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# PREVENTIVE MEDICINE FOR MIGRANE AND HEADACHE

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***Abstract:*** Migraine is a prevalent and occasionally incapacitating neurological and vascular condition that primarily impacts younger adults, with a notable prevalence among women. The term "migraine" finds its origins in Galen's use of "hemicranias" to describe a recurring condition characterized by severe, one-sided head pain, often accompanied by vomiting, sensitivity to light, regular episodic episodes, and relief through darkness and sleep. Migraine stands as a widespread headache disorder, and according to the World Health Organization, it holds a significant global ranking in terms of diseases that cause disability. Typically, diagnosis relies on clinical assessments, and in certain instances, neuroimaging is employed to rule out other potential sources of headaches. This article provides an overview of the current knowledge regarding the mechanisms at the core of migraine and various strategies for its management.

***KeyWords:*** **Headache, Epidemiology, Trigger factors, Prevention, Treatment.**

## I. INTRODUCTION

The term "migraine" originates from Galen's use of "hemicranias" to depict a recurring condition involving intense, one-sided head pain, accompanied by vomiting, sensitivity to light, regular episodic occurrences, and alleviation through darkness and sleep.[1] Migraine ranks as the third most widespread and holds the seventh position in terms of global disability causes.[2] It is a common source of headaches, primarily linked to the activation of meningeal perivascular pain fibers and heightened sensitivity in cerebral pain neurons that transmit signals from both intracranial structures and the skin and muscles outside the skull.[3] Migraines frequently cause headaches by stimulating pain fibers around the meninges and increasing the sensitivity of central pain neurons, which handle signals from both inside the head and external areas like the skin and muscles.[4] Several internal or external factors can initiate a migraine attack.[5] Key triggers include stress, variations in weather, tiredness, food and drinks, lack of sleep, hunger, and menstrual cycles. Understanding migraine triggers is crucial for effectively managing patients. Limited studies from India address these triggers. In this report, we explore migraine triggers, analyzing their correlation with clinical and prognostic variables.[3]

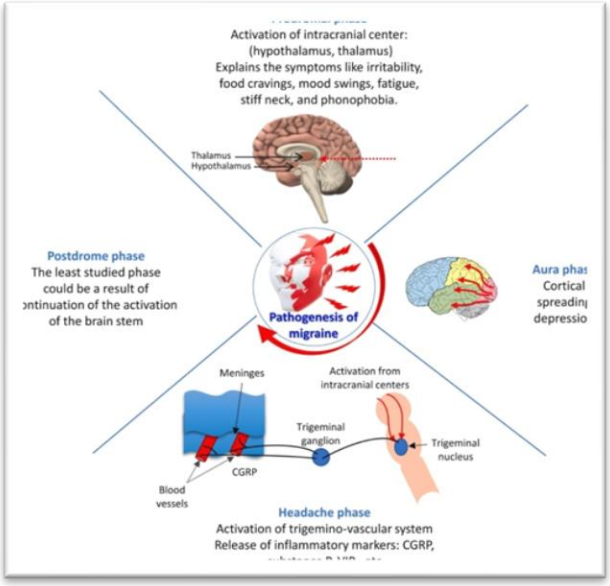
## II. EPIDEMIOLOGY

Extensive research has investigated the prevalence of migraines, which ranks 19$^{th}$ globally among all diseases causing disability. Approximately 11% of An active headache disorder which affects on the adult population worldwide. migraine being age and gender-specific.[2] Prior to puberty, it's more prevalent in boys than girls; however, during adolescence, migraines escalate more rapidly among girls in contrast to boys.[3] In 2019, over 213 million individuals in India were identified as experiencing migraines, with women accounting for 60 percent of these reported cases.[1] The prevalence of migraines in women rises steadily from childhood through early adulthood until around the age of 40, after which it gradually decreases.[2] Most commonly, migraines affect individuals aged between 15 and 55, with 70% to 80% of those experiencing migraines having a family history of the condition.[7] The prevalence rates of International Headache Society-defined migraines remain relatively steady in Western countries, ranging between 4% and 9.5% in men and 11.2% to 25% in women.[8] In the United States, approximately 6 % of men and 18% of women impacting 28 million Americans suffer from migraines. Data from the United Kingdom indicates an overall migraine prevalence ranging from 3.7% to 4.9 [9]

The prevalence of migraine disease among individuals aged 6 to 15 years in Saudi Arabia was recorded at 6.2%. Both males and females showed the highest incidence rate and number of new migraine cases within the age range of 10 to 14 years.[6]

## III. PATHOPHYSIOLOGY OF MIGRANE

The recognition of headaches dates back nearly 600 years, while the contemporary understanding of chronic migraines traces back to the early 17th century. Initially, the pathophysiology of migraine disorder focused on vascular mechanisms or neurological mechanisms, with Metabolic aspects have only been reported relatively recently. Migraines are categorized into four phases: (Premonitory, Aura, Headache, and Postdromal) (refer to Fig.1). These phases can unfold sequentially or display notable overlap.[5]




**(**Fig-1) illustrates the mechanisms underlying the various stages of a migraine, indicating the potential for overlap between these phases

Migraine pathophysiology involves the regulation of pain triggered by altered neural networks in the head. Research indicates that the brain stem and diencephalic nuclei play a role in overseeing the trigeminovascular system, which encompasses neurons controlling vascular networks (efferent) and those transmitting information to the trigeminal nucleus caudalis (afferent).[4]

The perception of head pain originates from the perceived inflammation of the meninges and vasodilation due to the activation of these networks.[3] Additionally, neurotransmitters like serotonin play crucial roles in both the pathophysiology and treatment of migraines. Serotonin triggers an internal network cascade that influences both inhibitory and excitatory neurotransmission. Serotonin receptors are spread throughout the brain, including those involved in pain-signaling pathways and blood vessels within the head. Migraine treatments are designed to target these serotonin receptors, aiming to enhance the serotonin signal, consequently providing pain relief by constricting blood vessels and inhibiting peptides like substance P21 and calcitonin gene-related peptide (CGRP).[5] The (ICHD) International Classification of Headache Disorders categorizes different types of headaches, serves as a standardized tool for distinguishing primary and secondary headaches. Diagnosis of headache disorders primarily relies on the clinical presentation across various phases. The headache and aura stages garner the main focus, often demanding medical attention.[7]

## IV. CLINICAL PHASE OF MIGRANE

**Premonitory phase-** This phase comes before the typical migraine headache, typically starting approximately 72 hours prior. Although these symptoms have been documented in literature for many years, they've often been overlooked. Symptoms encompass irritability, food cravings, mood swings, fatigue, stiff neck, and photophobia. These symptoms persist throughout the headache and aura stages, revealing a connection between The premonitory phase and its origin in the hypothalamus are significant in migraine onset.[2] Imaging studies have shown heightened flow of blood in the brain's hypothalamic region, Highlighting the role of the hypothalamus in the initial phases of a migraine episode. Migraineurs can experience triggers such as hunger, exposure to bright light, or sleep deprivation, which might also signify premonitory symptoms. However, there's a noticeable disparity in how triggering factors are described between clinical studies and questionnaire surveys. This variation could stem from patient misconceptions about these triggers and their association with migraine attacks.[8]

**Aura phase-** The aura phase is experienced by one-third of migraine patients, characterized by (CSD)cortical spreading depression, involving cortex depolarization and the formation of a transient wave. Researchers highlight CSD as the primary mechanism contributing to this phase.[2] The retinotopic propagation in the visual cortex indicates the potential involvement of CSD in migraines, supported by imaging studies. However, some studies have contradicted the connection between CSD and migraine.[2]

**Headache phase-** The headache phase involves severe, pulsating, unilateral pain ranging from moderate to extreme severity. The neurovascular theory explains this pain, attributing the activation of the trigemino-vascular system to earlier activity in higher intracranial centers like the thalamus and hypothalamus. Consequently, nociceptive fibers, The vascular system of the dura mater, which receives its blood supply from branches stemming from the trigeminal ganglion, undergoes sensitization and releases inflammatory mediators like calcitonin gene-related peptide (CGRP), substance P, and vaso-inhibitory peptide (VIP).[8] These mediators initiate signals along the trigemino-vascular pathway. Afferent nerve fibers to the trigeminal ganglion and those from the skin and muscles of the neck converge on second-order neurons within the trigeminal cervical complex (TCC), contributing to upper neck pain. Ascending fibers from the TCC transmit signals to various cortical areas after its passing through basal ganglia nuclei ,brainstem, and thalamic, hypothalamic , ultimately resulting in the experience of pain.[6]

**Thalamo-cortical and thalamic circuits and migraine-** Changes in brain function have been observed during the premonitory phase. Electrophysiological studies indicate heightened blood flow, notably within circuits linking the cortex and thalamus.[2] Both functional and structural imaging studies have noted variations in thalamic and thalamocortical activity. Moreover, in migraine

patients, electrophysiological research highlights changes in brain functionality, while imaging studies demonstrate fluctuations in thalamic activity during their attacks.[6]

**Postdromal phase-** The premonitory phase, often overlooked and underreported by patients, is the least studied in the literature. Yet, it can be a distinct phase of the disease or a continuation of the same pathology. Symptoms such as fatigue, muscle weakness, mood fluctuations, difficulty concentrating, and decreased appetite may be reported by patients during this phase. A potential explanation for the postdromal phase could involve the continued activation of the brainstem and diencephalon during and after processing pain stimuli.[8]

**triggering factors and Metabolic dysfunction-** Metabolic irregularities are predominantly linked to triggering factors for migraines. These include fasting, alterations in sleep patterns, fluctuations in ovarian hormone secretion (especially during menstruation), physical exercise, alcohol consumption, and changes in weather, all of which can lead to migraine headaches.[6]

## V. CLINICAL FEATURES

Women have an 18% greater likelihood of experiencing migraines compared to the 6% chance seen in men. The higher prevalence among women is often linked to hormonal fluctuations, particularly estrogen. Migraines typically commence during puberty or between the ages of 35 and 45.[5] Migraine presents in two major subtypes: Migraine with aura, characterized by transient focal neurological symptoms that generally precede or sometimes accompany the headache. Certain patients experience a premonitory phase that occurs hours or even days before the onset of the headache, followed by a headache resolution phase.[8] Symptoms observed during these phases encompass hyperactivity, hypoactivity, feelings of depression, cravings for specific foods, repetitive yawning, fatigue, and neck stiffness or pain. Migraine without aura is a clinical syndrome distinguished by a headache with specific features and Attached physiological signals like unilateral location, pulsating quality, moderate to severe pain intensity, aggravation or causing avoidance of routine physical activity. During the headache, individuals might experience nausea and/or vomiting, along with the sensitivity to the light (photophobia) and sound (phonophobia).[9]

## VI. DIAGNOSIS

The diagnosis of migraine it involves history taking, and alternately, it can be confirmed through the exclusion of other conditions using orthopedic tests, cranial nerve examination, a complete blood count, urinalysis, and if necessary, cranial magnetic resonance imaging.[4]

Individuals with migraines or a family history of migraines are often diagnosed by a neurologist specialized in headache treatment. This diagnosis is typically based on the individual's medical history, symptoms, and a thorough neurological and physical examination. In cases where the condition is atypical, intricate, or undergoes a sudden and significant change in severity, tests may be conducted to exclude other potential causes for the pain.[5]

- **A MRI scan-** Utilizing a robust magnetic field and radio waves, a magnetic resonance imaging (MRI) scan creates comprehensive images of the brain and blood vessels. This diagnostic tool assists in identifying conditions such as tumors, strokes, brain bleeding, infections, and various neurological disorders affecting the human brain and nervous system.[3]
- **A CT scan-** Employing a series of an X-rays, computerized tomography (CT) scan generates detailed cross-sectional images of the brain. This imaging method aids in the diagnosis of tumors, infections, brain damage, brain bleeding, and various potential medical issues that could be contributing to headaches.[3]

## VII. TREATMENT

Treatment for migraines targets symptom cessation and the prevention of future attacks. Medications for managing migraines are generally categorized into two main groups:

**Pain-relieving medications-** These medications, known as acute or abortive treatment, are taken Upon the onset of a migraine attack[4]

**Preventive medications-** Regularly taken, often on a daily basis, these Medications target reducing the severity or frequency of migraines.[4]

**A. Medications for relief-** The most effective relief from migraine pain is achieved when medications are taken at the initial indication of an impending migraine – right as the symptoms begin. Medications suitable for treating migraines include:

– **Pain relievers-** Over-the-counter or prescribed pain relievers such as aspirin or ibuprofen are available for alleviating migraine pain. Prolonged use of these medications can lead to medication-overuse headaches and potentially result in ulcers and gastrointestinal bleeding. Migraine relief medications containing a combination of caffeine, aspirin, and acetaminophen (Excedrin Migraine) might offer some relief, typically effective against mild type of migraine pain.[6]

– **Triptans-** To treat migraines, prescription medications like sumatriptan (Tosymra, Imitrex) and rizatriptan (Maxalt, Maxalt-MLT) are employed as they obstruct pain pathways in the brain. Available in pill form, shots, or nasal sprays, they effectively alleviate various migraine symptoms. However, caution is advised as they may not be safe for individuals at risk of a stroke or heart attack.[7]
– **Dihydroergotamine (Migranal, Trudhesa)–** Administered as a nasal spray or injection, this drug is most efficient when taken soon after the onset of migraine symptoms, particularly for migraines that persist for the more than 24 hours. Side effects may involve exacerbation of migraine-associated vomiting and nausea. Individuals with coronary artery disease, high (BP)blood pressure, or kidney and also liver disease should refrain from using dihydroergotamine.[6]
– **Lasmiditan-** Approved for treating migraines with and without aura, this newer oral tablet, lasmiditan, demonstrated significant improvement in headache pain during drug trials. However, lasmiditan can induce a sedative effect and dizziness, therefore individuals using it are cautioned against driving and operating machinery for at least eight hours.[4]
– **Opioid medications-**Narcotic opioid medications may offer relief for individuals unable to take other migraine medications. However, due to their high addictive potential, these are typically reserved for use only when other treatments prove ineffective.[2]
– **Oral CGRP Antagonists, Referred to as Gepants-** Ubrogepant (Ubrelvy) and rimegepant (Nurtec ODT) are oral gepants sanctioned for managing migraines in adults. Clinical trials demonstrated that medications within this class were is more effective than placebos in alleviating pain within two hours of ingestion. Additionally, they proved effective in addressing migraine symptoms like nausea, sensitivity to the light, and sound.[6]
– **Zavegepant for Nasal Administration (Zavzpret)-** Zavegepant, a newly FDA-approved nasal spray for migraine treatment, belongs to the gepant class and stands out as the only migraine medication administered via nasal spray. It provides relief from migraine pain within 15 minutes to 2 hours after a single dose, with effects lasting for up to 48 hours. Additionally, it can alleviate other Attached physiological signals with migraines, such as nausea, sensitivity to light, and sound. Typical side effects of Zavegepant encompass alterations in taste perception, nasal discomfort, and throat irritation.[4]

**B. Preventive Medication-** To address frequent, prolonged, or severe headaches unresponsive to standard treatment, preventive medications may be suggested by your healthcare provider. The objective of preventive medication is to decrease the frequency, intensity, and duration of migraines. Various options include:
– **Medications for Lowering Blood Pressure-** Examples of preventive medications for migraines encompass beta blockers like propranolol (Inderal, InnoPran, Hemangeol) and metoprolol (Lopressor), while calcium channel blockers such as verapamil (Verelan, Calan) can effectively deter migraines accompanied by aura.[3]
– **Atogepant-** This medication, a gepant, serves as a preventive measure for migraines. It's an oral tablet meant for daily consumption. Potential side effects of this medicine may encompass nausea, constipation, and fatigue.[2]
– **Anti-seizure drugs-** Valproate and topiramate (Topamax, Qudexy, among other names) may be beneficial for individuals experiencing less frequent migraines, but they can lead to side effects like dizziness, weight fluctuations, and nausea. However, it's important to note that these medications are not advised for pregnant women or those attempting to conceive.[2]
– **Antidepressants-**Amitriptyline, a tricyclic antidepressant, is effective in preventing migraines. Due to its side effects, like drowsiness, alternative antidepressants might be recommended instead.
– **Botox injections-** Injections of onabotulinumtoxin A (Botox), given approximately every 12 weeks, aid in preventing migraines in certain adults.[3]
– **Calcitonin gene-related peptides (CGRP) monoclonal antibodies-**Erenumab-aooe (Aimovig), fremanezumab-vfrm (Ajovy), galcanezumab-gnlm (Emgality), and eptinezumab-jjmr (Vyepti) are recent medications sanctioned by the Food and Drug Administration for migraine treatment. Administered monthly or quarterly through injections, the most frequent side effect is a reaction at the injection site.[3]

## VIII. CONCLUSION-

Migraine stands as a prevalent cause of headaches. Early diagnosis and swift treatment of migraine significantly improve the quality of life and deter the transition from episodic to chronic migraines. With an increasing focus on understanding the pathophysiology, there is a burgeoning discovery of new therapeutic tools targeting various pathways.

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