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RESEARCH ARTICLE

EVALUATION OF EFFICACY OF HINTS EXAMINATION IN DIFFERENTIATING BETWEEN POSTERIOR CIRCULATION STROKE FROM PERIPHERAL VESTIBULAR LESIONS IN PATIENTS PRESENTING WITH ACUTE VESTIBULAR SYNDROME: A PROSPECTIVE, CROSS-SECTIONAL STUDY

Raghavendra T. R.[1], Kallesh Shamanur.[2], Manjunath B. H.[3] Goutham S V.[4] and Veeresh S[5]
1. Professor, Department of Emergency Medicine, J. J. M. Medical College, Davangere, Karnataka, India.
2. Associate Professor, Department of Emergency Medicine, J. J. M. Medical College, Davangere, Karnataka, India.
3. Associate Professor, Department of Emergency Medicine, J. J. M. Medical College, Davangere, Karnataka, India.
4. Senior Resident, Department of Emergency Medicine, J. J. M. Medical College, Davangere, Karnataka, India.
5. Postgraduate Student, Department of Emergency Medicine, J. J. M. Medical College.

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Abstract

Background and Aim: Acute vestibular syndrome(AVS) is a subset of dizzines s typically accompanied by nausea, vomiting, nystagmus, gait imbalance, and continuous vertigo that may be due to a benign,peripheral cause versus a centra l cause. Differentiating between the two is challenging. We aimed to assess the efficacy and diagnostic accuracy of the HINTS examination in distinguishing posterior circulation stroke (PCS) from peripheral vestibular disorders (PVD) in patients presenting with AVS.

Methodology: This is a prospective, cross-sectional study consisting of total 100 patients presented with AVS. The HINTS examination was performed with three of its components *viz.*the Head Impulse Test(HIT),Nystagmus assessment ,and the Test of Skew(TS)by properly trained clinicians. All patients completed neuroimaging as reference standard. Final diagnosis and the results of HINTS examination were compared and analysed to determine the sensitivity (Sn), specificity(Sp),positive predictive value(PPV),negative predictive value (NPV) of HINTS examination along with its diagnostic accuracy.

Results: We found central AVS cases as dominant accounts for 98% followed by peripheral AVS cases (2%). Majorly, acute right cerebellar infarct and acute left cerebellar infarct were observed in 7% and 3% of the patients respectively. We found 100%,2.6%,25.5%, and 100% of Sn, Sp, PPV, and NPV respectively for HINTS examination in differentiation of PCS and PVD, along with the diagnostic accuracy of HINTS examination as 27%. The diagnostic accuracy of individual components of HINTS examination *viz.* HIT, Nystagmus, and TS were found to be 27%, 75%, and 75% respectively.

Conclusion: The HINTS examination is a simple, low-cost method that offers high sensitivity but moderate-to-low specificity for distinguishing PCS from PVD in patients with AVS, providing moderate overall diagnostic accuracy.

Corresponding Author:-Veeresh S
Address:-Postgraduate Student, Department of Emergency Medicine, J. J. M. Medical College.

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V distorted self-
m y the sudden
o l imbalance, autonomic disturbances, and intolerance to head movements with or without spontaneous nystagmus on examination.[2] When evaluating a patient with AVS, the primary concern for physicians is differentiating a central cause, such as posterior circulation stroke (PCS), from a peripheral cause (Figure 1). Identifying PCS which accounts for only 10–20% of ischemic strokes,[3-5] can be difficult, as it often manifests with varied neurological deficits lacking clear motor signs, including hemianopia, visual agnosia, amnesia, and neglect. The challenge is compounded by large emergency department (ED) studies showing that only about 25% of AVS presentations[6,7] or 3–5% of all dizziness-related visits are due to PCS.[8,9]The low incidence of AVS from stroke increases the risk of underdiagnosis in the ED, which can delay timely initiation of early reperfusion therapies such as intravenous recombinant tissue plasminogen activator (rtPA)[3,10] and endovascular thrombectomy,[11,12] both of which have proven safety and efficacy in treating strokes involving either the posterior or anterior circulation.

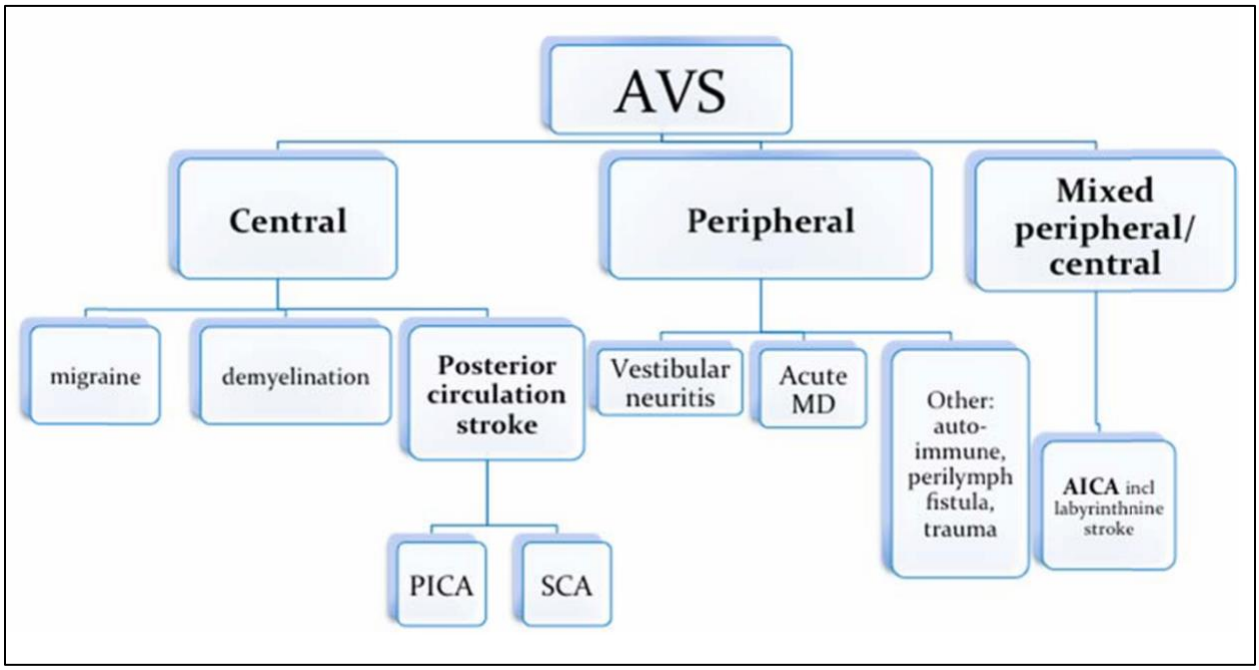

Figure 1. The acute vestibular syndrome and its localisation

AVS, Acute vestibular syndrome; MD, Meniere's disease; PICA, Posterior inferior cerebellar artery; SCA, Superior cerebellar artery; LMS, Lateral medullary stroke; AICA, Anterior inferior cerebellar artery

The HINTS examination (Head-Impulse Test [HIT], Nystagmus, Test of Skew [TS]) is a clinical tool used for patients with AVS.[2,13-17]It is considered the gold standard for distinguishing peripheral vestibular disorders from central causes. Research has shown that HINTS is more sensitive than neuroimaging methods such as computed tomography (CT) and diffusion-weighted magnetic resonance imaging (DW-MRI) in ruling out stroke in AVS patients.[2,18]This bedside test can be completed within minutes without specialized equipment. An abnormal HIT, characterized by vestibulo-ocular reflex (VOR) impairment with unilateral nystagmus and normal skew deviation, points toward a peripheral origin. Conversely, a normal HIT combined with direction-changing or vertical nystagmus, or skew deviation, suggests a central cause and calls for urgent further assessment.[2,13-15,17-19]

A limitation of the HINTS examination is that it demands specific skill and experience, meaning it is primarily carried out by neurologists and otorhinolaryngologists. In contrast, initial triage of AVS patients is often done by other healthcare providers without such expertise, potentially leading to misdirected referrals and delayed stroke management.[18,20]Other diagnostic options for evaluating vestibular function include Videonystagmography (VNG),

caloric reflex testing, and the Video Head-Impulse Test (vHIT).[21,22] These methods are highly effective for diagnosing vestibular disorders but are not widely accessible, especially in all emergency departments (EDs). They tend to be costly, non-portable, and less feasible for immediate use. In cases of ischemic stroke, however, rapid diagnosis and prompt treatment are critical to minimizing lasting brain damage.[23]

With this scenario, present study was conducted with the main purpose of evaluation of efficacy and diagnostic accuracy of the HINTS examination in distinguishing PCS from peripheral vestibular disorders (PVD) in patients presenting with AVS.

Methodology:-

Study population

This is a prospective, cross-sectional study conducted with patients presented with AVS at Department of Emergency Medicine, Bapuji hospital attached to J. J. M. Medical College (JJMMC), Davangere, Karnataka. The ethical committee approval and written informed consent were obtained before the conduct of study.

Inclusion criteria

1. Age: ≥18 years
2. Patients presenting with AVS viz. continuous vertigo, nausea, nystagmus, gait instability, with/without other neurological signs
3. Symptoms onset within 48-72 hours

Exclusion criteria

1. Patients with a known diagnosis of stroke or vestibular disorder
2. Those with altered mental status or unable to cooperate with the HINTS examination
3. Patients with a history of recent head trauma

Sample size

Sample size was calculated based on a previous study in which the sensitivity and specificity of HINTS score were 89.8% and 84.2% respectively using the following formulas;

$$N_{sen}= \frac{Z_\alpha{}^2 Sen(1-Sen)}{d^2}$$

$$N_{spec}= \frac{Z_\alpha{}^2 Sp(1-Sp)}{d^2}$$

Where,

Z_α: Standard normal deviation equal to 1.96 at 5% level of significance with 95% confidence level

Sensitivity=97.22%

Specificity=85.71%

d= allowable error=10%

Power of the study(1-β)=80%

Sample size based on sensitivity, n_{sen}=35

Sample size based on specificity, n_{spec}=51

Final sample size, n=86

Considering non response rate as 10%, the minimum sample size was 95 which was rounded off to 100.

Data collection workflow

- Clinical data including gender, age, hypertension, and diabetes were collected.
- All patients completed emergency brain CT examination to exclude hemorrhagic stroke
- Perform the HINTS examination to distinguish between PCS from PVD in patients presenting with AVS.
- All patients completed neuroimaging as reference standard.
- Final diagnosis and the results of HINTS examination were compared and analyzed to determine the Sensitivity (Sn), Specificity (Sp), Positive Predictive Value (PPV), Negative Predictive Value (NPV) along with diagnostic accuracy of HINTS examination

HINTS examination

The HINTS examination consists of three components: The Head Impulse Test (HIT), Nystagmus assessment, and the Test of Skew (TS). It is designed to evaluate the presence of specific signs that can indicate whether a patient's symptoms are likely to be caused by a stroke or a peripheral vestibular disorder.

1. Head impulse test (HIT):Have the patient look and maintain their gaze midline. Then ask them to try to maintain their gaze on you while quickly rotating the patient's head approximately 15-20 degrees to left/right. An intact vestibulo-ocular reflex (VOR) allows the patient to maintain their gaze throughout the rapid rotations. An abnormal response is one in which the patient is unable to maintain their gaze and their eyes have a corrective saccade back to midline upon rotation. An abnormal response is reassuring in that it usually indicates peripheral vertigo. Normal or eyes maintaining central position, is concerning for central vertigo
2. Gaze-evoked nystagmus (GEN): GEN is also known as direction-changing nystagmus. The subject was in an upright position; the examiner stood in front of the subject, and instructed the patient to follow the examiner's finger. During horizontal GEN examination, the patient looked at a target in a lateral eccentric position (about 30 degrees to the right and left of fixation). The examiner observed the direction of the horizontal nystagmus in left and right gaze. We identified the nystagmus as "direction changing" when the fast phase changed (Figure 2). If nystagmus fast phase does not change direction, regardless of eye position, then it is unidirectional.
   - In PCS, nystagmus may be persistent or direction-changing, which is a key differentiating feature from PVD.

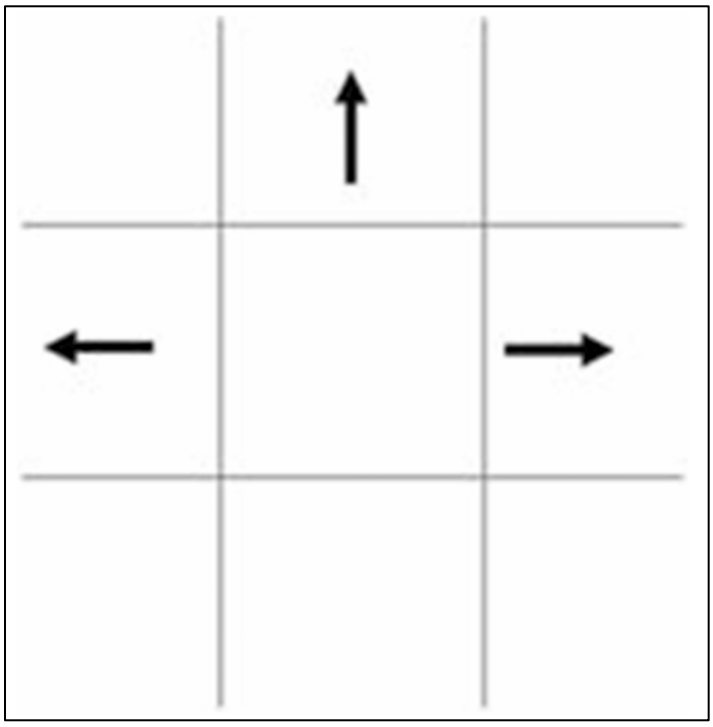

Figure 2. Schematic illustration of the direction in GEN

3. Test of skew (TS): The patient is fixating on a near target during the cross-cover test and that the movement of the eyes is vertical and dissociated, one eye is high: hypertropic and one low: hypotropic. After covering one eye with the palm for 1–3s, we covered the fellow eye in alternate fashion, and observed a vertical eye movement of the uncovered eye. The absence of vertical movement is the normal response.
   A positive test (presence of skew deviation) is highly suggestive of brainstem or cerebellar involvement, typical of a PCS. Whereas PVD does not result in skew deviation.
4. HINTS judging criteria for AVS: If any of the following 3 conditions is positive in the HINTS-Examination, the case is considered as central AVS, otherwise it is judged as peripheral AVS: (i). The horizontal head-impulse test is normal (negative), (ii). The direction of nystagmus changes with the direction of gaze GEN +, and (iii). The dissociated vertical deviation (skew) of both eyes on alternately covering the eyes, TS is positive.

Study outcomes

Primary outcome

- Sn, Sp, PPV, NPV, and diagnostic accuracy of HINTS examination in differentiating the PCS and PVD.

Secondary outcomes

- Diagnostic accuracy of individual components of HINTS examination viz. HIT, Nystagmus, and TS in differentiating the PCS and PVD.

Statistical analysis

Data was entered in Microsoft Excel 2021 and analysis was done using Statistical Software for Social Sciences (SPSS) version 21. Categorical variables were represented in the form of percentages, and frequencies. Continuous variables were presented as descriptive statistics (Mean and Standard deviation). Categorical variables were analysed using the Chi-square test. The Sn, Sp, PPV, NPV, and diagnostic accuracy of HINTS examination were calculated using the following formulas;

- Sensitivity (Sn) = TP / (TP + FN) × 100
- Specificity (Sp) = TN / (TN + FP) × 100
- Positive Predictive Value (PPV) = TP / (TP + FP) × 100
- Negative Predictive Value (NPV) = TN / (TN + FN) × 100
- Diagnostic Accuracy = (TP + TN) /N × 100

Where,

TP: True Positive; TN: True Negative; FP: False Positive; FN: False Negative

Results:-

Demographic characteristics

Majority of the patients i.e., 26% were belonged to age group of 51-60 and 61-70 years. The mean age of study subjects was found to be 61.62 years with 1:1 male to female distribution (Table 1).

Table 1: Demographic characteristics

Variables	Frequency (N)	Percentage (%)
Age (years)		
21–30	1	1.00
31–40	2	2.00
41–50	21	21.00
51–60	26	26.00
61–70	26	26.00
71-80	17	17.00
81-90	7	7.00
Mean ± SD	61.62 ± 12.32	
Gender		
Male	50	50.00
Female	50	50.00

Risk factors

The distribution of patients based on risk factors was illustrated in Figure 1. Results depicted that the top four ranked risk factors for AVS were found to be hypertension (41%) followed by hypertension & Type 2 Diabetes mellitus (17%), Type 2 Diabetes mellitus (16%), and smoking (10%). The Chi-square test revealed significant association (X^2 = 207.580; p=0.000) between distribution of risk factors among patients.

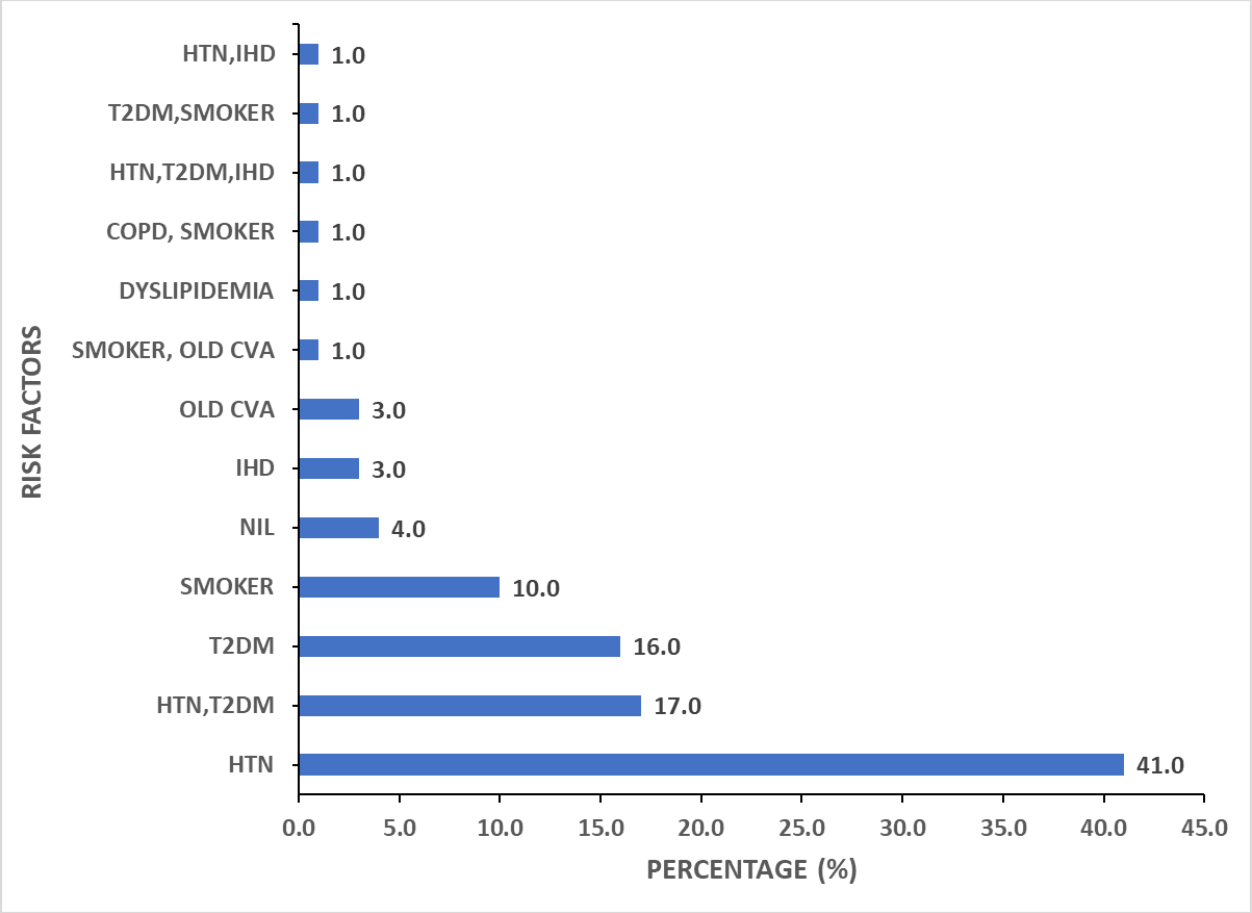

Figure 1. Distribution of patients based on risk factors

Neuroimaging findings

In majority of the patients the neuroimaging findings were normal. However, acute right cerebellar infarct and acute left cerebellar infarct were observed in 7% and 3% of the patients respectively. Other neuroimaging findings observed among study subjects were listed in Table 2. The Chi-square test revealed significant association (X^2 = 1036.40; p=0.000) between distribution of neuroimaging findings among patients.

Table 2: Distribution of patients based on neuroimaging findings

Neuroimaging Findings	Frequency (N)	Percentage (%)
Normal	75	75.00
Acute right cerebellar infarct	7	7.00
Acute left cerebellar infarct	3	3.00
Left posterolateral hemimedulla infarct	1	1.00
Subacute lacunar infarct in left parietal lobe	1	1.00
Acute infarct in B/L cerebellum	1	1.00
B/L PCA and MCA territory infarct	1	1.00
Right hemi PONS and cerebellar infarct	1	1.00
Acute infarct in PCA territory	1	1.00
Acute thalamic infarct	1	1.00
Acute infarct in right occipital region	1	1.00
Acute infarct in occipital region	1	1.00
Acute lacunar infarct in midbrain	1	1.00
Acute infarct in B/L cerebellar region	1	1.00
Acute infarct in left occipital region	1	1.00
Acute infarct in pons	1	1.00
Acute infarct in right hemi PONS	1	1.00
Subacute thalamic infarct	1	1.00

Type of AVS

The distribution of patients based on type of AVS was illustrated in Figure 2. Results implied that majority of the patients i.e., 98% having central type of AVS followed by peripheral type of AVS (2%). The Chi-square test revealed significant association (X^2 = 92.160; p=0.000) between central AVS and peripheral AVS distribution among patients.

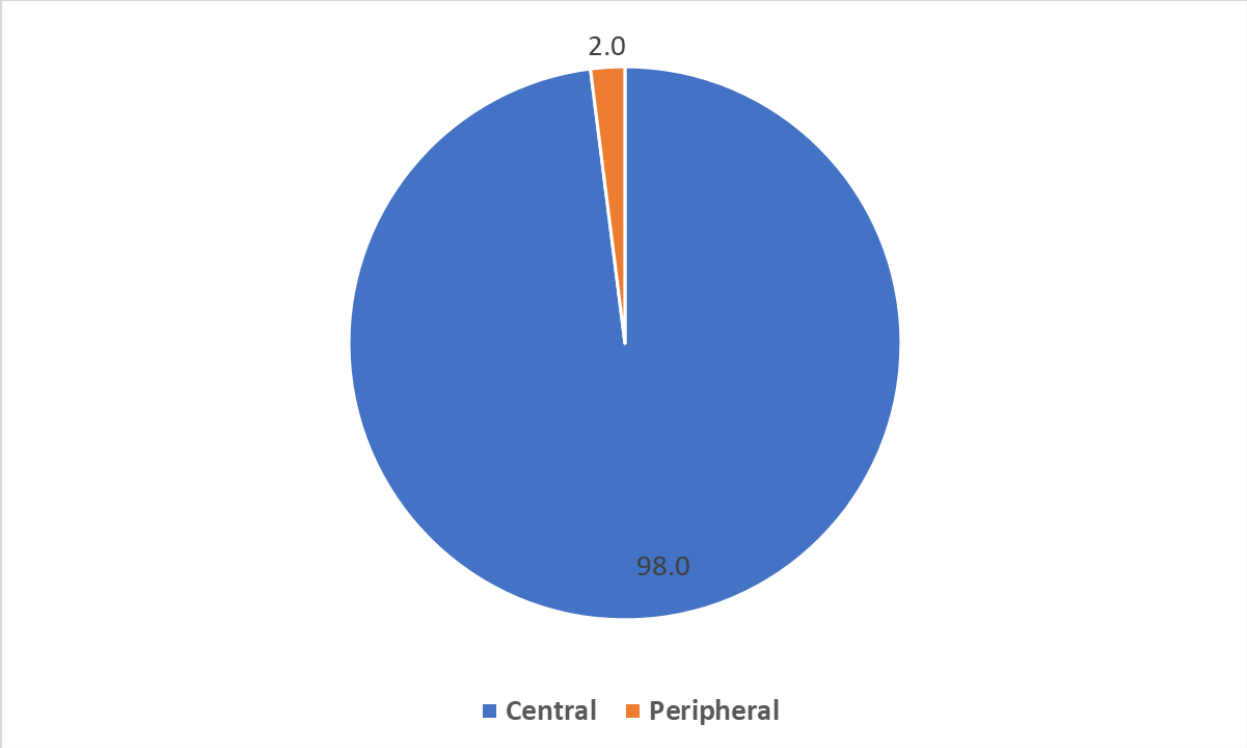

Figure 2. Distribution of patients based on type of AVS

Primary outcome

The Sn., Sp., PPV, NPV values of HINTS examination in differentiation of PCS and PVD were found to be 100%, 2.6%, 25.5%, and 100% respectively. The diagnostic accuracy of HINTS examination in differentiation of PCS and PVD was found to be 27% (Table 3).

Table 3: Primary outcome

Primary outcome	HINTS Exam
Sensitivity (Sn)	100%
Specificity (Sp)	2.6%
Positive Predictive Valus (PPV)	25.5%
Negative Predictive Valus (NPV)	100%
Diagnostic Accuracy	27%

Secondary outcomes

The results of secondary outcomes viz. diagnostic accuracy of individual components of HINTS examination in differentiating PCS and PVD were represented in Table 4. Results inferred that the diagnostic accuracy of HIT, Nystagmus, and TS were found to be 27%, 75%, and 75% respectively.

Table 4: Secondary outcomes

Components of HINTS	Diagnostic Accuracy
Head Impulse Test (HIT)	27%
Nystagmus	75%
Test of Skew (TS)	75%

Final diagnosis

The distribution of patients based on final diagnosis was illustrated in Figure 3. Results portray that in majority of the patients i.e., 77% were diagnosed as PVD using HINTS examination. Whereas, 23% of patients were diagnosed as PCS using the same HINTS examination. The Chi-square test revealed significant association (X^2 = 26.160; p=0.000) between PVD and PCS distribution among patients.

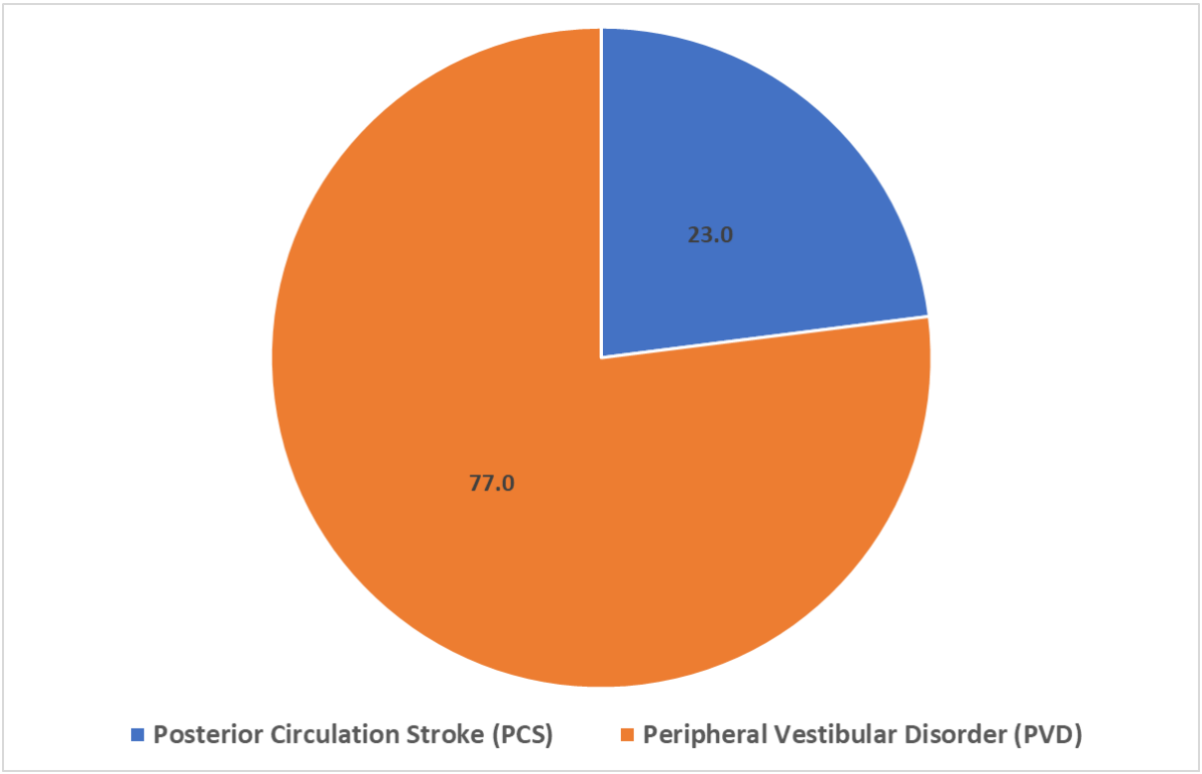

Figure 3. Distribution of patients based on final diagnosis

Discussion:-

Dizziness and vertigo are frequent reasons for presentation to the ED representing about 3% of all visits.[24,25] AVS is a specific form of dizziness usually accompanied by symptoms such as nausea,vomiting,nystagmus,gait disturbance, and persistent vertigo, which may stem from a benign peripheral cause (e.g., Ménière disease, vestibular neuritis) or a central cause (e.g., vertebrobasilar stroke, intracranial hemorrhage, cerebellar infarction).[26,27]Distinguishing between these causes can be difficult. Stroke remains the most frequently missed diagnosis in the ED. When conducted by clinicians with appropriate training, the HINTS examination offers high sensitivity and low-to-moderate specificity in detecting central causes of AVS. Nonetheless, the supporting evidence is of low quality, indicating the need for further prospective research before it can be broadly adopted in clinical practice.[27]

In our study the mean age of patients was found to be 61.62 years with 1:1 male to female distribution. These findings were comparable with the findings of literature studies reported by various other research investigators. In a prospective study carried out by Qiu et al., to evaluate the specificity and sensitivity of HINTS examination in distinguishing between central and peripheral AVS; the mean age of study subjects was found to 61.47 years in central AVS cases and 54.08 years in Peripheral AVS cases with similar distribution of male and female patients in central AVS cases like in our study. In majority of the patient's hypertension was found to be the major risk factor for AVS followed by Type 2 Diabetes mellitus, and smoking in our study. Concurrently, Qiu et al., also reported hypertension and Type 2 Diabetes mellitus as risk factors of central and peripheral AVS cases in their prospective study.[28]

In a prospective study carried out by Qiu et al., to evaluate the specificity and sensitivity of HINTS in distinguishing between central and peripheral AVS, reported peripheral AVS as dominant cases which accounts for 79.50%, and central AVS cases accounts for 20.50%.[28] However, these findings were in contrast with our findings of AVS distribution wherein we found central AVS cases as dominant accounts for 98% followed by peripheral AVS cases accounts for only 2%. Majorly, acute right cerebellar infarct and acute left cerebellar infarct were observed in 7% and 3% of the patients respectively in our study.

The meta-analysis study comprised 16 studies, including 14 prospective and 2 retrospective studies that evaluated 2,024 patients performed by Gottlieb et al., found that both HINTS- and HINTS Plus-Examinations yielded high sensitivity and reasonable specificity in identifying a central cause of AVS. However, individual components of the HINTS examination in isolation did not demonstrate high sensitivities.[27] In concurrence with these literature findings in our study also we found 100%, 2.6%, 25.5%, and 100% of sensitivity, specificity, PPV, and NPV respectively for HINTS examination in differentiation of PCS and PVD. Additionally, we determined the diagnostic accuracy of HINTS examination as 27% in differentiation of PCS and PVD. The diagnostic accuracy of individual components of HINTS examination viz. HIT, Nystagmus, and TS were found to be 27%, 75%, and 75% respectively. These findings depicted that Nystagmus and TS components of HINTS examination as pivotal for accurate differentiation of PCS and PVD in patients presented with AVS.

Moreover, literature reports evidenced that early discrimination between central and peripheral AVS is very important for early identification of possible PCS. CT is sensitive for hemorrhagic lesions, but not for ischemic lesions.[29] Although DWI of MRI can identify early ischemic lesions, the access to MRI examination is relatively limited.[30] Moreover, the false-negative rate of MRI diffusion-weighted imaging can still be as high as 12% and 48 h after the onset of symptoms of small posterior circulation cerebral infarction.[2] The HINTS examination test was developed by neuro-ophthalmologists as a bedside test to rule out central causes of vertigo in patients with AVS, which has been incorporated into clinical practice by frontline emergency physicians.[2,17] A systematic study showed that patients with a positive HINTS test had a 15-fold higher risk of developing PCS than those with a negative HINTS test, with a combined sensitivity of 95.5% and specificity of 71.2% using HINTS for any stroke. The overall PPV was 59.9% and the NPV was 97.2%.[31] These findings of PPV and NPV values of HINTS-Examination were comparable with our study.

The rationale and performance of HINTS examination could be understood from the literature that the neurophysiologic basis of HINTS was studied by Schmid-Priscoveanu et al., and the utilization of magnetic search coil recordings showed the loss of VOR in AVS among positive horizontal head impulse test (h-HIT) patients.[32] Additional tests potentially of diagnostic value include horizontal head-shake to examine the velocity storage mechanism in brainstem and the cerebellar nodulus.[33] The presence of horizontal directional-change or vertical post-head shaking nystagmus suggests brainstem or cerebellum abnormalities.[34] However, stroke in the AICA region remains a diagnostic challenge, as lesions affecting the vestibular root entrance, tract, or nucleus may be associated with a positive (abnormal h-HIT).

To address potential localization challenges, large skew deviation (>3 prism diopters) in AVS patients' needs special attention and is a good discriminator.[35] Hotson and Baloh, described the unidirectional horizontal nystagmus in peripheral vestibular lesions, following Alexander's law.[26] A group of researchers of Kattah and Kung have demonstrated that nystagmus increases with fixation block in central lesions, and, therefore does not have specific localization value.[13,36] Hotson, et al., and later Newman-Toker et al. further showed that horizontal gaze direction-change nystagmus (GEN) as a specific hallmark of central lesions.[26,37] The presence of vertical or pure torsional

nystagmus is also the result of central lesions. Central nystagmus symptoms are highly specific in their presentation, but unfortunately rarely present.[28]

Conclusion:-

In conclusion, the HINTS examination is a simple, low-cost, and highly sensitive tool with good specificity for distinguishing PCS from PVS in patients presenting with AVS, offering moderate overall diagnostic accuracy. The Nystagmus and Test of Skew components are particularly crucial for precise differentiation between PCS and PVD in such cases. Additionally, because the HINTS examination does not require specialized technical equipment, it is well-suited for use in EDs and can be broadly adopted in primary hospitals following thorough training of healthcare providers.

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