kurnia Bintang et al., in their study in 2019 stated that a significant difference in NLR was found among the mild, moderate and severe DHI categories, where NLR values rise with vertigo severity[2]. Hence, in our study we also evaluate the dizziness handicap inventory scores in the study subjects to quantify their association.

A systematic review and meta-analysis of studies on association of uric acid and benign paroxysmal positional vertigo by Xinglong Yang et al., in 2018 on a total

of 12 studies revealed serum uric acid was significantly higher among patients with BPPV than among controls.[14] Furthermore, Adi Putra et al., in his case control study in 2020 among 36 BPPV patients and 36 non-BPPV patients concluded that there was a significant relationship between uric acid levels with BPPV.[10] Similarly, Hyo Geun Choi et al., in his study in 2022 has reported that BPPV and Meniere's disease are novel comorbidities associated with gout. Thus, controlling gout will also contribute to lowering the risk of comorbid diseases such as BPPV and Meniere's disease.[11]

**Historical background**

The present knowledge we have of vestibular disorders and its function dates back to the eminent work of a group scientists belonging to the nineteenth century, e.g., Jan Evangelista Purkinje, Ernst Mach, Josef Breuer, Hermann Helmholtz, and Alexander Crum-Brown. [15] The eminent work put forth by them was what revealed the methods of sensing motion, the basis for modern vestibular and ocular motor research.

The most knowledgeable and infuential contemporary physician in the study of labyrinthine malfunction would be the otolaryngologist Harold Schuknecht (1917–1992). He presented controversial hypothesis and experimental evidence to explain the three most common forms of labyrinthine vertigo: benign paroxysmal positioning vertigo (first described in 1921 by Bárány), vestibular neuritis (by Ruttin in 1909), and Menière's disease (by Menière in 1861).[15]

Initially described in the medical literature by Adler, positionally generated vertigo was thought to be caused by an issue with the otolith organs. The presence of rotatory nystagmus in a 27-year-old woman who felt giddiness on turning her head

while lying down to the right was noted by Barany; where in an upward vertical component was seen; which, on looking to the right was entirely rotatory and to the left was completely vertical.[16] The term BPPV was later formulated in 1952, by two British otologists Margaret Dix and Charles Hallpike .

In 1952 at Queen Square Hospital, Margaret Dix (1911–1981) and Charles Hallpike (1900–1979) used 100 patients to create a diagnostic and provoking positioning examination for "positional nystagmus of the benign sort." "The complaints of patient were characteristically of dizziness on lying down or turning over in bed, or lying down below car or in throwing the head backward to paint a ceiling," as stated in the letter that they provided as supporting documentation. As part of the diagnostic procedure, the subject is made to sit on a sofa, their head tilted to one side, eyes fixed on examiner's forehead. Examiner pushes the patient back in critical position [30 degree below couch level and between his hands, holding the patient's forehead firmly in place].[20]

The resultant reaction where in superior pole of eye was beating directed towards ground, was when Barany first noticed nystagmus which was a torsional and later "fatigued" on subsequent testing.

As the patient sits up, a reaction delay of around 5 seconds followed by a crescendo nystagmus and drop, and a nystagmus reversal was noted by Barany. They evaluated individuals on a device that avoided neck rotation to rule out the idea that the response could be caused by vascular blockage. An identical reaction took place. Hallpike was a leader in the field of temporal bone histology in Great Britain. The otolithic membrane was said to be absent from the utricle's macula. In their conclusion, they stated that the overall picture was one of persistent tissue changes

brought on by either trauma or infection. The author concluded that the side of the nystagmus coincides with the side of the lesion. Hallpike strengthened the case about this theory by removing symptoms in two individuals with a chemical labyrinthectomy of an acoustically dead ear and in one patient with an eighth nerve slice. According to Barany, Dix, and Hallpike, the utricular macula condition was discovered to be the primary source of benign positional nystagmus.

Although the inner ear's bony and some membranous structures were physically well documented, till the 19th century their functions were unknown. The semicircular canals were held responsible for bone conduction of sound transmission and perception of sound directions, while the cochlea was thought to enunciate the pitch and type of sound, the saccule and utricle for loudness perception, and the cochlea itself to perceive loudness.[22]

Meniere was a French physician, who in January 1861, presented a paper where he described a subject who had presented with episodes of vertigo, tinnitus, and hearing loss with no evidence of cerebral disease. Thereby, this questioned the cerebral congestion theory as well as the treatments that were based on this theory.[21]

The criteria for Meniere's disease has undergone an evolution which started with the American Academy of Ophthalmology and Otolaryngology Committee on Hearing and Equilibrium presenting a proposal in 1972 of three categories of Meniere's disease stated as: 1) Classic Meniere's- which translated to vertigo with unilateral tinnitus and hearing loss, 2) Vestibular Meniere's: which meant vertigo without auditory symptoms, and 3) Cochlear Meniere's: which present with progressive but fluctuating hearing loss, aural fullness and tinnitus without vertigo.[21]

The International Bárány Society and the American Academy of Otolaryngology-Head and Neck Surgery in 2015, modified the Meniere's disease criteria to include only "Definite," and "Probable," categories; both of which can be translated as requiring at least two episodes of vertigo, tinnitus, or aural fullness, but with documented hearing loss required in only "Definite" Meniere's.[21]

**ANATOMY**

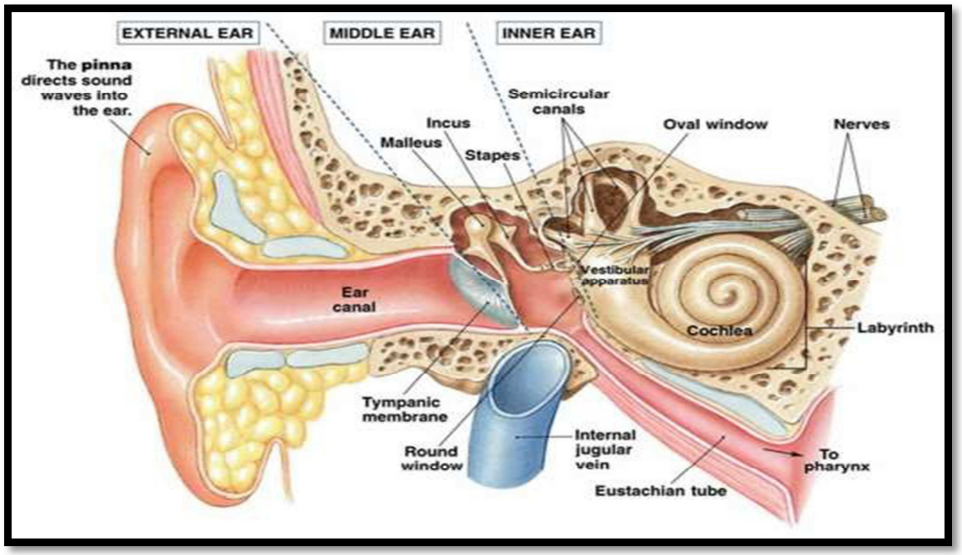



**Figure 1 : Compartments of the ear**

**The Inner Ear:**

The ear comprises of outer ear, inner ear and the middle ear. Of these the inner ear plays a crucial role in both hearing and balance.

Situated between the internal acoustic meatus lying medially and the middle ear lying laterally; the inner ear is a complex structure and a part of petrous part of temporal bone. It comprises the vestibulocochlear organs which pertains to — the cochlea, which is responsible for hearing and; the vestibular system, which is responsible for balance and spatial orientation.

The inner ear or the labyrinth consists of a membranous labyrinth and a bony labyrinth.

**Membranous labyrinth:**

The membranous labyrinth develops from Neuro-ectoderm or the optic placode, which then develops into the optic pit and then otic vesicle. The otic vesicle finally forms the membranous labyrinth. It is filled with endolymph and lies within the bony labyrinth. When fully developed, the membranous labyrinth has the cochlear duct, semicircular ducts, utricle, and saccule as its parts.

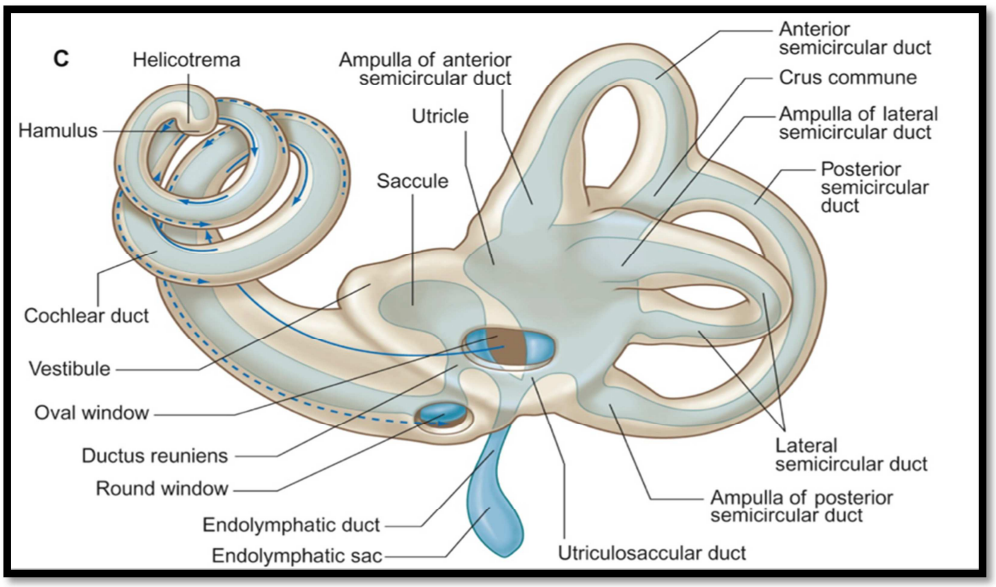



**Figure 2 : The labyrinth**

**Bony labyrinth:**

It is structured by three parts — the cochlea, the vestibule and the three semicircular canals. Perilymph is a fluid present within these structures.

Vestibule: It communicates anteriorly to the cochlea and posterior lay with the semicircular canals. It is the bony labyrinth around the utricle, the saccule.

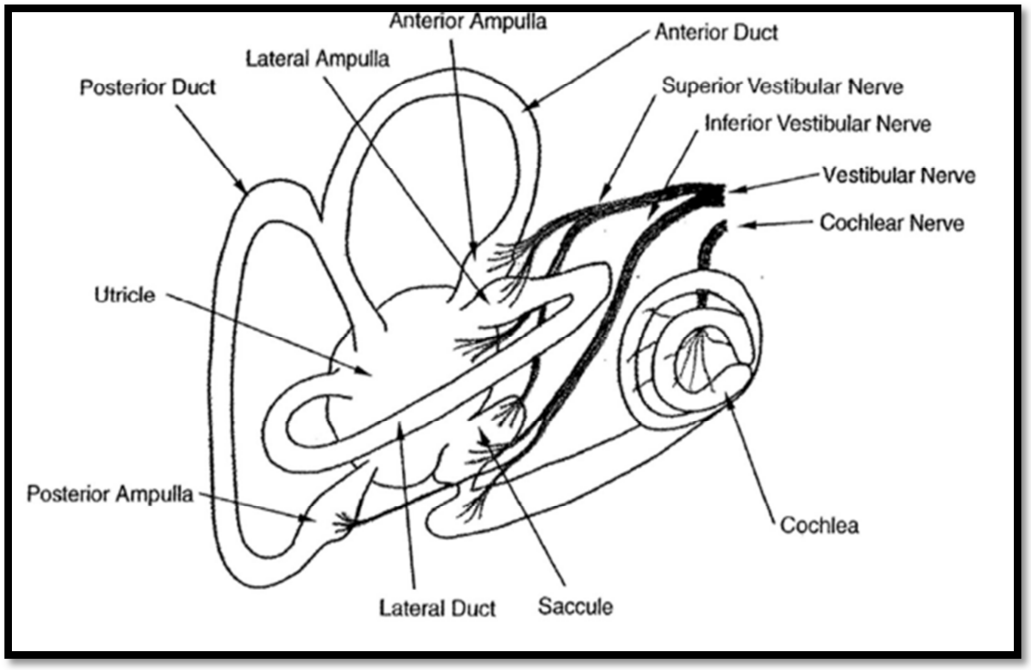



**Figure 3 : Nerve Innervation of the labyrinth**

**NERVE SUPPLY**

Each of the otolith organs and SCC are innervated by the vestibular nerve. These nerves are divided into an inferior and a superior vestibular nerve before they reach the Scarpa ganglion. The superior branch receives signals from the utricle, the LSCC, and the ASCC. Through the inferior vestibular nerve, signals are sent from the saccule and PSCC. This nerve, emerges from the porus acusticus internus porus which is the opening of the internal acoustic canal, forms the vestibulo-cochlear nerve, by joining the cochlear nerve. This is also known as the 8th cranial nerve.

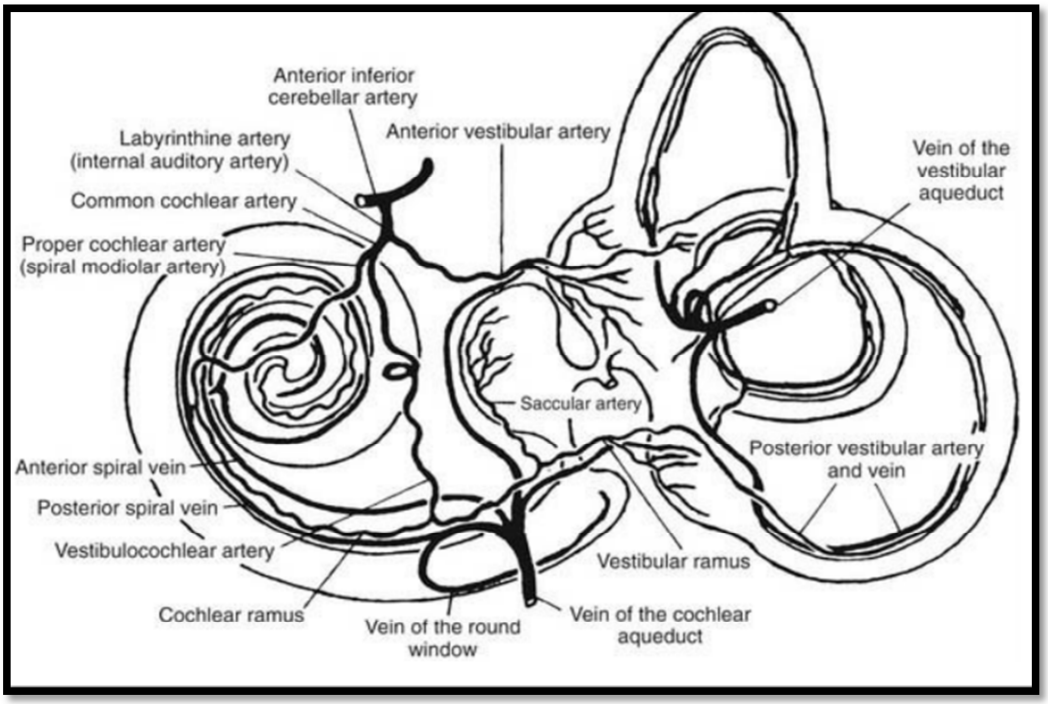



**Figure 4: Blood supply to labyrinth**

## BLOOD SUPPLY

The neuronal innervation is closely followed by the blood supply. Thus, the cochlear or the vestibular nerve may occasionally be affected by vascular lesions. The internal auditory artery supplies blood to the labyrinth. The IAA rises from the anterior AICA. On occasion, the basilar artery may directly branch into the internal auditory artery.

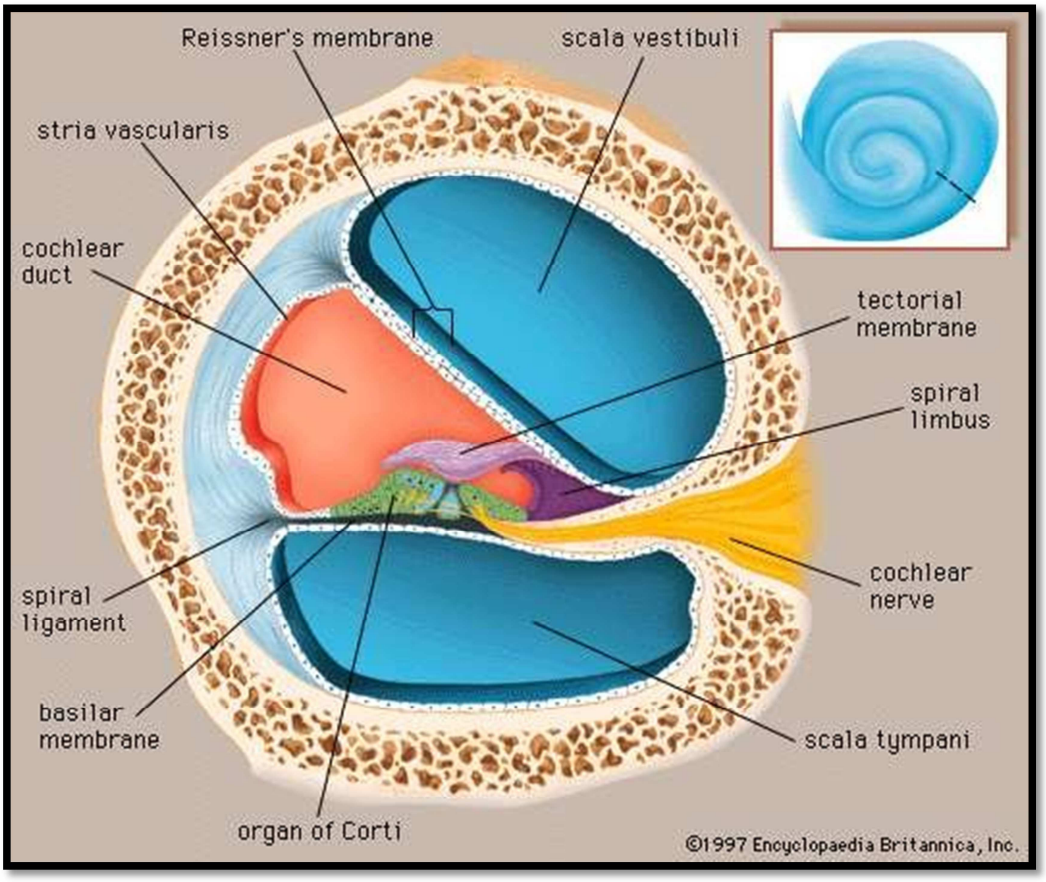



**Figure 5: The Cochlea**

**Cochlea.**: Cochlear duct, which is a component of the auditory portion of the membranous labyrinth, is housed within the cochlea. It forms a cone-shaped structure that points anterolaterally as it spirals around the modiolus, the middle section of the bone. Cochlear part of vestibulocochlear nerve gives its branches at base of modiolus.

A bone ledge called the spiral lamina, which extends from the modiolus and connects to the cochlear duct, holds it in place. Two perilymph-filled chambers are created above and below the cochlear duct:

**Scala vestibuli**: The location of it is above cochlear duct. It continues into vestibule.

**Semi-circular Canals**

There are anterior, lateral, and posterior semi-circular canals. They house the semi- circular ducts, which are in charge of maintaining equilibrium (along with the utricle and saccule).

In a superoposterior position to the vestibule, the canals are positioned at an angle to one another. They have an ampulla, or swelling, at one end.

The primary signal for the head's movement sensing is the moving endolymph in the SCCs.Transient rotations predominate in natural movements, such as head movements back and forth (such as nodding) or walking and sprinting. These movements are catered for by the SCC system.

The sensory epithelium is activated by head accelerations, but the signal that is sent to the brain is proportionate to head velocity. While head velocity is restricted to several hundred degrees per second, head accelerations can reach up to several thousand degrees per second square. Sustained velocity is no longer detected nor perceived after approximately 30 seconds. 3 forces act on endolymph & cupula in canal as it is rotated about an axis:

- Inertial force, proportional to the mass of the endolymph and cupula.
- Elastic restoring force of the cupula that positions the cupula back to the centre position after stimulation
- Fluid's resistance to sliding past the tube's internal wall due to viscous forces.

This viscous force is influenced by how quickly the endolymph moves relative to the wall.

**Cochlear Duct**

Within cochlea's bony framework is where the cochlear duct is situated. The spiral lamina keeps it in place. The duct's presence results in making of the scala vestibuli and scala tympani, two canals that run above and below the duct. It can be described as triangular in shape:

**Lateral wall** – called spiral ligament-thickened periosteum

**Roof** – which is formed by Reissner's membrane- separates the cochlear duct from the scala vestibuli.

**Floor** – formed by basilar membrane-separates cochlear duct & scala tympani. Organ of Corti present here .

**Saccule and Utricle**

The vestibule contains two membrane sacs called the saccule and utricle. They are balancing organs that are able to recognise when the head moves or accelerates in the vertical and horizontal planes, respectively.

The three semicircular ducts enter the utricle, which is the bigger of the two. The cochlear duct enters the globular-shaped saccule.

The utricle and saccule release endolymph into the endolymphatic channel. To reach the back of the petrous portion of temporal bone, the duct goes via the vestibular aqueduct. Here, duct widens into a sac that allows for the secretion and absorption of endolymph.

**Semi-circular Ducts**

The semicircular canals contain the semicircular ducts, which are oriented similarly. The endolymph flow within the ducts alters speed and/or direction in response to head movement. Sensory receptors in the semicircular canals' ampullae notice this change and communicate with the brain in order to process balance.

**FUNCTION:** The inner ear gathers, organises, and transmits sensory data pertaining to hearing through cochlea & balance through the vestibular system. It is in charge of mechanoelectrical transduction, which is the translation of movements—started by sound waves in the cochlea or by changes in the location of the head in space—into electrical signals that can then be transmitted to the brain via the auditory or vestibular nerves. It is formed by the series of bony channels that enclose interconnected fluid-filled tubes (the membranous labyrinth), the inner walls of which are lined by epithelial tissues. The bony channels are filled with perilymph, which surrounds the membranous canals. Perilymph is essentially a typical extracellular fluid which is similar, but not identical, to cerebrospinal fluid or serum; it has a higher Na+ and lower K+ concentration. The perilymphatic compartment joins the arachnoid space of the brain via the cochlear aqueduct so there is potential continuity between cochlear perilymph and CSF, although the exact compositions of the two fluids are different from each other and also from serum, indicating that perilymph is produced or at least significantly modified locally in the inner ear and is not derived directly from CSF (or serum). The fluid in the membranous canals - endolymph. It is higher in K+ (~140mM) and lower in Na+ (~1mM). Electric potential of endolymph is +80mV, the endocochlear potential (EP), but although the compartments are interconnected a similar electrical potential is not observed in the

vestibular system. The connections between the epithelial cells that enclose the endolymphatic regions mark the boundary between perilymph and endolymph. The preservation of this permeability barrier, which is formed by these junctions, is crucial for the inner ear's proper operation.

**THE VESTIBULAR SYSTEM**

The vestibular system comprises of the utricle and the three semicircular canals that begin and end in the utricle at orthogonal planes - (i)horizontal(lateral) SCC (ii)posterior SCC (iii)superior SCC. They form chambers anatomically distinct and via the utriculosaccular duct lead into the saccule. Majority of cases of BPPV shows involvement of the posterior semicircular canal.

**THE VESTIBULAR SYSTEM'S ROLE:** The vestibular system's primary job is to create info for the CNS, serving 4 purposes:

1. To guarantee eye stabilisation

2. To allow for balanced movement and posture.

3. To give the body an overall direction with respect to gravity.

4. To refocus the body after autonomic functions have been adjusted.

The optical, vestibular, and proprioceptive systems, as well as other signalslike hearing, even if they are of lesser importance, all provide information to the brain. The unique outcomes that result from the brain's core processing of all of this information are as follows:

- The vestibulo-ocular reflex (VOR) for gaze stability.
- The vestibulospinal reflex (VSR) and vestibulocollic reflex (VCR) maintain the body in an upright position and stabilize the trunk and head in space.
- Adjustments to autonomic function follow changes in body orientation.

Since the Vestibular system is proven that it affects circadian rhythm and related to cognitive performance, this list of outcomes is by no means limited to these four tasks.

It is evident that balance cannot rely just on eyesight when walking in the dark and must instead rely on somatosensory & vestibular senses. All systems are required for daily operations to run smoothly, and there is limited system redundancy.

## THE MICROSTRUCTURE OF THE VESTIBULAR SYSTEM

**Mechanosensitive hair cells** lend a major hand to **the maculae and crests** in the detection of head orientation with respect to gravity and changes in head movement.

These hair cells are in synaptic contact with afferent and efferent endings of the vestibular nerve on their basolateral aspect. There are two types of sensory hair cell in the vestibular system, type I and type II.

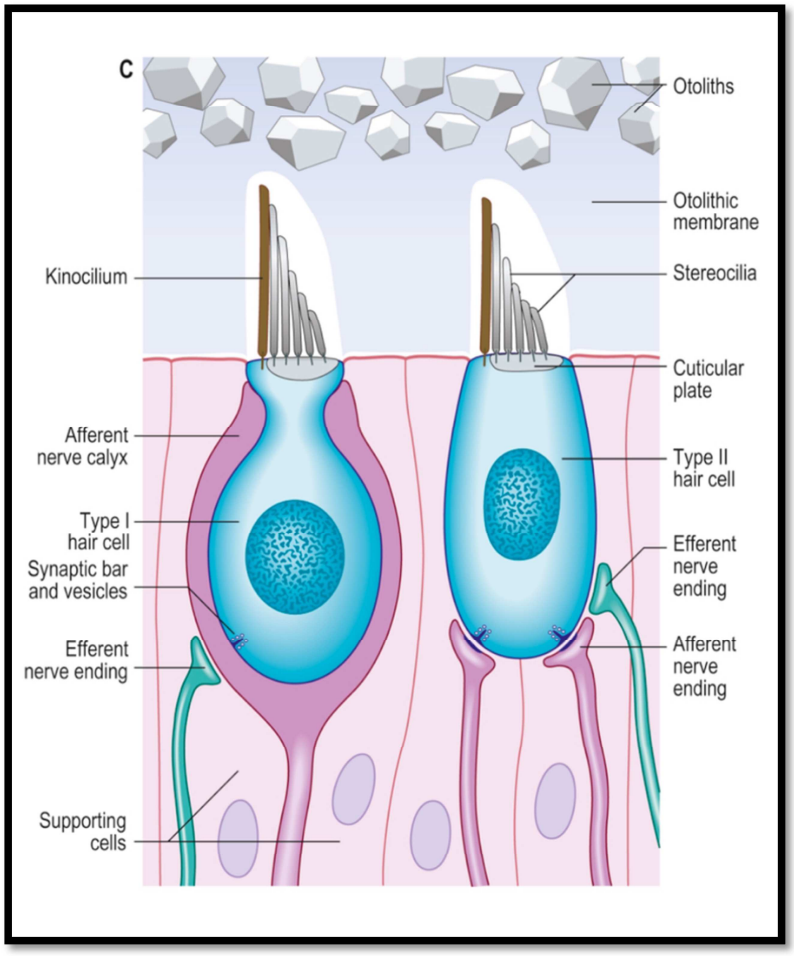



**Figure no 6: type I and II hair cell**

Type I vestibular sensory cells measure 25 μm in length, with a free surface of 6–7 μm in diameter. The basal part of the cell does not reach the basal lamina of the epithelium. Each cell is typically bottle-shaped, with a narrow neck and a rather broad, rounded basal portion containing the nucleus. The apical surface is characterized by 30–50 stereocilia (large, regularly arranged, modified microvilli about 0.25 μm across) and a single kinocilium (with the typical '9+2' arrangement of microtubules characteristic of true cilia). The kinocilium is considerably longer than the stereocilia, and may attain 40 μm, whereas the stereocilia are of graded lengths. The stereocilia and kinocilium are all interconnected by fine extracellular

filaments of various types, called cross links. One in particular, the tip link, connects the shorter stereocilia in each row with adjacent stereocilia in the taller row next to it. The tip link is common to all types of hair cell and is thought to play a central role in transduction.

Deflection of the bundle towards the kinocilium results in depolarization of the hair cell and increases the rate of neurotransmitter release from its base. Deflection away from the kinocilium hyperpolarizes the hair cell and reduces the release of neurotransmitter.

Type II sensory cells- Some are up to 45 μm long and almost span the entire thickness of the sensory epithelium, whereas others are shorter than type I cells. They are mostly cylindrical, but otherwise resemble type I cells in their contents and the presence of an apical kinocilium and stereocilia. However, their kinocilia and stereocilia tend to be shorter and less variable in length.

The otolithic membrane is a layer of extracellular material divided into two strata. The external layer is composed of otoliths or otoconia, which are barrel-shaped crystals of calcium carbonate with angular ends, up to 30 μm long, and heterogeneous in distribution. They are attached to a more basal gelatinous layer into which the stereocilia and kinocilia of the sensory cells are inserted. The gelatinous material consists largely of glycosaminoglycans associated with fibrous protein.[20]

**SEMICIRCULAR DUCTS:**

Medially the anterior and posterior ducts fuse to form the crus commune before ending at the utricle. The lateral end of each canal is dilated to form an ampulla, and crus ampullae is the duct segment between the ampullae and utricle.

The ampullary crest:

Each ampulla has septum transversum- a transverse elevation, on the centre of which is the ampullary crest. The ampullary crest is a saddle-shaped sensory ridge containing hair cells and supporting cells.

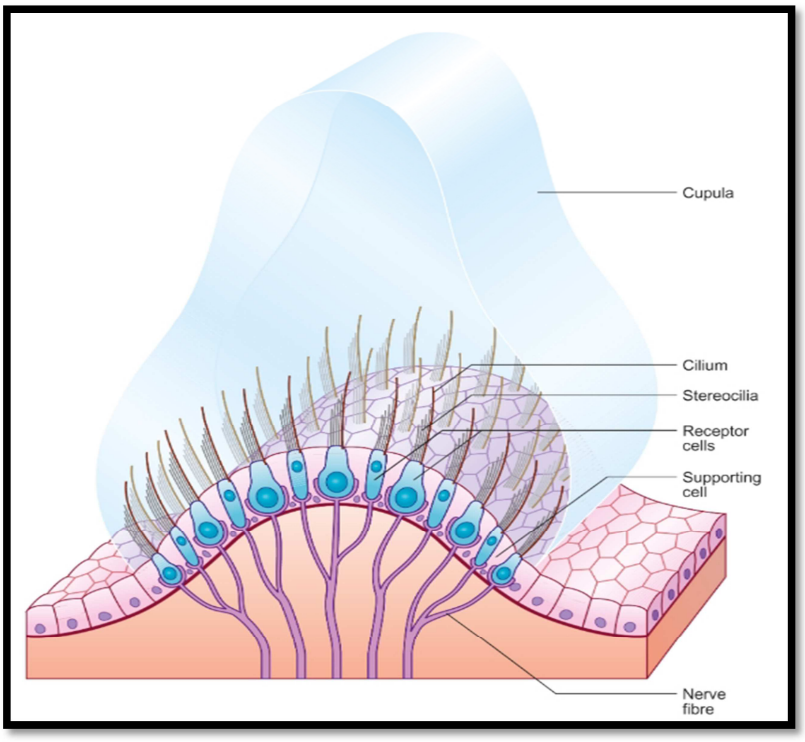



**Figure no 7 - The Ampullary crest**

**The cupula:**

The cupula is a vertical plate of gelatinous extracellular material attached along the free edge of the ampullary crest. It is readily deflected by endolymphatic flow derived from head rotations within the duct which is the source of stimuli delivered to the sensory hair cells. Thus during movements of the head in different planes of three dimensional space, angular accelerations are detected in the canals of the three semicircular ducts.

**UTRICLAR MACULA AND SACCULAR MACULA**

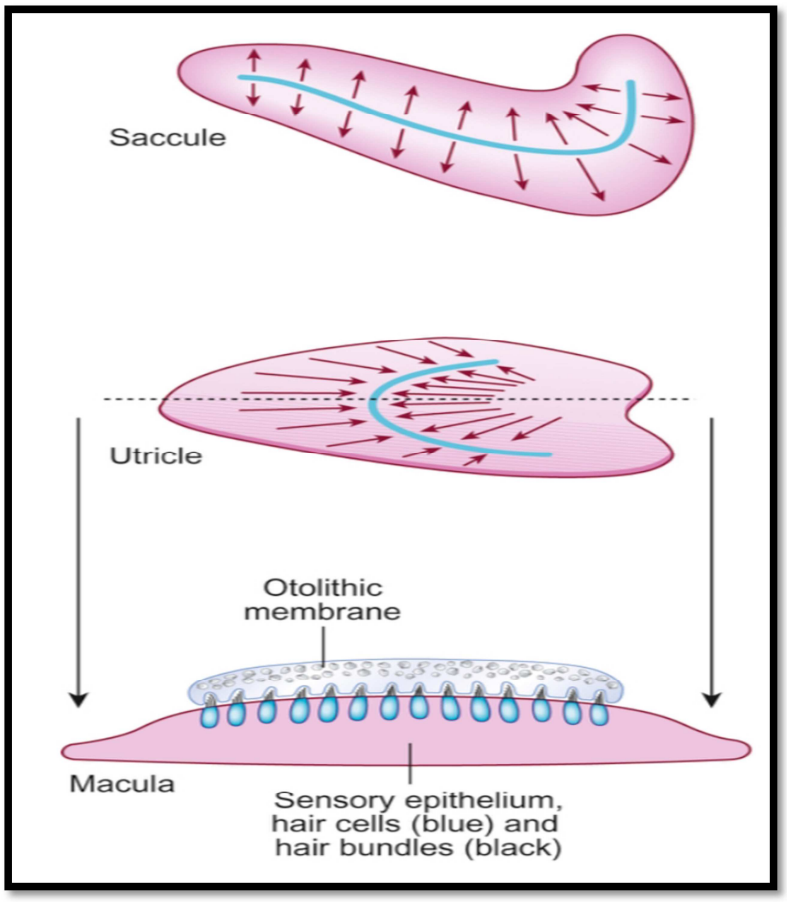



**Figure no.8: The utricle and saccule**

- UTRICLE - is an oblong, dilated sac that occupies the posterosuperior region of the vestibule.
- Utricular macula :

The **utriculus or macula of the utricle** is a specialized neurosensory epithelium lining the membranous wall and is the largest of the vestibular sensory areas.

It lies horizontally with its long axis anteroposteriorly oriented and its sharp angle pointing posteriorly (figure no.3). It is flat except at the anterior edge, where it is gently folded in on itself, and measures 2.8 mm in length and 2.2 mm in width.

The **<u>otolithic membrane or statoconial membrane</u>** is a gelatinous structure in which many small crystals-the otoconia (otoliths, statoliths) are embedded.

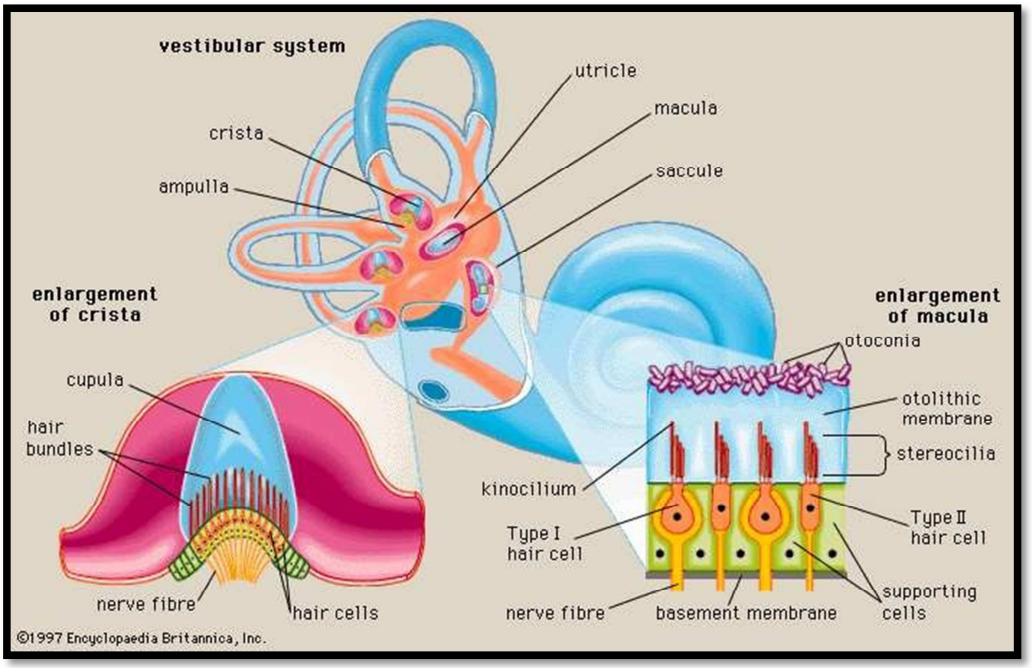



**Figure no 9 : Otoconial Membranes and Cupula**

'**<u>Snowdrift line'</u>** is a curved ridge running along the length of the otolithic membrane. It corresponds to an underlying sensory epithelium- **the striola** measuring 0.13 mm in width.

With respect to the midline of the striola the sensory cells are functionally and anatomically polarized.

**<u>Pars interna</u>** is the part of the macula medial to the striola and slightly larger than its latter the **<u>pars externa</u>** which is lateral to the macula.

In normal head position the macula in each utricle is almost horizontal.

In the horizontal plane linear acceleration of the head results in the otolithic membrane lagging behind the movement of the membranous labyrinth due to inertia produced by its mass.

Thus the membrane stimulates one group of hair cells by, deflecting their bundles towards the striola. All the while inhibiting other group of hair cells by deflecting their bundles away from the striola.

Thereby each horizontal movement of the head produces a specified pattern of firing in the utricular afferent nerve fibres.

- SACCULE - It is a globular, elongated sac located at the spherical recess near the scala vestibuli opening of cochlea.

The saccular macula has an elliptical structure, measuring 2.6 mm in length and 1.2 mm in its width. While the utricular macula lies in a horizontal plane, the saccular macula lies in a vertical plane on the wall of the saccule with its long axis orientated anteroposteriorly.

Similar to the utricular macula, the macula of the saccule is covered by an otolithic (statoconial) membrane. It has an S-shaped strip along its long axis- the striola - which is similar to that in the utricle; measuring 0.13 mm in width, along which the sensory cells are functionally and anatomically polarized.

With regard to its vertical orientation, the saccule is in particular sensitive to linear acceleration of the head in the vertical plane. Thus it acts as a gravitational sensor when the head is positioned upright. Furthermore, It is also sensitive to movement along the anteroposterior axis.

**Motion decomposition & orientation in head:**

Each movement in space is examined using 3 translational & 3 rotational degrees of freedom (yaw, pitch, and roll) (left–right, up– down, fore–aft). Anatomy of motion sensors in the peripheral vestibular system of the inner ear reflects these 6 degrees of freedom. Maculae detect primarily translation, whereas SCCs assess predominantly rotations. At first, one can assume the left & right canal as parallel systems, i.e. right anterior (RA) is parallel to left posterior (LP) and both lie in RALP plane.

The LARP plane is made up of LA and RP canal. Additionally both horizontal canals are parallel in lateral plane. The upright head's horizontal axis and horizontal SCC are around 30° angle to each other w.r.t sagittal plane of skull, vertical canal angle is roughly 45°.

**Movement detection:**

The vestibular system uses fundamental physical principles to sense movement or orientation. According to Newton's first law, "moving objects will continue to move until acted upon by a force." The direction or speed of the object may alter as a result of this force. According to the second law, an F(force) = m(mass) * a(acceleration).

Head and body are constantly moving throughout daily life (the head and body are even somewhat shaken during each pulse), & these movements are influenced by force or acceleration. The vestibular organ detects these movements thanks to a strict connection of the sensory epithelium to the bone structure. As a result, a system filled with fluid is fastened to the skull, and inertial forces cause the

fluid to move. Any movement of the head causes the fluid to travel more slowly & this displacement serves as signal for movement detection. Canal system is constructed so that the deflection of the hair cells is proportionate to the head velocity in order to reduce the movement of these cells caused by the accelerations that propel the head movements.

**Endolymphatic duct and sac**

The endolymphatic duct runs in the osseous vestibular aqueduct and becomes dilated distally to form the endolymphatic sac. This is a structure of variable size, which may extend through an aperture on the posterior surface of the petrous bone to end between the two layers of the dura on the posterior surface of the petrous temporal bone near the sigmoid sinus. Endolymph produced elsewhere in the labyrinth is absorbed in this region, probably mainly by the light cells. Damage to the sac, or blockage of its connection to the rest of the labyrinth, causes endolymph to accumulate; this produces hydrops, which affects both vestibular and cochlear function.[20]

**Mechanotransduction in hair cells**

Mechanotransduction is central to both hearing and balance and is a phenomenon that is shared by all the sensory hair cells of vestibular and auditory epithelia. The basic mechanism is the same in all of the different types of hair cell and is dependent on common features of the hair bundle: specifically, the 'staircase' array of stereocilia and the tip links connecting the tips of shorter and adjacent taller stereocilia. Deflections of the bundle in an excitatory (depolarizing) direction cause tension in the tip link, which acts to open non-specific cationic mechanoelectrical

transduction channels. Influx of potassium and calcium ions through these channels, depolarizes the cell and leads to calcium influx through basolateral voltage-gated calcium channels, which causes release of neurotransmitter. The hair cells also have basolateral potassium channels that allow efflux of potassium into perilymph.

The sensitivity of mechanotransduction is greatly increased by the combination of the hair-cell membrane potential (−70 mV) and the endolymphatic potential (+80 mV), producing an overall driving potential of up to 150 mV. It is therefore vital to maintain a high potassium concentration, despite its depletion from endolymph during detection of acoustic or balance stimuli.[20]

**COMMON PERIPHERAL CAUSES OF VERTIGO:[21]**

- Benign paroxysmal positional vertigo
- Meniere disease
- Third window syndrome
- Cochlea-facial nerve dehiscence
- Perilymph fistula
- Superior canal dehiscence
- Trauma
- Vestibular neuritis
- Drug induced toxicity- minocycline, phenytoin, quinidine, gentamicin, streptomycin
- other causes- bacterial labyrinthitis, otosclerosis, tumors

**Table 1:Physiologic Properties and Clinical Features of the Components of the Peripheral Vestibular System[22]**

| Localization | Component(s) | Triggered Eye Movements | Common Clinical Conditions | Localizing Features |
|---|---|---|---|---|
| Semicircular Canals | | | | |
| Posterior canal | PC | Vertical, torsional | BPPV-PC | Nystagmus |
| Anterior canal | AC | Vertical, torsional | BPPV-AC, SCD | Nystagmus, fistula test |
| Horizontal canal | HC | Horizontal ≫ torsional | BPPV-HC, fistula | Nystagmus |
| Vestibular Nerve | | | | |
| Superior division | AC, HC, utricle | Horizontal > torsional | VN, ischemia | Nystagmus, head-thrust test |
| Inferior division | PC, saccule | Vertical, torsional | VN, ischemia | Nystagmus |
| Common trunk (cranial nerve 8) | AC, HC, PC, utricle, saccule | Horizontal > torsional | VN, VP, ischemia | Nystagmus, head-thrust test, auditory findings |
| Labyrinth | AC, HC, PC, utricle, saccule | Horizontal > torsional | EH, labyrinthitis | Nystagmus, auditory findings |

*AC*, Anterior canal; *BPPV*, benign paroxysmal positional vertigo; *EH*, endolymphatic hydrops; *HC*, horizontal canal; *PC*, posterior canal; *SCD*,superior canal dehiscence; *VN*, vestibular neuritis; *VP*, vestibular paroxysmia.

**BENIGN PAROXYSMAL POSITIONAL VERTIGO:**

BPPV is a condition that causes an episodic vestibular syndrome of short duration of under a minute. This otoconial disorder presents with nystagmus triggered by the abnormal stimulation caused by otoconia in the affected semi-circular canal. It mostly aggravates when the patient turns over in the bed, bends the head down, or getting up from bed in the morning.[22]

It is a paroxysmal disorder and is not associated with hearing disorders (tinnitus and hearing loss) or headache, including migraine, associated with episodic vestibular symptoms.[22]

BPPV is characterized by giddiness that lasts for several seconds triggered by positional change with respect to gravity. The aetiology and pathogenesis of BPPV are controversial. It is mainly attributed to two forms- Canalolithiasis and Cupulolithiasis.

Cupulolithiasis causes the cupula to become sensitive to head movements and gravity because otoconia adhere to it. It has been widely speculated that canaliths responsible for development of illness may be caused by displaced otolithic membrane. Canalolithiasis may be converted to cupulolithiasis when floating otoconial debris in the canal attach to cupula.

**MENIERE DISEASE**

Ménière disease that is endolymphatic hydrops is an idiopathic condition of the membranous labyrinth. It is characterized by spontaneous bouts of prolonged vertigo, fluctuating hearing loss, and tinnitus. Histologically, the amount of endolymph within the scala media is excessive.[21]

The disease affects primarily adults between 30 and 60 years of age and is somewhat more common in women. The condition is unilateral in approximately 80% of affected patients, and when it is bilateral, the second ear generally becomes affected within 3 years of the first episode. Bilateral involvement has been reported in 16% to 50% of patients. [21]

The most common pattern by far is involvement of both the vestibular and the cochlear labyrinths; in rare instances, however, the disease may produce vestibular symptoms alone or episodes of fluctuating hearing loss alone.[21]

The vertiginous episodes last from twenty minutes to several hours and in special cases, subjects with Ménière disease experience vestibular otolith dysfunction, called 'otolithic crisis of Tumarkin', in which a sudden disorientation relative to the ground develops and the patient falls, but some patients have the illusion of being violently pushed to the ground.[21]

**VESTIBULAR NEURONITIS**

Vestibular neuronitis is characterized by a sudden onset of sustained and severe vertigo that worsens with head movements. This condition usually affects people in their 20s to 50s and is generally unilateral. It has various degrees of severity. Thought to be caused by a viral infection of the Scarpa ganglion, the condition is often preceded or accompanied by an obvious viral infection and may affect several individuals in a community at the same time, hence the term 'endemic vertigo or endemic labyrinthitis'. The most severe period of the attack usually lasts from 1 to 3 weeks and is characterized by an improvement in symptoms from day to day, although they may worsen with sudden movements of the head.

In addition to acute vestibular dysfunction, affected patients experience sudden, profound hearing loss in the affected ear. The vertigo subsides after 3 weeks, but it may still be provoked by sudden movements of the head in certain instances.[21]

**THIRD WINDOW SYNDROME**

The general term of third window syndrome has been adopted because the same spectrum of symptoms, signs on physical examination, and audiologic diagnostic findings are encountered with SSCD, cochlea-facial nerve dehiscence, cochlea-internal carotid artery dehiscence, cochlea-IAC dehiscence, lateral semicircular canal-superior semicircular canal ampulla dehiscence, modiolus, "perilymph fistula," posterior semicircular canal dehiscence, posterior semicircular canal–jugular bulb dehiscence, SSCD-subarcuate artery dehiscence, SSCD-superior petrosal vein dehiscence, vestibule-middle ear dehiscence, lateral semicircular canal-facial nerve dehiscence, wide vestibular aqueduct in children, posttraumatic hypermobile stapes footplate, otosclerosis with IAC involvement. The common structural finding in all of these conditions is an otic capsule defect that creates a "third window." [21]

**POSTTRAUMATIC VERTIGO**

Trauma to the temporal bone—common even with minor head injury —such as temporal bone fractures, labyrinthine concussion, posttraumatic positional vertigo, and perilymph fistulas can result in peripheral vestibular dysfunction. Central vestibular dysfunction, such as dizziness secondary to brainstem trauma or post-concussion syndrome, is also common.[21]

## URIC ACID:

Uric acid is generated as the end product of exogenous purines in the liver, intestines and tissues such as muscles, kidney and vascular endothelium while; endogenously it is derived from degradation of nucleic acids, adenine and guanine in live and dying cells.[23] Adenine and guanine is then deaminated and dephosphorylated to inosine and guanosine, respectively.[23] Inosine and guanosine is phosphorylated to the purine bases - hypoxanthine and guanine respectively, by enzyme purine nucleoside phosphorylase. These purine bases are then converted to xanthine, which is further oxidized by xanthine oxidase to uric acid.

## PHYSIOLOGICAL FUNCTIONS OF URIC ACID

Though uric acid is freely filtered in kidney glomeruli, 90% of this is reabsorbed in consideration of its physiological functions.

Antioxidant: Uric acid is a peroxynitrite scavenger, a strong antioxidant and reactive oxygen species; thereby high uric acid levels are detected in cytosol of normal individuals, especially in the cells of vascular endothelium, liver and nasal secretions.[23]

- **Mediator of type 2 immune responses :**

Discovered in the airways of asthmatic patients who were allergen challenged, uric acid was found to be a necessity for Th2 cell immunity, hyper reactivity of bronchia and airway eosinophilia.[23]

Furthermore, monosodium urate administered along with proteins inhaled elicited a type 2 immunity. Thus, uric acid was deemed to be an in vivo initiator and amplifier of allergic inflammation .[24]

Uric acid has been established as a pivotol player in regulating the rise of type 2 immune response to cysteine peptidase allergens. This was owed to the role of uric acid in the release of thymic stromal lymphopoietin (TSLP) and IL-33 via epithelial cell activation.[25]

- **Resistance to parasites:**

Owing to the anti-oxidants properties of uric acid, it interferes with lipoxygenases' functioning and acts as a substrate for cyclooxygenase enzyme. Thus, arachidonic acid deemed to be a potent schistosomicide; mediate parasite demise as seen in children infected with S.mansoni. When parasites infest, ingest blood, excrete and secrete cysteine peptidases in liver sinusoids, the type 2 immune effectors and cytokines, damage hepatocytes triggering the release of uric acid.[23] Found to be associated with non-alcoholic fatty liver disease, uric acid has a role in fatty liver through increased fatty acids synthesis and unsaturated fatty acids release, especially arachidonic acid from lipid depots and cell membrane. [23]

- **Defence against neurological and autoimmune diseases :**

Myelin degradation seen in multiple sclerosis is mediated by reactive oxygen species and peroxynitrites; both of which are blocked on elevated uric acid levels.[23] Thus, multiple sclerosis is mostly never seen among gout affected individuals.[23]

Lijun Wang et al., found that the serum uric acid levels of MS patients were lower than those of healthy controls, suggesting that low serum uric acid levels could be a possible biomarker for MS.[26]

Reduced levels of plasma uric acid have also been linked to neurological conditions like Parkinson's and Alzheimer's disease, pemphigus vulgaris, an autoimmune disease marked by skin blistering and mucous membrane erosion, and lichen planus, an inflammatory autoimmune disease of the mucocutaneous tissue that has also been linked to reduced levels of uric acid in saliva.[23]

- **Pathogenic role of serum uric acid**

Human blood contains a constitutive quantity of 40–60 µg/mL of uric acid, which is completely soluble in biological fluids up to 70 µg/mL. A quantity of uric acid that is higher than its solubility level causes monosodium urate crystals to precipitate, which can cause severe inflammatory episodes in certain people, particularly in the joint cavities.[23]

Since a continuous positive correlation has been shown between the severity of knee osteoarthritis and the synovia, but not the serum content of uric acid, IL-1β, and IL-18, uric acid is also thought to be a danger signal that contributes to the progression of osteoarthritis by inducing inflammasome activation.[23]

Furthermore, through the activation of growth factors, hormones, cytokines, and autacoids, hyperuricemia is strongly linked to the development of hypertension and cardiovascular disorders. Numerous studies have demonstrated that it is quite likely that uric acid enters the vascular smooth muscle fibers, activating a number of

signal transduction pathways before increasing the expression of inflammatory mediators.[23]

## NEUTROPHIL LYMPHOCYTE RATIO(NLR)

A biomarker that combines the two aspects of the immune system—the innate immune response, primarily driven by neutrophils, and adaptive immunity, primarily facilitated by lymphocytes—is the neutrophil lymphocyte ratio (NLR), which is computed as a straightforward ratio between the neutrophil and lymphocyte counts measured in peripheral blood.[27]

Acute stroke, myocardial infarction, atherosclerosis, severe trauma, cancer, post-surgery complications, bacterial or fungal infection, and any condition characterized by tissue damage that activates systemic inflammatory response (SIRS) can all be associated with an isolated rise in neutrophil count and, consequently, an elevated NLR.[27] This is due to the proinflammatory state that is driven by neutrophils and other inflammatory cells during the early hyperdynamic phase of infection. As a component of the innate response, SIRS is linked to the reduction of neutrophil apoptosis, which increases neutrophil-mediated death. [27] Consequently, a rise in neutrophils and a decrease in lymphocytes are frequently observed in NLR.

The rapid rise in NLR (less than 6 hours) that occurs after acute physiological stress may make NLR a more reliable indicator of acute stress than other laboratory indicators (such as white blood cell count, bacteremia and CRP).[27]

The host's response to viruses, tumor cells, atopy, and SIRS are all influenced by lymphocyte activity. In every field of application, lower NLR is typically linked to good prognostic variables, reflecting a conserved immunological balance.

**NLR AND ITS PATHOPHYSIOLOGY:**

- Sepsis:

For the accurate identification of sepsis and bacteremia, NLR has long been recognized as a trustworthy diagnostic.

- Pneumonia:

CAP, or community-acquired pneumonia, is a frequent cause of sepsis that requires hospitalization. When it comes to both short- and long-term mortality, the requirement for intensive care unit admission, and re-hospitalization, NLR has proven to have a good predictive value.[27]

Consequently, NLR showed a stronger correlation with post-CAP mortality than did the standard pneumonia scores (Pneumonia Severity Index; and CURB-65, Confusion, Urea, Respiratory rate and Blood pressure, aged 65 and older), WBC, and CRP.

It was predicted that patients with a prognosis worse than 28.3 would need to be admitted to a respiratory intensive care unit, whereas patients with a prognosis better than 11.12 may be safely released and followed up with outside care. Moreover, the chance of rehospitalization after three months rises in tandem with an increase in NLR, with a rate exceeding 75% when NLR exceeds twenty.[27]

- Cardiovascular Disease:

Numerous studies have demonstrated the ability of NLR to predict cardiovascular events. The well-established roles of inflammation and oxidative stress in the pathogenesis of atherosclerosis and endothelial dysfunction are the sole cause of NLR increase in cardiovascular disorders.[27]

- Surgery:

Regardless of the kind of operation (abdominal or cardiac), preoperative NLR values were found to be independent predictors for post-operative complications, as well as peri- and post-procedural death.

Although vertigo can manifest in a variety of ways, it also serves as a trigger for tension and worry, which raises stress hormone levels. This induces a range of symptoms that are exacerbated by elevated stress hormone levels and inflammatory indicators, most likely due to autonomic nervous system abnormalities. White blood cell count, ESR, and C-reactive protein are the three most widely used markers of inflammation. One quick and simple method to determine a subject's level of inflammation is to measure their neutrophil-to-lymphocyte ratio.[14] In a study by Isa Osbay et al., patients with vertigo were shown to have a considerably higher mean NLR than the vertigo were shown to have a considerably higher mean NLR than the control group.[20]

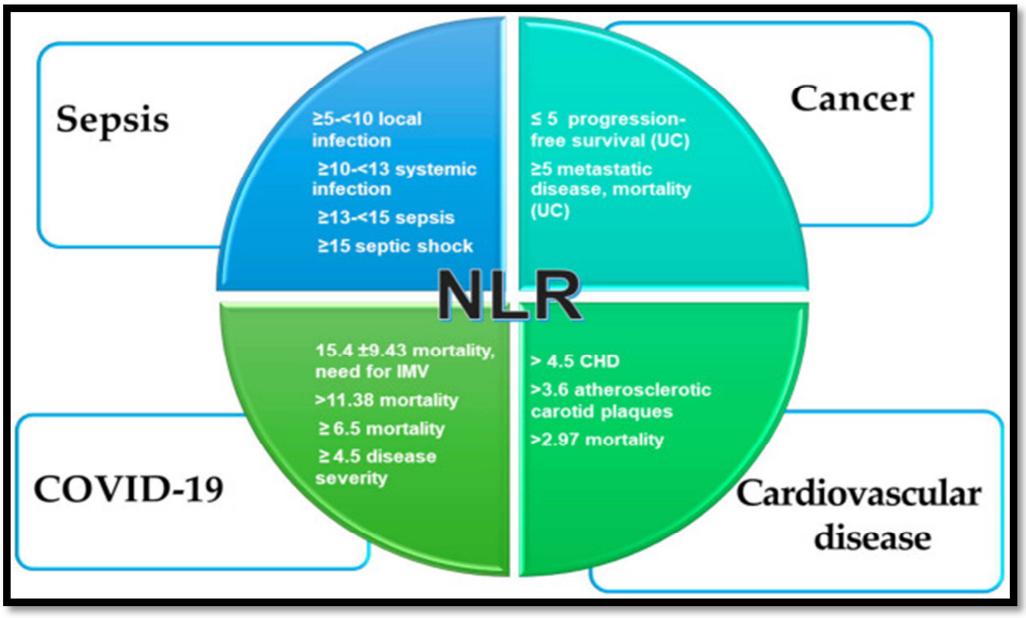



**Figure no 10: NLR cut-off values in the main pathophysiological states**[27]

## MARKERS TO DIFFERENTIATE PERIPHERAL VS CENTRAL VERTIGO

Distinguishing between peripheral and central causes of vertigo presents a challenge in clinical settings. Proteins that are commonly thought of as central nervous system(CNS) markers include S100β, glial fibrillary acidic protein, which is a marker of glial injury or activation, and neuron specific enolase(NSE), which is a marker of neuronal damage.[28] Brain-derived neurotrophic factor is a growth factor protein that is easily detectable in peripheral blood and is a member of the neurotrophin family.[28]

In a study conducted by Jong Hee Sohn et al., serum NSE and S100β levels was found to be significantly higher in patients with central vertigo whereas the peripheral vertigo group had an increased serum IL-6 level.[28]

In a study conducted by D V K Irugu et al., serum otolin-1 was found to be a reliable bio marker in BPPV patients where in the serum otolin-1 levels were found to be significantly higher compared with individuals without benign paroxysmal positional vertigo.[29] Furthermore, vertigo, anxiety and stress go hand-in-hand with each other as episodes of vertigo causes elevation of stress-hormones inflammatory markers.[30] While the counts of certain WBC subtypes are classic inflammatory markers, especially, in patients with cardiovascular diseases; a study conducted by Isa Ozbay et al., has established neutrophil-to-lymphocyte ratio (NLR) as a reliable marker in peripheral vertigo.[30]

According to Abdul Azeez et al., HDL, SGOT, ESR, Platelet to lymphocyte ratio, mean platelet value, neutrophil to lymphocyte ratio were significantly higher in BPPV patients; hence can be considered as indicators.[13]

# MATERIALS AND METHODS

## METHODOLOGY:

The Department of Otorhinolaryngology and Head & Neck Surgery at Jawaharlal Nehru Medical College conducted the current study over a period of one year to examine the variations of neutrophil to lymphocyte ratio and potential association of serum uric acid levels in patients with peripheral vestibular disorders: A cross sectional study in KLEs Dr. Prabhakar kore hospital, Belagavi. A total of 51 patients who were confirmed cases of peripheral vestibular disorders that came to the department of otorhinolaryngology were included in the study.

**STUDY PERIOD :** 1 year

**STUDY DESIGN:** A cross sectional study .

## STUDY POPULATION:

Study was conducted in 51 patients who are confirmed cases of Peripheral vestibular disorders above 18 years of age that came to department of Otolaryngology.

## INCLUSION CRITERIONS:

All patients who are confirmed cases of Peripheral vestibular disorders above 18 years of age that came to department of Otolaryngology.

**EXCLUSION CRITERIONS:**

All patients with forms of central vestibular disorders, individuals who have had middle ear surgeries, individuals with traumatic head injury, patients receiving chemotherapy, vestibulotoxic drugs, steroids or NSAIDs, patients with inflammatory diseases, patients with malignant, chronic renal, hepatic, cardiovascular or autoimmune diseases, gout, diabetes mellitus, thyroid disease and pregnancy patients were excluded.

**SAMPLE SIZE:**

The sample size taken was 51

**SAMPLING TECHNIQUE** :

The minimum sample size formula based on prevalence rate is

$$n = \frac{z_\alpha{}^2 P(1-P)}{d^2}$$

where P is the prevalence rate of peripheral vertigo among the vertigo cases and d is the percentage likely difference in the prevalence.

$z_\alpha$ is linked with the level of significance. For 5% level of the significance $z_\alpha = 1.96$.

Ref:

With P = 80% and d = 15% of P = 12%, the sample size is 43.

To get confirmative results the sample size will be increased to 50.

**STATISTICAL ANALYSIS:**

Since the study is of observational study the plan of analysis will be as follows.

For the continuous quantitative variables mean and standard deviation will be calculated. For the purpose of comparison, if the data is divided into two groups with respect to certain qualitative characteristic, the continuous variables will be compared using suitable tools of statistics like student's unpaired t test. The pre and post treatment measures will be compared using student's paired t test

Discrete variables will be represented by median.

The categorical data will be expressed in terms of rates, ratios and percentages. The association between the outcome, clinical and demographic characteristics will be tested using Chi-square test, test of proportion or Fisher's exact test.

For discrete variables nonparametric tests will be used.

Apart from the above suitable tools like ANOVA, correlation, regression etc., will be used according to the need.

Suitable graphs will be used to depict the comparison.

For all the tests the value of p less than 5% (0.05) will be considered significant.

**STUDY SETTING :**

**Data collection procedure:**

The patients coming to the Otolaryngology clinic with complaints of frequent attacks of dizziness will be evaluated for Vertigo using a Dizziness History Questionnaire.

- The subjects will be evaluated for signs of a peripheral vestibular disorder using Head Impulse test, Dix Hallpike Manoeuvre, tunning fork testing, fistula test.

- Once peripheral vestibular disorder is confirmed, the serum uric acid level is measured and the neutrophil lymphocyte ratio determined from the relative neutrophil and lymphocyte percentage.

- Informed consent will be taken before performing the procedure.

The levels of serum uric acid and neutrophil lymphocyte ratio is correlated with peripheral vestibular disorder patients.

# RESULTS

The study group was recorded over a period of one year at KLEs Dr.Prabhakar Kore Hospital ENT Outpatient Clinic.

Patients who came with complaints of giddiness and were clinically suspected to have peripheral vertigo were enrolled into the study. The study had a total of 51 participants.

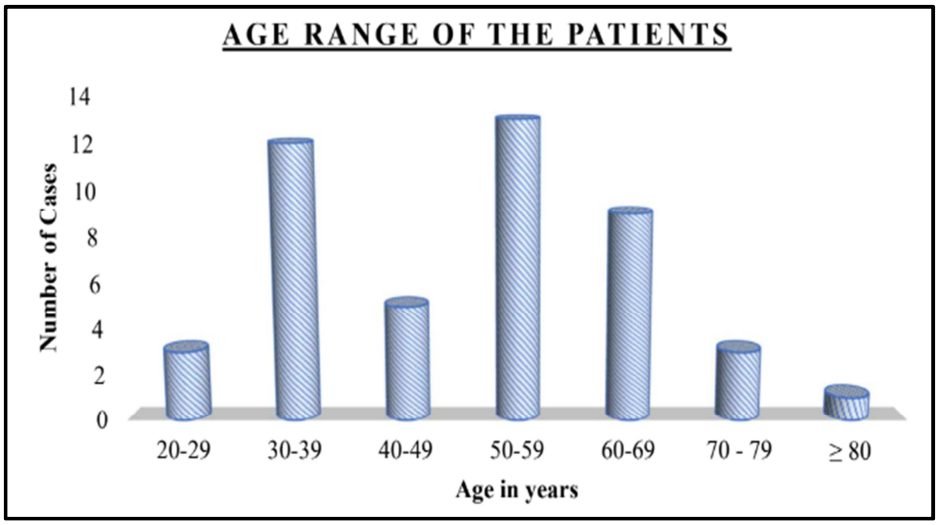
Neutrophil to lymphocyte ratio and serum uric acid levels were evaluated in patients with peripheral vestibular disorders.

Dizziness handicap inventory score(DHI) was also taken into account for each patient.

## DEMOGRAPHIC ANALYSIS

### AGE DISTRIBUTION:

The study group included participants with ages ranging from 20 to 85.



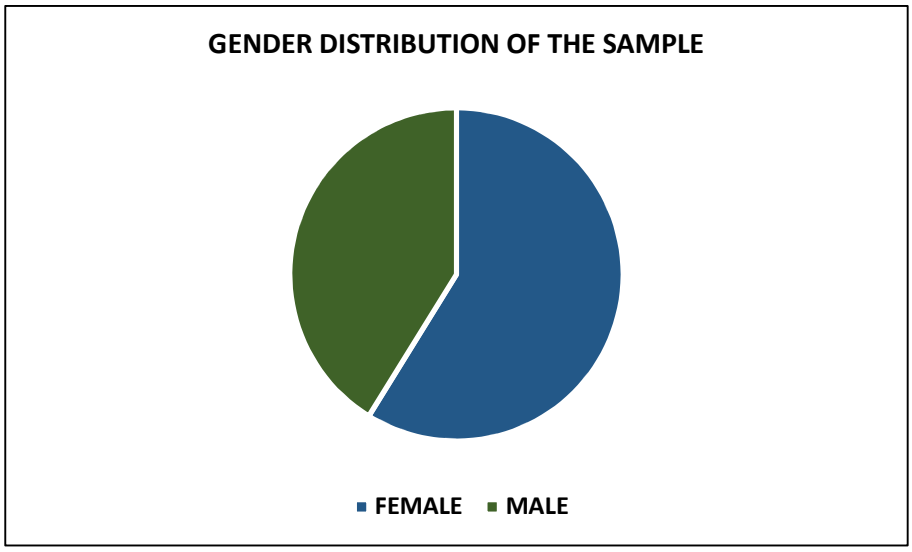

**Graph 1: Age range of the patients**

From the above data we can see that there were two peaks in incidence. The ages between 30-39 years and 50-59 years showed a spike in incidence and each contributed to one quarter of the study population.

The average age of incidence among our cases was 50.47 ± 15.31 years.

| GENDER | NUMBER | % |
|---|---|---|
| **FEMALE** | 30 | 58.82 |
| **MALE** | 21 | 41.18 |
| **TOTAL** | 51 | 100.00 |

**Table 2 : Gender Distribution:**




**Graph 2: Gender distribution of the sample**

In our study, a total of 30 men and 21 had women participated.

In other words, the study population constituted -

- 58.82% female students and 41.18% male students.
- Numerically the mean age of females(50.97) is more than mean age of males(48.43) but not significantly.

**OVERALL:**

| | **MEAN** | **S.D.** | **MIN** | **MAX** |
|---|---|---|---|---|
| **NLR** | 6.96 | 2.97 | 1 | 12 |
| **DHI SCORE** | 54.06 | 9.14 | 30 | 68 |

All patients clinically diagnosed with a peripheral vestibular dysfunction was taken into account and their absolute neutrophil and lymphocyte counts taken for the neutrophil to lymphocyte ratio followed by their serum uric acid levels.

As noted from the above and below data, the neutrophil to lymphocyte showed an overall mean of 6.96 and serum uric acid with a mean of 8.96. Both of which had a mean dizzines handicap inventory score of 54.06. This correlates to a significant portion of subjects showing severe handicap in accordance to the DHI scoring , where in – 16-34 points equates to mild handicap

36-52 points equates to moderate handicap

>or = 54 points equates to severe handicap

| | MEAN | S.D. | MIN | MAX |
|---|---|---|---|---|
| **SERUM URIC ACID mg/dl** | 8.96 | 1.32 | 3.4 | 11.2 |
| **DHI SCORE** | 54.06 | 9.14 | 30 | 68 |

**Table 3: Comparison of parameters with respect to gender**

In The Following Tables P Values Are Calculated Using Student's Unpaired T Test

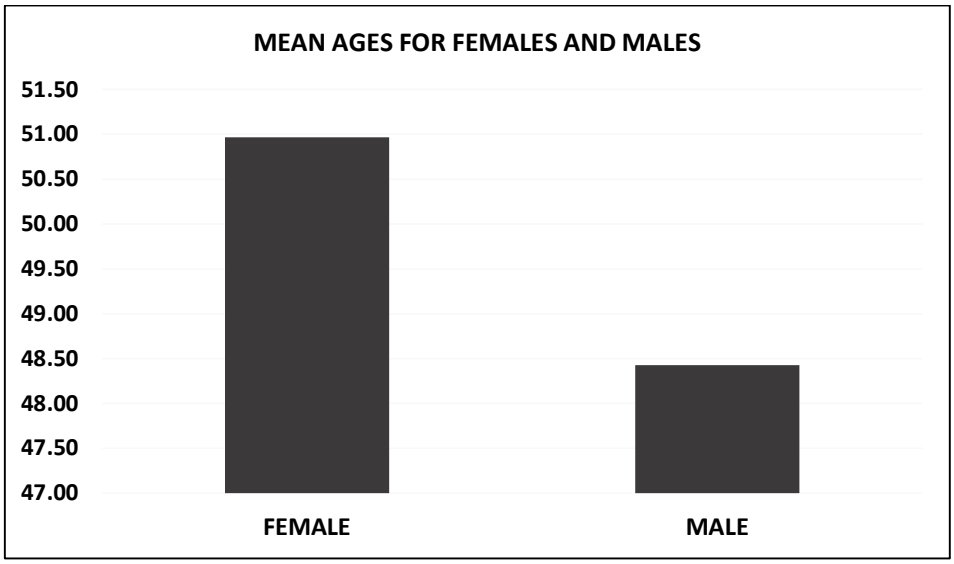
| | FEMALES | | | | MALES | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Age | Mean | S.D. | Min | Max | Mean | S.D. | Min | Max | p Value | Inference |
| | 50.97 | 16.31 | 25 | 87 | 48.43 | 11.29 | 31 | 74 | 0.5193 | NS |

(Abbreviations: NS -Not Significant S – Significant VS - Very Significant HS- Highly Significant)

**Table 4- Comparison of the Parameters With Respect To Gender**

As seen in the above table and depicted in the bar graph below, females had a mean age of 50.97 while male subjects had a mean age of 48.43. With a standard deviation of 16.31 and 11.29 in females and males respectively, they had a p value of 0.5193 hence deeming it not significant.

- Numerically the mean age of females is more than mean age of males but not significantly.




**Graph 3: Mean ages for females and males**

| | FEMALES | | | | MALES | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Mean | S.d. | Min | Max | Mean | S.d. | Min | Max | P value | Inference |
| NLR | 7.23 | 2.45 | 1 | 12 | 6.57 | 3.61 | 1 | 12 | 0.4384 | NS |
| Serum uric acid | 8.70 | 1.41 | 3.4 | 10.8 | 9.33 | 1.06 | 6.2 | 11.2 | 0.0953 | NS |

(Abbreviations: NS -Not Significant S – Significant VS - Very Significant HS- Highly Significant)

**Table 5: DHI score in females and males**

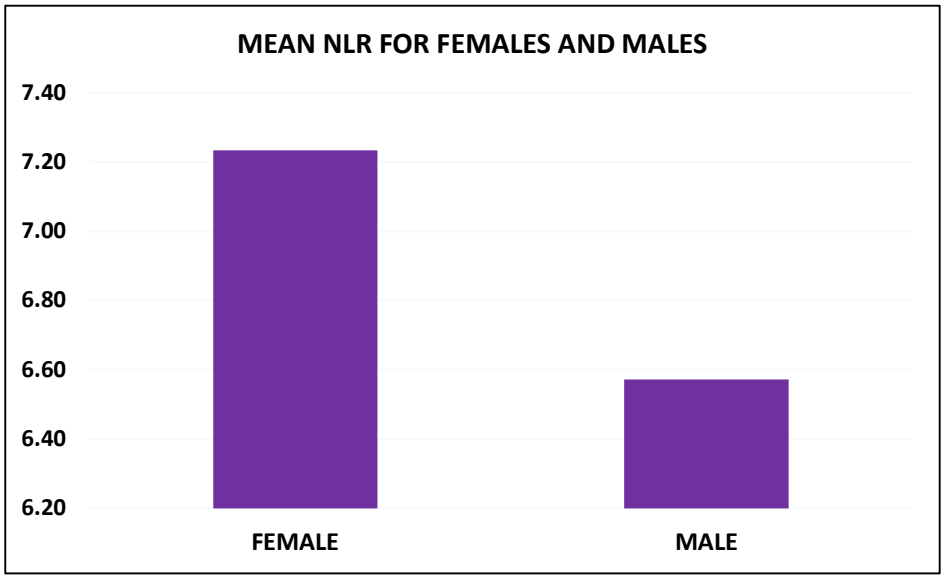
As seen in the above table, the female subjects showed a mean neutrophil to lymphocyte ratio(NLR) of 7.23 and mean serum uric acid of 8.70; while the males

subjects showcased a mean of 6.57 and 9.33 in NLR and serum uric acid level respectively.

NLR in females and males had a standard deviation of 2.45 and 3.61 respectively, giving a p value of 0.4384 and hence is not significant.

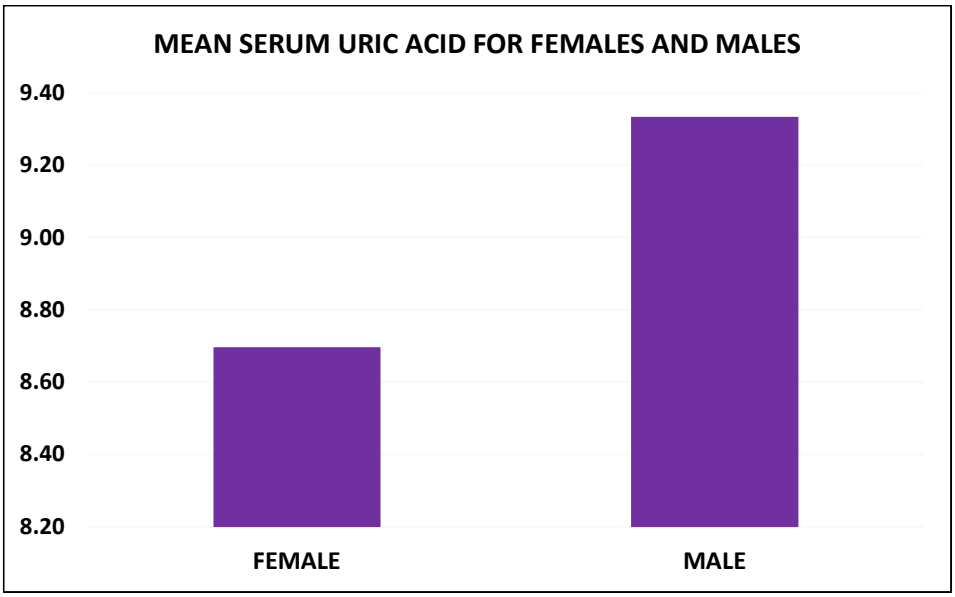
- Numerically the mean serum uric acid level of females is smaller than mean serum uric acid of males but not significantly.

- **Numerically the mean NLR of females is larger than mean NLR of males but not significantly.** In this sample there is little difference but in the population they are likely to be the same.




**Graph 4: Mean NLR for females and males**

The mean NLR of females (7.23) is larger than mean NLR(6.57) of males but not significantly.




**Graph 5: Mean serum uric acid for females and males**

- The mean serum uric acid level of females (8.70) is smaller than mean serum uric acid (9.33) of males but not significantly.

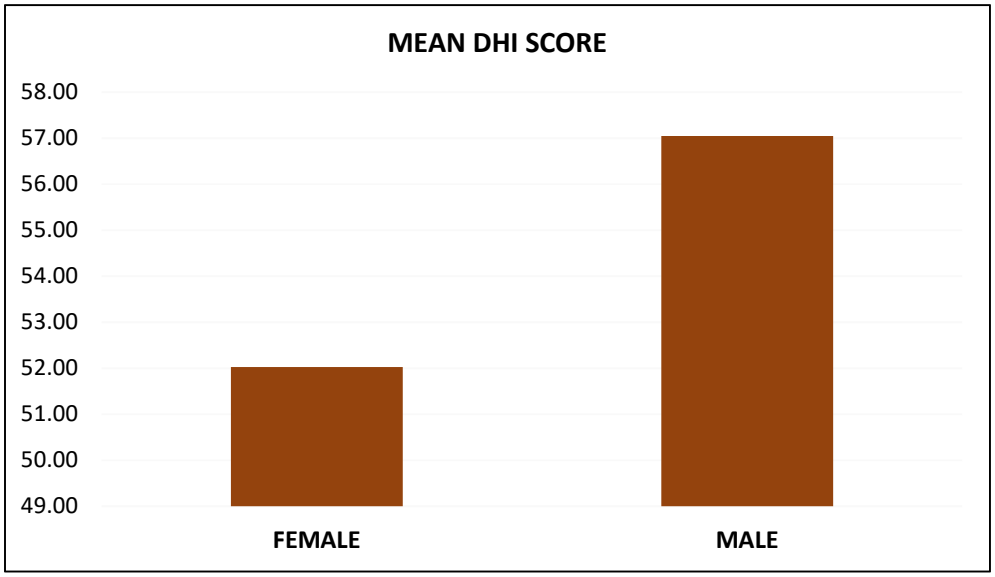
| | Females | | | | Males | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Mean | S.d. | Min | Max | Mean | S.d. | Min | Max | P value | Inferrence |
| Dhi score | 52.03 | 9.62 | 30 | 66 | 57.05 | 7.37 | 36 | 68 | 0.0497 | S |

(Abbreviations: NS -Not Significant S – Significant VS - Very Significant HS- Highly Significant)

**Table 6: Grades of DHI scoring among study population**

As seen in the above table, the female and male subjects had a mean DHI score of 52.03 and 57.05, and standard deviation 9.62 and 7.37 respectively resulting in a p value 0.0497 being significant.

The mean DHI score of females is significantly smaller than mean DHI score of males.

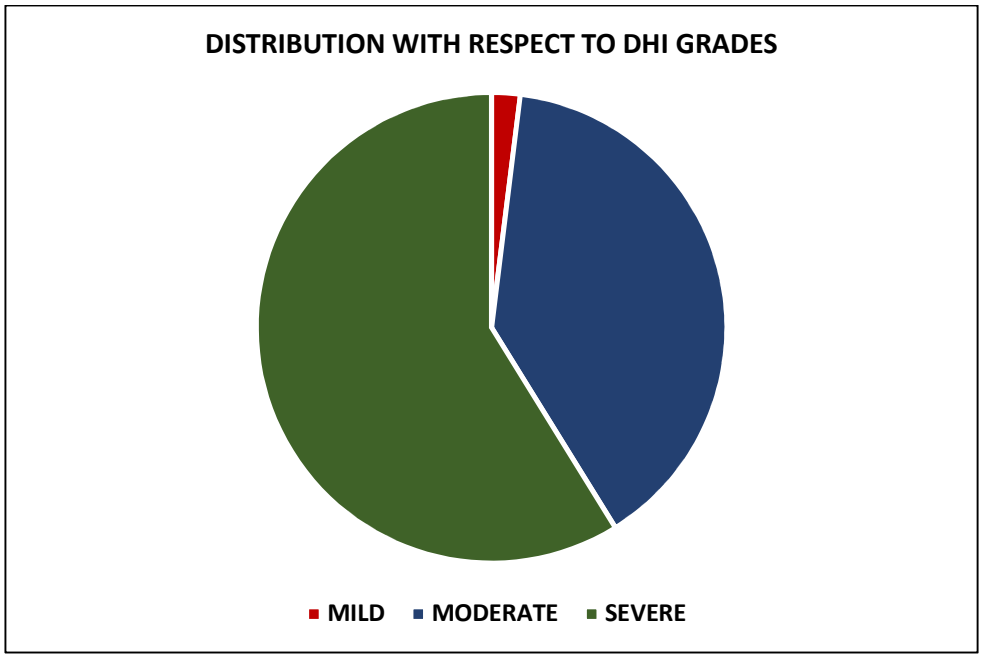



**Graph 6: Mean DHI score**

The cases are grouped with respect to the grades of dizziness handicap inventory score as follows –

| DHI | HANDICAP | NUMBER | % |
|---|---|---|---|
| **16 - 34** | **MILD** | 1 | 1.96 |
| **36 - 52** | **MODERATE** | 20 | 39.22 |
| **≥ 54** | **SEVERE** | 30 | 58.82 |
| | **TOTAL** | 51 | 100.00 |

**Table 7: NLR and Serum uric acid in moderate and severe handicap subjects**




**Graph 7 : Distribution with respect to DHI grades**

As noted in the above table, only one subject had a DHI score equating to mild handicap while; 20 subjects had moderate handicap and the remaining 30 study subjects had severe handicap. Furthermore,

- 58.82% of the study participants showed severe handicap with a mean NLR 6.93
- 39.22% participants showed moderate handicap with a mean NLR 7.20
- A mere 1.96% showed mild handicap and was excluded from comparison.
- The difference between the means of NLR for moderate handicap and severe handicap groups is not significant .

There is only one case of mild handicap (not a group) with value dhi as 30. This category is not included in the following comparison.

- 58.82% of the study participants showed severe handicap with a mean serum uric acid level 9.51
- 39.22% participants showed moderate handicap with a mean serum uric acid level 8.42
- A mere 1.96% showed mild handicap and was excluded from comparison.
- The difference between the means of serum uric acid for moderate handicap and severe handicap groups is **highly significant** .

| | Moderate handicap | | | | Severe handicap | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Mean | S.d. | Min | Max | Mean | S.d. | Min | Max | P value | Inferr ence |
| NLR | 7.20 | 2.19 | 1 | 9 | 6.93 | 3.38 | 1 | 12 | 0.7570 | NS |
| Serum uric acid | 8.42 | 1.14 | 6 | 10.2 | 9.51 | 0.75 | 8.4 | 11.2 | 0.0002 | HS |

(Abbreviations: NS -Not Significant S – Significant VS - Very Significant HS- Highly Significant)

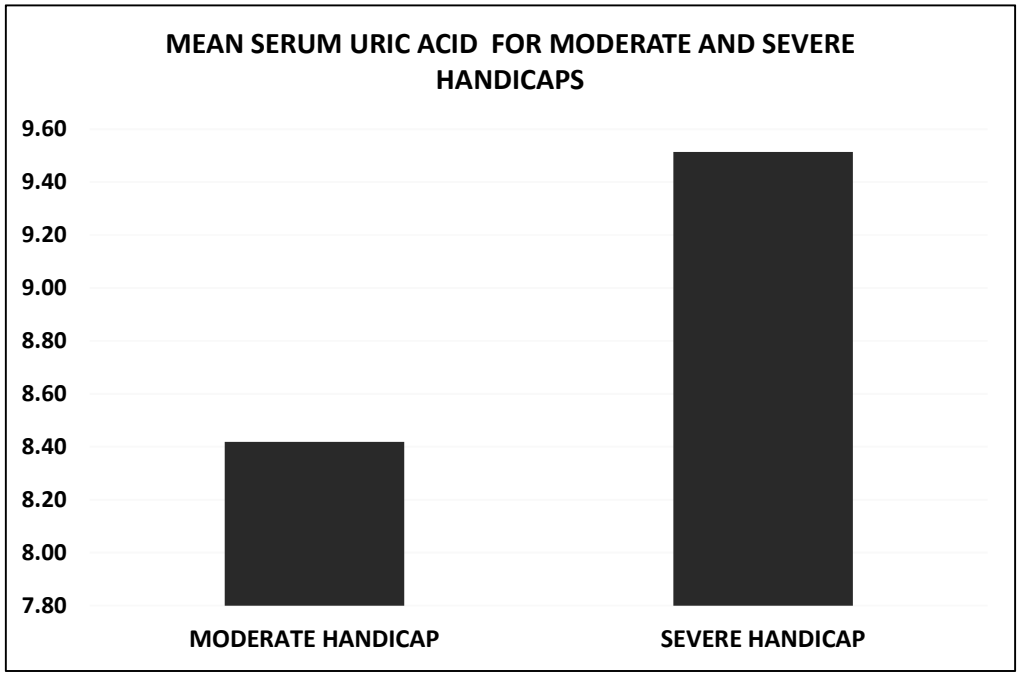
**Table 8: NLR and Serum uric acid among moderate and severe handicap**

As seen in the above table, the mean NLR in subjects with moderate handicap and severe handicap on DHI scoring was 7.20 and 6.93, and a standard deviation 2.19 and 3.38 respectively; resulting in a p value 0.7570 which was not significant.

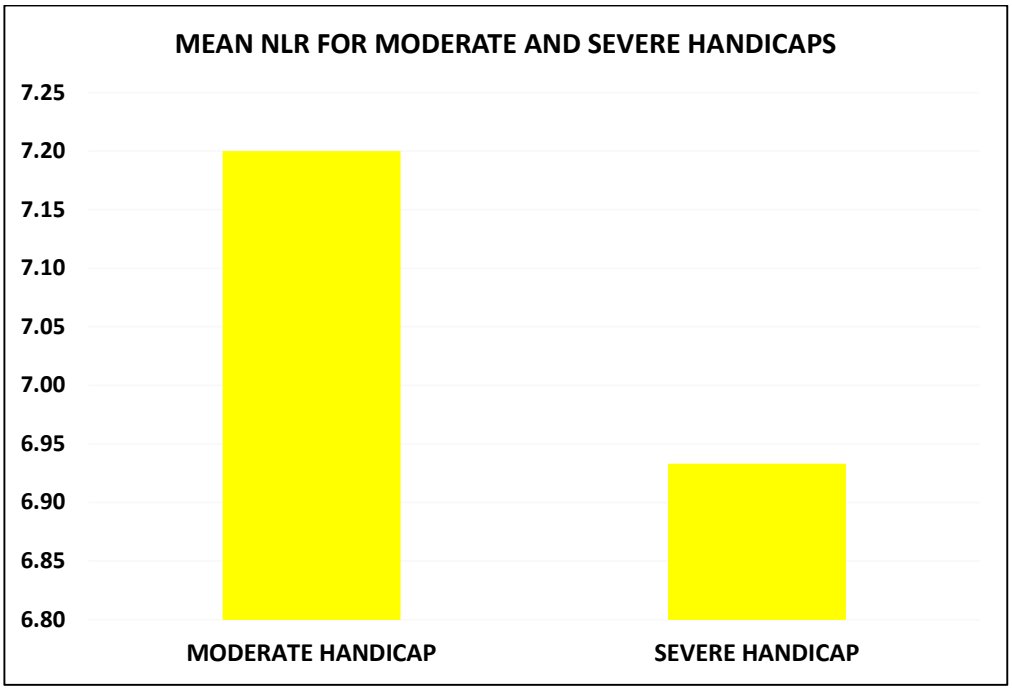
Futhermore, the mean serum uric acid in subjects with moderate handicap and severe handicap on DHI scoring was 8.42 and 9.51, and a standard deviation 1.14 and 0.75 respectively; resulting in a p value 0.0002 which was highly significant.

The difference between the means of nlr for moderate handicap and severe handicap groups is not significant.

The difference between the means of serum uric acid for moderate handicap and severe handicap groups is highly significant.




**Graph 8: Mean serum uric acid for moderate and severe handicaps**




**Graph 9: Mean NLR for moderate and severe handicaps**

| BETWEEN | r VALUE | p VALUE | INFERENCE |
|---|---|---|---|
| NLR AND DHI SCORE | 0.2066 | 0.1457 | NOT SIGNIFICANT |
| SERUM URIC ACID AND DHI SCORE | 0.3206 | 0.0125 | SIGNIFICANT |

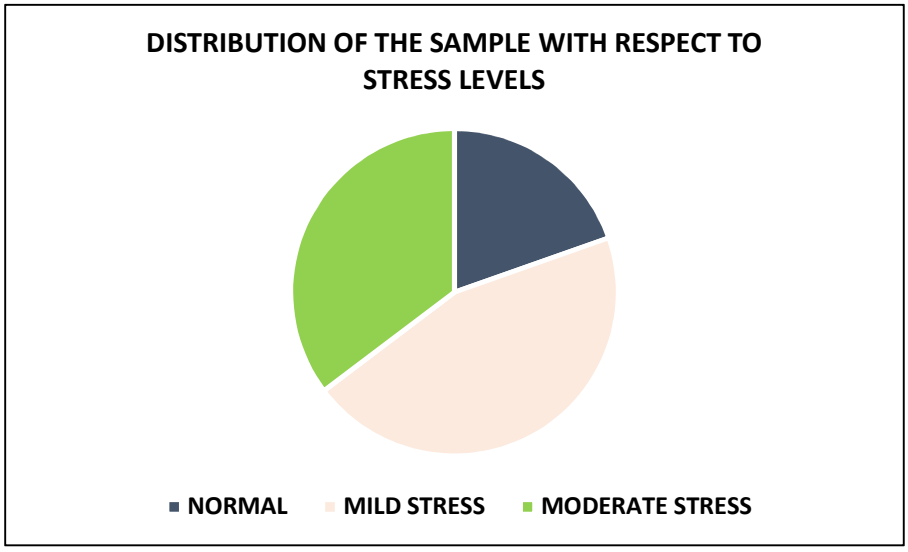
**Table 9: Karl Pearson's Coefficient Of Correlation (R) Is Given Above:**

According to the above table, there is no linear correlation between NLR and DHI Score; however, there is a significant linear correlation between serum uric acid and DHI score with r value 0.3206 and p value 0.0125.

| NLR | STRESS | NUMBER | % |
|---|---|---|---|
| **< 6** | **NORMAL** | 10 | 19.61 |
| **6 - 8** | **MILD STRESS** | 23 | 45.10 |
| **9 - 18** | **MODERATE STRESS** | 18 | 35.29 |
| | **TOTAL** | 51 | 100.00 |

**Table 10: The Cases Are Grouped With Respect To NLR As Above:**

As depicted in the above table, 10 subjects i.e. 19.61% of study subjects showed NLR of less than 6 which was normal while, 23 subjects i.e. 45% of study subjects showed moderate stress under NLR 6-8. 18 subjects accounting to 35% of study population showed moderate stress under NLR range 9-18.




**Graph 10: Distribution of the sample with respect to stress levels**

| | Normal stress | | | | Mild stress | | | | Moderate stress | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Mean | S.d. | Min | Max | Mean | S.d. | Min | Max | Mean | S.d. | Min | Max | P value | Inference |
| Dhi score | 50.00 | 11.66 | 30 | 64 | 54.39 | 8.05 | 36 | 66 | 55.89 | 8.74 | 40 | 68 | 0.2613 | NS |

(Abbreviations: NS -Not Significant S – Significant VS - Very Significant HS- Highly Significant)

**Table 11: In the Following Table P Value Is Calculated Using One Way Analysis Of Variance (ANOVA)**

- The DHI Scores are more or less at the same levels in the three groups

As seen in the above table, patients with normal stress levels in accordance with NLR showed a mean DHI score of 50.00 and standard deviation 11.66; while those established with mild stress had mean DHI score 54.39 and standard deviation 8.05. Lastly, the subjects with moderate stress showed 55.89 as mean DHI score and 8.74 standard deviation. The above mentioned variables accounted for a p value 0.2613 which was not significant.

# DISCUSSION

Vertigo is the sensation of movement, either in oneself or in the objects around oneself. It is a clinical symptom that typically manifests as a rotational, spinning movement and is associated with the most frequently diagnosed vestibular illnesses, including labyrinthitis, vestibular neuritis, acoustic neuromas, benign paroxysmal positional vertigo, and perilymph fistula.[30] With a 12-month prevalence of 5% and an incidence of 1.4% in adults, vertigo is a common symptom in the general population.[31] According to Raman Abrol et al., in an adult rural population, the overall prevalence of vertigo was determined to be 0.71%.[32] Furthermore, in 0.32% of the population, vertigo due to cardiovascular illness was the most common and prevalent symptom.[32] Vertigo was caused by neurologic disease in 0.14% of cases, metabolic disease in 0.09%, and otologic disease in 0.08%. The remaining 0.08% of the people under study had various ailments. [32] It has been established that a greater proportion of the general public and rural population experience non-otologic vertigo than otologic vertigo; hence early and accurate diagnosis of vertigo is critical. Hence, in our study we aim to establish simple parameters as a diagnostic tool in favor of peripheral vertigo.

An increasing percentage of visits to emergency departments (EDs) are due to dizziness and vertigo; at present, ED visits account for 2 to 3% of all consultations.[31] Identification of central vertigo or other severe vertigo is a critical concern in this context.

Our study's objective was to examine the variations of neutrophil to lymphocyte ratio and potential association of serum uric acid level in patients with peripheral vestibular disorders.

For a period of 1 year from 27th September 2022 to 26th October 2023, the study was carried out at the department of Otorhinolaryngology and head & neck surgery at Jawaharlal Nehru Medical College in Belagavi. 51 patients were considered in the study and the patients were all confirmed cases of peripheral vestibular disorders above 18 years of age.

Psychological issues may arise from vertigo and are not always associated with deficiencies in neurotologic examinations. Patients with Meniere's disease or vestibular migraine had higher levels of anxiety, sadness, and somatization than did those with vestibular neuritis and persistent vestibular impairments, according to a recent study. Notably, somatoform otoneurologic symptoms, such as somatoform dizziness, should be distinguished from concomitant mental symptoms in individuals with organic otoneurologic illnesses. [31]

In our study, patients with complaints of frequent attacks of dizziness were evaluated for vertigo using a Dizziness Handicap inventory score(DHI).

The subjects were then evaluated for signs of a peripheral vestibular disorder and once confirmed, the serum uric acid level was measured followed by the neutrophil lymphocyte ratio determined from the relative neutrophil and lymphocyte percentage.

NLR is a low-cost, easily obtained biomarker that reflects the equilibrium between two immune system components: adaptive immunity and acute and chronic inflammation. Variations in NLR over time are indicative of immune system dysfunction even if there are still no established cut-off values available. But when confounders are taken into consideration, together with the unique context of the disease, comorbidities, and treatment plan, NLR may be regarded as a strong predictive marker of disease severity and a predictor of mortality. Its range of normalcy, adjusted for age categories, may also be definitively identified with the use of additional case-control studies. Lastly, rather than using cut-off values, tertiles of range values based on illness severity may improve the performance of this intriguing biomarker.[27]

In our study, the levels of serum uric acid and neutrophil lymphocyte ratio were correlated with peripheral vestibular disorder patients.

58.82% of the study population were female students and 41.18% male students. Numerically the mean age of females(50.97) was found to be more than mean age of males(48.43).

According to a 2020 study by Adi Putra et al., the majority of BPPV traits linked to hormonal variables were observed in women rather than men.[5] Furthermore, it was concluded in the study that there was a significant relationship between uric acid levels and BPPV with the latter presenting with higher average of uric acid levels compared to the non affected subjects.[10]

58.82% of the study participants showed severe handicap pertaining to the DHI score; with a mean serum uric acid level 9.51. Of the study participants, 39.22%

showed moderate handicap with a mean serum uric acid level 8.42. The difference between the means of serum uric acid for moderate handicap and severe handicap groups was highly significant.

Serum uric acid levels were measured during vertigo episodes and were shown to be higher, whereas measurements taken following a vertigo episode revealed lower levels.[10] This is can be attributed to the disruption of enzyme urikinase formation with increasing age. Enzyme urikinase is pivitol in oxidizing uric acid into its disposable constituents and when this undergoes dysfunction it results in elevated serum uric acid levels.[10]

Hyperuricemia in men is when uric acid level is > 7 mg / dl while, in women it is when uric acid level is > 6 mg / dl.[10] In our study, all subjects who were confirmed cases of peripheral vestibular disorders were found to be hyperuricemic with majority showing severe handicap on DHI scoring.

High estrogen levels in women in the reproductive age group are essential for maintaining the kidneys' normal production of uric acid through urine; however, after menopause is reached, these levels disappear. Hence hyperuricemia is a cofactor aiding BPPV with women showing a higher incidence.[10]

Of the study subjects, 58.82% showed severe handicap with a mean NLR 6.93 while, 39.22% participants showed moderate handicap with a mean NLR 7.20. The difference between the means of NLR for moderate handicap and severe handicap groups is not significant.

The neutrophil-lymphocyte ratio, or NLR, is a commonly used indicator in non-infectious inflammatory illnesses. It is calculated by dividing the total or relative

neutrophil count by the total or relative lymphocyte count.[2] In a study conducted by Isa Osbay et al., the mean of NLR was found to be significantly high in vertigo affected patients than in the control subjects.[30]

According to Venkatesh Kasyapi V et al., an attack of vertigo is followed by an increase in anxiety levels.[2] Anxiety is known to cause symptoms such as autonomic nervous system abnormalities, elevated stress hormone levels, and inflammatory indicators.[2] As a result, we used the neutrophil to lymphocyte ratio in our investigation as a measure to determine the participants' level of inflammation.

Dizziness handicap inventory scoring:

Dizziness is described as a nonvertiginous experience of altered or impaired orientation in space without a false or distorted sense of motion in the Classification of Vestibular Disorders of the Barany Society.[33] One of the main causes of impairment and occupational incapacity is dizziness. When assessing the patient's clinical status, a self-reported questionnaire may be quite beneficial. Numerous questionnaires are available for the assessment of vertigo and dizziness handicap, such as the UCLA Dizziness Questionnaire, Activities-specific Balance Confidence, Vestibular Disorders of Daily Living Scale, and Vertigo Handicap Questionnaire.[33] The Dizziness Handicap Inventory (DHI) is a scoring system validated to assess a subject’s handicap caused by dizziness, and to asses effect of rehabilitation in the affected individual’s emotional, physical, and functional aspects of life.[11] To determine a person's disability grade, Jacobson and Newman created the DHI. With its 25 evaluates divided into three domains—functional, emotional, and physical—the DHI is intended to measure changes in dizziness that are depending on various factors.[33]

Twenty-five questions make up the DHI. The answers range from 0 to 4, with 4 denoting "severe problem" and 0 representing "no problem." The results of every question "Yes" receives a score of 4, signifying a serious issue. "Sometimes" receives a score of 2, signifying a moderate issue. "No" receives a score of 0, signifying that there is no issue. They are then added together to determine the final score. On the DHI, a total score might vary from 0 to 100. A higher score denotes a stronger influence of balance impairment and dizziness on an individual's life. The overall score can be interpreted as follows:

- 16-34 Points (mild handicap)
- 36-52 Points (moderate handicap)
- 54+ Points (severe handicap)

Of the study participants 58.82% showed severe handicap with a mean NLR 6.93 while 39.22% participants showed moderate handicap with a mean NLR 7.20 with no significant difference between the means. However, the difference between the means of serum uric acid for moderate handicap and severe handicap groups was found to be highly significant, with 58.82% of subjects showing severe handicap with a mean serum uric acid level of 9.51 and 39.22% showing moderate handicap with a mean serum uric acid level of 8.42.

Uric acid in correlation with NLR :

Cardiovascular and metabolic disorders are frequently marked by oxidative stress and inflammation. Depending on the surrounding microenvironment, uric acid (UA), a biomarker that can be easily and consistently detected in clinical practice, can serve as a pro-oxidant effector or as a potent scavenger of free radicals.

Hyperuricemia may be a maladaptive response to excessive oxidative stress, which may contribute to the onset and progression of cardiometabolic disease, even though UA is an effective oxygen scavenger and its antioxidant effects prevent metabolic alterations. The development of systemic inflammation and the regulation of several pathways linked to oxidative stress, insulin resistance/diabetes, and endothelial dysfunction are the main UA-related processes responsible for these harmful effects. Consequently, it has been discovered that blood uric acid is linked to coronary atherosclerosis, the degree of coronary artery lesions, and mortality from cardiovascular and other causes.[34]

An indicator of systemic inflammation and immunology, the neutrophil-to-lymphocyte ratio (NLR) is a straightforward hemochrome-derived metric that is nearly always available as part of the overall patient evaluation. It is also becoming recognized as a predictive biomarker in a variety of conditions, including cardiovascular disorders.[34]

Thus, a promising method for risk-stratifying patients with regard to arterial stiffness in CAD patients and thrombolysis in myocardial infarction risk score in STEMI patients is the use of UA and NLR.[34]

According to Peng Luo et al., Patients with Type 2 Diabetes Mellitus who also have hyperuricemia experience inflammation, and insulin resistance(IR) and inflammation are tightly associated.[35] Their research demonstrates that the group with hyperuricemia had significantly higher NLR and IR than the group with normal serum UA, and that among patients in the high serum UA group, UA is positively correlated with both NLR and IR.[35] These findings suggest that NLR may be used as a marker to

assess UA metabolism in type 2 diabetes mellitus patients and determine the level of inflammation among masses, thereby serving as a guide for clinical treatment.

Uric acid:

For decades, the definition of hyperuricemia has been constant: a plasma uric acid content of >416 μmol/L (7.0 mg/dl) in male adults and >357 μmol/L (6.0 mg/dl) in female adults.[36] It has been demonstrated that children's general serum uric acid (SUA) levels climb progressively from infancy through adolescence, with puberty bringing about the fastest increase in SUA .[36] This trend is attributed to hormonal changes.

Male and female SUA levels were nearly identical before to puberty. However, there was a gender difference in SUA following puberty.This phenomena could be explained by the shift in sex hormones that occurs throughout puberty. The body produces more androgens, particularly testosterone, during adolescence.[36] Since muscle hypertrophy is a primary source of purine, higher testosterone encourages muscular anabolism. As a result, SUA will rise in response to an increase in testosterone. Adenosine triphosphate metabolism will also increase with muscle development, and the production of additional purine intermediates in the muscle can have an impact on uric acid levels.[36] Conversely, estrogen in women can encourage the excretion of uric acid, whilst testosterone can hinder this process.[36] It is believed that adult women's lower serum urate concentration than that of males of comparable age is associated with women's higher renal clearance of urate, perhaps as a result of higher plasma estrogen levels.

Hyo Geun Choi et al., stated that lowering blood uric acid levels can help avoid the development or recurrence of comorbid conditions including Meniere's disease and BPPV, for which gout patients are more susceptible.[37] According to Hongsha Wang et al., the extremely damaging emission of reactive oxygen species (ROS) is caused by the release of inflammatory mediators in gout cases.[16] Similarly, hyperuricemia potentiates ROS release; thus, damaging blood vessels and causing disruption in inner ear blood supply.[16]

Very limited studies have been conducted in view of role of inflammatory markers as a diagnostic tool in peripheral vestibular disorders. Hence, in our study we have taken simple parameters- Neutrophil to lymphocyte ratio and serum uric acid to evaluate their association with peripheral vertigo. Though our study is only the tip of the iceberg among wide-ranging possibilities, it is a fruitful step in the ever evolving diagnostics for peripheral vertigo.

# CONCLUSION

Following our research we have come to a conclusion that hyperuricemia is a significant factor contributing to occurence of peripheral vestibular disorders. Neutrophil to lymphocyte ratio was found to be a significant parameter in assessing the inflammatory status of peripheral vertigo patients with a majority showing mild to moderate stress levels and ; moderate to severe handicap on DHI; thereby concluding that peripheral vertigo can be a byproduct of anxiety provoking release of stress hormones and inflammatory markers.

# SUMMARY

A very complicated sign of a malfunctioning balancing system is vertigo. Vertigo is a relatively common presenting symptom for people visiting the emergency room or outpatient clinic. It is challenging to diagnose vertigo due to the involvement of numerous clinical departments and specialties as well as the variety of medical histories.

In this cross sectional study conducted from 27th September 2023 to 26th October 2023 in the department of otorhinolaryngology and head and neck surgery at Jawaharlal Nehru medical college in Belagavi, the potential association of neutrophil lymphocyte ratio and serum uric acid levels in 51 patients with peripheral vertigo was studied.

A scoring system to analyse the severity of vertigo – 'The Dizziness Handicap Inventory'(DHI) score was used for all study participants; who were segregated into mild, moderate and severe handicap based on their DHI scores. As a result, majority of the subjects were found to have experienced moderate to severe handicap ;which pertained to the functional, emotional and physical distress they experienced. This was evaluated via a twenty five questions questionnaire with a total score of 100; a score of 0,2 and 4 given for answers - 'no', 'sometimes' and 'yes' respectively.

The absolute neutrophil count and absolute lymphocyte count was taken for each subject to estimate the neutrophil to lymphocyte ratio(NLR) which showed the presence of mild to moderate stress in majority of the subjects; thus, signifying the role of stress and anxiety as a contributing factor. Furthermore, serum uric acid levels taken into account for all study subjects were found to elevated.

A significant correlation was established between serum uric acid levels and DHI scores; wherein most of the patients reported moderate to severe handicap in accordance with their DHI scores.

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## ANNEXURES

## ANNEXURE-I

## KAHERs JNMC BELAGAVI

## INFORMED CONSENT FORM

## VARIATIONS OF NEUTROPHIL TO LYMPHOCYTE RATIO AND POTENTIAL ASSOCIATION OF SERUM URIC ACID LEVELS IN PATIENTS WITH PERIPHERAL VESTIBULAR DISORDERS: A CROSS SECTIONAL STUDY

Name of Student/Principal Investigator: **REG NO: BE0121005**

Name of Guide/Co Investigators:

**Objective:** To study the variations of neutrophil to lymphocyte ratio and potential association of serum uric acid level in patients with Peripheral vestibular disorders.

**Introduction:** The present study is conducted among patients who are confirmed cases of Peripheral vestibular disorders in ENT & HNS department in KLE's Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi .

**Explanation of procedure:** If you agree to participate in this study, the relevant data will be collected as per the proforma and the final diagnosis will be confirmed.

After getting enrolled in the study, you will be evaluated for Neutrophil lymphocyte ratio and Serum uric acid levels .

**Withdrawal from participation in the study:** Participation in this study is voluntary. You will be free to decide whether to participate in this study or continue participation once enrolled. In case you decide to withdraw your participation, you are free to do so. However, please convey the decision to the principal investigator.

**Possible benefits from participating in the study:** You will/will not have nor get any benefits by participating in this study. The data gathered will help the population at large.

**Possible risks from participating in the study:** There are no risks involved in participating in this study.

**Privacy and confidentiality:** The information collected from you will be coded, to prevent any person from identifying you. Your identity will never be revealed. The data collected from you will be kept confidential and only processed or aggregated data will be used for publication.

**Financial incentives:** You will not receive any payment for participating in this study.

**Authorization for publication of aggregated data:** Results obtained after processing of the aggregated data will be published for scientific purposes and or presented to scientific groups. However, your identity will never be revealed.

**Questions:** In case of any questions with regard to this study, you are free to contact: "Name of student/PI, mobile number, email ID" If you have any question or complaints with regard to your right as study participant you may contact Dr Harsha Hegde, Chairperson, Ethical committee of JNMC, 0831-2473777 Extension 4052.

**Legal rights:** By signing this consent form, we are not waving any of your legal rights.

## CONSENT STATEMENT

I am making a voluntary decision to participate in the study - Variations of neutrophil to lymphocyte ratio and potential association of serum uric acid levels in patients with peripheral vestibular disorders: a cross sectional study.

My signature below indicates that I have decided to participate and I have read the information provided above or the information provided above has been read to me in the language that I understand best. I was given the opportunity to ask questions and that they have been answered to my satisfaction.

**Name of the participant:**

**Signature or left thumb impression of the participant:**

**Name of the witness:**

**Signature or left thumb impression of the witness:**

**Name of the investigator: Signature of the investigator:**

**ANNEXURE II**

**PROFORMA FOR DATA COLLECTION**

**PROFORMA**

**VARIATIONS OF NEUTROPHIL TO LYMPHOCYTE RATIO AND POTENTIAL ASSOCIATION OF SERUM URIC ACID LEVELS IN PATIENTS WITH PERIPHERAL VESTIBULAR DISORDERS: A CROSS SECTIONAL STUDY**

Date:

O.P. No: IP No:

Name: Age:

Sex: Occupation:

Address: Phone No:

D.O.A D.O.D:

CLINICAL PROFILE:

Chief Complaint:

History of Present Illness

Past History:

Personal History:

Family History

Physical Examination:

I) General Physical Examination -

Vital signs: Pulse: Blood Pressure : Respiratory rate :

Pallor- Icterus - clubbing - cyanosis - Lymphadenopathy -

Oedema -

**II) ENT Examination**

**THROAT EXAMINATION -**

**ORAL CAVITY and OROPHARYNX:**

**1.2 INDIRECT LARYNGOSCOPY-**

**2. NECK EXAMINATION**

**3.NOSE EXAMINATION**

1.External appearance

| Root | Bridge | Dorsum | Alae | Tip | columella |
|---|---|---|---|---|---|

Cold spatula test

Cottle's test

Anterior Rhinoscopy

Posterior Rhinoscopy

Paranasal Sinus Examination

| **4. EAR EXAMINATION-** | **Right ear** | **Left ear** |
|---|---|---|
| | Pinna | |
| Preauricular area | | |
| Post auricular area | | |
| External auditory canal | | |
| Tympanic membrane | | |

| **Tuning Fork Test:** | **Right ear** | **Left ear** |
|---|---|---|
| Rinne's test: | | |

256hz

512hz

1024hz

Weber's test:

Absolute Bone Conduction test:

DIZZINESS HANDICAP INVENTORY SCORE:

INVESTIGATIONS:

NEUTROPHIL LYMPHOCYTE RATIO:

SERUM URIC ACID LEVEL

**DIAGNOSIS:**

**The Dizziness Handicap Inventory ( DHI )**

| | |
|---|---|
| P1. Does looking up increase your problem? | Yes<br>Sometimes<br>No |
| E2. Because of your problem, do you feel frustrated? | Yes<br>Sometimes<br>No |
| F3. Because of your problem, do you restrict your travel for business or recreation? | Yes<br>Sometimes<br>No |
| P4. Does walking down the aisle of a supermarket increase your problems? | Yes<br>Sometimes<br>No |
| F5. Because of your problem, do you have difficulty getting into or out of bed? | Yes<br>Sometimes<br>No |
| F6. Does your problem significantly restrict your participation in social activities, such as going out to dinner, going to the movies, dancing, or going to parties? | Yes<br>Sometimes<br>No |
| F7. Because of your problem, do you have difficulty reading? | Yes<br>Sometimes<br>No |
| P8. Does performing more ambitious activities such as sports, dancing, household chores (sweeping or putting dishes away) increase your problems? | Yes<br>Sometimes<br>No |
| E9. Because of your problem, are you afraid to leave your home without having someone accompany you? | Yes<br>Sometimes<br>No |
| E10. Because of your problem have you been embarrassed in front of others? | Yes<br>Sometimes<br>No |
| P11. Do quick movements of your head increase your problem? | Yes<br>Sometimes<br>No |
| F12. Because of your problem, do you avoid heights? | Yes<br>Sometimes<br>No |
| P13. Does turning over in bed increase your problem? | Yes<br>Sometimes<br>No |
| F14. Because of your problem, is it difficult for you to do strenuous homework or yard work? | Yes<br>Sometimes<br>No |
| E15. Because of your problem, are you afraid people may think you are intoxicated? | Yes<br>Sometimes<br>No |

| | |
|---|---|
| F16. Because of your problem, is it difficult for you to go for a walk by yourself? | Yes<br>Sometimes<br>No |
| P17. Does walking down a sidewalk increase your problem? | Yes<br>Sometimes<br>No |
| E18.Because of your problem, is it difficult for you to concentrate | Yes<br>Sometimes<br>No |
| F19. Because of your problem, is it difficult for you to walk around your house in the dark? | Yes<br>Sometimes<br>No |
| E20. Because of your problem, are you afraid to stay home alone? | Yes<br>Sometimes<br>No |
| E21. Because of your problem, do you feel handicapped? | Yes<br>Sometimes<br>No |
| E22. Has the problem placed stress on your relationships with members of your family or friends? | Yes<br>Sometimes<br>No |
| E23. Because of your problem, are you depressed? | Yes<br>Sometimes<br>No |
| F24. Does your problem interfere with your job or household responsibilities? | Yes<br>Sometimes<br>No |
| P25. Does bending over increase your problem? | Yes<br>Sometimes<br>No |

Used with permission from GP Jacobson.

Jacobson GP, Newman CW: The development of the Dizziness Handicap Inventory.

*Arch Otolaryngol Head Neck Surg*

1990;116: 424-427

## DHI SCORING INSTRUCTIONS

The patient is asked to answer each question as it pertains to dizziness or unsteadiness problems, specifically considering their condition during the last month. Questions are designed to incorporate functional (F), physical (P), and emotional (E) impacts on disability.

To each item, the following scores can be assigned:

No=0 Sometimes=2 Yes=4

Scores:

Scores greater than 10 points should be referred to balance specialists for further evaluation.

16-34 Points (mild handicap)

36-52 Points(moderate handicap)

54+ Points(severe handicap)

## ANNEXURE III

## KEY TO MASTER CHART

**Age**: in years

**Sex**: Male & Female

**N:L Ratio**: Neutrophil to lymphocyte ratio determined from the relative neutrophil and lymphocyte percentage

**Serum uric acid :** serum uric acid levels in mg/dl

**DHI Scoring** : Dizziness handicap inventory scoring done based on the DHI questionaire

**Diagnosis :** Diagnosed with any one of the peripheral vestibular disorders

# ANNEXURE IV MASTER CHART

| SL.NO | NAME | AGE | SEX | IP/OP NO. | N:L RATIO | SERUMURIC ACID(mg/dl) | DHI SCORE | DIAGNOSIS |
|---|---|---|---|---|---|---|---|---|
| 1 | Husenabi | 45 | Female | 1136289 | 9(92:10) | 8.4 | 48 | BPPV |
| 2 | Sharanavv a | 55 | Female | 1139101 | 6(90:15) | 7.4 | 44 | BPPV |
| 3 | Sadashiv | 46 | Male | 1160367 | 8(90:11) | 8.4 | 54 | BPPV |
| 4 | Nisha mohanan | 31 | Female | 6458497 | 3(75:20) | 3.4 | 30 | BPPV |
| 5 | Roopali vishal | 25 | Female | 1154400 | 6(89:14) | 6 | 36 | BPPV |
| 6 | Sandeep | 36 | Male | 6786512 | 4(80:20) | 6.2 | 36 | BPPV |
| 7 | Gangavva | 65 | Female | 1163200 | 7(88:12) | 7.8 | 37 | BPPV |
| 8 | Nagesh vasant | 56 | Male | 1138258 | 8(88:11) | 8.8 | 54 | MENIERE'S |
| 9 | Vanishri | 39 | Female | 6881716 | 4(88:18) | 6.4 | 36 | BPPV |
| 10 | Shivaji laxman | 53 | Male | 1139268 | 11(99:9) | 8.6 | 52 | BPPV |
| 11 | Elizabeth | 59 | Female | 1168867 | 6(88:14) | 9 | 66 | MENIERE'S |
| 12 | Kallappa | 35 | Male | 6917967 | 7(88:12) | 9 | 62 | BPPV |
| 13 | Minaxi | 87 | Female | 1167975 | 6(84:15) | 9 | 66 | BPPV |
| 14 | Changona manohar | 75 | Female | 1167324 | 6(88:14) | 8.4 | 58 | BPPV |
| 15 | Vishwanat h | 74 | Male | 1166811 | 15(91:6) | 9.2 | 60 | BPPV |
| 16 | Anita mane | 32 | Female | 6921263 | 8(88:11) | 8.8 | 58 | BPPV |
| 17 | Pratanya | 39 | Female | 6907116 | 7(88:12) | 9.4 | 60 | BPPV |
| 18 | Nitesh kakade | 31 | Male | 1164890 | 8(92:12) | 9.2 | 52 | BPPV |
| 19 | Aasiya ameerjan | 47 | Female | 6712192 | 9(96:11) | 9 | 48 | BPPV |
| 20 | Baburao | 71 | Male | 4799092 | 8(88:11) | 8.6 | 52 | BPPV |
| 21 | Vanishre | 39 | Female | 6682721 | 9(94:11) | 9.4 | 48 | BPPV |
| 22 | Shridevi | 65 | Female | 6832182 | 11(99:9) | 8.8 | 54 | BPPV |
| 23 | Jagadevi | 78 | Female | 6718602 | 9(94:11) | 9.2 | 44 | BPPV |
| 24 | Soundarya | 39 | Female | 6819309 | 9(96:11) | 8.4 | 46 | BPPV |
| 25 | Annapoorn a | 45 | Female | 6701601 | 7(88:12) | 8.2 | 48 | BPPV |
| 26 | Ranishekhar | 46 | Female | 6805805 | 9(96:11) | 9.2 | 40 | BPPV |
| 27 | Indutai | 81 | Female | 6610311 | 9(94:10) | 9.2 | 52 | BPPV |
| 28 | Raghu M. Talwar | 47 | Male | 6809564 | 8(92:12) | 10.2 | 56 | BPPV |
| 29 | Madhuri shamvargi | 42 | Female | 6917116 | 9(96:11) | 9.6 | 62 | BPPV |
| 30 | Basappa nagappa | 54 | Male | 6917998 | 9(92:10) | 9 | 64 | BPPV |
| 31 | Shweta mahesh | 40 | Female | 6915249 | 12(99:8) | 10.6 | 56 | BPPV |
| 32 | Bharat basu | 46 | Male | 6795227 | 6(88:14) | 9.4 | 52 | BPPV |
| 33 | Prakash sandeep | 49 | Male | 6909981 | 9(94:11) | 9.6 | 58 | BPPV |
| 34 | Manik ganesh | 42 | Male | 6909106 | 8(90:12) | 9.8 | 62 | BPPV |
| 35 | Shilpa malagi | 34 | Female | 6772979 | 7(88:12) | 9.4 | 54 | BPPV |
| 36 | Girish yallesh | 50 | Male | 6907477 | 11(99:9) | 10.2 | 58 | BPPV |
| 37 | Satish lohar | 34 | Male | 6773110 | 12(99:8) | 10 | 64 | BPPV |
| 38 | Deepali satyappa | 25 | Female | 4930268 | 9(92:10) | 9.6 | 56 | MENIERE'S |
| 39 | Bharamann a | 65 | Male | 1192454 | 10(90:9) | 8.8 | 54 | BPPV |
| 40 | Lakshmavv a | 54 | Female | 1182562 | 8(92:11) | 9 | 52 | BPPV |
| 41 | Bhairu K. Patil | 50 | Male | 1185936 | 7(88:12) | 8.6 | 48 | BPPV |
| 42 | Rebecca David | 63 | Female | 1187962 | 8(90:11) | 9 | 64 | BPPV |
| 43 | Asha | 64 | Female | 1186742 | 9(96:11) | 10.2 | 52 | BPPV |
| 44 | Shabeena | 62 | Female | 1187832 | 8(90:12) | 9.4 | 60 | BPPV |
| 45 | Sumaira | 58 | Female | 1184532 | 7(88:12) | 8.6 | 56 | BPPV |
| 46 | Shahida | 60 | Female | 1180100 | 9(92:10) | 9.6 | 64 | BPPV |
| 47 | Cha-ran- raj | 48 | Male | 10013269 | 11(99:9) | 10 | 62 | BPPV |
| 48 | Mohammad | 46 | Male | 10013011 | 12(99:8) | 10.8 | 66 | BPPV |
| 49 | Akash | 40 | Male | 10014467 | 9(92:10) | 10.4 | 68 | BPPV |
| 50 | Parasram | 44 | Male | 10012311 | 11(99:9) | 11.2 | 64 | BPPV |
| 51 | Shweta Mahesh | 40 | Female | 6915249 | 12(99:8) | 10.8 | 64 | BPPV |