Forgotten Psychiatric Comorbidity in Neurological Disorders

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ABSTRACT

Introduction: Neurological disorders like headache, stroke, and seizures are associated with many psychiatric comorbidities like anxiety, depression, psychosis, eating disorders, personality disorders, etc. In order to look for the association of psychiatric comorbidities in epilepsy, headache, and stroke, this study was undertaken as very few studies have been reported from this part of the country so that we can help patients in improving their quality of life.

Materials and methods: This study was done in Mahatma Gandhi Medical College and Hospital, Jaipur, India, by the Department of Neurology and the Department of Psychiatry at the time of 1st visit. Fifty patients each of proved epilepsy, stroke, and headache were enrolled after consent and they were put to screening using the Global Mental Health Assessment Tool (GMHAT) questionnaire and at the same time, Department of Psychiatry assessed comorbidities—depression and anxiety—and made diagnosis using Hamilton Anxiety Rating Scale (HAM-A) and Hamilton Depression Rating Scale (HAM-D) scale respectively.

Results: The GMHAT tool showed that 50% of the patients having headache, 80% of the patients who had stroke, and 72% of the patients suffering from epilepsy had psychiatric comorbidities. The HAM-A scale showed that 40% of the patients with headache, 16% of patients suffering from epilepsy, and 30% of patients with stroke had anxiety as psychiatric comorbidity. The HAM-D scale showed depression in 30% of the patients having headache, 36% of the patients with epilepsy, and 60% of the patients who had stroke.

Conclusion: Results of our study showed that depression and anxiety are the most frequently encountered psychiatric comorbidities in patients with epilepsy, headache, and stroke. In our study, it was seen that depression was more common as compared with anxiety in patients with epilepsy and stroke, and anxiety was more common as compared with depression

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in patients with headache. To confirm our findings further, larger multicenter studies are needed. Anxiety and depression should be evaluated by clinicians using these simple screening instruments that can rapidly detect symptoms of these comorbidities in their busy clinical settings.

Keywords: Epilepsy, Headache, Psychiatric comorbidity, Stroke.

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INTRODUCTION

The patients with neurological disorders have an increased risk for cognitive, behavioral, and psychosocial disorders. Neurological disorders like headache, stroke, and seizures cause emotional lability, a common syndrome of affective dysregulation. These disorders are associated with many psychiatric comorbidities like anxiety, depression, psychosis, eating disorders, personality disorders, etc.

The most frequent psychiatric comorbidities encountered in patients suffering from epilepsy are depression and anxiety, with a prevalence of depression ranging from 11 to 60% in patients having recurrent seizures. A meta-analysis done recently proved that patients suffering from epilepsy have several folds increased risk of depression as compared with the general population, but there is no meta-analysis done to study anxiety in such patients.³

The patients who suffered from stroke recently or in past are at significant risk for various psychiatric comorbidities. Poststroke depression (PSD) and poststroke dementia are the most commonly reported among them. These neuropsychiatric complications that are associated with stroke have negative effect on the social functioning and overall quality of life of these patients. Several studies have shown that there is also a delay in the recovery of their motor functioning.⁴

Anxiety and depression are also commonly associated with recurrent and chronic headaches. Migraine is associated with comorbidities, such as anxiety disorder, ranging from 18 to 58% and depression, ranging from 17 to 47%.⁵

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In order to look for the association of psychiatric comorbidities in epilepsy, headache, and stroke, this study was undertaken as very few studies have been reported from this part of the country so that we can help patients in improving their quality of life.

MATERIALS AND METHODS

The study was done in Mahatma Gandhi Medical College and Hospital by the Department of Neurology and the Department of Psychiatry at the time of first visit. Fifty patients each of confirmed diagnosis of epilepsy, headache, and stroke were enrolled after consent. They were put to screening using GMHAT questionnaire, responses were noted, and final diagnosis was recorded as per GMHAT (which is a well-rated tool and has been used to look for psychiatric comorbidities). The GMHAT-Primary Care Version (GMHAT/PC) is a computerized tool and is used for clinical assessment of a wide range of psychiatric problems in a hospital setting and is very convenient to be used in busy outpatient departments as well. A computer diagnosis, a symptom rating, a self-harm risk assessment, and a referral letter can be generated by this tool.⁶

At the same time, the Department of Psychiatry assessed comorbidities—depression and anxiety—and made diagnosis using HAM-A and HAM-D scale respectively. These scales are the first rating scales to measure anxiety and depression and are still widely used today in both clinical and research settings.

RESULTS

Epilepsy

Fifty patients with epilepsy were interviewed using the GMHAT tool. The aim was to study mental health problems related to psychiatry in patients suffering from epilepsy. The age of the patients varied from 16 to 60 years with a mean value of 35.2 years. Of the 50 patients with epilepsy studied, 27 (54%) were males and 23 (46%) were females (Table 1). The most common psychiatric disorder in subjects with epilepsy was depression (16%) (Table 2). The prevalence of organic disorder among epileptics was 16%, psychosis was 12%, and anxiety was 8% (Table 2). Other psychiatric comorbidities found were phobia, mania, eating disorders, and personality problems.

Using HAM-A scale, it was seen that 16% of the patients (8 patients) with epilepsy had anxiety, out of

Table 1: Sex distribution of patients

	Stroke $(n = 50)$	Headache (n = 50)	Epilepsy (n = 50)
Males	26%	21%	27%
Females	24%	29%	23%

Table 2: The GMHAT score for comorbidities in patients of stroke, headache, and epilepsy

	Stroke	Headache	Epilepsy
Primary diagnosis	(n = 50)	(n = 50)	(n = 50)
		,	(11 - 30)
Psychotic disorder	11	2	6
Organic disorder	4	3	8
Eating disorder	0	0	2
Normal	10	25	14
Personality problems	0	0	2
Depression	15	5	8
Mania	0	0	3
Anxiety	7	9	4
Phobia	0	2	3
Drug abuse	3	4	0

Table 3: The HAM-A scale in patients with stroke, headache, and epilepsy

Score	Stroke (n = 50)	Headache (n = 50)	Epilepsy (n = 50)
<17 mild	10	10	3
18-24 moderate	2	10	4
25-30 severe	3	0	1
Others	35	30	42

Table 4: The HAM-D scale in patients with stroke, headache, and epilepsy

Score	Stroke (n = 50)	Headache (n = 50)	Epilepsy (n = 50)
8–13 (mild depression)	15	8	12
14-18 (moderate)	10	5	5
19-22 (severe)	5	2	1
≥23 (very severe)	0	0	0
Others	20	35	32

which three were males and five were females; 6% of patients (3 patients) had mild anxiety, 8% of patients (4 patients) had moderate anxiety, and 2% (1 patient) had severe anxiety (Table 3).

The HAM-D scale showed depression in 36% of the patients (18 patients) with epilepsy, of which 10 were males and 8 were females. It was seen that 24% patients (12 patients) had depression of mild grade, 10% of patients (5 patients) had depression of moderate grade, and 2% of patients (1 patient) with epilepsy had severe depression (Table 4).

Stroke

Fifty patients with stroke participated in this study. This included 26 males (52%) and 24 females (48%) (Table 1). The age of the patients ranged from 18 to 74 years (the mean age was 60.6 years). In GMHAT scoring, a total of 40 patients (80%) were identified to have psychiatric comorbidities (Table 2). Depression (30%) was most commonly seen in our study population. Others included psychotic disorders (22%), organic disorders (8%),



generalized anxiety disorders (GADs) (14%), and drug abuse (6%) (Table 2).

Using HAM-A scale, it was seen that 30% patients (15 patients) had anxiety out of which 11 patients were males and 4 were females. Of them, 20% of patients (10 patients) had anxiety of mild grade, 4% of patients (2 patients) had anxiety of moderate grade, and 6% of patients (3 patients) had anxiety of severe grade (Table 3).

Using HAM-D scale, it was seen that 60% of patients (30 patients) had depression out of which 15 patients were males and 15 were females. Of them, 24% of patients (12 patients) had mild depression, 10% of patients (5 patients) had moderate depression, and 2% of patients (1 patient) had depression of severe grade (Table 4).

Headache

We included 50 patients with headache. Out of 50 patients, 29 (58%) were females, and 21 (42%) were males (Table 1). The GMHAT tool, HAM-A, and HAM-D were used to identify psychiatric comorbidities in these patients. The GMHAT tool showed that 50% of the patients with headache suffer from psychiatric comorbidities (Table 2); 18% of the patients with headache suffered from anxiety disorder and 10% of the patients had depression (Table 2); 8% of the patients with headache had history of drug abuse (Table 2). Other psychiatric comorbidities found were psychosis, organic disorder, and phobia.

The HAM-A scale showed that 40% of the patients (20 patients) had psychiatric comorbidity (anxiety) which was equal in both males and females. Out of these, 20% of patients (10 patients) had anxiety of mild grade and 20% (10 patients) had anxiety of moderate grade. It was seen that none of the patient with headache had severe anxiety (Table 3).

The HAM-D scale showed depression in 30% of the patients (15 patients), out of which 5 patients were males and 10 were females. Out of these, 16% of the patients (8 patients) had depression of mild grade, 10% (5 patients) had depression of moderate grade, and 4% (2 patients) had depression of severe grade. None of our patients with headache had depression of very severe grade (Table 4).

DISCUSSION

Epilepsy

People with epilepsy very commonly suffer from depression and anxiety disorders. Depressed mood can be caused by the altered brain activity which can further lead to the increase in frequency of seizures, leading to difficulty in management of the disease. These feelings of anxiety and depression can be worsened by the stress of living with a chronic condition. A strong link between

epilepsy, depression, and anxiety disorders has been reported in the literature.⁷ In this study, the prevalence of anxiety was 16% and that of depression was 36%. Depression was greater than the result reported in Ethiopia (32.8%), but prevalence of anxiety was lower than that seen in Ethiopia (33.5%). In our study, 36% of the patients with epilepsy had depression which was also more when compared with the result reported from Thailand (20%). The prevalence of anxiety was much lower when compared with studies done in China (30%), 9 Brazil (33–39%),¹⁰ Thailand (39%),⁸ and Egypt (47%).¹¹ The differences found could be attributed to methodological issues, difference in procedures of collecting samples, and different scales used to look for psychiatric comorbidities. The increased incidence of suicide in patients with psychiatric disorders and epilepsy has been reported in several studies.³ In a population-based case-control study in Denmark, 32-fold increased risk of suicide was seen in patients who had epilepsy and affective disorder, whereas 11-fold increased risk in patients who had epilepsy and anxiety. 12 Jones et al 13 in his review of literature identified a life time average suicide rate of 12% in people with epilepsy which was much more as compared with 1.1 to 1.2% in the general population.

Stroke

One of the commonest neuropsychiatric complications associated with stroke is PSD. Its prevalence varies depending on the hospital setting in which the patient has been examined. The prevalence rate of 21.6% has been reported for major depression and 20.0% for minor depression in acute rehabilitation hospitals in the studies from developed countries, and 24% for major depression and 23% for minor depression in outpatient clinics in which the duration of stroke varies between 3 months and 3 years. There is a significant association between location of the lesion and development of PSD. The physical disability has significant association with increased frequency in PSD.¹⁴ The prevalence of psychiatric comorbidity recorded in this study was 80%. The prevalence is much higher than the prevalence of 36% reported by Ajiboye et al, ¹⁴ 9.1% by Williams et al, ¹⁵ and 49 to 54.7% reported by other researchers. 16,17 This wide variations in prevalence rates could be due to differences in methods and the settings in which the studies were conducted. The psychiatric comorbidities which were found in this study were 30% for depression, 14% for GAD, 8% for organic disorder, and 6% for drug abuse. We reviewed several studies that focused mainly on PSD or poststroke anxiety and were conducted in developed countries; it was seen that 20 to 40% of patients had depression 18-20 and 20 to 30% of patients had GAD. 21,22 The prevalence rate for depression in our study was quite similar to other studies, but for anxiety disorder, it was lower when compared with the studies that focus mainly on poststroke anxiety disorder. Some studies that focused on three or more psychiatric disorders in stroke patients can be said to be more comparable to our study. 15-17 In an Italian study, depression was reported in 27% of the patients (mild depression in 14.6%, moderate depression in 4.9%, and severe depression in 7.2%), anxiety disorder in 12% of patients, and personality disorders in 10.2% of patients. 16 In our study, the prevalence of depression was 30% which was also slightly higher than that of Oladiji et al²³ where the reported prevalence of depression was 25.5% among stroke survivors. A longer duration of depression is seen in patients with comorbidity of PSD and GAD together than PSD alone, and this may lead to more intense adverse physical and social functioning outcome.²⁴ It has been reported that stroke outcome can be improved profoundly by early identification and treatment of these psychiatric disorders. 18,24,25 For patients with PSD and other psychiatric disorders after hospitalization, a higher 3-year mortality risk has been reported for stroke.¹⁵ A similar study found that there was an increased 10-year mortality in poststroke psychosis patients.²⁶

Headache

Headache is a very common disorder with a 1-year prevalence rate of 10 to 18.6% for migraine and 31 to 90% for tension-type headache (TTH), and it is often so troubling that it interferes with everyday life. Psychiatric comorbidities, such as anxiety disorders and depression are associated with headache, especially migraine.⁵ There are 2 to 5 times more chances to have these symptoms in patients with migraine than patients without migraine. Depression is seen in about 25% of patients with migraine, and anxiety in about 50%.²⁷ In our study, 40% of patients (20 patients) had anxiety which was equal in both males and females. Out of these, 20% of patients (10 patients) had anxiety of mild grade and 20% (10 patients) had anxiety of moderate grade which was less when compared with other studies. Anxiety disorder is more common than panic disorder in patients of headache as reported by other studies. A study done by Mehlsteibl et al²⁸ showed that headache patients are more likely to suffer from GAD (37%) than from the panic disorder (27%). The HADAS study and a study by Merikangas et al²⁹ confirmed this result.³⁰ Chronic migraine was associated with GAD in 44.6% of patients in study by Corchs et al,31 which was quite similar to the results found in our study. In our study, 30% of the patients (15 patients) had depression, which was more when compared with other

studies. Out of these, 16% of the patients (8 patients) had depression of mild grade, 10% (5 patients) had depression of moderate grade, and 4% (2 patients) had depression of severe grade. None of our patients with headache had depression of very severe grade. In a study by Song et al,³² it was seen that 9.5% of patients of TTH had anxiety and 4.2% had depression and which were higher as compared with nonheadache cases; 53.4 and 36.9% of TTH patients had anxiety and depression respectively, in an Italian study.³³ Anxiety and depression were seen in 17 and 21% of patients respectively, in another study done in America.³⁴ Anxiety and depression among patients with TTH have rarely been studied and reported using population-level data. The findings are heterogeneous given the current state. The quality of life in patients with migraine and chronic daily headache is low and lots of work hours and work days are lost in household activities, and family and social and leisure activities.⁵ Researchers do not know the exact reason why all these psychiatric comorbidities are so common in patients with headache. Serotonin, a brain chemical, is believed to be involved in all these conditions. Both these conditions can be triggered by hormone changes in women.²⁷ There are different theoretical approaches that indicate that GAD is more commonly seen in headache patients. It has been suggested recently that emotional and somatic arousal can be dampened by "worrying" (which constitutes the main feature of GAD). 35,36 Worry may be used by patients with headache as a tool to reduce the somatic arousal known to exist with pain and eventually may develop GAD.³⁷

CONCLUSION

Results of our study showed that depression and anxiety are the most frequently encountered psychiatric comorbidities in patients of epilepsy, headache, and stroke. In our study, it was seen that depression was more common as compared with anxiety in patients with epilepsy and stroke, and anxiety was more common as compared with depression in patients with headache. To confirm our findings, further larger multicenter studies are needed. Anxiety and depression should be evaluated by clinicians using these simple screening instruments that can rapidly detect symptoms of these comorbidities in their busy clinical settings.

REFERENCES

- Bragatti JA, Torres CM, Isolan GR, Bianchin MM. Psychiatric comorbidities of epilepsy: a review. J Neurol Neurophysiol 2011 Dec;52:002.
- Choi DH, Jeong BO, Kang HJ, Kim SW, Kim JM, Shin IS, Kim JT, Park MS, Cho KH, Yoon JS. Psychiatric comorbidity and quality of life in patients with post-stroke emotional incontinence. Psychiatry Investig 2013 Dec;10(4):382-387.



- Alsaadi T, El Hammasi K, Shahrour TM, Shakra M, Turkawi L, Nasreddine W, Raoof M. Depression and anxiety among patients with epilepsy and multiple sclerosis: UAE comparative study. Behav Neurol 2015 Oct;2015:196373.
- Hilty, DM.; Chang, CH.; Servis, ME. Post-stroke psychiatric syndromes: diagnosis and pharmacologic intervention. Psychiatric Times; 2005. [cited 2014 Jul 10]. Available from: www.psychiatrictimes.com.
- Zebenholzer K, Lechner A, Broessner G, Lampl C, Luthringshausen G, Wuschitz A, Obmann SM, Berek K, Wöber C. Impact of depression and anxiety on burden and management of episodic and chronic headaches—a cross-sectional multicentre study in eight Austrian headache centres. J Headache Pain 2016 Feb;17:15.
- Sharma VK, Lepping P, Cummins AG, Copeland JR, Parhee R, Mottram P. The Global Mental Health Assessment Tool– Primary Care Version (GMHAT/PC). Development, reliability and validity. World Psychiatry 2004 Jun;3(2):115-119.
- Tegegne MT, Mossie TB, Awoke AA, Assaye AM, Gebrie BT, Eshetu DA. Depression and anxiety disorder among epileptic people at Amanuel Specialized Mental Hospital, Addis Ababa, Ethiopia. BMC Psychiatry 2015 Sep;15:210.
- 8. Phabphal K, Sattawatcharawanich S, Sathirapunya P, Limapichart K. Anxiety and depression in Thai epileptic patients. J Med Assoc Thai 2007 Oct;90(10):2010-2015.
- 9. Kwan P, Yu E, Leung H, Leon T, Mychaskiw MA. Association of subjective anxiety, depression, and sleep disturbance with quality-of-life ratings in adults with epilepsy. Epilepsia 2009 May;50(5):1059-1066.
- Stefanello S, Marín-Léon L, Fernandes PT, Li LM, Botega NJ. Depression and anxiety in a community sample with epilepsy in Brazil. Arq Neuropsiquiatr 2011 Apr;69(2-B):342-348.
- 11. Hamed SA, Metwaly NA, Hassan MM, Mohamed KA, Ahmad MA, Soliman AA, Elsaied AR. Depression in adults with epilepsy: relationship to psychobiological variables. World J Neurol 2012 Feb;2(1):1-10.
- 12. Christensen J, Vestergaard M, Mortensen PB, Sidenius P, Agerbo E. Epilepsy and risk of suicide: a population-based case—control study. Lancet Neurol 2007 Aug;6(8):693-698.
- Jones JE, Hermann BP, Barry JJ, Gilliam FG, Kanner AM, Meador KJ. Rates and risk factors for suicide, suicidal ideation, and suicide attempts in chronic epilepsy. Epilepsy Behav 2003 Oct;4(Suppl 3):S31-S38.
- 14. Ajiboye PO, Abiodun OA, Tunde-Ayinmode MF, Buhari OI, Sanya EO, Wahab KW. Psychiatric morbidity in stroke patients attending a neurology clinic in Nigeria. Afr Health Sci 2013 Sep;13(3):624-631.
- 15. Williams LS, Ghose SS, Swindle RW. Depression and other mental health diagnoses increase mortality risk after ischemic stroke. Am J Psychiatry 2004 Jun;161(6):1090-1095.
- Beghi M, Cornaggia CM, Di Giacomo E, Primati C, Clerici M. Stroke and psychiatric disorders. Riv Psichiatr 2009 Jan-Feb;44(1):55-63.
- 17. Wang X, Chung MC, Hyland ME, Bahkeit M. Posttraumatic stress disorder and psychiatric co-morbidity following stroke: the role of alexithymia. Psychiatry Res 2011 Jun;188(1):51-57.
- 18. Robinson RG, Spalletta G. Poststroke depression: a review. Can J Psychiatry 2010 Jun;55(6):341-349.
- Aström M, Adolfsson R, Asplund K. Major depression in stroke patients. A 3-year longitudinal study. Stroke1993 Jul;24(7):976-982.

- 20. Hackett ML, Anderson CS. Predictors of depression after stroke: a systematic review of observational studies. Stroke 2005 Oct;36(10):2296-2301.
- Castillo CS, Schultz SK, Robinson RG. Clinical correlates of early-onset and late-onset poststroke generalized anxiety. Am J Psychiatry 1995 Aug;152(8):1174-1179.
- Aström M. Generalized anxiety disorder in stroke patients.
 A 3-year longitudinal study. Stroke1996 Feb;27(2):270-275.
- 23. Oladiji JO, Akinbo SR, Aina OF, Aiyejusunle CB. Risk factors of post-stroke depression among stroke survivors in Lagos, Nigeria. Afr J Psychiatry (Johannesbg) 2009 Feb;12(1):47-51.
- Chemerinski E, Robinson RG. The neuropsychiatry of stroke. Psychosomatics 2000 Jan-Feb;41(1):5-14.
- Angelelli P, Paolucci S, Bivona U, Piccardi L, Ciurli P, Cantagallo A, Antonucci G, Fasotti L, Di Santantonio A, Grasso MG, et al. Development of neuropsychiatric symptoms in poststroke patients: a cross-sectional study. Acta Psychiatr Scand 2004 Jul;110(1):55-63.
- Almeida OP, Xiao J. Mortality associated with incident mental health disorders after stroke. Aust N Z J Psychiatry 2007 Mar;41(3):274-281.
- 27. Smitherman, TA.; Baskin, SM. Depression and anxiety in migraine patients. Mount Royal (NJ): American Migraine Foundation; 2015.
- Mehlsteibl D, Schankin C, Hering P, Sostak P, Straube A. Anxiety disorders in headache patients in a specialised clinic: prevalence and symptoms in comparison to patients in a general neurological clinic. J Headache Pain 2011 Jun;12(3):323-329.
- 29. Merikangas KR, Angst J, Isler H. Migraine and psychopathology. Results of the Zurich cohort study of young adults. Arch Gen Psychiatry 1990 Sep;47(9):849-853.
- 30. Beghi E, Bussone G, D'Amico D, Cortelli P, Cevoli S, Manzoni GC, Torelli P, Tonini MC, Allais G, De Simone R, et al. Headache, anxiety and depressive disorders: the HADAS study. J Headache Pain 2010 Apr;11(2):141-150.
- 31. Corchs F, Mercante JP, Guendler VZ, Vieira DS, Masruha MR, Moreira FR, Bernik M, Zukerman E, Peres MF. Phobias, other psychiatric comorbidities and chronic migraine. Arq Neuropsiquiatr 2006 Dec;64(4):950-953.
- Song TJ, Cho SJ, Kim WJ, Yang KI, Yun CH, Chu MK. Anxiety and depression in tension-type headache: a population-based study. PLoS One 2016 Oct;11(10):e0165316.
- 33. Puca F, Genco S, Prudenzano MP, Savarese M, Bussone G, D'Amico D, Cerbo R, Gala C, Coppola MT, Gallai V, et al. Psychiatric comorbidity and psychosocial stress in patients with tension-type headache from headache centers in Italy. The Italian Collaborative Group for the Study of Psychopathological Factors in Primary Headaches. Cephalalgia 1999 Apr;19(3):159-164.
- 34. Holroyd KA, Stensland M, Lipchik GL, Hill KR, O'Donnell FS, Cordingley G. Psychosocial correlates and impact of chronic tension-type headaches. Headache 2000 Jan;40(1):3-16.
- 35. Borkovec, TD.; Alcaine, O.; Behar. E. Avoidance theory of worry and generalized anxiety disorder. In: Heimberg RG, Turk CL, Mennin DS, editors. Generalized anxiety disorder in research and practice. New York: Guilford Press; 2004. pp. 77-108.
- 36. Behar E, DiMarco ID, Hekler EB, Mohlman J, Staples AM. Current theoretical models of generalized anxiety disorders (GAD): conceptual review and treatment implications. J Anxiety Disord 2009 Dec;23(8):1011-1023.
- 37. McWiliams LA, Goodwin RD, Cox BJ. Depression and anxiety associated with three pain conditions: results from a nationally representative sample. Pain 2004 Sep;111(1-2):77-83.