CRANIAL AUTONOMIC SYMPTOMS AMONG MIGRAINE DIAGNOSED PATIENTS: PREVALENCE AND CLINICAL IMPLICATIONS

Manoj Dhungana,[1] Sanjeev Shah,[2] Rajesh Shrestha,[1] Arpana Pokhrel[1]

ABSTRACT

INTRODUCTION

Cranial autonomic symptoms (CAS) are increasingly identified in migraine patients, making diagnosis more challenging due to similarities with Trigeminal Autonomic Cephalagias (TACs). This study is conducted to determine the prevalence of CAS in Nepalese migraine cohort and highlight their importance in improving diagnostic accuracy and guiding individualized treatment in resource limited setting.

MATERIAL AND METHODS

This cross-sectional study involved 150 migraine patients at a Medical College Headache clinic, Department of Psychiatry in Nepal. Psychiatrists applied ICHD-3 beta criteria for diagnosis and assessed the presence of CAS. Data were collected using a pretested structured interview questionnaire and analyzed with SPSS version 16, using both descriptive and inferential statistics. Ethical approval was obtained from the Institutional review Committee (IRC-DMCRI/047/2022) of Devdaha Medical College, and written informed consent was secured. Strict confidentiality of participants' information was maintained throughout the study.

RESULTS

At least one CAS was reported by 73.3% of patients. The most common symptoms were eyelid edema (54.5%), conjunctival injection (49.1%), lacrimation (47.3%), and aural fullness (45.5%). CAS occurred more often in males (86.7% vs. 70% in females) and was most frequent in the 20-30 year of age group (85.0%).

CONCLUSION

CAS is common in migraine and may mimic TACs or other secondary headaches. Routine screening can improve diagnostic accuracy and guide individualized treatment plans.

KEYWORDS

Cranial autonomic symptoms, Migraine, Clinical significance

1. Department of Psychiatry, Devdaha Medical College and Research Institute, Bhaluhi, Nepal
2. Department of Psychiatry, Universal College of Medical Sciences, Bhairahawa, Nepal

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For Correspondence
Dr. Manoj Dhungana
Department of Psychiatry
Devdaha Medical College and Research Institute
Bhaluhi, Nepal
Email: drmanoj3536@gmail.com

INTRODUCTION

Migraine is a common primary headache disorder characterized by recurrent attacks of moderate to severe headache, often accompanied by nausea, photophobia, and phonophobia. It is a highly prevalent neurological condition affecting approximately 14% of the global population, ranking among the leading causes of disability worldwide.[1] Migraine is disabling primary headache disorder, affecting over 1 billion individuals' worldwide.[2] While traditionally characterized by recurrent attacks of moderate-to-severe headache, often accompanied by nausea, photophobia, and phonophobia, migraine can also present with a range of cranial autonomic symptoms (CAS).[3] These include lacrimation, conjunctival injection, eyelid edema, nasal congestion, rhinorrhea, facial sweating or flushing, aural fullness, and miosis.[4,5]

CAS has been extensively described in trigeminal autonomic cephalalgias (TACs), such as cluster headache, but accumulating evidence indicates that they are also highly prevalent among migraine patients.[6,7] Reported prevalence rates vary between 50% and 80%, with symptom patterns differing by attack laterality, chronicity, and patient demographics.[3,8] These symptoms can lead to diagnostic confusion, particularly with secondary headache disorders such as sinusitis, or psychiatric conditions when misinterpreted as somatic complaints.[5,9]

Several studies have shown that CAS occurs in up to one-third of migraine patients, though prevalence rates vary depending on the population studied and the diagnostic criteria applied.[4,10] The presence of CAS in migraine may lead to diagnostic challenges, as it can mimic TACs, potentially resulting in misclassification and inappropriate management.[10]

The pathophysiology of CAS in migraine is believed to involve activation of the trigeminovascular system, leading to parasympathetic outflow via the superior salivatory nucleus and sphenopalatine ganglion.[3,4] Hypothalamic dysregulation may also play a role, influencing autonomic expression and potentially contributing to differences between migraine subtypes.[6] Recognizing CAS is essential for accurate diagnosis, avoiding unnecessary investigations, and guiding individualized treatment strategies, including targeted preventive therapies such as CGRP antagonists.[3,7]

The occurrence of CAS in migraine is also associated with higher headache frequency, increased headache-related disability, and greater allodynia.[11] Despite increasing recognition of CAS in migraine, there is a paucity of data from low and middle-income countries, including Nepal, where access to specialized headache services and advanced neuroimaging is limited. Understanding the prevalence and clinical implications of CAS in such settings may improve diagnostic accuracy, reduce mismanagement, and support tailored therapeutic approaches.[10]

In Nepal, where primary headache disorders are highly prevalent, determining the prevalence of CAS can help develop cost-effective diagnostic approaches in resource-limited settings.[9] Overlap between CAS and TACs can result in misdiagnosis, leading to inappropriate treatment (e.g., unnecessary use of antibiotics or wrong medications like indomethacin) and delayed management.[3] The presence of CAS in migraine has clinical implications for treatment and prognosis, including tailoring therapist such as gene-related peptide (CGRP) antagonists.[4,7]

This study aims to measure the prevalence of CAS in a Nepalese migraine cohort and provide practical insights for headache specialists to improve diagnosis and management in both neurological and psychiatric care.

MATERIAL AND METHODS

This cross-sectional study included 150 migraine patients diagnosed using the ICHD-3 (Beta version) criteria at the Headache clinic, Department of Psychiatry, Devdaha Medical College, Lumbini Province, Nepal, between August 2023 and July 2024. Data were collected using a pretested structured interview questionnaire and analyzed using descriptive and inferential statistics in SPSS version 16. An enumerative sampling technique was applied.

Ethical approval was obtained from the Institutional review Committee (IRC-DMCRI/047/2022) of Devdaha Medical College and Research Institute, Rupandehi. Written informed consent was obtained from all participants after clearly explaining the study objectives and strictly confidentiality of participants' information was maintained throughout the study.

Inclusion Criteria:
- Age >18 to 55 years
- Confirmed diagnosis of migraine (with or without aura)

Exclusion criteria:
- Previously diagnosed TACs (e.g., cluster headache, paroxysmal hemicrania)
- Presence of sinusitis, orbital pathologies, or other secondary headache causes
- Neuropsychaitric disorders that could mimic CAS (e.g., somatoform disorders)

Data were gathered through face-to-face structured interviews using a standardized proforma to record demographic details (age, sex), migraine characteristics (episodic vs. chronic, presence of aura), and cranial autonomic symptoms (CAS) (yes/no), including their type and laterality (unilateral, bilateral, alternating). CAS assessment for migraine patients covered symptoms such as lacrimation, conjunctival injection, eyelid edema, aural fullness, nasal congestion, rhinorrhea, facial sweating, facial flushing, ptosis, and miosis, based on established headache literature. Trained psychiatrists conducted the interviews to ensure consistency. Collected data were entered into a secure database and analyzed descriptively using SPSS Statistics (version 16). Prevalence was defined as the percentage of patients reporting each symptom, with subgroup analyses by sex and age group (18–30, 31–40, 41–55 years). As this was a descriptive study, no inferential statistical tests were applied.

RESULTS

Out of 150 patients (120 females, 30 males, mean age 32.4± 8.7 years), 110 (73.3%) experienced at least one cranial autonomic symptom (CAS) during migraine episodes. The highest prevalence was found in patients aged 20-30 years (85.0%)

Table 1. CAS prevalence by age group (n=150)

Age group (years)	Frequency	CAS-positive (n)	Prevalence (%)
20–30	60	51	85.0
31–40	50	41	82.0
41–55	40	18	45.0
Total	150	110	73.3

Table 1 shows CAS prevalence by age group. The highest prevalence was in patients aged 20–30 years (85.0%).

Table 2. Individual CAS Prevalence (n=110)

Symptom	Number (n)	Prevalence (%)
Eyelid edema	60	54.5
Conjunctival injection	54	49.1
Lacrimation	52	47.3
Aural fullness	50	45.5
Facial sweating	39	35.5
Facial flushing	18	16.4
Nasal congestion	15	13.6
Rhinorrhea	8	7.3
Ptosis	7	6.4

Table 2 lists individual CAS frequencies among the 110 CAS-positive patients. Eyelid edema (54.5%) was most common followed by conjunctival injection (49.1%).

Table 3. Gender Distribution (n=110)

Gender	Number (n)	Percentage (%)
Female	84	76.4
Male	26	23.6

Table 3 shows CAS-positive patient gender distribution: 76.4% female, 23.6% male (ratio 3.2:1).

Table 4. Number of CAS Symptoms (n=110)

Number of Symptoms	Number (n)	Percentage (%)
One	58	52.7
Two	42	38.2
Three or more	10	9.1

Table 4 shows the number of CAS symptoms per patient. Most had one or two symptoms.

Table 5. CAS Laterality (n=110)

Laterality	Number (n)	Percentage (%)
Unilateral	66	60.0
Bilateral	33	30.0
Alternating	11	10.0

Among CAS-positive patients, 60% reported unilateral, 30% bilateral, and 10% alternating laterality (Table 5).

DISCUSSION

This study demonstrate that cranial autonomic symptoms are highly prevalent among migraine patients, with 73.3% experiencing at least one symptom consistent with previous reports indicating prevalence rates 50-80%.[2-5] The most frequently observed symptoms were eyelid edema (54.5%), conjunctival injection (49.1%), lacrimation (47.3%), indicating a significant overlap with trigeminal autonomic cephalgias (TACs). Such overlap can increase the risk of misdiagnosis as cluster headache or paroxysmal hemicraniation.[4]

In this Nepalese cohort, the high CAS prevalence corresponds with regional data on primary headache disorders and may be influenced by genetic or environmental factors.[8] A prospective study also reported similar CAS prevalence, linking these symptoms to central sensitization, which could explain their prominence in our cohort.[5]

The higher prevalence observed in males (86.7% vs. 70% in females) and in younger patients (85.0% in those aged 20-30 years) suggests possible demographic influences, though the descriptive nature of this study limits causal interpretation. The underlying pathophysiology of CAS in migraine involves activation of the trigemino vascular system, which stimulates parasympathetic outflow via the superior salivatory nucleus and the sphenopalatine ganglion.[6]

Hypothalamic dysregulation, implicated in both migraine and TACs, may further contribute to CAS expression-particularly in chronic migraine. However, our findings indicate lower CAS prevalence in chronic migraine (64.0%) compared to episodic migraine (78.0%).[6] Routine CAS screening especially for eyelid edema, lacrimation, and aural fullness is crucial for accurate diagnosis, particularly in resource-limited settings like Nepal, where access to neuroimaging may be limited.[9]

Future research should investigate whether CAS prevalence differs across ethnic or geographic groups and explore targeted treatment strategies, such as CGRP antagonists, for migraine patients with CAS.[5,7]

Cranial autonomic symptoms present several clinical challenges. First, they can resemble secondary headaches-such as sinusitis leading to unnecessary ENT referrals or antibiotic prescriptions. In Nepal, where access to otolaryngology services or neuroimaging is limited, this may delay effective migraine management.[9] Second, in psychiatric contexts, CAS such as lacrimation or facial flushing may be misinterpreted as psychosomatic symptoms, increasing the risk of misdiagnosis as somatoform disorders.[4] This is especially concerning in regions where mental health stigma may discourage patients from seeking neurological evaluation.

Third, the presence of CAS may indicate a distinct migraine subtype with unique therapeutic implications. Evidence suggests that patients with CAS positive migraine may respond more favorably to CGRP antagonists than to triptans, potentially due to increased trigemino vascular activation.[4,7] The study finding that the majority of CAS positive patients (90.9%) reported only one or two symptoms further supports the potential value of a targeted screening approach to efficiently identify phenotype.

For headache specialists, systematic CAS screening particularly for eyelid edema, lacrimation, and aural fullness is vital for accurate diagnosis. In resource-limited settings, a targeted clinical assessment can reduce reliance on costly diagnostic tools such as MRI, preventing unnecessary referrals and promoting patient-centered care.[8]

Future research should explore whether the gender and age differences observed in CAS prevalence are linked to biological or environmental factors, and whether patients with CAS positive migraine benefit from tailored preventive strategies, including topiramate or CGRP targeted monoclonal antibodies.[6]

CONCLUSION

Cranial autonomic symptoms were present in 73.3% of migraine patients, frequently resembling trigeminal autonomic cephalalgias or secondary headaches. Systematic screening for CAS especially eyelid edema, lacrimation, and aural fullness can improve diagnostic accuracy and guide personalized management. These findings are particularly relevant in resource-limited settings like Nepal, where a targeted history taking approach can optimize headache diagnosis and minimize diagnostic delays.

This study has several limitations. Being conducted at a single center may restrict the generalizability of findings. Reliance on patient reported symptoms introduces the possibility of recall bias. Additionally, the descriptive study design did not allow for inferential statistical analysis of demographic associations, such as the higher CAS prevalence observed in males or younger patients. Future research could address these gaps by incorporating objective measures (e.g., tear production quantification) or using longitudinal designs to track CAS stability and treatment outcomes.

CONFLICT OF INTEREST

None

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