The incidence of fibromyalgia in migraine sufferers — a prospective study from South Kerala

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Abstract
Background and Objectives: Migraine is commonly associated various painful syndromes. The Objective of Study is to determine the incidence of fibromyalgia in association with migraine. The clinical profiles of patients with migraine associated with other painful symptoms were studied. Secondary headache syndromes and other causes of generalized body aches were excluded using appropriate investigations. Cases were selected on outpatient basis over a period of 5 years.

Materials and Method: 278 Patients with migraine were enrolled in this study based on ICHD II (First revision). The incidence of fibromyalgia was detected on the basis of ACR criteria 2010. The data collected was analyzed systematically.

Results and Interpretations: Out of 278 patients, 68 had features of fibromyalgia. This constitute about 24.46 % of total subjects was studied.

Conclusions: The present study revealed that 24.46% of patients with migraine having associated symptoms and signs suggestive of fibromyalgia.

Keywords: Migraine, Fibromyalgia, secondary headache syndrome.

Introduction
Migraine is a common primary headache syndrome, which affects primarily children and young adults. Migraine affects around 10-15% of the human population. Females are affected twice as compared to males. (2) The head ache in migraine is pulsating in character. But, the majority of migraine sufferers presented with a non pulsating head ache during the illness. The symptoms started unilaterally and become diffuse as time goes. At times headache can be bilateral and there can be aching sensation over the back of the neck and over shoulders. The headache usually evolved over a period of thirty minutes to three hours. By definition pain in migraine typically lasts more than four hours. Migraine headaches usually subside within three days. The severity of pain varies in different population and even within the same family. Head ache may subside after vomiting or after a sleep. Most patients with migraine complain of any one of the additional symptoms like phonophobia, photophobia and prefer to lie down in dark calm room. Fasting, certain food items, travel and menstruation are important triggers of this type of head ache. Migraine with visual or other sensory auras is less common compared to migraine without aura. Basilar migraine is an atypical variant of migraine. In this category, patients develop aura and other symptoms in relation vestibular dysfunction of transient nature. Basilar migraine may precede or follow migraine with or without aura. Recently developed diagnostic criteria have helped clinical research, allowing a complete understanding of the clinical aspects of basilar migraine. The challenge now is to better understand the pathophysiology of vestibular migraine from both a clinical and basic science perspective to enable improved rational management of this disorder. An expanded view of the migraine circuit motivates basic science studies of the individual and interactive roles of vestibular and nociceptive mechanisms in basilar migraine. The atypical presentation is more common in children and this includes paroxysmal torticollis, paroxysmal vertigo, cyclical vomiting etc.

Patients with migraine are prone to develop other co-morbid conditions like fibromyalgia, cardiac diseases neuropsychiatric illness. Most common psychiatric illness associated with migraine are anxiety, depression panic attacks and obsessive compulsive disorder. Migraine with co morbid psychiatric conditions cause functional impairment across various aspects of life which in turn may leads to reduced health-related quality of life. Migraine and depression are mutually perpetuating disease entities. Depression and anxiety in association with migraine cause greater impairment of quality of life. Restless legs syndrome is a well-known comorbid condition associated with migraine. Co morbidities provide novel therapeutic options but also impose therapeutic limitations. Certain treatment options are relatively contraindicated in presence of co morbidities. So co morbid illnesses make the treatment strategies of migraine challenging.

Fibromyalgia is one of the most common chronic pain conditions. This disease entity affects around five
percent of people in the world. Most common age group affected by fibromyalgia is between thirty and fifty-five. The female population is mostly affected and it constitutes about eighty-five percentage of sufferers. Only rarely it affects males. Fibromyalgia is characterized by generalized pain involving muscles and ligaments, commonly associated with multiple somatic complaints. Even though it may cause pain over the muscles tendons and ligaments there will not be any definite evidence of tissue inflammation. The pathophysiological mechanism of Fibromyalgia resembles a model of severe central non-organic pain. In this model, even a non-nociceptive stimulus delivered over tender or non-tender points are capable of inducing pain due to cortical hyperactivation. The recent experiments in migraine models suggested that neuropeptides play an important role in the pathogenesis of migraine. The most important one is the Calcitonin gene related peptide. Fibromyalgia frequently associated with other primary headache syndromes as well. The pathophysiological mechanism behind this association is not well-established. In a study conducted in Brazil showed there is a prevalence fibromyalgia in 35.6% of patients with chronic migraine. In fibromyalgia, in spite of extensive investigation, no tissue pathology or structural abnormalities could be identified and there is no evidence for continuous activation nociceptive afferent stimulation. At the same time, there is ample evidence for temporal summation of pain and central sensitization as suggested by various investigators. In short, the co-occurrence of fibromyalgia and migraine can be explained on the basis of the common pathophysiological mechanism. Migraine is frequently associated with fibromyalgia syndrome, which may have a common pathophysiologic basis.

Materials and Method
This is a prospective study conducted in the Department of Neurology, Government Medical College, Trivandrum and Government T D Medical College, Alappuzha over a period of 5 years. Diagnosis of migraine was made based on ICHD II R1 criteria. Overall 278 patients between the age of 13 and 50yrs with migraine were enrolled for this study. Of the total subjects 84 (30.215%) were males and 194 (67.784%) were females. The majority of patients were between the age of 21 and 40 yrs (65.41%). Refer Table 1 & 2. Secondary headache syndromes were ruled out using brain imaging (contrast CT scan brain/MRI Brain), MR Venogram, CSF study (done for selected 15patient). Detailed history and physical examination were done to look specifically for co morbid painful syndromes. Patients with preexisting inflammatory conditions were excluded using laboratory investigations including complete blood count, C-reactive protein, Antinuclear Antibody, Rheumatoid factor, CCP, CK, Thyroid function Test, liver function test, Renal function test, serum Electrolytes, Anti-HCV & Blood sugar estimation. Diagnosis of fibromyalgia was made on the basis of ACR criteria 2010.

Results
Results were analyzed at the end of study period. Migraine with aura was noticed in 46 patients (16.54%) and 31(11.15%) patient developed transformed migraine during follow-up. Basilar migraine was noted in 47 patients (16.9%). Migraine associated with anxiety/ depression noted in 50 patients (18%), 78 patients (28%) had sleep disturbance and 108 patients (38.84%) had nonspecific body aches. Most common pain syndromes noticed were cervical and lower back pain (107, 38.48%). Only 8 patient had history of systemic hypertension. No patient is noticed to have Diabetes Mellitus. In this study, of the 278 patients 67satisfy the criteria for fibromyalgia of which all of them were females. This will constitute about 24.46 of total subjects were studied.

Table 1: Gender distribution of migraine sufferers

<table>
<thead>
<tr>
<th>Gender</th>
<th>Number of Cases</th>
<th>%</th>
</tr>
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<tbody>
<tr>
<td>Male</td>
<td>84</td>
<td>30.215</td>
</tr>
<tr>
<td>Female</td>
<td>194</td>
<td>69.785</td>
</tr>
<tr>
<td>Total</td>
<td>278</td>
<td>100</td>
</tr>
</tbody>
</table>

Table 2: Age distribution of migraine sufferers

<table>
<thead>
<tr>
<th>Age(yr)</th>
<th>Number of patients</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>13-20</td>
<td>62</td>
<td>22.3</td>
</tr>
<tr>
<td>21-30</td>
<td>103</td>
<td>37</td>
</tr>
<tr>
<td>31-40</td>
<td>79</td>
<td>28.41</td>
</tr>
<tr>
<td>41-50</td>
<td>34</td>
<td>12.23</td>
</tr>
</tbody>
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Discussion
Migraine is most commonly seen in females between puberty and menopause and is associated with various nonspecific pain syndromes. Migraine usually associated with various co morbidity illnesses which in turn negatively affect the quality of life in migraine sufferers. Sleep disturbances, RLS, neuropsychiatric manifestations may mask the underlying migraine. Identification of co existing illness was our aim of the study. In this present study, we focused mainly on one of the most disabling pain syndromes that can co-occur in patients with migraine. Study revealed that there is a strong association between migraine and fibromyalgia compared to general population. Migraine is common primary headache syndrome in which sensory sensitivity play a major role. Neurobiology of migraine is only poorly understood. Various mechanisms of migraine had been proposed by different investigators. These include neurogenic inflammation of meninges and peripheral and central trigeminal sensitization. Sensory supply of face, scalp, and dura mater is sub served by the trigeminal nerve. Various investigators showed that prostaglandins are distributed throughout...
the trigemino vascular system and are capable of producing intra and extra cranial vasodilatation. Sensitization of ophthalmic division causes pain within the cranial cavity and over the scalp and activation of the maxillary division is responsible for facial pain syndromes. The convergence of cervical and trigeminal afferent explains why neck stiffness or pain is so common in primary headache. Episodic nature of pain can explain on the basis of channelopathies that are genetically determined. Electrophysiological changes in our brain are usually wrongly designated as hyper excitability. But the same phenomenon can be better explained as disinhibition of neuronal circuits. If migraine was basically a sensory attentional problem with changes in cortical synchronization, hyper synchronization, all its manifestations could be accounted for in a single overarching pathophysiological hypothesis of a disturbance of the subcortical sensory modulation systems. Multisensory integration is the ability of brain to co process and co modulate different modalities of stimuli for unique perception of the world. While it seems likely that the trigeminovascular system and its cranial autonomic reflex connections, the trigeminal autonomic reflex, act as a feed-forward system to facilitate the acute attack, the fundamental problem in migraine is in the brain. Functional imaging has identified different mechanisms involved in the transformation of episodic migraine to transformed migraine syndrome.

Methods to explain the pain sensitive afferent system suggests that fibromyalgia resembles severe central organic pain in which even non-nociceptive stimuli may induce pain over the tender and non-tender points. This phenomenon can be explained hyperalgesia in fibromyalgia patients. Fibromyalgia and episodic or chronic migraine very frequently co-occur, suggesting common pathophysiological mechanisms; both conditions display generalized somatic hyperalgesia. Understanding the genetic basis of migraine is important to develop new prophylactic treatment strategies and to prevent co morbid conditions like stroke, epilepsy, depression etc. Basic principle of prophylactic strategy is to improve compliance, reduce adverse effects and improve long term outcomes. In our study, all the patients with fibromyalgia with migraine are young and middle aged females. This constitutes about 24.46% of the total subjects studied. No male patient with migraine in our study had evidence of fibromyalgia based on ACR criteria 2010. Co-occurrence of migraine with fibromyalgia will increase the morbidity in migraine sufferers.

Conclusions
This study revealed that there is a strong association between migraine and fibromyalgia (24.46%) compared to general population (5%). The concurrence and migraine and fibromyalgia in same patients suggest that there is probably a common mechanism triggering both these pain syndromes. Co-occurrence of fibromyalgia and migraine involves heightened somatic hyperalgesia compared to any one of these pain syndromes. Increased migraine frequency with a shift towards transformed migraine enhances both hyperalgesia and increased incidence of fibromyalgia, which is reversed by effective migraine prophylaxis. Early detection and intervention of fibromyalgia associated with migraine improved the long-term outcome in most of the patients with a long-standing migraine.

Conflict of Interest: None

Source of Support: Nil

References