



# **A Study of Etiopathogenesis of Different Vertigo Syndromes**

**Vaidehi Hande <sup>a\*</sup> and Shraddha Jain <sup>a#</sup>**

<sup>a</sup> *Department of Otorhinolaryngology, Jawaharlal Nehru Medical College, Datta Meghe Institute of Medical Sciences, Sawangi (Meghe), Wardha, India.*

## **Authors' contributions**

*This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.*

## **Article Information**

DOI: 10.9734/JPRI/2021/v33i61A35592

## **Open Peer Review History:**

This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: <https://www.sdiarticle5.com/review-history/81050>

**Study Protocol**

**Received 20 October 2021**

**Accepted 26 December 2021**

**Published 28 December 2021**

## **ABSTRACT**

**Background:** Dizziness or disturbed postural awareness is common presentation in varying age groups. Dizziness can be classified into various types like Rotatory Vertigo, Imbalance/disequilibrium, Pre syncope/Light headedness and Psychogenic. Classically, there are four vertigo syndromes which are most commonly accepted among Otolaryngologists. However, cervicogenic vertigo is missing from the list of these vertigo syndromes. This study aims to assess the etiological factors for vestibular and central vertigo and other non-vestibular forms of vertigo and dizziness.

**Methodology:** This will be a prospective observational study conducted in the Department of Otorhinolaryngology, Jawaharlal Nehru Medical College, Wardha. About 75 patients presenting with symptoms of dizziness, tinnitus with associated nausea vomiting in the out-patient department will be included in this study. Patients will undergo clinical examination including Special Clinical Tests for vertigo like Dix-Hall pike Manoeuvre, Tandem walking and Dysdiadokokinesis. Collected data will be fed to appropriate statistical programme and analysed.

**Expected Results:** Relevant data on different etiopathogenic causes of vertigo will be obtained.

**Conclusion:** Better understanding of the various etiologies of various vertigo syndromes, their associations in various age groups and systemic diseases help better treatment outcomes.

<sup>‡</sup> Junior Resident;

<sup>#</sup> Professor and Unit Head;

<sup>\*</sup> Corresponding author: E-mail: [handevaidehi96@gmail.com](mailto:handevaidehi96@gmail.com);

*Keywords: Dizziness; vertigo; meniere's disease; cervicogenic giddiness; vestibular neuronitis.*

## 1. INTRODUCTION

Vertigo/ dizziness is defined as disturbed postural awareness and could range from feeling of sensation of spinning of self or surrounding. Dizziness or disturbed postural awareness is common presentation in varying age groups. Dizziness can be classified into various types like Rotatory Vertigo, Imbalance/disequilibrium, Pre syncope/Light headedness and Psychogenic. Classically, there are four vertigo syndromes which are most commonly accepted among Otolaryngologists. However, cervicogenic vertigo is missing from the list of these vertigo syndromes, as pointed out by the authors of this article [1].

**Vertigo:** Vertigo refers to a sensation of movement which may be perceived as own self moving with respect to the surrounding or as surrounding moving with respect to the person and is the most common type. It may be associated with head movements and nystagmus. The causes can be attributable to the vestibular labyrinth (Meniere's disease, BPPV, Labyrinthitis), some conditions of central nervous system (CNS) like posterior circulation stroke and Vertebrobasilar insufficiency and cervicogenic giddiness (Barre Leiou Syndrome and Rotational Vertebral Artery Occlusion). The last category of cervicogenic giddiness has not been included as a differential diagnosis in otolaryngologists list [2,3].

**Presyncope:** Presyncope or light-headedness or blackouts may be described as a feeling of fainting and may be associated with excessive salivation, heat, or diplopia and may last for seconds and minutes. It typically occurs on getting up from lying position in sitting or standing posture and may represent underlying cardiovascular conditions [4,5]. It can also be sometimes vestibular but needs independent evidence, which may not be found on vestibular testing like caloric test [6].

**Disequilibrium:** Disequilibrium or imbalance is sensation of falling down mostly while walking. Patients indicate that they are dizzy but "not at the head" and prefer sitting or lying down [7]. It is usually seen in neurological disorders like Parkinson's Disease and peripheral neuropathies. Medications like benzodiazepines and TCAs may also cause disequilibrium [4].

Cerebellar and spinal cord pathologies can also cause such symptoms [2]. There may be associated symptoms like weakness, ataxia or memory loss. Proprioceptive cervical vertigo may also cause disequilibrium but is not mentioned in any Otolaryngology textbooks [2,3].

**Non- Specific Dizziness:** Some patients may not be able to describe their symptoms and may give vague complaints most of the time may be due to psychiatric disorder [4,7]. Psychiatric causes are 2<sup>nd</sup> most prevalent type accounting for 15 percent for giddiness in patients [6,7]. No otorhinolaryngology textbook mentions cervicogenic dizziness as a separate entity. There is no mention of cervicogenic giddiness as a cause of imbalance. Vertigo syndromes have been masked as there are lot of overlaps between them also there are few missing from the link. Senior author has observed, that there is a link missing between cervicogenic and vestibular dizziness [1]. There are certain overlaps in these vertigo syndromes observed by the authors of this article. They have noted that cervicogenic dizziness can coexist with vestibular syndromes in a majority of cases [eg. cervicogenic dizziness and Meniere's or BPPV] and have hypothesized that the same pathophysiology causing cervicogenic dizziness may also be responsible for giving rise to these vestibular syndromes. The concept that Vestibular and Cervicogenic dizziness, could be spectrum of the same disease, in some cases, is a novel hypothesis proposed by the authors [1]. We are undertaking this research to study the various etiologies involved in these syndromes and to help unmask the overlaps between them.

Vertigo syndromes have similar clinical presentation but underlying cause can be classified mainly as peripheral/central or vestibular/non-vestibular. Benign Paroxysmal Positional Vertigo, Meniere's disease, Vestibular neuritis, canalolithiasis, perilymph fistulas, are most common vestibular causes of vertigo [8].

It has been well established that vertigo occurs with acute suppurative otitis media, acute suppurative labyrinthitis and chronic suppurative otitis media with or without cholesteatoma [9]. Meniere's disease is an important cause of giddiness arising from the inner ear [10]. Psychogenic vertigo, pregnancy related vertigo,

vertigo induced by vestibulotoxic drugs also have similar presentations.

Cervical spine abnormalities like spondylosis, inflammatory conditions like rheumatoid arthritis, degenerative diseases like spondylotic myopathies trigger the proprioceptors and the vestibular nucleus causing cervicogenic dizziness. Cervicogenic dizziness is defined as having presence of disorientation, neck pain, limited cervical range of motion, imbalance, unsteadiness, [11]. Those who believe in cervicogenic dizziness consider it as most common cause of vertigo. Whether cervicogenic dizziness is a diagnosis of exclusion (when all other causes of vertigo are ruled out) or a separate entity associated with underlying cause is controversial. There are 4 types of cervicogenic dizziness, namely Proprioceptive cervical vertigo, Barre'le'ou Syndrome, Rotational vertebral artery vertigo (Bow Hunter syndrome) and Migraine associated cervicogenic vertigo [12]. Central causes of vertigo are-Vertebrobasilar insufficiency, Posterior inferior cerebellar artery syndrome, Basilar migraine, Multiple sclerosis, Epilepsy, tumors of brainstem and fourth ventricle.

Auto-immune conditions like Systemic sclerosis characterized by fibrosis of blood vessels, compromises the inner ear especially cochlea. As cochlea is highly sensitive to blood changes and hypoxia, patients have vestibular symptoms [13]. It has been found that people with sensorineural hearing loss are more prone to vertigo [11]. A lot of research is going on in this field and much more is needed to further ascertain the multiple sites, causes and interconnected syndromes which give rise to vertigo [14]. As auditory and vestibular systems are anatomically proximal, a basis for correlation between them can be drawn stating, any compromise in auditory system will lead to a pathology in the vestibular system. An association between the degrees of hearing loss and postural instabilities and balance changes in children with SNHL has been found in previous studies [14]. Diagnosis of aetiologies of vertigo syndromes is often difficult, may require elaborate history taking, examination and vestibular assessment protocols to come to a diagnosis. Diagnosis of vertigo syndromes is mainly clinical and majority are diagnosed by history alone. Patients with aural symptoms have mainly vestibular vertigo, however certain cases of cervicogenic vertigo also may have aural symptoms. Patients with central causes of

vertigo present with unsteadiness of gait, however cervicogenic causes also present with unsteadiness of gait, which can be seen in rotational vertebral artery vertigo/ Bow Hunter syndrome. Tumarkin's otolithic crisis presents with drop attacks. Light headedness or presyncope directs towards cardiovascular causes of vertigo like cardiac tamponade, sick sinus syndrome, arrhythmias. Diagnosis of cervicogenic vertigo requires history taking with clinical examination in addition requires proper cervical tests which are gold standard for diagnosing Benign Paroxysmal Positional Vertigo like Dix Hallpike Manoeuvre, Meniere's disease is diagnosed clinically primarily on history of episodes of vertigo. Various investigation modalities are currently being developed in diagnosis of dizziness like electro-nystagmography, video nystagmography, vestibular evoked myogenic potential. Diagnosis may also be supported from radiological investigations like CT scans.

Vertigo has varied clinical presentations. It is a challenge for ENT practitioners to diagnose etiologies of vertigo. Opinions from Neurophysicians, Neurosurgeons, Orthopedicians and Internal medicine physicians are essential.

Though diagnosis of this condition is primarily clinical and patients respond to medical management, a study into the various causative factors to aid in better management and long term prognosis is proposed. There are very few studies regarding protocol for diagnosis of etiopathogenesis of vertigo. The present study is being undertaken to study different etiologies for vertigo syndromes, and possible overlaps, to hypothesize the likely pathophysiology, which could help develop a comprehensive management protocol for vertigo of any origin.

## 1.1 Rationale

- As vertigo is a symptom, not a disease, a primary concern for this is that though maximum cases present to otolaryngologists, same symptom can be byproduct of numerous pathologies.
- There could be likely overlaps in various vertigo syndromes, with a common underlying pathology, with divergent pathophysiology for vertigo at different levels, which if addressed could aid in better management of the patient.

## 1.2 Aim

To study the aetiopathogenesis of different vertigo syndromes

## 1.3 Objectives

1. To study the etiological factors associated with vestibular vertigo.
2. To study the etiological factors associated with central vertigo.
3. To study etiological factors associated with other non-vestibular forms of vertigo and dizziness.

## 2. METHODS

### 2.1 Study Setting

A study will be conducted in the Department of Otorhinolaryngology, of Jawaharlal Nehru Medical College, Sawangi(Meghe), in Wardha district of Maharashtra. Population under study will be local patients presenting with symptoms of dizziness, tinnitus with associated nausea vomiting in the out-patient department as well as patients referred from other departments with similar complaints among the age group of elder than 4 years excluding children below age of 4 years and genetic diseases.

### 2.2 Sample Size

In terms of research sample is a group of people, that are taken from a larger population for measurement. The sample is a representative of the population to ensure that we are able to generalize the findings from the research sample selected to the whole population.

Sample size with designed error of margin formula:

$$n \text{ equals to } (Z \text{ alpha}/2 \text{ square} \times P (1-P))/d \text{ square}$$

Where,

Z alpha/2 is the level of significance at 5% =1.96

P= Prevalence of vertigo = 0.71%=0.071

So minimum sample size required will be 75 patients.

75 patients with complaints of dizziness above the age of 4 years will be enrolled.

## 2.3 Study Design

This is a Prospective observational study which will be conducted in the Department of Otorhinolaryngology Acharya Vinoba Bhave Rural Hospital, Sawangi (Meghe), Wardha, attached to Jawaharlal Nehru Medical College, Sawangi (Meghe), Wardha, located in Central India comprising of predominantly rural population of east Maharashtra including all the patients with dizziness or vertigo in the age group of elder than 4 years excluding children below age of 4 years and genetic diseases. Sample size including 75 patients studied from November 2020 to November 2022 including patients attending Otorhinolaryngology OPD or emergency with complaints of giddiness or dizziness, or referred from -General Medicine, Pediatrics, Neurology, Orthopedics and other departments for the above complaints.

In all the 75 patients of dizziness or vertigo, a detailed history will be obtained according to a pre-designed proforma. This will be followed by a general and systemic examination with special emphasis on cardiovascular and a detailed neurological assessment. Special Clinical Tests for vertigo of different origin like Dix-Hall Pike Manoeuvre, Tandem walking, Dysdiadokokinesis, tests for postural hypotension, Vertebro-basilar insufficiency, cervicogenic dizziness will be carried out. A detailed E.N.T evaluation will be done with the help of a Bull's lamp, head mirror, otoscope and microscope. In all the patients' blood profile investigations and other relevant investigation will be performed for finding association with other systemic diseases. Audiological investigations will include Pure Tone Audiometry and Impedance Audiometry where indicated. Pure tone audiometry will be conducted in all patients as a baseline investigation for assessing the type and degree of hearing loss. It will be carried out in a sound treated room with ALPS AD 2000 where least is 250 Hz and highest is 8000 Hz and from 5db to 100 db. The frequency dial will be adjusted to 1000 Hz. And the minimum intensity at which the subject hears will be taken as a threshold for air conduction (AC) at the frequency. Similarly, all the other frequencies 250 Hz, 500 Hz, 2000 Hz, 4000 Hz and 8000 Hz will be tested for air conduction threshold and measured by 5 'up' and 'down' technique. The bone conduction threshold will similarly be measured. The pure tone average of the air conduction threshold will be calculated by taking the mean of the hearing thresholds at 500 Hz,

1000 Hz and 2000 Hz. Then, according to the WHO classification of hearing impairment, the degree of hearing loss will be assessed. Also, the hearing thresholds at each frequency will be noted. Brain Stem Evoked Response Audiometry (BERA) will be done, where indicated.

Radiological investigations like X ray cervical spine will be done in all cases and MRI brain, CT/ MRI Cervical spine, Vertebral artery Doppler, MR Angiogram of vertebral artery to diagnose vascular occlusions leading to dizziness where indicated. MRI brain (1.5 Tesla) for ruling out central vertigo, where indicated. High Resolution Computed Tomography (CT) temporal bone and contrast-enhanced CT of brain will be done in cases of suspected complicated otitis media or cases of post-traumatic vertigo. Videonystagmography will be done and Vestibular Evoked Myogenic Potential will be Recorded (from cervical musculature in suspected cervicogenic dizziness patients) where indicated. Findings thus obtained will be entered in the proforma meant for the study.

## 2.4 Inclusion Criteria

1. All the patients with dizziness or vertigo in the age group of more than 4 years.

## 2.5 Exclusion Criteria

1. Children below the age group of 4 years.
2. Genetic diseases.

## 3. EXPECTED RESULTS

Relevant data on different etiopathogenic causes of vertigo will be obtained.

## 4. DISCUSSIONS

A common symptom for patients seen by primary care doctors, neurologists, and otolaryngologists is dizziness. Peripheral vestibular disorders are among the most common causes of dizziness, but central nervous system disorders must be omitted. An overview of the epidemiology of dizziness, the distinction between central and peripheral vertigo, and the key causes of dizziness is given in this article. As one of the most common medical concerns, it affects about 20 percent to 30 percent of people.

For a sense of disequilibrium, dizziness is a general term. Vertigo is a subtype of dizziness, described as a movement illusion

caused by the vestibular system's asymmetric involvement.

Vertigo, nausea, vomiting, extreme ataxia, multidirectional nystagmus that is not suppressed by optic fixation, and other neurologic symptoms are caused by central vestibular lesions affecting the pons, medulla, or cerebellum. Dysequilibrium without vertigo, presyncope, and psychophysiology are the other forms of dizziness [15].

The peripheral vestibular organ within the bony labyrinth of the inner ear is closely connected to the other parts of the equilibrium system. As a result of its constant active interaction with the other elements, it plays a major role in ensuring that we can maintain our balance. In the event of a disorder, otogenic vertigo can occur. Important evidence of a peripheral-vestibular disturbance is provided by the patient's history of dizziness, and confirmation of the suspected diagnosis is achieved by clinical and other appropriate examinations and tests. Common differential diagnoses include benign paroxysmal positional vertigo, Ménière's disease, and vestibular neuropathy. These can be readily differentiated by applying a systematic approach, and usually respond to treatment [16]. Related studies were reviewed [17-21].

Cervicogenic vertigo is not mentioned in any otolaryngological textbooks, however, those who believe cervicogenic dizziness consider it to be the most common cause of dizziness. There are various etiologies of cervicogenic dizziness which includes abnormal afferents from cervical proprioceptors due to spasms or abnormalities in cervical spine configurations, decreased blood flow in vertebral arteries due to excessive sympathetic activity or direct compression of vertebral artery and it is also frequently associated with migraine [17]. Vestibular dizziness are also associated with cervical symptoms, suggesting that both vestibular and cervical dizziness may coexist and both may have common underlying aetiology in neck [22-26].

### 4.1 Disorders of Vestibular System

Cervical vertigo is caused by an irregular afferent feedback from joint receptors in the upper cervical region to the vestibular nucleus. Whiplash injuries also cause disturbances of cervical proprioception, leading to vertigo in the cervix. BPPV or Benign Paroxysmal Positional

Vertigo is due to fractured utricle otoconia dislodged into endolymph that interferes with normal dynamics of endolymph. Meniere's disease occurs when the system has elevated endolymphatic fluid leading to high system pressure leading to dysfunction in hearing and balance. In superior semicircular canal there is erosion of superior bony canal causing erratic pressure system in the canals and therefore dizziness. Vestibular migraine is seen in migraineurs as they have heightened sensitivity of vestibular system.

## 5. CONCLUSION

All the data collected will be evaluated, and conclusions will be derived for better understanding of the various etiologies of various vertigo syndromes, their associations in various age groups and systemic diseases for better treatment outcome.

## CONSENT

As per international standard, parental written consent will be collected and preserved by the author(s).

## ETHICAL APPROVAL

As per international standard or university standard written ethical approval will be collected and preserved by the author(s).

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

## REFERENCES

1. Jain S, Jungade S, Ranjan A, et al. Revisiting Meniere's Disease as Cervicogenic Endolymphatic Hydrops and Other Vestibular and Cervicogenic Vertigo as Spectrum of Same Disease: A Novel Concept. *Indian J Otolaryngol Head Neck Surg*; 2020. Available: <https://doi.org/10.1007/s12070-020-01974-y>
2. Watkinson JC, Clarke RW, editors. Evaluation of Balance. In: Bronstein A., editors. *Scott-Brown's Otorhinolaryngology and Head and Neck Surgery*. 8th edition Great Britain. CRC Press. 2018;2:775-815.
3. Attry S, Gupta VK, Marwah K, Bhargav S, Gupta E, Vashisth N. Cervical vertigo- pathophysiology and management: an update. *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*. 2016;1: 98-107.
4. Post RE, Dickerson LM. Dizziness: a diagnostic approach. *American Family Physician*. 2010;82:361.
5. Runser LA, Gauer R, Houser A. Syncope: Evaluation and differential diagnosis. *American family physician*. 2017;95:303-12.
6. Kroenke K, Lucas CA, Rosenberg ML, Scherokman B, Herbers Jr JE, Wehrle PA, Boggi JO. Causes of persistent dizziness: A prospective study of 100 patients in ambulatory care. *Annals of internal medicine*. 1992;117:898-904.
7. Kelm Z, Klapchar K, Kieliszak CR, Selinsky C. Psychogenic dizziness: An important but overlooked differential diagnosis in the workup of the Dizzy patient. *J Am Osteopath Assoc*. 2018;118:e22-7.
8. James A. Nelson, Erik Viirre. The clinical differentiation of cerebellar infarction from common vertigo syndromes the clinical differentiation of cerebellar infarction from common vertigo syndromes. *Western Journal of Emergency Medicine*; 2009
9. Michael J. LaRouere, Michael D. Seidman, Jack M. Kartush. Medical and surgical treatment of vertigo. *Vertigo - Medical and Surgical Treatment*; March 1998. Available: [http://timesofindia.indiatimes.com/articleshow/68570219.cms?utm\\_source=contentofinterest&utm\\_medium=text&utm\\_campaign=cppst](http://timesofindia.indiatimes.com/articleshow/68570219.cms?utm_source=contentofinterest&utm_medium=text&utm_campaign=cppst)
10. Alexander S Reiley, Frank M Vickory, Sarah E Funderburg, Rachel A Cesario, Richard A Clendaniel. How to diagnose cervicogenic dizziness – *Archives of Physiotherapy*; 2017
11. Furman JM, Cass SP. *Balance Disorders: A Case-Study Approach*. Philadelphia: F.A. Davis; 1996
12. Maysa Bastos Rablo, Ana Paula Corona. Auditory and vestibular dysfunctions in systemic sclerosis: Literature Review.
13. Strupp M, Brandt T: Diagnosis and treatment of vertigo and dizziness. *Dtsch Arztebl Int*. 2008p105:173–180.
14. Karatas M. Central vertigo and dizziness: Epidemiology, differential diagnosis, and common causes. *The neurologist*. 2008 Nov 1;14(6):355-64.
15. Krause E, Gürkov R, Hempel JM. Otogenic (labyrinthine) vertigo--when the ear fails to

- keep us in equilibrium. *MMW Fortschritte der Medizin*. 2007 Jan 1;149(1-2):29-32.
16. Ciquinato DS, Silva RA, Oliveira MR, Gil AW, Marchiori LL. Posturographic Analysis in the Elderly with and without sensorineural Hearing Loss. *International Archives of Otorhinolaryngology*. 2020 Dec;24(4):496-502.
  17. Murray, Christopher J L, Aleksandr Y Aravkin, Peng Zheng, Cristiana Abbafati, Kaja M Abbas, Mohsen Abbasi-Kangevari, Foad Abd-Allah, et al. Global Burden of 87 Risk Factors in 204 Countries and Territories, 1990–2019: A Systematic Analysis for the Global Burden of Disease Study 2019. *The Lancet*. 2020;396(10258):1223–49. Available:[https://doi.org/10.1016/S0140-6736\(20\)30752-2](https://doi.org/10.1016/S0140-6736(20)30752-2)
  18. Vos Theo, Stephen S Lim, Cristiana Abbafati, Kaja M Abbas, Mohammad Abbasi, Mitra Abbasifard, Mohsen Abbasi-Kangevari, et al. Global Burden of 369 Diseases and Injuries in 204 Countries and Territories, 1990–2019: A Systematic Analysis for the Global Burden of Disease Study 2019. *The Lancet*. 2020; 396(10258):1204–22. Available:[https://doi.org/10.1016/S0140-6736\(20\)30925-9](https://doi.org/10.1016/S0140-6736(20)30925-9)
  19. Wang, Haidong, Kaja M Abbas, Mitra Abbasifard, Mohsen Abbasi-Kangevari, Hedayat Abbastabar, Foad Abd-Allah, Ahmed Abdelalim, et al. Global Age-Sex-Specific Fertility, Mortality, Healthy Life Expectancy (HALE), and Population Estimates in 204 Countries and Territories, 1950–2019: A Comprehensive Demographic Analysis for the Global Burden of Disease Study 2019. *The Lancet*. 2020;396(10258) :1160–1203. Available:[https://doi.org/10.1016/S0140-6736\(20\)30977-6](https://doi.org/10.1016/S0140-6736(20)30977-6)
  20. Khatib M, Sinha A, Gaidhane A, Simkhada P, Behere P, Saxena D, et al. A systematic review on effect of electronic media among children and adolescents on substance abuse. *Indian Journal of Community Medicine*. 2018;43(5):S66–72. Available:[https://doi.org/10.4103/ijcm.IJCM\\_116\\_18](https://doi.org/10.4103/ijcm.IJCM_116_18).
  21. James SL, Castle CD, Dingels ZV, Fox JT, Hamilton EB, Liu Z, Roberts NL, Sylte DO, Bertolacci GJ, Cunningham M, Henry NJ. Estimating global injuries morbidity and mortality: Methods and data used in the Global Burden of Disease 2017 study. *Injury Prevention*. 2020 Oct 1;26(Suppl 2):i125-53.
  22. Kumar A, Chery L, Biswas C, Dubhashi N, Dutta P, Dua VK, Kacchap M, Kakati S, Khandeparkar A, Kour D, Mahajan SN. Malaria in South Asia: prevalence and control. *Acta tropica*. 2012 Mar 1;121(3):246-55.
  23. Chole RH, Patil RN, Basak A, Palandurkar K, Bhowate R. Estimation of serum malondialdehyde in oral cancer and precancer and its association with healthy individuals, gender, alcohol, and tobacco abuse. *Journal of Cancer Research and Therapeutics*. 2010 Oct 1;6(4):487.
  24. Pradhan S, Madke B, Kabra P, Singh AL. Anti-inflammatory and immunomodulatory effects of antibiotics and their use in dermatology. *Indian Journal of Dermatology*. 2016 Sep;61(5):469.
  25. Acharya S, Shukla S, Mahajan SN, Diwan SK. Acute dengue myositis with rhabdomyolysis and acute renal failure. *Annals of Indian Academy of Neurology*. 2010 Jul;13(3):221.
  26. Gadbail AR, Chaudhary M, Patil S, Gawande M. Actual Proliferating Index and p53 protein expression as prognostic marker in odontogenic cysts. *Oral Diseases*. 2009 Oct;15(7):490-8.

© 2021 Hande and Jain; This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

*Peer-review history:*

*The peer review history for this paper can be accessed here:*

<https://www.sdiarticle5.com/review-history/81050>