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Review Of Impact Of Migraine: Neuropsychiatric Aspects, Quality Of Life And Disability

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Abstract: Migraine is one of the most common type of headache worldwide. Mostly it's seen that the pain and associated physical symptoms of migraine are a major concern for its management. What we often overlook is the impact of migraine on a person's daily activities, sleep pattern, and mental health; that substantially affects the quality of life and adds to disability for people with migraine.

INTRODUCTION:

Migraine is a hereditary condition characterized by recurrent episodes of headaches that vary widely in intensity, frequency, and duration. These headaches typically affect one side of the head and are often accompanied by symptoms such as loss of appetite, nausea, and vomiting. Additionally, they may be preceded by or associated with neurological and mood disturbances, as noted by CRITCHLEY in 1969. (1)

HISTORICAL BACKGROUND:

The term "migraine" originates from the Latin word "hemicrania," which translates to "half" (hemi) and "skull" (crania). This term was first employed by Galenus of Pergamum around 400 B.C., while Hippocrates described aura as the flashing of lights preceding migraine attacks. The earliest recorded instances of painful headaches date back to 1200 B.C. in Egypt. (2)

Aretaeus of Cappadocia, in the 2nd century, described typical migraine features such as one-sided or unilateral headaches and associated vomiting. Freud also discussed the psychopathological aspects of migraine, a concept further elaborated upon by Harold Wolff in 1930, building upon Freud's ideas. (2)

Migraine presents as a frequently occurring disorder characterized by recurrent episodes of headaches and accompanying symptoms. It is often associated with various somatic and psychiatric conditions as comorbidities. Both migraine and psychiatric disorders pose significant challenges to healthcare systems globally due to their prevalence and burdensome nature. (3)

Epidemiology of Migraine:

According to Global, regional, and national burden of migraine and tension-type headache, 1990–2016, a systematic analysis for the Global Burden of Disease Study 2016, the worldwide prevalence of migraine is approximately 15%, with women being affected three times more often than men. It typically begins between the ages of 15 and 24 years and is most common in individuals aged 30 to 45 years (Figure no. 1).

Figure no. 1: Global Burden of Disease Study 2016

Prevalent cases and YLDs for migraine	Prevalence 2016	YLD 2016
Global	**~ 1000 million**	**45million**
South Asian Region	~300 million	**12 million**
India	~230 million	9 million

Diagnostic criteria:

The International Classification of Headache Disorders, Third Edition (ICHD-3) provides specific diagnostic criteria for migraines. To be diagnosed with migraine, a patient should have experienced at least five attacks that fulfil the following criteria:

1. Headache Duration:

   The headache attack must last between 4 and 72 hours (when untreated or unsuccessfully treated).

2. Headache Characteristics:

   The headache should exhibit at least two of the following four characteristics:

   Unilateral Location: The pain is typically on one side of the head.

   Pulsating Quality: The headache throbs or pulses.

   Moderate or Severe Pain Intensity: The pain is significant.

3. Associated Symptoms:

   The headache must be accompanied by at least one of the following symptoms:

   Nausea and/or vomiting.

   Photophobia (sensitivity to light) and/or phonophobia (sensitivity to sound).

4. Exclusion Criteria:

   The diagnosis should not be better accounted for by another ICHD-3 diagnosis

INTERPLAY OF MIGRAINE WITH NEURO-PSYCHIATRIC DISORDERS, QOL AND DISABILITY:

Migraine and psychiatric disorders are widespread and imposing conditions, presenting significant challenges to healthcare systems globally. The overlap between these two conditions is substantial. Epidemiological research indicates that individuals with migraine face an elevated likelihood of experiencing major depression, anxiety, or suicidal tendencies.

Genome-wide association studies have revealed that migraine exhibits a heightened genetic correlation with psychiatric disorders, implying shared genetic foundations or pathways. Along with neurological and psychiatric disorders related impact on the quality of life, migraine related dysfunction further worsens the QOL and adds on to the associated disability.

Following is the detailed description of the impact of migraine on various aspects:

1. Depression:

Depression often coexists with migraine, presenting a challenge in treating both conditions. Individuals experiencing migraines have 2.5 times higher odds of also experiencing depression. Notably, this risk is more pronounced among women. Furthermore, individuals with a longer history of migraines and higher attack frequency tend to exhibit a greater prevalence of depressive symptoms.

Individuals experiencing anxiety-type headaches do not face an increased risk of depression when compared to control groups. Furthermore, there is no evidence suggesting that migraine frequency is heightened due to the presence of anxiety or depression.

When migraines transition from an episodic to a chronic form, the risk of comorbid psychiatric conditions significantly increases. A study revealed that 78% of individuals with persistent migraines also experience psychiatric disorders. Among these, major depression occurred in 57% of cases, dysthymia in 11%, panic disorder in 30%, and generalized anxiety in 8%. Notably, female migraineurs were more commonly affected by depression and anxiety disorders. However, there was no elevated risk of generalized anxiety disorder specifically within this group. (3)

Among individuals experiencing persistent daily headaches, the risk of major depression and panic disorder is 1.5 to 2 times higher in females compared to the general population. Sex-related differences exist in the occurrence of comorbid conditions. A study indicated that female migraineurs, but not male migraineurs, faced an increased risk of anxiety, depression, somatic complaints, and hysteria.

The connection between affective disorders and migraines remains uncertain. Does migraine cause affective disorders in some individuals, while affective disorders trigger migraine attacks in others? Generally, affective disorders manifest before migraine symptoms, and depressed individuals may have a lower pain threshold, potentially leading to a wider range of headaches. However, no genetic link between migraines and depression has been established.

Venlafaxine has a greater ability to inhibit serotonin reuptake compared to norepinephrine. It seems that doses ranging from 75mg to 150mg may effectively manage migraines. Additionally, Mirtazapine, known for enhancing serotonergic and noradrenergic neurotransmission, could be beneficial in treating both conditions.

2. Suicide attempts:

While the evidence linking migraine and depression is compelling, the extrapolation of an elevated risk of suicide associated with migraines is particularly concerning. A study conducted by Breslau et al. in 1991 indicated that both female and male individuals with migraines (of either subtype) had higher rates of attempted suicide compared to those without migraines.

When comparing migraine without aura to individuals without migraines, the adjusted odds ratio for suicide attempts was 1.6. However, for those with migraine with aura, the odds ratio increased significantly to 3.0. These results highlight a threefold higher risk of suicide attempts associated with migraine with aura, regardless of major depression, other psychiatric comorbidities, and sex.

The diagnosis of migraine headache by a physician was discovered to be connected to a higher likelihood of deliberate self-harm in the future, though no evidence suggested a correlation with mortality due to suicide (4).

3. Anxiety:

The findings revealed a significant connection between anxiety and migraine headaches. Individuals who reported experiencing migraine headaches were more likely to also experience symptoms of anxiety compared to those without migraines. This suggests that there may be a bidirectional relationship between migraine headaches and anxiety, where each condition can potentially exacerbate the other.

Understanding this association is crucial for healthcare professionals in effectively managing and treating individuals with migraine headaches. Addressing both the physical pain of migraines and the accompanying anxiety symptoms can lead to more comprehensive and successful treatment outcomes for patients (5).

The connection between anxiety disorders and migraines appears to work both ways. A study investigating the 5HTTLPR polymorphism of the serotonin transporter gene found that both anxiety and migraines are linked to a higher occurrence of the s allele, indicating a shared genetic predisposition. Current theories regarding the neurobiological mechanism linking anxiety and migraines encompass various factors, including serotonin dysfunction, dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis, hormonal impacts, and psychological elements such as interoceptive conditioning, pain-related cognition, avoidance learning, and anticipatory anxiety (6).

4. Panic disorder:

Panic disorder (PD) is characterised by unexpected recurrent panic attacks, followed by physical symptoms consisting of sweating, trembling, palpitations, dizziness, chest pain, the worry of going crazy or dying, frequently co-happening with agoraphobia (7). The odds ratio (OR) of panic disorder (PD) in individuals with migraine stands at 3.76, with an even higher likelihood observed in patients experiencing migraine with aura. PD correlates with heightened migraine frequency, greater disability, an elevated risk of chronic migraine, and an increased likelihood of medication overuse. Migraine and PD exhibit similarities in various aspects, including functional limitations, gastrointestinal symptoms like nausea, autonomic symptoms such as dizziness, and affective symptoms like fear during attacks, and concerns about future episodes between attacks (6).

5. Bipolar disorder:

BD is characterized via a periodic course of depressive episodes and episodes with highly extended mood (mania or hypomania). It is normally divided into BD type I (as a minimum one manic or blended episodes) and BD type II (at least one hypomanic, but no complete manic phase), with BD I generally impairing more severely the individual functioning (7).

Bipolar spectrum disorder (BPAD) and migraine share a bidirectional relationship, with over three times more migraine with aura patients experiencing BPAD compared to the general population, or approximately one-third of individuals with bipolar disorder suffering from migraines. The prevalence of migraine among those with bipolar disorder varies between subtypes, with 54.17% of individuals with bipolar disorder type II and 32.7% with bipolar disorder type I reporting migraine (8).

Both conditions exhibit shared features, including episodic nature, exacerbation by stress, familial association, and responsiveness to anticonvulsant medications such as valproate. Migraine and BPAD are more prevalent in females, with the unstable rapid cycling course subtype being particularly associated with both conditions. Possible mechanisms underlying their co-occurrence involve heritability factors and alterations in neurotransmitter systems such as serotonin, dopamine, and glutamate, as well as changes in sodium/calcium channels and pro-inflammatory processes (9).

Treatment strategies often involve antiepileptic drugs like valproate and topiramate, which have demonstrated efficacy for both migraine and BPAD. Psychotherapy, when added to pharmacotherapy for BPAD, may improve treatment adherence. However, caution is advised with selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs) due to the risk of exacerbating mania, potentially leading to non-adherence to medication regimens during manic episodes (6).

6. Personality traits/ disorders:

Wolff is acknowledged for pioneering the significant concept of the 'migraine personality,' which he described as a combination of 'personality traits and responses prevalent in individuals with migraine,'

encompassing 'feelings of insecurity coupled with tension, exhibited as rigidity, conscientiousness, attention to detail, perfectionism, and resentment (10).

While there is even less empirical or systematic data regarding other personality disorders, it is believed that they can, in certain instances, complicate headache treatment due to the challenging interpersonal behaviour of the patient. For example, histrionic patients may overly dramatize physical symptoms, passive/dependent patients may excessively depend on healthcare providers, and narcissistic patients may exhibit demanding behaviour (11).

The subset of migraine patients with concurrent Borderline personality disorder exhibited a correlation with female gender, higher incidence of medication overuse headache, elevated rates of self-reported depression, heightened migraine-related disability, and a reduced responsiveness to pharmacological migraine treatment (12).

Compared to controls, women of age 18–65 years with migraine had better rating in the Harm Avoidance (HA) and Persistence (P) sections and decrease rating in the Self-Directness sections of the Temperament and Character Inventory, therefore, certain traits may have been associated with increased migraine severity or decreased response to treatment (13,14).

7. Eating disorders:

Eating disorders encompass a range of psychological conditions characterized by abnormal eating habits and attitudes towards food and weight. Common types include anorexia nervosa, bulimia nervosa, and binge-eating disorder. They often co-occur with other mental health issues like depression and can have severe physical and emotional consequences (7).

In the general female population, migraine was present in 12%, while among individuals with Anorexia Nervosa (AN) and Bulimia Nervosa (BN), it was 22% (odds ratio 2.0, $p = .04$). Women with an eating disorder showed a high prevalence of Major Depressive Disorder (MDD) at 42%. MDD was strongly linked with migraine (odds ratio 3.0, $p < .0001$) and accounted for the connection between eating disorders and migraine. The highest prevalence of migraine (36%) occurred in women with both an eating disorder and MDD (15).

Eating problems may raise the probability of increasing migraine attacks. Persons suffering from eating disorders tend to skip meals or prolonged fasting, which can act as a trigger (16).

7. Quality of Life and Disability:

A cross-sectional study by G M Terwindt et al (2000) in a Dutch population of 5998 people out of which 620 had migraine to study the quality of life. Results showed that migraineurs were seen to have compromised physical, mental, and social functioning, particularly those with a high frequency of attack (17).

Al Ghadeer HA (2021) conducted a study in Saudi Arabia where 101 out of 359 participants were identified to have a migraine. In this study, 57.3% suffered from a severe disability caused by migraines while only 20.7% had a moderate disability. Low QOL scores were associated with females and a significant relationship was found between migraine-associated disability and patients' emotional function in QOL (18).

Recently, OVERCOME study by Etsuko Awaki (2024) was conducted to see the impact of migraine on daily life. In this study, among 17,071 respondents with migraine, 24.8% required assistance with housework at least sometimes. It was also seen that Migraine interfered with relationships, leisure, and social activities at least sometimes for 31.8%, 41.6%, and 18.0% of respondents, respectively. Another interesting finding was that between headache days, 26.8% of respondents worried about planning social/leisure activities at least sometimes. These would affect the quality of life of these participants (19).

DISCUSSION AND CONCLUSION:

Psychiatric co-occurring conditions are more prevalent among migraine patients compared to the general population, particularly in those with chronic migraine rather than episodic migraine. Various hypotheses exist to elucidate the complex connections between psychiatric comorbidities and migraine. However, the biological mechanisms behind these relationships remain poorly understood. The presence of psychiatric comorbidities appears to elevate the risk of chronic migraine development, diminish the quality of life for migraine patients, and complicate migraine treatment. A significant proportion of females, children, and adolescents with migraine experience concurrent psychiatric disorders. Further research is warranted to explore this intersection thoroughly, especially regarding therapeutic interventions, given their clinical, functional, and economic ramifications.

Migraine commonly co-occurs with mental health conditions such as anxiety, depression, bipolar disorders, and panic attacks. It is crucial for psychiatrists, therapists, and neurologists to be well-versed in both psychiatric diagnoses and headaches. The presence of psychiatric comorbidity in headache disorders is prevalent and significantly impacts patients' lives. Specifically, utilizing DSM-V criteria to diagnose disorders across all three axes is essential for effectively treating many migraine patients. Thorough consideration of patient history and diagnostic methods related to migraine should account for the presence of comorbidities.

Despite extensive research, our understanding of the biological underpinnings of migraine and its comorbidities remains incomplete. Factors such as heritability, specific genes, and neurotransmitter systems play significant roles in various comorbid disorders. Due to the complex and dynamic nature of these influences over time, comprehensive treatment strategies are necessary, including combined approaches.

Diagnostic clarification is essential, as is navigating the intricate therapeutic interplay between these conditions. A multimodal treatment perspective must carefully consider each patient's disorder and treatment history to effectively manage comorbidity between migraine and psychiatric disorders. Hence, would help to improve the quality of life and lessen the disability related to the impact of migraine.

DECLARATION OF CONFLICT: None.

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