

# CLINICAL AND EPIDEMIOLOGICAL CHARACTERISTICS OF MIGRAINE IN LATVIA

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*The aim of this study was to explore clinical-epidemiological characteristics of migraine in Latvia and the disability of migraine patients, to determine the optimal options for care of these patients. Patients selected from three headache centres were asked 40 questions by phone. Among 116 patients, the dominant age group was 25–34 (41.4%) and most patients were women (87.9%). 52.6% of patients were highly educated, and 53.4% had a job involving communication with people. In 56.9% of cases headaches started at the age of 15–24. About 25% migraine attacks lasted for 25–48 hours. The diagnosis “Migraine with aura” was confirmed in 50% of the patients. Headaches were quite frequent: 4–8 times a month or more in 22.4% of patients and 2–4 times a month in 29.3%. As medication, 50.9% used selective serotonin 5-HT (5-hydroxytryptamine) receptor agonists for migraine attacks treatment, 35.3% — nonsteroidal anti-inflammatory drugs (NSAIDs) and 30.2% — acetaminophen-containing medicines. The average quality of life estimated by migraine disability assessment questionnaire (MIDAS) was 13.0, which equates to moderate disability. According to our study clinical characteristics of migraine in Latvia do not differ significantly from that of other European countries. Most of the patients are educated, working women of childbearing age. Migraine diagnosis and treatment seems to be appropriate, but nevertheless, too many sufferers have frequent and persistent headache attacks that require further investigation.*

**Key words:** *migraine headache, Latvians, clinical-epidemiological characteristic, International Classification of Headache Disorders — III (ICHD-III), disability.*

## INTRODUCTION

Half to three quarters of the adults aged 18–65 years in the world have had a headache at least once during the last year and among those individuals more than 10% have reported migraine (Jensen and Stovner, 2008; Anonymous, 2011). The epidemiological profile of headaches including migraine varies in different regions of the world. It is known that there is lower prevalence of migraine in Africa, Asia, and the Middle East than in Europe and North America (Merikangas, 2013; Chawla *et al.*, 2014). A large survey of chronic pain conducted in 16 European countries and Israel revealed headache in 15% of all chronic pain patients and migraine in 7% (Breivik *et al.*, 2006). A similar study in Latvia showed a higher proportion of chronic headache sufferers (23% of chronic pain patients), but a similar proportion of those with migraine — 6% (Logina *et al.*, 2008).

In general, migraine is one of the most common reasons that make people seek help in primary care settings (Buse *et al.*,

2012). According to the World Health Organization Global Burden of Disease Study, migraine is the third most prevalent disorder and the seventh most disabling medical disorder worldwide (Anonymous, 2013; Lipton and Silberstein, 2015). It significantly restricts the patients' physical activity and working capacity, and reduces the patient's ability to form social contacts. It is found that men suffering from migraine require on average 3.8 bed-days per year, whereas women — 5.6 bed-days per year (Chawla *et al.*, 2014), causing economic damage to the employer as well as the entire economy of the state. This raises a great need for studies to further understand the features and mechanisms of migraine, and to find ways to treat and to prevent disability from migraine.

Migraine is a primary headache disorder characterised by attacks of moderate to severe headache that are typically unilateral with pulsating quality, aggravated by physical activity and associated with nausea, photophobia or phonophobia (Goadsby *et al.*, 2002). Two major subtypes of

migraine have been recognised by the International Classification of Headache Disorders (Anonymous, 2013): 1.1. Migraine without aura — a clinical syndrome of headache with specific features and associated symptoms, and 1.2. Migraine with aura — primarily characterised by transient focal neurological symptoms that usually precede or sometimes accompany the headache. The most common visual aura is flashing lights or loss of vision, but it may be in the form of pins and needles or other sensory, motor or speech disturbances, which can last from 5 to 60 minutes (Buse *et al.*, 2012; Anonymous, 2013). Migraine can begin at any age, but most often it occurs between 25–55 years. About 6% of men and 18% of women in the US suffer from migraine attacks Lipton *et al.*, 2002).

Migraine mechanisms are various. It is considered to be a neurovascular disorder, but the cortex-enhanced response and the release of neurotransmitters, which leads to the activation of trigeminal conduction pathway, has also been involved. That promotes cerebral vascular dilation and neurogenic inflammation in primary neuron terminals localised in cerebral vascular walls, brain membranes and nasal cavities (Jones *et al.*, 2012). The underlying triggering pathophysiology of migraine with aura is thought to be a decrease of circulating blood (Rogawski *et al.*, 2012).

Many factors can initiate a pathophysiological mechanism, and the migraine attack can occur at any given moment. In a retrospective study of 1207 migraine patients (Kelman, 2007), 75.9% reported at least one migraine attack provocative factor: stress (79.5%), female hormonal disturbance (65.1%), not eating (57.3%), weather (53.2%), sleep disturbance (4.8%), perfume or odour (43.7%), neck pain (38.4%), light(s) (38.0%), alcohol (37.8%), smoke (35.7%), sleeping late (32.0%), heat (30.3%), food (26.9%), exercise (22.1%), and sexual activity (5.2%).

Although the debate on mechanisms of migraine is continuing, several pharmacological anti-migraine treatment options are available, which significantly improve the patients' quality of life. Unfortunately, different treatment regimes can fail, and among such patients many have begun to perceive headache as a life-changing disturbance in their lives, and have lost faith that it is possible for it to change.

The aim of our study was to explore clinical-epidemiological characteristics of migraine in Latvia and the disability of migraine patients, to determine optimal options for care for these patients.

## MATERIALS AND METHODS

Migraine sufferers were chosen from three specialized headache consultancy centres. 258 clinical records of patients were checked, and out of them — 178 out-patient clinical cards were selected coded as “G43 Migraine” according to International Classification of Diseases or ICD-10. 62 patients were excluded from the further investigation: 12 because of possible secondary cause of headache

(head injury, toxic influence, cerebral ischemia), 33 phone calls were incorrect or not answered, 17 patients refused to participate in the survey.

In total, 116 patients fulfilled inclusion criteria of the study:

- 1) The diagnosis of migraine completely corresponded to proposed criteria by International Classification of Headache Disorders - III (ICHD-III) — at least five headache attacks, lasted 4–72 hours (untreated or unsuccessfully treated); headache must have had at least two of the following characteristics: unilateral location, pulsating quality, moderate or severe pain intensity, aggravation by or causing avoidance of routine physical activity (e.g., walking or climbing stairs), and during the headache the patient must have had at least one of the following: nausea and/or vomiting, photophobia and phonophobia;
- 2) No other any primary or secondary headache disorder registered;
- 3) No other somatic or neurological disease detected;
- 4) The respondent's consent acquired.

The data of all included 116 migraine sufferers were obtained from their clinical cards, and standardized survey of patients by phone was made during period from 1 December 2014 to 31 January 2015. Questionnaire includes 40 items on patients' age, education levels, profession, age on onset of migraine headaches, migraine in their relatives, attack's character, associated symptoms, pattern, attack durations, medication history, treatment and its effectiveness. Maximum pain intensity during attack was self-evaluated by patients using 0–10 Numeric Rating Scale (NRS) (where 0 being no pain and 10 being the worst pain patients can imagine) (McCaffery, 1999).

Disability of patients related to migraine was measured by Migraine Disability Assessment Questionnaire or MIDAS (Stewart *et al.*). It is a set of questions on how many days in the last three months the patient missed work/school, his/her productivity was reduced, household work was lost or reduced, and life activities were put on hold because of their headaches. The total number of days has been scored as points, and it corresponds to a certain degree of MIDAS level of disability: grade I — little or no disability (MIDAS score 0–5 points); grade II — mild disability (MIDAS score 6–10 points); grade III — moderate disability (11–20 points), and grade IV — severe disability (21 and more points). The test helps to assess not only disability, but also the disease severity and treatment effectiveness.

Before completing the questionnaire, each respondent received an explanation on the study objectives. The ethical standards and confidentiality of the patients' information were guaranteed according to the regulations and permission of Rīga Stradiņš University Ethics Committee from 27 November 2014.

Descriptive statistical calculations were made using Microsoft Excel 2010 and IBM (International Business Machines Corporation) SPSS (Statistical Package for the Social Sciences) Statistics for Windows Version 20.0.

## RESULTS

Demographic and other characteristics of the studied migraine patients were summarized in Table 1. The majority of responders who suffered from migraine were female (88%). Age distribution among them was from 15 to 64 years, and the prevailing group had age 25–34 years (41%). There is noticeable tendency that the number of patients decreased with age, i.e. 17.2% of patients with age 45–54 years, and only 7.6% with age in 55–64 years.

Among those who suffered from migraine, about a half had a university education (53%), followed by those with secondary (20%) and vocational (17%) education, and only 2.6% of patients had finished basic school.

Half (53%) of patients had an occupation related to communication with people, followed by people involved in a job with intensive use of a computer (19%) and those employed in manual labour (12%).

The diagnosis of migraine without aura was confirmed in 56 (48.3%) of the 116 patients and migraine with aura in 58 (50%), and in the remaining two patients probable migraine

was diagnosed. More than a half of the respondents (55.7%) had one or more relatives suffering from migraine.

In most patients (66 or 57%) headaches started at the age of 15–24, for 17% the attacks began earlier, but in only seven (6%), migraines started after the age of 35. An oncoming migraine attack or prodrome was not felt by 67.2% of the observed (78 of 116), but some of them had some unspecific sensation: tiredness or weakness (21 or 18%), nausea, excitation or other symptoms (14 or 12.5%).

Usually, a headache attack was provoked by stress (68 or 58.6%), fatigue (38 or 32.8%), sleep disturbances (26 or 22.4%) and female hormonal disturbances (29, or 25%, of 102 women). Less common provocative factors included weather changes (13 or 11.2%), strong odour (16 or 13.8%), and certain kinds of food (12 or 10.3%). Only 16 of 116 (13.8%) did not associate their headaches with a provocation.

In 20 of 116 (17.3 %) patients the length of migraine attack was less than 12 hours (Fig. 1). Half of the respondents underwent headaches lasting for one (30 patients) and two (29) days and nights. One-fourth of patients (26) suffered from prolonged attacks lasting for 49–72 hours, and 10% (11) for more than 72 hours. Headaches were quite frequent in half of respondents: 4–8 times a month or more in 26 (22.4%), 34 patients had migraine 2–4 times per month (29.3%), 42 (36.2%) — 1–2 times per month, but only 13 (11%) had headaches less often (Fig. 2).

Table 1

### CHARACTERISTICS OF MIGRAINE PATIENTS

	Number of patients, (% of group)			
	Total	Migraine without aura	Migraine with aura	Probable migraine
Gender, including:	116	56 (48.3%)	58 (50%)	2 (1.7%)
women	102 (87.9%)	50 (43.1%)	51 (44%)	1 (0.9%)
men	14 (12.1%)	6 (5.2%)	7 (6.0%)	1 (0.9%)
Age:				
15–24 years	17 (14.7%)	5 (4.3%)	12 (10.3%)	0
25–34 years	48 (41.4%)	23 (19.8%)	24 (20.7%)	1 (0.9%)
35–44 years	24 (20.7%)	14 (12.1%)	9 (7.8%)	1 (0.9%)
5–54 years	18 (15.5%)	9 (7.8%)	9 (7.8%)	0
55–64 years	9 (7.8%)	5 (4.3%)	4 (3.4%)	0
Education :				
higher education	61 (52.6%)	27 (23.3%)	34 (29.3%)	0
incomplete higher education	9 (7.8%)	5 (4.3%)	3 (2.6%)	1 (0.9%)
secondary education	23 (19.8%)	9 (7.8%)	14 (12.1%)	0
vocational education	20 (17.2%)	13 (11.2%)	6 (5.2%)	1 (0.9%)
elementary education	3 (2.6%)	2 (1.7%)	1 (0.9%)	0
Occupation profile:				
unemployed	8 (6.9%)	5 (4.3%)	3 (2.6%)	0
student	10 (8.6%)	3 (2.6%)	7 (6.0%)	0
related to communication with people	62 (53.4%)	32 (27.6%)	27 (23.3%)	2 (1.7%)
job with intensive use of computer	22 (19.0%)	8 (6.9%)	14 (12.1%)	0
employed in manual labour	14 (12.1%)	7 (6.0%)	7 (6.0%)	0

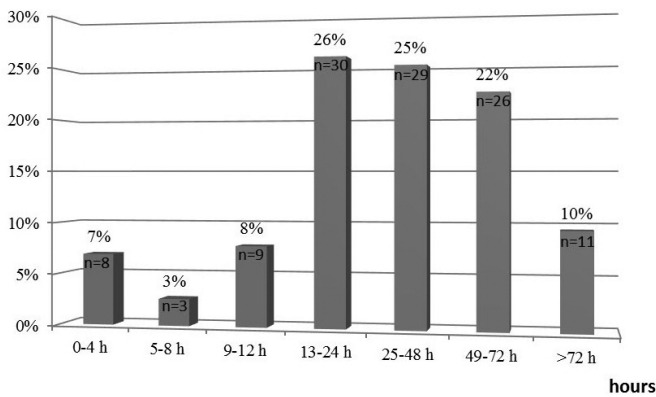


Fig. 1. The average duration of migraine attacks (in hours). Columns, % of patients (n = 116) with different length of migraine attack; n, number of patients in each frequency group.

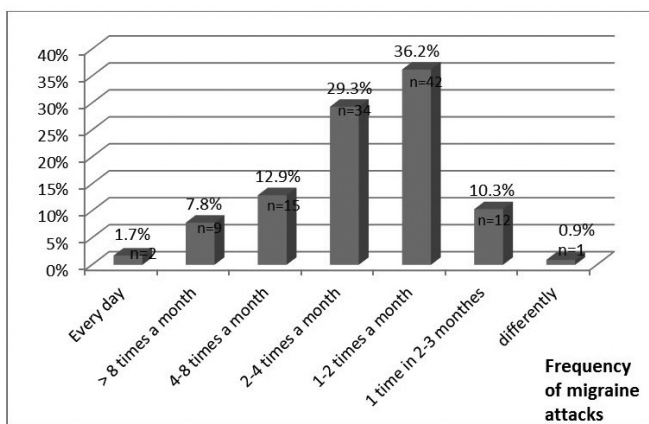


Fig. 2. Frequency of migraine attacks among patients. Columns, % of patients (n = 116); n, number of patients in each frequency group.

Migraine attacks were usually accompanied by nausea 67.2% (78), vomiting 51.7% (60), photophobia 77.6% (90), and phonophobia 61.2% (71); less common accompanied symptoms were increased sensitivity to odours 13.8% (16). Weakness (15 or 12.9%) and fatigue (45 or 38.8%) were the main causes of discomfort after attack in part of patients. In patients who had diagnosis of migraine with aura, the phenomena of aura were more often expressed as changes of vision in 49.1% (57), dizziness in 21.5% (25), mild pain in

5.2% (5) and numbness of some parts of the body in 4.3% (5).

The migraine patients included in this study were sufficiently investigated: with the magnetic resonance investigation of brain in 56.0% (65 of 116 patients), computed tomography — 52.6% (61), duplex sonography of cerebral blood vessels — 29.3% (34) and electroencephalography in 5.2% (6).

Most of the patients (50.9% or 59 of 116) had used specific medicines — selective serotonin 5-HT<sub>1</sub>-receptor agonists (triptans) at least several times for treatment of their migraine attacks. Other treatment options were use of non-steroidal anti-inflammatory drugs (NSAIDs) (41 or 35.3%), medicines containing acetaminophen (35 or 30.2%), and analgin or metamisole (8 or 6.9%). To manage headache, the patients also tried to fall asleep (30 or 25.9%), to move into a dark and quiet place (16 or 13.8%) or take a shower (9 or 7.8%).

Analysis of disability and quality of life by MIDAS (migraine disability assessment) showed some association with migraine profile, characteristic and treatment. Pain intensity during attack was estimated as  $8.5 \pm 2.2$  by NRS in all patient groups without significant difference between males and females —  $8.0 \pm 1.3$  and  $7.9 \pm 1.5$ , respectively. MIDAS disability grade for males was assessed as mild (MIDAS score  $9.1 \pm 7.2$ ), but moderate in women (MIDAS score  $13.5 \pm 9.5$ ); however, this difference was not statistically significance ( $p \geq 0.05$ ) (Table 2). More than one-third of patients 37.1% (43) reported that, during the headaches, they were not able to work, and approximately the same number (40.5% (47) still coped with their daily duties by taking medication. Both migraine with aura and migraine without aura had caused moderate degree of disability, but differences in MIDAS scores in our patients were not significant —  $14.2 \pm 10.4$  and  $11.6 \pm 7.8$  ( $p > 0.05$ ). Patients from different educational groups noticed a similar quality of life by MIDAS scores (Fig. 3), but there was a tendency for patients with higher education to have a higher disability grade.

Despite different numbers of patients using different treatment regimens, a better quality of life was found in those

Table 2

MIGRAINE SUBTYPE, HEADACHES PAIN INTENSITY AND DISABILITY

	All patients (n = 98)	Male (n = 11)	Female (n = 87)	p
MIDAS score (mean, SD)	13 ± 9.3	9.1 ± 7.2	13.5 ± 9.5	p = 0.15
NRS score (mean, SD)	8.5 ± 2.2	8.0 ± 1.3	7.9 ± 1.5	p = 0.9
		Migraine without aura pts (n = 42)	Migraine with aura pts (n = 54)	
MIDAS score (mean, SD)	n.a	11.6 ± 7.8	14.2 ± 10.4	p = 0.3
NRS score (mean, SD)	n.a	7.8 ± 1.5	8.0 ± 1.4	p = 0.3

MIDAS, Migraine Disability Assessment Questionnaire; NRS, Numeric pain rating scale; SD, standard deviation; pts, patients; n.a, not applicable; p, significance level of correlation between gender and pain intensity or disability. No correlations were statistically significant.

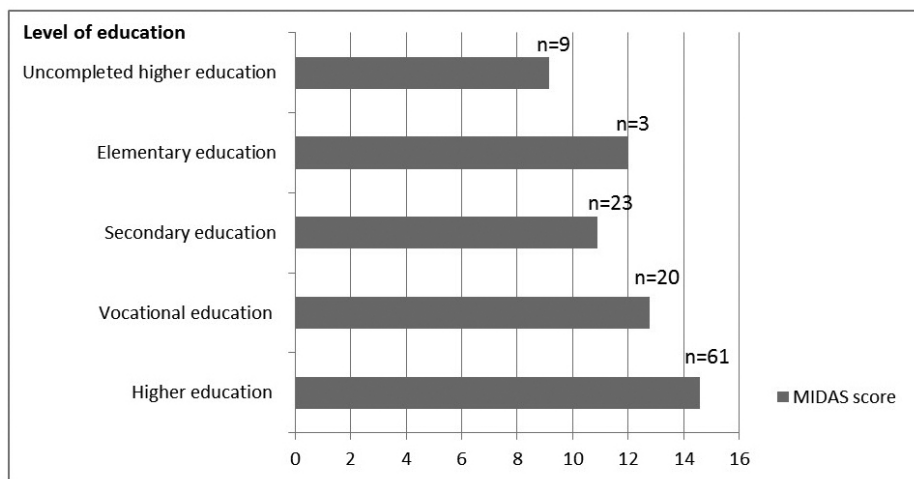


Fig. 3. MIDAS score according to level of patients education. MIDAS, Migraine Disability Assessment Questionnaire; n, number of patients in each educational group.

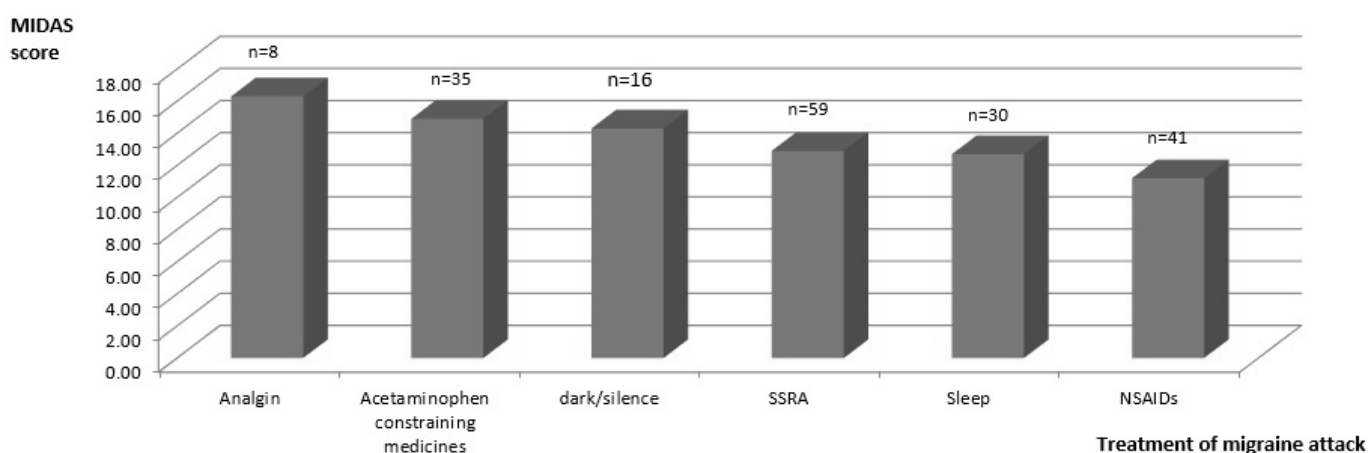


Fig. 4. MIDAS scores according to type of the treatment of acute migraine attack. MIDAS, Migraine Disability Assessment Questionnaire; n, number of patients in each treatment group; NSAIDs, non-steroidal anti-inflammatory drugs; SSRA, selective serotonin receptor agonists.

migraine patients who used NSAIDs, selective serotonin 5-HT<sub>1</sub> (5- hydroxytryptamine-1) receptor agonists (triptans) and tried to fall asleep (Fig. 4); however, this difference was not significant ( $p > 0.05$ ).

## DISCUSSION

Migraine is one of the most common disorders of the nervous system. Every 10 seconds, someone in the United States enters an emergency room with a headache or migraine (Anonymous, 2015), and it is acknowledged as the third most prevalent disorder in the world (Kurth *et al.*, 2011; Anonymous, 2013). The population of our study was selected from specialised centres and does not reflect prevalence of migraine in our country fully. However, the data are representative for an analysis of clinical epidemiology and the influence on patients' quality of life.

Remarkable female predominance has been shown in many studies — up to 75% of all experienced migraine (Chawla *et al.*, 2014) and 88% in our study. Much evidence exists connecting hormonal fluctuations and migraine (Sacco *et al.*, 2012), but not all migraines are hormonal. Recent research has found that women may be more susceptible than

men to depression of cortical spreading and brain excitation that is thought to lead to migraine (Anonymous, 2015). Regarding men, some features of their help-seeking behaviour have been mentioned. Masculinity ideologies emphasise self-reliance, competitiveness, emotional control, power over others and cultural stereotypes — men might believe that they should keep their emotions under control, and that by extension they should not be emotional when under stress to not to appear “girlish” (Mansfield *et al.*, 2003; Smith *et al.*, 2006). That may be the reason why men do not go to the doctor, offering the false notion that women get sick more often. It has been shown that men do feel illness symptoms as women or a little less symptoms than women, but they tend to ignore them: “minor illness can be fought off if you don't give in to it”, “I often ignore symptoms hoping they will go way” and “I have to be really ill before I go and see the doctor” (Galdas *et al.*, 2005). Data obtained in our study partly confirm such suggestions — the pain intensity by NRS in men and women is practically identical ( $8.0 \pm 1.3$  and  $7.9 \pm 1.5$ ), but the disability grade differs ( $9.1 \pm 7.2$  and  $13.5 \pm 9.5$  by MIDAS score).

In general, the clinical epidemiological data from our study on migraine in the Latvian population corresponds to the

epidemiological findings in other countries — the majority of the migraine patients are well-educated women of working age (25–34 years old).

Despite having no consent on a correlation between migraine and level of education, some studies showed a higher rate of migraine in persons with lower education (Breslau *et al.*, 1991; Scher *et al.*, 1998) and a lower rate in those with a lower educational (Buse *et al.*, 2010; Ertas *et al.*, 2012). Of all the patients included in our study, more than one half (53%) had a higher education. This might be explained partly by the selected population from specialised cabinets where mainly responsible and self-made persons seek help. Also, higher education is available and popular in Latvia, where there are 57 higher education institutions and three branches of foreign universities, and 29 112 students in 2014 from a total population of 2.013 million (Anonims, 2014).

We observed an unusually high proportion of patients who suffered from migraine with aura — 50% of those selected from the specialised headaches out-patient centres. This study certainly approves the existence of higher disability ( $14.2 \pm 10.4$  MIDAS score) and pain intensity ( $8.0 \pm 1.4$ ) in migraine with aura, in comparison with migraine without aura ( $11.6 \pm 7.8$  and  $7.8 \pm 1.5$ , respectively)

The study shows the need for extensive investigation of patients, and it is incorrect to assume that migraine is a clinical diagnosis (Chawla *et al.*, 2014) for which there is no need for additional studies. Usually, visual and other diagnostic tests are used to rule out other diseases that could mimic or co-exist with migraine (differential diagnoses), and to determine whether there is a clear change in the aura symptoms or recurrence of migraine with atypical features (Buse *et al.*, 2012). There are some studies using magnetic resonance scans that showed association of migraine with a variety of structural brain lesions in cerebellum, including clinically silent infarct-like lesions in mid-life (Kurth *et al.*, 2011; Scher *et al.*, 2009). This suggests that a remote history of migraine with aura may be a strong risk factor for brain lesions commonly found in older populations (Scher *et al.*, 2009).

Almost half of the respondents in our study had used specific treatment for migraine — selective serotonin 5-HT (5-hydroxytryptamine) receptor agonists and, to a lesser extent, other medicines and non-medical activities. This means that the level of the diagnosis and treatment of migraine is relatively high. However, there was a high proportion of patients with frequent and persistent migraine attacks, which requires analysis of the situation for the improvement of patient education and promotion of their compliance.

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## KLĪNISKI EPIDEMIOLOĢISKS MIGRĒNAS RAKSTUROJUMS LATVIJĀ

Migrēna ir hroniska slimība, kam raksturīgas vidēji vai stipri izteiktas lēkmjveida galvassāpes, visbiežāk viļņveidīgas. Slimības epidemioloģiskā izpēte palīdz precīzēt migrēnas pacientu aprūpes uzdevumus un plānot nepieciešamos resursus. No trīs Galvassāpju kabinetu datu bāzēm tika atlasītas pacientu ambulatorās kartes ar diagnozi G43 „Migrēna” pēc starptautiskās slimību klasifikācijas (SSK-10). Tika veikta telefoniska pacientu standartizēta anketēšana, ietverot 40 jautājumus. Tika iegūti dati par 116 pacientiem, ar lielāko īpatsvaru vecuma grupā no 25 līdz 34 gadiem (41,4%). Minētajā pacientu grupā sievietes prevalēja (87,9%), puse (52,6%) no migrēnas pacientiem bija ar augstāko izglītību, 53,4% strādāja, komunicējot ar cilvēkiem. Diagnoze „Migrēna ar auru” bija izlikta 58 jeb 50% pacientu. Vairākumam (56,9%) pacientu galvassāpes sākās tipiskajā vecumā jeb 15–24 gados. 1/5 daļai (26 jeb 22,4%) lēkmes bija biežas (4–8 un vairākas reizes mēnesī). Galvassāpju epizožu ilgumi biežāk bija 13–24 (25,9%) un 25–48 (25,0%) stundas. 50,9% lēkmju kupēšanai tika lietota specifiskā terapija, izvēloties selektīvos serotonīna 5-HT<sub>2</sub> (5-hidroksitriptamīna) receptoru agonistus, taču 35,3% pacientu bija izvēlējušies nesteroidos pretiekaisuma līdzekļus un 30,2% — paracetamolu saturošus līdzekļus. Pusei pacientu veikta magnētiskā rezonanse (56,0%) un datortomogrāfija (52,6%). Var secināt, ka migrēnas epidemioloģiskie dati Latvijā neatšķiras no citu Eiropas valstu datiem, t.sk. lielākā pacientu daļa ir izglītotas, publiskā darbā strādājošas sievietes reproduktīvā vecumā. Migrēnas diagnostika un ārstēšana ir salīdzinoši augstā līmenī, taču liels ir pacientu īpatsvars ar biežām un ilgstošām galvassāpju lēkmēm.