AUDIOLOGICAL FINDINGS AND NON-AUDIOLOGICAL CORRELATES IN INDIVIDUALS WITH ACOUSTIC NEUROMA: A SYSTEMATIC REVIEW

J. CHINNARASU

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August 2022

CERTIFICATE

This is to certify that this dissertation entitled "**Audiological Findings and Non-audiological Correlates in Individuals with Acoustic Neuroma: A systematic review**" is a bonafide work submitted as a part of the fulfilment of the degree of Master of Science (Audiology) of the student with Registration Number: 20AUD014. This has been carried out under the guidance of the faculty of this institute and has not been submitted earlier to any other University for the award of any other Diploma or Degree.

Mysuru

August, 2022

Dr. M. Pushpavathi

Director

All India Institute of Speech and Hearing

Manasagangothri, Mysuru-570006

CERTIFICATE

This is to certify that this dissertation entitled "**Audiological Findings and Non-audiological Correlates in Individuals with Acoustic Neuroma: A systematic review**" has been prepared under my supervision and guidance. It is also being certified that this dissertation has not been submitted earlier to any other University for the award of any other Diploma or Degree.

Mysuru

August 2022

Dr Devi N

Associate professor in Audiology

All India Institute of Speech and Hearing

Manasagangothri, Mysuru-570006

DECLARATION

This is to certify that this dissertation entitled "**Audiological Findings and Non-audiological Correlates in Individuals with Acoustic Neuroma: A systematic review**" is the result of my own study under the guidance of Dr. Devi N, Associate professor in Audiology, Department of Audiology, All India Institute of Speech and Hearing, Mysuru and has not been submitted earlier to any other University for the award of any other Diploma or Degree.

Mysuru **Registration No: 20AUD014**

August 2022

Dedicated to My

APPA (நா. ஜெயகோபி)

INDIRAMMA (இந்திரா)

CHITRAMMA (சித்ரா)

AND MY BIG FAMILY……

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"Yaadhum Oore Yaavarum Kelir"

The World is My town and its people are My kinsmen

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ABSTRACT

Tumors affecting the eighth cranial are often referred to as eighth nerve tumors, acoustic neuromas or vestibular schwannoma, acoustic neurilemomas, acoustic neurinomas, and acoustic tumors. Many individuals with vestibular schwannoma experience hearing loss along with tinnitus and dizziness. The accurate diagnosis of acoustic neuromas requires audiological evaluation, radiological evaluations, and other brain imaging findings. This review study aims to compile the articles comprising audiological and non-audiological evaluations of computed tomography (CT) and Magnetic resonance imaging (MRI) and their correlations in individuals with acoustic neuroma. The full-length articles published in the English language during the past ten years (2011 – 2021) were selected for this systematic review. These selected studies were analyzed using the CASP (Critical Appraisal Skills Programme) checklist for qualitative research to avoid the risk of bias. Of 38 full-length articles, 13 studies were included in the systematic review. The results of these articles reported that most patients with acoustic neuroma have significant unilateral hearing loss, mostly descending or sloping type. Along with the hearing loss, these individuals showed marked abnormality in auditory brainstem response (ABR) peaks and a decrement in the speech discrimination scores. About 4 to 6% of the patients with acoustic neuroma did not show any symptoms of hearing loss. The audiological test results did not significantly correlate with the tumor size or the site. However, small tumors or tumors at the early stage are difficult to find and diagnose through audiological tests alone. Non-audiological evaluations such as CT and MRI have increased the diagnosis of acoustic neuroma at the early stage. The incidence of vestibular schwannoma has increased globally during the past thirty years. This systematic review insists on the utility of non- audiological evaluation in diagnosing

acoustic neuroma, even though the patient shows no audiological symptoms such as hearing loss and tinnitus. Also, it recommends the audiologist consider the radiological findings while determining the diagnosis in patients indicating unilateral hearing loss, sudden SNHL, tinnitus, reduced speech understanding, and dizziness.

CHAPTER 1

INTRODUCTION

Hearing impairment or hearing loss is the reduction in the hearing ability. It is also called ‘hypacusis' or hard of hearing. Majorly it was classified into two types; conductive and sensorineural hearing loss. The most common type was sensorineural hearing loss (SNHL), which refers to any cause of hearing loss due to a cochlea, auditory nerve, or central nervous system pathology. The diseases or disturbances in the cochlea which cause hearing impairment are known as cochlear pathology. The diseases or disturbances which affect the vestibulocochlear nerve and neural auditory pathway are termed retro cochlear pathology, and that type of hearing loss is called neural hearing loss (Dhingra & Dhingra, 2021; Gelfand, 2015; Katz., Chasin, English, Hood, and Tillery, 2015; Zahnert, 2011).

The common cause of neural hearing loss are tumors such as meningioma, acoustic neuroma, and other cerebellopontine angles (CPA) tumors. Tumors affecting the eighth cranial nerve are often referred to as eighth nerve tumors, acoustic neuromas, acoustic neurilemomas, acoustic neurinomas, and acoustic tumors. However, the technically preferred term is vestibular schwannomas because most eighth cranial nerve tumors involve the Schwann cells, which are present in the vestibular division of the nerve (Consensus Developmental Panel, 1994). The great majority of them are unilateral. However, ~ 5% of them are bilateral and are associated with a genetic syndrome called neurofibromatosis type 2. Acoustic tumors in the CPA are also called cerebellopontine angle or posterior fossa tumors. Acoustic neuroma constitutes 90% of all cerebellopontine angle tumors and 10% of all brain tumors (Sekhar & Jannetta, 1984).

Regarding pathology, vestibular schwannomas (VS) are often encapsulated round or oval lesions and originate from the vestibular division of the eighth cranial nerve. VS often develops at the intersection of the schwann and glial cells and extends into the CP angle. They are also typically seen in the internal auditory canals. A significant lesion can occasionally compress the fifth cranial nerve in addition to the cochlear nerve and the lower cranial nerves. A large lesion may compress the brain stem. Early signs of tumors include hearing loss, ringing in the ears, giddiness, and headache due to compression on the vestibulocochlear nerve (Zamani, 2000). Acoustic neuroma might occur sporadically or might be inherited as part of NF2. The autosomal dominant disorder of the 22nd chromosome is associated with acoustic neuroma, meningiomas, neurofibromas, and gliomas (Black, 1983). The tumor may appear in. every age of life, but the main manifestation is between the 3rd and 5th decade (Rosahl et al., 2017).

Traditionally, vestibular schwannomas have been classified according to the tumor size (Tos et al., 1992). But the problem with the traditional classification method was that it was based on the tumor's diameter. Sekiya et al. (2000) proposed classifying vestibular schwannoma based on Magnetic Resonance Imaging (MRI) to precisely delineate the extent of the tumor into the internal auditory canal (IAC) or IAC plus Cerebellopontine angle. The incidence rates of VS vary worldwide from 1 to 20 cases per million inhabitants per year and are reported to be on the increase globally (Hoffman et al., 2006; Howitz et al., 2000; Lanser et al., 1992). More than 3300 vestibular schwannoma cases are diagnosed yearly in the United States. The study findings on the African population strongly suggest that VS is very rare in the African population (Ohaegbulam et al., 2017).

Acoustic neuroma can be diagnosed in many ways, such as through audiological evaluations, radiological testing, and histopathological examination of the temporal bone (Mahmud et al., 2003). Radiological testing includes Magnetic Resonance Imaging (MRI), Computed Tomography (CT), and X-ray imaging (Crabtree & House, 1964) .Much literature supports the use of Magnetic Resonance Imaging in diagnosing acoustic neuroma since it visualizes the internal parts of the brain and neural pathways (Consensus Developmental Panel, 1994; Reznitsky et al., 2019; Stangerup & Caye-Thomasen, 2012). Since unilateral hearing loss is the primary symptom of vestibular schwannoma, audiological evaluation could be used to diagnose the patients. The audiological tests used in diagnosis were pure tone audiometry, speech audiometry, acoustic reflex testing, and auditory brainstem response. Auditory brainstem response audiometry was considered the best audiological diagnostic tool for acoustic neuroma (Schmidt et al., 2001).

The sensitivity and specificity of research articles that compare Brainstem Evoked Response Audiometry (BERA) with MRI were not similar (Haapaniemi et al., 2000; Moffat et al., 1993; Quaranta et al., 2001). BERA measurement has high sensitivity compared with MRI for acoustic neuromas, which are larger by 1cm (Chandrasekhar et al., 1995; Dhingra & Dhingra, 2021; Wilson et al., 1992). Many patients with vestibular Schwannoma experience hearing loss and tinnitus. Suppose hearing impairment is present along with tinnitus. In that case, reduced speech identification scores (SIS) and absent ABR peaks with poor morphology, acoustic neuroma could be suspected, and MRI scans were performed on those individuals (Gelfand, 2015; Katz, Chasin, English, Hood, 2015). Since hearing loss could be the earlier symptom of acoustic neuroma, an audiological diagnosis should be made before the MRI (Dhingra & Dhingra, 2021; Gelfand, 2015; Katz, Chasin, English, Hood, 2015). With the increasing research in using the different test battery approaches and higher correlations among the different tests to diagnose individuals with AN, it is required to systematically compile and correlate the audiological and non-audiological findings of acoustic neuroma.

1.1 Need for the study

Vestibular schwannoma or acoustic neuroma is a rare disease, but it accounts for 80% of cerebellopontine (CP) angle 6–7% of all intracranial and tumors (Butowski, 2015; Sanna & Hamada, 2011; Zamani, 2000). Due to the mass effect, vestibular schwannoma, despite being benign, poses a risk to intracranial structures and has a slight risk of developing into malignancy (Gupta et al., 2020). It could cause severe damage to the auditory system of the individual. Jeong et al. (2016), Sakamoto et al. (2001), Zamani, (2000) have concluded that progressive sensorineural hearing loss (SNHL) is one of the prominent symptoms of vestibular schwannoma (VS). There would be a significant difficulty in understanding speech out of proportion to the pure tone hearing threshold (Dhingra & Dhingra, 2021). Only 5 to 10% of tumors have an origin from the auditory branch. However, the early symptoms were mostly auditory, and vestibular symptoms generally occur later (Clemis et al., 1986). The auditory symptoms will manifest earlier than the vestibular symptoms, but a deficiency in vestibular function is most typically found when the AN is already rather substantial (Quaranta et al., 2001). Though some patients with acoustic neuroma exhibit no hearing loss, the percentage in such cases do not exceed 5%. Almost 90% of the patients with acoustic neuroma showed sensorineural hearing loss (Dhingra & Dhingra, 2021; Quaranta et al., 2001). The prognosis of the condition depends on a timely diagnosis of vestibular schwannoma. All patients with sensorineural hearing loss must have vestibular schwannoma ruled out, especially if the hearing loss is asymmetric (Bento et al., 2012). Due to the loss of normal physiology of hearing in patients with acoustic neuroma, audiological evaluation plays a vital role in identifying acoustic neuromas even at the early stage.

At the same time, radiological evaluations such as Magnetic Resonance Imaging (MRI) and Computed tomography (CT) have improved the detection rate of the lesion in acoustic neuroma. Acoustic/vestibular schwannoma develops gradually, growing at roughly 1–2 mm each year (Gupta et al., 2015). It often may not manifest any obvious symptoms in the earlier stages. Early diagnosis is crucial because surgical therapy leads to better hearing and facial nerve outcomes when the tumor is smaller at the time of diagnosis (Lee et al., 2015). The detection of small size tumors might be difficult in CT, but MRI could detect even the intra-canalicular lesions, which are smaller in size (Lhuillier et al., 1992; Mark et al., 1993). Due to the frequent use of MRI scanning, the percentage of tumors diagnosed in the early stages has increased (Selesnick & Jackler, 1993; Stangerup & Caye-Thomasen, 2012). Through coronal and axial thin sections of MRI, the relation of the tumor to the brainstem and cranial nerves might be seen. Acoustic neuroma detection via MRI has gained popularity due to its increased accuracy and low incidence of false negative instances (Kabashi et al., 2020). In Minnesota, the USA, computed tomography (CT) was utilized for VS diagnosis for the first time in 1978, while MRI for VS diagnosis debuted in 1984. Pre-CT, CT, and MRI incident rates were 1.4, 1.4, and 3.3 per one lakh people year, respectively. Diagnosis of Vestibular schwannoma has been increased due to the utility of non- audiological evaluations such as Magnetic Resonance Imaging and computed tomography (Marinelli et al., 2018).

Many audiological studies, as well as radiological evaluations, have been done on patients with vestibular schwannoma. But collective data and the recent updates in the findings are not reviewed much. Also, a systematic review study which comprises the recent audiological findings, comparison and correlation of audiological and non-audiological findings such as CT, MRI, and the incidence and prevalence among the various people, is much needed to know more about the disease.

1.2 Aim of the study

The current study aims at reviewing the significant audiological and non-audiological correlates in the studies conducted in the past ten years (2011 – 2021) on individuals diagnosed with acoustic neuroma.

1.3 Objectives of the study:

The specific research questions for the study include:

1. What are the audiological findings in individuals with acoustic neuroma over the past ten years?
2. What are the comparison and correlations between audiological and non – audiological findings in patients with an acoustic neuroma?

Chapter 2

METHODS

The systematic review was conducted based on the Preferred Reporting Systematic Review and Meta-Analysis Statement (PRISMA) (Page et al., 2021). A systematic literature search was carried out for peer-reviewed articles published from 2011-2021.

2.1 Information Source

The databases for the following were extensively searched for studies on audiological findings and non- audiological correlates in individuals with acoustic neuroma in databases such as Pub Med, Google Scholar, and Science Direct. Lists of references and citations were searched manually for further relevant studies.

2.2 Search Strategy

The search in the informational source was carried out using key terms, related search phrases, derivatives, and MeSH words relevant to the study combined with Boolean operators such as 'AND,' 'OR,' 'NOT’. "Acoustic neuroma" OR "Vestibular schwannoma" OR "Auditory tumors" OR "Acoustic tumors" AND "Cerebello pontine angle tumors" AND "Space occupying lesions in the auditory pathway" NOT "Brain tumors" NOT "Neurofibromatosis type-2" were used as the key terms for searching studies. The lists of references and citations were manually checked to find more relevant studies.

2.3 Study Selection

The specific inclusion and exclusion criteria for the selection of studies were as follows.

2.3.1 Inclusion Criteria:

- Original articles containing human participants with appropriate samples and relevant diagnostic tests were considered.
- Articles focused on the audiological and non-audiological findings of acoustic neuroma were included.
- The articles published in the English language were considered for the review.
- The selection was based on the PECOS criteria (Methley et al., 2014)

Participant	Individuals diagnosed with acoustic neuroma
Exposure	Audiological tests and non-audiological evaluations such as CT and MRI
Control	Individuals without acoustic neuroma or with other types of tumors
Outcomes	Findings, comparisons, and correlations of audiological and non-audiological evaluations
Study design	Retrospective and prospective studies

2.3.2 Exclusion Criteria:

- Articles with low methodological quality and language apart from English were excluded.

- Case reports, systematic reviews, meta-analysis letters to editors, and editorials were excluded.

2.4 Data extraction:

The review results were analyzed using the Rayyan QCRI systems (Qatar Computing Research Institute) and Mendeley desktop reference manager system, and the duplicate studies were eliminated. The studies that met the inclusion criteria were identified by screening the titles and abstracts retrieved from the search strategies. After that, the full text of the potential studies was retrieved and matched to see if they were eligible. The extracted data included article title, author detail with their affiliation, year of publication, research design, study, population sample size, age group comparison group method of outcome measures, and keyword specific to the title of this study.

2.5 Quality assessment:

The Critical Appraisals Skills Programme for Diagnostic test study (CASP) was used to assess the quality of the individual studies. The findings have been shown in the result section in detail.

Chapter 3

RESULTS

A total of 4180 articles were identified using database searches, references, and citations. With 14 duplicates eliminated, the remaining 4166 articles were included for title/ abstract screening. Following the title and abstract review, 38 articles were selected for the full-length article screening. Out of 38 full-length articles chosen for the eligibility assessment, 20 were excluded due to the irrelevant study design (only audiological findings or the radiological evaluations). Of the left out 18 articles, one article was excluded again as it was a case report study, one article was removed because it was a background article about Cerebello pontine angle tumors, and at last three articles were removed because they consisted of the irrelevant study population (patients with tumors other than acoustic neuroma and vestibular schwannoma). Finally, 13 articles were selected for this study. A detailed Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flowchart for the selection of the study is shown in Figure 3.1

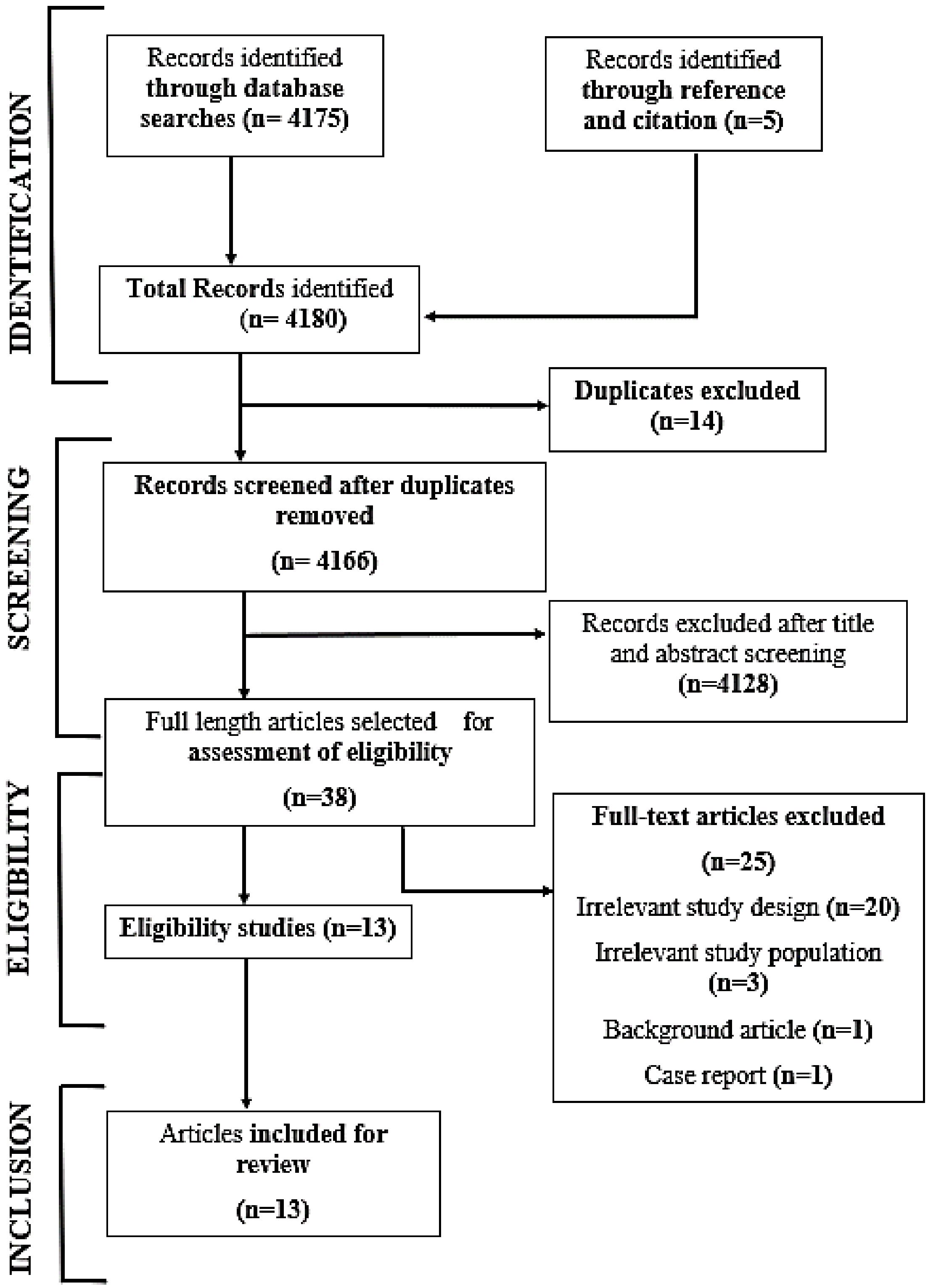

Figure 3.1: PRISMA flowchart for the selection process of articles included in the review

3.1 Study Characteristics

All articles that were finalized and selected for the review focused on the retrospective analysis of audiological evaluation, such as pure tone audiometry, non-audiological evaluation, such as Magnetic Resonance Imaging, and five articles focused on the diagnostic results of auditory brainstem response (ABR) audiometry. One article thoroughly evaluated the medial acoustic neuroma – a type of acoustic neuroma.

Population: The participants in the included studies are individuals with acoustic neuroma, and they are all in the age range of 11 to 81 years. The total population in these 13 studies was 6797 patients.

Exposure: In this study, the exposure of interest was audiological and non-audiological evaluations in individuals with acoustic neuroma. The audiological test analyzed in these studies were pure tone audiometry, speech audiometry, tinnitogram, and auditory brainstem response, and one study even included Cervical VEMP. The non-audiological evaluations examined are Magnetic Resonance Imaging and Computed Tomography.

Comparators: The outcomes of both audiological tests and non-audiological evaluations such as CT and MRI of individuals with acoustic neuroma are compared with individuals without acoustic neuroma (Ahsan et al., 2015; Jeong et al., 2016; Lee et al., 2011), individuals with tumors other than acoustic neuroma (Kim et al., 2016). In some studies, the results are compared within individuals with acoustic neuroma or vestibular schwannoma (Bento et al., 2012; Eliezer et al., 2019; Kim et al., 2014; Lee et al., 2015; Patel et al., 2015; Salem et al., 2019; Valame & Gore, 2017). One article compared the results of cerebellopontine angle tumors with or without internal acoustic canal extension (Tutar et al., 2013).

Outcomes: All articles were based on the retrospective analysis of audiological findings and non-audiological evaluations of individuals with acoustic neuroma or vestibular schwannoma. The audiological and non-audiological correlates of acoustic neuroma were the primary outcome interest in all the selected articles.

Table 3.1 Summarizes study design, research question, study population details, testing parameters, and study outcomes focusing on the audiological and non-audiological correlates of acoustic neuroma.

Sl.no	Author & year	Title	Study design and Research question	Study Population	Testing parameters used	Results	Inference
1.	Jeong et al. (2016)	Abnormal Magnetic Resonance Imaging Findings in Patients with Sudden Sensorineural Hearing Loss	Retrospective study design. →To evaluate MRI findings of patients with Sudden sensorineural hearing loss	291 patients with sudden sensorineural hearing loss(SSNHL) → 153 women and 138 men →Mean age- 45.7 years (11- 81 years)	Pure tone audiometry (PTA), Magnetic resonance imaging (MRI)	**Audiological findings: -** → Out of 291, 13 had MRI abnormality, in that nine patients had a vestibular schwannoma → In that nine patients with vestibular schwannoma, i) Mean PTA threshold was 56 ± 23 dB ii) Mean speech discrimination score was 63% ± 34% → In one patient with a nodular enhancing lesion in the left internal auditory canal fundus and basal turn of the cochlea compatible with Intra labyrinthine schwannoma, low frequency mixed hearing loss (46 dB threshold) was found in the left ear →In the 14-year-old	→ MRI of the internal auditory canal revealed abnormalities in 4.5% (13 of 291) of SSNHL patients; the vestibular schwannoma was the most frequent abnormality found in these patients.. → Compared to medium-sized (1.1-2.9 cm) and big tumours (>3 cm), SSNHL is more commonly found in tiny tumours (1 cm). → There was no relationship between tumor size and the incidence of SSNHL. → The MRI findings for intralabyrinthine schwannoma typically showed a lack of normal fluid density on T2-weighted images and a comparable enhancement

						patient with subacute labyrinthine hemorrhage, the right ear which had vestibular schwannoma showed a hearing threshold of 106 dB → For a 56-year-old patient with distant metastasis into the internal auditory canal from stomach cancer, pure tone audiometry revealed total hearing loss on the ear with tumor. → In a 17-year-old patient with a dermoid cyst, the right ear threshold was 71 dB, and the SDS was 24%. **Non-audiological findings: -** →Out of 291, 13 patients had an abnormality in MRI, and the most common finding was vestibular schwannoma	on gadolinium-enhanced T1-weighted images. → Patients with SSNHL who might have a labyrinthine haemorrhage may not be detected by an MRI performed at early stage. → In patients with IAC metastasis, gadolinium-enhanced MRI findings of heterogeneous nodular enhancement in the internal auditory canal and cerebellopontine angle with leptomeningeal enhancement may contribute to a differential diagnosis. → Due to the leakage of lipid metabolites into the endolymphatic system following a dermoid cyst rupture, which may have altered endolymphatic homeostasis and resulted in SSNHL, precontrast T1 weighted MRI might

						involving IAC or cerebellopontine angle (n=9) and the age range of those nine patients was 40 to 65years. →One patient showed well defined nodular enhancing lesion in the left IAC fundus and basal turn of the cochlea compatible with Intra labyrinthine schwannoma, who has low frequency mixed hearing loss →Subacute labyrinthine haemorrhage was found in the MRI findings of a 14-year-old patient → In a 56-year-old patient with distant metastasis into the internal auditory canal from stomach cancer, the findings of MRI revealed the presence of leptomeningeal carcinomatosis with	reveal lipid metabolites inside the endolymphatic space.

						enhancing lesions in the right IAC →Based on MRI findings, a 17-year-old patient with sudden SNHL was diagnosed with a dermoid cyst. → Hearing loss has been more frequently linked to lateral tumours that originate in or extend to the internal auditory canal.	

Sl.no	Author & year	Title	Study design and Research question	Population	Testing parameters used	Results	Inference
2.	Kim et al. (2016)	Audiologic evaluation of vestibular schwannoma and other cerebellopontine angle tumors	Retrospective study design → To evaluate the clinical difference between Vestibular schwannoma (VS) and other CPA tumors	171 patients with cerebellopontine angle tumors →They were separated into two groups:- 1) Patients with vestibular schwannoma (number of patients =116) →46 males and 70 females. → The mean age of this group was 53.9 ± 14.4 years, and the mean duration of symptoms was 16.3± 13.1 months. 2) Patients with	Pure tone audiometry (PTA), speech audiometry, tinnitogram, auditory brainstem response (ABR) and Magnetic resonance imaging (MRI)	**Audiological findings:** In the vestibular schwnnoma group, → the mean hearing threshold was 38.9 ±34.3 dB → Average speech discrimination score was 73.1±34.1% →In tinnitogram findings, 1) Average frequencies = 5012.5 ± 3504.9 Hz. 2) Average loudness = 62.5±27.4 dB. → Out of 116 patients with vestibular schwannoma, ABR was present in 92, complete absent in 24, and abnormal in 104. → Measurement values of ABR in VS group as follows: - i) wave V latency - 4.57 ± 2.36 ii) ILD of wave V - 3.22 ± 2.93	→ Cerebellopontine angle constitutes about 5 to 10% of intracranial tumors. →Vestibular schwannoma accounted for 70-90% of CPA tumors, 5-10% being meningiomas, and 3 to 7% were epidermoid cysts. → In this study, vestibular schwannoma accounted for 65% of the tumors in the cerebellopontine angle → Sensorineural hearing loss was

				non- VS tumors (number of patients is 55) →17 males and 38 females. →The mean age of the non- VS group was 49.3±15.8 years, and the mean duration of symptoms was 15.5±13.7 months.		iii) I-V interval - 3.14 ± 2.43 iv) I-III interval - 1.78 ± 1.63 v) III-V interval – 2.20 ± 2.47 In the non- vestibular schwannoma group, →the mean hearing threshold was 31.2±28.3 dB → Average speech discrimination score was 80.3±37.2% →In tinnitogram findings, 1) mean frequencies = 4281.2 ± 3504.9 Hz 2) loudness = 61.3± 25.3 dB. → Out of 55 patients, ABR was present in 45 and absent in 10. → Measurement values of ABR in the non- vestibular schwannoma group are as follows: - i) wave V latency - 5.46 ± 2.47 ii) ILD of wave V - 3.45 ± 2.62	one of the strongest clinical signs of the presence of vestibular schwannoma. → Non- vestibular schwannoma type of tumors differ from vestibular schwannoma through different symptom patterns, shapes, and neuro anatomic locations. → The sloping sensorineural hearing loss was the characteristic of vestibular schwannoma, which was not a clinical sign of patients with meningioma.

						iii) I-V interval - 3.46 ± 2.62 iv) I-III interval - 1.42± 1.26 v) III-V interval – 2.82 ± 2.36 → There was no difference between audiological test results and the tumor site in both groups. → Sensorineural hearing loss was considered the strongest clinical sign of vestibular schwannoma → During the early stage of the tumor, hearing loss might occur at all frequencies → The characteristic of a large tumor was low-frequency hearing loss, specifically at 500 Hz. → Most typical audiometric configuration in patients	→ Though the size of the tumor is similar, the hearing level of the patients with vestibular schwannoma were poorer than those of patients with non- VS tumor → This study concludes that the most typical combination was hearing loss and tinnitus in patients with vestibular schwannoma. Of symptoms, whereas, in patients with non-vestibular schwannoma type of tumor, hearing loss with dizziness was more common in

						with vestibular schwannoma was the sloping hearing loss which is also mentioned as a descending type →Compared with the non-VS type of tumor, the hearing level in patients with vestibular schwannoma was significantly poor. **Non-audiological findings:** → In this study, vestibular schwannoma accounted for 65% of the tumors in the cerebellopontine angle → The internal auditory canal and cerebellopontine angle, IAC with CPA plus brainstem compression, and internal auditory canal alone were the areas where vestibular schwannoma was most frequently seen. → Non-vestibular schwannoma type of tumors were most often	combined symptoms

						present in the cerebellopontine angle alone, followed by Cerebellopontine angle plus brainstem compression	

Sl.no	Author & year	Title	Study design and Research question	Population	Testing parameters used	Results	Inference
3.	Tutar et al. (2013)	Audiological correlates of tumor parameters in acoustic neuroma	Retrospective study design → To determine whether PTA and SDS are correlated with the size of the tumor and the presence of intrameatal extension in the acoustic neuroma	115 patients with CPA tumor with/without IAC extension →Thirty-seven patients were excluded because of neurofibromatosis →76 unilateral Acoustic neuroma patients included →43 Male and 33 Female. → Mean age at diagnosis was 46.10 years	PTA, Speech audiometry, Magnetic Resonance Imaging	**Audiological findings** → Out of 76 patients, 73 with unilateral Acoustic neuroma were affected with a unilateral SNHL, and three patients had normal hearing at the time of diagnosis. →A high-frequency sloping hearing loss was present in most of the patients with Acoustic neuroma (61%); about 12% of cases had a flat configuration, and the audiogram was U shaped in 8% of cases. → In the contralateral ear, 48 individuals had normal hearing, and 28 indicated sensorineural hearing loss. → On the tumor ear;- 1) Mean SDS =57%, 2) Mean SRT = 46 dB → On the opposite ear 1) Mean SDS = 96% 2) Mean SRT = 10 dB	→ One of the most vital clinical signs for the presence of acoustic neuroma is sensorineural hearing loss. →High-frequency slope had the highest occurrence in acoustic neuromas, followed by flat loss. → There was a marked decrease in speech discrimination scores and speech recognition scores → The tumor's size and hearing

							→ There was a statistically significant difference between SDS of ear with tumor and opposite ears ($p < 0.001$) → Pure tone thresholds, SRT, and SDS did not significantly correlate with the tumor size or its expansion into the IAC **Non-audiological findings** →Of 76 patients, 33 had an extension to the internal auditory canal; the mean tumor size was 18.58 mm → The patients were divided into two groups based on the tumor size, 1) group 1 → < 20 mm 2) group 2 → > 20 mm. → The findings of the t-tests did not reveal a significant difference between the two groups thresholds at each frequency, SRT, and SDS.	level at each frequency did not correlate with one another.. → Additionally, there is no apparent relationship between the tumor's size, its extent to the internal auditory canal, and other factors like the speech recognition threshold, maximal speech discrimination scores, the configuration of the audiogram, and other variables.

Sl.no	Author & year	Title	Study design and Research question	Population	Testing parameters used	Results	Inference
4.	Salem et al. (2019)	Audiological Evaluation of Vestibular Schwannoma Patients with Normal Hearing	Retrospective study design → to examine the characteristics of the ABR and the prevalence of normal hearing among patients with vestibular schwannoma. → To investigate the relationship between ABR abnormalities and the degree of tumour involvement in the vestibulocochlear nerve or brainstem, as well as the impact of tumour size or location	4000 patients were diagnosed with vestibular schwannoma between 1986 and 2017	PTA, Auditory Brainstem Response, Computed Tomography, and Magnetic Resonance Imaging	→ Out of 4000 clinical reports of patients with vestibular schwannoma, 3768 were selected for this study. **Audiological findings:** - → ABR data were available for 114 patients out of 162 with normal hearing. → The sensitivity of the ABR test was 73.6% (98/133. →In findings of ABR, there was a statistically significant relationship between tumor grade and ABR → Small tumours (grades 0 and 1) had a sensitivity of 64.5%, while tumours of medium to large size	→ The female to male patient ratio reported in this study was 2.3:1, and it was similar to the ratio of 3:1 given by various authors → There was a slight predominance of the vestibular schwannoma on the left side (51.9%) found in this study. → In this study, the majority of the patients (64.7%) were between the ages of 30 and 50. → Tinnitus was the most frequent symptom among the patients (54.4%), followed by subjective hearing loss (43.3%) and vertigo (35.3%).

						had a sensitivity of 97.2%. **Non- audiological findings: -** →The tumors were classified from grade 0 to grade 5 according to their size through imaging techniques. → Grade 0 (intrameatal) was the most prevalent tumour grade, occurring in 64 cases, followed by grade 1 (48 patients).	→As the tumor size increased; abnormality of the auditory brainstem response also increased. → For contralateral ABR recording, giant tumors altered the measurements. → There was no evident association between the ABR results and symptoms. Additionally, the occupation of the fundus at the tumor's site has no impact on ABR results. → Even if the patient has normal hearing, ABR testing should be a part of the usual test battery on the patient's initial appointment. Given the incidence of

							vestibular schwannoma, starting with ABR testing rather than going to the MRI would be more cost-effective..

Sl.no	Author & year	Title	Study design and Research question	Population	Testing parameters used	Results	Inference
5.	Ahsan et al. (2015)	Clinical Predictors of Abnormal Magnetic Resonance Imaging Findings in Patients with Asymmetric Sensorineural Hearing Loss	Retrospective study design →To assess the relationship between asymmetrical SNHL patients' abnormal MRI findings and clinical and audiometric factors.	615 patients with asymmetrical SNHL received MRI	PTA, Speech audiometry, Magnetic Resonance Imaging	**Audiological findings: -** → Out of 615 patients, 451 fulfilled the criteria for asymmetric hearing loss, and they are included in this study. → The minimum 10-dB difference at three consecutive frequencies or the highest 15-dB difference at two consecutive frequencies were seen in all patients with the difference of 15 dB at 3 kHz. **Non- audiological findings: -** → Of the 451patients, 48 had abnormal MRI findings (10.6%) → CPA or IAC tumor was the most typical abnormality found. The most common MRI abnormality noted in CPA or IAC mass (n=21;	→ This study did not examine the correlation between audiometric criteria and tumor size due to the small number of patients with CPA or IAC tumor. → They observed that the presence of a CPA mass was substantially correlated with unilateral tinnitus and a difference of 15 dB at 3 kHz. → Retro cochlear pathology cannot be diagnosed directly using standard audiometry. Retro cochlear pathology could be detected by an abnormal acoustic reflex.

						40%) → An abnormal MRI finding was associated with sudden hearing loss, however the association did not reach statistical significance (p=0.054). → This study found that only patients with a difference of 15 dB between ears at 3 kHz significantly increased abnormal MRI results.	→ ASNHL may be screened on patients using ABR. A vestibular schwannoma larger than 1 cm can be detected by the ABR test, since the ABR sensitivity is higher for larger tumors. → This study also concluded that an abnormal MRI did not significantly indicate a CPA/IAC mass in cases of sudden acute hearing loss. → However, those patients who have asymmetric SNHL that contains this audiometric feature should undergo a MRI. → If a patient also has unilateral tinnitus, vertigo, or

							dizziness in addition to having asymmetric SNHL, they are more certain to have abnormal findings in MRI.

Sl.no	Author & year	Title	Study design and Research question	Population	Testing parameters used	Results	Inference
6.	Patel et al. (2015)	Hearing in Static Unilateral Vestibular Schwannoma Declines More Than in the Contralateral Ear	Retrospective study design → In order to determine if the IAC/CPA mass itself causes the affected ear's hearing loss to progress more rapidly than the opposite ear	One hundred fifty patients with a diagnosis of acoustic neuroma. →Only patients with static acoustic neuroma were included. → Patients with other otological history were excluded. → Patients who had progressive tumors were excluded → Finally, 15 patients were included.	Pure tone audiometry, speech audiometry, Magnetic Resonance Imaging.	**Audiological findings: -** → There was a significant difference between the unaffected and damaged ears in audiometric measurements (*P* <.05) → The average increase in the 4 kHz level difference between ears was 10.9 dB, which reaches a maximum difference increase of 45 dB. → The average increase in the difference between the ears' speech discrimination scores was 24%, with a maximum increase of 100%. → It should be mentioned that most patients' hearing	→ The results of this study showed that, when compared to the opposite ear, hearing thresholds and speech discrimination gradually decline in the ear with a static AN. → The difference in speech discrimination scores tended to expand however some patients displayed transient reduction or widening of the difference. → It is concluded that even if an acoustic neuroma is not growing, hearing thresholds and speech discrimination scores will decline in the affected ear. → Finally, this study revealed that even while patients with static

				→ 4 males and 11 females. → Age range – 32 to 78 years old		deteriorated with time. However, a small number of them retained stable hearing in some measurements. **Non- audiological findings: -** → Reviewing the MRI images revealed no evidence of tumor growth. → All patients had tumors that affected the internal auditory canal, and five of them also had tumors that affected the cerebellopontine angle. → The IAC tumor's involvement ranged from 3 to 14 mm. The dimensions of cerebellopontine angle tumor ranged from 3 to 15 mm.	IAC/CPA masses may still have "serviceable hearing," it is likely that their hearing may decline with time.

Sl.no	Author & year	Title	Study design and Research question	Population	Testing parameters used	Results	Inference
7.	Dunn et al. (2014)	Medial acoustic neuromas: clinical and surgical implications	Retrospective study design To evaluate the clinical and imaging features of medial acoustic neuroma	52 adult patients who were identified with medial acoustic neuroma → 33 Women, 19 Men. → Age range- 19 to 74 years. Mean 43 years and median 45 years	Pure tone audiometry, speech audiometry, MRI and CT	**Audiological findings: -** →Most common Symptoms were progressive hearing loss, about 88% of patients, and unsteady gait (38%). → 46 out of 52 patients with Medial acoustic neuroma reported hearing loss. → Preoperatively, out of 46 patients, 10 had hearing levels ≤ 30dBHL and > 70% speech discrimination, 10 had > 30dBHL but ≤ 50dBHL and > 50% speech discrimination, 6 patients had > 50 dBHL and ≥ 50 speech discrimination and 26 had < 50% speech discrimination with any level of pure tone threshold.	→ Acoustic neuroma occupies the cisternal compartment with no extension into the lateral IAC and is termed "medial acoustic neuroma." → Some level of hearing could be present despite a larger tumor size. This study showed that hearing preservation is an achievable goal in these patients, especially if they had goa od hearing before surgery. →Tumor adherence to the cochlear nerve in the IAC3 and increases in IAC pressure from tumor13 may be responsible for hearing loss in the acoustic neuroma patient. But the absence of significant

						→ Postoperatively, of 10 patients with ≤ 30dBHL before surgery, functional hearing was preserved in 5 of 10 patients with postoperative audiograms **Non- audiological findings: -** → The tumor size ranged from 13 mm to 53 mm in maximum diameter, with an average size of 34.5 mm →Forty-seven patients (90.4%) had tumors of 25 mm or larger, and five patients had small tumors (<25 mm). →In addition to CN involvement, larger tumors compress and displace the brainstem, distorting the usual view of the brain tumor interface; draining veins in large and giant tumors may be unusually	intracanalicular extension may provide an opportunity to preserve hearing despite the large size of the medial tumor. → Understanding this variant of acoustic neuroma, a high rate of hearing preservation will be achievable even with the larger size of the medial tumor

						distended and fragile, increasing the risk of hemorrhage	

Sl.no	Author & year	Title	Study design and Research question	Population	Testing parameters used	Results	Inference
8.	Lee et al. (2015)	Otologic manifestations of acoustic neuroma	To investigate the otorhinolaryngological factors associated with acoustic neuroma	114 patients with acoustic neuroma → 46 males 68 females Mean age = 52.2 ± 13.1 years. → 63 had AN on the right ear, and 51 had AN on the left ear.	Pure tone audiometry (PTA), speech discrimination scores, tinnitogram, auditory brainstem response (ABR), and Magnetic resonance imaging (MRI)	**Audiological findings:** → The most common AN symptoms were dizziness (31.8%), tinnitus (7.7%), and hearing loss (51.7%). → The sloping hearing loss was the most prevalent, followed by flat-concave and ascending patterns. →16.3% of 114 patients, or 19 people, had acute sensorineural hearing loss symptoms. → The convex pattern of the audiogram showed the greatest SDS reduction. →Tinnitogram findings revealed, 1) Average frequency = 5012 ± 3379 Hz	→ There was no correlation between tumour size or location and the degree of hearing loss, speech discrimination scores, tinnitogram findings, or ABR results. →Sudden Sensorineural hearing loss was the initial symptom of acoustic neuroma. → One of the key symptoms in individuals with small tumours is dizziness. As the tumor increases

						2) Average loudness = 62.5 ± 27.4 dB → Waves I, III, and V latency durations were prolonged or absent in 30.3%, 52.9%, and 49.9% of patients with ABR, respectively. → The interaural wave I-V latency difference is more than 4.4 ms in 30.3% of cases. **Non- audiological findings:** → Acoustic neuroma was primarily located in the internal auditory canal and Cerebellopontine angle (43.9%), followed by the IAC + CPA + brainstem compression (29.3%) and IAC alone (26.7%). → There were no	in size, a compensatory mechanism is activated. → Tinnitus could get worsen as the tumor grows. → According to the results of this study, those who experience otologic symptoms like hearing loss, tinnitus, poor speech discrimination scores, and abnormal ABR should get an MRI to rule out an acoustic neuroma.

						acoustic neuromas in the CPA and CPA plus brainstem compression in any patients. → Most tumors had a dimension of 10 to 20 mm. Only two patients had a size of less than 10mm.	

Sl.no	Author & year	Title	Study design and Research question	Population	Testing parameters used	Results	Inference
9.	Valame and Gore (2017)	Role of cervical vestibular evoked myogenic potentials and auditory brainstem response in the evaluation of vestibular schwannoma	Retrospective study design To determine whether cervical VEMP, in conjunction with the ABR, is useful in the diagnosis of vestibular schwannoma	15 cases of vestibular schwannoma, from May 2012 to May 2014 →Age range 19 to 68 years. Mean age – 43.6 years	Pure tone audiometry, cervical VEMP auditory brainstem response (ABR), and Magnetic resonance imaging (MRI)	Out of 15 patients, unilateral sporadic vestibular schwannoma was present in thirteen, and bilateral neurofibromatosis type2 was present in two. **Audiological findings: -** → There was a significant severity of hearing loss found in all the patients with large tumors → Out of nine patients with small tumors, three (33.3%) showed severe to profound hearing loss in the ear with vestibular schwannoma. →ABR was absent in the ears of seven patients with large tumors (87.5%). → Only three patients with a small tumor showed an absent ABR (33.33%).	→ Large tumours that have displaced or compressed the brainstem to the opposite side may exhibit abnormal response in the contralateral ear while passing through the lower brainstem in the cVEMP's descending course → In 80% of patients with large unilateral tumors, the cVEMP was absent or had a lower amplitude in the contralateral ear. It might be caused by the mass effect of the tumor on the descending MVST or the contralateral inferior vestibular nuclei.

						→ All patients in this study, with the exception of one with a small tumour, showed abnormalities in cVEMP on the tumor side, regardless of the size of the tumour or the degree of hearing loss. **Non- audiological findings** → The fifteen patients were classified into two groups based on their tumor size. 1) Small tumors (<2.5 cm) (n=9) 2) Large tumors (>2.5 cm) (n=8)	→ The cVEMP is an important tool in the differential diagnosis of the lesion site in addition to the ABR. → Since cVEMP does not require residual hearing for diagnosis, it may be essential to detect retrocochlear pathology when other audiological procedures, like ABR and acoustic reflex, are ineffective since they need residual hearing.

Sl.no	Author & year	Title	Study design and Research question	Population	Testing parameters used	Results	Inference
10.	Bento et al. (2012)	Vestibular schwannoma: 825 cases from a 25-years experience	Retrospective study design → To assess the indications and symptoms seen in the 825 vestibular schwannoma cases that underwent surgery between 1981 and 2006. → To describe the pertinent features of medical diagnosis using audiometry and imaging	825 Individuals diagnosed with vestibular schwannoma and underwent surgery between January 1984 and August 2006. →467 (56.6%) were female, and 358 (43.4%) were male. →Age range and number of patients 0–20 years: 12 (1.5%) 21–30 years: 55 (6.7%) 31–40 years: 108 (13.1%) 41–50 years: 329 (39.8%) 51–60 years: 216	PTA, speech audiometry, ABR, and MRI.	**Audiological findings:** → The most common condition was unilateral progressive hearing loss, which affected 656 patients (79.5%), followed by vertigo (5.1%), tinnitus (8.1%), and sudden hearing loss (48, 5.8%). →Before surgery, there were 220 patients (26.7%) with profound hearing loss, 261 (31.6%) with severe hearing loss, 279 (33.8%) with moderate hearing loss, 53 (6.4%) with mild hearing loss, and 12 (1.5%) with normal thresholds. → In 146 patients (17.7%), the spondee recognition score on the tumor side was 100%; in 212 patients (25.7%); in 241 patients (29.2%); in	→ 90% of acoustic neuroma begin with progressive, unilateral hearing loss as a symptom, and in the current study, 80% of cases had this as their main complaint. → There is no relationship between speech discrimination scores, hearing thresholds, or tumor size. → Most of the patients were between 41 years to 60 years of age. → Female preponderance was more in this study (60%).

				(26.2%) 61–70 years: 82 (9.9%) 71–80 years: 23 (2.8%).		97 patients (11.8%); and in 129 patients (30%).. → 352 people (42.7%) had abnormal ABR results, whereas 29 (3.5%) had results that were within the normal range. In the charts of 111 patients, there were no ABR data (13.4%). **Non-audiological findings:** → On MRI, the tumour size was consistent with Grade I in 189 cases (22.9%), Grade II in 401 (48.6%), Grade III in 188 (22.8%), and Grade IV in 47 (5.7%). → In 813 patients (98.5%), there were no indications of recurrence or persistent tumor after a minimum 5-year follow-up.	→ Imaging tests should be done for definitive diagnosis when there is clinical or audiological suspicion of CPA tumor. → For a certain diagnosis, MRI was the method of choice.

Sl.no	Author & year	Title	Study design and Research question	Population	Testing parameters used	Results	Inference
11.	Kim et al. (2014)	Clinical Significance of an Increased Cochlear 3D fluid-attenuated Inversion Recovery Signal Intensity on an MR Imaging Examination in Patients with Acoustic Neuroma	Retrospective study design →To compare imaging results with audiometric findings and hearing problems in many patients with acoustic neuroma to investigate the clinical implications of an elevated cochlear 3D FLAIR signal.	122 patients with acoustic neuroma between 2008 and 2012. → 20 patients were excluded because of various reasons. → 102 patients were included → 58 males; 44 females → Mean age – 49.9 ± 12.4 years	Pure Tone Audiometry, Magnetic Resonance Imaging	**Audiological findings:** → In the Internal auditory canal group (ANIAC), 11 out of 22 patients (50%) had hearing disturbance →In the ANCPA group, 59 out of 80 patients (74%) had hearing disturbance. → Out of 102 patients, 45 had tinnitus (44%) – 9 in the ANIAC group and 36 in the ANCPA group. **Non-audiological findings:** → The 102 patients are divided into two groups: - 1) Acoustic neuroma limited to the IAC (ANIAC) = 22 patients 2) Acoustic neuroma limited to the IAC and the CPA cistern (ANCPA) = 80 patients	→ There were no discernible differences between patients with ANIAC and those with ANCPA in terms of age, sex, or the duration between the PTA and MR imaging evaluation. → According to the PTA, this study showed that patients with ANCPA had considerably worse hearing function than those with ANIAC. → In patients with ANCPA compared to ANIAC, the cochlear signal strength on 3D FLAIR pictures was considerably higher. → In patients with

						→ Additionally, mean rSI (relative signal intensity) was significantly higher in ANCPA patients compared to ANIAC patients.	ANCPA, there was no relationship between the cochlear rSI on 3D FLAIR MR images and the hearing impairment assessed by PTA. → In patients with ANIAC, there was a moderate correlation between the cochlea's rSI on 3D FLAIR MR images and hearing impairment as evaluated by PTA.. → This study found that for small tumors restricted to the internal auditory canal, an enhanced cochlear signal on 3D FLAIR pictures correlated with the degree of hearing impairment assessed by PTA.

Sl.no	Author & year	Title	Study design and Research question	Population	Testing parameters used	Results	Inference
12.	Eliezer et al. (2019)	Sensorineural hearing loss in patients with vestibular schwannoma correlates with the presence of utricular hydrops as diagnosed on heavily T2-weighted MRI	Retrospective study design → To assess whether the volume of the vestibular endolymphatic space correlates with the degree of hearing loss	32 patients were recruited between December 2015 and May 2017 → 23 patients were included. → 13 Female and 10 Male → Mean age of 63.5 ± 9.3 years	PTA hearing levels of bone conduction and 3T Magnetic Resonance Imaging	**Audiological findings:** → Mean PTA level on the tumor side (57.9 ± 26.5 dBHL) was higher than on the contralateral side →Two patients had Normal hearing, 3 patients had Mild SNHL, 9 patients had Moderate SNHL, 6 patients had Severe SNHL, and 3 patients had Profound SNHL → The mean SRT on the tumor side was 60.2 ± 31 dB SPL, higher than on the contralateral side. **Non-audiological findings:** → Mean tumor volume of the 23 included patients was 1.74 ± 2.5 cubic cm. → All these patients had	→ This study has found a moderate correlation between the utricular volume and the degree of hearing loss, but not significant between saccular volume and the levels of PTA. → There was a significant correlation between the volume of vestibular endolymphatic space and the degree of hearing loss. →There was no significant correlation between tumor volumes and PTA levels → There was a possible mechanism in Vestibular schwannoma which

						obstructive VS → Mean saccular volume was 3.17 ± 1.1 mm3, and the mean utricular volume was 14.4 ± 5 mm3. →The mean volume of the vestibular endolymphatic space was 17.45 ± 5.5 mm3	leads to hearing loss-Endolymphatic hydrops. →MR Imaging can reveal Endolymphatic hydrops associated with schwannoma. → FIESTA C sequence can enable the assessment of vestibular endolymphatic space.

Sl.no	Author & year	Title	Study design and Research question	Population	Testing parameters used	Results	Inference
13.	Lee et al. (2011)	Vestibular schwannoma in patients with sudden sensorineural hearing loss	Retrospective study design To determine the incidence of vestibular schwannoma in individuals with sudden sensorineural hearing loss	Two hundred ninety-five patients with SSNHL between 2002 to 2008.	PTA and Magnetic Resonance Imaging, 3D (FIESTA) temporal MRI	**Audiological findings:** → Out of 295, vestibular schwannoma was found in 12 patients (4%). • seven females and five males; Age range- 32 to 69 years → Three cases of sudden SNHL in one ear and a coincidental discovery of vestibular schwannoma in the opposite ear were reported. → Hearing loss and vertigo were present in both patients in two cases of	→ Hearing loss, loss of balance, and tinnitus are some of the symptoms of vestibular schwannoma. The most typical sign of vestibular schwannoma is progressive hearing loss. → In patients with vestibular schwannoma, sudden sensorineural hearing loss has been linked to several causes, including endolymphatic oligohydramnios, conduction blockage of the auditory nerve, and microvascular constriction in the cochlea. →All of the patients in this study had intrameatal tumours ranging in size from small to medium. Small

						vestibular schwannoma that imitated labyrinthitis. **Non-audiological findings:** → There were small to medium-sized intrameatal tumors present in every subject.	tumours are more likely than larger ones to cause sudden sensorineural hearing loss. → Due to the widespread of MRI, a greater number of VS cases are detected. This study also recommended that all Sudden SNHL cases should undergo MRI

3.2 Quality Assessment

The Critical Appraisals Skills Programme (CASP) was used to assess the quality of the studies. It is a generic tool for appraising the strengths and limitations of any qualitative researchmethodology. It consists of 12 questions to assess the article in depth across each section to reduce bias. The questions in the tool are marked as "Yes', 'No' or "Can't tell," depending on the question's requirement. The results of the quality assessment for allthe selected studies are provided in Table 3.2

Table 3.2. Results of the quality assessment for all of the selected studies

Questions													
	Section A: Are the results of the trial valid?						***Section B:*** What are the results?				***Section C:*** Will the results help locally?		
Authors & Years	**Q1**	**Q2**	**Q3**	**Q4**	**Q5**	**Q6**	**Q7**		**Q8**		**Q9**	**Q10**	**Q11**
							a)	**b**	**a)**	**b)**			
Jeong et al., (2016)	Yes	Yes	Yes	Can't Tell	Yes	Yes	No	Yes	No	No	Can't Tell	Yes	No
Kim et al., (2016)	Yes	Yes	Yes	Can't Tell	Yes	Yes	Yes	Yes	No	No	Yes	Yes	No
Tutar et al., (2013)	Yes	Yes	Yes	Can't Tell	Yes	Yes	No	Yes	No	No	Yes	Yes	No
Salem et al., (2019)	Yes	Yes	Yes	Can't Tell	Yes	Yes	Yes	Yes	No	No	Yes	Yes	No

Ahsan et al., (2015)	Yes	Yes	No	Can't Tell	Yes	Yes	Yes	Yes	No	No	No	Yes	No
Patel et al., (2015)	Yes	Yes	No	Can't Tell	Yes	Yes	No	Yes	No	No	No	No	No
Dunn et al., (2014)	Yes	Yes	Yes	Can't Tell	Yes	No	No	Can’t Tell	Can’t Tell	No	Yes	Yes	No
Lee et al., (2015)	Yes	Yes	Yes	Can't Tell	Yes	Yes	Yes	Yes	No	No	Yes	Yes	No
Valame and Gore, (2017)	Yes	Yes	Yes	Can't Tell	Yes	Yes	No	No	Can’t Tell	No	No	Yes	No
Bento et al., (2012)	Yes	Yes	Yes	Can't Tell	Yes	No	No	Yes	Can’t Tell	No	Yes	Yes	No

Kim et al., (2014)	Yes	Yes	Yes	Can't Tell	Yes	Yes	No	Yes	No	No	Yes	Yes	No
Eliezer et al., (2019)	Yes	Yes	No	Can't Tell	Yes	Yes	No	Yes	No	No	Yes	No	No
Lee et al., (2011)	Yes	Yes	Yes	Can't Tell	Yes	No	No	Yes	No	No	No	No	No
Total % of yes	100%	100%	77%	0%	100%	77%	30%	77%	0%	0%	70%	84%	0%

CASP Checklist – Diagnostic Test Study

Questions:

Q1. Was there a clear question for the study to address?

Q2. Was there a comparison with an appropriate reference standard?

Q3. Did all patients get the diagnostic test and reference standard?

Q4. Could the results of the test have been influenced by the results of the reference standard?

Q5. Is the disease status of the tested population clearly described?

Q6. Were the methods for performing the test described in sufficient detail?

Q7. What are the results?

a. Are the sensitivity and specificity and/or likelihood ratios presented?
b. Are the results presented in such a way that we can work them out?

Q8. How sure are we about the results? consequences and cost of alternatives performed?

a. Could they have occurred by chance?
b. Are there confidence limits?

Q9. Can the results be applied to your patients/the population of interest?

Q10. Can the test be applied to your patient or population of interest?

Q11. Were all outcomes important to the individual or population considered?

Chapter 4

DISCUSSION

The space bounded by the petrous temporal bone, pons, and anterior cerebellum, represents the Cerebellopontine angle (CPA) (Bonneville et al., 2007). It is a triangular space in the posterior cranial fossa that is superiorly bounded by the tentorium, posteromedially by the brainstem, and posterolaterally by the petrous part of the temporal bone. Since it houses the trigeminal nerve, abducens nerve, facial nerve, vestibulocochlear nerve, and the anterior inferior cerebellar artery, anatomically and clinically, it is an important landmark (Samii & Gerganov, 2012). Any lesions in the CP angle can cause severe problems in the function of those cranial nerves. So, it is essential to have various diagnostic procedures that will show the effect of the lesion on CP angle anatomically and physiologically. The CP angle tumors account for about 5 to 10% of intracranial tumors. Vestibular schwannoma is 70 to 90%, 5 to 10% are meningiomas, and 3 to 7% are epidermoid cysts (Butowski, 2015). The diagnostic procedures such as audiological and non-audiological evaluations such as Magnetic Resonance Imaging and Computed Tomography are well proven and show greater sensitivity while diagnosing the presence of vestibular schwannoma.

4.1 Audiological findings in individuals with Acoustic neuroma.

The findings through the audiological tests such as pure-tone audiometry, speech discrimination score, and auditory brainstem response are majorly affected in individuals with acoustic neuroma. Almost all the articles reviewed in this study reported that sensorineural hearing loss was one of the strongest signs in individuals with acoustic neuroma. About 4 – 4.5% of the patient with sudden sensorineural hearing loss exhibited the presence of acoustic neuroma in this systematic review (Jeong et al., 2016; Lee et al., 2011).

The hearing loss pattern is variable in individuals with acoustic neuroma (Van Abel et al., 2013). Kim et al. (2016) reported that sudden or progressive hearing loss is the key symptom in individuals with acoustic neuroma. Patel et al. (2015) found that progressive hearing loss could be present in the ear with acoustic neuroma, even if the tumor is not growing. Dunn et al. (2014) reported that progressive hearing loss (88%) was the most common initial symptom in patients with medial acoustic neuroma. By analyzing the 825 cases with vestibular schwannoma throughout the 25 years, Bento et al. (2012) found that progressive hearing loss was the chief complaint in 656 patients (79.5%). Some studies in this review found the highest prevalence of high frequency sloping hearing loss or descending type, followed by flat hearing loss in acoustic neuroma patients (Lee et al., 2015; Tutar et al., 2013), which was supported by various literature (Johnson, 1977; Moffat et al., 1993; Pensak et al., 1985). In up to 95% of their patients with acoustic neuromas, the majority of authors have described unilateral hearing loss or bilateral asymmetric hearing loss, and in 4-5% of these individuals, normal hearing function (Beck et al., 1986; Johnson, 1977; Kanzaki et al., 1991; Musiek et al., 1986; Roland et al., 1987; Selesnick & Jackler, 1993). In accordance with the previous statement, one article in this systematic review has found that 4.2% of the patients with acoustic neuroma showed normal hearing sensitivity (Salem et al., 2019).

The Speech Discrimination Score is a test usually done at a suprathreshold level, about 40 dB above the Speech Recognition Threshold of the patient. It tests the patient's ability to identify monosyllabic words or phonemes (Kung & Willcox, 2007). It was reported that speech discrimination scores were mostly affected in the ear with acoustic neuroma, which decreased with an increase in tumor size (Johnson, 1977; Selesnick & Jackler, 1993). The results of the studies included in this review also supported the previous statement (Ahsan et al., 2015; Bento et al., 2012; Dunn et al., 2014; Lee et al., 2015; Patel et al., 2015; Tutar et al., 2013).

Recent studies like Koors et al. (2013) reported that auditory brainstem response (ABR) has a sensitivity of 93.4% in detecting vestibular schwannomas of any size, with a relatively higher sensitivity of 95.6% for larger tumors and a slightly lower sensitivity of 85.8% for smaller tumors, which was also supported by various other authors (Barrs et al., 1985; Glasscock et al., 1979; Guyot et al., 1992; Pensak et al., 1985; Pfaltz et al., 1991; Telian et al., 1989). Five out of thirteen articles selected for this systematic review focused on the diagnostic results of ABR. Kim et al. (2016) found that ABR waves were abnormal in 104 patients out of 116. Salem et al. (2019) reported that ABR testing yielded a sensitivity of 73.6%). The sensitivity of ABR for small tumors (64.5%) was lesser than for larger tumors (97.2%), which was disagreed by Berrettini et al. (1996). They concluded that there is no significant difference in the presence or absence of ABR waves based on the tumor size. Prolonged or absent wave I, III, and V were observed in patients with acoustic neuroma by Bento et al. (2012) and Lee et al. (2015). Bento et al. (2012) observed abnormal ABR waves as a sign of retro cochlear dysfunction in 352 patients out of 825. Valame and Gore, (2017) have analysed the cervical VEMP of 15 patients with vestibular schwannoma along with the ABR. They reported that ABR was absent in the ear with large tumors, and 33% of patients with small tumors. Cervical

VEMP waves are abnormal in all patients with vestibular schwannoma, except one with a small tumor.

Tinnitogram evaluated the frequency and loudness of the tinnitus in the ear with acoustic neuroma. Out of 13 articles reviewed, only 2 evaluated the tinnitogram in patients with acoustic neuroma. Kim et al. (2016) found that 7.6% of patients with vestibular schwannoma (116 patients) reported tinnitus as the chief complaint in the ear with the tumor. As well as, 59 out of 116 patients, who complained of hearing disturbance, also reported tinnitus as an accompanying symptom in them. The mean pitch was 5012.5 ± 3504.9 Hz, and loudness matchings were at 62.5±27.4 dB. Lee et al. (2015) showed tinnitogram findings according to the tumor size. Out of 114, 8 patients reported the symptom of tinnitus. The mean pitch was 5012 ± 3379 Hz, and loudness matched at 62.5 ± 27.4 dB.

4.2 Non- audiological findings in individuals with Acoustic neuroma.

The advancements in imaging techniques made it possible to identify the small and asymptomatic neuromas. As a result, the incidence of acoustic neuroma increased in the past 30 years (Fortnum et al., 2009; Patel et al., 2015; Tutar et al., 2013). The non-audiological techniques reviewed in this study are Computed Tomography (CT) and Magnetic Resonance Imaging (MRI). All the studies included in this review have reported the findings of the MRI, and two studies have evaluated CT along with the MRI (Dunn et al., 2014; Salem et al., 2019).

Jeong et al. (2016) found that 13 out of 291 patients with sudden sensorineural hearing loss showed MRI abnormality. In that 13, 9 patients had vestibular schwannoma. Three patients had only intrameatal tumors, and six patients had intrameatal tumors with extension out of porous medially. Kim et al. (2016) evaluated 171 patients with CPA tumors and found that 116 patients were those with vestibular schwannoma. And most often, vestibular schwannoma was located in the internal auditory canal and CP angle, followed by IAC plus CPA plus brainstem compression. Vestibular schwannoma in IAC alone is less prevalent compared to others. By analyzing 115 patients with tumors in CP angle with or without IAC extension, Tutar et al. (2013) reported that the average size of the tumors is 18.58 mm.

Salem et al. (2019) classified the tumor grade according to size in 162 patients with vestibular schwannoma who had normal hearing. Grade 0 (64 out of 162) was the most frequent tumor grade, followed by grade 1 (48 out of 162). Ahsan et al. (2015) showed CPA or IAC mass was the common cause of MRI abnormality in patients with asymmetrical hearing loss. The tumor dimension ranged from 0. 3 cm to 3.6 × 2.7cm, which presents as intracochlear mass to CPA tumor. Patel et al. (2015) classified 15 patients with non-growing acoustic neuroma into two categories. All the patients had tumors involving the IAC, and five patients had additional CPA involvement. The extent of the tumor in IAC ranges from 3 to 14 mm, and in CPA ranges from 3 to 15 mm.

Medial acoustic neuroma, a variant of acoustic neuroma, was thoroughly examined in 52 patients retrospectively by Dunn et al. (2014). It has been reported that the size of the tumor in medial acoustic neuroma ranged from 1.3 cm to 5.3 cm. This medial acoustic neuroma occupies only the cisternal compartment and has no lateral extension into the IAC. Lee et al. (2015) reported that tumor in patients with acoustic neuroma was located mostly in the internal auditory canal plus CP angle than the IAC plus CPA plus brainstem compression. Most patients had tumor sizes ranged from 10mm to 2 cm.

After retrospectively reviewing the 825 cases with acoustic neuroma, Bento et al. (2012) classified the tumors into four grades based on their size. The most common grade was Grade II (48.6%) which was nothing but the tumor extending into the posterior fossa, with or without an intracanalicular component, without touching the brainstem. Valame and Gore, (2017) reported that larger tumors (> 2.5 cm) have more severity than smaller tumors (< 2.5 cm). The tumor size in this study ranges from 5.4 mm to 5 cm. Kim et al. (2014) have investigated the clinical significance of increased cochlear signal on 3D FLAIR in patients with acoustic neuroma. The study reported that on 3D FLAIR images, cochlear signal intensity was significantly higher in patients with acoustic neuroma confined to CP angle and IAC than in the patients with acoustic neuroma confined to IAC alone. Eliezer et al. (2019) attempted to correlate the presence of utricular hydrops in patients with vestibular schwannoma using the T2 weighted MRI. FIESTA-C, a refocused steady state gradient echo sequence, was used in this study. The average tumor volume was 1.74 ± 2.5 cubic cm. Lee et al. (2011) reported that all 12 patients out of 295, who had vestibular schwannoma, have intrameatal or small to medium-sized tumors.

4.3 Correlation between the audiological and non- audiological findings of individuals with Acoustic neuroma

Acoustic neuromas arise at the junction of the peripheral and central myelin of the vestibular nerve. Based on the position of the junction or the site of the tumor development, the severity of the dysfunction also varies (Moffat et al., 1993; Nager, 1969; Neely, 1981; Thomsen & Tos, 1993). Berrettini et al. (1996) found the most significant differences between the lateral and medial tumors, in that lateral tumors are smaller than the medial tumors. Lateral tumors are associated with early audiovestibular symptoms, while medial tumors show insidious or atypical symptoms. In accordance with previous literature (Berrettini et al., 1996; Moffat et al., 1994), the articles reviewed in this study also showed no significant differences in subjective hearing loss between the size of tumors (Bento et al., 2012; Dunn et al., 2014; Eliezer et al., 2019; Jeong et al., 2016; Kim et al., 2016; Lee et al., 2015; Patel et al., 2015; Tutar et al., 2013).

In agreement with Moffat et al., (1993), Dunn et al. (2014) concluded that hearing function preservation could be achieved even with large-sized tumors in patients with medial acoustic neuroma. The comparison between the vestibular schwannoma and non-vestibular schwannoma tumors showed that patients with vestibular schwannoma reported high-frequency sloping hearing loss. In contrast, the patient with non-VS has been reported with a flat type of hearing loss pattern. Hearing thresholds were worse in a patient with VS than a patient with non- VS tumors, supported by the review article on non-vestibular schwannoma (Springborg et al., 2008). Kim et al. (2016) concluded that it might be due to the origin of the tumors. Most often, non-VS tumors are present in the CP angle alone, but vestibular schwannoma is often located in the internal auditory canal and the CP angle.

Kanzaki et al. (1991) found that there was no relationship between the speech discrimination scores and tumor size, and the above statement is supported by some articles reviewed in this study (Bento et al., 2012; Dunn et al., 2014; Kim et al., 2016; Lee et al., 2015; Patel et al., 2015; Tutar et al., 2013). Specifically, Patel et al. (2015) reported that speech discrimination scores would decrease in the ear with a tumor, even if it is not growing. Along with hearing loss, tinnitus occurs in the first stage of tumor development (Selesnick & Jackler, 1993). The other audiological symptoms represent the involvement of the vestibular and cochlear nerves with gradual impairment of function. Berrettini et al. (1996) reported tinnitus in 51% of the patients with acoustic neuroma. Ogawa et al. (1991) concluded that tinnitus accompanied by subjective hearing loss was one of the major symptoms in patients with acoustic neuroma. It was supported by Curati et al., (1986). Two articles reviewed in the current study have evaluated tinnitogram, and its results are discussed previously. Kim et al. (2016) concluded that the presence of hearing loss and tinnitus was the symptom present mostly in the patients with vestibular schwannoma, and hearing loss with dizziness was present mostly in the patients with non- vestibular schwannoma type of CP angle tumor. Lee et al. (2015) reported tinnitogram findings are not associated with the site of lesion or tumor site.

Magnetic resonance imaging (MRI) is the diagnostic tool of choice for all CPA tumors (Wilms et al., 1992; Zamani, 2000). Along with MRI, auditory brainstem response (ABR) also showed higher sensitivity in detecting vestibular schwannomas (Barrs et al., 1985; Glasscock et al., 1979; Koors et al., 2013; Moffat et al., 1989; Pensak et al., 1985). In the current study, 5 articles have evaluated and reported the ABR findings of patients with acoustic neuroma. Kim et al. (2016) found ABR abnormality in 89.7% of patients with vestibular schwannoma and 81.8% in the non- VS group. Salem et al. (2019) reported ABR findings in 162 normal hearing patients with acoustic neuroma. The incidence is 4.2%. ABR in normal hearing patients with acoustic neuroma could be because of desynchronization of firings in the auditory nerve due to the pressure of the tumor against it (Eggermont et al., 1980; Selters & Brackmann, 1977). At last, they concluded that abnormal ABR in normal hearing patients strongly indicates the presence of the acoustic neuroma. This study found a significant relationship between the size of the tumor and ABR abnormality. That is ABR abnormality increases as the tumor grade increases. Large-sized tumors could alter the contralateral recordings of ABR (Salem et al., 2019).

In contrast to the findings of the previous studies, Lee et al. (2015) observed no correlation between the ABR results and the size of the tumor or site of the tumor. Though the ABR is cost-effective compared to MRI, it is less sensitive for small-sized tumors. It has also been reported that dizziness was one of the major symptoms observed in patients with small tumors. Small acoustic tumors may compress the vestibular nerve in the internal auditory canal, impairing its function or the labyrinth and causing vertigo. A compensatory mechanism is engaged when these tumors grow, resulting in less vestibular nerve compression and more brainstem and cerebellum compression (Park et al., 2004). The only article reviewed in the current study, which has ABR findings along with the cervical VEMP, was done by Valame and Gore, (2017). They have reported that, except for one patient with a small tumor, all patients with tumors, irrespective of size. As the cervical VEMP descends into the lower brainstem, large tumours that have compressed or shifted the brainstem to the opposite side may show abnormalities in the response in the contralateral ear. Four out of five patients with large tumors showed absent cervical VEMP on the contralateral recording. The mass impact of the lesion on the contralateral inferior vestibular nuclei or the descending medial vestibulospinal tract (MVST) in the brainstem may cause the high percentage of large tumors exhibiting inappropriate response when the other ear was examined (Valame & Gore, 2017).

Finally, they concluded that, along with ABR, cervical VEMP findings could be crucial in identifying the retro cochlear pathology. Through the retrospective analysis of 825 cases, Bento et al. (2012) observed signs of retro cochlear dysfunction in 42.7% of patients.

When a cerebellopontine angle tumor is suspected, MRI is undoubtedly the imaging modality of choice. The reliability of gadolinium contrast-enhanced MRI is approximately 100 % (Bento et al., 2012). The high cost of MRI is a major limiting factor in screening protocol (Robinette et al., 2000). On the other hand, ABR testing is less expensive, takes less time, and is more accessible. Patients who cannot have an MRI because of ferromagnetic implants, obesity, or claustrophobia can have an ABR instead (Cheng & Wareing, 2012). ABR testing also aids in deciding on approaches to hearing preservation during surgery of vestibular schwannomas (Stucken et al., 2012). Because of these considerations, the ABR can be used as a first screening test for VS. Still, there would be a definitive exclusion of acoustic neuroma in individuals with normal audiological parameters that can be accomplished only with advanced radiographic imaging techniques, such as MRI. So, audiological and non-audiological test batteries should be administered for the early diagnosis of tumors, even if they are smaller in size.

Chapter 5

SUMMARY AND CONCLUSION

The present systematic review was taken to document the recent audiological findings and the correlation of audiological and non- audiological findings such as computed tomography and Magnetic Resonance Imaging in individuals with acoustic neuroma during the past ten years. Of 38 articles selected for the full-length article screening, 13 articles were selected for this systematic review. . Almost all the articles have concluded that patients who have unilateral or asymmetrical hearing loss, tinnitus, low speech discrimination scores, and abnormal peaks in auditory brainstem response (ABR) should undergo Magnetic resonance imaging (MRI), in suspicion of acoustic neuroma. Some populations are diagnosed with normal hearing in the audiological evaluations and excluded from the differential diagnosis of retro cochlear pathology, though they might have an acoustic neuroma. In these situations, diagnosing acoustic neuroma or vestibular schwannoma at an early stage might be hindered. Hence, there is a need to include imaging protocols such as CT, and MRI should be demanded the correct diagnosis of acoustic neuroma. This systematic review did not find any correlation between the tumor size or site of lesion and hearing loss. Also, from the combination of symptoms, the type of tumor in the cerebellopontine angle could be suspected. In patients with vestibular schwannoma, the most common symptom was unilateral hearing loss with tinnitus, and hearing loss with dizziness. In individuals reporting a sudden sensorineural hearing loss and asymmetrical sensorineural hearing loss, the most common MRI abnormality was small or medium-sized vestibular schwannoma. Hearing loss could deteriorate even in the ear with static vestibular schwannoma.

Along with the ABR results, the abnormal findings in the contralateral cervical VEMP have also been reported as a strong indicator of a large tumor (>2.5 cm). Finally, this systematic review study concludes that MRI and other imaging tests should be considered as the modality of choice for the definitive diagnosis of vestibular schwannoma or acoustic neuroma. All individuals suspected of acoustic neuroma in the audiological evaluation should be administered non-audiological evaluations such as CT and MRI for the correct diagnosis, increasing the diagnosis of acoustic neuroma even at the earlier stage.

5.1 Clinical implication:

- The study can provide valuable information on the various audiological and non-audiological findings and their co-relation in individuals with acoustic neuroma.
- It can also help to get more information about the recent updates in the findings and the test used for diagnosing acoustic neuroma.

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