CLINICAL PROFILE OF THE PREMONITORY PHASE OF MIGRAINE AMONG THE PATIENTS AT NEUROLOGY DEPARTMENT OF A TERTIARY CARE HOSPITAL OF PAKISTAN

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ABSTRACT

Objective: To assess the clinical profile of the premonitory phase of migraine among the patients presenting with acute attack of migraine at a neurology unit of a tertiary care teaching hospital of Pakistan.

Study Design: Cross sectional study.

Place and Duration of Study: Neurology department, Pak Emirates Military Hospital Rawalpindi. One year, from 1st May 2017 to 30th April 2018.

Methodology: The sample population comprised of 201 patients of new or previously diagnosed migraine presenting with acute attack at neurology department of PEMH Rawalpindi. Migraine was diagnosed by the consultant neurologist on the basis of International Classification of Headache Disorders diagnostic criteria for migraine. Symptoms of the premonitory phase were classed as Fatigue and musculoskeletal problems, cognitive and affective problems, homeostatic alterations, perceptual abnormalities, affective symptoms and others.

Results: Out of 201 patients of migraine reporting in neurology OPD, 90.1% patients reported at least one symptom of premonitory phase. Male to female ratio of the patients was 1:3. Affective symptoms including low mood was the commonest symptoms reported among the target population followed by fatigue. Mean age of patients included in the study was 33.43 ± 3.845 years. Sleep disturbance was the least reported premonitory phase symptom among the patients of migraine in our study.

Conclusion: There was high frequency of premonitory phase symptoms among the patients of migraine headaches in Pakistan. Sensitivity and severity of these symptoms need to be assessed routinely among the target population in order to effectively treat this headache syndrome with holistic approach.

Keywords: Clinical profile, Migraine, Premonitory phase.

INTRODUCTION

Headache is one of the most commonly encountered medical symptom in the outpatient department of various specialities[1]. One of the primary headaches which is most prevalent in Pakistan and other countries is migraine[1,2]. Migraine have been associated with many health problems and diseases including epilepsy, irritable bowel syndrome, menstrual problems and anemia[3-5].

Premonitory symptoms associated with migraine have been under consideration for long. It includes set of all those non painful symptoms which occur hours or days before the actual

attack of heaedache[6]. They not only serve as an alarm for the attack of migraine but also add to the misery of actual painful symptoms of migraine. Various treatment options have also ben tried to minimize these premonitory symptoms[7].

Various studies done in recent past have focused on this interesting phenomenon associated with migraine headache. Fatigue was most commonly reported symptom in the premonitory phase reported by the patients of migraine in a study done in UK[8]. In another large study around 85% of the participants reported the presence of premonitory symptoms of one type or another[9]. Fatigue and mood changes were the commonest symptoms in the premonitory phase reported by the pediatric population with migraine in a study done in a recent past[10]. Another large review reported that prevalence of premonitory symp-

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toms among the patients of migraine ranged between 33-87%[7]. These findings make this phenomenon really relevant for the physicians treating migraine in order to treat migraine as a whole instead of just focusing on the headache and painful symptoms.

The mechanisms by which premonitory phase occurs and linked with the onset of migraine are complex and poorly understood. Not much work has been done in this aspect but few brain areas have been linked with premonitory phase in the imaging studies. These include posterolateral hypothalamus, periaqueductal gray area, midbrain tegmental area and substantia nigra, dorsal pons, and various cortical areas including prefrontal cortex, occipital and temporal regions[11]. Activation of these structures may be linked with both premonitory phase and actual migraine symptoms.

In addition to different areas of brain various neurochemicals have also been linked with premonitory phase of migraine. Orexin, cholecystokinin, dopamine, somatostatin, anti-diuretic hormone (ADH) and melatonin haven studied with the symptoms of premonitory phase[12,13].

Local data was limited regarding this aspect of migraine headache. Some work has been done on the epidemiology of migraine along with other neurological disorders in our country[14]. This study was planned with the objective to determine the burden of premonitory symptoms among the patients of migraine headache and analyze the spectrum with which patient of migraine go through before the onset of headache.

METHODOLOGY

This cross sectional study was conducted at the neurology department of a tertiary care hospital of Rawalpindi between 1st May 2017 to 30th Apr 2018. Sample size was calculated with the help of WHO sample size calculator. Screening was performed on all the patients of migraine diagnosed by a consultant neurologist on International Classification of Headache Disorders diagnostic criteria for migraine (ICHD). Non probability consecutive sampling technique

was used. Exclusion criteria were the patients more than 50 years of age or those who did not consent to or those with a past or current history of any chronic physical or psychiatric illness or current history of substance use. Patients with dual medical or neurological diagnosis were also not included in the study. Those could not read or perform the study questionnaire or had a mild illness like common cold or upper respiratory infection one week prior to onset of migraine headache were also excluded from the study.

International Classification of Headache Disorders diagnostic criteria for migraine

(1) At least five attacks fulfilling criteria (2)-(4)

(2) Headache attacks lasting 4-72 h (untreated or unsuccessfully treated)

(3) Headache has at least two of the following four characteristics:

(a) Unilateral location.

(b) Pulsating quality.

(c) Moderate or severe pain intensity.

(d) Aggravation by or causing avoidance of routine physical activity (e.g. walking or climbing stairs).

(4) During headache at least one of the following:

(a) Nausea and/or vomiting.

(b) Photophobia and phonophobia.

(5) Not better accounted for by another ICHD-3 diagnosis[15].

After ethical approval from the ethical review board committee and written informed consent from the potential participants, patients diagnosed with migraine at neurology department of MH RWP fulfilling the above mentioned inclusion and exclusion criteria were included in the study. Data were collected on a structured proforma specially designed for this study. Symptoms were divided into cognitive, affective, perceptual, homeostatic alterations, fatigue, musculoskel problems and others. A clinician was present at the time of filling of proforma to answer the quarries of the

participants. Detailed history taking general physical examination and reviewing of previous record was done to pick the confounding factors. All the efforts were made to distinguish the premonitory symptoms from routine fatigue or other minor illnesses at that time such as common cold or GI disturbances.

Statistical analysis required for the study data was performed by using the Statistics Package for Social Sciences version 23.0 (SPSS-

Table-I: Characteristics of participants included in the final analysis (n=201).

Variables	n (%)
Age (years)	
Mean ± SD	33.43 ± 3.845
Range (min-max)	18-50 years
Gender n(%)	
Male	70 (34.8)
Female	131 (65.2)
Duration of illness	
Mean ± SD	9.23 ± 2.585)
Range (min-max)	1 month – 19 years
No of premonitory symptoms n(%)	
No symptom	20 (9)
1 symptom	96 (48)
2 symptoms	64 (32)
>2 symptoms	21 (10)

23.0). Frequency and percentages for gender, type of premonitory symptoms, and number of premonitory symptoms was calculated. Mean ± standard deviation (SD) for age and duration of illness was calculated.

RESULTS

A total of 219 patients of migraine headache were approached to participate in the study. Ten refused participation or were unable to diffe-rentiate between symptoms of premonitory phase or general medical illness and 08 were ineligible due to exclusion criteria (04 gave history of depression, 02 had epilepsy, 01 was pregnant and 01 had carcinoma of thyroid gland). After excluding all these patients, 201 participants were left behind who underwent the detailed history taking and questionnaire filling. Male to female

ratio was 1:3. Other characteristics of study population have been summarized in table-I. Low mood was the commonest premonitory symptom among the target population followed by fatigue. Sleep problems were the least reported symptoms among the patients. Other symptoms included cognitive decline, visual

Table-II: Premonitory symptoms among the patients reporting with migraine headaches at neurology department (n=201).

Medical conditions	n (%)
Abdominal discomfort	33 (16.4)
Visual disturbances	10 (4.9)
Low mood	69 (34.3)
Neck stiffness	39 (19.4)
Sleep disturbances	14 (6.9)
Feeling hot	19 (9.4)
Cravings	21 (10.4)
Fatigue	44 (21.9)
Irritability	05 (2.5)
Memory problems	21(10.4)
Concentration difficulties	19 (9.4)
Vertigo	22 (10.9)
Yawning	31 (15.4)
Others	19 (9.4)

Table-III: Frequency of different symptom groups in premonitory phase (n=201).

Medical Conditions	n (%)
Cognitive problems	46 (22.9)
Homeostatic alterations	22 (10.9)
Perceptual abnormalities	39 (19.4)
Fatigue and musculoskeletal problems	55 (27.3)
Others	39 (19.4)

blurring and neck stiffness (table-II). Mean age of patients included in the study was 33.43 ± 3.845. Mean duration of illness among the patients participating in the study was 9.23 ± 2.58 years.

DISCUSSION

A large number of studies have been done to look into the phenomenon of painful symptoms of migraine but limited work has been done on other aspects of this multidimensional illness. Our study was planned with a unique objective to look into the symptoms which occur prior to the headache or painful symptoms of migraine.

Understanding of these symptoms is not only important in prediction of actual painful symptoms after them but also significant in management of this headache syndrome as a whole. Using a simple questionnaire we found that more than 90% of our sample population showed the presence of one or more premonitory symptoms. This is similar to the other studies done on migraine patients in other parts of the world[8,10]. Migraine is a complex disorder with various manifestations before and after the actual headache phase. The premonitory phase and postdrome are often overlooked and missed which hinders both clinicians and researches to understand this phenomenon completely[11,16].

There was a clear female predominance in our study sample. It was in accordance with the existing literature[17]. More prevalence of affective symptoms in our population can also be explained on these findings as affective symptoms and illnesses are more prevalent in the female population across all the cultures of the world. Different neurobiology and neurochemistry of female brain may also contribute to this fact.

Various physical and physiological aspects of premonitory symptoms have been discussed in the past. Functional imaging and neurochemical studies have also unveiled few facts but still it was an under discovered phenomenon. A complex and multidimensional basis exist for the premonitory symptoms and link them with the actual painful symptoms of migraine. Activation of various cortical and subcortical structures may be responsible for these premonitory symptoms along with the change in levels of various neurotransmitters. Actual painful symptoms and premonitory symptoms may also share a common etiology and all the prodromal symptoms, headache and postdrome may be part of one neurophysiological process[11,17].

Low mood was the commonest symptom reported in premonitory phase by our target population. It was different from other studies done in the recent past[18,19]. Difference in our population may be due to underlying comorbid undetected depression or due to more suffering of long standing untreated illness. Genetic and hormonal factors may be responsible for this comorbidity[20]. Functional studies have opened a new dimension for this comorbidity by detecting the changes in the brain metabolites[21].

Fatigue was also a common symptom reported by patients of migraine in our study during the premonitory phase. Studies done in other parts of the world have also shown similar results[9]. Fatigue is a subjectively reported phenomenon which may be difficult to get interpreted by the interviewer. Fatigue may serve as a trigger for the onset of migraine or it may be part of the premonitory phase of migraine. Clear open ended questions can reduce this subjectivity but it cannot be completely eliminated.

Sleep problems and migraine headaches have complex and multiple links. Sleep problems have been reported by patients of migraine in all the phase including the premonitory phase, actual headache phase and the postdrome. They also have been nominated as a triggering factor for the acute attack of migraine[22]. These problems were the least reported symptoms in our study. Poor sleep quality have also been reported by the patients of migraine[23]. Restless leg syndrome is also associated with both migraine premonitory phase and sleep problems[24].

Our study has few limitations as well. Randomized selection of study subjects from all the migraine patients was not done. Therefore, this study lacks generalizability. We did not use a validated tool for assessing the premonitory symptoms rather we used a self-made questionnaire to record the symptoms during the premonitory phase. Relying on the recall capability of patients and possibility of comorbid minor illnesses raises issues regarding different types of biases. Classifying symptoms as triggers or premonitory symptoms is also difficult in the study design followed in this particular study. More studies with a larger sample size from multiple centers using sophisticated tolls and study design can give more generalizable results.

CONCLUSION

There was high frequency of carotid artery stenosis among the patients of ischemic stroke in Pakistan. Special attention should be paid to the patients who have been suffering from a metabolic disorder like DM. Long duration of DM also emerged as independent risk factor for carotid artery stenosis in our study population.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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