

**MIGRAINOUS INFARCTION: A CLINICAL REVIEW OF PATHOPHYSIOLOGY,
DIAGNOSIS, AND MODERN THERAPEUTIC STRATEGIES**

Dilfuza Abdukadirova

PhD, Associate Professor

Sakhobiddin Nematjonov

Department of Neurology, Andijan State
Medical Institute, Andijan, Uzbekistan

Abstract. Migraine represents one of the most prevalent neurological disorders globally and is increasingly recognized as a complex brain disease with significant cerebrovascular implications. Among its rare but severe complications, migrainous infarction constitutes a critical entity that bridges primary headache disorders and ischemic stroke. This narrative review examines the current understanding of migrainous infarction, with particular emphasis on epidemiological data from Central Asia, underlying pathophysiological mechanisms, diagnostic challenges, and emerging therapeutic approaches. The analysis reveals that Central Asian countries demonstrate a disproportionately high burden of both migraine and stroke, with Uzbekistan ranking among the top nations globally for age-standardized stroke incidence. The pathophysiology of migrainous infarction involves cortical spreading depression, neurovascular dysfunction, and prothrombotic changes, predominantly affecting young women with migraine with aura in the posterior circulation territory. Diagnosis remains challenging due to the necessity of excluding alternative stroke etiologies, particularly in young patients without traditional vascular risk factors. The advent of calcitonin gene-related peptide (CGRP)-targeted therapies represents a paradigm shift in migraine management, offering effective prevention without vasoconstrictive effects and demonstrating favorable cardiovascular safety profiles in recent large-scale studies. However, caution is warranted in patients with established cerebrovascular disease. The review underscores the importance of individualized risk assessment, comprehensive diagnostic evaluation, and integration of modern preventive strategies in clinical practice across Central Asia and globally.

Keywords: Migrainous infarction; Migraine with aura; Ischemic stroke; Cortical spreading depression; CGRP-targeted therapy; Central Asia; Young stroke; Neurovascular dysfunction; Preventive treatment; Cerebrovascular risk.

Migraine affects approximately one billion people worldwide and ranks as the second leading cause of disability-adjusted life years among neurological disorders. The Global Burden of Disease Study 2021 identified Central Asia as having the highest prevalence of tension-type headache among Asian regions, with migraine affecting over 13,000 per 100,000 population. In Uzbekistan specifically, population-based studies demonstrate a migraine prevalence of 7.2%, indicating substantial medico-social significance. Concurrently, the Central Asian region bears a disproportionately high stroke burden, with age-standardized mortality rates exceeding those of most European and American countries. Uzbekistan currently ranks fourth globally for stroke incidence, with ischemic strokes comprising 84.7% of all cerebrovascular events. This convergence of high migraine prevalence and substantial stroke burden creates a compelling public health imperative, particularly given the established association between migraine with aura and increased ischemic stroke risk.

The relationship between migraine and stroke has been recognized for decades, yet the precise mechanisms linking these conditions remain incompletely understood. Migrainous infarction, defined by the International Classification of Headache Disorders, Third Edition (ICHD-3) as ischemic brain infarction occurring during a typical migraine attack with aura, represents the

most direct manifestation of this association. The condition predominantly affects young women under 45 years of age, with the posterior circulation territory involved in over three-quarters of cases. Despite its rarity, accounting for less than 2% of all ischemic strokes, migrainous infarction carries significant diagnostic and therapeutic implications.

The relevance of this review is determined by several factors. First, the rising stroke incidence in Central Asia, particularly among younger populations, necessitates heightened awareness of non-traditional risk factors such as migraine. Second, recent advances in CGRP-targeted therapies have fundamentally altered the preventive treatment landscape, offering new possibilities for reducing cerebrovascular risk in susceptible individuals. Third, diagnostic challenges persist due to the necessity of excluding alternative stroke etiologies in young patients, requiring comprehensive neurovascular evaluation. Finally, the integration of modern therapeutic strategies into clinical practice across Central Asian healthcare systems remains an important area for development.

The aim of this review is to synthesize current evidence regarding the epidemiology, pathophysiology, diagnostic approach, and modern therapeutic strategies in migrainous infarction, with particular attention to regional data from Central Asia and the clinical implications of emerging CGRP-targeted therapies.

Materials and Methods. This narrative review was conducted through a comprehensive search of peer-reviewed literature published between 2018 and 2025. Electronic databases including PubMed, Scopus, Web of Science, and Google Scholar were systematically searched using combinations of keywords: "migrainous infarction," "migraine with aura," "ischemic stroke," "cortical spreading depression," "CGRP-targeted therapy," "Central Asia," and "young stroke."

Inclusion criteria encompassed clinical trials, systematic reviews, meta-analyses, epidemiological studies, and clinical guidelines focusing on the migraine-stroke association, pathophysiological mechanisms, diagnostic criteria, and therapeutic interventions. Particular emphasis was placed on studies reporting data from Central Asian populations and recent investigations evaluating CGRP-targeted therapies. Exclusion criteria included non-peer-reviewed publications, case reports with insufficient methodological quality, and studies not directly relevant to the migraine-stroke relationship or modern therapeutic approaches.

Data extraction focused on epidemiological patterns, pathophysiological mechanisms, diagnostic criteria according to ICHD-3, neuroimaging characteristics, differential diagnosis, and therapeutic outcomes. Special attention was given to studies evaluating the cardiovascular and cerebrovascular safety profiles of CGRP-targeted therapies. The collected evidence was analyzed using descriptive and comparative methods, with emphasis on clinical applicability in Central Asian healthcare settings.

Results. The analysis of contemporary literature reveals several critical findings regarding the epidemiology, pathophysiology, diagnostic challenges, and management of migrainous infarction.

Epidemiological data demonstrate that migrainous infarction occurs with an estimated frequency of 3.36 per 100,000 person-years, accounting for 0.5% to 1.5% of all ischemic strokes. Meta-analytic evidence indicates a significantly elevated stroke risk among patients with migraine with aura, with odds ratios ranging from 2.16 to 3.0 compared to individuals without migraine or those with migraine without aura. Recent large-scale database analyses, including the All of Us study involving over 400,000 participants, confirm a 33% higher stroke risk in migraine with aura patients after adjustment for comorbidities. Population-attributable risk estimates suggest that migraine with aura contributes to approximately 46% of cryptogenic ischemic strokes in young adults with patent foramen ovale and 23% in those without.

Central Asian countries demonstrate particularly concerning epidemiological patterns. The Global Burden of Disease 2021 data identify Central Asia as having the highest tension-type headache prevalence in Asia, with migraine affecting approximately 13,584 per 100,000 population. Uzbekistan-specific data reveal a migraine prevalence of 7.2% and a stroke incidence rate of 248.95 per 100,000 population, placing the country fourth globally. The standardized stroke mortality in Central Asian nations ranges from 83.74 to 170.80 per 100,000 population, substantially exceeding rates in Western Europe and North America. These figures underscore the urgent need for targeted prevention strategies addressing modifiable risk factors, including migraine.

The clinical presentation of migrainous infarction typically evolves during a characteristic migraine attack with aura. Visual aura symptoms predominate, observed in approximately 50% of cases, followed by sensory and nonspecific manifestations. The posterior circulation territory is affected in over 77% of cases, consistent with the neuroanatomical distribution of cortical spreading depression and the particular susceptibility of posterior circulation arteries to vasospastic changes. Functional outcomes are generally favorable, with complete recovery reported in nearly half of cases, although persistent visual field defects may occur following severe occipital lobe infarction.

Pathophysiological mechanisms underlying migrainous infarction involve multiple interacting pathways. Cortical spreading depression represents the primary neurophysiological substrate, characterized by a slowly propagating wave of neuronal depolarization accompanied by transient hyperperfusion followed by prolonged hypoperfusion. While typically insufficient to cause ischemia independently, cortical spreading depression renders brain tissue vulnerable through metabolic mismatch, glutamate excitotoxicity, and inflammatory mediator release. Neurovascular coupling disturbances induced by cortical spreading depression may precipitate ischemic injury in the presence of additional risk factors.

Arterial vasospasm, documented through magnetic resonance angiography and transcranial Doppler studies in affected patients, represents another potential mechanism. Sympathetic activation during severe prolonged migraine attacks may induce vasoconstriction, particularly in posterior circulation arteries that demonstrate heightened sensitivity to autonomic influences. Prothrombotic changes, including increased platelet aggregation and elevated von Willebrand factor levels, further contribute to cerebrovascular vulnerability during migraine attacks.

Diagnostic evaluation of suspected migrainous infarction requires systematic exclusion of alternative etiologies. Essential investigations include magnetic resonance imaging with diffusion-weighted sequences to confirm acute ischemia, magnetic resonance or computed tomography angiography to exclude arterial dissection and vasculitis, transcranial Doppler sonography for hemodynamic assessment, and echocardiography with bubble study to evaluate for patent foramen ovale. Laboratory evaluation should address hypercoagulable states, antiphospholipid syndrome, and autoimmune vasculitis. The diagnosis can only be established when cerebral infarction occurs during a typical migraine attack with aura, after comprehensive exclusion of other stroke mechanisms.

Differential diagnosis encompasses several critical conditions that may mimic migrainous infarction. Transient ischemic attack typically demonstrates sudden onset with maximal deficit at presentation, contrasting with the gradual symptom spread characteristic of migraine aura. Reversible cerebral vasoconstriction syndrome presents with thunderclap headache and multifocal arterial narrowing, distinguishable through angiographic findings. Cervical and intracranial arterial dissection may produce headache followed by focal deficits, with characteristic imaging findings including intimal flap or double lumen. Epileptic seizures with postictal paresis usually resolve within hours and are preceded by ictal activity. Systematic

exclusion of these conditions through comprehensive clinical evaluation and advanced neuroimaging is essential for accurate diagnosis.

Neuroimaging findings in migraine extend beyond acute infarction. White matter hyperintensities, predominantly localized in frontal and parietal lobes and the limbic system, are more prevalent in migraineurs compared to controls and correlate with disease duration and attack severity. Silent brain infarcts, particularly in the posterior circulation territory, occur with increased frequency and may represent subclinical manifestations of the same pathophysiological processes underlying migrainous infarction. These neuroimaging changes serve as potential markers of increased stroke risk and support the conceptualization of migraine as a progressive brain disorder.

Modern therapeutic strategies have undergone substantial evolution with the introduction of CGRP-targeted therapies. Monoclonal antibodies directed against CGRP or its receptor, including erenumab, fremanezumab, galcanezumab, and eptinezumab, demonstrate significant efficacy in reducing migraine attack frequency across both episodic and chronic migraine populations. Small-molecule CGRP receptor antagonists (gepants), such as rimegepant, ubrogepant, and atogepant, provide options for both acute treatment and preventive therapy. Crucially, unlike triptans and ergot derivatives, these agents do not induce vasoconstriction, rendering them particularly suitable for patients with vascular risk factors or history of cerebrovascular events.

Large-scale observational studies support the cardiovascular safety of CGRP-targeted therapies. Medicare database analyses involving over 260,000 patients demonstrate no increased cardiovascular event risk with anti-CGRP monoclonal antibodies compared to alternative preventive treatments. A 2025 study among US veterans showed association with reduced myocardial infarction risk and no significant association with ischemic stroke or intracranial hemorrhage. The 2024 American Headache Society consensus statement recommends CGRP-targeted therapies as first-line preventive options for episodic migraine with moderate to severe disability.

However, specific precautions apply to patients with established cerebrovascular disease. Current recommendations suggest temporary discontinuation of CGRP-targeted therapies in the acute or recent post-stroke period, with reinitiation considered no earlier than three months following the event depending on stroke etiology and individual patient factors. Patients with small vessel disease, distal arterial stenosis, or Raynaud phenomenon may require alternative therapeutic approaches. The decision to administer thrombolysis in suspected migrainous infarction requires careful consideration of the therapeutic window and exclusion of underlying vasculopathy.

Discussion. The findings of this review confirm that migrainous infarction represents an important clinical entity at the intersection of primary headache disorders and cerebrovascular disease. The disproportionately high burden of both migraine and stroke in Central Asian countries, particularly Uzbekistan, underscores the regional significance of this association and the need for heightened clinical awareness.

The pathophysiological complexity of migrainous infarction, involving cortical spreading depression, neurovascular dysfunction, and prothrombotic changes, explains the diagnostic challenges encountered in clinical practice. The necessity of excluding alternative stroke etiologies, including arterial dissection, vasculitis, hypercoagulable states, and cardioembolic sources, requires comprehensive neurovascular evaluation. This is particularly relevant in Central Asian healthcare settings, where access to advanced neuroimaging and specialized diagnostic testing may be limited. The development of standardized diagnostic algorithms and regional referral pathways could improve diagnostic accuracy and timeliness.

The advent of CGRP-targeted therapies represents a fundamental paradigm shift in migraine management with important implications for cerebrovascular risk reduction. The absence of vasoconstrictive effects distinguishes these agents from traditional migraine-specific medications, offering a safer alternative for patients with vascular risk factors. However, several considerations warrant attention in clinical practice across Central Asia.

First, the accessibility and cost-effectiveness of CGRP-targeted therapies in regional healthcare systems require evaluation. These medications, while demonstrating clear clinical benefits, may present economic challenges in resource-limited settings. Strategies for integrating these therapies into national formularies and insurance coverage frameworks need development. Generic alternatives and biosimilar preparations may eventually improve accessibility, though regulatory pathways in Central Asian countries require strengthening.

Second, the long-term cerebrovascular safety data, while encouraging, remain relatively limited given the recent introduction of these agents. Continued pharmacovigilance and post-marketing surveillance are essential, particularly in populations with high baseline cerebrovascular risk such as those in Central Asia. Regional stroke registries and migraine databases could contribute valuable real-world evidence.

Third, patient selection for CGRP-targeted therapy requires careful individualized assessment. Young women with migraine with aura, particularly those using hormonal contraceptives or with additional vascular risk factors, represent a population requiring particular attention. The contraindication of estrogen-containing contraceptives in migraine with aura patients remains an important counseling point. Smoking cessation, blood pressure control, and management of metabolic syndrome complement pharmacological prevention.

The role of non-pharmacological interventions, including lifestyle modification, regular physical activity, and stress management, complements pharmacological prevention. Multidisciplinary approaches involving neurologists, cardiologists, rehabilitation specialists, and primary care physicians offer the most comprehensive risk reduction strategies. Patient education regarding warning symptoms and the importance of timely medical evaluation during prolonged or atypical aura episodes is essential.

Modern rehabilitation technologies, including telerehabilitation and wearable monitoring devices, may expand access to specialized care in remote Central Asian regions. However, infrastructure development, healthcare professional training, and patient digital literacy are prerequisites for effective implementation. The potential for artificial intelligence-assisted diagnostic tools to support stroke recognition in migraine patients deserves exploration.

Traditional preventive medications, including beta-blockers, antiepileptic drugs, and calcium channel blockers, remain widely available and economically accessible in Central Asian healthcare systems. However, their variable efficacy, limited tolerability, and lack of specificity for migraine pathophysiology restrict their utility in high-risk patients. The transition from traditional to CGRP-targeted therapies should be viewed as complementary rather than replacement, with individualized selection based on clinical profile, comorbidities, and resource availability.

Practical implementation of modern migraine management in Central Asian healthcare systems requires several strategic steps. Development of regional clinical guidelines incorporating local epidemiological data and healthcare infrastructure capabilities is essential. Training programs for primary care physicians and neurologists should emphasize recognition of atypical aura symptoms and appropriate referral pathways. Establishment of multidisciplinary headache centers in major regional hospitals could improve diagnostic accuracy and therapeutic outcomes. Integration of migraine screening into routine cardiovascular risk assessment protocols may facilitate early identification of high-risk individuals.

Limitations of this review include the narrative rather than systematic methodology, potential publication bias favoring positive therapeutic outcomes, and limited availability of Central Asian-specific epidemiological and clinical data. Future research priorities should include population-based studies determining migrainous infarction incidence in Central Asian countries, investigation of region-specific genetic and environmental risk modifiers, evaluation of CGRP-targeted therapy accessibility and outcomes in regional healthcare systems, and development of culturally adapted patient education materials.

Conclusion. Migrainous infarction represents a rare but clinically significant complication of migraine that highlights the important relationship between primary headache disorders and cerebrovascular disease. The high prevalence of migraine and stroke in Central Asia, particularly in Uzbekistan, underscores the regional importance of this association.

Current evidence indicates that migrainous infarction results from complex interactions between cortical spreading depression, neurovascular dysfunction, and prothrombotic changes, predominantly affecting young women with migraine with aura. Diagnosis requires meticulous exclusion of alternative stroke etiologies and remains challenging, particularly in resource-limited settings.

The introduction of CGRP-targeted therapies has fundamentally transformed migraine prevention, offering effective attack reduction without vasoconstrictive effects and demonstrating favorable cardiovascular safety profiles. These agents should be considered as first-line preventive options in appropriate patients, with individualized risk assessment guiding therapeutic decisions. However, specific precautions apply to patients with recent cerebrovascular events.

Comprehensive management of patients with migraine and cerebrovascular risk requires integration of pharmacological prevention, modification of vascular risk factors, and multidisciplinary care coordination. Further research is needed to optimize therapeutic protocols, establish region-specific guidelines, and improve access to modern treatments across Central Asian healthcare systems. The evolving understanding of migraine-associated cerebrovascular risk holds significant promise for improving patient outcomes in this vulnerable population. Collaborative efforts between regional healthcare systems, international research consortia, and pharmaceutical stakeholders will be essential for translating scientific advances into tangible clinical benefits across Central Asia and beyond.

References

1. Headache Classification Committee of the International Headache Society. The International Classification of Headache Disorders, 3rd edition. *Cephalalgia*. 2018;38(1):1-211.
2. The burden of migraine and tension-type headache in Asia from 1990 to 2021. *The Journal of Headache and Pain*. 2025. (GBD 2021 data for Central Asia)
3. Kilichev IA, Adambayev ZI, Matyokubov MO. Dynamics of some epidemiological indicators of stroke in the desert-steppe zones of Uzbekistan during the period of independence of the republic. *Medical News*. 2022;1:76-78.
4. Epidemiological trends and forecasts in stroke. *Stroke Journal*. 2025. (GBD 2021: Uzbekistan 4th globally in stroke incidence)
5. Eller MT, Schwarzova K, Gufler L, et al. CGRP-targeted migraine therapies in patients with vascular risk factors or stroke: a review. *Neurology*. 2025;105(2):e213852(1)-e213852(9).
6. American Headache Society. Position Statement: CGRP Inhibitors should now be considered a first-line option for migraine prevention. 2024.
7. Dodick DW, Tepper SJ, Ailani J, et al. Effect of erenumab versus other migraine preventive medications on cardiovascular and cerebrovascular outcomes: a United States claims database-based observational cohort study. *Headache*. 2025.
8. Chen SP, Ayata C. Migraine and stroke: an update. *Current Opinion in Neurology*. 2023;36(3):197-204.