



## Relation of sinonasal anatomic variants with the frequency, pain severity and time off work in patients with migraine

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### Abstract

**Aim:** Chronic migraine (CM) is a condition characterized by attacks of severe headaches leading to an increase in time off work, decrease in work productivity and in physical functioning. The aim of this study was to investigate the role of sinus anatomic variants (SAV) on the evolution of migraine from episodic to chronic form.

**Methods:** Two hundred and seven migraineurs [110 with episodic migraine (EM) and 97 with CM] with no evidence of nasal septal deviation with a contact point on the lateral nasal wall were evaluated for endoscopic, radiologic and anatomic variant (AV) abnormalities using Lund-Kennedy endoscopy (LKES) and Lund-Mackay radiology scores (LMRS). Headache day frequency, duration, severity and lost time at work were compared with regard to the presence of any AV and concha bullosa (CB) as well.

**Results:** There was a very significant difference between EM and CM patients with regard to overall SAV and endoscopy scores. However, no significant difference was seen between the groups with regard to radiology scores and headache pain severity. The presence of one AV increased headache day frequency, severity and days off work in all patients. CB was found to worsen headache severity and lost time at work in all patients.

**Conclusions:** Patients with CM have more SAV and worse endoscopy scores than patients with EM. The presence of any of the AVs increases headache day frequency, pain severity and days off work in migraineurs.

### Keywords

Chronic migraine, episodic migraine, sinonasal anatomic variants, headache severity, sinus endoscopy, concha bullosa, Lund-Mackay scores, Lund-Kennedy scores



## Introduction

Migraine is a chronic disorder characterized by attacks of severe headaches leading to increased time off work, decreased work productivity and impaired physical functioning. The global prevalence of current migraine and lifetime prevalence are estimated by the WHO to be 10% and 14%, respectively [1].

In a review of epidemiologic studies, 10.3% of men and 23.1% of women in Turkey were identified as having migraine [2].

Headache attacks of moderate or severe pain intensity lasting 4 to 72 hours (if unresponsive to treatment) associated with nausea and/or vomiting or photophobia and phonophobia, which may be aggravated by routine physical activity, are the typical symptoms of migraine [3].

More recently, in June 2013, the International Classification of Headache Disorders, third edition (ICHD-III, beta version) added chronic migraine (CM), which occurs on at least 15 days of the month for more than 3 months. The chronic form usually evolves from the episodic form and causes significant functional disability and morbidity [4].

Migraineurs, both men and women, have a 2.5-fold increased risk of subclinical cerebellar stroke, and those with migraine with aura and increased headache frequency have the highest risk [5]. This explains why prophylactic therapy is almost always used in combination with acute migraine treatment. Acute treatment aims to eliminate the headache, while preventive treatment, which is given even when the headache is not present, aims to reduce the frequency and severity of migraine attacks to prevent progression from an acute form to a CM and to improve the patient's quality of life [6].

In addition to various factors (hormonal changes, stress, sleep disorders, head trauma, etc.) that are thought to exacerbate migraine attacks, endonasal contact points and concha bullosa (CB), which is one of the main anatomic variants (AVs), are thought to trigger various forms of headache via the trigeminovascular system and the release of substance P [7].

In view of these studies suggesting that sinonasal pathologies may trigger migraine attacks, we aimed to investigate the role of CB and other sinus AV (SAV) in the progression of migraine from episodic to chronic form.

## Materials and methods

### Study design and patient selection

This cross-sectional clinical study was designed to evaluate the effect of SAV, endoscopy, and radiology scores on daily headache frequency, pain severity, pain duration, and time lost from work per month in patients with migraine.

The study was approved by the Institutional Review Board of Haydarpaşa Numune Educational and Research Hospital Istanbul with study identification number (HNEAH-KAEK 2012/40) and included patients  $\geq 18$  years of age with migraine who were treated for migraine attacks at the neurology outpatient clinic based on ICHD-III, beta version [4]. Informed consent to participate in the study was obtained from all participants. Patients were selected from those with no evidence of intracranial pathology on cranial magnetic resonance imaging already obtained at the request of the neurology clinic. Patients were excluded if they had a history of chronic rhinosinusitis (CRS), nasal septal deviation with a contact point on the lateral nasal wall, or any other systemic disease such as hypertension, diabetes, etc., and intracranial pathologies that might bias the study toward other types of headache. Patients who did not undergo cranial MRI were also excluded.

Patients meeting the criteria for migraine and reporting an average of 15 or more headache days/month over the previous 3 months were classified as having CM, whereas those reporting an average of less than 15 headache days/month over the previous 3 months were classified as having episodic migraine (EM).

## Main outcomes and measures

Outcomes were self-reported headache frequency, headache pain severity, pain duration, and days of work lost per month.

Migraine pain severity was rated on a global scale from 0 to 10 (0 = no pain; 10 = most pain imaginable) using a visual analog scale (VAS). Headache duration was recorded in hours from onset to resolution.

The following assessments were also included in the study to compare the groups. These were: patients' endoscopic scoring, radiologic grading, and AV grading by another colleague blinded to patient history using Lund-Kennedy endoscopy (LKES) and Lund-Mackay radiology scores (LMRS). LMRS was performed according to the most recent MRI. Additional sinus imaging was not performed [8, 9].

LKES is a three-point scale (0, 1, 2) that assesses the presence of polyps, edema, and discharge.

LMRS (0–12, for each side) and AV [absent frontal sinus, CB, agger nasi cell (AN), Haller cell (HC), paradoxical middle turbinate, everted uncinate process; 1 = present, 0 = absent] are adapted from the Lund-Mackay staging system.

## Sample size

The G\*Power program (v3.1.7) was used for the power analysis of the study. Power and sample size were calculated based on the frequency of AVs between EM and CM groups by comparing left and right sinonasal cavities. Sensitivity analysis and power calculation using our own estimates of AV scores from our previous data showed that a sample size of at least 94 patients would give us the ability to detect significant differences in the means of AV between the EM and CM groups ( $\delta = 0.463$  for the right side;  $\delta = 0.420$  for the left side; power 80%;  $\alpha = 0.05$ ).

## Statistical analysis

NCSS (Number Cruncher Statistical System) 2007 & PASS (Power Analysis and Sample Size) 2008 statistical software (UT, USA) were used for statistical analysis of the results.

Descriptive (mean, standard deviation, frequency, median, percentage, minimum and maximum) and quantitative statistical methods were used to evaluate the study data. For quantitative analyses, the Mann Whitney *U* test was used to compare two groups with parameters that did not have a normal distribution, and the Student *t*-test was used to compare two groups with parameters that did have a normal distribution. Pearson Chi-square, Fisher's exact and Yates continuity correction tests were used to compare qualitative data. The relationship between parameters was analyzed using Spearman's correlation test. Results were evaluated with 95% confidence interval with accepted significance level of  $P < 0.01$  and  $P < 0.05$ .

## Results

Two hundred and seven patients (66 males, 31.9%; 141 females, 68.1%) with a mean age of approximately  $39.43 \pm 8.54$  years (range: 22–53 years) were included in the study. Among them, 110 were diagnosed with EM and 97 with CM. The duration of symptoms ranged from 2 to 32 years with a mean of  $14.51 \pm 8.62$  years. Hundred and forty-three (69.1%) patients had the characteristics of migraine with aura. Headache duration ranged from 4 to 24 hours with a mean of approximately  $14.73 \pm 9.24$  hours. Migraine frequency ranged from 2.5 to 16 days with a mean of  $11.37 \pm 4.15$  days. Pain severity (VAS) ranged from 6 to 10 points with a mean of  $9.35 \pm 1.05$  points. Mean lost work time was  $5.56 \pm 3.34$  days (range: 1–15 days) (Table 1).

No statistically significant difference was found between EM and CM groups with regard to gender and age distribution of patients (Pearson Chi-square for gender, Student *t*-test for age distribution  $P > 0.05$ ).

**Table 1.** Distribution of descriptive characteristics of the patients

Characteristics		Min-Max	Mean $\pm$ SD
Age (years)		22–53	39.43 $\pm$ 8.54
Duration of symptoms (years)		2–32	14.51 $\pm$ 8.62
Headache duration (hours)		4–24	14.73 $\pm$ 9.24
Frequency of migraine (days)		2.5–16	11.37 $\pm$ 4.15
Pain severity (VAS)		6–10	9.35 $\pm$ 1.05
Lost time at work (days)		1–15	5.56 $\pm$ 3.34
		<i>n</i>	%
Gender	Female	141	68.1
	Male	66	31.9
Aura	Present	143	69.1
	Absent	64	30.9

VAS: visual analog scale

The mean total AV frequency of EM and CM patients were  $1.05 \pm 0.80$ ;  $1.46 \pm 0.68$  on the right side and  $1.34 \pm 1.00$ ;  $1.78 \pm 0.91$  on the left side. There was a very significant difference between patients with EM and CM regarding total right SAV (Mann Whitney *U* test,  $P = 0.001$ ). Patients with CM had more SAV on the right sinonasal cavity than those with EM (Table 2).

**Table 2.** Analysis of overall anatomic variants, Lund-Mackay radiology and Lund-Kennedy endoscopy scores according to migraine types

Sinus and nasal evaluation scores		Migraine types		<i>P</i>
		Episodic migraine < 15 days ( <i>n</i> = 110)	Chronic migraine $\geq$ 15 days ( <i>n</i> = 97)	
Overall right anatomic variant	Min-Max (median)	0–2 (1)	0–2 (2)	0.001**
	Mean $\pm$ SD	$1.05 \pm 0.80$	$1.46 \pm 0.68$	
Overall left anatomic variant	Min-Max (median)	0–3 (2)	0–3 (2)	0.002**
	Mean $\pm$ SD	$1.34 \pm 1.00$	$1.78 \pm 0.91$	
Right Lund-Mackay radiology scores	Min-Max (median)	0–2 (0)	0–6 (0)	0.060
	Mean $\pm$ SD	$0.43 \pm 0.77$	$1.32 \pm 2.24$	
Left Lund-Mackay radiology scores	Min-Max (median)	0–1 (0)	0–6 (0)	0.317
	Mean $\pm$ SD	$0.37 \pm 0.49$	$1.33 \pm 2.23$	
Right Lund-Kennedy endoscopy scores	Min-Max (median)	1–4 (2)	2–6 (4)	0.001**
	Mean $\pm$ SD	$1.89 \pm 0.81$	$3.28 \pm 1.34$	
Left Lund-Kennedy endoscopy scores	Min-Max (median)	1–4 (2)	2–6 (4)	0.001**
	Mean $\pm$ SD	$2.09 \pm 0.81$	$3.28 \pm 1.34$	

Mann Whitney *U* test indicates statistically significant differences, \*\*:  $P < 0.01$

Similarly, total left AV were very significantly higher in patients with CM (Mann Whitney *U* test,  $P = 0.002$ ;  $P < 0.01$ ). Patients with CM had more AV on the left sinonasal cavity than those with EM (Table 2).

Mean LMRS of EM and CM patients were  $0.43 \pm 0.77$ ;  $1.32 \pm 2.24$  on the right side and  $0.37 \pm 0.49$ ;  $1.33 \pm 2.23$  on the left side.

No statistically significant difference was found between CM and EM patients regarding right and left LMRS. However, although not statistically significant, the difference between right LMRS of the groups was close to the significance level (Mann Whitney *U* test,  $P = 0.06$ ) (Table 2).

Mean LKES of EM and CM patients were  $1.89 \pm 0.81$ ;  $3.28 \pm 1.34$  on the right side and  $2.09 \pm 0.81$ ;  $3.28 \pm 1.34$  on the left side.

Endoscopy scores of CM patients were very significantly higher than those of EM patients on the right side (Mann Whitney *U* test,  $P = 0.001$ ;  $P < 0.01$ ). Patients with CM had worse (higher) scores on their right endoscopy. Similarly, left LKES were very significantly higher (worse) in CM than in EM patients (Mann Whitney *U* test,  $P = 0.001$ ;  $P < 0.01$ ) (Table 2).

Statistical analysis of AV showed that CB was the most frequent anatomical variant in migraineurs, followed by AN, HC and paradoxical middle turbinate. CB was present in 67/110 patients in EM and 74/97 patients in CM on the right side. CB was significantly more frequent in the right nasal cavity in CM than in EM patients (76.3% vs. 60.9%; Yates continuity correction test,  $P = 0.026$ ;  $P < 0.05$ ). On the other hand, no statistically significant difference was observed between the patient groups regarding the presence of left CB (76.3% vs. 70.9%; Yates continuity correction test,  $P = 0.474$ ;  $P > 0.05$ ) (Table 3).

**Table 3.** Analysis of concha bullosa, agger nasi cell, Haller cell, paradox concha according to migraine types

Nasal anatomic variations		Migraine types		P
		Episodic migraine < 15 days (n = 110)	Chronic migraine ≥ 15 days (n = 97)	
		n (%)	n (%)	
Right concha bullosa	Absent	43 (39.1%)	23 (23.7%)	<sup>a</sup> 0.026*
	Present	67 (60.9%)	74 (76.3%)	
Left concha bullosa	Absent	32 (29.1%)	23 (23.7%)	<sup>a</sup> 0.474
	Present	78 (70.9%)	74 (76.3%)	
Right agger nasi	Absent	61 (55.5%)	44 (45.4%)	<sup>b</sup> 0.147
	Present	49 (44.5%)	53 (54.6%)	
Left agger nasi	Absent	61 (55.5%)	34 (35.1%)	<sup>b</sup> 0.003**
	Present	49 (44.5%)	63 (64.9%)	
Right Haller cell	Absent	110 (100%)	87 (89.7%)	<sup>c</sup> 0.001**
	Present	0 (0%)	10 (10.3%)	
Left Haller cell	Absent	100 (90.9%)	77 (79.4%)	<sup>a</sup> 0.031*
	Present	10 (9.1%)	20 (20.6%)	
Right paradoxical concha	Absent	110 (100%)	97 (100%)	-
	Present	0 (0%)	0 (0%)	
Left paradoxical concha	Absent	100 (90.9%)	87 (89.7%)	<sup>a</sup> 0.952
	Present	10 (9.1%)	10 (10.3%)	

<sup>a</sup> Yates continuity correction test; <sup>b</sup> Pearson Chi-square test; <sup>c</sup> Fisher's exact test. \*\*:  $P < 0.01$ ; \*:  $P < 0.05$ ; -: not applicable

No significant difference was observed between the patient groups regarding the presence of right AN (54.6% vs. 44.5%; Pearson Chi-square test,  $P = 0.147$ ;  $P > 0.05$ ). However, AN in the left nasal cavity was significantly more frequent in CM patients (64.9% vs. 44.5%; Pearson Chi-square test,  $P = 0.003$ ;  $P < 0.01$ ) (Table 3).

HC was significantly more frequent in both right and left sides in CM patients (Fisher's exact test,  $P = 0.001$ ;  $P < 0.01$ ; Yates continuity correction test,  $P = 0.031$ ). CM patients had more HCs on both right and left sinuses than EM patients (Table 3).

There was no statistically significant difference between groups regarding the frequency of right and left paradoxical middle concha (Yates continuity correction test,  $P > 0.05$ ). No everted uncinate process was observed in any patient (Table 3).

Mean headache severity of EM and CM patients was  $9.18 \pm 1.27$  and  $9.54 \pm 0.69$ , respectively.

Group analysis of headache pain severity revealed no significant difference between CM and EM groups in pain severity on VAS (Mann Whitney  $U$  test,  $P = 0.258$ ;  $P > 0.01$ ). However, a very significant difference was found between CM and EM patients regarding the number of days lost from work per month ( $3.98 \pm 2.49$  days for EM;  $7.36 \pm 3.28$  days for CM; Mann Whitney  $U$  test,  $P = 0.001$ ;  $P < 0.01$ ). Patients with CM were more frequently absent from work (Table 4).

Correlation analysis between headache duration (hours) and work absenteeism showed no correlation between headache duration and work absenteeism in both groups (Spearman's correlation  $r$ :  $-0.170$ ,  $P = 0.076$ ;  $r$ :  $-0.179$ ,  $P = 0.080$ ;  $P > 0.05$ ). Headache duration was not a factor influencing lost work days in migraineurs (Table 5).

**Table 4.** Comparison of VAS scores and time off-work according to the types of migraine

Headache impact metrics	Migraine types		<i>P</i>
	Episodic migraine < 15 days ( <i>n</i> = 110)	Chronic migraine ≥ 15 days ( <i>n</i> = 97)	
	Mean ± SD (median)	Mean ± SD (median)	
Migraine VAS	9.18 ± 1.27 (10)	9.54 ± 0.69 (10)	0.258
Time off-work (days)	3.98 ± 2.49 (3)	7.36 ± 3.28 (7)	0.001**

VAS: visual analog scale. Mann Whitney *U* test indicates statistically significant differences, \*\*: *P* < 0.01

**Table 5.** Relation of time off-work to the duration of headache in episodic and chronic migraine

Migraine type	Time off-work (days) * Duration (hours)	
	<i>r</i>	<i>P</i>
Episodic migraine < 15 days ( <i>n</i> = 110)	−0.170	0.076
Chronic migraine ≥ 15 days ( <i>n</i> = 97)	−0.179	0.080
Total ( <i>n</i> = 207)	0.058	0.403

*r*: Spearman's correlation coefficient

Statistical analysis was also performed to define the role of AV on migraine day frequency, headache severity, and work loss in all patients. Headache day count, pain severity, and lost work days were significantly higher in patients with the presence of an AV. The presence of any of these AVs was found to increase headache daily frequency, pain severity and days lost from work in all migraineurs (Kruskal Wallis test; \*: *P* < 0.05, \*\*: *P* < 0.01, Table 6).

**Table 6.** Evaluation of migraine frequency, pain severity and days off work according to the presence of an anatomic variant

Characteristics	Right anatomic variant			Left anatomic variant		
	Absent	Present	<i>P</i>	Absent	Present	<i>P</i>
<i>n</i>	45	71	-	45	40	-
Migraine frequency (days)	10.78 ± 2.97	12.32 ± 3.14	0.013*	10.78 ± 2.97	12.13 ± 3.55	0.001**
Days off work (days)	3.14 ± 0.88	6.16 ± 3.07	0.001**	3.14 ± 0.88	5.13 ± 3.80	0.001**
Pain severity VAS	9.04 ± 1.66	9.55 ± 0.75	0.219	9.04 ± 1.66	10.00 ± 0.00	0.001**

VAS: visual analog scale. Kruskal Wallis test indicates statistically significant differences, \*: *P* < 0.05; \*\*: *P* < 0.01; -: not applicable

However, except for headache frequency, pain severity and time off work were significantly higher in patients with CB. CB was found to be a factor that may have an influence on increasing headache severity and loss of productivity in patients (Mann Whitney *U* test; \*: *P* < 0.05, \*\*: *P* < 0.01, Table 7).

**Table 7.** Headache day frequency, pain severity (VAS) and time off work per month according to concha bullosa

Characteristics Mean ± SD (median)	Right concha bullosa			Left concha bullosa		
	Absent	Present	<i>P</i>	Absent	Present	<i>P</i>
Migraine frequency (days)	11.29 ± 2.92 (10)	11.41 ± 4.63 (15)	0.157	11.54 ± 3.14 (10)	11.31 ± 4.47 (12)	0.398
Time off work	4.15 ± 1.80 (3)	6.22 ± 3.68 (7)	0.001**	3.48 ± 1.07 (3)	6.31 ± 3.56 (7)	0.001**
Pain severity VAS	8.71 ± 1.45 (9)	9.65 ± 0.61 (10)	0.001**	8.85 ± 1.56 (10)	9.53 ± 0.73 (10)	0.027*

VAS: visual analog scale. Mann Whitney *U* test indicates statistically significant differences, \*: *P* < 0.05; \*\*: *P* < 0.01

## Discussion

Although some headache experts have not endorsed the concept of peripheral conditions activating migraine, there is a large body of literature that has defined processes involving the nasal passages and paranasal sinuses as triggering factors for migraine.



Since the late 1980s, the pathophysiology of contact point headaches has been discussed by Stammberger and Wolf as being caused by the release of substance P, a neuropeptide with potent vasodilatory effects that are transmitted via afferent C-fibers as a result of thermal, toxic, infectious and/or traumatic stimuli [10].

The correlation between migraine and the paranasal structures is further explained by the activation of the trigeminovascular system, which is distributed in the paranasal structures via the ophthalmic and maxillary branches and, when stimulated, produces inflammatory responses mediated by a peptide related to the calcitonin gene (CGRP) and substance P, causing headache. Both peptides, which are widely distributed in the nervous system, play a role in pain transmission, inflammation, and vasodilation in migraine [11].

Although the pathophysiology of migraine is considered by some authors to be relevant to rhinogenic headaches, many others believe that the central nervous system is the initiator of the migraine process, followed by sensitization of the peripheral neurons of the trigeminal nerve. This sensitization is thought to be often accompanied by cutaneous pain associated with normally mild stimuli in the paranasal area [12].

Migraine complaints are multifactorial in many patients and it is debated whether peripheral factors such as nasal contact points on the lateral nasal wall, rhinosinusitis symptoms, SAV or central activation of the trigeminal nerves innervating the meninges play a role in triggering episodic or daily headaches [13].

AVs affecting the nasal septum, AN, CB, ethmoid bulla narrowing the nasal cavities have been suggested in previous studies to cause nasal mucosal edema resulting in tissue hypoxia, release of serotonin and other vasoactive substances triggering the crisis. This contention was further supported in these studies by the relief of pain following surgical treatment of the AVs [14].

In contrast to the aforementioned authors, Bolger [15] conducted a review of sinus CT, analyzing middle concha pneumatization, AN and HC, and found no clear correlation between these conditions and migraine.

In the context of these conflicting judgments, our aim in the present study was to verify the association of sinonasal AVs, sinus endoscopic and radiological findings with the presence of episodic or CM.

Contrary to Bolger's statements, our study found that patients with CM had more AVs in the right and left sinonasal cavities than those with EM. Of the AVs, CB (76.3%) was the most common, followed by AN (64.9%) and HC (20.6%) in CM. Paradoxical middle concha was rare and equally seen in both groups. Furthermore, the analysis of migraine frequency, pain severity and days of work lost showed significant differences regarding the presence of AVs (Table 6). Considering the presence of more frequent SAVs in CM patients and their effect on increasing headache severity, frequency, and time off work, we may suggest that even in the absence of septal contact points, AVs may play a role in the progression of migraine headache from episodic to chronic form. Our findings are consistent with those of Stammberger et al. and Novak et al. in the context of AVs being considered headache-triggering factors [10, 14].

More recently, the impact of nasal abnormalities on headache severity was highlighted by Yazici et al. [16] in 2010. In their series of 99 patients, 70% were diagnosed with migraine. Of these, 73% were found to have nasal abnormalities consisting of septal deviation, turbinate hypertrophy, contact points, and CB. Headache severity based on VAS 3 and 6 months after surgery was reported to be significantly reduced in those who underwent surgery.

Later in 2011, the assertion that surgical correction of the nasal contact point could reduce headache duration and pain severity in migraine was strengthened by the study of Abu-Samra et al. [17] who found that elimination of the nasal contact points can improve the outcome for drug therapeutic effect in unresponsive chronic headache patients.

Our study differs from the study by Yazici et al. and Abu-Samra et al. in terms of study groups, exclusion of septal deviation with a contact point, and lack of surgical treatment. We preferred to compare all SAVs between EM and CM patients and analyze their effect on pain severity, chronicity, and loss of productivity. Although our study has some similarities, the presence of CB in worsening headache severity

was consistent with the aforementioned authors. In addition, other AVs such as AN, HC were also found to be more frequent in CM.

In addition to anatomical variations, subclinical inflammation found on CT or nasal endoscopy in migraine was again verified in 2008 in the series of Mehle et al. [18] with the surprising frequency of positive CT findings showing sinus abnormalities with extensive disease (LMRS > 5). Based on their findings, the authors declared that migrainous “sinus headache” and sinonasal disease often occur simultaneously. However, they were unable to interpret the nature of this association.

In 2009, it was reported that radiographic abnormalities on sinus CT in patients with sinus headaches with migraine and CRS were factors in worsening the course of migraine [19].

In our series, the mean LMRS of EM and CM patients were  $0.43 \pm 0.77$ ;  $1.32 \pm 2.24$  on the right side and  $0.37 \pm 0.49$ ;  $1.33 \pm 2.23$  on the left side. The sinonasal mucosa of all patients was affected by CRS to some extent in the CT images. In addition, although not statistically significant, the difference between right-side LMRS of the groups was close to the significance level ( $P = 0.06$ ). However, in our study, patients with CM did not show significant radiographic sinus disease and were not in agreement with the CT findings of Mehle et al. and Cady et al. [18, 19]. In contrast to these authors, we do not believe that the high radiographic scores seen in migraineurs are a consequence of real mucociliary dysfunction and chronic inflammation. Rather, based on the pathophysiological characteristics of migraine, positive sinus radiographic findings may be due to activation of the parasympathetic nervous system via the superior salivatory nucleus of the seventh cranial nerve, resulting in mucosal edema.

Mean LKES of EM and CM patients were  $1.89 \pm 0.81$ ;  $3.28 \pm 1.34$  on the right side and  $2.09 \pm 0.81$ ;  $3.28 \pm 1.34$  on the left side, respectively. Patients with CM showed more edema and discharge on endoscopy than those with EM on both sides.

Worse endoscopic scores (edema and discharge) in CM patients may be related to parasympathetic nervous system activation, which is more frequent in CM (> 15 days/month) than in EM (< 15 days/month). The nasal mucosal edema seen in our series supports the endoscopic evidence of nasal mucosal swelling, which has been shown to occur during a migraine attack and to resolve after administration of sumatriptan [20].

In our opinion, the reason for the worse nasal congestion in CM patients was primarily based on more migrainous days and secondarily on the presence of more frequent AVs, which are known to promote local inflammatory processes.

Although the headache pain severity did not show a significant difference between the groups in our study, the pain severity (mean  $9.35 \pm 1.05$ ) was consistent with the view that migraine is one of the most severe headaches, as reported by the National Health Interview Survey in the USA [21]. In addition, the time lost from work in CM patients exceeded 7 days per month (mean  $7.36 \pm 3.28$  days), resulting in increased loss of productivity, cost effectiveness, and additional medication costs. The headache-related disability in the present series was even worse than that reported by Buse et al. [22]. In addition, the frequency of headache days, pain severity, and work loss were associated with the presence of AV in all patients.

Based on the results of the present study, our consideration that AVs, including CB, are factors that increase headache frequency, severity, and time off work per month in migraineurs is in line with recent authors [12, 16, 18, 19].

The shortcoming of this study was the lack of surgical treatment to investigate how removal of AVs would affect migraine progression and time off work in this cohort. However, the present study was conducted to analyze the association of all SAVs in CM.

CM usually evolves from the episodic form and causes significant functional impairment, poorer quality of life and cost effectiveness than in patients with EM. Regarding the headache burden of CM patients compared to EM patients, the evaluation of all sinonasal anatomic factors is an important issue for physicians to define treatment strategies for effective disease management.



The results of the present study showed no significant difference between CM and EM patients in terms of radiological sinus mucosal disease. SAVs (CB, AN, HC) were found to be significantly more frequent in CM patients. Endoscopy scores were significantly worse in patients with CM than in those with EM. The presence of any of these AVs seems to increase chronicity, pain severity and work disability in migraineurs.

## Abbreviations

AN: agger nasi cell

AVs: anatomic variants

CB: concha bullosa

CM: chronic migraine

CRS: chronic rhinosinusitis

EM: episodic migraine

HC: Haller cell

LKES: Lund-Kennedy endoscopy scores

LMRS: Lund-Mackay radiology scores

SAV: sinus anatomic variants

VAS: visual analog scale

## Declarations

### Author contributions

AV: Conceptualization, Investigation, Writing—original draft, Writing—review & editing. SK: Conceptualization, Writing—original draft, Writing—review & editing. TÇ: Investigation, Writing—review & editing, Validation, Supervision. All authors read and approved the submitted version.

### Conflicts of interest

The authors declare that they have no conflicts of interest.

### Ethical approval

The study was approved by the Institutional Review Board of Haydarpaşa Numune Educational and Research Hospital Istanbul with the study Identification Number (HNEAH-KAEK 2012/40).

### Consent to participate

Informed consent to participate in the study was obtained from all participants.

### Consent to publication

Not applicable.

### Availability of data and materials

The data are not publicly available due to government restrictions on patient privacy.

### Funding

Not applicable.

### Copyright

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