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Original Article

Psychiatry/Mental Health Section

Psychiatric Morbidity in Migraine and its Impact on Quality of Life: A Hospital-based Cross-sectional Study

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ABSTRACT

Introduction: Migraine is a disabling headache disorder. Many psychiatric disorders co-exist with migrainous headache which largely remain undiagnosed leading to greater risk of morbidity and significantly impacts quality of life. Migraine patients are particularly at risk for mood and anxiety disorders which negatively impact the prognosis and poor headache outcome. Hence, defining the exact nature of underlying psychiatric conditions in migraine are relevant issues in the clinical practice.

Aim: To find the association of psychiatric morbidity and quality of life in migrainous (with and without aura) and non migrainous subjects and to assess the correlation between severity of migraine and quality of life.

Materials and Methods: It was a hospital-based cross-sectional study conducted amongst the patients and their healthy attendants visiting the Psychiatry OPD of Rajindra Hospital, Patiala from May 2018 to April 2019, after obtaining ethical clearance. A total of 392 subjects of both gender and in the age group 18-65 years, who gave informed consent were enrolled. Group 1 (n=196) consisted of cases i.e., migrainous patients as per International Classification of Headache Disorders 3rd Edition, β version (ICHD-3) criteria and Group 2 (n=196) consisted non migrainous controls. Psychiatric morbidity was assessed using Mini International Neuropsychiatric Interview (MINI) and confirmed on International Classification of Diseases 10th edition (ICD-10). Severity of migraine was assessed on Migraine Disability Assessment Test (MIDAS) and its impact on quality of life (QOL) by using 36 Item Short Form questionnaire (SF-36 questionnaire). Variables were compared using the independent t-test and Chi-square test. Pearson correlation was used to study the relationship between severity of migraine with QOL in subjects with and without psychiatric morbidity.

Results: Psychiatric morbidity was found among 65.3% (n=128) and 19.9% (n=39) subject in Group 1 and Group 2, respectively. Major Depressive Disorder (37.2%, n=73) was the most common psychiatric morbidity, followed by Generalised Anxiety Disorder (8.7%, n=17), Manic episode and Panic disorder each (5.1%, n=10), Hypomanic episode and Obsessive Compulsive Disorder each (3.1%, n=6), Dysthymia (2%, n=4) and Post Traumatic Stress disorder (1%, n=2). Between groups, the association of migraine with Major Depressive Disorder ($p \leq 0.001$), General Anxiety Disorder (GAD) (p=0.024), Manic episode (p=0.005), Hypomanic episode (p=0.048) was statistically significant but more in migrainous patients than non migrainous subjects. Migrainous patients had lower QOL in physical and psychological health domains of SF-36 than in non migrainous subjects. Furthermore, migrainous patients with or without psychiatric morbidity had significantly negative correlation in all domains of SF-36.

Conclusion: Psychiatric morbidity was significantly higher in migrainous patients than non migrainous subjects with poor quality of life in migrainous patients causing significant disability with an increase in severity of migraine.

Keywords: Generalised anxiety disorder, Headache, Major depressive disorder

INTRODUCTION

Migraine is a disabling headache disorder with an yearly prevalence of about 15% in the general population [1,2]. According to the Global Burden of Disease Study, migraine is the second most prevalent neurological disorder worldwide which causes greater disability than all other neurological disorders combined [2,3]. According to World Health Organisation (WHO), severity of migrainous attacks are classified as the most disabling illness comparable to dementia, quadriplegia and active psychosis [4,5]. The prevalence of migraine is three times more common in women than in men with peak appearing during middle ages [6]. Although migraine is an episodic disorder but it can progress to chronic disease [7,8]. The majority, self-medicate using non prescription (over-the-counter) medication and do not seek medical help [9]. Migraine has two major subtypes: Migraine Without Aura (MOA) which is a recurrent headache, lasting for 4-72 hours, mostly unilateral, pulsating, moderate or severe in intensity, aggravated by routine physical activity, associated with nausea and/or photophobia and phonophobia, and Migraine With Aura (MA) which is described as recurrent attacks of fully reversible visual, sensory or other central nervous system symptoms lasting minutes that develop gradually followed by headache and associated migraine symptoms [10].

Both migraine and psychiatric disorders are widely prevalent and cause huge burden challenging the healthcare systems worldwide. The high co-occurrence of psychiatric disorders with migraine suggests bi-directional relationship and common pathophysiologic mechanisms. Pathophysiology of migraine is neurovascular in nature. The sensory sensitivity is due to dysfunction of monoaminergic systems located in brainstem and thalamus [11]. Epidemiological studies have shown that there is a convincing association between primary headaches and psychiatric disorders with prevalence of 66.1% [12-14]. These conditions show a large overlap and studies suggest that patients with migraine especially those with chronic course are at increased risk for depression and anxiety, which were present in 19.7% and 13.7% of cases of primary headaches respectively [15,16]. The presence of psychiatric conditions increases the chances of conversion of migraine into chronic form leading to poor QOL [17].

Migrainous patients with psychiatric disorders are at greater risk for morbidity and users of health resources than migrainous patients without psychiatric conditions. Despite its widespread prevalence, migraine associated with psychiatric disorders remains under-diagnosed and under-treated. The co-morbid psychiatric disorders

in migraine are highly relevant in the clinical practice, as it might impact both the response to treatment and likelihood to achieve remission. Hence, recognising psychiatric co-morbidities is vital for early remission and recovery. In addition, the effect of migraine on Health Related Quality of Life (HRQoL) poses important public health problem and studying its effects would further quantify its impact which can serve as a baseline for subsequent measures for effective management [18-21]. There are limited studies from northern region highlighting the association of psychiatric morbidity with migraine [18,19]. Therefore, the current study was undertaken to find out the association of psychiatric morbidity and quality of life among migrainous (with and without aura) and non migrainous subjects diagnosed under the most recent International Classification of Headache Disorders 3rd Edition, β version (ICHD-3), [10] and to assess correlation between severity of migraine and quality of life.

MATERIALS AND METHODS

This hospital-based cross-sectional study was conducted amongst the patients and their healthy attendants visiting the Psychiatry OPD of Rajindra Hospital, Patiala over a period of twelve months (May 2018 to April 2019). A total of 392 subjects were enrolled by purposive sampling. Group 1 (n=196) consisted of cases i.e, migrainous patients diagnosed on the basis of International Classification of Headache Disorders 3rd Edition, β version (ICHD-3) and Group 2 (n=196) of healthy non migrainous controls [10]. Institute's Ethics Committee (IEC) clearance was obtained (No. BFUHS/2K18p-TH/5257 dated 09/05/2018). The study was conducted as per the declaration of Helsinki, Geneva. Tools were applied by mental health professionals and diagnosis was confirmed by consultants of the department.

Sample size calculation: The sample size was calculated based upon the prevalence of migraine using sample size proportion formula with confidence limit of 95% and precision of 5%.

The formula used was $n=z^2\times p(1-p)\div d^2$

p=0.15, z=1.96, d=0.05, n=196 where 15% prevalence was taken for the purpose of current study [1,2].

Inclusion and Exclusion criteria: Patients of migraine as defined by ICHD-3, β version in age group of 18-65 years, who gave voluntary written informed consent were included in the study [10]. Any patient having history of cluster headache or Medication Overuse Headache (MOH) other than migraine or secondary headache syndromes, history or presence of any other medical illness, epilepsy, intellectual disability, pregnancy and those who refused to give written informed consent were excluded from this study.

After completing socio-demographic proforma, selected patients were subjected to Mini International Neuropsychiatric Interview (MINI) for assessment of psychiatric co-morbidity [22]. The diagnosis of psychiatric illness was confirmed on the basis of International classification of diseases, 10th edition (ICD-10) [23]. The severity of depression and anxiety symptoms was assessed on Hamilton Depression Rating Scale (HAM-D) and Hamilton Anxiety Rating Scale (HAM-A), respectively. Further assessment to evaluate disability was done on Migraine Disability Assessment Scale (MIDAS) and quality of life was assessed on 36-Item Short Form Questionnaire (SF-36) [24-27].

Study Tools

1. **Proforma for socio-demographic variables:** A semi-structured proforma was used to gather socio-demographic details such as age, gender, education, marital status, socio-economic status according to BG Prasad classification [28], occupation and residential background.
2. **International Classification of Headache Disorders 3rd Edition, β version (ICHD-3), [10]:** The diagnosis of migraine was confirmed on the basis of ICDH-3, β version developed by Headache classification committee of the International Headache Society (IHS).
3. **Mini International Neuropsychiatric Interview (MINI), [22]:** It is a short, structured diagnostic interview developed by an international group of psychiatrists and clinicians to diagnose psychiatric disorders. It has good validity, reliability (inter rater and test-retest), sensitivity and specificity indices.
4. **International classification of diseases, 10th edition (ICD-10), [23]:** The diagnosis of psychiatric illness was confirmed on the basis of ICD-10, by World Health Organisation.
5. **Hamilton Depression Rating Scale (HAM-D), [24]:** It is the most widely used clinician-rated scale for the assessment of depression severity in patients who were already diagnosed with a depressive disorder. Its original version contains 17 items and where item is scored on a 3 or 5 point scale.
6. **Hamilton Anxiety Rating Scale (HAM-A), [25]:** It is used to measure the severity of anxiety symptoms. It consists of 14 item designed to assess the severity of a patient's anxiety. Each of the 14 items contains a number of symptoms and each group of symptoms is rated on a scale of 0-4. It yields a comprehensive score in the range of 0-56. It has a very good internal consistency with Cronbach's alpha of 0.79-0.86 and test-retest reliability value of 0.64.
7. **Migraine Disability Assessment Scale (MIDAS), [26]:** It is a 5 item questionnaire to evaluate disability within the most recent three months. Patients are asked questions about the frequency, duration of their headaches, and how often these headaches limited their ability to participate in activities at work, at school, or at home. Grade I- Little or no disability (0-5), Grade II- Mild disability (6-10), Grade III- Moderate disability (11-20), Grade IV- Severe disability (>20). The test-retest reliability of the overall MIDAS score was approximately 0.8.
8. **36-Item Short Form Questionnaire (SF-36), [27]:** It is a self-reported Short Form Health Survey with 36 item and measures physical and mental health status. It has Cronbach's alpha greater than 0.85 and reliability coefficient greater than 0.75 for all the dimensions. The SF-36 consists of eight scaled scores. Each scale is directly transformed into a 0-100 scale on the assumption that each question carries equal weight. The lower score imply more disability and higher score indicates less disability i.e., a score of zero is equivalent to maximum disability and a score of 100 is equivalent to no disability.

STATISTICAL ANALYSIS

The data was analysed for descriptive statistics which include frequency, mean, percentage, median, standard deviation. Inferential statistics for group comparison applied independent t-test and Chi-square (χ^2) test. Software Statistica 7.0 was used. A p-value ≤0.05 was considered as significant and p-value ≤0.001 as highly significant. Pearson correlation coefficient was used to study the correlation between of severity of migraine with QOL in subjects with and without psychiatric morbidity.

RESULTS

A total of 392 subjectes were enrolled. Overall socio-demographic data of the participants divided into migrainous and non migrainous subjects. The subjects were age and gender matched. Mean age in both groups was 35.53 (±9.146) years. Majority of subjects were females i.e., 152 (77.6%) and aged 31-40 years i.e., 73 (37.2%) each in both groups. 155 (79.1%) subjects were married, 114 (58.2%) were housewives and 155 (79.1%) belonged to rural areas in migrainous group comparable to 158 (80.6%)

married, 125 (63.8%) housewives and 160 (81.6%) subjects from rural areas in non migrainous group. But statistical difference was observed in education and socio-economic status categories. Majority of subjects in migrainous group studied upto higher secondary i.e., 64 (32.7%) than 43 (21.9%) in non migrainous group i.e., while 102 (52%) of matriculate subjects belonged to non migrainous group. Subjects belonging to upper middle and lower middle class were higher in migrainous group i.e; 34 (17.3%) and 39 (19.9%) than non migrainous group i.e; 25 (12.8%) and 32 (16.3%), respectively [Table/Fig-1].

Category	Variables	Group 1 (migrainous) n=196		Group 2 (Non migrainous) n=196		Chi-square (χ^2)	p-value
		No.	% age	No.	% age		
Gender	Female	152	77.6	152	77.6	-	1.000
	Male	44	22.4	44	22.4		
Age (in years)	18-30	57	29.1	57	29.1	-	1.000
	31-40	73	37.2	73	37.2		
	41-50	50	25.5	50	25.5		
	51-65	16	8.2	16	8.2		
Marital status	Married	155	79.1	158	80.6	0.709	0.701
	Unmarried	37	18.9	36	18.4		
	Others	4	2	2	1		
Education status	Illiterate	26	13.3	11	5.6	18.643	0.001
	Primary	34	17.3	40	20.4		
	Matriculation	70	35.7	102	52		
	Higher secondary	64	32.7	43	21.9		
	Graduate	2	1	-	-		
Occupation	Student	23	11.7	28	14.3	8.256	0.143
	Housewife	114	58.2	125	63.8		
	Labourer/Farmer	26	13.3	28	14.3		
	Professional	5	2.6	2	1		
	Unemployed	1	0.5	-	-		
	Semi-professional	27	13.8	13	6.6		
Socio-economic status [28]	Upper class	-	-	14	7.1	20.211	≤0.001
	Upper middle class	34	17.3	25	12.8		
	Middle class	119	60.7	125	63.8		
	Lower middle class	39	19.9	32	16.3		
	Lower class	4	2	-	-		
Background	Rural	155	79.1	160	81.6	3.502	0.320
	Urban	41	20.9	36	18.4		

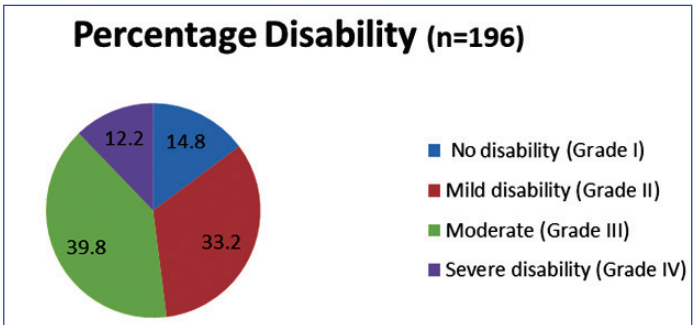
[Table/Fig-1]: Socio-demographic details of the study sample (n=392).
p≤0.05*=significant; p≤0.001**=highly significant; Chi-square test; if more than 20% cells had the cell counts less than 5 (fisher exact test was used)

Out of 196 cases in migrainous group, 128 (65.3%) had some psychiatric disorder wherein MDD was the most common psychiatric morbidity which was found in 73 (37.2%) subjects, followed by GAD in 17 (8.67%), Manic episode and Panic disorder in 10 (5.1%) each, Hypomanic episode and Obsessive Compulsive Disorder (OCD) in 6 (3.1%) each, Dysthymia in 4 (2%) and Post Traumatic Stress Disorder (PTSD) in 2 (1%) subjects. However, in non migrainous group, psychiatric morbidity was present in 39 (19.87%) of subjects. Majority had MDD i.e., 27 (13.8%) followed by Panic disorder and GAD in 5 (2.6%) each and OCD in 2 (1%) subjects. Chi-square test was applied to test the association i.e., for MDD, it was (p≤0.001), GAD (p=0.024), manic episode (p=0.005), hypomanic episode (p=0.048). It had statistically significant difference between them but more in migrainous group [Table/Fig-2]. The mean scores of HAM-D in patients of Migraine with aura (MA) and Migraine without aura (MOA) were 17.17±4.064 and 15.62±4.063 respectively while mean scores of HAM-A were 23.50±3.536 and 18.40±4.925 respectively in both groups, respectively. The difference was not statistically significant among the groups for severity of MDD and GAD.

Psychiatric disorder (ICD-10)	Group 1 (Migrainous) (n=196)			Group 2 (Non migrainous) (n=196)	Chi-square (χ^2)	p-value
	Migraine with aura (n=33) 16.8%	Migraine without aura (n=163) 83.2%	Total			
	No. (%age)	No. (%age)	No. (%age)			
Major Depressive Disorder	12 (36.4)	61 (37.4)	73 (37.2)	27 (13.8)	28.423	≤0.001
Dysthymia	-	4 (2.5)	4 (2.04)	-	5.678	0.058
Manic Episode	2 (6.1)	8 (4.9)	10 (5.1)	-	10.408	0.005
Hypomanic Episode	1 (3.0)	5 (3.1)	6 (3.06)	-	6.094	0.048
Panic Disorder	1 (3.0)	9 (5.5)	10 (5.1)	5 (2.6)	2.196	0.334
OCD	1 (3.0)	5 (3.1)	6 (3.06)	2 (1.0)	2.042	0.360
PTSD	1 (3.0)	1 (0.6)	2 (1.02)	-	5.168	0.075
GAD	2 (6.1)	15 (9.2)	17 (8.67)	5 (2.6)	7.446	0.024
Total	20	108	128 (65.3)	39 (19.87)		

[Table/Fig-2]: Psychiatric morbidity in migraine (with and without aura) and non migrainous (n=392).
p≤0.05*=significant; p≤0.001**=highly significant; Chi-square test; if more than 20% cells had the cell counts less than 5 (fisher exact test was used); OCD: Obsessive compulsive disorder; PTSD: Post traumatic stress disorder; GAD: General anxiety disorder

[Table/Fig-3] shows distribution of subjects on the basis of disability due to migraine on MIDAS. 167 (85%) of them were having some disability with overall mean Disability MIDAS score of 11.71±6.468 SD. Majority of subjects had moderate disability i.e., 78 (39.8%) subjects with mean score of 14.15±2.634 SD, while mild and severe disability was seen in 65 (33.2%) and 24 (12.2%) subjects, with mean scores being 7.62±0.995 SD and 24.58±2.185 SD respectively. On comparing the severity score on MIDAS in migrainous group, patients MA had higher severity with mean of15.33±7.684 as compared to MOA i.e., 10.98±5.957 which was found to be statistically significant (p=0.004).



[Table/Fig-3]: Percentile distribution of disability on Migraine Disability Assessment Scale (MIDAS).

[Table/Fig-4] shows comparison of QOL between migrainous (with and without aura) and non migrainous cases. All domain scores of SF-36 were statistically significantly (p=0.05) lower in migrainous compared to non migrainous group, which means poor QOL. Comparison of QOL within subtypes of migraine (Migraine with aura and Migraine without aura) showed that mean SF-36 score was lower in all the domains in patients of MA. The difference was statistically significant in all domains except for emotional well-being domain.

[Table/Fig-5] shows correlation of severity of migraine with quality of life assessed on MIDAS which depicts significant negative relationship with all domains of quality of life in migrainous subjects with and without psychiatric co-morbidity.

SF36 domains	Group-1 (Migrainous) (n=196)				Group-2 (Non Migrainous) (n=196)	p value (t test)
	Migraine with aura (n=33)	Migraine without aura (n=163)	p-value	Total (n=196)		
	Mean±SD	Mean±SD		Mean±SD	Mean±SD	
sf36-1 Physical functioning	76.67±14.289	87.98±12.785	≤0.001	86.07±13.686	98.29±5.065	≤0.001
sf36-2 Role limitations due to physical health	21.97±34.094	68.56±30.377	≤0.001	60.71±35.536	95.15±11.412	≤0.001
sf36-3 Role limitations due to emotional problems	40.37±35.097	58.67±41.378	0.019	55.59±40.886	91.48±17.762	≤0.001
sf36-4 Energy/fatigue	44.39±22.939	57.91±21.522	0.001	55.64±22.291	87.53±17.071	≤0.001
sf36-5 Emotional well-being	55.70±20.899	59.51±18.529	0.293	58.87±18.946	87.40±19.258	≤0.001
sf36-6 Social functioning	41.29±22.204	54.83±25.847	0.003	52.55±25.724	92.14±16.687	≤0.001
sf36-7 Pain	49.31±19.276	60.81±17.224	0.001	58.87±18.057	89.10±12.000	≤0.001
sf36-8 General health	26.71±10.879	32.12±12.145	0.018	31.20±12.087	69.16±20.088	≤0.001

[Table/Fig-4]: Quality of life between migrainous (with and without aura) and non migrainous SF 36: 36-Item Short Form Questionnaire.
p≤0.05*=significant; p≤0.001**=highly significant; t-test

Parameters	SF36-1	SF36-2	SF36-3	SF36-4	SF36-5	SF36-6	SF36-7	SF36-8
MIDAS (migraine with psychiatric morbidity)	-0.656**	-0.766**	-0.571**	-0.576**	-0.557**	-0.674**	-0.793**	-0.553**
MIDAS (migraine without psychiatric morbidity)	-0.388**	-0.721**	-0.388**	-0.624**	-0.772**	-0.388**	-0.760**	-0.769**

[Table/Fig-5]: Correlation of severity of migraine with Quality of life with and without psychiatric morbidity (n=196).
p≤0.05*=significant; p≤0.001**=highly significant (Pearson correlation test); MIDAS: Migraine disability assessment scale

DISCUSSION

There is wide variation regarding age of migraine ranging 20-45 years [29,30]. In present study, majority of patients in both the groups were from age group 31-40 years. Females outnumbered males significantly. Majority of them were married and housewives. Similar findings were reported by Bansal PD et al., here maximum number of patients were females, married and housewives [31]. The probable causes for migraine in married individuals were psychosocial problems compared to unmarried persons. Most of the migrainous subjects belonged to middle class which is in line with study conducted by Renjith V et al., who on evaluating (n=60) participants also reported that majority of migrainous patients belonged to upper and lower middle class [32].

Review of literature showed 78% of migrainous patients had some psychiatric disorder wherein MDD was (57%), Dysthymia (11%), Panic disorder (30%) and GAD (8%) [33,34]. The present study showed that psychiatric morbidity was found in 65.3% of migrainous cases and 19.9% in non migrainous subjects. MDD (37.2%) was most common disorder, followed by GAD (8.67%), Manic episode and Panic disorder (5.1%) each. Among migrainous subgroups, psychiatric morbidity was found in 83.2% MOA subtype whereas it was present in 16.8% cases of MA which is in agreement to earlier study conducted by Seilberstein SD et al., who reported psychiatric morbidity was present in 78.5% and 21.5% of MOA and MA subtypes respectively [35]. The mean severity scores of HAM-D and HAM-A were higher in patients of MA as compared to MOA but this difference was statistically not significant among subgroups for severity of MDD and GAD. In migrainous group, MIDAS disability scores were 14.8%, 33.2%, 39.8% and 12.2% for minimal, mild, moderate and severe disability respectively. Almost similar findings were reported by Semiz M et al., in migrainous patients i.e., 34.9%, 18.9%, 22.5% and 23.7% for minimal, mild, moderate and severe disability respectively [36]. Within migrainous group, patients of MA had higher severity score on MIDAS as compared to MOA.

The high co-occurrence of psychiatric disorders with migraine suggests bidirectional relationship. The possible mechanisms are dysfunction in central serotonergic availability, fluctuations in ovarian hormone levels (for women), dysregulation of the hypothalamic-pituitary adrenal (HPA), and sensitisation of both sensory and affective neural networks. The presence of psychiatric co-morbidities may transform migraine into a chronic form. Therefore, identifying the psychiatric conditions in patients of migraine is important for early management and prognosis of disease. Migraine is regarded as an incapacitating disease that can notably reduce the QOL of sufferers [37]. The SF-36 (QOL) scores were significantly lower in migrainous as compared to non migrainous subjects. Subgroup analyses between MA and MOA showed that patients with MA scored lower in all QOL domains.

Disability due to migraine had a negative relationship with all domains of QOL in migrainous subjects with psychiatric morbidity, which means more severe the migraine, poorer the quality of life. After migraine attacks, patients tend to be physically weak, which may disrupt their daily routines. Majority of clinicians or general practitioners often underestimate the burdens caused by migraine, which may affect its management. Healthcare professionals should routinely evaluate quality of life and related disability to determine whether patients are receiving effective treatment or any additional treatment strategies are required to improve quality of life.

Limitation(s)

There are few limitations to the study. The data was collected from patients visiting psychiatry OPD of a tertiary level hospital only, study had cross-sectional research design and lacks follow-up analysis of the patients. Further studies with a larger sample size and follow-up can be conducted in future.

CONCLUSION(S)

Psychiatric morbidity was significantly higher in migrainous than non migrainous subjects. Within migrainous subtypes, it was significantly high in MOA than MA. QOL was significantly lower in migrainous than non migrainous group. Within subtypes of migraine (Migraine with aura and Migraine without aura), QOL was lower in all the domains in patients of MA. Majority of them had moderate degree of disability. Disability due to migraine had a negative relationship with all domains of QOL but more in migrainous patients with

psychiatric morbidity. Therefore, healthcare professionals should routinely evaluate psychiatric co-morbidity in migrainous patients for early detection to improve their quality of life.

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