

## Original Research Article

# A study on prevalence and co-morbidity of bipolar and anxiety disorders in chronic headache patients

Sivaji M.<sup>1\*</sup>, Manickavasagam J.<sup>1</sup>, Indumathi Sundaramurthi<sup>2</sup>, Gopinathan S.<sup>1</sup>

<sup>1</sup>Department of Neurology, Institute of Neurology, Madras Medical College, Chennai, Tamil Nadu, India

<sup>2</sup>Department of Anatomy, Chettinad Health and Research Institute, Kelambakkam, Kanchipuram, Tamil Nadu, India

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### \*Correspondence:

Dr. Sivaji M,

E-mail: [sivajimuruga@gmail.com](mailto:sivajimuruga@gmail.com)

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## ABSTRACT

**Background:** Co morbidity between headache and psychiatric disorders is more prevalent in chronic headache patients. The bipolar disorders and anxiety disorders are predominant in migraine and TTH respectively. This co morbidities have a poor reflection and impact on quality and outcome of chronic headache patients and results in worst prognosis and poor response to medical treatment.

**Methods:** The chronic headache patients especially migraine and tension type of headache were analyzed with following materials such as the structured psychiatric clinical interview with ICD-10 mental and behavioural disorder, DSM-5 criteria. HAM-A, HAM-D, BDI-2, BPRS, young mania rating scale, Yale-Brown Obsessive Compulsive Scale (Y-BOCS) and panic disorder scale.

**Results:** Various subsets of bipolar disorder and anxiety disorder were found as follows: 74% of migraineurs are associated with psychiatric disorders in which bipolar affective disorder 6%, depressive episode 48%, dysthymia 30%, GAD 10% and Panic disorder 6%. 52% of TTH are associated with psychiatric disorders as follows: major depressive episode 52%, GAD 30%, separation anxiety disorder 6%, PTSD 7%, OCD 3% and panic disorder 2%.

**Conclusions:** From previous and future studies the headache can be identified according to subsets of headache with psychiatric disorders make easier to provide appropriate pharmacological and psychological treatment which may reduce the chronicity and intractability of headache.

**Keywords:** GAD-generalized anxiety disorder, Headache, Psychiatry comorbidity, PTSD-post traumatic stress disorder, TTH- Tension type of headache

## INTRODUCTION

Headache occurs with number of psychiatric disorders, including depressive disorders, anxiety disorders, post-traumatic and stress-related disorder. There is always a common causative factors and reciprocal influence between headache and psychiatric disorders. Psychological and psychopathological analysis discloses the genesis of the headache mostly the psychological, social and occupational stressors which play an important role for the transformation of migraine into chronic one. Most recent studies also report that stress-related

disorders and post-traumatic stress disorders are closely associated with migraine. One theory strongly suggest that migraine and psychiatric comorbidity share the common genetic factors, serotonergic processing and oestrogen response. In women, the prevalence of migraine and mood disorders are more common when compared to men. According to B Lee, Peter line study hypothesis states that oestrogen plays a role in the pathophysiology of migraine and mood disorders. Limbic system and HPA axis are inter linked in human beings and the estrogen modulates and exerts agonistic action on serotonergic system.<sup>1</sup>

## METHODS

In this study 486 daily headache patients were randomly selected from Neurology OPD and referral from other specialty OPDs Government General Hospital, Madras Medical College Chennai, from March 2016 to February 2017. The patients with normal investigation parameters and normal CT/MRI Imaging were selected for the study. The patients who had major organic psychosis and secondary to general medical causes were excluded from this study.

### Headache diagnosis

Patients who are satisfying the criteria classified under the International Classification of Headache Disorders, 3rd edition (beta version)- (IHS) were selected in this study.

### Psychiatric assessment

These selected patients were subjected for the following methods of examinations viz. the structured psychiatric clinical interview with ICD-10 mental and behavioural disorder, DSM-5 criteria. HAM-A, HAM-D, BDI-2, BPRS, YMRS, Y-BOCS and panic disorder scale were administered.

## RESULTS

The study included 486 (380 female 106 male) population. Age group between 15-55 years. Literacy rate range from illiterate 6% to 94% high school and degree level. 65 % were employed, 10% were students and 25% were not employed.

**Table 1: Migraine with psychiatric diseases.**

Diagnostic categories	No. of patients	%
Psychiatric morbidity	150	74%
Bipolar affective disorder	9	6%
Depressive episodes	72	48%
Dysthymia	45	30%
Generalised anxiety disorder	15	10%
Panic disorder	9	6%

**Table 2: Tension type headache and psychiatric diseases.**

Diagnostic categories	No. of patients	%
Psychiatric morbidity	53	52%
Major depressive episodes	27	52%
Generalized anxiety disorder	15	30%
Separation anxiety disorder	3	6%
Post-traumatic stress disorder	4	7%
Obsessive compulsive disorder	2	3%
Panic disorder	1	2%

Under daily chronic headache screening showed migraine 204(42%) and tension type of headache 102 (21%). 74 % of 204 migraine patients had psychiatric morbidity (150) (Table 1). 52 % of 102 tension type headache patients has psychiatric morbidity (53) (Table 2).

## DISCUSSION

A person with headache may complain of short- and long-term episodes of pain which is not related with his or her symptoms. The underlying psychotic disorder plays a role in intensifying the headache. Structured psychiatric clinical interview schedule revealed an Intensive, agonizing pain, often provoked by stress, psycho-social factors. The pain occurs most commonly in depression, dysthymia, somatoform, stress and anxiety disorders. Sigmund Freud categorized the psychopathology of migraine, during Harold Golf's era, who conceived a notion of "the migraine personality" in the genesis of headache. After that many studies revealed that there is a definite interrelationship between headache and psychological factors. Psychologic stressor, familial, behavioural, social and environmental factors augments and precipitate recurrent headaches. Patients having migraine are more sensitive to dopamine stimulation and the drugs acting on serotonergic receptors and neurons also induce migraine. The neuronal calcium channels dysfunction found in familial hemiplegic migraine which was started by Hargreaves and Shephard. In headache disorders hypothalamus involved in the development of anxious and depressive symptoms.<sup>2-4</sup>

### Migraine and psychiatry co morbidity

Co-morbidity of migraine are associated with various disorders such as cardiovascular disease, stroke, subclinical vascular lesions, coronary heart disease, hypertension, gene polymorphisms, patent foramen oval and psychiatric disorders. In this study, bipolar and anxiety disorders were taken into account. Two previous studies states that strong relationship prevails between migraine and major affective disorder found Breslau et al, and a definite threefold increase of migraine within one year of prevalence of bipolar disorders and two-fold increase in prevalence of depression. Merikangas et al, Juang et al, study showed 78% having migraine had psychiatric comorbidity, including major depression (57%), dysthymia (11%), panic disorder (30%), and generalized anxiety disorder (8%). Ajay Kumar Singh study states that study conducted by Cardona Castrillon, et al, evaluated patients aged 18-65 years with migraine observed major depression in 21.3%, dysthymic disorder 4.5%, panic disorders 5.6%, GAD 14.6%, PTSD 4.5%, social phobia 6.7%, specific phobia 5.6%, OCD 2.2%, and 19.1% had two mental disorders. In this present study migraine with psychiatric morbidity is 74%, bipolar affective disorder 6%, depressive episode 48%, dysthymia 30%, generalized anxiety disorder 10%, panic disorder 6%.<sup>5-8</sup>

### *The genesis of bidirectional causal theory for migraine and psychiatric comorbidity<sup>9</sup>*

- For migraine, psychiatric disorders are casual factors and responsible for the occurrence of chronic migraine
- Chronic migraine precipitates the development of anxiety and depression in migraine patients
- Showed either common aetiological factors or no association, deranged activity of neurotransmitters and receptors, low activity of enzymes plays a role in the occurrence of migraine and psychiatric disorders.

Berslau et al, states that migraine patients have strong association with anxiety disorders including phobia, panic disorder, GAD and obsessive-compulsive disorder. Ferrari proposed three biomarkers and their mechanisms are involved commonly between migraine and mood disorders which includes a decrease of platelet serotonin concentration, an increase of urinary 5-hydroxytryptamine and a possible increase of 5-hydroxyindole acetic acid.<sup>10,11</sup>

### ***Migraine and bipolar affective disorder***

The studies related on the association of migraine and bipolar affective disorders are less when compared than those for anxiety and depression. Breslau et al and Merikangas et al, conducted two population based studies and reported that the prevalence of migraine and bipolar disorder very common in young adults and have a strong and positive association. Ortiz et al, found comorbid migraine in 24.5%, McIntyre et al 24.8%, Holland et al, found a much lower prevalence of 4.7%. This present study showed 6%.<sup>5,6,12-14</sup>

The etiology for the occurrence bipolar affective disorder in migraine are polymorphisms of ANK3 and CACNA1C genes, genome wide associations, neuropathological mechanisms, neurotrophic factors, neuronal loss and in cellular level altered calcium and endoplasmic reticulum function. Gunde et al argued hyperintensities of white matter detected in neuroimaging plays an important role and its relation between migraine and bipolar affective disorder. Bigal et al hypothesis says that there may be an activation of HPA axis with reduced serotonin synthesis in comorbidity of migraine and bipolar disorders. Hamel proposed that serotonergic dysfunction mechanism involved between affective disorders and migraine. Martin and Behbehani proposed decreased oestrogen level induce down regulation of serotonergic system and up regulation of sympathetic system that leads to association of migraine and effective problems.<sup>15-19</sup>

### ***Migraine and depression***

The longitudinal population studies done by Breslau et al, showed strong bidirectional association between migraine and depression. Depression with migraine was studied using HAM D scales in the present study showed among

204 migraine patients 48% had depression and it was similar to the studies conducted by Fasmer OB and Lee B et al which showed 47% and 50%. Mathew et al, Juang et al, Singh AK showed 61%, 57%, 38.4% respectively. De Fillipis et al in 28% and Verri et al in 25% found association of migraine and depression in their studies. Kececi et al study with Turkish population showed occurrence of depression in 32% of migraine patients. There was always higher risk for the onset of depression in migraine patients and threefold higher risk of migraine onset in patients with pre-existing major depression.<sup>1,5,7,8,10,21-24</sup>

### ***Migraine and persistent depressive disorder (Dysthymia)***

Dysthymic disorder is a chronic, mild depressive mood state that does not meet the full criteria for major depression and exists for at least 2 years duration. In this present study dysthymia occurring in migraine patients was 30%, while studies by Verri AP et al, Bhuvana RC showed 17% and 9% respectively.<sup>23,25</sup>

### ***Migraine and generalized anxiety disorder***

Merikangas et al reported Generalized anxiety disorder found in 9.8% of migraine patients. Verri, et al found an association between generalized anxiety disorders and migraine in 69.3% cases. The community based studies conducted by Merikangas et al, Breslau et al, Mc Williams et al showed the incidence and prevalence of GAD is five times higher in migraine. In this present study 10% had GAD which was similar to Mc Williams study which showed 9.1% of patients with migraine had GAD.<sup>5,6,23,26</sup>

### ***Migraine and panic disorder***

Patients with migraine 3 to 10 times more likely to suffer from panic disorder. More prevalence of panic disorder shown by the studies conducted on migraine patients by Breslau et al and vice versa Stewart et al, Marazziti et al, Breslau et al by population based study assessed the temporal relation of migraine and panic disorder. In the present study 6% of patients showed panic disorder which was similar to Cardona-Castrillon et al study.<sup>5,10,27-29</sup>

### ***Tension Type of Headache and psychiatry co morbidity***

Tension-type headache (TTH) is third most common headache occurs both in males and females. The patients usually describe TTH as a pain felt over the head as though a weight is placed over the head or a tight band tied around the head. TTH also associated with pain over the neck and shoulder muscles and lasts from 30 mins to several days. Normal activities do not intensify the TTH unlike migraine and head and neck movements plays as a triggering factor in TTH. Co morbidity of psychiatric disorders such as depression, OCD, GAD, panic disorders

occur along with TTH. In the present study, the psychiatry comorbidity associated with TTH was 52%. Guidetti Vet al reported that the rates of psychiatric comorbidity ranged between 45-56% in tension type of headache.<sup>30</sup>

#### ***TTH with depression***

A population based study by Tae-Jin Song showed participants with TTH (7.7%) had anxiety alone, 14 (2.5%) had depression alone, and 10 (1.8%) had both anxiety and depression. Desai SD study reported TTH was seen in 23 (22.8%), 48.5% suffered from depression. In the present study 52% had major depressive disorder along with TTH. A study by Robbins reported bipolar spectrum patients with chronic tension-type headache as 4.5%.<sup>31-33</sup>

#### ***TTH with GAD***

Desai SD reported among the patients with TTH 17.9% suffered from GAD. An Italian study reported that 53.4% TTH participants had anxiety and another clinical based study in America showed 17% had anxiety in chronic TTH. The present study showed about 30% of GAD prevalent in patients with TTH.<sup>33-35</sup>

#### ***TTH with separation anxiety disorder and panic disorder***

Livingston et al stated that adolescent and young adults presented with somatic complaints of headache were associated with various anxiety disorders. The prevalence of panic attack and separation anxiety disorder found to be high. Last stated the prevalence of separation anxiety disorder was around 78% in adolescents. Many studies showed the associations between separation anxiety disorder and panic disorder in young adulthood, Roberson et al, Silove et al, those studies proved the possibility of the co-occurrence of headaches and separation anxiety disorder in childhood which might be a developmental antecedent of co-morbid headaches and panic disorder that occurs during adolescence and young adulthood. The present study reveals 6% of separation anxiety disorder and 2% of panic disorder.<sup>36-39</sup>

#### ***TTH with post-traumatic stress disorder(PTSD)***

Incidence of PTSD is around 5-8% and more common in women than men. PTSD is more common in certain occupational sphere like military combat camps and refugee camps. In the present study, the structured clinical interview schedule revealed that more intrapersonal and interpersonal trauma prevail in the causation of PTSD like loss of loved object in natural disaster, accidents and sexual abuse. Many studies stated the occurrence of morbidity of PTSD associated with migraine. The present study reveals 7% of PTSD on TTH.

#### ***TTH with obsessive compulsive disorder (OCD)***

Beghi et al observed 2.3%, Kumar A et al 9% of OCD. In the present study TTH with OCD found in 3%. Cupini LM et al states that there is a strong association between chronic headache with medication overuse and obsessive-compulsive disorder. Individuals with drug-seeking behaviour, drug dependence or with sense of craving for substance share with the compulsive component of OCD. The presence of subclinical obsessive-compulsive disorder is underestimated in chronic headache patients most of the time. Co-morbidity of OCD has to be evaluated in patients with chronic headache. If the compulsive behaviour is found in chronic headache analyse the presence of underlying co-morbid OCD. Cognitive behavioural therapy may reduce the severity of headache and tendency of overuse of medications.<sup>8,40,41</sup>

#### **CONCLUSION**

Psychiatric comorbidity must be recognized efficiently at the earliest in order to plan for effective management of headache patients. Hence bipolar and anxiety disorders significantly impair and disable the quality of life in patients with migraine and TTH. Early identification and psychiatric treatment of comorbid conditions may prevent fallacies of diagnostic dilemma in labeling the appropriate diagnostic entity and increase the outcome of headache disorder with appropriate insight oriented psychotherapy, cognitive therapy and cognitive-behavioural therapy. In present study, we observed a correlation between frequency of headache and depressive disorders is increased in migraine disorder whereas anxiety disorder is more predominant in TTH. Improvement in mental health knowledge and research may reduce chronicity and intractability in the therapeutics of headache disorders.

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