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ORIGINAL RESEARCH

Preventive treatment status among adults presenting with status migrainosus: a retrospective emergency department cohort study

Shimrit Heiliczer[1,2,*], Galit Almoznino[3,4], Oved Daniel[1]

[1]Neurology Division, Tel Aviv Sourasky University Medical Center (Ichilov), 6423906 Tel Aviv, Israel
[2]Oral Medicine Unit, Department of Otolaryngology, Head and Neck Surgery, and Maxillofacial Surgery, Tel Aviv Sourasky University Medical Center (Ichilov), 6423906 Tel Aviv, Israel
[3]Big Biomedical Data Research Laboratory, Faculty of Dental Medicine, Hebrew University of Jerusalem, Hadassah Medical Center, 91120 Jerusalem, Israel
[4]Department of Oral Medicine, Sedation & Maxillofacial Imaging, Faculty of Dental Medicine, Hadassah Medical Center, Hebrew University of Jerusalem, 91120 Jerusalem, Israel

***Correspondence**
Shimrith@tlvmc.gov.il
(Shimrit Heiliczer)

Abstract

Background: Status migrainosus (SM) is a disabling migraine complication that remains poorly characterized in emergency settings, particularly regarding prevention at presentation. We aimed to characterize documented preventive-treatment status among adults presenting to the emergency department (ED) with SM and explore associated baseline clinical characteristics. **Methods**: We conducted a single-center retrospective cohort study of adults with International Classification of Headache Disorders, 3rd edition (ICHD-3)-defined SM between January 2017 and August 2025. The screening frame comprised 1426 migraine-coded ED discharges; all 19 SM-coded encounters and 187 predefined high-suspicion encounters underwent manual chart review. The first confirmed SM presentation was the index presentation. Between-group comparisons were exploratory, with Benjamini-Hochberg false discovery rate (FDR) correction across 24 comparisons as a sensitivity analysis. **Results**: Forty-two patients met ICHD-3 criteria and accounted for 65 SM-related ED presentations. At index presentation, 10/42 (23.8%; exact 95% confidence interval 12.1–39.5%) had documented ongoing preventive therapy and 32/42 (76.2%) did not. Patients presenting despite preventive therapy had nominally higher rates of chronic migraine (62.5% *vs.* 10.0%, $p = 0.009$), anxiety disorders (40.0% *vs.* 6.2%, $p = 0.021$), chronic pain comorbidity (30.0% *vs.* 3.1%, $p = 0.036$), selective serotonin reuptake inhibitor use (40.0% *vs.* 6.5%, $p = 0.024$), and cannabis use (33.3% *vs.* 3.4%, $p = 0.035$). None remained significant after FDR correction (minimum $q = 0.174$). **Conclusions**: Most identified patients with ICHD-3-confirmed SM in this cohort were not receiving documented migraine preventive therapy. Exploratory secondary analyses identified nominal differences in several baseline clinical characteristics according to preventive-treatment status, but none remained significant after FDR correction. These findings provide a rationale for prospective investigation of the clinical significance of preventive-treatment status in SM, including whether SM occurring without prevention identifies an opportunity for preventive reassessment and whether SM occurring during prevention reflects underlying disease burden, treatment-related factors, or true preventive-treatment failure.

Keywords

Status migrainosus; Chronic migraine; Migraine prevention; Emergency department; Migraine chronification

1. Introduction

Status migrainosus (SM) is classified by the International Classification of Headache Disorders, 3rd edition (ICHD-3), as a debilitating migraine attack lasting longer than 72 hours [1]. Although SM is considered an uncommon migraine complication, observational studies have described substantial associated burden, including hospitalization, poorer migraine-related outcomes, and acute treatment difficulty [2–6]. Nevertheless, SM remains understudied across several clinically relevant domains, and important aspects of its epidemiology, precipitating factors, clinical course, pathophysiology, and the baseline clinical characteristics of affected patients remain incompletely defined [2, 7].

Among these gaps, the preventive-treatment status of patients at the time of SM presentation has received little attention. Determining whether SM occurs in the absence of preventive therapy or despite ongoing prevention is clinically

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relevant because the same severe migraine complication may arise in different treatment contexts. SM occurring without preventive therapy may identify an opportunity for preventive reassessment, whereas SM occurring despite prevention must be interpreted in the context of the underlying disease burden and treatment history of patients selected for preventive therapy. Because preventive therapy is typically prescribed to patients with higher attack frequency, disability, treatment exposure, or comorbidity burden [8], treatment status at presentation may, therefore, provide important insight into the baseline clinical context in which SM occurs. However, neither the distribution of preventive treatment status at SM presentation nor the clinical characteristics associated with it have been systematically characterized.

Accordingly, the primary aim of this study was to characterize documented migraine preventive treatment status among adults presenting with ICHD-3-defined SM. The secondary aim was to explore baseline clinical characteristics according to preventive-treatment status, thereby providing insight into the clinical context in which SM occurs.

2. Methods

2.1 Study design and setting

We conducted a single-center retrospective observational cohort study at Tel Aviv Sourasky Medical Center, a tertiary academic medical center in Tel Aviv, Israel. The study included adult patients who presented to the emergency department (ED) with SM between 01 January 2017 and 31 August 2025.

The study was approved by the Institutional Review Board of Tel Aviv Sourasky Medical Center (approval number: 0305-25-TLV). The requirement for informed consent was waived by the Institutional Review Board because the study involved retrospective analysis of existing medical-record data.

2.2 Patient identification and case ascertainment

Patients were screened through an electronic search of ED discharge diagnoses using all International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) migraine-related diagnosis codes within category 346.xx, including all fifth-digit subclassifications from 346.00 to 346.93. ICD-9-CM codes were used only as a screening tool and were not considered sufficient for final diagnosis.

Between 01 January 2017 and 31 August 2025, 1426 ED discharges carried a migraine-related diagnostic code. From this screening frame, 206 encounters were selected for manual chart review: all 19 SM-coded encounters and 187 additional migraine-coded encounters meeting predefined high-suspicion criteria. The latter included encounters with documentation suggestive of a prolonged migraine attack, repeated migraine-related ED presentations, neurology consultation or hospitalization.

Final inclusion required manual confirmation that the episode fulfilled ICHD-3 criteria for SM: the attack occurred in a patient with established migraine with or without aura; was typical of previous migraine attacks except for its duration and severity; was unremitting for >72 hours; produced debilitating pain and associated symptoms; and was not better accounted for by another diagnosis. The reviewer assessed the documented headache history, neurological examination, clinician impression, and diagnostic testing when performed. Of the 206 manually reviewed encounters, 141 were excluded because the documented presentation either did not meet criteria for a migraine attack or had a documented migraine duration of <72 hours; none were excluded solely because documentation was insufficient to adjudicate SM status. All suspected cases were reviewed by one physician (SH) using the same predefined criteria across records. The screening and inclusion process is shown in Fig. 1.

2.3 Differentiation of SM from baseline chronic migraine

In patients with chronic migraine or frequent baseline headache, SM was diagnosed only when the medical record clearly described a continuous attack lasting longer than 72 hours that was exceptional in severity and/or associated disability relative to the patient's usual baseline pattern. Documented prolonged worsening without a clearly distinguishable attack was excluded.

2.4 Index presentation and unit of analysis

For the present phenotypic analysis, the first confirmed SM presentation during the study period was defined as the index presentation.

Baseline demographic, clinical, comorbidity, and medication variables were extracted as documented at or before the index presentation. Preventive treatment status was defined according to documented migraine preventive therapy at the time of the index SM presentation.

All analyses in this manuscript were performed at the patient level.

2.5 Data collection

Data were extracted from the electronic medical records using a standardized Microsoft Excel data collection sheet. Variables were selected based on their clinical relevance to migraine and SM, as well as the feasibility of reliable extraction from the retrospective medical records.

Extracted variables included demographic characteristics, migraine-related characteristics, preventive treatment status at the index ED presentation, psychiatric comorbidities, chronic pain comorbidities, psychiatric medication use, substance use, SM-associated clinical features, migraine-related ED utilization during the study period, and ED diagnostic evaluation variables.

Demographic variables included age, sex, marital status, and contraceptive use.

Migraine-related variables included chronic migraine, abortive medication use, triptan use, analgesic use, and migraine-related ED utilization during the study period. Chronic migraine was classified as present if it was explicitly documented by a treating clinician or if the documented headache frequency met ICHD-3 criteria for chronic migraine. When insufficient information was available to determine

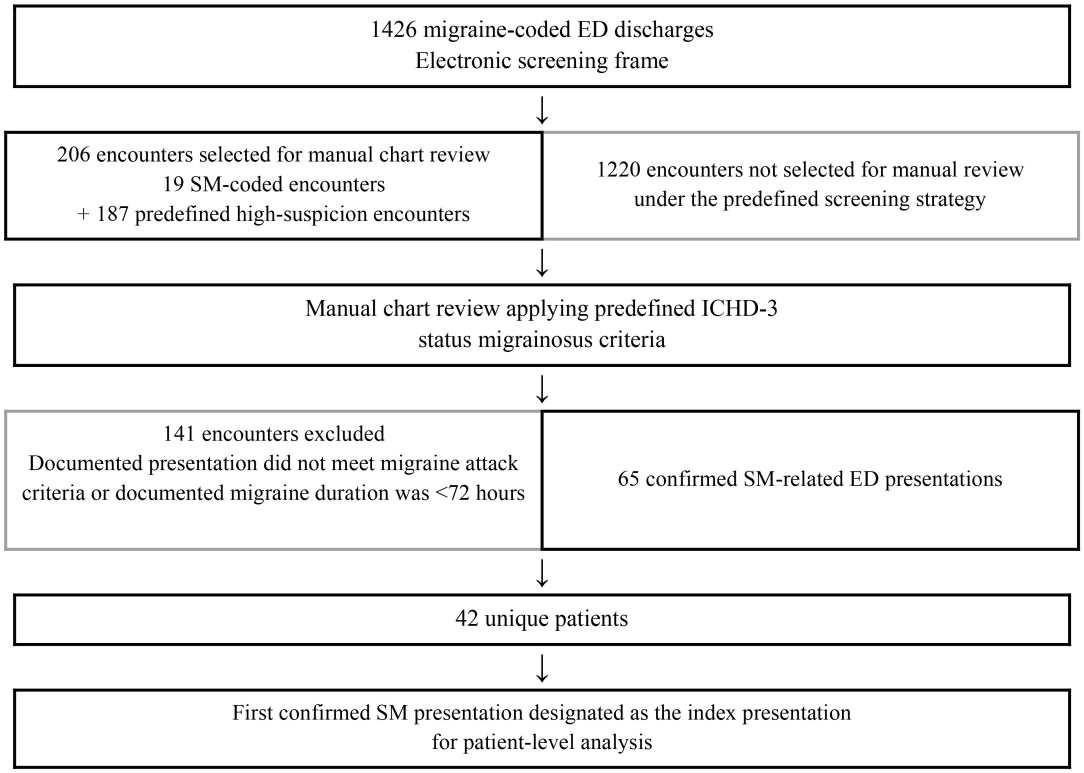


FIGURE 1. Study cohort identification and case ascertainment flowchart. ED, emergency department; SM, status migrainosus; ICHD-3, International Classification of Headache Disorders, 3rd edition.

chronic migraine status, the variable was recorded as missing. Aura was recorded as present only when explicitly documented during the index SM presentation. Migraine-related ED utilization during the study period was recorded as the total number of migraine-related ED presentations documented for each patient between 01 January 2017 and 31 August 2025. Because this variable could include visits occurring after the index SM presentation and follow-up opportunity differed by index date, it is reported descriptively only, as a measure of overall healthcare utilization rather than as a baseline predictor.

Psychiatric comorbidities included anxiety disorder, depression, obsessive-compulsive disorder, and post-traumatic stress disorder.

Psychiatric medication use included selective serotonin reuptake inhibitors (SSRIs), benzodiazepines, and atypical antipsychotics.

Chronic pain comorbidities included chronic back pain and irritable bowel syndrome. Substance use variables included nicotine smoking and cannabis use.

SM-associated clinical features included headache laterality, aura during the index presentation, nausea and/or vomiting, and photophobia and/or phonophobia.

ED diagnostic evaluation variables, including neuroimaging and lumbar puncture when performed, were collected to characterize the emergency presentation and diagnostic assessment of the cohort. These variables were not analyzed as study outcomes.

2.6 Preventive treatment status

The primary study variable was preventive treatment status at the index ED presentation. Patients were classified as receiving preventive therapy when ongoing pharmacotherapy prescribed for migraine prevention was documented at the index presentation. Preventive-treatment status was determined by systematic review of all medication sources available in the medical record for each patient, including the regular medication history documented during the ED assessment, the electronic chronic-medication record, and medication information contained in primary-care referral letters when present. Preventive treatment included established conventional classes, such as antiseizure medications, antidepressants, beta-blockers, and other standard oral preventives, as well as calcitonin gene-related peptide (CGRP)-targeted therapies, including monoclonal antibodies and gepants. For all preventive medications, the documented dose was required to fall within a therapeutic dosing range used for migraine prevention according to published clinical guidance [8]. This classification was intended to characterize preventive-treatment exposure at presentation rather than treatment adequacy or efficacy. The individual preventive agents and documented doses are provided in **Supplementary Table 1**. Treatment duration, adherence, dose optimization, and prior preventive-treatment history could not be determined consistently and were not evaluated.

2.7 Study outcome

The primary outcome was the proportion of patients with documented ongoing migraine preventive therapy at the in-

dex SM presentation. Between-group comparisons of demographic, migraine-related, psychiatric, chronic pain, medication, substance-use, and acute SM-associated features were secondary exploratory analyses.

2.8 Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics, version 29 (IBM Corp., Armonk, NY, USA).

Patients were stratified according to preventive treatment status at the index SM presentation: those receiving documented ongoing preventive therapy and those without documented preventive therapy.

Categorical variables were summarized as n/N (%) and compared using two-sided Fisher's exact test. Continuous variables were summarized as mean ± standard deviation (SD) and compared using independent-samples *t*-tests, with Welch's correction when the assumption of equal variances was not met.

Missing data were handled by available-case analysis. Therefore, the denominator for each variable reflects the number of patients with available data.

All between-group comparisons were secondary and exploratory. For categorical variables, between-group effect estimates were reported as differences in proportions (preventive-therapy group minus the group without preventive therapy), expressed in percentage points with Newcombe 95% confidence intervals (CIs); continuous variables were reported as mean differences with 95% CIs. Nominal statistical significance for categorical comparisons was based on Fisher's exact test p values. All statistical tests were two-sided, with nominal significance defined as $p < 0.05$. A Benjamini-Hochberg false discovery rate (FDR) sensitivity analysis was performed across the 24 secondary inferential comparisons to assess the impact of multiple comparisons. Multivariable modeling was not performed because of the limited sample size.

3. Results

3.1 Patient identification and cohort overview

The electronic screening frame comprised 1426 migraine-coded ED discharges. Of these, 206 encounters underwent manual chart review, including all 19 SM-coded encounters and 187 additional encounters meeting the predefined high-suspicion criteria. Among the 206 reviewed encounters, 141 did not meet the study criteria for SM. Sixty-five SM-related ED presentations were confirmed, involving 42 unique patients who met the study criteria for ICHD-3-defined SM and were included in the patient-level analysis. The case ascertainment process is shown in Fig. 1.

The primary finding was that 32/42 patients (76.2%) were not receiving documented ongoing preventive therapy at the index SM presentation, whereas 10/42 (23.8%; exact 95% CI 12.1–39.5%) were receiving documented prevention.

3.2 Baseline demographic and clinical characteristics

The cohort was predominantly female, with 39/42 patients (92.9%) women, and the mean age was 36.6 ± 11.5 years. Most patients with available data were married, 22/39 (56.4%). Nicotine smoking was reported in 14/38 patients (36.8%), and cannabis use in 4/38 patients (10.5%) (Table 1).

Psychiatric comorbidities were identified in 9/42 patients (21.4%), most commonly anxiety disorders, 6/42 (14.3%), and depression, 4/42 (9.5%). Psychiatric medication use was reported in 7/41 patients (17.1%), including SSRIs in 6/41 (14.6%), atypical antipsychotics in 3/41 (7.3%), and benzodiazepines in 2/41 (4.9%). Chronic pain comorbidities were identified in 4/42 patients (9.5%), mainly chronic back pain, 3/42 (7.1%) (Table 1).

3.3 Migraine phenotype and index SM presentation characteristics

Chronic migraine status was retrievable for 28/42 patients (66.7%). Among these, chronic migraine was present in 7/28 (25.0%). Acute migraine medication use was reported in nearly all patients with available data (40/41, 97.6%), including triptans in 21/41 (51.2%) and analgesics in 19/41 (46.3%).

Aura was recorded only when explicitly documented during the index SM presentation, and was present in 9/42 patients (21.4%).

Among patients with documented headache laterality (n = 34), the index SM headache was unilateral in 20/34 (58.8%) and bilateral in the remainder. Nausea and/or vomiting were documented in 36/40 patients (90.0%), and photophobia and/or phonophobia in 28/40 (70.0%) (Table 2).

ED diagnostic evaluation was performed when clinically indicated. Neuroimaging was performed in 18/42 patients (42.9%), including computed tomography (CT) in 16/42 (38.1%) and magnetic resonance imaging (MRI) in 2/42 (4.8%). Lumbar puncture was performed in 1/42 patients (2.4%).

No imaging or lumbar puncture finding led to an alternative diagnosis explaining the SM presentation.

3.4 Comparison by preventive-treatment status

Secondary exploratory comparisons according to preventive-treatment status are presented in Tables 1 and 2. Migraine phenotype: Chronic migraine was documented in 5/8 patients (62.5%) receiving preventive therapy compared with 2/20 (10.0%) without documented preventive therapy (difference in proportions +52.5 pp, 95% CI +14.8 to +77.4; p = 0.009). Chronic migraine status was missing in 2/10 patients (20.0%) receiving preventive therapy and 12/32 (37.5%) without documented preventive therapy.

Psychiatric and chronic pain comorbidity: Anxiety disorders were documented in 4/10 patients (40.0%) receiving preventive therapy compared with 2/32 (6.2%) without documented preventive therapy (difference in proportions +33.8 pp, 95% CI +6.7 to +62.8; p = 0.021). Chronic pain comorbidity was documented in 3/10 (30.0%) and 1/32 (3.1%), respectively

TABLE 1. Sociodemographic and clinical characteristics of patients with SM, stratified by preventive-treatment status.

Variable	All patients	With preventive therapy	Without preventive therapy	Effect estimate (95% CI)	*p* value	BH-FDR *q*
Demographics & Social						
Patients	42	10	32			
Female	39/42 (92.9%)	9/10 (90.0%)	30/32 (93.8%)	−3.8 pp (−34.5 to +12.4)	1.000	1.000
Age, yr, mean ± SD	36.6 ± 11.5	35.9 ± 13.2	36.9 ± 11.2	−0.97 yr (−9.52 to 7.59)	0.821	0.938
Married	22/39 (56.4%)	6/10 (60.0%)	16/29 (55.2%)			
Single	16/39 (41.0%)	4/10 (40.0%)	12/29 (41.4%)			
Divorced	1/39 (2.6%)	0/10 (0.0%)	1/29 (3.4%)			
Hormonal/contraceptive therapy	10/42 (23.8%)	4/10 (40.0%)	6/32 (18.8%)	+21.3 pp (−7.2 to +51.6)	0.213	0.381
Medical Comorbidities						
Psychiatric comorbidity	9/42 (21.4%)	4/10 (40.0%)	5/32 (15.6%)	+24.4 pp (−3.9 to +54.4)	0.181	0.361
Anxiety	6/42 (14.3%)	4/10 (40.0%)	2/32 (6.2%)	+33.8 pp (+6.7 to +62.8)	0.021	0.174
Depression/affective disorder	4/42 (9.5%)	2/10 (20.0%)	2/32 (6.2%)	+13.8 pp (−6.2 to +45.1)	0.236	0.381
OCD	2/42 (4.8%)	1/10 (10.0%)	1/32 (3.1%)	+6.9 pp (−8.2 to +37.4)	0.424	0.565
PTSD	3/42 (7.1%)	2/10 (20.0%)	1/32 (3.1%)	+16.9 pp (−2.2 to +48.0)	0.136	0.310
Chronic pain comorbidity	4/42 (9.5%)	3/10 (30.0%)	1/32 (3.1%)	+26.9 pp (+3.9 to +57.3)	0.036	0.174
Chronic back pain	3/42 (7.1%)	2/10 (20.0%)	1/32 (3.1%)	+16.9 pp (−2.2 to +48.0)	0.136	0.310
IBS	1/42 (2.4%)	1/10 (10.0%)	0/32 (0.0%)	+10.0 pp (−3.5 to +40.4)	0.238	0.381
Medications & Substance Use						
Current smoker	14/38 (36.8%)	4/9 (44.4%)	10/29 (34.5%)	+10.0 pp (−21.4 to +42.3)	0.699	0.839
Cannabis use	4/38 (10.5%)	3/9 (33.3%)	1/29 (3.4%)	+29.9 pp (+4.6 to +61.3)	0.035	0.174
Psychiatric medication use	7/41 (17.1%)	4/10 (40.0%)	3/31 (9.7%)	+30.3 pp (+2.6 to +59.7)	0.047	0.188
SSRI	6/41 (14.6%)	4/10 (40.0%)	2/31 (6.5%)	+33.5 pp (+6.3 to +62.7)	0.024	0.174
Benzodiazepine	2/41 (4.9%)	2/10 (20.0%)	0/31 (0.0%)	+20.0 pp (+1.9 to +51.0)	0.055	0.188
Atypical antipsychotic	3/41 (7.3%)	2/10 (20.0%)	1/31 (3.2%)	+16.8 pp (−2.6 to +47.9)	0.142	0.310

Categorical comparisons used two-sided Fisher's exact tests. Age was compared using an independent-samples t-test. Categorical effect estimates are differences in proportions (preventive-therapy group minus the group without preventive therapy), expressed in percentage points with Newcombe 95% CIs; for age, the effect estimate is the mean difference with 95% CI. BH-FDR q values reflect correction across 24 secondary inferential comparisons. Denominators reflect available data. OCD, obsessive-compulsive disorder; PTSD, post-traumatic stress disorder; IBS, irritable bowel syndrome; SSRI, selective serotonin reuptake inhibitor; BH-FDR, Benjamini-Hochberg false discovery rate; CI, confidence interval; SD, standard deviation.

TABLE 2. Migraine and SM characteristics stratified by preventive-treatment status.

Variable	All patients	With preventive therapy	Without preventive therapy	Effect estimate (95% CI)	*p* value	BH-FDR *q*
Migraine Characteristics						
Chronic migraine	7/28 (25.0%)	5/8 (62.5%)	2/20 (10.0%)	+52.5 pp (+14.8 to +77.4)	0.009	0.174
Triptan use	21/41 (51.2%)	7/10 (70.0%)	14/31 (45.2%)	+24.8 pp (−10.0 to +49.8)	0.277	0.416
Analgesic use	19/41 (46.3%)	2/10 (20.0%)	17/31 (54.8%)	−34.8 pp (−56.3 to +0.5)	0.075	0.226
Documented preventive therapy	10/42 (23.8%)	10/10 (100.0%)	0/32 (0.0%)	—	—	—
Conventional oral preventive therapy	6/42 (14.3%)	6/10 (60.0%)	0/32 (0.0%)	—	—	—
CGRP-targeted preventive therapy	5/42 (11.9%)	5/10 (50.0%)	0/32 (0.0%)	—	—	—
ED migraine visits during study period, mean ± SD	2.52 ± 1.85	3.80 ± 3.39	2.13 ± 0.71	—	—	—
SM Characteristics						
Aura	9/42 (21.4%)	1/10 (10.0%)	8/32 (25.0%)	−15.0 pp (−34.0 to +17.6)	0.416	0.565
Unilateral headache	20/34 (58.8%)	5/8 (62.5%)	15/26 (57.7%)	+4.8 pp (−31.3 to +35.1)	1.000	1.000
Nausea/vomiting	36/40 (90.0%)	9/10 (90.0%)	27/30 (90.0%)	+0.0 pp (−31.1 to +17.6)	1.000	1.000
Photophobia/phonophobia	28/40 (70.0%)	8/10 (80.0%)	20/30 (66.7%)	+13.3 pp (−20.7 to +36.3)	0.693	0.839

Categorical comparisons used two-sided Fisher's exact tests. Effect estimates for categorical variables are differences in proportions (preventive-therapy group minus the group without preventive therapy), expressed in percentage points with Newcombe 95% CIs. BH-FDR q values are based on 24 secondary inferential comparisons across Tables 1 and 2. Chronic migraine status was missing in 2/10 patients receiving preventive therapy and 12/32 without documented preventive therapy. Conventional oral and CGRP-targeted preventive-treatment categories are not mutually exclusive: one patient received combination therapy. ED migraine visits are descriptive only because observation opportunity differed according to index date. ED, emergency department; CGRP, calcitonin gene-related peptide; BH-FDR, Benjamini-Hochberg false discovery rate; CI, confidence interval; SD, standard deviation; SM, status migrainosus.

(difference in proportions +26.9 pp, 95% CI +3.9 to +57.3; $p = 0.036$).

Psychiatric medication and substance use: Psychiatric medication use was documented in 4/10 patients (40.0%) receiving preventive therapy and 3/31 (9.7%) without documented preventive therapy (difference in proportions +30.3 pp, 95% CI +2.6 to +59.7; $p = 0.047$). SSRI use was documented in 4/10 (40.0%) and 2/31 (6.5%), respectively (difference in proportions +33.5 pp, 95% CI +6.3 to +62.7; $p = 0.024$).

Cannabis use was documented in 3/9 patients (33.3%) and 1/29 (3.4%), respectively (difference in proportions +29.9 pp, 95% CI +4.6 to +61.3; $p = 0.035$).

Healthcare utilization: Migraine-related ED utilization during the study period was 3.80 ± 3.39 visits among patients receiving preventive therapy and 2.13 ± 0.71 among those without documented preventive therapy. Because observation opportunity differed according to index date, this variable was reported descriptively only and no inferential comparison was performed.

In the Benjamini-Hochberg FDR sensitivity analysis across the 24 secondary inferential comparisons, none of the individual associations remained statistically significant at an FDR threshold of 0.05 (minimum $q = 0.174$). Accordingly, the nominally significant between-group associations should be interpreted as exploratory and hypothesis-generating findings rather than confirmatory evidence.

4. Discussion

4.1 Principal findings

The principal finding of this retrospective ED cohort was that approximately three-quarters of patients with ICHD-3-

confirmed SM in this cohort were not receiving documented migraine preventive therapy at the index ED presentation. To the best of our knowledge, this study is the first to systematically characterize preventive-treatment status among adults presenting with physician-confirmed ICHD-3-defined SM.

Secondary exploratory comparisons showed nominally higher rates of chronic migraine, anxiety disorders, chronic pain comorbidity, SSRI use, and cannabis use among patients presenting with SM despite documented preventive therapy than among those without documented preventive therapy. However, none of these associations remained significant after correction for multiple comparisons (minimum $q = 0.174$). These findings should therefore be regarded as exploratory and hypothesis-generating.

4.2 SM despite preventive therapy: exploratory observations

The largest observed difference between groups was the higher prevalence of chronic migraine among patients who presented with SM despite documented preventive therapy. Higher rates of anxiety disorders, chronic pain comorbidity, SSRI use, and cannabis exposure were also observed in this group. These patterns may reflect greater underlying migraine and comorbidity burden among patients developing SM despite preventive therapy.

These observations are consistent with the broader migraine literature. Chronic migraine is associated with greater attack frequency, disability, central sensitization, impaired descending pain modulation, and structural and functional alterations in pain-processing networks [9, 10]. Similarly, anxiety disorders and overlapping chronic pain conditions are associated with migraine-related disability, central sensitization, and reduced treatment responsiveness, particularly in patients with chronic migraine [11–18].

These observations raise the possibility that SM occurring during preventive therapy may reflect several overlapping factors, including greater underlying migraine and comorbidity burden, treatment-related factors such as adherence or optimization, and true preventive-treatment failure.

Prospective studies are needed to clarify how underlying disease burden, treatment adequacy, and preventive-treatment response interact in the development and clinical course of SM.

4.3 Patients without preventive therapy: an opportunity for preventive reassessment

Most patients in this cohort were not receiving documented migraine preventive therapy at the time of their index SM presentation. Although the present study cannot determine whether these patients fulfilled contemporary criteria for preventive-treatment before developing SM, this finding highlights an important clinical question: should an episode of SM itself prompt structured reassessment of preventive-treatment eligibility?

Current recommendations for migraine prevention are primarily based on attack frequency, disability, response to acute treatment, medication overuse, contraindications to acute therapies, and patient preference [19]. Although SM is recognized by ICHD-3 as a complication of migraine [1], it is not currently included among the migraine subtypes or complications that independently support consideration of preventive therapy [19].

This represents an important conceptual gap. Recurrent SM has been associated with accelerated progression from episodic to chronic migraine [20], and episodic status migrainosus has been linked to a high rate of subsequent chronification in a small case series [21]. Although these observations do not establish that preventive therapy should routinely be initiated after a first episode of SM, they support the rationale for systematic post-SM reassessment of preventive-treatment eligibility. Such reassessment should consider not only attack frequency, but also disability, previous prolonged attacks, medication overuse, acute treatment response, comorbidities, and the overall trajectory of migraine disease [19].

This perspective is consistent with the broader shift toward earlier preventive intervention to modify migraine disease course rather than simply treating individual attacks [22]. Whether SM itself should influence preventive-treatment decisions beyond current guideline criteria remains an important question for future prospective studies.

5. Limitations

This study has several limitations. First, its retrospective single-center design limits causal inference and generalizability. Second, case ascertainment was based on all SM-coded encounters and a predefined high-suspicion subset of migraine-coded ED presentations rather than manual review of all 1426 migraine-coded encounters. This targeted strategy may have preferentially captured clinically conspicuous presentations or patients with greater healthcare utilization and may have missed SM cases among the 1220 encounters not manually reviewed. Consequently, the cohort may not represent the full spectrum of SM presenting to the ED, and the direction and magnitude of any resulting selection bias cannot be determined. Third, both comparison groups were defined among patients who had already developed SM. Therefore, the study cannot determine whether preventive therapy modifies the risk of developing SM. Fourth, the sample size was small, particularly in the preventive-treatment group, resulting in imprecise effect estimates and precluding reliable multivariable adjustment. Although several between-group comparisons reached nominal statistical significance, none remained significant after FDR correction. These associations should, therefore, be considered exploratory and hypothesis-generating. Future multicenter studies or registries using systematic case ascertainment may provide more precise and generalizable estimates. Fifth, preventive-treatment status was determined from the medication information available in the medical record, including the ED medication history, electronic chronic-medication record, and primary-care referral information when available. Direct patient verification was not possible, and treatment adherence, duration, detailed prior preventive-treatment exposure, prior preventive failures, and use of non-pharmacologic preventive strategies could not be fully assessed. Accordingly, documented preventive therapy should not be interpreted as evidence of treatment adequacy or treatment failure. Sixth, psychiatric and chronic

pain comorbidities were extracted from medical records and may have been underreported. Seventh, all case ascertainment and variable extraction were performed by a single reviewer using predefined criteria; independent second-reviewer confirmation was not performed, and inter-rater reliability could not be assessed. Eighth, chronic migraine status was missing in 14/42 patients. Because the mechanism of missingness cannot be determined retrospectively, differential or non-random missingness may have influenced the observed difference in chronic migraine prevalence. Ninth, the study spans 2017–2025, during which preventive-treatment options and prescribing patterns evolved substantially, particularly with the introduction of CGRP-targeted therapies. The observed prevalence and type of preventive-treatment exposure may, therefore, not fully reflect current practice. Finally, medication overuse, sleep disturbance, and menstrual-cycle factors were not systematically captured, limiting a full characterization of SM precipitants and modifiers.

6. Conclusions

In this retrospective ED cohort, most identified patients with ICHD-3-confirmed SM were not receiving documented migraine preventive therapy at index presentation, whereas a smaller subgroup developed SM during ongoing prevention. Exploratory differences in chronic migraine and several comorbid clinical features did not remain significant after FDR correction. Together, these findings highlight preventive-treatment status as a relevant clinical context in SM and suggest that SM arising without prevention and SM arising during preventive therapy may represent distinct management questions. Prospective studies should determine whether the former identifies an opportunity for preventive reassessment and whether the latter reflects underlying disease burden, suboptimal treatment implementation, or true preventive-treatment failure.

ABBREVIATIONS

SM, Status Migrainosus; ED, Emergency Department; ICHD-3, International Classification of Headache Disorders, 3rd edition; SSRI, Selective Serotonin Reuptake Inhibitor; OCD, Obsessive-Compulsive Disorder; PTSD, Post-Traumatic Stress Disorder; IBS, Irritable Bowel Syndrome; CGRP, Calcitonin Gene-Related Peptide; FDR, False Discovery Rate; CI, Confidence Interval; SD, Standard Deviation; CT, Computed Tomography; MRI, Magnetic Resonance Imaging; ICD-9-CM, International Classification of Diseases, Ninth Revision, Clinical Modification.

AVAILABILITY OF DATA AND MATERIALS

The data presented in this study are available on reasonable request from the corresponding author.

AUTHOR CONTRIBUTIONS

SH—conceptualization and writing, original draft preparation. OD and GA—writing–review and editing. All authors have read and agreed to the published version of the manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study was approved by the Institutional Review Board of Tel Aviv Sourasky Medical Center (approval number: 0305-25-TLV). The requirement for informed consent was waived by the Institutional Review Board of Tel Aviv Sourasky Medical Center because the study involved retrospective analysis of existing medical-record data.

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CONFLICT OF INTEREST

The authors have declared no conflict of interest. Oved Daniel is serving as one of the Editorial Board members of this journal. We declare that Oved Daniel had no involvement in the peer review of this article and has no access to information regarding its peer review. Full responsibility for the editorial process for this article was delegated to RB.

SUPPLEMENTARY MATERIAL

Supplementary material associated with this article can be found, in the online version, at https://files.jofph.com/files/article/2120764823195009024/attachment/Supplementary%20material.docx.

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